Clinical Translation of a Simple Cognitive Task to Reduce the Occurrence of Intrusive Memories after a Psychological Trauma

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Abstract

Preventive interventions after psychological trauma are lacking. Intrusive memories in the first few weeks after a traumatic event can be highly distressing, and also predict later post-traumatic stress disorder (PTSD). Laboratory studies with healthy volunteers have found that engaging in a visuospatial cognitive task soon after an experimental trauma film can reduce the frequency of intrusive memories over the following week. The aims of this research were to a) develop the a simple cognitive task intervention (a memory reactivation cue followed by playing the computer game "Tetris") for use in a hospital emergency department (ED) with patients who had experienced a road traffic accident, and b) provide a preliminary test of the efficacy of the intervention using a randomised controlled trial design.

First, the current evidence base for preventive interventions after trauma was reviewed, and theory was drawn from experimental psychology and clinical psychology to propose that delivering a simple cognitive task involving playing Tetris in the immediate aftermath of trauma may offer a novel preventive intervention for PTSD symptoms (Chapter 1). Next, the laboratory procedure was adapted for use in a hospital ED, based on direct observation in the ED, and existing literature (Chapter 2).

An initial pilot study (n = 10) tested key procedures in the ED, namely recruitment of road traffic accident patients, practical delivery of the intervention and completion of an intrusion diary over the first week (Chapter 3). A second pilot study (n = 23) was conducted to improve the study procedures, test both the intervention and control conditions, and assess participant experience (Chapter 4). The recruitment rate, eligibility criteria, drop-out rate and completion rate of the intrusion diary were all improved. Participant feedback was used to refine the intervention and control procedures.

Finally, a main randomised controlled study (n = 71) was conducted, comparing the simple cognitive task intervention with usual care in the emergency department (with a simple activity diary). As predicted, participants in the intervention group had fewer intrusive memories in the first week, and less severe clinical intrusion symptom scores, than those in the control group. Further, participant feedback highlighted the value of being offered an intervention in the emergency department. This research was the first to successfully translate laboratory findings to a clinical emergency department setting. Findings provide a first step towards developing an accessible, low intensity preventive intervention to target intrusive memories after trauma. Further trials and mechanism studies are warranted.

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List of Abbreviations

ASD	Acute Stress Disorder
APA	American Psychiatric Association
BAI	Beck Anxiety Inventory
BDI-II	Beck Depression Inventory, 2nd Edition
CAPS	Clinician-Administered PTSD Scale
CBT	Cognitive Behavioural Therapy
CTRG	Clinical Trials & Research Governance, University of Oxford
DSM-IV	Diagnostic and Statistical Manual of Mental Disorders, 4th Edition
DSM-5	Diagnostic and Statistical Manual of Mental Disorders, 5th Edition
ED	Emergency Department
EMDR	Eye Movement Desensitisation and Reprocessing
HADS	Hospital Anxiety and Depression Scale
MRC	Medical Research Council
RTA	Road traffic accident
NICE	National Institute for Health and Care Excellence
NIHR	National Institute for Health Research
NRES	National Research Ethics Service
PDS	Posttraumatic Diagnostic Scale
PTSD	Post-Traumatic Stress Disorder
REC	Research Ethics Committee
R&D	Research and Development, NHS Trust
RN	Research Nurse
SPSS	Statistical Package for the Social Sciences

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Overarching framework for this research

The overall aim of this research was to develop and test a simple cognitive task intervention (a memory reactivation cue followed by playing the computer game Tetris) as a novel preventative intervention to reduce the occurrence of intrusive memories after a traumatic event. This involved translating research from previous laboratory-based studies with healthy participants (Holmes et al., 2009; Holmes et al., 2010) to a hospital emergency department setting with patients who had experienced a road traffic accident. The stages in this research were informed by the MRC guidelines for the development and evaluation of complex interventions (Medical Research Council, 2008), which highlights four key stages in the development of novel interventions: development; feasibility and piloting; evaluation; and implementation. Figure 1 shows how the MRC framework was adapted for this research.

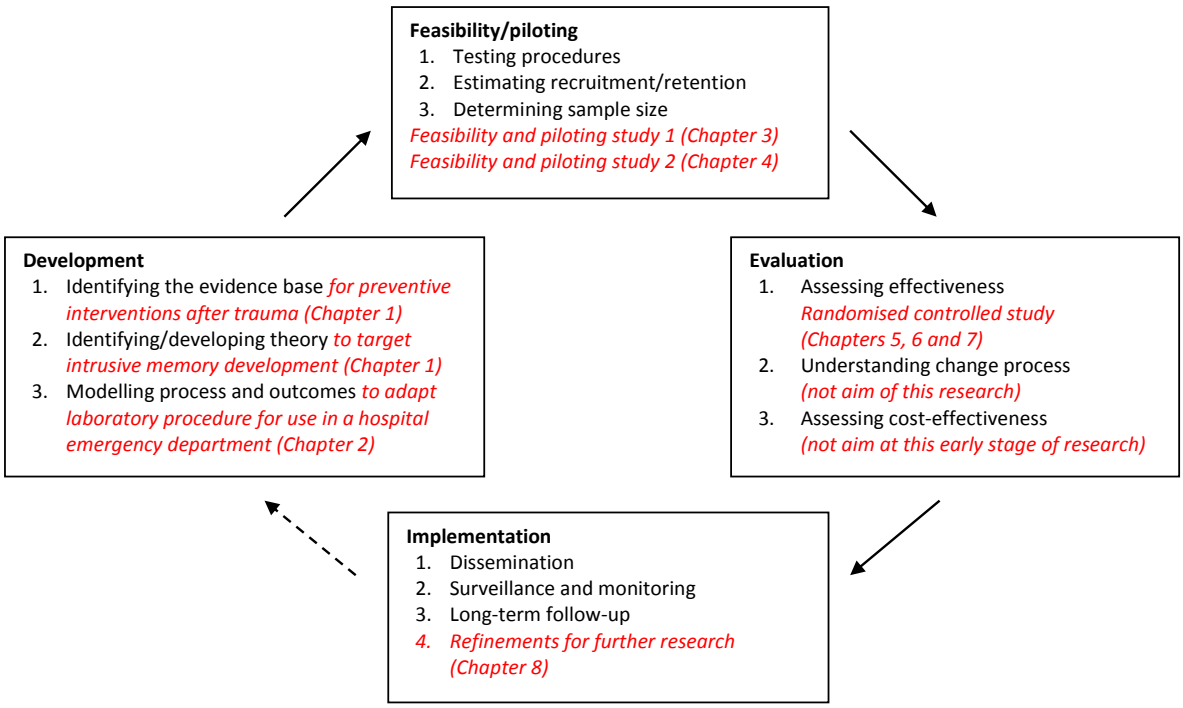


Figure 0.1. Key stages in the development and evaluation of a novel preventive intervention after trauma, modelled on the MRC Complex Interventions Guidance (2008). Adaptations for this research are shown in red italics.

CHAPTER 1. Introduction: A novel preventive intervention after a trauma to target intrusive memory development

Overview

This chapter begins by introducing background regarding the impact of psychological trauma, with a focus on post-traumatic stress disorder (PTSD) and acute stress disorder (ASD). It then discusses the evidence base for preventive interventions after trauma (part of the "Development" stage in the adapted MRC framework for complex interventions; see Figure 1.1), and identifies gaps in the target and timing of current approaches. The chapter then presents theory from clinical psychology to propose that early intrusive memories may be a suitable target for a preventive intervention after trauma, and theory from experimental psychology showing that intrusive memory development can be targeted using simple cognitive tasks within the first few hours after a laboratory-based trauma film (also part of the "Development" stage in Figure 1.1). It is proposed that administering a simple cognitive task soon after real-world trauma might offer a novel preventive intervention based on cognitive science to target early intrusive memories and later PTSD. The feasibility of translating this approach to real-world trauma is discussed. The chapter concludes by presenting the aims of this research: to develop and test the simple cognitive task intervention to reduce intrusive memories after a road traffic accident with patients in a hospital emergency department.

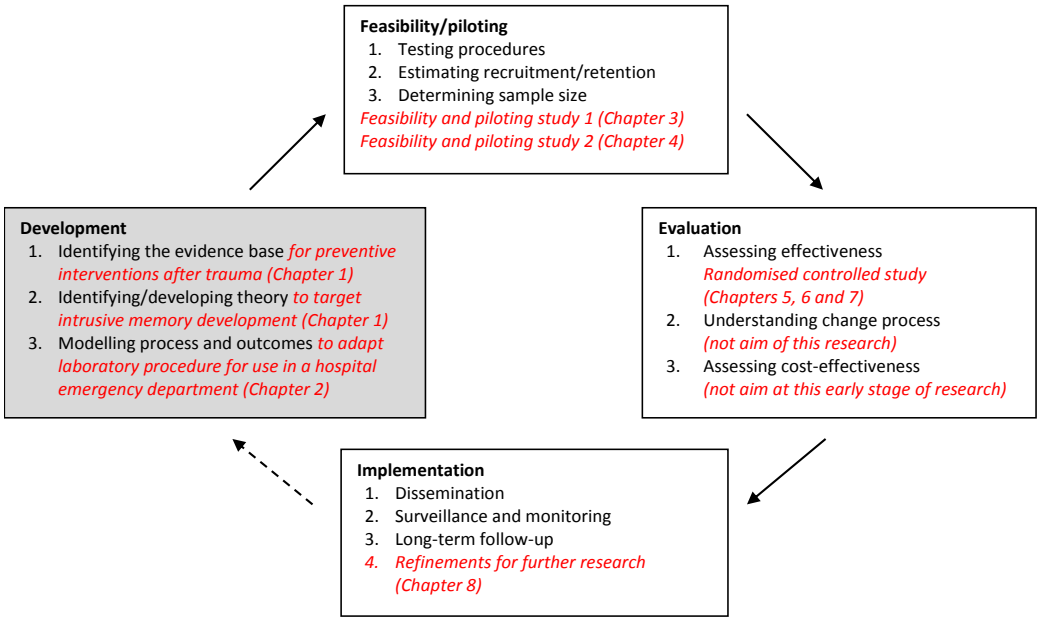


Figure 1.1. Key stages in this research to develop and evaluate a novel preventive intervention after trauma, based on the MRC Complex Interventions Guidance (2008).

Background: The impact of psychological trauma

Traumatic events are common. Most people will experience at least one traumatic event in their lifetime (R. C. Kessler, Sonnega, Bromet, Hughes, & Nelson, 1995; Norris, 1992). The most commonly reported traumas are witnessing someone being killed or severely injured, being in a life-threatening accident, or being involved in a fire, flood or natural disaster (R. C. Kessler et al., 1995). Traumatic events typically elicit high levels of emotional distress, and in some cases may lead to mental health problems, most notably post-traumatic stress disorder (PTSD; American Psychiatric Association, 2013).

Post-traumatic stress disorder

Post-traumatic stress disorder (PTSD) has attracted a great deal of research since its appearance in the third edition of the Diagnostic and Statistical Manual of Mental Disorders (DSM-III; American Psychiatric Association, 1980). It is prominent for being defined by the occurrence of a triggering traumatic event. In this research, a traumatic event was defined in line with criterion A1 of the DSM-IV (American Psychiatric Association, 1994), which was available at the time of starting the research: "the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others" (see Figure 1.2). During the course of this research, a new edition of the DSM was published (the DSM-5; American Psychiatric Association, 2013), with the following notable changes to the definition of a trauma event: a) criterion A2 "the person's response involved intense fear, helplessness, or horror" was removed, and b) indirect exposure (e.g. through electronic media) in the course of professional duties was added (see Figure 1.3).

PTSD is further characterised by the following clusters of symptoms, which must have been present for more than one month.

1. Persistent re-experiencing of the trauma, such as recurrent intrusive memories
2. Avoidance of things that act as reminders of the trauma, such as avoiding the place where the trauma occurred
3. Increased physical arousal, such as startling easily
4. Negative changes in cognitions and mood, such as feelings of fear, anger or guilt (added in DSM-5).

Figure 1.2. DSM-IV criteria for PTSD (available at the time of starting this research)

Criterion A: The person has been exposed to a traumatic event in which both of the following have been present:

1. The person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
2. The person's response involved intense fear, helplessness, or horror. **Note:** In children, this may be expressed instead by disorganized or agitated behavior.

Criterion B: The traumatic event is persistently reexperienced in one (or more) of the following ways:

1. Recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions. **Note:** In young children, repetitive play may occur in which themes or aspects of the trauma are expressed.
2. Recurrent distressing dreams of the event. **Note:** In children, there may be frightening dreams without recognizable content.
3. Acting or feeling as if the traumatic event were recurring (includes a sense of reliving the experience, illusions, hallucinations, and dissociative flashback episodes, including those that occur upon awakening or when intoxicated).**Note:** In young children, trauma-specific reenactment may occur.
4. Intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event.
5. Physiological reactivity on exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event.

Criterion C: Persistent avoidance of stimuli associated with the trauma and numbing of general responsiveness (not present before the trauma), as indicated by three (or more) of the following:

1. Efforts to avoid thoughts, feelings, or conversations associated with the trauma
2. Efforts to avoid activities, places, or people that arouse recollections of the trauma
3. Inability to recall an important aspect of the trauma
4. Markedly diminished interest or participation in significant activities
5. Feeling of detachment or estrangement from others
6. Restricted range of affect (e.g., unable to have loving feelings)
7. Sense of a foreshortened future (e.g., does not expect to have a career, marriage, children, or a normal life span)

Criterion D: Persistent symptoms of increased arousal (not present before the trauma), as indicated by two (or more) of the following:

1. Difficulty falling or staying asleep
   Irritability or outbursts of anger
   Difficulty concentrating
   Hypervigilance
   Exaggerated startle response

Criterion E: Duration of the disturbance (symptoms in Criteria B, C, and D) is more than one month.

Criterion F: The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.

Figure 1.3. DSM-5 criteria for PTSD (published during this research)

Criterion A: The person was exposed to: death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence, as follows: *(one required)*

1. Direct exposure.
2. Witnessing, in person.
3. Indirectly, by learning that a close relative or close friend was exposed to trauma. If the event involved actual or threatened death, it must have been violent or accidental.
4. Repeated or extreme indirect exposure to aversive details of the event(s), usually in the course of professional duties (e.g., first responders, collecting body parts; professionals repeatedly exposed to details of child abuse). This does not include indirect non-professional exposure through electronic media, television, movies, or pictures.

Criterion B: The traumatic event is persistently re-experienced in the following way(s): (*one required*)

1. Recurrent, involuntary, and intrusive memories.
2. Traumatic nightmares.
3. Dissociative reactions (e.g., intrusive memories) which may occur on a continuum from brief episodes to complete loss of consciousness.
4. Intense or prolonged distress after exposure to traumatic reminders.
5. Marked physiologic reactivity after exposure to trauma-related stimuli.

Criterion C: Persistent effortful avoidance of distressing trauma-related stimuli after the event: (*one required*)

1. Trauma-related thoughts or feelings.
2. Trauma-related external reminders (e.g., people, places, conversations, activities, objects, or situations).

Criterion D: Negative alterations in cognitions and mood that began or worsened after the traumatic event: (*two required*)

1. Inability to recall key features of the traumatic event (usually dissociative amnesia; not due to head injury, alcohol, or drugs).
2. Persistent (and often distorted) negative beliefs and expectations about oneself or the world (e.g., "I am bad," "The world is completely dangerous").
3. Persistent distorted blame of self or others for causing the traumatic event or for resulting consequences.
4. Persistent negative trauma-related emotions (e.g., fear, horror, anger, guilt, or shame).
5. Markedly diminished interest in (pre-traumatic) significant activities.
6. Feeling alienated from others (e.g., detachment or estrangement).
7. Constricted affect: persistent inability to experience positive emotions.

Criterion E: Trauma-related alterations in arousal and reactivity that began or worsened after the traumatic event: (*two required*)

1. Irritable or aggressive behavior
2. Self-destructive or reckless behavior
3. Hypervigilance
4. Exaggerated startle response
5. Problems in concentration
6. Sleep disturbance

Criterion F: Persistence of symptoms (in Criteria B, C, D, and E) for more than one month.

Criterion G: Significant symptom-related distress or functional impairment (e.g., social, occupational).

Criterion H: The disturbance is not due to medication, substance use, or other illness.

Lifetime prevalence of PTSD has been estimated at 7.8% (R. C. Kessler et al., 1995), and even higher rates are found after specific types of trauma, such as 23% after a road traffic accident (Ehlers, Mayou, & Bryant, 1998), 25% in women after miscarriage (Engelhard, van den Hout, & Arntz, 2001), and 47% after rape (Rothbaum, Foa, Riggs, Murdoch, & Walsh, 1992). Occupational groups with repeated exposure to trauma, such as emergency first responders (Kleim & Westphal, 2011) or the military (Hoge et al., 2004) may be at particular risk for developing PTSD. Further, PTSD symptoms can develop through vicarious traumatisation in families or professionals supporting trauma survivors (e.g. Dirkzwager, Bramsen, Adèr, & van der Ploeg, 2005). PTSD is often accompanied by concurrent depression or substance abuse (R. C. Kessler et al., 1995), and has been associated with considerable societal and economic burden (Hidalgo & Davidson, 2000).

The main risk factors for developing PTSD after a traumatic event relate to a person's reaction at the time of the event (their "peritraumatic" reaction), in particular perceived threat to life, dissociation, and distress, as well as a lack of social support after the event (Ozer, Best, Lipsey, & Weiss, 2003). Pre-trauma factors such as a person's demographic background, experience of previous traumas and previous psychiatric problems have weaker predictive effects (Brewin, Andrews, & Valentine, 2000).

With regards to evidence-based treatments for PTSD, current UK clinical guidelines (National Institute for Health and Clinical Excellence, 2005) recommend psychological interventions such as trauma-focused cognitive behavioural therapy (CBT) (e.g. Ehlers, Clark, Hackmann, McManus, & Fennell, 2005) and eye-movement desensitization and reprocessing (EMDR: Shapiro, 1989, 1996). Studies have shown good efficacy of these interventions, for example 74.1% recovery with trauma focused CBT (Ehlers et al., 2005) and 83% recovery with EMDR (C. Lee, Gavriel, Drummond, Richards, & Greenwald, 2002). There is also evidence for the effectiveness of some pharmacological treatments, in particular selective serotonin reuptake inhibitors (SSRIs), found to be effective in 59.1% of cases (D. J. Stein, Ipser, & Seedat, 2006). However, these treatments are only recommended at one month or more after the trauma, once PTSD has fully developed.

Early post-traumatic stress symptoms and acute stress disorder

Distressing psychological symptoms are common within the first month after a traumatic event, and in fact tend to have the highest rates within this early period. For example, 51% of road traffic accident survivors experienced moderate to severe post-traumatic stress symptoms within the first two weeks (Bryant & Harvey, 1996), and 94% of rape victims reported post-traumatic stress symptoms at two weeks, dropping to 65% at one month (Rothbaum et al., 1992).

The diagnosis of acute stress disorder (ASD) was originally introduced into the DSM-IV (American Psychiatric Association, 1994) to identify people with severe psychological reactions within the first month of trauma who were at risk of later PTSD. The diagnostic criteria were similar to those for PTSD, except for a) the additional requirement that dissociative symptoms were present during or after the traumatic event, and b) the time frame of symptoms being between 2 days and 4 weeks after the traumatic event (see Figure 1.4). However, the diagnosis was found to have poor predictive ability for PTSD (Bryant, Friedman, Spiegel, Ursano, & Strain, 2011), leading to a change in criteria in the DSM-5, such that the diagnosis simply required the presence of nine out of 14 potential symptoms, within a time frame of three days to one month after the trauma (see Figure 1.5). Symptoms include those common to PTSD (e.g. symptoms of re-experiencing, avoidance, negative mood and hyperarousal) as well as dissociative symptoms (e.g. losing awareness of one's surroundings).

With regards to treatment for ASD, a Cochrane review found psychological interventions such as trauma-focused CBT to be effective (Roberts, Kitchiner, Kenardy, & Bisson, 2010). However, interventions in this review were delivered within the first three months after a trauma, suggesting that PTSD as well as ASD was potentially targeted, rather than symptoms within the first month specifically.

Figure 1.4. DSM-IV criteria for Acute Stress Disorder

Criterion A: The person has been exposed to a traumatic event in which both of the following were present:

1. The person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others
2. The person's response involved intense fear, helplessness, or horror.

Criterion B: Either while experiencing or after experiencing the distressing event, the individual has three (or more) of the following dissociative symptoms:

1. A subjective sense of numbing, detachment or absence of emotional responsiveness
2. A reduction in awareness of his or her surroundings (e.g., "being in a daze")
3. Derealization
4. Depersonalization
5. Dissociative amnesia (i.e., inability to recall an important aspect of the trauma)

Criterion C: The traumatic event is persistently reexperienced in at least one of the following ways: recurrent images, thoughts, dreams, illusions, flashback episodes, or a sense of reliving the experience; or distress on exposure to reminders of the traumatic event.
or perceptions. **Note:** In young children, repetitive play may occur in which themes or aspects of the trauma are expressed.

Criterion D: Marked avoidance of stimuli that arouse recollections of the trauma (e.g., thoughts, feelings, conversations, activities, places, people).

Criterion E: Marked symptoms of anxiety or increased arousal (e.g., difficulty sleeping, irritability, poor concentration, hypervigilance, exaggerated startle response, motor restlessness).

Criterion F: The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning or impairs the individual's ability to pursue some necessary task, such as obtaining necessary assistance or mobilizing personal resources by telling family members about the traumatic experience.

Criterion G: The disturbance lasts for a minimum of 2 days and a maximum of 4 weeks and occurs within 4 weeks of the traumatic event.

Criterion H: The disturabance is not due to the direct physiological effects of a substance (e.g., a drug of abuse, a medication) or a general medical condition, is not better accounted for by Brief Psychotic Disorder, and is not merely an exacerbation of a pre-existing Axis I or Axis II disorder.

Figure 1.5. DSM-5 criteria for Acute Stress Disorder

Criterion A: The person was exposed to: death, threatened death, actual or threatened serious injury, or actual or threatened sexual violence, as follows: *(one required)*
1) Direct exposure; 2) Witnessing, in person; 3) Indirectly, by learning that a close relative or close friend was exposed to trauma. If the event involved actual or threatened death, it must have been violent or accidental; 4) Repeated or extreme indirect exposure to aversive details of the event(s), usually in the course of professional duties (e.g., first responders, collecting body parts; professionals repeatedly exposed to details of child abuse). This does not include indirect non-professional exposure through electronic media, television, movies, or pictures.
Criterion B: Presence of nine (or more) of the following symptoms from any of the five categories of intrusion, negative mood, dissociation, avoidance, and arousal, beginning or worsening after the traumatic event occurred:
Intrusion symptoms
1) Recurrent, involuntary, and intrusive distressing memories of the traumatic event(s).
2) Recurrent distressing dreams in which the content and/or affect of the dream is related to the event(s).
3) Dissociative reactions (e.g., flashbacks) in which the individual feels or acts as if the traumatic event(s) were recurring (such reactions may occur on a continuum, with the most extreme expression being a complete loss of awareness of present surroundings).
4) Intense or prolonged psychological distress or marked physiological reactions in response to internal or external cues that symbolise or resemble an aspect of the traumatic event(s).
Negative mood
5) Persistent inability to experience positive emotions (e.g., inability to experience happiness, satisfaction, or loving feelings).
Dissociative symptoms
6) An altered sense of the reality of one's surroundings or oneself (e.g. seeing oneself from another's perspective, being in a daze, time slowing).
7) Inability to remember an important aspect of the traumatic event(s) (typically due to dissociative amnesia and not to other factors such as head injury, alcohol or drugs).
Avoidance symptoms
8) Efforts to avoid distressing memories, thoughts, or feelings about or closely association with the traumatic event(s).
9) Efforts to avoid external reminders (people, places, conversations, activities, objects, situations) that arouse distressing memories, thoughts or feelings about or closely association with the traumatic event(s).
Arousal symptoms
10) Sleep disturbance (e.g. difficulty falling or staying asleep, restless sleep).
11) Irritable behaviour and angry outbursts (with little or no provocation), typically expressed as verbal or physical aggression toward people or objects.
12) Hypervigilance
13) Problems with concentration
14) Exaggerated startle response
Criterion C: Duration of the disturbance (symptoms in Criterion B) is 3 days to 1 month after trauma exposure. (Note: Symptoms typically begin immediately after the trauma, but persistence for at least 3 days and up to a month is needed to meet disorder criteria).
Criterion D: The disturbance causes clinically significant distress or impairment in social, occupational, or other important areas of functioning.
Criterion E: The disturbance is not attributable to the physiological effects of a substance (e.g., medication or alcohol) or another medical condition (e.g., mild traumatic brain injury), and is not better explained by brief psychotic disorder.

Identifying the evidence base for preventive interventions after trauma

The fact that PTSD and ASD are defined by the occurrence of a triggering traumatic event holds a rare opportunity in psychological disorders: to intervene in the immediate aftermath of the traumatic event in an attempt to prevent the disorder from developing. This approach, known as "secondary prevention" in the preventive medicine literature (N. Gordon, 1983), has been a popular topic of research in the field of post-traumatic stress. Intervention approaches have included those that can be delivered to everyone after a traumatic event ("universal" prevention) as well as those targeted at people at risk of developing PTSD ("selective" prevention). They have also covered a variety of time frames after trauma, from as early as the first few hours and days (the "immediate" aftermath) to the first few weeks or months (the "early" period; Agorastos, Marmar, & Otte, 2011). A number of different categories of intervention approaches are discussed below, with a brief description of each and a summary of the evidence to date.

Psychological debriefing

Psychological debriefing is perhaps the most widely researched intervention approach aimed at preventing post-traumatic stress symptoms after a trauma. The intervention is a single-session talking therapy consisting of a series of phases, typically including recall of the trauma, expression of emotional reactions (termed 'emotional ventilation') and psychoeducation/normalisation (Rose, Bisson, Churchill, & Wessely, 2002). The exact structure varies slightly between different models (van Emmerik, Kamphuis, Hulsbosch, & Emmelkamp, 2002), with the predominant model being Critical Incident Stress Debriefing (Mitchell, 1983).

A substantial number of studies were conducted in the 1980s and 1990s to test the efficacy of psychological debriefing, covering a range of traumatic events, various time frames for delivery of the intervention (from as early as a few days after the trauma to a few weeks), and individual and group debriefing. Meta-analysis results indicated that single-session psychological debriefing was not effective in preventing the development of post-traumatic stress symptoms (Rose et al., 2002; van Emmerik et al., 2002), and even suggested increased risk of PTSD in some cases (Rose et al., 2002). Consequently, single-session psychological debriefing is no longer recommended for routine use following psychological trauma.

Whilst research into psychological debriefing has declined, it has been argued that Critical Incident Stress Debriefing is effective for use in organisational contexts with emergency personnel (Hawker, Durkin, & Hawker, 2011). It is also notable that it is still used by some humanitarian organisations, such as by UNICEF and Save the Children (Summerfield, 1999). However, it does not appear to be effective as a universal preventive intervention for all survivors of trauma.

Pharmacological interventions

A number of candidate pharmacological agents have been proposed as preventive interventions for PTSD. These include the beta-blocker propranolol (Pitman et al., 2002), hydrocortisone (Schelling et al., 2001), morphine (Bryant, Creamer, O'Donnell, Silove, & McFarlane, 2009), ketamine (McGhee, Maani, Garza, Gaylord, & Black, 2008), imipramine (Robert, Blakeney, Villarreal, Rosenberg, & Meyer Iii, 1999), and benzodiazepines (Gelpin, Bonne, Peri, Brandes, & Shalev, 1996). These medications have been proposed on the basis that high emotional arousal in the immediate aftermath of a trauma enhances the consolidation of memories of the trauma (McCleery & Harvey, 2004). Therefore administering drugs in the immediate aftermath of a trauma that either reduce physiological arousal or disrupt memory consolidation may attenuate memory for the traumatic event and reduce PTSD symptoms (see Steckler & Risbrough, 2012 for a review). Whilst pre-clinical and observational studies have suggested that some of these drugs show promise, evidence from clinical studies remains scarce.

To date, only propranolol and hydrocortisone have been tested in randomised controlled studies. A small trial of a 10-day course of propranolol (n = 18) versus placebo (n = 23), first administered to emergency department patients within six hours of injury, found a non-significant reduction in one month PTSD symptoms in the propranolol group compared to the placebo group (Pitman et al., 2002). However, drop-out in the propranolol group was high, such that only 11 patients (61%) returned at one month follow-up. Stein et al. (2007) subsequently compared a 14-day course of propranolol (n = 17), gabapentin (n = 14) and placebo (n = 17) administered within 48 hours of injury, and found no effect of either propranolol or gabapentin relative to placebo on PTSD symptoms at 1-, 4- and 8-month follow-up.

Evidence for hydrocortisone has been more promising. Schelling and colleagues conducted a series of randomised controlled studies testing hydrocortisone in patients who

required treatment in an intensive care unit (ICU) following septic shock (Schelling et al., 2001) and cardiac surgery (Schelling et al., 2004; Schelling et al., 2006). All of the studies suggested a lower risk of PTSD in the hydrocortisone group compared to the placebo group, but none of the differences were statistically significant.

Therefore, whilst pharmacological preventive intervention after trauma may hold promise, there is currently insufficient clinical evidence to indicate their use in clinical practice (Bisson, 2007). Further, pharmacological treatments may hold drawbacks, such as the potential for side-effects (Steckler & Risbrough, 2012) and ethical concerns regarding "erasing" memories of trauma (Henry, Fishman, & Youngner, 2007; Holmes, Sandberg, & Iyadurai, 2010). Large, well-controlled trials are clearly warranted before the use of medication to prevent post-traumatic stress symptoms can be advocated in routine clinical practice.

Multiple session psychological interventions

Various multiple-session psychological interventions have been investigated as preventive interventions after trauma. One body of research has explored the use of trauma-focused cognitive behavioural therapy (TF-CBT): a talking therapy that is effective in treating PTSD (Ehlers & Clark, 2000). TF-CBT typically involves education about the psychological effects of trauma, imaginal reliving of the traumatic event, cognitive restructuring (a method of reappraising the meaning of the event), and reducing avoidance behaviours (Ehlers, Clark, et al., 2003). A meta-analysis of five randomised controlled trials comparing TF-CBT to supportive counselling, delivered within three months of trauma, reported a reduced rate of PTSD in the TF-CBT group than in the supportive counselling group at three to six months (Kornor et al., 2008). However, these trials all included patients with initial acute stress disorder (ASD), and the review concluded that there was insufficient evidence for the effectiveness of TF-CBT for traumatised patients without an ASD diagnosis.

A subsequent Cochrane review examined multiple-session psychological interventions delivered within three months of a traumatic event to trauma survivors who did not meet a particular symptom profile. Interventions included CBT, counselling, and memory structuring interventions. The review found no evidence for the efficacy of these interventions in preventing PTSD in people who were not already symptomatic, and in fact reported a trend for increased PTSD symptoms at three to six month follow-up in those

who received an intervention relative to control. The review concluded that multiple-session psychological interventions aimed at *all* individuals exposed to trauma, like single-session psychological debriefing, should not be used in routine practice (Roberts, Kitchiner, Kenardy, & Bisson, 2009).

Since Roberts et al.'s (2009) review, a randomised controlled trial of a modified prolonged exposure therapy to prevent PTSD has been published (Rothbaum et al., 2012). The therapy involved three 1-hour sessions commenced in a hospital emergency department and completed within the first two weeks after the trauma. It consisted of multiple components, such as imaginal exposure, behavioural exposure and self-care tasks, designed to target broad aspects of PTSD. The intervention was found to reduce PTSD symptom severity at 4- and 12-week follow-up in the intervention group compared to an assessment only group (Rothbaum et al., 2012), but drop-out rates were relatively high (26% at 4 weeks and 34% at 12 weeks). To date, this seems the most promising finding regarding a multiple-session psychological intervention to prevent PTSD that can be delivered to all trauma survivors (i.e. not just those who are already symptomatic). However, the intervention was somewhat intensive (involving three hour-long sessions), required trained therapists to deliver it, and involved multiple therapeutic components. Arguably there is still need for a simpler, lower-intensity and more cost-effective intervention that can be delivered in the immediate aftermath of trauma to target key processes in the development of PTSD.

Current early intervention guidelines

Given the paucity of effective secondary preventive interventions for PTSD, many clinical guidelines now advise against the use of specific preventive interventions in the immediate aftermath of trauma. For example, the UK National Institute for Health and Clinical Excellence (NICE) guidelines recommend "watchful waiting" within the first month after a trauma (National Institute for Health and Clinical Excellence, 2005). Even advocates of a "screen and treat" model do not recommend screening trauma survivors until three to four weeks after the trauma (Brewin et al., 2008).

Other organisations recommend "psychological first aid" in the immediate aftermath of a disaster, with the context of a stepped care model (North Atlantic Treaty Organization (NATO), 2008; World Health Organization, 2011). Psychological first aid refers to the provision of safety, practical help and information to assist people in the

immediate aftermath of a traumatic event, but does not include specific preventive interventions for PTSD (World Health Organization, 2011). This approach has not yet been empirically tested, but may be considered a consensus current best practice (Wessely et al., 2008).

Summary

Despite a wealth of research into the secondary prevention of post-traumatic stress, there remains a lack of evidence-based interventions. Based on this review, there still appears to be a need for preventive interventions after trauma that a) can be delivered in the immediate aftermath of trauma (i.e. within the first few hours and days), b) can be offered universally to all trauma survivors, regardless of whether or not they exhibit acute stress symptoms, c) are low-intensity in nature and d) target specific processes known to be important in the development of early post-traumatic symptoms as well as later PTSD.

Identifying/developing theory to target intrusive memory development

Theory from clinical psychology: why target early intrusive memories after trauma?

What are intrusive memories?

"Recurrent, involuntary and intrusive memories" are a hallmark symptom of PTSD in the DSM-5 (American Psychiatric Association, 2013; see Figure 1.3). Intrusive memories are predominantly fragmented sensory impressions of the traumatic event (van der Kolk & Fisler, 1995). They most commonly take the form of visual mental images, such as a snapshot pictures or "film clips"; however, they may also consist of bodily sensations, sounds, smells and tastes, or have several sensory components simultaneously (Ehlers, Hackmann, & Michael, 2004; Ehlers & Steil, 1995). For example, Ehlers et al. (2004) reported the case of a man who had repeated intrusive memories of seeing headlights coming towards him, as he had seen just before having a head-on road traffic collision at night.

Intrusive memories are thought to be functionally distinct from voluntary verbal thoughts about the traumatic event, such as deliberately mulling over what happened (Ehlers & Clark, 2000). However, they may include intrusive, unwanted thoughts that occurred at the time of the trauma, such as "I am going to die" (Holmes, Grey, & Young, 2005).

Interestingly, problematic mental images occur not only in PTSD, but across a wide range of psychological disorders, and are typically intrusive (occur involuntarily) and highly emotional (for reviews see: Brewin, Gregory, Lipton, & Burgess, 2010; Hirsch & Holmes, 2007; Holmes & Mathews, 2010). It is these characteristics of intrusive memories that are often targeted in established treatment techniques such as imagery rescripting (Arntz, 2012).

Why are early intrusive memories after a traumatic event important?

Intrusive memories are very common within the early aftermath (the first few weeks) of a traumatic event. For example, in a sample of 188 road traffic accident survivors attending a hospital emergency department, Mayou, Bryant, and Duthie (1993) found that 76% reported intrusive memories in the first few weeks after the accident. For the majority of people, post-traumatic stress symptoms diminish over time as the person adapts to the trauma and its impact on their life (McNally, Bryant, & Ehlers, 2003). So why should we be concerned with the presence of intrusive memories in the early stages after a trauma?

One reason is that intrusive memories elicit high levels of emotional distress (Ehlers & Steil, 1995; Foa & Riggs, 1993). By definition, they are emotion-laden memories, and typically involve emotions of fear, helplessness or horror (Hellawell & Brewin, 2002), but also other emotions such as anger, shame and guilt (Holmes et al., 2005; D. A. Lee, Scragg, & Turner, 2001). As such, targeting early intrusive memories may be a means to reducing distress after a traumatic event.

Another reason is that the presence of early intrusive memories may predict later PTSD. For example, Harvey and Bryant (1998) found in a sample of 92 road traffic accident survivors that the presence of "recurrent images and thoughts" in the first month predicted the presence of PTSD at six months. Similarly, in a sample of 337 severely injured trauma survivors in hospital, the presence of intrusive memories at a mean of eight days post-injury predicted PTSD diagnosis at three and twelve months (Creamer, O'Donnell, & Pattison, 2004).

Finally, it is not just the presence of early intrusive memories, but also how distressing people find them, which may predict later PTSD. Longitudinal studies have found an association between the distress of early intrusive memories and the presence or severity of later PTSD in road traffic accident survivors (Mayou et al., 1993), assault

victims (Michael, Ehlers, Halligan, & Clark, 2005), and female rape victims (Rothbaum et al., 1992). These findings raise the possibility that targeting the occurrence of early intrusive memories after a traumatic event, but also how distressing they are, might prevent PTSD from developing at a later stage.

How might early intrusive memories lead to later PTSD?

Psychological theories of PTSD propose that the nature of the memory of the traumatic event is a central feature of the disorder (Brewin, Dalgleish, & Joseph, 1996; Ehlers & Clark, 2000; Foa & Rothbaum, 1998). These models suggest that traumatic events, relative to other experiences, are encoded in memory to form strong sensory representations of the event, that are poorly integrated with autobiographical memory (see Brewin & Holmes, 2003 for a review). In this form, unconscious sensory cues (which act as reminders of the trauma) may trigger the trauma memory, bringing about the experience of an intrusion.

Ehlers & Clark (2000) have proposed that particular strategies that people employ to cope with intrusive memories of trauma, such as trying to push them away ("suppression") or mulling over them ("rumination"), may maintain the disjointed, sensory nature of the trauma memory and result in the persistence of PTSD (see Figure 1.6). Consistent with this theory, studies have shown that suppression and rumination in response to intrusive memories is associated with greater PTSD severity (Clohessy & Ehlers, 1999; Ehlers et al., 1998). This raises the possibility that attempts to cope with the distressing impact of early intrusive memories after trauma using these unhelpful strategies may inhibit normal recovery following trauma, and in time lead to PTSD. Whilst specific mechanisms are speculative at this stage, future research may help to shed light on the relationship between early intrusive memories and later PTSD.

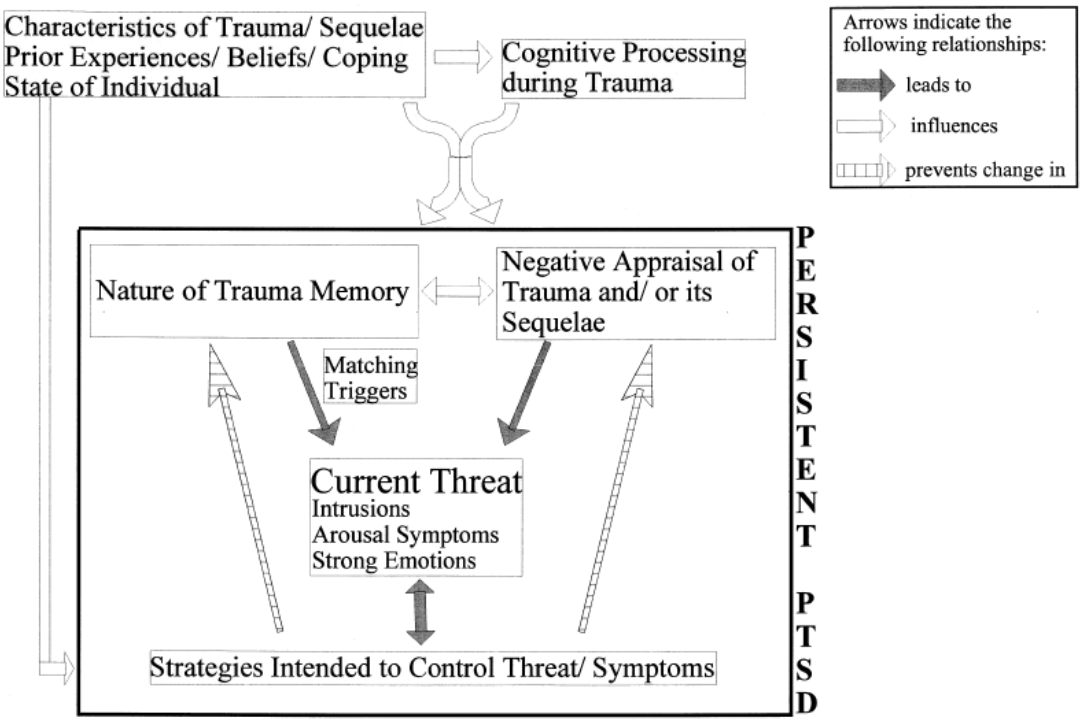


Figure 1.6. A cognitive model of PTSD. Taken from Ehlers, A., & Clark, D. M. (2000). A cognitive model of posttraumatic stress disorder. *Behaviour Research and Therapy, 38*(4), p.321. Copyright 2000 by Elsevier Ltd. Reproduced with permission.

Summary

Intrusive memories in the first few weeks after a traumatic event can be highly distressing for trauma survivors. Further, the frequency of their occurrence, and how distressing they are, may predict later PTSD. Therefore targeting the occurrence of early intrusive memories after a traumatic event may not only alleviate early psychological distress but also prevent PTSD from developing. The next section describes evidence from experimental research showing that the frequency and distress of intrusive memories can be targeted using particular types of cognitive tasks.

Theory from experimental psychology: targeting intrusive memories using simple cognitive tasks

Modulating the vividness and distress of mental images using concurrent cognitive tasks

As explained earlier, intrusive memories of trauma predominantly take the form of visual mental images. Mental imagery can be described as having a sensory experience in the absence of a physical sensory stimulus, in other words "seeing with the mind's eye,

hearing with the mind's ear" and so on (Kosslyn, Ganis, & Thompson, 2001). Two decades of experimental research has investigated the effect of performing concurrent cognitive tasks on the experience of mental imagery, based on the working memory model of Baddeley and Hitch (1974).

This model proposes that visual and verbal information are represented in separate systems: the "visuospatial sketchpad" is proposed to hold and manipulate visual information and to be involved in visual mental imagery (such as holding in mind a picture of someone's face), whilst the "phonological loop" is proposed to hold verbal and auditory information, and to be involved in auditory mental imagery (such as holding in mind the pitch of a particular musical note). Each of these systems is proposed to have limited capacity, and is regulated by a common attentional control system, termed the central executive. The model was later updated to include a component termed the episodic buffer, which provides an interface between working memory and long-term memory (Baddeley, 2003; see Figure 1.7 for a diagram of the revised working memory model).

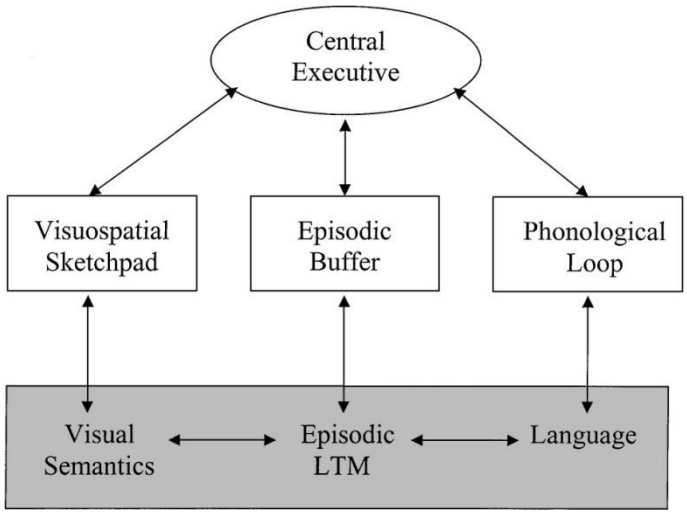


Figure 1.7. The revised working memory model. Adapted from Baddeley, A. D. (2003). Working memory: looking back and looking forward. *Nature Reviews Neuroscience, 4*, p.835.

The working memory model postulates that visual mental images would be disrupted by performing concurrent visuospatial tasks due to competition for storage capacity or rehearsal processes in the visuospatial sketchpad, whilst auditory images would be disrupted by performing concurrent verbal tasks due to competition for resources in the phonological loop. Findings from dual-task experiments, in which participants are asked to hold a mental image in mind whilst at the same time performing a cognitive task, support

this hypothesis. Studies have shown that visuospatial tasks such as bilateral saccadic eye movements and spatial pattern tapping, relative to verbal or control tasks, reduce the vividness and emotionality of visual mental images, whilst verbal tasks such as counting aloud, relative to visuospatial or control tasks, reduce the vividness and emotionality of auditory images (Baddeley & Andrade, 2000; see Figure 1.8; Kemps & Tiggemann, 2007).

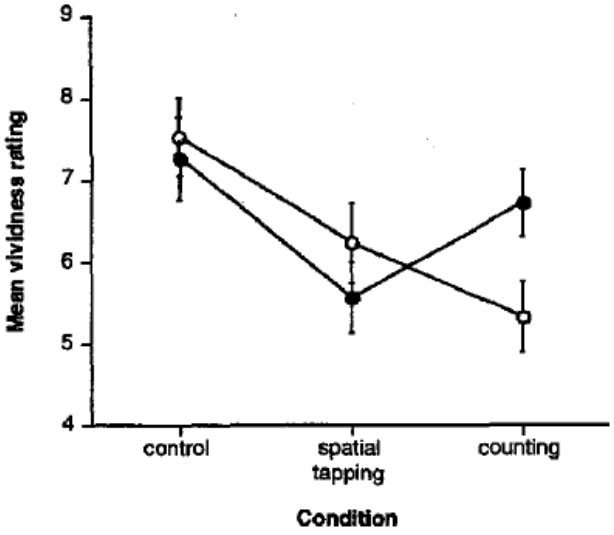


Figure 1.8. Rated vividness of visual (closed circles) and verbal (open circles) mental images in control (no task), visual (spatial tapping) and verbal (counting aloud) concurrent task conditions. Taken from Baddeley, A. D., & Andrade, J. (2000). Working memory and the vividness of visual imagery. *Journal of Experimental Psychology: General, 129*(1), p.130. Copyright 2000 by the American Psychological Association.

Critically, similar findings have been demonstrated for mental images in the form of distressing autobiographical memories, such as intrusive memories (Andrade, Kavanagh, & Baddeley, 1997; Kavanagh, Freese, Andrade, & May, 2001), and even for images of feared future events, termed "flashforwards" (Engelhard, van den Hout, Janssen, & van der Beek, 2010). However, more general effects that are not linked to task modality have been found. For example, tasks hypothesized to tax the central executive of the working memory model, such as performing a concurrent mental arithmetic task, have also been found to reduce the vividness and emotionality of distressing autobiographical memories (Engelhard, van den Hout, & Smeets, 2011; van den Hout et al., 2010), suggesting more than one possible mechanism.

In conclusion, evidence from two decades of dual-tasks experiments suggest that it is possible to target the vividness and emotional impact of distressing visual images of

autobiographical events (such as intrusive memories) using concurrent visuospatial tasks and/or tasks that tax working memory.

Modulating intrusion frequency using cognitive tasks during or soon after an experimental trauma film

Experimental psychology research has not only investigated the effect of performing concurrent cognitive tasks on the vividness and emotional impact of distressing mental images, but also the effect of performing cognitive tasks during or soon after stressful events on the frequency of subsequent intrusive memories. This research has predominantly used the "trauma film paradigm" as an experimental analogue of real-world stressful or traumatic events. This paradigm involves showing healthy participants a film with traumatic footage, such as scenes of injury and death, which has been shown to elicit a variety of stress responses, such as changes in heart rate and skin conductance and the occurrence of intrusive memories of the film (Horowitz, 1969; Lazarus & Alfert, 1964).

The trauma film paradigm has been used to investigate the effect of a variety of cognitive processing manipulations on the frequency of intrusive memories of the film over the following week (see Holmes & Bourne, 2008 for a review). Figure 1.9 shows the basic procedure, taken from Holmes & Bourne (2008). A key finding across a number of studies is that performing a concurrent visuospatial task during the film, such as spatial pattern tapping or clay modelling, compared to performing no task or a concurrent verbal task, such as counting aloud, reduces the number of intrusive memories of the film in the following week (Holmes, Brewin, & Hennessy, 2004; Stuart, Holmes, & Brewin, 2006).

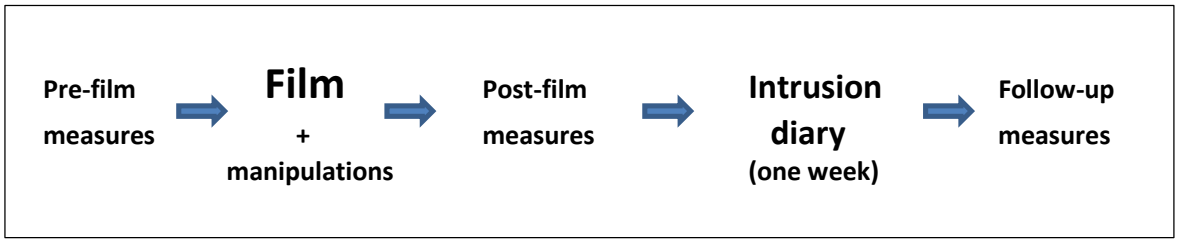


Figure 1.9. The basic procedure for the trauma film paradigm. Adapted from Holmes, E. A., & Bourne, C. (2008). Inducing and modulating intrusive emotional memories: A review of the trauma film paradigm. *Acta Psychologica, 127*(3), p.555.

Unfortunately, the translational implications of these findings may be limited, given that it may be challenging to intervene during a real-world traumatic event.

However, there may be greater scope for intervening in the immediate aftermath, alongside emergency or disaster relief services. Consequently, studies have sought to test the effect of using cognitive tasks *soon after* a trauma film on the frequency of subsequent intrusive memories. Deeprose, Zhang, Dejong, Dalgleish, and Holmes (2012) asked participants to complete a visuospatial finger tapping task, a verbal counting task and no task 30 minutes after watching a trauma film. Consistent with studies using concurrent tasks, the visuospatial finger tapping task reduced the number of intrusive memories in the following week relative to the verbal counting task and no task.

A novel approach has been to use visuospatial or verbal computer games as cognitive tasks soon after a trauma film. Holmes, James, Coode-Bate, and Deeprose (2009) asked healthy volunteers to play the visuospatial computer game "Tetris", versus no task, 30 minutes after watching a trauma film. Tetris is a popular computer game that involves moving and rotating falling shapes to create complete rows of blocks across the screen (see Figure 1.10). As predicted, those who played Tetris reported fewer intrusive memories in the following week than those who completed no task. Further, playing Tetris reduced intrusive memory frequency when played 4 hours after watching a trauma film, compared to no task or playing a verbal "Pub Quiz" game (Holmes, James, Kilford, & Deeprose, 2010; see Figure 1.11).

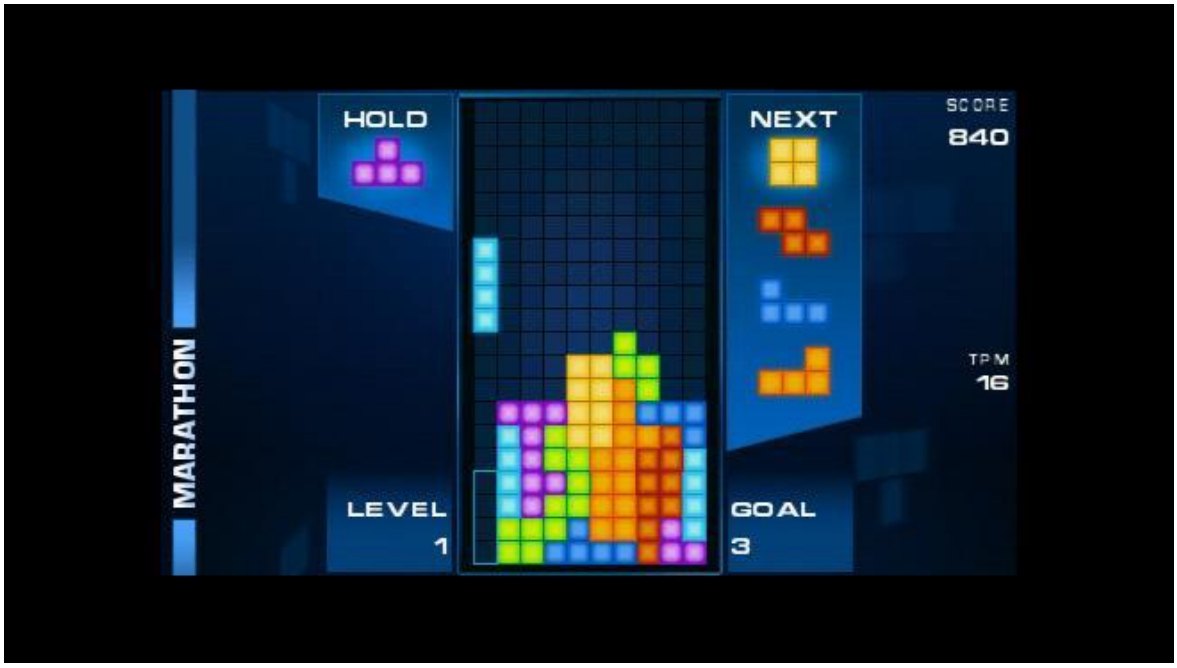


Figure 1.10. The computer game Tetris.

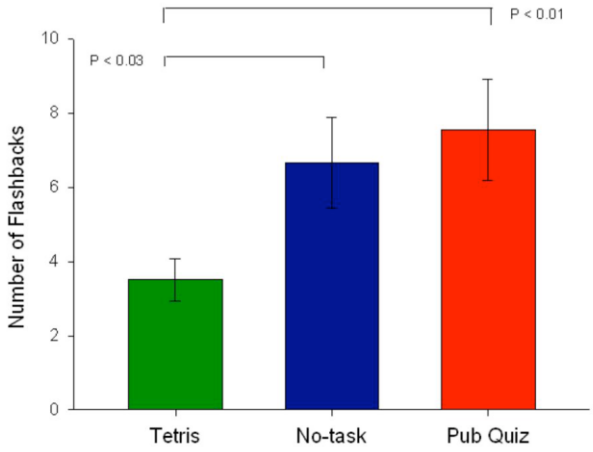


Figure 1.11. Number of intrusive memories in the week after a trauma film for participants who played Tetris, no task or Pub Quiz 4 hours after watching the film. Taken from Holmes, E. A., James, E. L., Kilford, E. J., & Deeprose, C. (2010). Key steps in developing a cognitive vaccine against traumatic flashbacks: visuospatial Tetris versus verbal Pub Quiz. *PLoS ONE, 5*(11), p.8.

Why might completing a visuospatial cognitive task, such as the computer game Tetris, soon after an experimental trauma analogue (a film with traumatic footage) reduce later intrusive memories? The memory consolidation hypothesis suggests that memories are initially malleable and liable to disruption before they become fixed or "consolidated" into long-term memory (Nader, 2003; Walker, Brakefield, Hobson, & Stickgold, 2003). Studies of motor memory tasks (e.g. learning of a finger tapping sequence) suggest that there is approximately a 6-hour "window" within which memories can be disrupted by competing information (Walker et al., 2003). This suggests that performing a competing visuospatial cognitive task within 6 hours after a trauma film, whilst visual memories of the film are still labile, may disrupt the consolidation of visual trauma memories, thereby reducing later intrusive memories (Deeprose et al., 2012; Holmes et al., 2009; Holmes, James, Kilford, & Deeprose, 2010).

This research holds promising translational implications, as it suggests that completing a simple visuospatial cognitive task in the immediate aftermath of a traumatic event may reduce intrusive memories and post-traumatic stress symptomatology in the early period e.g. the first week.

A proposal: a novel preventive intervention based on cognitive science

In summary so far, there is a lack of evidence-based interventions after psychological trauma that: a) can be delivered in the immediate aftermath of trauma (i.e. within the first few hours and days), b) can be offered universally to all trauma survivors, regardless of whether or not they exhibit acute stress symptoms, c) are simple and low-intensity in nature and d) are targeted at specific processes known to be important in the development of early post-traumatic symptoms as well as later PTSD. Findings from clinical research suggest that targeting early intrusive memories after trauma might reduce initial distress and also prevent PTSD from developing at a later stage. Experimental research based on cognitive psychology theory has shown that engaging in a visuospatial cognitive task, compared to no task or a verbal task, four hours after an experimental trauma film reduces the number of intrusive memories of the film in the following week. Therefore completing a simple cognitive task procedure in the immediate aftermath of a real-world trauma may offer a means of reducing early post-traumatic distress and preventing later PTSD symptoms. Given the gap in preventive interventions for post-traumatic stress, there is an impetus to work towards translating this experimental research to real-world trauma.

Translation to real-world trauma

In translating this novel intervention approach to a real-world setting, there are a number of key considerations, which are discussed below.

Selection of an appropriate cognitive task

A variety of visuospatial cognitive tasks have been shown to reduce the occurrence of intrusive mental images in laboratory studies, including tapping a pattern on a keyboard (Deeprose et al., 2012), clay modelling (Stuart et al., 2006), eye movements (van den Hout et al., 2001) and the computer game Tetris (Holmes et al., 2009). There are a number of reasons to believe that a procedure involving playing the computer game Tetris may be particularly suitable for use following real-world trauma.

First, the intervention showed a particularly strong effect size in reducing the number of intrusive memories in the week after a trauma film (d = 0.91[1] in Holmes et al., 2009), suggesting that the effect may withstand translation to a less controlled environment. Supporting this from a mechanism perspective, Tetris appears to tax working memory more strongly than eye movements (Engelhard, van Uijen, & van den Hout, 2010).

Second, a computer game such as Tetris may be more practical to implement in a real-world setting than other visuospatial tasks, as it can be played on small mobile devices such as a Nintendo gaming device or a smartphone.

Finally, Tetris is likely to be more accessible and acceptable than other visuospatial tasks. Tetris is one of the most popular and well-known computer games in history, and is played across ages, genders and cultures ("About Tetris," 2013). It now available on numerous platforms, including online, via social media websites such as Facebook and as a smartphone application, with over 425 million paid mobile downloads to date (Merlo, Milton, Gooze´e, Theobald, & Everitt, 2014). Playing a computer game at the scene of a trauma, compared to carrying out guided eye movements or tapping tasks, may be viewed by trauma survivors as a familiar, acceptable and non-stigmatising activity.

Efficacy after real-world trauma

To date, the use of visuospatial tasks in the immediate aftermath of real-world trauma to prevent the development of intrusive memories has not been empirically tested. However, there are a number of reasons to believe that the effect found after a laboratory-based trauma film will translate to real-world trauma. First, watching traumatic film footage, similar to experiencing a traumatic event first-hand, can elicit distressing post-traumatic stress symptoms, such as intrusive memories. In the most recent version of the diagnostic manual for mental health disorders, the DSM-5, the definition of a traumatic event includes “repeated or extreme indirect exposure to aversive details of the event(s), usually in the course of professional duties”, such as work-related exposure through electronic media, television, movies, or pictures (American Psychiatric Association, 2013). Furthermore, exposure to media images of the September 11, 2001 terrorist attacks were

[1] Cohen’s d (*d*) is a standardised measure of effect size. Values d> 0.2 are taken to indicate a "small" effect, values > 0.5 indicate a "medium" effect and values > 0.8 indicate a "large" effect (Barker, Pistrang, & Elliot, 1996).

found to elicit post-traumatic stress symptoms such as intrusive memories up to 6 months later in London school children (Holmes, Creswell, & O'Connor, 2007) and up to 3 years later in a US national sample (Silver et al., 2013), and the quantity of disaster-related footage watched by children after Hurricane Gustav predicted the severity of their PTSD symptoms at one month (Weems, Scott, Banks, & Graham, 2012).

Second, intrusive memories elicited by watching a trauma film appear to be qualitatively similar to intrusive memories following real-world trauma, even if they might be less distressing. Examples of intrusive memories recorded in a written diary by healthy participants to sections of a trauma film involving road traffic accidents included "car crashing into couple on wall", "child's arm cracking into place" "hearing crash", "car crashing over garden wall and crushing little boy" (obtained from James et al., 2015). In comparison, examples of intrusive memories recorded by patients with PTSD following real-world road traffic accidents include "sound of glass shattering", "seeing the bus double doors buckle into the bus", "glass windscreen shattering and hear tinkling", "head hitting pavement" and "twisting of bike and body at impact" (obtained from Holmes, Grey & Young, 2005). On face value, there appear to be qualitative similarities between the two sets of descriptions. For example, both involve vivid sensory information, are described as if they are occurring in the present, and tend to elicit an emotional response. As such, intrusive memories to a traumatic film and intrusive memories to real-world trauma may lie along a continuum.

Third, there is already evidence to suggest that visuospatial tasks can be used therapeutically with clinical patients after a real-world trauma. In a laboratory study with patients with PTSD, Lilley, Andrade, Turpin, Sabin-Farrell, and Holmes (2009) found that the vividness and emotionality of distressing intrusive memories of trauma were reduced by recalling the traumatic image and performing concurrent eye movements, relative to counting or no concurrent task. Further, eye movements are used as a therapeutic technique within EMDR (Shapiro, 1989; 1996), which is a well-established and evidence-based treatment for PTSD (National Institute for Health and Clinical Excellence, 2005).

Therefore, there is reason to believe that completing a visuospatial cognitive task procedure in the immediate aftermath of real-world trauma will have a similar effect in reducing the occurrence and distress of subsequent intrusive memories as it does after a laboratory-based trauma film.

Feasibility of implementation in the immediate aftermath of real-world trauma

Given that other preventive intervention approaches have been tested in the immediate aftermath of real-world trauma, such as psychological debriefing (Hobbs, Mayou, Harrison, & Worlock, 1996) and the drug propranolol (Pitman et al, 2002), it is likely to be feasible to implement a simple cognitive task procedure within this timeframe. A number of humanitarian organisations and emergency services already implement incident-management procedures soon after an event occurs, providing a potential opportunity to incorporate a simple preventive intervention. For example, the Royal Berkshire Fire and Rescue Service hold a group debriefing meeting for employees soon after any major incident (B. Jeffries, personal communication, June 2010).

Uptake by traumatised individuals

Even if it is feasible to implement a cognitive task intervention soon after a trauma, what is the evidence to suggest that traumatised individuals will be willing to engage in such an intervention? Individual testimonies from survivors of trauma have highlighted the need for psychological support in the immediate aftermath of trauma (National Institute for Health and Clinical Excellence, 2005), suggesting an openness to psychological interventions at this stage. However, playing a computer game as part of a psychological intervention is not a traditional approach, and motivating traumatised individuals to play a computer game within six hours of a traumatic event may be a challenge (Dyregrov & Regel, 2011). Encouragingly, however, following publication of Holmes et al.'s (2009) laboratory study, Holmes received feedback from members of the public of their own accord via email and letter, describing their spontaneous use of playing Tetris and other computer games in a therapeutic way after experiencing trauma (James, 2013). Whilst anecdotal, these reports suggest that the concept of playing computer games like Tetris as a therapeutic intervention after trauma may not be entirely unprecedented.

In contrast to existing psychological interventions after trauma, such as trauma-focused CBT (Ehlers & Clark, 2000), the proposed cognitive task intervention is not a talking therapy. It therefore has the advantage of potentially targeting people who find it hard to access traditional psychological therapies, such as those who perceive stigma over talking about their experiences (Pietrzak, Johnson, Goldstein, Malley, & Southwick, 2009), or those for whom language is a barrier (see Kung, 2004).

Conclusion

To date, there is a lack of preventive interventions after trauma that a) can be delivered in the immediate aftermath of trauma (i.e. within the first few hours and days), b) can be offered universally to all trauma survivors, regardless of whether or not they exhibit acute stress symptoms, c) are low-intensity in nature and d) target specific processes known to be important in the development of early post-traumatic symptoms as well as later PTSD.

Intrusive memories are distressing, predominantly visual memories of a traumatic event that pop into the mind unbidden. Clinical literature suggests that early intrusive memories after trauma may be a suitable target for preventive intervention, as they are not only distressing in their own right, but may also predict later PTSD. Experimental studies based on cognitive science have shown that a simple cognitive task intervention delivered within the first few hours after a trauma analogue (a film with traumatic footage) reduces the occurrence of intrusive memories over the following week in healthy volunteers. This approach may offer a simple, low-intensity intervention that could be delivered in the immediate aftermath of real-world trauma to target intrusive memories in the first week and possibly prevent the development of PTSD. A cognitive task intervention involving playing the visuospatial computer game Tetris holds particular translational potential, as it may be practical to implement in the immediate aftermath of trauma and acceptable for trauma survivors. The next step to progress this research is to develop and evaluate a simple cognitive task intervention involving Tetris game play to reduce intrusive memories after a real-world traumatic event.

Aims of this research

The overarching aim of this research was to develop and evaluate a simple cognitive task intervention involving Tetris game play as a novel preventive intervention to reduce the occurrence of intrusive memories after a real-world traumatic event. This involved translating research from previous laboratory studies to a hospital emergency department setting with patients who had experienced a road traffic accident. The research consisted of a series of stages:

1. Adapting the procedure used in the laboratory with healthy volunteers (Holmes et al., 2009) for a randomised controlled study in a hospital emergency department with patients who have had a road traffic accident (Chapter 2)
2. Piloting key parts of the adapted procedure in the emergency department with road traffic accident patients (Chapters 3 and 4)
3. Conducting a preliminary test of the efficacy of the simple cognitive task intervention to reduce the occurrence intrusive memories after a road traffic accident using a randomised controlled study design (Chapters 5, 6 and 7)
4. Identifying refinements for further research (Chapter 8).

The next chapter describes how the procedure used in the laboratory by Holmes et al. (2009) was adapted for a randomised controlled study in a hospital emergency department setting.

CHAPTER 2. Study Design and Development: Modelling process and outcomes to adapt the laboratory procedure for use in a hospital emergency department

Overview

The main study in this research was a randomised controlled study to test the efficacy of a simple cognitive task intervention in reducing intrusive memories after a real-world traumatic event. This chapter describes how the study was designed and planned, by adapting the procedures used in previous laboratory studies for use in a hospital emergency department with road traffic accident patients. The chapter begins by introducing randomised controlled trial (RCT) literature that informed adaptations and decisions in the design of the study[2]. This literature relates to widely used RCT frameworks and key issues in RCT design, such as internal and external validity, systematic error and practical feasibility. The chapter then describes how these considerations informed the main decisions in the design of the study, using a recommended structure for defining clinical research questions (the PICO framework; Richardson, Wilson, Nishikawa, & Hayward, 1995). Modelling of the sample, intervention procedure, control procedure and outcomes was based on previous experimental and clinical literature in the area, as well as observation and liaison with staff in the Emergency Department.

Randomised controlled trials framework

The main study in this research may be described as a randomised controlled trial, in that it is "a prospective study comparing the effect and value of intervention against a control in human beings" (Friedman, Furberg, & DeMets, 2010, p.2). Randomised controlled trials can be categorised according to the phase of development of the intervention, whereby different phases aim to answer different research questions. In the development of pharmaceutical interventions, trials are often described in sequential phases from I to IV. The different phases examine issues such as drug tolerance and metabolism (*Phase I*), dosage (*Phase II*), efficacy (*Phase III*), and effectiveness and safety in clinical practice (*Phase IV*) (International Conference on Harmonisation, 1997). In

[2] Training was received in randomised controlled trial design and implementation, including a 5-day Randomised Controlled Trial course run by the Oxford Centre for Statistics in Medicine, and the University of Oxford Good Clinical Practice Online Course (see Appendix 2.1 for course certificates).

practice, trials of pharmaceutical interventions do not always fit neatly into these phases, and therefore it has been argued that it may be more helpful to think of *early phase* and *late phase* trials (Friedman et al., 2010, p.4). In the development of complex interventions involving several components (such as the current intervention), trials may be better described within an iterative framework, rather than in sequential phases (Campbell et al., 2000; see Figure 2.1). Within this framework, *explanatory* trials typically aim to establish the efficacy of an intervention under tightly controlled conditions, whilst *pragmatic* trials aim to establish the effectiveness of the intervention in everyday clinical practice (Roland & Torgerson, 1998).

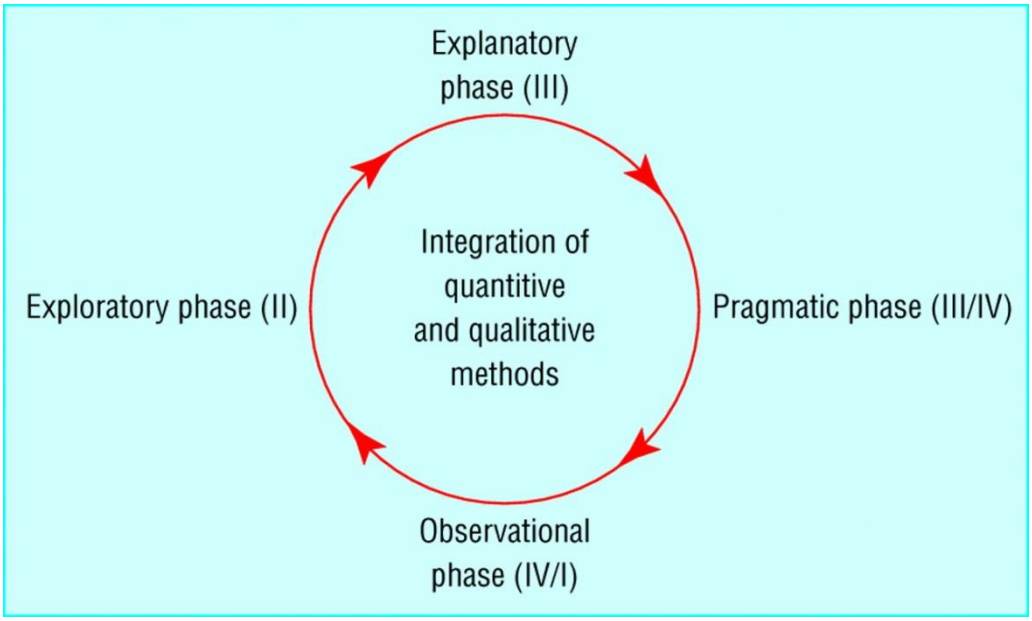


Figure 2.1. Iterative view of development of randomised controlled trials of complex interventions. Taken from Campbell, M., Fitzpatrick, R., Haines, A., Kinmonth, A. L., Sandercock, P., Spiegelhalter, D., & Tyrer, P. (2000). Framework for design and evaluation of complex interventions to improve health. *British Medical Journal, 321,* p.695. Copyright 2000 by BMJ Publishing Group Ltd. Reprinted with permission.

The aims of this research were to: a) translate a simple cognitive task intervention to reduce intrusive memories after a traumatic event from a laboratory setting (following a trauma film) to a clinical setting (following a real-world traumatic event) and b) provide a preliminary test of the efficacy of the intervention. The feasibility and piloting stage of this research addressed issues such as the acceptability of the intervention and a feasible duration for the intervention (comparable to issues of drug tolerability and dosage in phase I and II drug studies). The main study for this research may be viewed as an *early-phase*,

or *explanatory*, randomised controlled trial, as it sought to answer whether or not the simple cognitive task intervention could reduce intrusive memories after a real-world traumatic event under ideal conditions. The results of the study aimed to inform the development of *late-phase*, or *pragmatic*, clinical trials to answer whether or not the simple cognitive task intervention reduces intrusive memories after real-world traumatic events in clinical practice.

Key issues in randomised controlled trial design

Planning of the study was informed by a number of key issues in trial design: internal and external validity of the study; systematic error or bias in the study design; and practical considerations concerning the feasibility of the study design.

Internal and external validity

Important considerations in any study design are the extent to which the results can be attributed to the effect of the intervention on the outcome (the "internal validity" of the study) and the extent to which the results can be generalised to the wider population (the "external validity" of the study). In an early-phase explanatory trial, the emphasis is often on enhancing the internal validity of the study, to determine the efficacy of an intervention as accurately as possible (Godwin et al., 2003). To achieve this, it is important to protect the power of the study i.e. the likelihood of detecting the effect of the intervention over the effect of other possible confounding factors on outcome. The internal validity of a study may be compromised by error due to variation caused by chance ("random error") and errors due to factors in the study design or implementation that bias the results ("systematic error").

Random error

Random error, also known as "noise", refers to the impact of chance variations or chance inconsistencies in measurement on the study results, which can distort the results in either direction. The impact of random error can be reduced by increasing the study sample size.

Systematic error

Systematic error, also known as "bias", refers to deviations that are not simply due to chance but instead reflect issues in the study design or procedures. Systematic error is more problematic than random error, as it leads to consistent inaccuracies that bias the study results in a particular direction, which cannot be minimised by increasing the study sample size. Systematic errors can occur in a number of places in a randomised controlled trial. The main potential sources of bias are as follows (see Geddes, 2011):

- Selection bias – bias in the way that participants are allocated to treatment group, e.g. preferentially allocating a patient to the treatment or control group based on baseline characteristics, prognostic factors or clinician preference
- Performance bias – bias in the way that patients are treated depending on the group to which they have been allocated, e.g. giving patients different amounts of support or encouragement depending on whether they are in the treatment or control group
- Attrition bias – bias due to differential drop-out of patients in the different treatment groups, e.g. if more participants drop out in one group than the other
- Detection bias – bias in the way that outcomes are measure in the different treatment groups, e.g. clinicians inadvertently (or deliberately) rating symptom scores as higher in one group than the other.

Figure 2.2 shows where these biases can occur in the course of a randomised controlled trial.

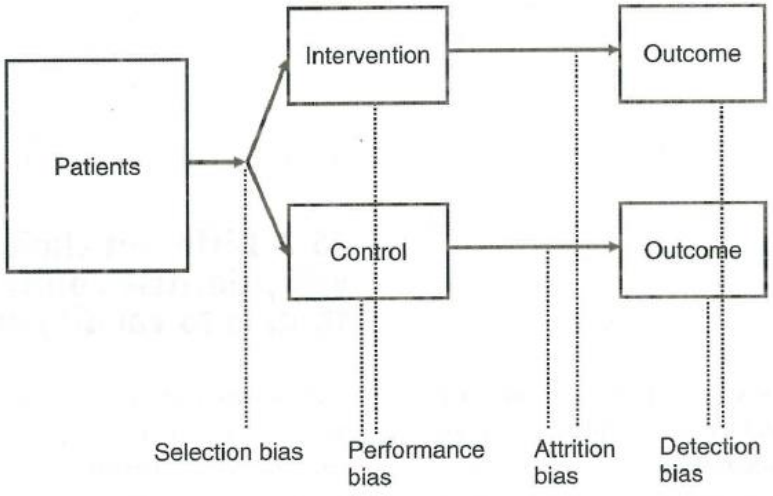


Figure 2.2. Specific sources of bias in a randomised controlled trial. Taken from Geddes, J. (2011). Experimental epidemiology. In M. T. Tsuang, M. Tohen, & P. Jones (Eds.), *Textbook of Psychiatric Epidemiology, 3rd Edition*, p. 247. Copyright 2011 by John Wiley & Sons, Inc. Reprinted with permission.

To maximise confidence in the validity of a study's results, choices in the study design should aim to reduce random and systematic error and enhance the power of the study. A useful way of viewing this is in terms of the "signal to noise ratio" of a study i.e. the ratio of the size of the intervention effect (the "signal") in relation to variation due to other confounding factors ("noise"). Geddes (2011) has suggested some potential ways of maximising the treatment signal, minimising noise and protecting the sample size in the design of a study (see Figure 2.3). These suggestions were used to inform choices in the design of this early-phase randomised controlled trial.

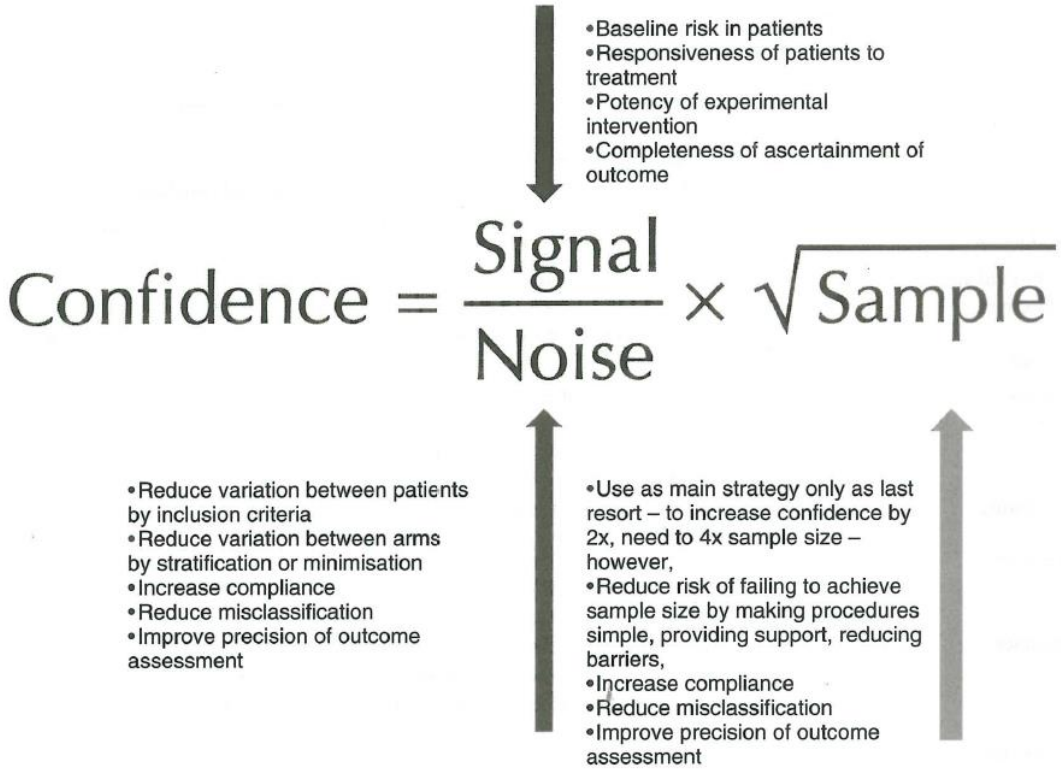


Figure 2.3. Relationship between confidence, signal to noise ratio and sample size in randomised controlled trials. Taken from Geddes, J. (2011) Experimental epidemiology. In M. T. Tsuang, M. Tohen, & P. Jones (Eds.), *Textbook of Psychiatric Epidemiology, 3rd Edition*, p. 249. Copyright 2011 by John Wiley & Sons, Inc. Reprinted with permission.

Practical feasibility

The feasibility of implementing a study is an important early consideration in the design of the study (Hulley, Cummings, Browner, Grady, & Newman, 2007, p.20). The following practical considerations were particularly relevant in designing the current study:

1. Feasibility of recruiting participants after real-world trauma: Recruiting people to a research study in the immediate aftermath of a real-world traumatic event might pose practical challenges that would limit the study sample size, participant eligibility criteria and recruitment strategy. Decisions were made in consultation with research staff at the John Radcliffe Hospital Emergency Department, who were familiar with the practical limitations of recruiting this type of patient group.
2. Scope within the time available: The study design had to be feasible within the three-year doctoral research period. This would be likely to constrain the sample size, duration of follow-up and general complexity of the study (e.g. involvement of other people and procedures).
3. Research support in the context of a DPhil: The size and design of the study had to be appropriate to the research-training context of a DPhil. This might affect decisions about whether or not to outsource components of the research such as trial management, data monitoring and data analysis.

Structure for defining the research question

A widely recommended structure for defining research questions in healthcare is the PICO framework (defined below; Thabane, Thomas, Ye, & Paul, 2009), which was first introduced as a structure for formulating clinical questions in evidence-based medicine (Richardson et al., 1995). The PICO framework helps researchers to consider key parts of the research question: the target Population or Participants, the Intervention, the Control or Comparator intervention and the key Outcomes of interest. This framework was used to consider the key aspects of the study that needed to be modelled. The following plans for the study design and translation of procedures from the laboratory to the real world were informed by theoretical considerations in randomised controlled trials design, existing clinical research literature and clinical observation and liaison in the emergency department (to inform the feasibility of the planned procedures).

Population/participants

Population

The population chosen for testing the simple cognitive task intervention was adult patients (aged 18 and over) presenting to the John Radcliffe Hospital Emergency

Department after a road traffic accident. Road traffic accident survivors recruited through a hospital emergency department have been widely used in prospective psychological studies of trauma reactions (e.g. Ehlers, Mayou, & Bryant, 2003; Holeva & Tarrier, 2001). Consequently a good deal is known about baseline characteristics and typical rates of early post-traumatic stress symptoms and PTSD in this group. For example, 51% experience moderate to severe post-traumatic stress symptoms in the first two weeks after the accident (Bryant & Harvey, 1996) and 23% have PTSD at 3 months (Ehlers et al., 1998). This existing body of research provided a useful context and comparison to evaluate a novel intervention in the current study, to indicate how representative the study sample was of the wider population, and how well the results of the study may be generalised (i.e. the external validity of the study).

Setting

The research was based at the John Radcliffe Hospital Emergency Department in Oxford. This is a highly research-active department, which hosts a large number of local, national and international research trials. It holds strong collaborative links with the University of Oxford. Of particular relevance, a number of previous University of Oxford studies based at the John Radcliffe Hospital Emergency Department have investigated the psychological impact of road traffic accidents. These studies include a large prospective study (Ehlers et al., 1998), an intervention trial (Hobbs et al., 1996), and a previous DPhil study (Murray, Ehlers, & Mayou, 2002). This suggested that recruitment would be feasible, and that the department would be likely to provide a practical and supportive setting for this research.

A number of additional features of the emergency department suggested it would offer a suitable setting for this research:

1. Patients have a *waiting time of up to 4 hours*, suggesting there would be sufficient time to implement an intervention before they were discharged.
2. The John Radcliffe Hospital ED is now the *major trauma hospital* in the locality, meaning that people who have road traffic accidents in a wide area are brought to this department.
3. *Attendance figures* for the department for March 2012 to March 2013 (i.e. one year) showed that 830 people attended the department after a road traffic accident, indicating an ample pool of potential participants for the study.

Participant eligibility criteria

In this early-phase trial, it was considered important to have a relatively homogenous sample, to reduce random error (or "noise") caused by confounding participant factors and improve the chance of detecting an intervention effect (i.e. increase the "signal") (Geddes, 2011). To enhance the treatment signal and power of the study, inclusion criteria were selected to identify participants at risk of developing post-traumatic stress symptoms who were most likely to benefit from the intervention (e.g. experienced an accident meeting the DSM-IV criteria for a traumatic event, alert and orientated, reported memory of the accident, fluent in English, physically able to use the intervention). However, it was not possible to screen participants and select them specifically on the basis of high risk for developing intrusive memories, as there was currently insufficient evidence regarding known risk factors for intrusive memories after trauma. To minimise potential participant non-adherence and drop-out, and preserve the power of the study, exclusion criteria were selected to rule out participants who were intoxicated, had moderate to severe brain injury, had a pre-existing neurological condition or had a severe mental illness[3]. These eligibility criteria are listed in the "Method" section of the first feasibility and piloting study (Chapter 3).

Recruitment strategy

The procedure for recruiting participants was developed in liaison with the Consultant in Emergency Medicine/Research Lead and an ED Research Nurse, to inform a feasible recruitment process. The planned strategy was for ED staff to screen all patients presenting to the ED and contact the researcher by telephone if a patient met a minimum subset of inclusion criteria and gave verbal consent to be approached by a researcher. The researcher would be available during the hours of 8am and 8pm Monday to Friday. This recruitment strategy aimed to minimise selection bias by ensuring that all patients meeting a minimum subset of inclusion criteria between the specified hours would be invited to take part in the study.

[3] The eligibility criteria were amended slightly following the results of the first feasibility and piloting study (see Chapter 3), and to bring them in line with those used in a recently-published trial of an early preventive psychological intervention commenced in a hospital emergency department (Rothbaum et al., 2012) before commencing the second feasibility and piloting study (see Chapter 4).

Sample size

In determining the sample size for the study, key considerations were: the power of the study to detect a treatment effect and the feasibility of recruiting the sample within the available time frame. A power calculation was based on Holmes et al.'s (2009) study, which found a large effect size of $d = 0.91$ for the reduction in the number of intrusive memories in the Tetris condition ($M = 6.70$, $SD = 5.47$) compared to a no-task control condition ($M = 2.80$, $SD = 2.65$). In this study, a more conservative effect size of $d = 0.7$ was employed.

A sample size of $N = 33$ per group was required to ensure 80% power to detect an effect size of $d = 0.7$ at the 5% significance level using a two-tailed test. A previous randomised controlled trial recruiting road traffic accident patients from the John Radcliffe Hospital ED reported a 14% loss to follow-up rate (Hobbs et al., 1996). The total sample size was estimated at 76 to allow for a similar attrition rate. A brief audit of attendees at the ED over a one-month period, in consultation with an ED Research Nurse, indicated that approximately seven potential participants were admitted per week. Taking into account researcher availability and a likely consent rate of 40% (Murray et al., 2002), a recruitment rate of one participant per week was estimated. This would allow the sample of 76 participants to be recruited in approximately 18 months, excluding follow-up.

Intervention

The simple cognitive task intervention was modelled on that used in previous laboratory studies (Holmes et al., 2009; Holmes, James, et al., 2010) – i.e. a memory reactivation cue followed by playing the visuospatial computer game "Tetris". In translating the intervention from the laboratory to a real-world setting, the aim was to preserve its potential potency (to enhance the treatment signal) whilst ensuring that the intervention would be tolerable for patients who had just experienced a traumatic accident.

Memory reactivation cue

In the laboratory, Holmes et al. (2009) gave all participants a brief film reminder (viewing neutral still images from the film) just prior to playing the visuospatial computer game Tetris or sitting quietly, to reactivate the memory of the film so that it was labile and open to modification using a competing visuospatial task. In the case of real-world trauma,

the reactivation cue may need to be tailored to the particular individual's experience (Pitman, Orr, Forgue, Dejong, & Claiborn, 1987). Previous clinical intervention studies have used different approaches to reactivate trauma memories in participants who have experienced distressing or traumatic events (see Table 2.1).

In this study the main considerations were to maximise the efficacy of the memory reactivation cue whilst minimising any potential distress it may elicit, given that participants would have just experienced a traumatic event. A manipulation similar to that used by Santa Maria, Reichert, Hummel, and Ehring (2012) was felt to be most suitable for the following reasons: a) it was designed to reactivate the visual memories of the worst moments of the trauma ("hotspots"), which are those that tend to recur as intrusive memories (Holmes et al., 2005) and b) it was relatively brief (20 to 30 seconds), so might minimise any distress for participants. The memory reactivation cue was hypothesized to be particularly important as part of the intervention in this study, as patients would be seen in a different environment to the one in which the accident took place, containing fewer environmental contextual cues to enable memory reactivation (S. M. Smith, 1988).

As this study involved a very recently traumatised sample who might find picturing the worst moments of the accident distressing, only participants in the intervention condition would be asked to picture the worst moments. Whilst this differed from Holmes et al.'s (2009) laboratory study, in which all participants received a neutral reactivation cue, this was felt to be appropriate for the following reasons: a) to avoid causing unnecessary distress for participants in the control condition, b) because the aim of this study was to test the efficacy of the intervention as a whole rather than to test the relative impact of its components, and c) if anything, minimising distress in the control group would result in a more conservative indication of the intervention effect.

Table 2.1. Memory Reactivation Cues Used in Previous Studies of Clinical Interventions for Trauma Memories, to Inform Development of the Memory Reactivation Cue in the Current Randomised Controlled Study

Paper	Sample	Type of intervention	Memory reactivation cue
Cognitive task interventions with healthy volunteers with distressing/traumatic memories			
Santa Maria et al. (2012)	57 university students who had experienced a distressing life event within the last 5 years.	Abstract versus concrete processing: participants wrote about their negative experience in either an abstract-evaluative or a concrete-experiential way.	Asked to think back to the negative experience and select the "hotspot" – the moment that was experienced as most distressing. They were then instructed to close their eyes and imagine the hotspot as vividly as possible for 30 seconds, letting images and associated emotions come up without trying to suppress them.
Engelhard et al. (2011)	80 university students who had seen images of the Queen's Day tragedy on the TV or internet.	Concurrent cognitive tasks that taxed working memory to varying degrees: exposure alone or exposure with concurrent 'simple' subtraction, 'intermediate' subtraction, or 'complex' subtraction.	Participants were asked to select a negative visual image of the Queen's day tragedy which had an emotional impact on them. They were asked to bring the image to mind as vividly as possible as if it were happening right now for 20 seconds, and rate its vividness and emotionality.
Lilley et al. (2009)	18 participants awaiting psychological treatment for PTSD	Competing concurrent tasks: Bilateral eye movements v. counting v. no task (exposure alone). Within-subjects design.	Asked to identify three images that intruded involuntarily and represented the most distressing parts of the memory for the event i.e. their traumatic hotspots. They were then asked to bring each to mind and rate its vividness and emotionality (0 to 10).

Table 2.1 continued.

Paper	Sample	Type of intervention	Memory reactivation cue
Pharmacological interventions with PTSD patients			
Brunet et al. (2008)	19 participants with chronic PTSD	Propranolol v. placebo	Participants were guided through a script preparation procedure, in which they described their most distressing trauma incident(s) in writing on a standard script preparation form (based on Pitman et al., 1987).
Suris, North, Adinoff, Powell, and Greene (2010)	22 male combat veterans diagnosed with PTSD	Glucocorticoid v. placebo	
Suris, Smith, Powell, and North (2013)	51 male combat veterans diagnosed with PTSD	Sirolimus v. placebo	
Eye Movement Desensitization and Reprocessing (EMDR)			
Shapiro (1989)	22 participants who were experiencing traumatic memories following a variety of traumatic events.	Exposure with bilateral eye movements v. exposure only.	Participants were asked to identify a single picture that represented the entire traumatic memory (preferably the most traumatic point of the incident) and indicate who and what was in the picture. They were then asked to visualise the traumatic scene, rehearse a negative statement that went with the picture (e.g. "I am helpless") and follow the experimenter's finger with their eyes in bilateral rhythmic movements.

Tetris game play

In a laboratory setting, Holmes et al. (2009) asked healthy volunteers to play the computer game "Tetris"[4] for 10 minutes on a personal computer (PC). The PC version of the game involved using the cursor keys to move and rotate the shapes as they fell from the top of the screen. A period of clinical observation in ED indicated that it would not be feasible to ask patients to play Tetris on a PC. A number of key differences were observed between the laboratory and ED settings with relevance for how Tetris was administered (see Table 2.2).

Table 2.2. Comparison of the Physical Environment Between the Laboratory and the Emergency Department, Used to Inform How Tetris was Administered in the Randomised Controlled Study

Laboratory	Emergency Department
Quiet, controlled environment	Noisy, unpredictable environment with patients in different areas (waiting room, bays on ward)
Participants sitting upright, with full physical ability	Patients may be seated in waiting area or lying on a bed, and may have physical injuries.
Access to computer on a desk	No computer or desk access available to patients

In consultation with ED staff, it was agreed that the intervention would be best administered on a handheld device that did not require a table. This would enable it to be used flexibly in different parts of the ED, and by patients lying on a bed. A Nintendo DS was selected as a possible platform for Tetris play (see Figure 2.4), using the Tetris DS[5] version of the game. Patients who were unable to sit or did not have use of both arms would be excluded. Instructions for delivering the simple cognitive task intervention were adapted from those used in the laboratory studies. A standard set of wording was used to ensure consistency of delivery of the intervention across participants.

[4] Copyright 1985–2008, Tetris Holdings LLC. from Blue Planet Software (Honolulu, HI).

[5] Published by Nintendo, released March 20, 2006.

Figure 2.4. Nintendo DS (handheld gaming device) selected for delivering the computer game Tetris in the Emergency Department.

Dose

In trials of pharmacological treatments, the optimal dose of treatment is one that has the highest efficacy whilst remaining safe (i.e. with minimum side effects and drop-out). For the simple cognitive task intervention, one hypothesis is that the optimal "dose" of Tetris would be at a level of difficulty that mildly to moderately taxes visual working memory, as opposed to minimally or overly taxing working memory (Engelhard et al., 2011). The PC version of the game used by Holmes and colleagues (Holmes et al., 2009; Holmes, James, et al., 2010) increased in difficulty level as the participant's performance improved, which potentially "titrated" the dose of the intervention to an optimal level for each participant. For this study, the "marathon" version of Tetris DS was selected, which similarly increases in difficulty level as the participant's performance improves. This would hope to maintain the efficacy of the task, whilst remaining engaging and tolerable for participants.

Duration

Holmes et al. (2009) asked participants to play Tetris for 10 minutes after watching a 12-minute trauma film. However, there was no precedent for an optimal duration for playing Tetris after a real-world traumatic event to effectively reduce intrusive memories. A minimum period of 10 minutes of uninterrupted Tetris game play was selected initially, with the option for participants to play Tetris for as long as the participant wished.

One of the aims of the feasibility and piloting stage of this research would be to identify a feasible duration for playing Tetris (see Chapter 3).

Control

In an early phase (exploratory or explanatory) trial, the ideal control condition is identical to the intervention condition with the only exception that the active treatment is omitted (Hulley et al., 2007, p.149). Therefore any difference between the two groups can be attributed to the hypothesized active "ingredients" of treatment, rather than any noise due to non-specific effects of the intervention condition (such as participant expectation or contact with the clinician). This is important for the internal validity of the study, so that accurate conclusions can be drawn from the study results. In the case of medication trials, this usually involves administering a placebo pill that is indistinguishable from the treatment pill in appearance, dose and timing. In trials of behavioural or psychological interventions the selection of an appropriate control is often less clear-cut as there may be a number of "active" components of the intervention.

Within this simple cognitive task intervention, the active component was hypothesized to be engagement in a visuospatial task whilst the trauma memory is labile in working memory. Therefore a suitable control might be to engage in a non-visuospatial task or no task while the trauma memory is labile, as modelled in preceding laboratory studies (Holmes et al., 2009; Holmes, James, et al., 2010). Other (non-visuospatial) tasks, such as a Pub Quiz computer game or psychological debriefing intervention, have been found to increase intrusive memories and PTSD symptoms after trauma, and may not be ethical as a control condition in a recently traumatised population. Therefore a no-task control condition involving sitting quietly for the same length of time as the intervention, was initially selected. However, liaison with clinical staff at the ED indicated that it might not be feasible to ask patients to "sit quietly", given that there is constant noise and distractions in the ED environment. The Consultant in Emergency Medicine and ED Research Lead suggested that a "usual care" control would be most appropriate, which may include waiting, assessment and medical treatment by emergency department staff, but no specific intervention designed to reduce intrusive memories or other post-traumatic stress symptoms.

As a point of note, the most suitable control condition in a late phase trial is often the current best treatment available, or usual clinical care if the best treatment is not widely used in clinical practice (Friedman et al., 2010, p.22). Given that at present there is no recommended preventive intervention after trauma, usual care may offer the most suitable control if this research is to be extended to a larger pragmatic trial. Hence findings from

this study may be relevant to inform the next stage of research (i.e. hold external validity). Also of note, participants in the intervention condition would receive the simple cognitive task intervention in addition to usual care in the emergency department.

Outcomes

Selection of the primary outcome measure

The primary outcome is the main outcome of interest, on which the intervention effect is evaluated and the study is powered. Randomised controlled trials typically have a single primary outcome measure (Friedman et al., 2010, p.43). It is recommended that the primary outcome is sensitive to the effect of the intervention, clinically relevant, can be measured reliably (i.e. is free from detection bias), and is easy to measure (Everitt & Wessely, 2008, p.69; Heyse, 2005). These recommendations are discussed further below.

1. Theoretically sensitive to the intervention effect: Ideally, previous research would have shown that the outcome measure can be modified using a visuospatial cognitive task intervention. A stronger effect size would indicate that the outcome measure is more sensitive to the effect of the intervention, and thus better able to detect a treatment signal in this study.
2. Clinical validity of the measure: The ability of the measure to assess a clinically relevant construct enables valid clinical inferences to be drawn from the study results (Gebski, Marschner, & Keech, 2002). In this study, the primary outcome measure would ideally: a) be a validated measure of intrusive memories or post-traumatic stress symptoms, b) have high predictive validity for these constructs, and/or c) be associated with clinical distress or impairment in functioning. Further, outcome measures would ideally be validated in road traffic accident patients or patients recruited from a hospital emergency department.
3. Reliability (or "precision") of the measure: Using measures that yield similar results over time and between different people helps to reduce noise and increase the power of the study. For example, using measures with standardised instructions may reduce assessor and participant bias and improve the consistency of measurement. Again, outcome measures would ideally be tested for reliability in road traffic accident patients or patients recruited from a hospital emergency department.

4. Ease of completion: Participants may be more likely to complete simple outcome measures that are quick and easy to complete. A high completion rate is important as it helps to improve the ability to detect the treatment signal, reduce noise due to missing data and preserve the power of the study.

The primary aim of this explanatory trial was to translate the simple cognitive task intervention from the laboratory to a clinical setting; at this stage of the research, the aim was not to provide a pragmatic test of effectiveness in clinical practice. Therefore the primary outcome was modelled on and translated from the laboratory studies on which this research was based (Holmes et al., 2009; Holmes, James, et al., 2010), i.e. the number of intrusive memories in the first week after the road traffic accident. This primary outcome was considered an important target in its own right, as well as a possible predictor of other clinical outcomes (e.g. PTSD). To select a suitable primary outcome measure to assess the number of intrusive memories in the first week after the road traffic accident, a number of candidate measures were compared on the four considerations described above. Table 2.3 shows a comparison of potential primary outcome measures on the key criteria for selection.

Given that in an early-phase trial it is important to enhance the likelihood of detecting a treatment effect, in this study the sensitivity of the primary outcome measure to the effect of the simple cognitive task intervention was considered key. Only the intrusion diary and the Impact of Events Scale – Intrusion Subscale (IES-I) have been found to have reduced scores following a visuospatial task intervention. Whilst the intrusion diary has not been tested for reliability, the strong effect size for the reduction in the number of intrusive memories following a visuospatial cognitive task compared to no task (d = 0.91; Holmes et al., 2009) suggested that this may be a suitable and sensitive primary outcome measure for this translational study.

Table 2.3. Comparison of Potential Primary Outcome Measures for the Randomised Controlled Study on Key Criteria for Selection

Measure	Sensitivity to intervention effect	Reliability	Clinical validity	Ease of completion
Intrusion diary – number of intrusive memories (Holmes et al., 2009; Holmes, James, et al., 2010)	**Yes:** Participants recorded fewer intrusive memories in a pen-and-paper intrusion diary following a visuospatial cognitive task than a verbal or control task e.g. effect size of $d = 0.91$ (Holmes et al., 2009).	Not reported.	The number of intrusive memories recorded in an intrusion diary in the week after a trauma film was significantly correlated with a clinical measure of PTS symptomatology, the IES-I, in 302 healthy volunteers ($r = .334$, $p < .001$) (Clark, 2013; unpublished raw data).	High completion rates in laboratory studies with healthy volunteers (e.g. 100% of participants who were followed up in Holmes et al., 2009). Similar to diaries used routinely with patients in cognitive behavioural therapy.
IPT – frequency of intrusions in a 2-minute period following viewing of trauma-related pictures (Michael et al., 2005)	Not reported as an outcome measure following visuospatial task interventions.	Not reported.	Percentage of time that the intrusions were present during the task was significantly correlated with concurrent PTSD severity and PTSD severity 6 months later	Brief experimental task, requiring presence of a researcher to administer.
Intrusion Interview – frequency item (Hackmann, Ehlers, Speckens, & Clark, 2004; Michael et al., 2005)	Not reported as an outcome measure following visuospatial task interventions. May hypothesise that a retrospective report of the the number of intrusive memories in the last week would be sensitive to the intervention effect.	Not reported.	Correlation with corresponding frequency item on the Intrusion Questionnaire was r = .94 (Hackmann et al., 2004).	Retrospective clinician-administered interview. Single frequency item may be brief to administer, but is delivered as part of a comprehensive interview.

Table 2.3 continued.

Measure	Sensitivity to intervention effect	Reliability	Clinical validity	Ease of completion
Intrusion Questionnaire – frequency item (Hackmann et al., 2004)	Not reported as an outcome measure following visuospatial task interventions. May hypothesise that a retrospective report of the the number of intrusive memories in the last week would be sensitive to the intervention effect.	1-week test–retest reliability was between r = .61 and r = .72 (Speckens, Ehlers, Hackmann, & Clark, 2006).	Correlation with corresponding frequency item on the Intrusion Interview was r = .94 (Hackmann et al., 2004).	Retrospective self-report questionnaire. Single frequency item may be brief to complete, but is delivered as part of a comprehensive questionnaire.
Symptom Questionnaire (Halligan, Clark, & Ehlers, 2002)	Not reported as an outcome measure following visuospatial task interventions. May hypothesize that items assessing daily frequency of intrusions would be sensitive to the intervention effect.	Internal consistency of 4 items assessing analogue PTSD intrusion symptoms was alpha =.81 (Halligan et al., 2002).	No relevant data reported.	Brief 16-item retrospective self-report questionnaire.
IES – Intrusion subscale score (IES-I; Weiss & Marmer, 1997)	**Yes:** Healthy volunteers reported lower IES-I scores following a visuospatial cognitive task than a no-task control (Holmes et al., 2009; Krans, Janecko, & Bos, 2013) e.g. effect size of d = 0.74 (Holmes et al., 2009).	High internal consistency in motor vehicle accident (MVA) survivors (alpha = .90; J. G. Beck et al., 2008).	Validated measure of the severity of distress caused by intrusion symptoms after trauma. Significantly correlated with CAPS reexperiencing score (r = .66) and PSS-SR reexperiencing score (r = . 86) in MVA survivors (J. G. Beck et al., 2008). Injured trauma survivors with PTSD v. no PTSD at 6 months had higher IES-I scores at 1 week (Shalev, Peri, Canetti, & Schreiber, 1996).	Completed as part of the IES-R, a brief 22-item self-report questionnaire.

Table 2.3 continued.

Measure	Sensitivity to intervention effect	Reliability	Clinical validity	Ease of completion
PDS – Re-experiencing symptoms score (Foa, 1995)	Not reported as an outcome measure following visuospatial task interventions.	Good internal consistency (alpha = .78) and test-retest reliability (*r* = .77) in 248 people with mixed traumas (Foa et al., 1997) .	Validated measure of the severity of PTSD intrusion symptoms. Correlation of *r* = .77 with IES-I subscale score in a sample of 248 people with mixed traumas (Foa et al., 1997).	Completed as part of the PDS, a 49-item self-report questionnaire assessing PTSD symptoms, taking approx. 15 minutes to complete.
DTS – Re-experiencing symptoms score (Davidson et al., 1997)	Not reported as an outcome measure following visuospatial task interventions.	Not reported for re-experiencing symptoms.	Significantly correlated with IES-I score (.77) in 350 mixed trauma survivors (Davidson et al., 1997). Correlation of .70 with CAPS re-experiencing subscale (Zlotnick, Davidson, Shea, & Pearlstein, 1996).	Completed as part of the DTS, a brief 17-item self-report questionnaire assessing PTSD symptoms.
PTSD Checklist – Civilian Version (PCL-C) – re-experiencing subscale score (Blanchard et al., 1996)	Not reported as an outcome measure following visuospatial task interventions.	High internal consistency (alpha = .935) in MVA survivors (Edward B. Blanchard et al., 1996).	Significant correlations with CAPS on individual re-experiencing symptom items (.617 to .788) in MVA survivors (Edward B. Blanchard et al., 1996) and with IES-I in students (Ruggiero, Ben, Scotti, & Rabalais, 2003).	Completed as part of the PCL-C, a brief 17-item self-report questionnaire assessing PTSD symptoms.
CAPS – reexperiencing symptoms subscale score (Blake et al., 1995)	Significantly reduced following EMDR which included a visuospatial eye-movement task but no significant difference between EMDR with and without eye movements (Boudewyns & Hyer, 1996).	Adequate internal consistency (e.g. alpha of .76 in MVA survivors: Beck et al., 2008), test-retest reliability (.88 to .99; Weathers et al., 1999) and inter-rater reliability (.92 to .97; reported in Weathers, Keane, & Davidson, 2001).	Validated clinical measure of the severity of re-experiencing symptoms, matching the DSM-IV diagnostic symptoms for PTSD (American Psychiatric Association, 1994; Weathers et al., 2001). Score at a mean of 8 days post trauma predicted diagnosis of PTSD at 3 and 12 months (Creamer et al., 2004).	Completed as part of the CAPS, a comprehensive clinician-administered interview to assess PTSD symptoms, which takes approximately 45 minutes to administer.

Selection of secondary outcome measures

In addition to the primary outcome, it is usual for trials to be interested in other outcomes to assess the wider impact of the intervention and safety of the intervention (Everitt & Wessely, 2008, p.69). In this study, secondary outcomes of interest were acute stress symptoms (within the first month after the trauma), post-traumatic stress symptoms (from one month after the trauma), possible diagnosis of PTSD (from one month after the trauma), other mental health outcomes (e.g. anxiety and depression), work and social functioning, and overall quality of life. Given that the primary outcome measure (a self-report intrusion diary) was not a standardised clinical outcome measure, additional secondary outcome measures were also included to provide convergent information to the intrusion diary: a) a retrospective self-report interview (the Intrusion Interview) and b) a retrospective self-report questionnaire (the Intrusion Questionnaire).

Secondary outcome measures were selected on the basis of their reliability and validity, ideally in road traffic accident survivors recruited via a hospital emergency department, as well as their use in previous randomised controlled trials of interventions after trauma. Hypothesized sensitivity to the effect of the intervention was not a required criterion, as the study was not powered to detect an effect of the intervention on secondary outcome measures. Liaison with the ED Consultant indicated that patients may reside anywhere in the country, hence outcome measures would need to be administered remotely using telephone interviews and online/postal questionnaires. Therefore secondary outcome measures would ideally be validated for use in this way. Details of secondary outcome measures can be found in Figure 2.5.

Timing of outcome assessments

The main outcomes in this study were: a) intrusive memories and acute stress symptoms within the first month after the trauma and b) post-traumatic stress symptoms from one month after the trauma. The following time points for follow-up assessments were selected, based on previous literature:

- One week: To assess early intrusive memories and acute stress symptoms predictive of later PTSD. Intrusive memories in the first week after a trauma film have been shown to be reduced using a simple cognitive task intervention (e.g. Holmes et al., 2009), and intrusive memories and re-experiencing symptoms at 8 days after a trauma predict PTSD symptoms at 3 months (Creamer et al., 2004).
- One month: To assess post-traumatic stress symptoms and possible diagnosis of PTSD (American Psychiatric Association, 2013).
- Three months: To assess "chronic" post-traumatic stress symptoms, predictive of longer-term problems. Post-traumatic stress symptoms at three months have been shown to predict PTSD at 1 year (Ehlers et al., 1998)
- Six months: To assess chronic PTSD at longer-term follow-up.

Figure 2.5 shows the planned timing for administering baseline and outcome measures.

Other key design issues

Baseline variables

Baseline measures were selected to assess known pre- and peri-traumatic risk factors for post-traumatic stress symptoms, to assess balance between the intervention and control groups on potential confounding factors. Risk factors were identified from two meta-analyses of PTSD predictors (Brewin et al., 2000; Ozer et al., 2003) as well as additional studies of risk factors for PTSD symptoms in road traffic accident survivors recruited from a hospital emergency department (Coronas et al., 2011; Ehlers et al., 1998). Measures were selected to be as brief as possible (maximum 15 minutes) to a) minimise participant burden, given that they may be traumatised and in pain and b) allow sufficient time for the procedure to be completed before discharge from the ED (usually within 4 hours). Details of baseline variables can be found in Figure 2.5.

	Eligibility	Baseline	1 week	1 month	3 months	6 months
Emergency Department						
Ambulance/medical records						
Demographics	X					
Details of accident	X					
GCS	X					
ISS		X				
Heart rate/medication		X				
Face-to-face assessment						
Informed consent	X					
Eligibility questions	X					
Self-report measures						
Psychiatric/trauma history		X				
Perceived life threat		X				
SDQ		X				
PDI		X				
After Discharge						
Self-report measures						
Intrusion diary			X			
Intrusion Questionaire questions			X			
IES-R			X	X	X	X
BDI-II			X	X	X	X
BAI			X	X	X	X
WSAS			X	X	X	X
EQ-5D			X	X	X	X
Treatment/life stress/post-trauma factors			X	X	X	X
Expectancy Questionnaire						X
Feedback Questionnaire						X
Clinical interviews						
Intrusions Interview questions			X			
CAPS			X	X	X	X

Figure 2.5. Planned timing of assessments for the randomised controlled study.
GCS = Glasgow Coma Scale; ISS = Injury Severity Score; SDQ = State Dissociation Questionnaire; PDI = Peritraumatic Distress Inventory; IES-R = Impact of Events Scale-Revised; BDI-II = Beck Depression Inventory-II; BAI = Beck Anxiety Inventory; WSAS = Work and Social Adjustment Scale; EQ-5D = EuroQol-5D; CAPS = Clinician Administered PTSD Scale.

Randomisation

Random allocation of participants to comparison groups aims to reduce selection bias (so that outcome is not biased by baseline prognosis or clinician preference), produce groups that are comparable on known and unknown prognostic factors and provide a valid foundation for statistical testing (Armitage, 1982; Friedman et al., 2010). In small trials like this, however, randomisation may not always result in groups that are balanced on prognostic factors, which may confound the interpretation of the results (Altman & Bland, 1999). Minimisation is an acceptable method of ensuring that groups are balanced on several prognostic factors (Altman & Bland, 2005), particularly when the sample size is less than 100 and the number of prognostic factors is greater than 3 (S. J. Pocock & Simon, 1975; Scott, McPherson, Ramsay, & Campbell, 2002).

In this study, potential baseline prognostic factors were identified from two meta-analytic reviews of risk factors for PTSD (Brewin et al., 2000; Ozer et al., 2003). Perceived life threat, peritraumatic dissociation and peritraumatic distress were the strongest peritraumatic predictors of PTSD (weighted r = .26, .35 and .26 respectively; Ozer et al., 2003). Age and gender were also included as key demographic variables that would ideally be balanced between the two groups, even though they are relatively weak predictors of PTSD (weighted r = .13 and .06 respectively: Brewin et al., 2000).

An online randomisation programme was developed and managed by the Oxford Cognitive Health and Neurosciences Clinical Trials Unit (OCHNCTU), who remained independent of the day-to-day management of the trial. The programme used the minimisation method outlined by S. J. Pocock and Simon (1975), with a small random component to ensure that allocations remained unpredictable. To ensure that participant's group allocation remained unknown until the point of randomisation (referred to as "allocation concealment"; Schulz & Grimes, 2002), thereby minimising selection/allocation bias, the randomisation programme would be accessed online from the emergency department only after participants had completed the relevant baseline measures. Baseline scores would be input to reveal the participant's group allocation.

Blinding

Blinding refers to the participant and/or investigator being unaware of the group to which the participant has been allocated. The purpose of blinding is to minimise bias caused by conscious or unconscious factors influencing the way the participant behaves or

is treated (performance bias) and the way outcome is assessed (detection bias), according to the group to which they have been assigned. In an ideal design, neither the participants nor the investigators having contact with participants, assessing outcome and analysing the data would know to which group the participant had been assigned (a *double-blind* or *triple-blind* study). In trials of pharmaceutical agents this is usually achieved by using a placebo intervention that is identical to the treatment intervention in all ways (e.g. appearance, smell, taste, method of administration etc.) with the exception of containing the active ingredient. The intervention would be assigned and monitored for safety by someone other than the investigator. In the case of complex interventions, such as this cognitive task intervention, blinding may not be possible. In this study, by nature of the intervention being a behavioural task, it was necessary for the participant and researcher administering the intervention to know which intervention was being administered (an *un-blinded* or *open* study). However, the following measures were planned to help minimise or assess bias:

a) Participants were told that they would be randomly assigned to either: 1) being asked to picture the accident for 30 seconds (to bring back the memory), followed by completing a simple computer task for a minimum of 10 minutes or 2) to continue waiting in the emergency department. They were not informed that the simple computer task was hypothesized to reduce intrusive memories of the accident.
b) Participants' expectation of the effect on their intrusive memories of what they had been asked to do in the emergency department would be assessed at follow up, to identify any difference between the intervention and control groups.
c) Clinician-administered outcome measures (e.g. the CAPS) would be administered by a researcher who did know to which group the participant had been allocated.
d) The majority of outcome measures were participant self-report measures, administered remotely (online or by post), thereby minimising the opportunity for detection bias.
e) A standard protocol was developed for running the study, to ensure that wording, instructions and measurement methods were consistent across participants.
f) All researchers administering the protocol would be trained and checked at regular intervals to minimise performance and detection bias.

Trial management and data monitoring

Given that the study was a small early-phase trial involving a single centre, and part of a doctoral research qualification, the student was responsible for the majority of the day-to-day management of the trial, including coordination of the trial and data handling. However, a trial management group was set up, consisting of research supervisors, other researchers with experience of conducting similar intervention trials and a trial statistician. The trial management group was responsible for independent oversight and data monitoring of the trial; consistent with the small size of the study, there were no separate trial steering or independent data monitoring committees. The trial management group would be responsible for monitoring the following aspects of the study's progress: recruitment and retention of participants, protocol adherence, any safety issues or adverse events, data monitoring and data analysis (towards the end of the study) (see Appendix 2.2 for a template of the trial management group meeting agenda). Meetings were planned to occur fortnightly at the start of the trial, and every one to two months thereafter. In addition, weekly updates would be circulated to the study investigators to ensure regular monitoring of the study's progress.

The trial management plan was reviewed and approved by the Oxford Cognitive Health and Neurosciences Clinical Trials Unit (OCHNCTU). Conduct of the trial, documentation and reporting would be conducted in accordance with OCHNCTU Standard Operating Procedures and Good Clinical Practice guidelines. A study monitoring plan was created to specify how the study progress would be monitored, including: verification of source data, handling of protocol deviations, monitoring the completeness of data collection, data checking, database integrity, data storage, monitoring visits and safety reporting (see Appendix 2.3 for the monitoring plan).

Summary of adaptations to the laboratory procedure for the emergency department

Figure 2.4 shows an overview of the laboratory procedure used by Holmes et al. (2009) and how it was adapted for this research in a hospital emergency department.

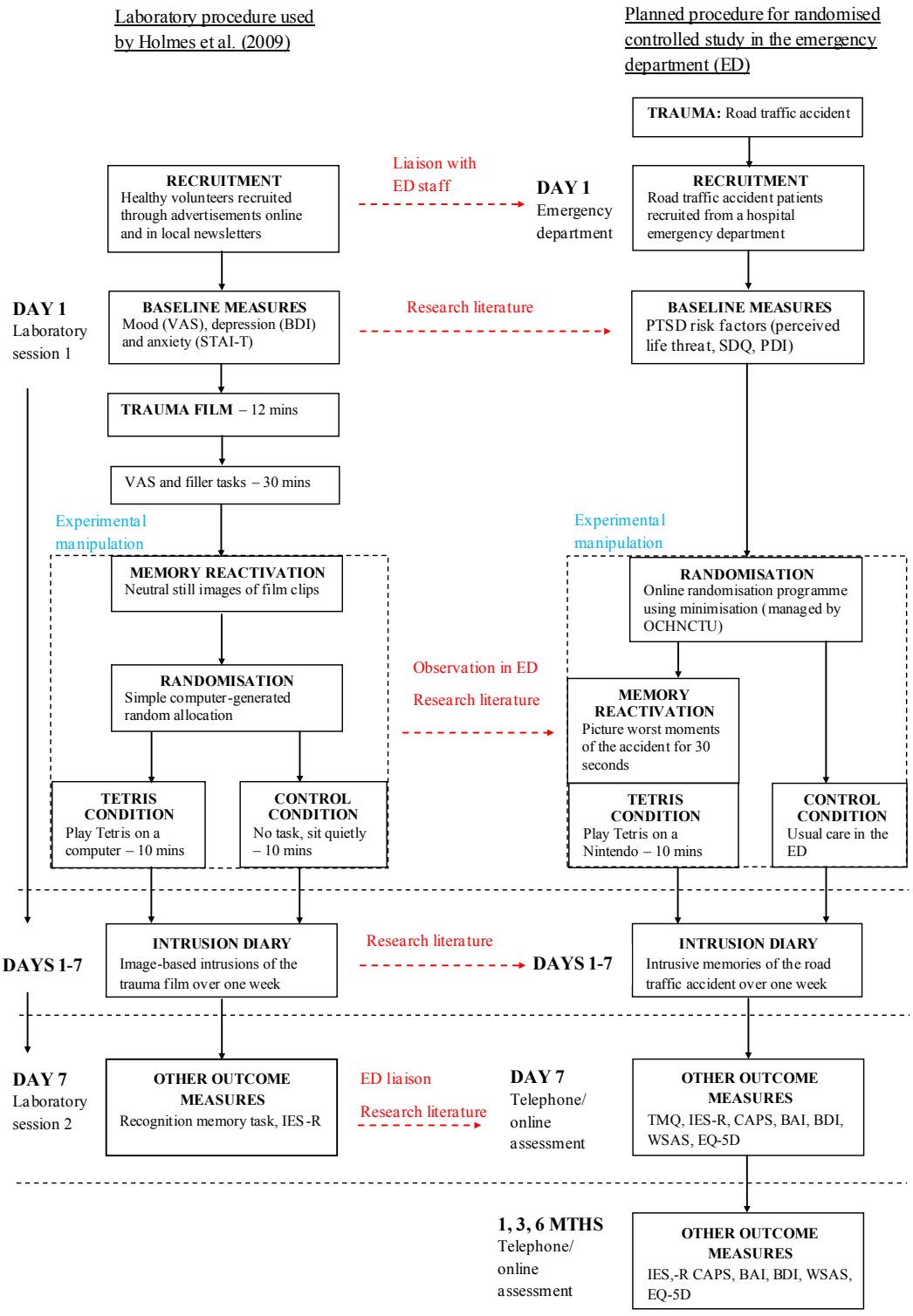


Figure 2.6. Overview of the laboratory procedure used by Holmes et al. (2009) (left hand side) and how it was adapted for a hospital emergency department (right hand side). VAS = visual analogue scale, BDI = Beck Depression Inventory, BAI = Beck Anxiety Inventory, IES-R = Impact of Events Scale-Revised, SDQ = State Dissociation Questionnaire (Halligan, Michael, Clark, & Ehlers, 2003), PDI = Peritraumatic Distress Inventory (Brunet et al., 2001), TMQ = Trauma Memory Questionnaire, CAPS = Clinical-Administered PTSD Scale, WSAS = Work and Social Adjustment Scale, EQ-5D = EuroQoL-5D.

Development and review of the study protocol

The proposal for this research was reviewed by a number of stakeholders at various stages. Figure 2.5 illustrates the development process for the study protocol. Ethical approval was obtained from the local NRES Research Ethics Committee (REC) to conduct a small feasibility/pilot study and a randomised controlled study to test the simple cognitive task intervention in the John Radcliffe Hospital Emergency Department with patients who had experienced a road traffic accident. The REC approval letter (REC reference 12/SC/0485, dated 18/10/12) is given in Appendix 2.4.

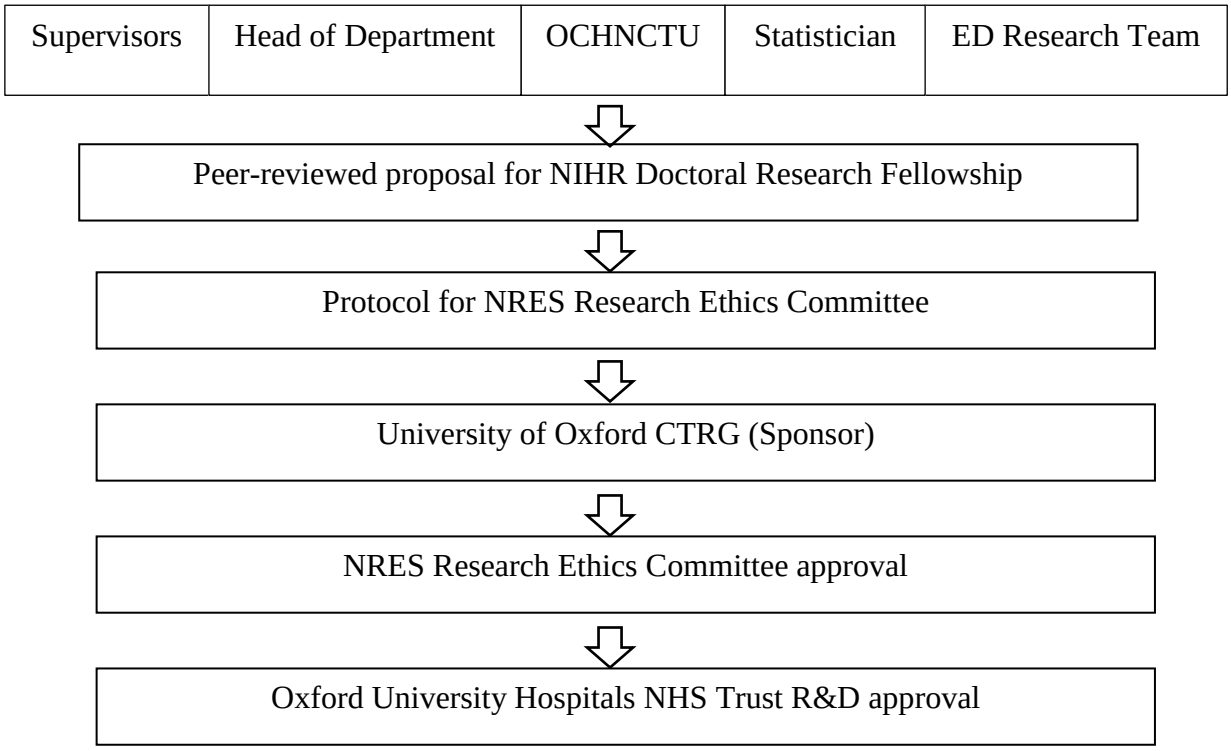


Figure 2.7. Development and review of the study protocol.
OCHNCTU = Oxford Cognitive Health and Neurosciences Clinical Trials Unit; ED = Emergency Department; NIHR = National Institute for Health Research; NRES = National Research Ethics Service; CTRG = Clinical Trials and Research Governance; R&D = Research and Development.

CHAPTER 3. Feasibility and Piloting Study 1: A first test of key procedures for the randomised controlled study

Introduction and aims

As discussed in Chapter 1, laboratory studies with healthy volunteers found that completing a simple cognitive task (a memory reactivation cue followed by playing the computer game Tetris), compared to a no-task control, soon after watching a trauma film (an experimental analogue of trauma) reduced the number of intrusive memories of the film over the following week (Holmes et al., 2009; Holmes, James, et al., 2010). Intrusive memories were recorded using a pen-and-paper intrusion diary. Chapter 2 described how the laboratory study procedures were adapted for use with patients in a hospital emergency department (ED) following a road traffic accident. This chapter describes the first of two studies conducted as part of the feasibility and piloting stage of this research (see Figure 3.1).

A key aim of piloting is to assess the feasibility of processes that are critical to the success of the main study (Thabane et al., 2010). These processes might typically include recruitment and retention of participants, assessment and suitability of eligibility criteria, and the feasibility of the intervention and outcome assessment procedures. In line with this, the current study aimed to test the practical implementation of key procedures for the main randomised controlled study, namely 1) recruiting road traffic accident patients in the ED, 2) delivering the simple cognitive task intervention (picturing the accident for 30 seconds followed by playing Tetris for at least 10 minutes), and 3) measuring the primary outcome using a pen-and-paper intrusion diary. The results were used to inform refinements for a second feasibility and piloting study (Chapter 4).

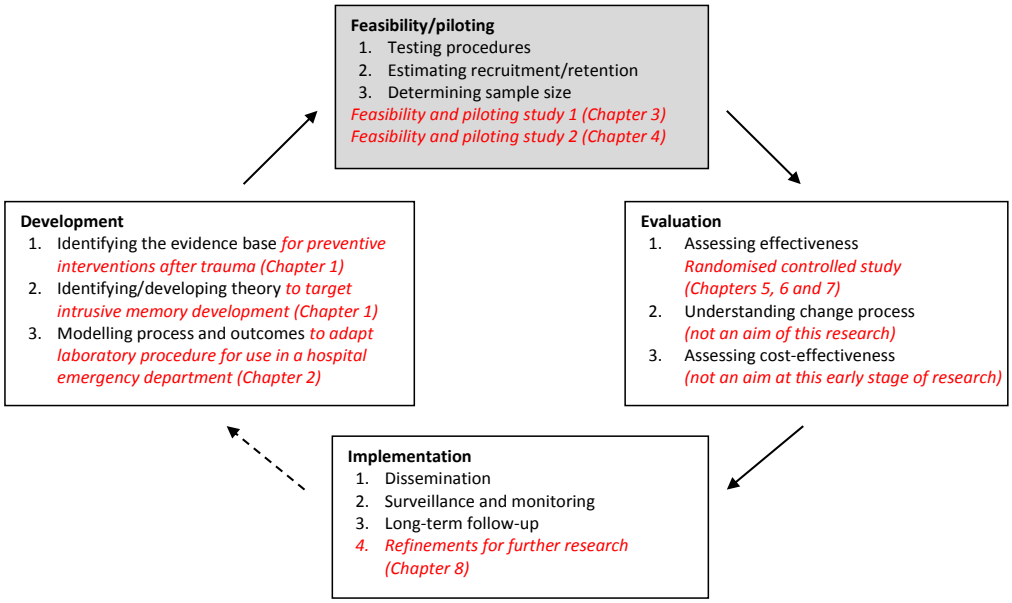


Figure 3.1. Key stages in this research to develop and evaluate a novel preventive intervention after trauma, based on the MRC Complex Interventions Guidance (2008).

Background

Aim 1: Recruiting road traffic accident patients in the emergency department

1. What is the recruitment rate of participants to the study?

A recruitment rate of one participant per week was previously estimated (see Chapter 2). This figure was based on the following assumptions: a) approximately two to three potential participants would be identified per week during the hours when the researcher would be available to approach them (8am to 8pm from Monday to Friday), and b) 40% of participants approached about the study would consent to take part. However, these estimates were not sufficiently well informed. The estimate of two to three potential participants was based on the examination of a database of patients presenting to the ED, which did not detail all of the relevant eligibility criteria. Further, the estimated 40% consent rate was drawn from an earlier study that was not an intervention study (Murray et al., 2002). Therefore, the first aim of this study was to determine the recruitment rate, using the recruitment procedure described in the methods section below.

Aim 2: Delivering the simple cognitive task intervention

1. What proportion of patients presenting to the ED after a road traffic accident are willing to complete the simple cognitive task (picturing the accident for 30 seconds followed by playing Tetris for at least 10 minutes)?

In previous laboratory studies, participants were healthy volunteers who requested information about the study in response to an advertisement (Holmes et al., 2009; Holmes et al., 2010). In the current study, patients in the emergency department might be less willing to consent to completing the intervention because a) they will not be expecting to be invited to take part in a research study and b) they may be distressed, tired or in pain as a result of the accident. On the other hand, they will already have been asked by emergency service staff to recall what happened in the accident, so picturing the accident again may be relatively well tolerated. Further, Tetris is a popular and well known game, and is played across ages, genders and cultures ("About Tetris," 2013), suggesting it may be relatively acceptable as part of the intervention. Therefore, the aim of this study was to determine the proportion of potential participants willing to complete the simple cognitive task (a memory reactivation cue followed by playing Tetris).

2. What proportion of participants are able to complete the simple cognitive task (picturing the accident for 30 seconds followed by playing Tetris on a hand-held gaming device for at least 10 minutes)?

Whilst patients presenting to the ED after a road traffic accident might be willing to complete the simple cognitive task, a number of factors may affect their ability to complete the task as instructed. First, patients may find the memory-reactivation cue (closing their eyes and picturing the accident for 30 seconds) too distressing to complete. Second, patients may find it difficult to play Tetris for as long as 10 minutes due to tiredness, pain, or difficulty concentrating as a result of the accident. Third, patients may be unable to play Tetris for as long as 10 minutes due to distractions in the environment, including interruptions by ED staff, noise in the ED, or the arrival of family or friends. Therefore the study assessed what proportion of participants would be able to complete the simple cognitive task as instructed.

3. What is the maximum length of time participants report they would have been able to play Tetris for, assessed using a simple feedback questionnaire?

In laboratory studies, the simple cognitive task was effective in reducing the number of intrusions of a trauma film when Tetris was played for 10 minutes. To date, no studies have used Tetris in a clinical population after real-world trauma; hence it is uncertain if a 10-minute "dose" of Tetris will be sufficient to have a significant effect. Whilst a longer period of playing Tetris may be optimal after real-world trauma, there may be a number of potential challenges to patients playing Tetris in the emergency department, such as being tired or in pain, or being interrupted by staff or family members. Therefore one aim of the study was to ascertain the maximum length of time for which participants felt they would have been able to play Tetris, assessed using a simple questionnaire.

4. What is participants' experience of playing Tetris in the ED, as assessed using a simple feedback questionnaire?

To date, the computer game Tetris has not been used as part of an intervention with patients presenting to an ED after a road traffic accident. Whilst Tetris is popular across a range of populations, e.g. it has been translated into over 50 languages ("About Tetris," 2013), it is plausible that in patients who have recently experienced a trauma, playing Tetris will be considered difficult, distressing, or trivial. Therefore this study evaluated participants' experience of playing Tetris using a simple feedback questionnaire, which included open questions designed to indicate what might improve the experience of playing Tetris.

In summary, the second aim of the study was to assess the proportion of patients willing and able to complete the simple cognitive task intervention and to gather feedback on their experience of completing the task, including obtaining an estimate of the maximum length of time for which they would be willing to play Tetris.

Aim 3: Measuring the primary outcome using a pen-and-paper intrusion diary

1. What proportion of participants complete and return the intrusion diary in the week after the accident?

The sample size calculation for the randomised controlled study was based on an attrition rate of 14%, drawn from a previous randomised controlled trial recruiting road traffic accident patients from the John Radcliffe Hospital ED (Hobbs et al., 1996). Therefore, for the randomised controlled study to have sufficient power to detect a treatment effect, the primary outcome measure must have at least an 86% completion rate (i.e. 86% of participants given the intrusion diary must complete it). In previous laboratory studies with healthy volunteers, completion rates of the pen-and-paper intrusion diary have been found to be high (e.g. 100% of participants who were followed up in Holmes et al., 2009). However, the intrusion diary has not previously been used as an outcome measure in patients recruited from a hospital emergency department following a road traffic accident. In this sample, completion rates may be lower, due to factors such as a disrupted routine in the week after the accident. Therefore, an additional aim of this study was to assess the proportion of participants that complete the pen-and-paper intrusion diary in the week after the accident.

2. What is participants' experience of completing the intrusion diary in the week after the accident, as assessed using a simple feedback questionnaire?

Another aspect of the suitability of the intrusion diary for use as the primary outcome measure is how easy participants find it to fill in, how accurately they report filling it in, and whether there are any difficulties with filling in the diary in the week after the accident. Therefore the study assessed these aspects of participants' experience of filling in the intrusion diary, using a simple feedback questionnaire.

In summary, the third aim of the study was to assess the proportion of participants that completed the intrusion diary outcome measure in the week after the accident, and to gather feedback on participants' experience of completing the intrusion diary.

Method

Design

A within-subjects design was used in which all participants were offered the simple cognitive task intervention in the ED and asked to complete an intrusion diary in the week after the accident. The first eight participants were given the intrusion diary described in the method section of this chapter. The last two participants were given an amended version of the intrusion diary and delivery method (see Chapter 4), in response to the results from the first eight participants. Further details are given in the results and discussion sections.

Participants

Participants were patients presenting to the John Radcliffe Hospital ED after a road traffic accident. Patients were included in the study if they met the following eligibility criteria:

Inclusion criteria

- Aged 18 or over
- Involved as a driver, passenger, motorcyclist, cyclist or pedestrian in a road traffic accident meeting the DSM-IV A1 criterion for PTSD ("experienced, witnessed, or confronted with an event that involved actual or threatened death or serious injury, or a threat to the physical integrity of oneself or others")
- Seen in the ED within 6 hours of leaving the scene of the accident
- Fluent in written and spoken English
- Willing and able to provide informed consent and complete study procedures

Exclusion criteria

- Moderate to severe traumatic brain injury, indicated by any of:
    - Glasgow Coma Scale score < 13
    - Post-traumatic amnesia (PTA) > 1 hour
    - Loss of consciousness of > 30 minutes
- Currently receiving treatment for mania, psychotic symptoms, substance abuse or neurological condition.

A sample of 10 participants was recruited, consisting of seven men and three women, with a mean age of 33.7 years (SD 14.9). Additional demographic information for the sample is given in Table 3.1.

Table 3.1. Demographic Information for the Sample (N = 10)

Demographic variable	*n* (unless stated otherwise)
Marital status	
Single	3
Married or cohabiting	6
Divorced	1
Widowed	0
Employment status	
Employed	6
Unemployed	0
Student	3
Retired	1
Years in education, Mean (*SD*) (*n* = 9)[a]	14.3 (4.7)
Highest educational qualification (*n* = 9)[a]	
None	3
GCSE or equivalent	2
A-Level or equivalent	3
University Degree or equivalent	0
Master's Degree or equivalent	1
Doctorate or equivalent	0
Household income (*n* = 9)[b]	
£0 – 19, 999	3
£20,000 – 29,999	2
£30,000 – 39,999	4
£40,000 – 49,999	0
£50,000 +	0
Housing status	
Home owner	2
Tenant	5
Living with relatives	3
University accommodation	0
English as first language	
Yes	6
No	4
Ethnicity	
White British	5
White Other	2
Asian Other	3

[a] Missing response for one participant
[b] One participant did not wish to answer this question

Materials and measures

Baseline measures

a) Self-report measures:

Clinical history form. This form assessed personal and family history of mental health problems, and history of prior trauma (see Appendix 3.1).

Perceived life threat. Participants were asked to rate "to what extent did you feel your life was in danger?" and "to what extent did you feel that someone else's life was in danger?" each on a 10-point Likert scale from 0 (*not at all*) to 10 (*extremely*). This rating was based on ratings of perceived life threat used in previous prospective studies following trauma (e.g. Heir, Piatigorsky, & Weisaeth, 2009; Holbrook, Hoyt, Stein, & Sieber, 2011) (see Appendix 3.2).

State Dissociation Questionnaire (SDQ; Halligan et al., 2002; Halligan et al., 2003; Murray et al., 2002). This nine-item measure assesses peri-traumatic dissociative experiences such as derealisation, depersonalization, detachment, altered time sense, and emotional numbing. Items are rated on a Likert scale from 0 (*not at all*) to 4 (*very strongly*), and the mean score is calculated. The SDQ shows good reliability and validity (Halligan et al., 2002; Halligan et al., 2003; Murray et al., 2002) (see Appendix 3.3).

Peritraumatic Distress Inventory (PDI; Brunet et al., 2001). This 13-item measure was used to assess the extent to which participants experienced a number of emotional reactions during the accident. Items such as "I felt helpless to do more" and "I was horrified by what happened" are rated on a 5-point Likert scale (0 = not at all, 1 = slightly, 2 = somewhat, 3 = very, 4 = extremely) and summed to give a total score. The PDI was found to be internally consistent, with good reliability and validity. PDI score has been found to predict the development of PTSD symptoms (e.g. Nishi et al., 2010) (see Appendix 3.4).

Hotspots of the accident form. Participants were asked to write down the worst moments of their accident (see Appendix 3.5).

Activity diary. A simple activity diary was used for participants to record each activity they did, and for how long, during their time in the ED. The diary was adapted from the activity log used by Porcheret et al. (2012) (see Appendix 3.6).

b) Information collected from participants' medical notes:

Details of the accident e.g. time of accident, type of vehicle, driver or passenger.

Injury Severity Score (ISS; Baker, O'Neill, Haddon, & Long, 1974). The ISS is a widely used measure of the overall severity of physical injury. The ISS was calculated from information regarding participants' injuries.

Medication administered following the accident. The type and dose of any medication administered in the ambulance or ED was recorded.

Outcome measures

Tetris feedback questionnaire. This 13-item feedback questionnaire was used to assess the maximum length of time for which participants felt they would have been able to play Tetris (aim 2, question 3) and participants' experience of playing Tetris in the ED (aim 2, question 4). The first 7 items were designed to give ratings of participants' experience of playing Tetris (aim 2, question 4). Each item was rated on a 9-point Likert scale from 1 (*not at all*) to 9 (*extremely*), and included questions such as "how enjoyable did you find playing Tetris?", "how easy did you find playing Tetris," and "how distressing did you find playing Tetris?" The next two items asked for how long participants would be willing to play Tetris (aim 2, question 3). The last 4 items asked open questions about participants' experience of playing Tetris (aim 2, question 4), such as what they found positive or difficult. This questionnaire was adapted from a previous study of a novel computerised intervention (Blackwell & Holmes, 2010). The measure is given in Appendix 3.7.

Intrusion diary. A pen-and-paper diary was used to assess the number of intrusions participants had in the week after the accident (aim 3, question 1). Participants were asked to write down the following information each time they had a intrusion of the accident: the date and time of the intrusion, the content of the intrusion, what (if anything) triggered it, and its vividness and emotionality, both rated on a scale of 0 (*not at all*) to 10 (*extremely*). The diary was adapted from the one used by Holmes et al. (2009; 2010), as described in Chapter 2 (see Appendix 3.8).

Intrusion diary feedback questionnaire. This seven-item feedback questionnaire was used to assess participants' experience of filling in the intrusion diary (aim 3, question 2). The first four items were rated on a 9-point Likert scale from 1 (*not at all*) to 9 (*extremely*), and asked questions such as "how easy did you find it to fill in the intrusion

diary?" and "how accurately do you think you filled in the intrusion diary?". The last three items asked open questions about participants' experience of filling in the intrusion diary, such as what they found positive or difficult. This measure is given in Appendix 3.9.

Tetris computer game

The computer game Tetris DS was played on a Nintendo DS Lite: a hand-held gaming device with a screen size of 62 mm by 46 mm (see Chapter 2 for a photograph).

Procedure

Ethical approval for the study was gained from a local NRES Research Ethics Committee as part of the application for the randomised controlled study (REC reference 12/SC/0485, approval letter dated 18/10/12; see Appendix 2.4). Details of the study were clarified in an amendment (Amendment 1 approval letter dated 22/01/13; see Appendix 3.10). Figure 3.2 shows a diagram to summarise the procedure for the study. The procedure is described in more detail below.

Identification. Potential participants were identified by ED staff. Staff were asked to contact the researcher by telephone if a suitable patient presented to the ED between the hours of 8am and 8pm from Monday to Friday. The researcher was predominantly based within 15 minutes of the ED, and travelled in to the ED on receiving a call. A poster was positioned at all the main staff stations in the ED, which summarised the aims of the study, participant inclusion criteria, the role of ED staff and the researcher's contact number (see Appendix 3.11). The researcher attended regular staff meetings to remind staff about the study and encourage their role in the recruitment procedure. In addition, the researcher prompted the coordinating nurse two to three times a day, either in person or by telephone, to identify if any potential participants were present in the ED.

Screening. Potential participants were screened for eligibility by ED staff, based on information available on the ED online patient database ("FirstNet"[6]) and patients' handover notes. Screening aimed to determine if patients met the following subset of

[6] "FirstNet" is part of the Electronic Patient Record (EPR) system used by the John Radcliffe Hospital Emergency Department to register patients presenting to the department and record their clinical management.

eligibility criteria: aged 18 or over; experienced or witnessed a road traffic accident; fluent in English; no moderate to severe traumatic brain injury. If a patient met the above criteria, a member of staff gained verbal consent from the patient to speak to the researcher.

Informed consent. Participants were approached during a settled time whilst they were waiting in the ED and provided with an information sheet about the study (similar to Appendix 5.7). They were given time to read this, ask questions, and consider whether or not they wished to participate. Those who decided to take part signed a consent form to indicate their decision (similar to Appendix 5.8).

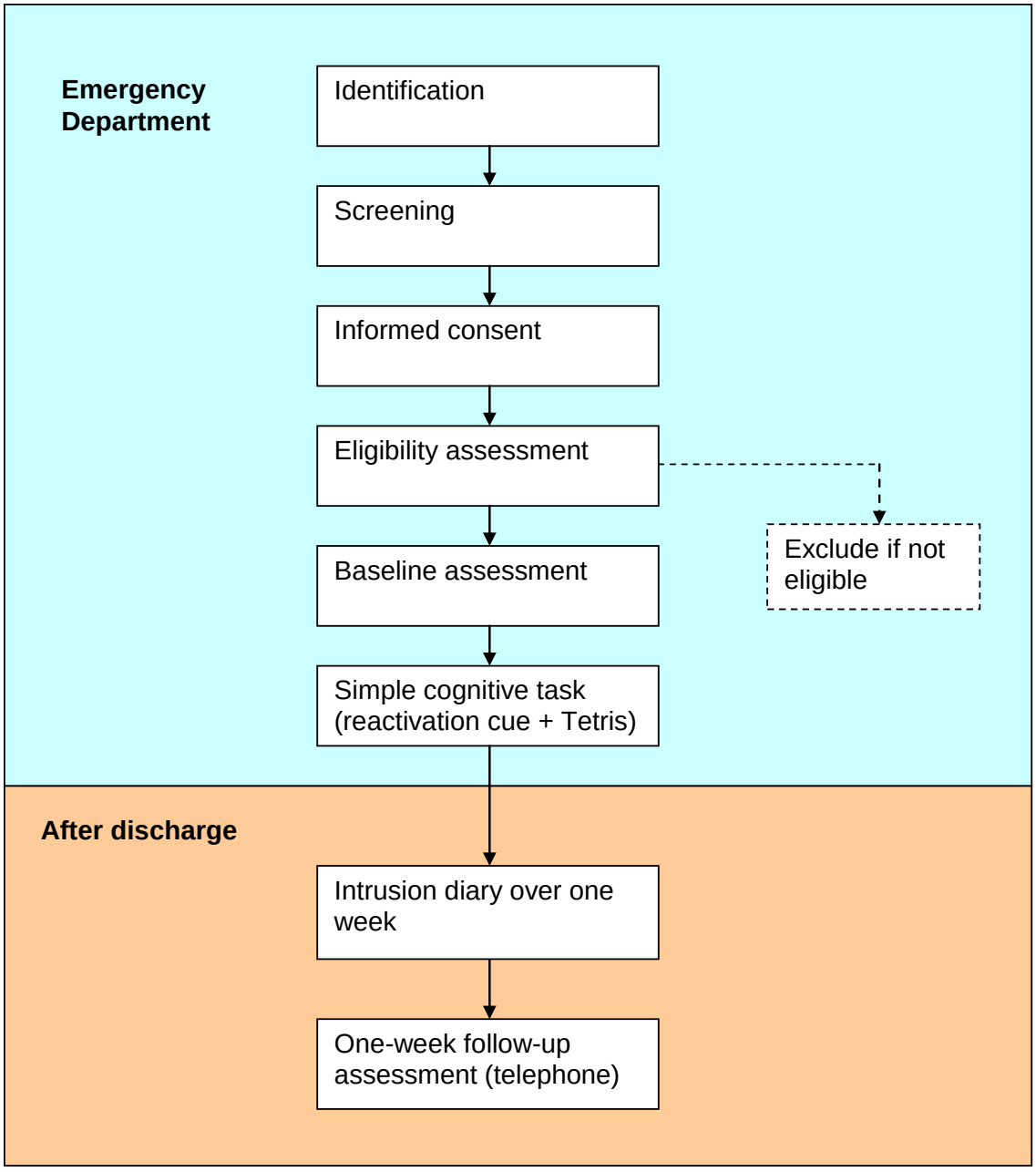


Figure 3.2. Diagram of the procedure for the first feasibility and piloting study.

Eligibility assessment. Participants were then asked a series of questions to assess the remaining eligibility criteria, such as whether they reported current mania, psychotic symptoms, substance abuse or a neurological condition. Participants who no longer met eligibility criteria were excluded from the study.

Baseline assessment. Eligible participants completed the baseline measures in their own time. The researcher was present to assist them with any queries. The researcher recorded additional baseline information from participants' medical notes.

Simple cognitive task intervention. All participants were asked to complete the simple cognitive task intervention. Participants were asked to close their eyes and picture the worst moments of the accident for 30 seconds (a cue designed to reactivate visual memories of the accident, as used in Santa Maria et al., 2012). The researcher then demonstrated how to play the computer game Tetris, and participants were given a chance to practice (up to a maximum of 3 minutes), until they understood how to play the game. Participants were then asked to play Tetris for at least 10 minutes, but for as long as they wished. The researcher timed the duration of play using a stopwatch, and told participants when 10 minutes had elapsed. If the participant needed to be seen by a professional during the 10-minute period, they were required to complete a further 10 minutes once they had been seen. Immediately after playing Tetris, participants were asked to complete the Tetris feedback questionnaire.

Intrusion diary. Finally, participants were given instructions on how to fill in the intrusion diary over the next week. A time was arranged to contact them in a week's time.

One-week follow-up assessment. After one week, participants were contacted by telephone to complete the intrusion diary feedback questionnaire. Participants were asked to post their intrusion diary back in the stamped addressed envelope provided. They were then debriefed about the study and had the chance to ask any questions. If the diary was not received after a few days, the researcher contacted the participants again to remind them to post it back.

Results

Participant baseline characteristics

Table 3.2 shows baseline characteristics of the sample of patients presenting to the John Radcliffe Hospital ED after a road traffic accident.

Table 3.2. Baseline Characteristics of the Sample (N = 10)

Baseline variable	*n*
Type of vehicle	
Car/Van	9
Bicycle	1
Role in accident	
Driver	8
Passenger	1
Current mental health problem	2
Previous mental health problem	1
Family history of mental health problem	2
Prior trauma	8
Analgesic medication administered after the accident	6
Loss of consciousness during accident	1
Post-traumatic amnesia	1
	M (*SD*)
Perceived life threat (*n* = 9)	
Self (0 – 10)	6.33 (3.04)
Other (0 – 10)	4.44 (3.71)
State Dissociation Questionnaire score (*n* = 9)	1.58 (0.85)
Peritraumatic Distress Inventory score (*n* = 9)	22.8 (15.4)
Number of hotspots of the accident	1.70 (0.82)
Duration of activities in the ED (mins)	
Talking to people (staff, family, friends) (*n* = 9)	41.67 (21.21)
Undergoing investigations or treatment e.g. scans	20.50 (16.06)
Other visuospatial activities e.g. texting, puzzles	0.00 (0.00)
Sleeping (*n* = 1)	180.00
Length of loss of consciousness in mins (*n* = 1)	10.00
Length of post-traumatic amnesia in mins (*n* = 1)	50.00

Only one participant lost consciousness during the accident, for 10 minutes. This participant reported post-traumatic amnesia of 50 minutes, and was unable to recall any details of the accident itself. The implications of this are raised in the discussion.

Aim 1: Recruiting road traffic accident patients in the ED

1. What is the rate of recruiting participants to the study?

Ten participants were recruited to the study over a period of 12 weeks of active recruitment, indicating a recruitment rate of just under one participant (a mean of 0.83) per week. Figure 3.3 shows a recruitment flowchart for the study.

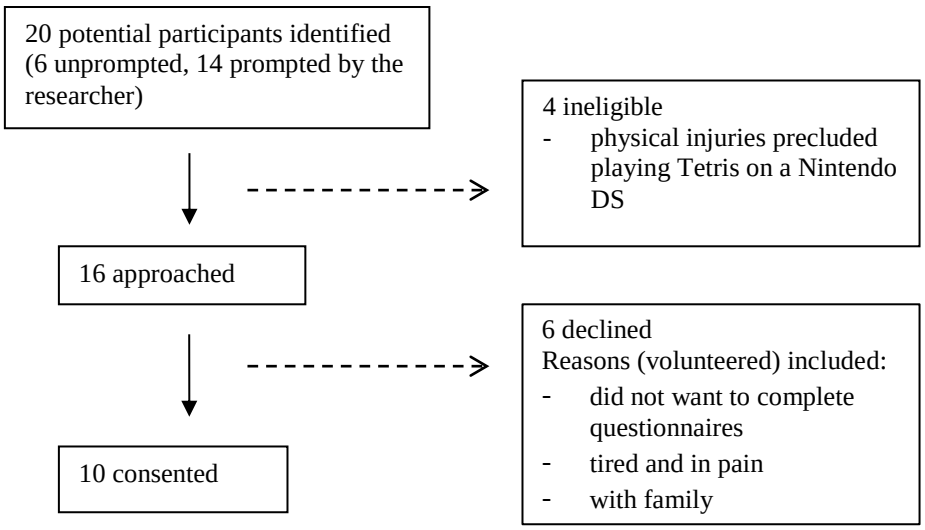


Figure 3.3. Recruitment flowchart for the first feasibility and piloting study.

a) How many potential participants were identified per week? During the hours in which the researcher was available to approach participants, 20 potential participants were identified over a 12-week period. This suggests that a mean of 1.67 potential participants were identified per week.

b) What proportion of participants approached about the study consented to take part? Of the 20 potential participants identified, it became immediately apparent that 4 would be ineligible to take part due to physical injuries that rendered them unable to play Tetris on a Nintendo DS. Therefore, whilst they met the screening criteria, these four patients were not approached about the study. The implications of this for the screening criteria are raised in the discussion. Of the 16 participants approached about the study, 10 (62.5%) consented to take part.

Aim 2: Delivering the simple cognitive task intervention

1. What proportion of patients presenting to the ED after a road traffic accident are willing to complete the simple cognitive task (picturing the accident for 30 seconds followed by playing Tetris for at least 10 minutes)?

The recruitment flowchart (Figure 2) shows that 10 out of 16 (62.5%) patients who were approached about the study consented to take part, indicating that they were willing to complete the simple cognitive task i.e. willing to close their eyes and picture the accident for 30 seconds followed by completing a computer task for 10 at least 10 minutes). These 10 patients comprised the final recruited sample. Of those who declined to take part, reasons volunteered by patients included not wanting to fill in questionnaires, being tired and in pain, and being with family.

2. What proportion of participants are able to complete the simple cognitive task (picturing the accident for 30 seconds followed by playing Tetris on a hand-held gaming device for at least 10 minutes)?

Figure 3.4 shows a flowchart of the number of participants able to complete the simple cognitive task intervention. 70% of the participants who were willing to complete the simple cognitive task intervention were actually able to complete the simple cognitive task *as instructed* (i.e. pictured the accident for 30 seconds followed by playing Tetris for at least 10 minutes). All participants who were unable to complete the simple cognitive task as instructed were immobilised (lying down and unable to move their head) at the point of taking informed consent. All were initially included in the study following liaison with ED staff indicating that they would gain mobility after undergoing a scan. One of the participants who was immobilised was still able to complete the cognitive task, but was only able to play Tetris for 8 minutes 53 seconds, after which time they requested to stop because their arms were tired. Of note, all eight participants who were given the simple cognitive task intervention were able to complete the memory reactivation cue (closing their eyes and picturing the worst moments of the accident for 30 seconds). The mean duration of playing Tetris was 13.75 minutes (SD 3.06). The minimum length of time was 8 minutes 53 and the maximum was 18 minutes. After this time, participants stopped playing Tetris for a number of reasons, including being discharged from the ED, being tired or in pain, being interrupted by a member of staff, and being bored of the game.

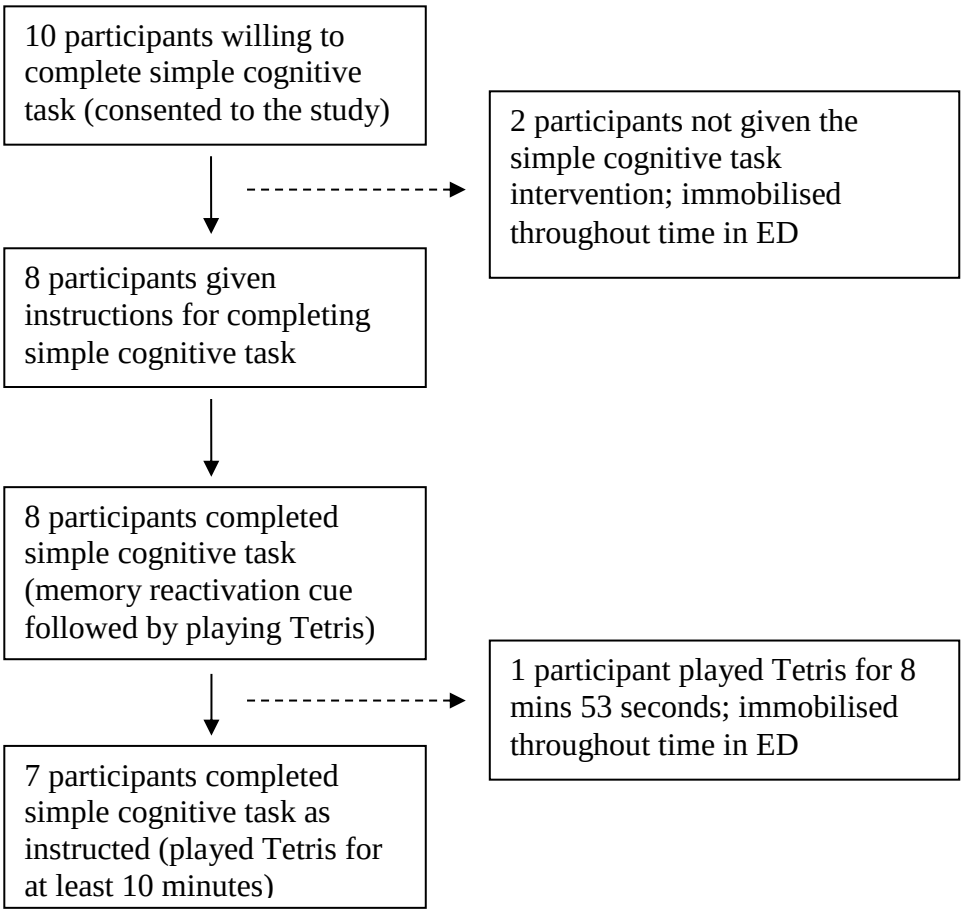


Figure 3.4. Number of participants able to complete the simple cognitive task intervention.

3. What is the maximum length of time participants report they would be willing to play Tetris for, assessed using a simple feedback questionnaire?

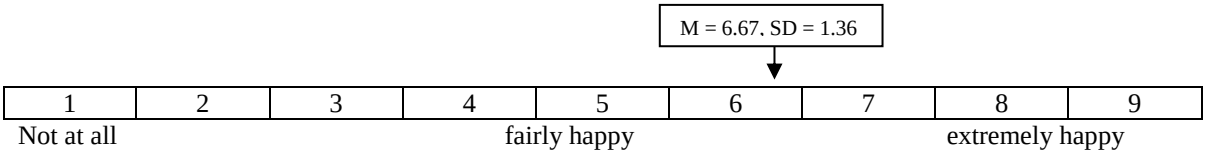
The eight participants who were able to play Tetris reported a mean duration of 32.5 minutes (SD 19.8) for the maximum length of time for which they would have been able to play Tetris. Exact responses were as follows (in minutes, from lowest to highest): 10, 10, 20, 30, 30, 30 in one go but 60 altogether, 40, 60. One of the participants who responded 10 minutes was the participant who was immobilised, who reported verbally that they would have been able to play Tetris for longer if they were mobile. Only two out of eight participants responded that they would have been able to play Tetris for as long as an hour.

4. What is participants' experience of playing Tetris in the ED, as assessed using a simple feedback questionnaire?

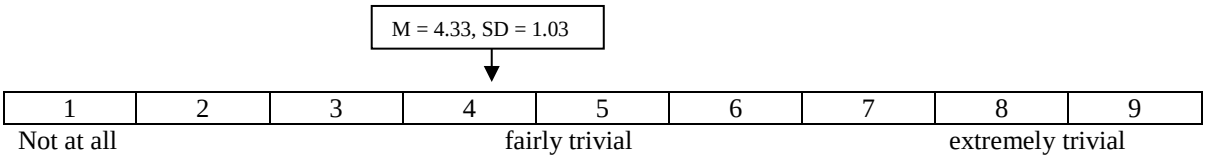
Figure 3.5 shows means and standard deviations of participants' ratings on the feedback questionnaire regarding their experience of playing Tetris in the ED. Results are shown for the eight participants who played Tetris. Ratings indicate that overall participants were happy to be offered something to do whilst waiting in the ED, and found playing Tetris fairly enjoyable and minimally distressing.

Table 3.3 shows participants' verbatim responses to open questions in the feedback questionnaire regarding their experience of playing Tetris. Responses are shown for the eight participants who played Tetris. Responses indicate that the main perceived benefit was that it gave participants a distraction in the ED. However, potential difficulties were raised, such as being in pain and being in a noisy or busy environment. Improvements were suggested, such as using a bigger screen and being in a more comfortable position.

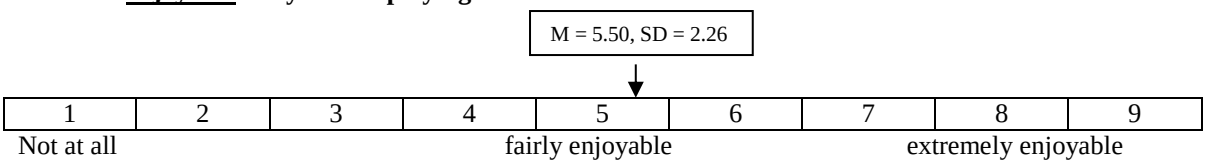
1. How happy were you to be offered something to do whilst waiting?



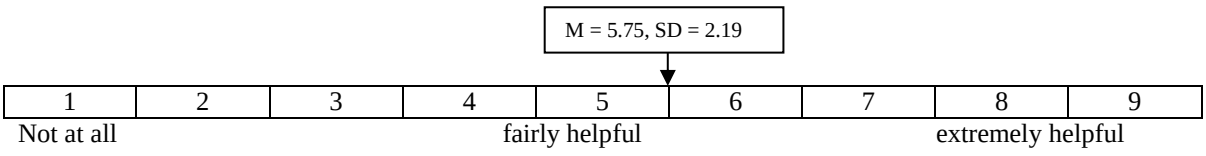
2. How trivial did you find it being asked to play Tetris?



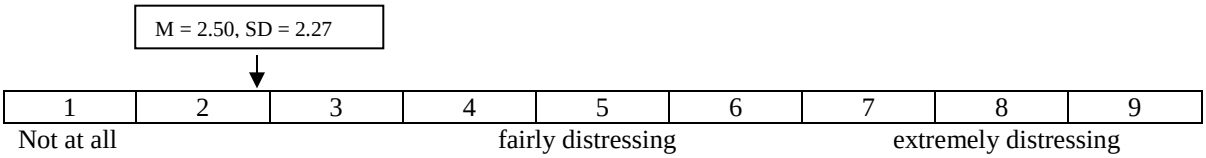
3. How <u>enjoyable</u> did you find playing Tetris?



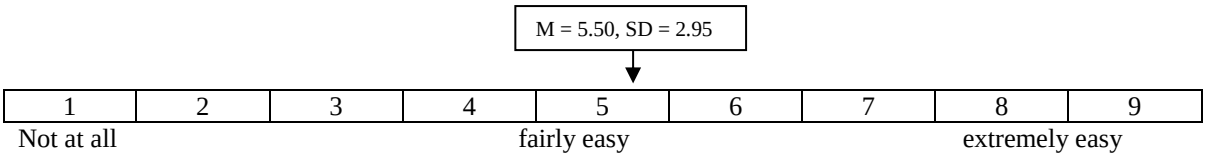
4. How <u>helpful</u> did you find playing Tetris?



5. How <u>distressing</u> did you find playing Tetris?



6. How <u>easy</u> did you find playing Tetris?



7. How <u>easy</u> did you find it <u>to concentrate</u> on playing Tetris?

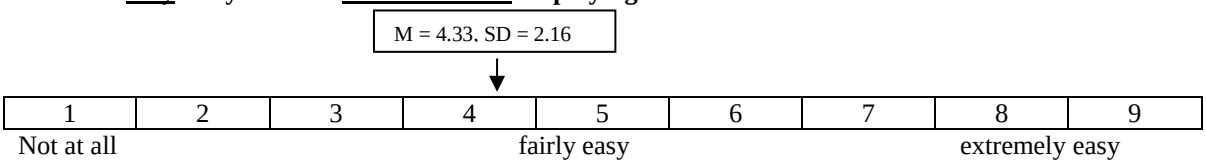


Figure 3.5. Means and standard deviations of participant ratings on the Tetris feedback questionnaire.

Table 3.3. Participant Responses to Open Questions on the Tetris Feedback Questionnaire for Participants Who Played Tetris (N = 8)

Feedback questionnaire item	Verbatim responses
What was positive about playing Tetris? (*n* = 7)	"You need someone to talk to, you've got a lot on your mind" "It was easy, kept me busy for a while" "Takes your mind off it" "Having something to do while I wait" "It was distracting and helped spend time" "Helped me think" "Takes your mind off what's happened"
What was difficult about playing Tetris? (*n* = 6)	"Not difficult" "I'd had an accident" "In pain physically" "None once I knew how. Could be annoying if the doctor/nurse kept coming in every 5 minutes" "Eyes were flickering from the anaesthesia"
What would improve your experience of playing Tetris? (*n* = 5)	"No" "If no injuries, could have played for 1 hour. Should play Donkey Kong or other computer games, something with a bit of humour" "Bigger screen" "The bed position could be more comfortable if the bed was bent towards a seated position" "No"
Any other comments? (*n* = 2)	"Unsure how Tetris could be played if it was rather noisy or busy in the ward" "Headphones to block out the noise might have helped"

Aim 3: Measuring the primary outcome using a pen-and-paper intrusion diary

1. What proportion of participants complete and return the intrusion diary in the week after the accident?

The first eight participants were given the intrusion diary as described in the method section to complete over the following week. Of these eight participants, one was lost to follow-up (i.e. could not be contacted after leaving the ED), four participants (50%) reported at the one-week follow up telephone call that they had filled the diary in, but none of the participants (0%) returned the diary in the post. Difficulties reported by participants

with filling in the diary are described in the next section. As a result of the poor completion rate, the final two participants were given an amended version of the diary and delivery method.

2. What is participants' experience of completing the intrusion diary in the week after the accident, assessed using a simple feedback questionnaire?

Figure 3.5 shows means and standard deviations of participants' ratings on the telephone-administered feedback questionnaire for the first eight participants, regarding their experience of filling in the intrusion diary in the week after the accident. Item 1 was rated by all seven participants who were contacted at one week follow-up, whilst items 2, 3, and 4 were only rated by the four participants who reported filling in the diary.

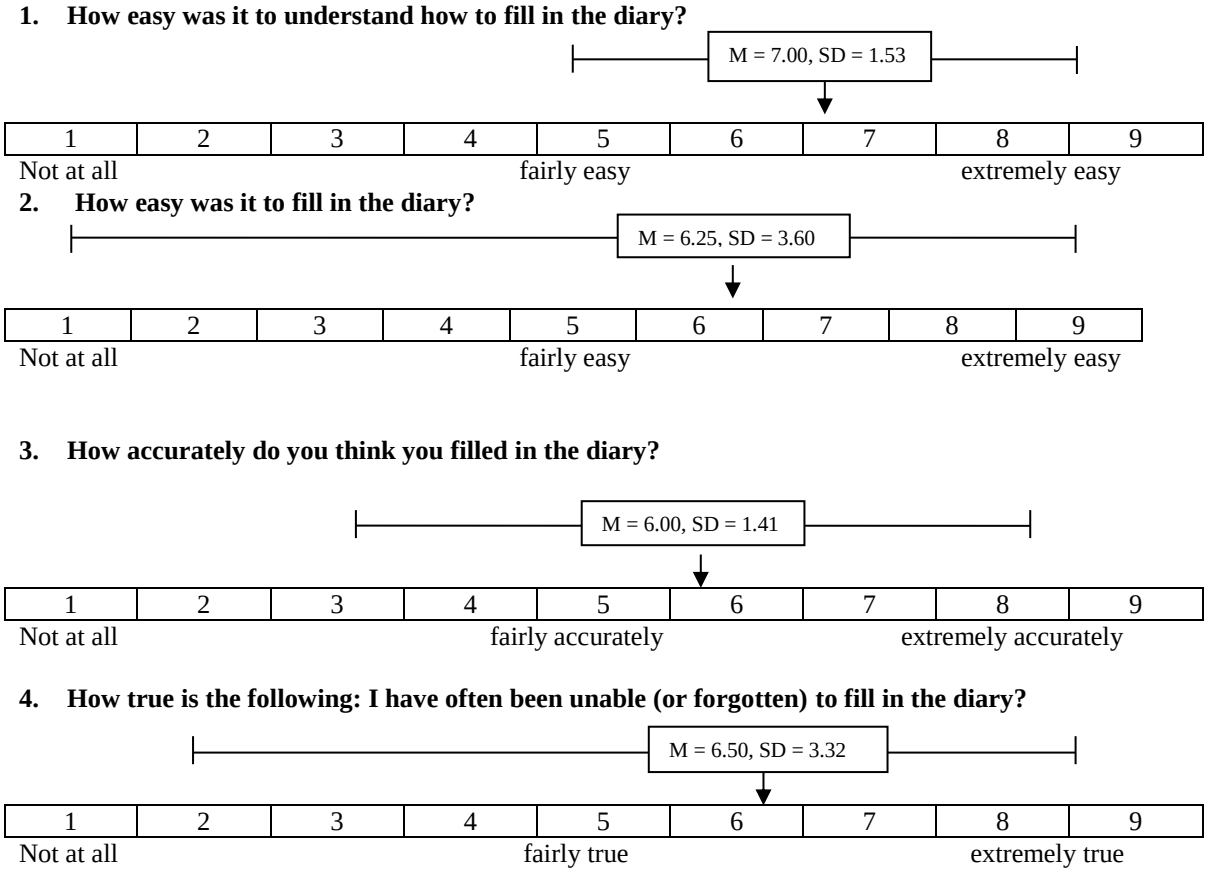


Figure 3.6. Means, standard deviations and ranges (shown by the horizontal lines) of participant ratings on the intrusion diary feedback questionnaire.

Table 3.4 shows participants' verbatim responses to open questions in the feedback questionnaire regarding their experience of filling in the intrusion diary. Responses are shown for the first eight participants in the study, seven of whom were contacted at one week follow-up.

Table 3.4. Participant Responses to Open Questions on the Intrusion Diary Feedback Questionnaire for the First Eight Participants (N = 7)

Feedback questionnaire item	Verbatim responses
What was positive about filling in the diary? (*n* = 5)	"It helps me to recover and understand that life is good, feel blessed that I'm still alive and given a second chance. Although that accident give me a very traumatic memory and experience." "If you write it down you can forget about it" "Makes you aware of what you're going through - not that helpful now, but might be 6 months down the line" "To think back and look back" "If it helps other people"
What was difficult about filling in the diary? (*n* = 6)	"Too much going on e.g. GP appointments. Don't want to write it down, don't want to think about it" "I feel upset most of the time whenever the flashback comes to my mind. I thought it's just all a dream." "Remembering the detail" "Reminder of what you've gone through - bad enough having the intrusion and then it's having to remember to write it down" "Nothing" "Nothing"
What would improve your experience of filling in the diary or make it easier? (*n* = 6)	"Use email" "Mark it on a mobile phone" "Maybe just mark a tick box (rather than write the content). Having a piece of paper reminds you you've got to do it." "Nothing" "Nothing"

Participants' ratings (Figure 3.6) and verbatim responses (Table 3.4) on the feedback questionnaire indicated that their experience of filling in the intrusion diary varied considerably. The implications of this are discussed later.

In the light of the results from the first eight participants in this study, the intrusion diary and the way in which it was delivered was amended before it was delivered to the last two participants. The following amendments were made, based on the results of the feedback questionnaire from the first eight participants: 1) the format of the diary was simplified so that participants only had to put a tick in a box for each intrusion they had, and a brief (one to two word) description of the content of the intrusion; 2) the researcher spent more time in the ED helping the participant to think through when and how they would complete the diary, and additionally sent reminders to complete the diary by text or email over the following week.

The results of the last two participants, who were given the amended intrusion diary and delivery method, are presented below.

1. What proportion of participants complete the intrusion diary in the week after the accident?

One of the two participants completed and returned the diary in the post (50%). The other participant was lost to follow-up (did not respond to contact by telephone, email or post). Table 3.5 shows a comparison of the completion rate for the two versions of the intrusion diary.

Table 3.5. Completion Rates of the Original and Amended Versions of the Intrusion Diary (N = 10)

	Original intrusion diary (*n* = 8; 1 lost to follow-up)	Amended intrusion diary (*n* = 2; 1 lost to follow-up)
Reported filling in diary	4 / 8 (50%)	1 / 2 (50%)
Diary received in post	0 / 8 (0%)	1 / 2 (50%)

2. What is participants' experience of completing the intrusion diary in the week after the accident, assessed using a simple feedback questionnaire?

For the participant who was successfully followed up after one week, their responses on the feedback questionnaire are shown in Table 3.6.

Table 3.6. Participant Response to Open Questions on the Intrusion Diary Feedback Questionnaire for the Last Two Participants (N = 1)

Feedback questionnaire item	Rating 0-10
How easy was it to understand how to fill in the diary?	9
How easy was it to fill in the diary?	9
How accurately did you think you filled in the diary?	9
How true is the following: I have been unable (or forgotten) to fill in diary	1
	Verbatim response
What was positive about filling in the diary?	"If it helps other people"
What was difficult about filling in the diary?	"Nothing"
Improvement suggestions	"Nothing"

Discussion

The aim of this first feasibility and piloting study was to test the practical implementation of key procedures for the randomised controlled study, namely: 1) recruiting road traffic accident patients in the ED, 2) delivering the simple cognitive task intervention (a memory reactivation cue followed by playing Tetris) and 3) measuring outcome using a pen-and-paper intrusion diary. General results and the results for each aim are discussed below.

Baseline assessment

Nine out of 10 participants completed all the baseline measures, suggesting that in general baseline assessment was well tolerated. The baseline assessment for the participant who did not complete all the measures was interrupted on numerous occasions by staff and family, and by the time there was an opportunity to complete the assessment the participant reported feeling too tired, but agreed to be given instructions on completing the intrusion diary.

Compared to a previous study assessing peri-traumatic distress in the immediate aftermath of a road traffic accident, the current sample appeared to have a relatively high level of peri-traumatic distress. Nishi et al. (2010) reported a median PDI score of 15.0, and a subsequent diagnosis of PTSD in 7.8% of participants after one month and 21.1% of participants after two months. In the current study, the mean PDI score was 22.8 (SD 15.4) for the sample, suggesting we might expect higher rates of PTSD than found in the study by Nishi et al. (2010).

Only one participant in the sample lost consciousness during the accident for 10 minutes, and had subsequent post-traumatic amnesia of 50 minutes. This participant was unable to recall any details of the accident itself. Whilst this participant met the eligibility criteria, their lack of memory of the accident raised concerns given that the primary outcome for the randomised controlled study is the number of intrusions of the accident. Whilst it is possible for patients with PTA following a trauma to develop later PTSD (King, 1997), longer periods of PTA are associated with fewer re-experiencing symptoms (Bryant, Creamer, O'Donnell, Silove, Clark, et al., 2009). In light of this, the eligibility criteria were subsequently amended to exclude patients with no memory of the accident, and the maximum period of loss of consciousness will be changed from 30 minutes to 5 minutes, in line with a recently published trial of an early psychological intervention after trauma delivered in an ED (Rothbaum et al., 2012).

Aim 1: Recruiting road traffic accident patients in the ED

1. What is the rate of recruiting participants to the study?

The recruitment rate for this study was just under one participant per week. This was in line with an initial estimate of the recruitment rate based on examining a database of patients presenting to the ED over a one-month period. On average, 1.67 potential participants were identified per week, which is slightly lower than the estimate of two to three potential participants, based on an examination of an ED patient database. However, the consent rate of 62.5% was higher than the initial estimate of 40%, taken from a previous prospective study recruiting road traffic accident patients from the John Radcliffe Hospital ED (Murray et al., 2002).

The recruitment procedure used in this study may not have been optimal. The lower-than-estimated rate of identifying potential participants suggests that some potential participants were being missed. Further, the researcher was not based in the ED, and relied on ED staff contacting her by telephone if a potential participant presented to the ED between 8am and 8pm Monday to Friday. Six out of 20 potential participants were approached following an unprompted telephone call from ED staff. The other 14 potential participants were identified when the researcher prompted staff by calling in or visiting the ED. This suggests that ED staff did not consistently contact the researcher when a potential participant presented. Therefore, this recruitment strategy may not offer an accurate picture of the potential recruitment rate for the randomised controlled study.

A more accurate indication of the potential for recruitment might be gained if the researcher was present in the ED themselves for as much time as possible, to check regularly with staff for the arrival any potential participants. Further, patients could be offered the opportunity of opting in to the study themselves, by advertising the study in the ED waiting room. In the light of this, an amended recruitment strategy was implemented in the next stage of this research, which is a pilot study in the emergency department. The researcher aimed to be present in the ED themselves for at least 80% of the time between 9am and 5pm from Monday to Friday. The rationale was that this would offer a more accurate indication of the number of potential participants presenting to the ED during these times. Further, an advertisement for the study was put up in the ED waiting room, with contact details for the researcher. An amendment to the ethical approval of the study was submitted with this change.

Aim 2: Delivering the simple cognitive task intervention

1. What proportion of patients presenting to the ED after a road traffic accident are willing to complete the simple cognitive task (picturing the accident for 30 seconds followed by playing Tetris for at least 10 minutes)?

As described in Aim 1, 62.5% of participants approached about the study consented to take part, indicating that they were willing to complete the simple cognitive task intervention i.e. that they were willing to close their eyes and picture the accident for 30 seconds, following by completing a computer task for 10 minutes. This consent rate is higher than the initial estimate of 40%, taken from a previous prospective study recruiting road traffic accident patients from the John Radcliffe Hospital ED (Murray et al., 2002). Further, it is considerably higher than the 10.9% consent rate found in a recent trial of an early intervention after trauma, commenced in the ED (Rothbaum et al., 2012). In the current study, of the eligible participants who declined taking part, none voluntarily reported that the reason was because they were not willing to complete the simple cognitive task intervention. However, potential participants were not explicitly asked about their willingness to complete the simple cognitive task as this did not fall under the ethical approval for the study. One participant did report that they were unwilling to fill in questionnaires, suggesting that their reason for declining was related to the study procedure, but not the simple cognitive task specifically. Taken together, these results tentatively suggest that the simple cognitive task does not discourage participants from

taking part in the study, and that the intervention is considered acceptable at the point of taking consent. However, one limitation was that potential participants were not explicitly asked about their willingness to complete the simple cognitive task.

2. What proportion of participants are able to complete the simple cognitive task (picturing the accident for 30 seconds followed by playing Tetris on a hand-held gaming device for at least 10 minutes)?

Seventy percent of the participants were able to complete the cognitive task as instructed, which included playing Tetris for a minimum of 10 minutes. All three participants who were not able to complete the task as instructed were strapped lying down on a board at the point of taking consent, on the assumption that they would become mobile following a scan. However, by the time one participant gained mobility they no longer wanted to continue with the study, and the other two remained lying down throughout their time in the ED. One of these participants was able to complete the reactivation cue followed by playing Tetris, but for less than 10 minutes due to their arms getting tired. This suggests that the main barrier to participants completing the simple cognitive task was their physical mobility. The proportion of participants able to complete the intervention might be increased by ensuring that all potential participants have sufficient physical mobility to play Tetris on a hand-held gaming device at the point of taking informed consent, for example that they are able to sit upright and have use of both their arms. This amendment was will be made to the screening criteria for the next stage of the research, as discussed in the earlier section on recruitment.

Of the eight participants given instructions on completing the simple cognitive task, all were able to successfully complete the memory reactivation cue (closing their eyes and picturing the accident for 30 seconds). This suggests that participants do not find the memory reactivation cue too distressing to complete.

3. What is the maximum length of time participants report they would be willing to play Tetris for, assessed using a simple feedback questionnaire?

Participants reported a mean maximum duration of 32.5 minutes. Only two out of eight participants reported they would be willing to play Tetris for a maximum duration of 10 minutes, one of whom reported verbally that it would have been longer if they were not immobilised. The rest reported they would be willing to play Tetris for 20 minutes or

longer. This suggests that the "dose" of the simple cognitive task might feasibly be increased from a minimum of 10 minutes to a minimum of 20 minutes. A duration of 20 minutes was therefore chosen to be used in the next stage of the research (with a break allowed after 10 minutes). Only two out of 10 participants reported that they would be able to play Tetris for as long as an hour. This indicated that, whilst spontaneous anecdotal reports from people who had played Tetris following stressful experiences suggested that an hour of play might have a therapeutic effect (see Chapter 2), for patients in an ED who have had a road traffic accident, an hour might not be an acceptable length of time to play Tetris.

4. What is participants' experience of playing Tetris in the ED, assessed using a simple feedback questionnaire?

Overall, participants' responses on a feedback questionnaire regarding their experiencing of playing Tetris were encouraging. On average, participants were happy to be offered something to do whilst waiting in the ED. Whilst participants found being asked to play Tetris fairly trivial, they also found playing Tetris fairly enjoyable, helpful and easy, and, importantly, minimally distressing. Open questions in the feedback questionnaire were designed to indicate how the experience of playing Tetris might be improved. Within participants' responses were a number of issues or improvement suggestions that could be feasibly addressed. These were:

1) Potential difficulty playing Tetris if there were distractions on the ward (such as noise or being seen by staff)
2) Being in an uncomfortable seating position
3) Using a bigger screen for playing Tetris.

In response to these comments, the following amendments might improve participants' experience of playing Tetris in the ED.

1) Offer participants the option of using ear protectors to block out noise and distractions in the ED.
2) Ensure participants are as physically comfortable as they can be before they play Tetris, e.g. by asking if they would like to make any changes to their position to make them more comfortable. Allow participants a break after they have played Tetris for 10 minutes, in case they are in pain or uncomfortable.
3) Use a gaming device with a slightly larger screen.

These amendments were implemented in the next stage of the research.

A few of the comments made by participants were not open to feasible amendment, namely using a different computer game such as Donkey Kong (which has not been tested as an intervention to reduce intrusions post-trauma), and being in pain and having a flickering eye due to anaesthesia. Whilst it was not possible to directly address the latter two comments within the study procedure, it may help to ensure participants are as comfortable as they can be before they start playing Tetris, and to allow them a break after 10 minutes of playing Tetris, to help alleviate any pain or discomfort.

Aim 3: Measuring the primary outcome using a pen-and-paper intrusion diary

1. What proportion of participants complete and return the intrusion diary in the week after the accident?

These results presented the greatest challenge. For the first eight participants who were given the intrusion diary in the ED, the results of this study indicated that 50% of participants reported completing their intrusion diary in the week after the accident, but 0% of participants returned their diary in the post. A limitation to the procedure used in this study was that the researcher only contacted participants once more to remind them to post back their diaries, and did not ask if there was any difficulty with returning the diary or what might be helpful. However, the following are suggested reasons that may account for why none of the participants who reported completing their diary returned it in the post. First, they may not have fully completed the diary, or may have lost the diary or stamped addressed envelope, and felt too worried to tell this to the researcher over the telephone. Second, they may have found it hard to find the time or means to post the diary, or forgotten to post it. To address these possible limitations, it was decided to introduce a number of refinements to the procedure in the subsequent feasibility and piloting study to try to improve rates of returning the diary in the post.

1) Participants would be offered extra support e.g. thinking through when to fill it the diary and where to keep it, being reassured that it may not be easy to fill in the diary, so they would feel able to tell the researcher if any problems arose, such as losing the diary or envelope. They would also be contacted by phone the day after the accident to check that they were still happy with what they have been asked to do, and to help solve any problems such as losing the diary, or not understanding the instructions.

2) Participants would be offered the option of the researcher coming to pick up the diary from them.

The return rate may also have been affected by difficulties with completing the intrusion diary. Even if all participants who reported completing the diary returned it, the completion rate for the first eight participants would still only have been 53.7%. This does not meet the 86% completion rate required for the estimated sample size for the randomised controlled study to have sufficient power to detect a treatment effect. This indicates that in the form in which it was delivered in this study, the pen-and-paper intrusion diary would not be suitable as the primary outcome measure. Therefore, either the intrusion diary and/or the way in which it is delivered would need to be amended to improve the completion rate, or an alternative measure would need to be selected as the primary outcome measure for the randomised controlled study.

The intrusion diary was initially selected as the primary outcome measure to parallel the procedure used in previous laboratory studies as closely as possible. In the light of this, the next logical step would be to try and improve completion rates of the intrusion diary by amending the way in which it is delivered. If this is unsuccessful, then an alternative primary outcome measure may need to be selected from those included in the study protocol, such as the Intrusion Interview (Hackmann et al., 2004), Impact of Events Scale-Revised (Weiss & Marmer, 1997), or Clinician-Administered PTSD Scale (Blake et al., 1995). Participants' responses on the feedback questionnaire regarding their experience of completing the intrusion diary provided clues as to how the intrusion diary might be amended to improve completion rates (see below).

2. What is participants' experience of completing the intrusion diary in the week after the accident, assessed using a simple feedback questionnaire?

The first eight participants' responses on a feedback questionnaire regarding their experience of filling in the intrusion diary indicated that their experience varied a great deal. All participants rated it to be "fairly easy" to "extremely easy" to understand how to fill in the diary, suggesting that the instructions were clear. However, participants' ratings of how easy they found it to fill in the diary in practice ranged from "not at all" to "extremely", suggesting that amendments would need to be made to make sure all participants found the diary easy to fill in. Further, participants' ratings suggested that their accuracy of filling in the diary varied considerably.

Responses to open questions regarding what participants found positive or difficult about filling in the diary, and what might improve their experience of filling in the diary, pointed to a number of refinements that might improve participants' completion of the diary, as described below.

It is worth noting that two participants reported a beneficial effect of filling in the diary. One participant reported that writing down their intrusions helped to forget about them, and another reported that it made them aware of what they were going through, which might be helpful in the future. Interestingly, symptom monitoring in patients with PTSD has been associated with improvement of symptoms in studies with adults (Tarrier, Sommerfield, Reynolds, & Pilgrim, 1999) and children and young people (P. Smith et al., 2007). This may have implications for the main randomised controlled study, as the process of monitoring symptoms using the intrusion diary in the week after the accident may have a therapeutic effect, which could interact with the effect of the intervention. This issue was considered further in the next stage of the research.

Reported difficulties with filling in the diary came under the following themes: remembering to fill it in; remembering the details of the intrusions, finding time to fill it in, and not wanting to be reminded of/think about the accident. These difficulties pointed towards a number of refinements that might improve rates of completing the diary:

1) Being given a reminder at the end of every day to fill in the diary
2) Simplifying the diary, so that it takes less time to fill in
3) Minimising the amount of information that participants have to write down regarding the content of intrusions.

These refinements were implemented in the next feasibility and piloting study.

With regards to improvement suggestions, some participants suggested alternatives as to how they would have liked to record their intrusions, including using email, text, and mobile phone technology. However, given that this research was a first step in translating the laboratory procedure to a clinical setting, it was considered important to parallel the laboratory procedure as closely as possible to minimise the effect of confounding factors that might account for any difference in the results. Therefore, the pen-and-paper diary was considered the optimal method of assessing intrusions at this stage, incorporating the above refinements. However, participants' comments suggest that it may help to offer them support with filling the diary (e.g. reminders) using other media such as text or email. Therefore, the next study would include sending participants a text (or email, if preferred) at the end of every day to remind them to fill in their diary.

The amendments described here for aim 3 were implemented for the final two participants. One of the two participants (50%) completed and returned the diary, in comparison a return rate of 0% in the first eight participants. The other participant was entirely lost to follow-up. Responses on the feedback questionnaire of the participant who was followed up indicated that the amended diary was extremely easy to understand and fill in, and did not identify anything difficult about filling in the diary. Whilst it was not possible to draw any firm conclusions from such a small number, there was some suggestion that the amended diary and delivery method might offer an improvement over the original diary and delivery method in terms of the completion rate and participant experience. Therefore it was decided to continue with implementing these amendments in the pilot study.

Summary

In summary, this first feasibility and piloting study found a) a recruitment rate of just under one participant per week, b) that 62.5% of road traffic accident patients approached in the ED were willing to take part in the study and complete the simple cognitive task intervention, and c) that 70% of participants were able to complete the intervention for at least 10 minutes of Tetris play. Possible amendments to improve these procedures were brought to light, such as improving the recruitment strategy and refining the participant eligibility criteria. However, the completion rate of the pen-and-paper intrusion diary for the first eight participants was a clear problem (0% return rate). Participant feedback indicated a number of amendments that might help to improve the completion rate of the intrusion diary, which were implemented for the last two participants with encouraging results (50% return rate). The main amendments were to simplify the format of the intrusion diary and to send participants a daily reminder to fill it in. Therefore, before proceeding to the randomised controlled study, it was decided that these amendments should be implemented and evaluated in the next stage of the research: an additional second feasibility and piloting study in the emergency department.

CHAPTER 4. Feasibility and Piloting Study 2: Refining procedures for the randomised controlled study

Introduction and aims

A first feasibility and piloting study in the emergency department (Chapter 3) highlighted the need for further piloting before proceeding to the randomised controlled study. The results indicated that a number of issues needed addressing: a) a suboptimal recruitment rate of road traffic accident patients in the Emergency Department (just under one participant per week), b) inability of some participants to complete the simple cognitive task intervention (70% were able to complete the intervention for at least 10 minutes of Tetris play), c) a slightly higher drop-out rate than initially estimated (20% rather than 14%), and d) a serious drawback in the completion rate of the proposed primary outcome measure (0% return rate in the first eight participants). Therefore the first aim of this second feasibility and piloting study was to improve: a) the recruitment rate, b) the eligibility criteria, c) the drop-out rate, and d) the completion rate of the primary outcome measure. To achieve these aims, this study implemented a number of refinements to the eligibility criteria and study procedures, based on the results of the previous study, and tested them in a series of additional patients (n = 23).

Further, the first feasibility and piloting study only tested the procedure for the simple cognitive task intervention, and not for the control condition (usual care). Therefore this study tested the procedures for both conditions, and provided a preliminary comparison of outcome between the two. A final aim was to evaluate participants' overall experience of taking part in the study, to inform any additional improvements for the randomised controlled study.

As the overall aim of this pilot work was to improve the procedure for the randomised controlled study (see MRC framework diagram, Figure 3.1, Chapter 3), minor amendments were made during the course of the study based on accumulating observational data, outcome data, and participant feedback. These refinements are described in the section "Procedural changes made during the study".

Background and development

Aim 1: Improvements from Feasibility and Piloting Study 1

a) Recruitment rate

The previous feasibility and piloting study yielded a recruitment rate of just under one participant (a mean of 0.83) per week. However, the recruitment strategy may not have been optimal. The researcher contacted emergency department (ED) staff two to three times a day to check if any potential participants were present, and the rest of the time relied on ED staff to contact her by telephone when a potential participant presented. The results suggested that ED staff were not consistently able to call the researcher when a potential participant presented. Therefore, the recruitment strategy was amended, so that the researcher was present in the ED for at least 80% of the time between 9am and 5pm from Monday to Friday, to check regularly with ED staff for the arrival of potential participants. Further, advertisement posters were placed in the ED waiting room so that patients could contact the research team if they were interested in taking part in the study.

b) Eligibility criteria

In the previous study, two out of 10 participants were unable to play the computer game Tetris at all, and one participant was unable to play Tetris for the full 10 minutes, due to all three being immobilised (strapped lying down on a stretcher) throughout their time in the ED. To improve the suitability of recruited participants to complete the study procedures, an inclusion criterion was added to state that participants must have sufficient physical mobility to complete a computer game on a Nintendo DS at the point of taking informed consent (e.g. be able to sit up and have use of both arms).

Further, one participant in the previous study had post-traumatic amnesia of 50 minutes. This participant had no recollection of the accident, and described the worst moment as "trying to remember what happened when I got into hospital". This was qualitatively very different to other participants' worst moments (or "hotspots"; Holmes, Grey & Young, 2005), which related to the accident itself (e.g. "hurtling into the lorry in front", "being upside down"). Further, the participant had the lowest perceived life threat score (1 out of 10) in the sample. Given that homogeneity of the sample is important in an early-phase randomised controlled trial (Everitt & Wessely, 2008), the exclusion criterion

of "post-traumatic amnesia greater than one hour" was removed, and replaced with the inclusion criterion "report memory of the accident".

Following the start of the previous feasibility and piloting study, Rothbaum et al. (2012) published a trial of a modified prolonged exposure therapy to prevent post-traumatic stress disorder. This study is notable in that it is the only recent, relatively large trial (N = 137) of a preventative psychological intervention initiated within a hospital ED within a few hours of a trauma. Therefore other eligibility criteria were refined to bring them in line with Rothbaum et al., to allow potential comparison between the two studies. The exclusion criterion of "moderate to severe traumatic brain injury (TBI)", indicated by a) Glasgow Coma Scale score (GCS) of less than 13, b) loss of consciousness greater than 30 minutes, or c) post-traumatic amnesia (PTA) greater than one hour was changed to a) alert and oriented, GCS = 15, b) loss of consciousness greater than five minutes, and c) report memory of the accident (i.e. no PTA). Current intoxication and suicidality were added to the exclusion criteria.

c) Drop-out rate

In this study, drop-out was defined when no outcome data were obtained from a participant, and included loss to follow-up (i.e. no response from a participant to any form of contact from one week onwards). The previous feasibility and piloting study showed a drop-out rate of two out of 10 participants (20%) over one week. This was slightly higher than the estimated drop-out rate of 14%, based on a previous randomised controlled trial recruiting road traffic accident patients from the John Radcliffe Hospital ED (Hobbs et al., 1996).

A number of factors were hypothesised to affect drop-out in this research. First, participants who were unable to complete their intrusion diary might drop out if they felt they had not complied with the study instructions. To address this, participants in this study were given extra support in the ED with how to fill in their intrusion diary, and were telephoned the next day to check that they still understood the instructions and to answer any questions. Second, certain baseline characteristics might be associated with drop-out, such as injury severity or perceived life threat. Therefore, this study compared baseline variables between those who dropped out and those who stayed in the study to identify any relevant factors. Third, participants who dropped out might find aspects of the study burdensome or distressing. Therefore this study evaluated participants' experience of

taking part in the study, to identify any problematic aspects of the study that might be changed.

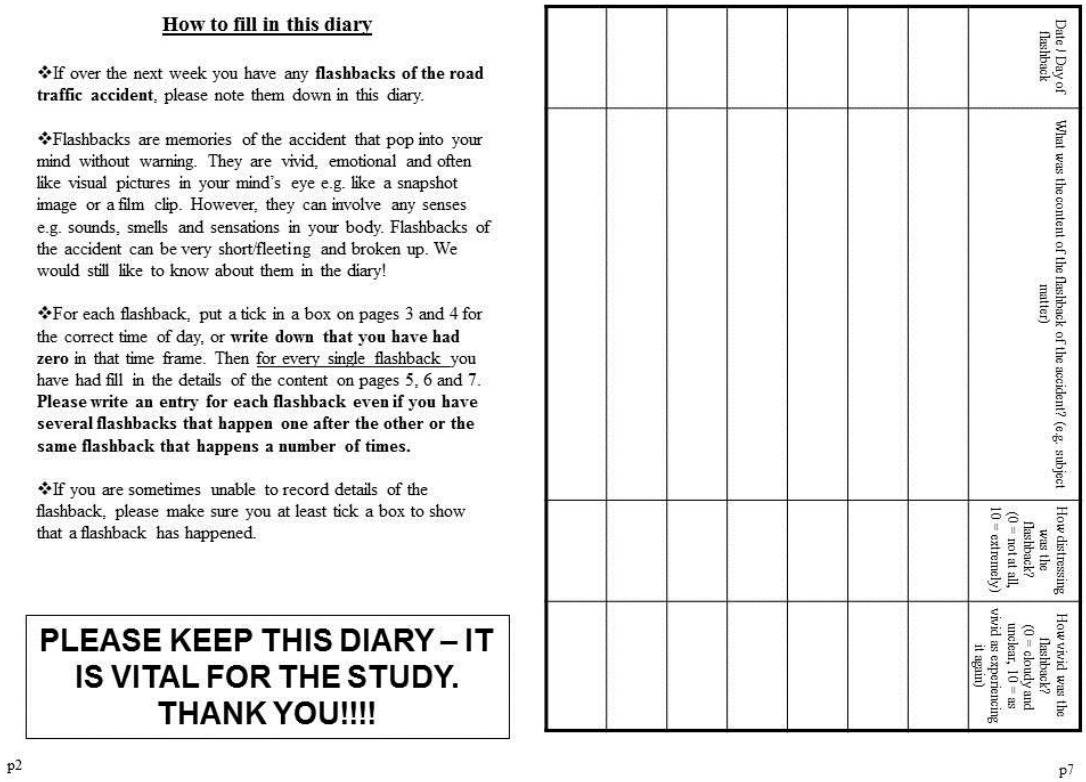
In the event that participant drop-out was associated with factors after participants left the ED (e.g. ongoing health problems, unpredictable circumstances over the next week), which could not be measured, the drop-out rate would be used to inform a new sample size calculation for the randomised controlled study.

d) Completion rate of the primary outcome measure

The main problem identified in the previous feasibility and piloting study was the completion rate of the pen-and-paper Intrusion Diary, filled in by participants in the week after the accident. Out of the first eight participants, four (50%) reported that they had filled in the diary, but none (0%) returned the diary in the post. This suggested that the diary itself, the way in which it was delivered, and/or the way in which participants were required to return the diary, were problematic. A number of amendments were implemented in this study, based on participant feedback from the previous study:

1) The diary format was simplified, so that participants had to put a tick in a box for each intrusion and write a brief description of the content, instead of filling in detailed information about the trigger, content, vividness and distress of each intrusion. Figure 4.1 shows excerpts from the previous and current versions of the Intrusion Diary.
2) Participants were provided with more support in the ED to ensure that they understood the diary instructions, and had thought about when they could fill it in each day and where they would keep it.
3) Participants were contacted by telephone the day after the accident to check that they still understood the instructions, and to help solve any problems such as losing the diary.
4) Participants were sent a daily text (or email if preferred) to remind them to fill in the diary if they had had any intrusions of the accident that day.
5) Participants were offered the option of the researcher picking up the diary in person after one week, instead of returning the diary in the post.

Version 1 of the Intrusion Diary used in feasibility and piloting study 1



How to fill in this diary

❖If over the next week you have any **flashbacks of the road traffic accident**, please note them down in this diary.

❖Flashbacks are memories of the accident that pop into your mind without warning. They are vivid, emotional and often like visual pictures in your mind's eye e.g. like a snapshot image or a film clip. However, they can involve any senses e.g. sounds, smells and sensations in your body. Flashbacks of the accident can be very short/fleeting and broken up. We would still like to know about them in the diary!

❖For each flashback, put a tick in a box on pages 3 and 4 for the correct time of day, or **write down that you have had zero** in that time frame. Then for every single flashback you have had fill in the details of the content on pages 5, 6 and 7. **Please write an entry for each flashback even if you have several flashbacks that happen one after the other or the same flashback that happens a number of times.**

❖If you are sometimes unable to record details of the flashback, please make sure you at least tick a box to show that a flashback has happened.

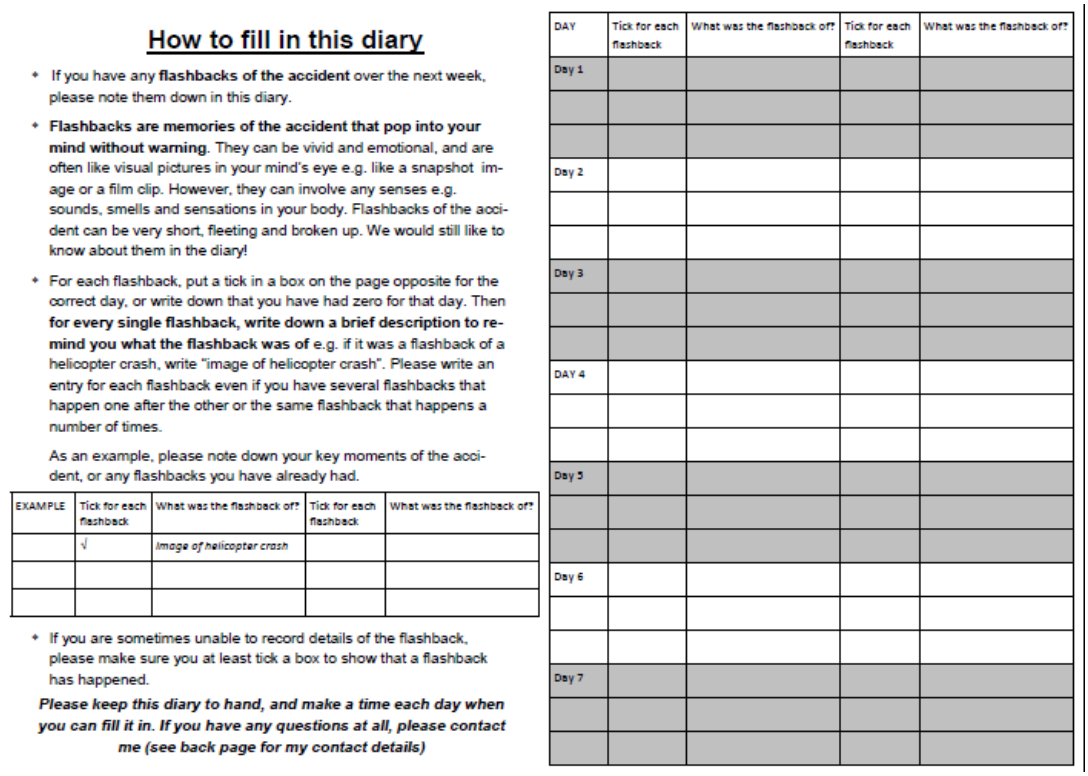
PLEASE KEEP THIS DIARY – IT IS VITAL FOR THE STUDY. THANK YOU!!!!

p2

Date / Day of flashback	What was the content of the flashback of the accident? (e.g. subject matter)	How distressing was the flashback? (0 = not it all, 10 = extremely)	How vivid was the flashback? (0 = cloudy and unclear, 10 = as vivid as experiencing it again)

p7

Version 2 of the Intrusion Diary used in feasibility and piloting study 2



How to fill in this diary

- If you have any **flashbacks of the accident** over the next week, please note them down in this diary.
- **Flashbacks are memories of the accident that pop into your mind without warning**. They can be vivid and emotional, and are often like visual pictures in your mind's eye e.g. like a snapshot image or a film clip. However, they can involve any senses e.g. sounds, smells and sensations in your body. Flashbacks of the accident can be very short, fleeting and broken up. We would still like to know about them in the diary!
- For each flashback, put a tick in a box on the page opposite for the correct day, or write down that you have had zero for that day. Then **for every single flashback, write down a brief description to remind you what the flashback was of** e.g. if it was a flashback of a helicopter crash, write "image of helicopter crash". Please write an entry for each flashback even if you have several flashbacks that happen one after the other or the same flashback that happens a number of times.

  As an example, please note down your key moments of the accident, or any flashbacks you have already had.

EXAMPLE	Tick for each flashback	What was the flashback of?	Tick for each flashback	What was the flashback of?
	√	*Image of helicopter crash*		

- If you are sometimes unable to record details of the flashback, please make sure you at least tick a box to show that a flashback has happened.

Please keep this diary to hand, and make a time each day when you can fill it in. If you have any questions at all, please contact me (see back page for my contact details)

DAY	Tick for each flashback	What was the flashback of?	Tick for each flashback	What was the flashback of?
Day 1				
Day 2				
Day 3				
DAY 4				
Day 5				
Day 6				
Day 7				

Figure 4.1. Excerpts from version 1 (used in the feasibility and piloting study 1) and version 2 (used in feasibility and piloting study 2) of the Intrusion Diary.

In the event that the completion rate of the Intrusion Diary remained low, this study also assessed the completion rate of a few additional outcome measures, which might offer suitable alternatives for the primary outcome measure. These measures had already been included as secondary outcome measures in the protocol, and included items or subscales that assessed intrusive memories in the week after the accident. The relevant items/subscales were:

1. Interview-based measures administered by telephone at one week:
    a) Intrusion Interview – number of intrusive memories over the last week
    b) Clinician-Administered PTSD Scale – Re-experiencing symptoms score
2. Self-report measures administered online or by post at one week:
    a) Intrusion Questionnaire – number of intrusive memories over the last week
    b) Impact of Events Scale-Revised – Intrusion subscale score

This study compared the Intrusion Diary to each of these alternative measures in relation to the completion rate and participant preference (for the diary, telephone assessment or online/postal assessment). These results would be used to select an alternative primary outcome measure if necessary.

Aim 2: Testing and refining the intervention and control procedures

The previous feasibility and piloting study only assessed the implementation of the intervention condition (a simple cognitive task procedure). Therefore this study tested the procedures for both the simple cognitive task intervention and the usual care control condition. Refinements were made during the course of the study based on observation and examination of the accumulating data. At the end the study, baseline and outcome data were examined to provide a preliminary comparison between the intervention and control groups.

Aim 3: Assessing participants' experience of the study

The final aim of this study was to assess participants' experience of taking part, using a feedback questionnaire. This was used to gain an indication of the acceptability of the study procedures and identify any further improvements for the randomised controlled study.

Method

Design

A quasi-experimental between-groups design was used in which participants were alternately allocated to one of two conditions: 1) a simple cognitive task (a memory reactivation cue followed by playing Tetris for approximately 20 minutes) or 2) usual care in the emergency department. Participants were followed up one week later to assess intrusive memories of the accident, post-traumatic stress symptoms and associated health outcomes (e.g. anxiety, depression and quality of life).

Participants

Participants were patients presenting to the John Radcliffe Hospital Emergency Department (ED) after a road traffic accident. The refined eligibility criteria were as follows.

Inclusion criteria

- Aged 18 or over
- Experienced or witnessed a road traffic accident (as a driver, passenger, motorcyclist, cyclist or pedestrian)
- Met the DSM-IV criterion A1 for PTSD ("experienced, witnessed, or confronted with actual or threatened death or serious injury)
- Can be seen in the ED within 6 hours of leaving the scene of the accident
- Report memory of the accident
- Alert and orientated, GCS = 15
- Fluent in written and spoken English
- Willing and able to provide informed consent and complete study procedures
- Willing and able to be contacted following discharge to complete follow-up assessments
- Have sufficient physical mobility to play a computer game on the intervention platform (a Nintendo DS) at the point of taking informed consent.

Exclusion criteria

- Loss of consciousness > 5 minutes
- Report a history of severe mental illness
- Current substance abuse or neurological condition
- Current intoxication
- Currently suicidal

Twenty-three participants were recruited: 14 men and nine women with a mean age of 36.7 years (*SD* = 11.2). Table 4.2 in the results section shows full demographic details for the intervention and control groups.

Materials and measures

Baseline measures

Baseline measures were identical to the first feasibility and piloting study (see Chapter 3 for details), with the exception of using the Peritraumatic Dissociative Experiences Questionnaire (PDEQ; Marmar, Weiss, & Metzler, 1997) instead of the State Dissociation Questionnaire (SDQ; Halligan et al., 2002; Halligan et al., 2003; Murray et al., 2002) to assess dissociation during the accident (see Appendix 4.1). The PDEQ is a widely used 10-item self-report questionnaire assessing dissociative symptoms at the time of the trauma. It has good reliability and validity (Marmar, Weiss, & Metzler, 1998) and predicts later PTSD (Birmes et al., 2003). The PDEQ has stronger psychometric properties than the SDQ, but was not selected initially as it takes slightly longer to administer. Given that baseline measures were tolerated well in the previous study, the PDEQ was substituted for the SDQ in this study.

Self-report baseline measures were as follows: clinical history form; perceived life threat; Peritraumatic Dissociative Experiences Questionnaire (PDEQ; Marmar et al., 1997); Peritraumatic Distress Inventory (PDI; Brunet et al., 2001); hotspots of the accident form; activity diary.

Baseline information collected from participants' medical notes was as follows: details of the accident; medication administered after the accident; admission to a hospital ward; Injury Severity Score (Baker et al., 1974).

Outcome measures

a) Measures of intrusive memories in the week after the accident:

Amended Intrusion Diary (adapted from Holmes et al., 2009; Holmes, James, et al., 2010). Participants recorded each intrusion they had in the first week after the accident using a pen-and-paper diary. In this simplified version of the diary, participants were asked to put a tick in a box for the day on which each intrusion occurred, and to write a brief description (one or two words) to remind them of the content of each intrusion. The full version of the amended Intrusion Diary (version 2) is shown in Appendix 4.2.

Intrusion Interview (Hackmann et al., 2004; Michael et al., 2005). The Intrusion Interview is a structured interview in which participants are asked to describe the content of each of their intrusive memories in turn. For each intrusive memory, respondents indicate its frequency in the past week, and rate its vividness, the distress associated with it and the extent to which it seemed to be happening now instead of being something from the past ("nowness"), each on a scale of 0 (*not at all*) to 100 (*very much*). In the current study, participants were asked to describe the content of each of their intrusions using their Intrusion Diary as a prompt. The researcher used this opportunity to verify that what they had written in the diary were indeed intrusions of the accident. The total frequency of all intrusions in the previous week was noted, and participants rated the overall vividness, distress and nowness of their intrusions.

Intrusion Questionnaire (Hackmann et al., 2004). The Intrusion Questionnaire includes similar items to the Intrusion Interview, but in questionnaire form. Respondents are asked to indicate for each intrusive memory how often it occurred in the previous week, and to rate its vividness, distress and nowness each on a scale of 0 (*not at all*) to 100 (*very much*). Test-retest reliability of the items over one week ranged between $r = .61$ and $r = .72$ (Speckens et al., 2006). Correlations with corresponding items on the Intrusion Interview were: frequency $r = .94$, distress $r = .74$, vividness, $r = .70$ and nowness $r = .84$ (Hackmann et al., 2004). In the current study participants indicated the frequency of all intrusions in the previous week, and rated the overall vividness, distress and nowness of their intrusions.

b) Measures of post-traumatic stress symptoms:

Clinician-Administered PTSD Scale (Blake et al., 1995). The CAPS is a well-established structured clinical interview to assess PTSD diagnosis and symptom severity. It includes 17 items corresponding to the DSM-IV symptoms of PTSD. Each item is rated for frequency in the past week (or month; 0-4) and intensity (0-4). Frequency and intensity scores are added to give a total severity score and subscales scores for re-experiencing, avoidance and hyperarousal symptoms. The CAPS has excellent reliability and validity (Weathers et al., 2001), and has been widely used in high-quality trials of early interventions after trauma (Bryant et al., 2008; Ehlers, Clark, et al., 2003; Shalev et al., 2012).

Impact of Events Scale-Revised (IES-R; Weiss & Marmer, 1997). The IES-R is a 22-item self-report measure of the subjective distress caused by a traumatic event (see Appendix 4.3). It has good reliability and validity, and has been widely used as an outcome measure in randomised controlled trials of interventions after trauma (e.g. Bryant et al., 2008). It consists of three subscales, designed to parallel the DSM-IV criteria for PTSD: Intrusion, Avoidance and Hyperarousal. Participants were asked to rate items with reference to the impact of the road traffic accident.

c) Measures of other psychiatric symptoms:

Beck Anxiety Inventory (BAI; A. T. Beck, Brown, Epstein, & Steer, 1988). This 21-item self-report measure is a well-established measure of the severity of anxiety symptoms, and has been used in previous randomised controlled trials of interventions after trauma (e.g. Bryant et al., 2008; Ehlers et al., 2003).

Beck Depression Inventory-II (BDI-II; A. T. Beck, Steer, & Brown, 1996). This 21-item self-report measure is a well-established measure of the severity of depression symptoms, and has been used in previous randomised controlled trials of interventions after trauma (e.g. Bryant et al., 2008; Ehlers et al., 2003).

d) Measures to assess wider outcomes:

Work and Social Adjustment Scale (WSAS; Mundt, Marks, Shear, & Greist, 2002). The WSAS is a simple measure of impairment in social and occupational functioning, widely used in primary healthcare settings (e.g. Improving Access to Psychological Therapies (IAPT) services). It has good reliability and validity in patient samples (e.g.

Cronbach's α of 0.70 to 0.94, test-retest correlation of 0.73, and correlations of 0.81 and 0.86 with clinician interviews).

EuroQol-5D-5L (EQ-5D-5L; Kind, 1996). The EuroQol-5D-5L is a brief measure for assessing general quality of life and health status. Items assess mobility, self-care, usual activities, pain and anxiety/depression using a 5-item scale. It is frequently used as an outcome measure in clinical trials (e.g. D. Kessler et al., 2009).

e) Measures to assess participants' experiences and expectations of the study:

Feedback Questionnaire. This 13-item questionnaire was designed to assess participants' experience of completing the study (see Appendix 4.4). Items 1 to 7 were each rated on a 9-point Likert scale from 1 (*not at all*) to 9 (*extremely*), and asked how easy, helpful, difficult, distressing and burdensome participants found the study, as well has how happy they were to be randomised to completing a computer task or not. Items 8 to 11 asked free response questions to assess what participants found positive or difficult, and how the study might be improved. Item 12 asked participants to rate their preferred method of telling the researcher about their intrusions – using the Intrusion Diary, by interview over the telephone after one week or by questionnaire after one week – and to give their reason for choosing this method. Finally, item 13 asked for any other comments about the study.

Expectancy Questionnaire. A single item was used to assess participants' expectation of the effect of the study on their intrusions. Participants were asked to rate how much they predicted that what they had been asked to do in the emergency department would increase or decrease their intrusions of the accident, on a scale of -10 (*extreme decrease*) to 10 (*extreme increase*).

Tetris computer game

The computer game Tetris DS was played on a Nintendo DS XL: a hand-held gaming device with a screen size of 85 mm by 64 mm. This was a slightly larger device than that used in the first feasibility and piloting study, following the suggestion from a participant to use a bigger screen.

Procedure

Substantial amendments were approved by the NRES Research Ethics Committee (REC) to amend the study procedures and eligibility criteria based on the results of the first feasibility and piloting study (see Amendment 2 approval letter dated 04/06/13; Appendix 4.5) and to conduct a second feasibility and piloting study (see Amendment 3 approval letter dated 24/06/13; Appendix 4.6).

Figure 4.2 summarises the procedure for this second feasibility and piloting study. The procedure is described in more detail below.

Identification. The researcher was present in the ED on average 80% of the time from Monday to Friday 9am to 5pm. During this time, the researcher regularly prompted ED staff to identify any potential participants presenting to the ED. In addition, posters were placed around the ED so that patients could contact the researcher directly if they were interested in taking part (see Appendix 4.7).

Screening. Patients were screened based on information from the ED online patient database ("FirstNet"[7]) and their ambulance and ED notes. Screening aimed to determine if patients met the following subset of inclusion criteria: aged 18 or over; experienced or witnessed a road traffic accident meeting the DSM-IV A1 criterion for PTSD; report memory of the accident; alert and orientated, GCS = 15; fluent in English; have sufficient physical mobility to use a hand-held gaming device (e.g. able to sit upright, use of both arms). If these criteria were met, a member of the ED staff asked the patient for verbal consent to speak to the researcher.

Informed consent. Participants were approached during a settled time whilst they were waiting in the ED and provided with an information sheet about the study (similar to Appendix 5.7). They were given time to read this, ask questions, and consider whether or not they wished to participate. Those who decided to take part signed a consent form to indicate their decision (similar to Appendix 5.8).

Eligibility assessment. Participants were asked a series of questions to assess any remaining eligibility criteria, such as a reported history of severe mental illness, current substance abuse or a current neurological condition. Participants who no longer met eligibility criteria were excluded from the study.

[7] "FirstNet" is part of the Electronic Patient Record (EPR) system used by the John Radcliffe Hospital Emergency Department to register patients presenting to the department and record their clinical management.

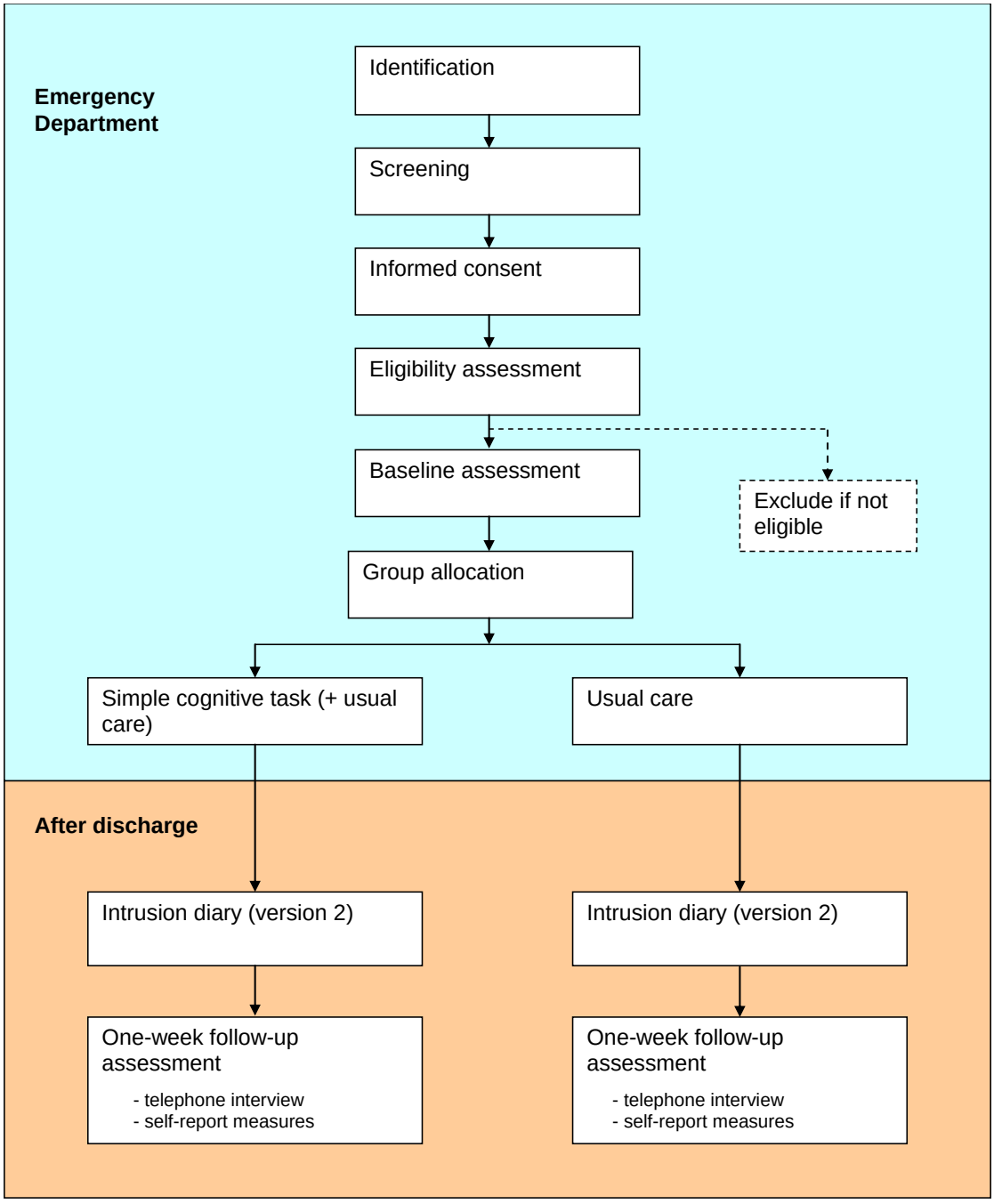


Figure 4.2. Diagram of the procedure for the second feasibility and piloting study.

Baseline assessment. Eligible participants completed the baseline measures in their own time. The researcher was present to assist them with any queries. The researcher recorded additional baseline information from participants' medical notes.

Group allocation. Participants were alternately allocated to the simple cognitive task and usual care groups, to ensure that both procedures were piloted early on in the study.

Simple cognitive task intervention. Participants in the simple cognitive task condition were asked to close their eyes and picture the worst moments of the accident for 30 seconds (a cue to reactivate visual memories of the accident). The researcher then demonstrated how to play the computer game Tetris on a Nintendo DS XL, and participants were given a chance to practice until they understood how to play the game. Participants were asked to play Tetris for approximately 20 minutes, but for as long as they wished. This had to consist of at least one uninterrupted period of 10 minutes. If the participant needed to be seen by a professional during the 10-minute period, they were required to complete a further 10 minutes uninterrupted once they had been seen. Participants were offered a break after 10 minutes, but could continue playing if they wanted to. The researcher timed the duration of play, and told participants when 20 minutes had elapsed. Participants were told that they were welcome to play Tetris over the following week at home, by downloading it on their phone or playing it online for free, particularly if they had an intrusion of the accident. However, this was not obligatory.

Usual care. Participants in the usual care condition were not given any additional instructions before continuing to the next stage of the procedure.

Intrusion diary. Finally, participants were given instructions on how to fill in the Intrusion Diary over the next week. This included encouraging participants to think about where they would keep the diary and how they would remember to fill it.

Instructions for one week follow-up. The researcher then explained the next stages of the study, and how they would stay in touch with the participant over the next week. A time was arranged to contact the participant in a week's time, and this was noted down for the participant on the Intrusion Diary. Participants were given a stamped addressed envelope in which to post back the diary, but were also given the option of the researcher picking the diary up from them at a convenient time.

Additional support with filling in the intrusion diary. Participants were contacted by telephone the day after the accident to check that they still had the diary and understood the instructions, and to confirm the time of the one week follow-up telephone call. The researcher helped to solve any problems that had arisen. Participants were sent a text towards the end of every day to remind them to fill in the diary if they had had any intrusions that day.

One week follow-up assessment. After one week, participants were contacted by telephone to complete the Intrusion Interview, CAPS[8] and EQ-5D-5L. Participants in the simple cognitive task condition were asked if they had played Tetris at home and details of when and for how long were recorded. Participants were then asked to fill in the remaining questionnaires either online (using the software Qualtrics, which involved emailing participants a link to a secure online survey) or by post. Finally, participants were asked to post their Intrusion Diary back in the stamped addressed envelope provided, or a time was arranged to collect it from them. If necessary, participants were contacted again to remind them to return the diary and/or questionnaires.

Statistical analysis plan

Data were recorded and analysed using SPSS Version 20.

Statistical analyses for this study were exploratory, as the study was not sufficiently powered to test the efficacy of the intervention. However, between-groups analyses were used to compare baseline and outcome data to inform refinements to the procedure for the randomised controlled study. The distribution of data for continuous variables was determined by examining boxplots, histograms and skewness and kurtosis statistics. Where data for both groups were approximately normally distributed, an independent samples *t*-test was used; otherwise the Mann Whitney U test was used. Differences in categorical variables were analysed using a Chi-square test (or Fisher's Exact test for small frequencies). Two-tailed tests were used at the 5% significance level.

In this pilot study it was considered important to detect any differences that were present, and therefore preferable to make a type I error (i.e. incorrectly detect a difference that was not present) than a type II error (i.e. incorrectly reject a difference if one was present). Therefore, multiple-comparison corrections (e.g. Bonferroni) were not applied.

Qualitative data from the Feedback Questionnaire were recorded verbatim and examined for possible themes.

[8] Administration of the CAPS over the telephone has been shown to be as valid and reliable as face-to-face interviews (Aziz & Kenford, 2004).

Procedural changes made during the study

Given that one of the aims of this study was to develop optimal procedures for the randomised controlled study, refinements to the procedure were made during the course of the study. The changes are described below.

1) Method of allocation to group

After recruiting 15 participants to the study, an examination of the data revealed poor balance between the intervention and control groups on the Peritraumatic Distress Inventory (PDI) score, which is a key baseline predictor of post-traumatic stress symptoms (simple cognitive task n = 8, M = 19.4, SD = 11.7; usual care n = 7, M = 11.3, SD = 7.7). Therefore, the remaining participants were allocated to each group in such a way as to minimise the difference in mean PDI score between the two groups, akin to minimisation (Taves, 1974). This was done by conducting a brief analysis to determine the participant's group allocation after obtaining baseline measures. By the end of this study, the balance on PDI score between the groups was improved (simple cognitive task n = 9, M = 16.3, SD = 11.3; usual care n = 10, M = 14.9, SD = 8.4).

2) Memory reactivation cue in the simple cognitive task condition

After 15 participants had reached their one-week follow-up assessment, an examination of the data revealed that all three participants who had dropped out of the study had been allocated to the intervention condition. This raised the concern that an aspect of the intervention procedure might be related to participant drop-out. The key components of the intervention procedure that differed from the control procedure were:

- A memory reactivation cue (asking participants to close their eyes and picture the worst moments of the accident for 30 seconds)
- Playing the computer game Tetris for at least 20 minutes
- The additional time required from participants in the emergency department (approximately 20 to 25 minutes)

Participant ratings on the Feedback Questionnaire indicated that the study procedures were minimally distressing (n = 5, M = 2.40, SD = 2.07; 1 = *not at all distressing* to 9 = *extremely distressing*), and that the length of time required in the study was minimally burdensome (n = 5, M = 3.40, SD = 1.82; 1 = not at all burdensome to

9 = extremely burdensome). However, one possibility was that asking participants to close their eyes and picture the worst moments of the accident was having an adverse effect for some participants. From reviewing notes regarding participants' responses to the reactivation cue, it was noticed that, perhaps contrary to what might be expected, the three participants who were lost to follow up showed no emotional response during the reactivation cue. In contrast, the other participants either expressed some distress, or indicated sufficient involvement in the image to re-experience sensory aspects of the accident. Psychological theories of PTSD suggest that dissociating or avoiding memories of trauma is associated with greater risk of PTSD (see Brewin & Holmes, 2003 for a review). Therefore it is possible that the intensity of the reactivation cue caused some participants to avoid the memory, with potential adverse effects.

In consultation with the trial management group, it was agreed to use a less intense reactivation cue. Given that participants were already asked to note down the worst moments of the accident on the "hotspots of the accident" form, this procedure was now used as the memory reactivation cue, as it acted as a reminder of the accident prior to playing Tetris. The instruction to participants to close their eyes and picture the worst moments of the accidents was omitted from the procedure. Whilst it was not possible to evaluate formally the impact of this change on the loss-to-follow up rate (due to the small numbers), some observations suggested that this change might be beneficial. First, of the additional four participants recruited to the simple cognitive task group, no further participants were lost to follow-up. Second, all four participants indicated on the Feedback Questionnaire that they found taking part in the study "not at all distressing".

3) Error in baseline procedure in the usual care condition

In reviewing the procedure for the intervention condition (a memory reactivation cue followed by playing the computer game Tetris, as described above), it became apparent that part of the memory reactivation cue (asking participants to note down the worst moments of the accident on a form) was included in error in the control condition as part of the baseline assessment. This suggested that the procedure in the control condition was not congruent with a "usual care" control. Therefore the "hotspots of the accident" form was removed from the baseline assessment in the control condition. Only two further participants were recruited into the control condition after implementing this change, so it was not possible to evaluate its impact.

Results

Recruitment rate

Recruitment took place over a period of 14 weeks. On average the researcher was present in the ED for 77.7% of the time between 9am and 5pm from Monday to Friday. The mean recruitment rate was 1.7 participants per week.

Figure 4.3 shows a flowchart of recruitment for this second feasibility and piloting study.

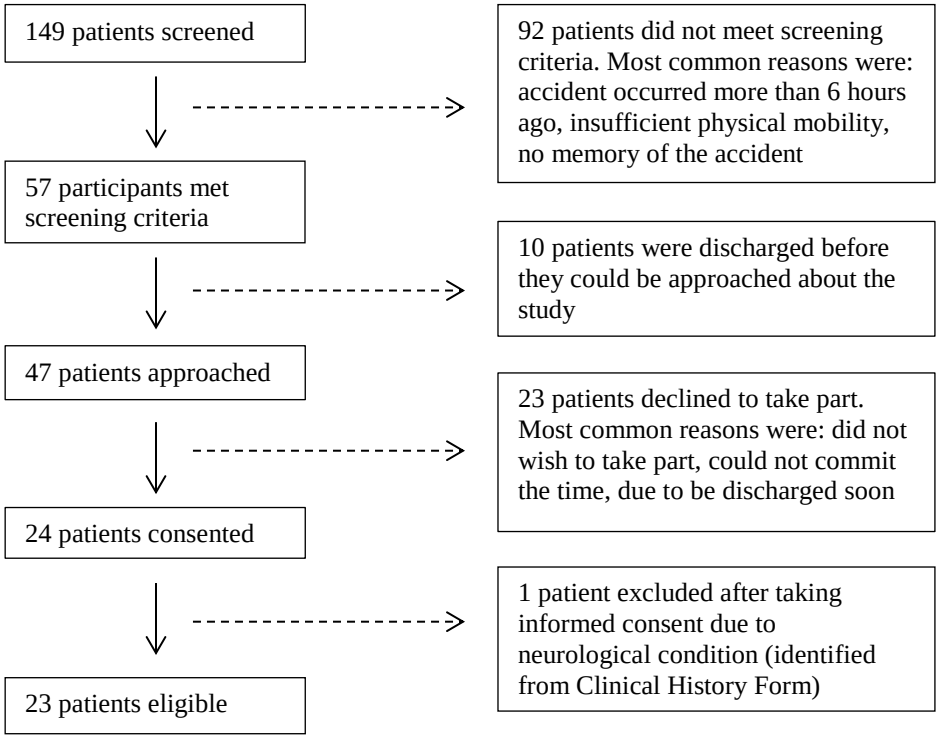


Figure 4.3. Recruitment flowchart for the second feasibility and piloting study.

Eligibility criteria

Changes to the eligibility criteria were implemented from the previous feasibility and piloting study, as only 70% of participants in the preceding study were able to complete the study procedures. In this study, all 23 eligible participants (100%) were able to complete the study procedures in the emergency department.

Drop-out rate

Figure 4.4 shows that four out of 23 participants (17.4%) in this study dropped out at follow up. Three were lost to follow-up (i.e. could not be contacted after leaving the ED).

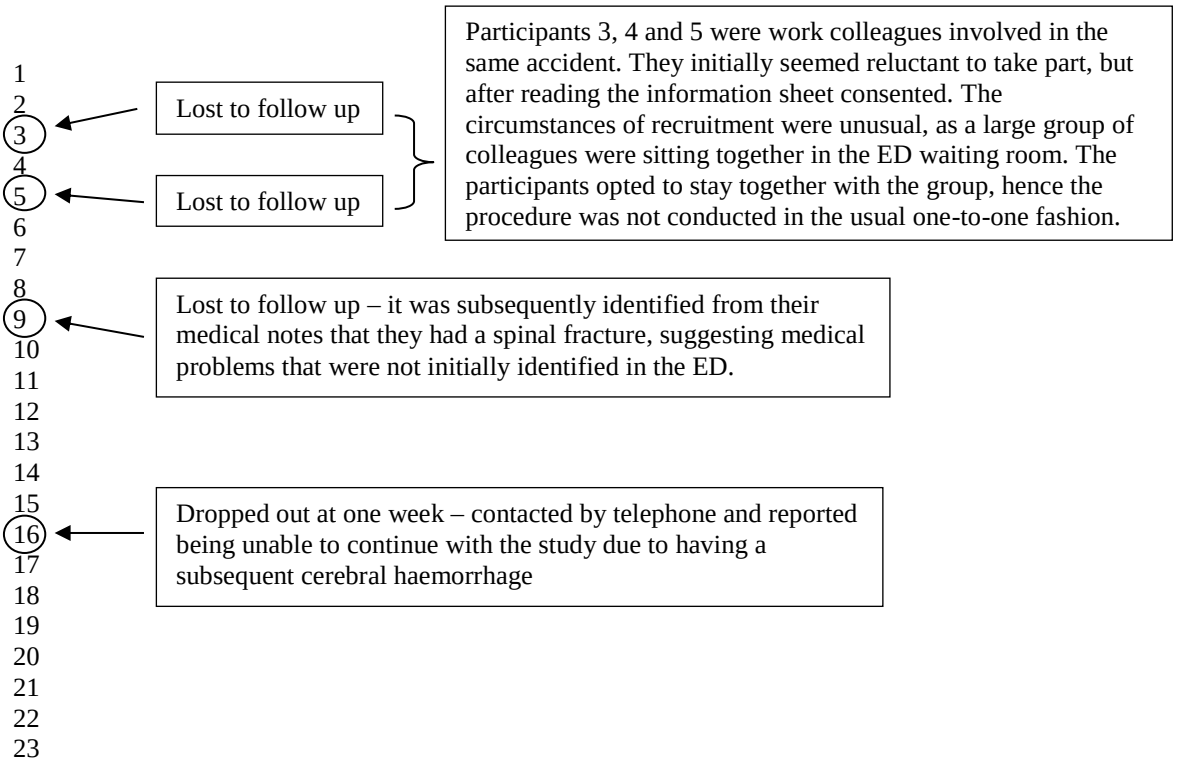


Figure 4.4. Observational details of participants who dropped out of the study

During the study observational information was used to improve the way in which participants were approached about the study, to reduce the likelihood of drop-out. For example, participants were only approached during a settled time, and willingness to complete all the study procedures, including follow-up assessments, was thoroughly assessed. Consequently, whilst three participants were lost to follow up in the first half of the study (26%), only one participant dropped out in the second half of the study (9%).

Table 4.1 shows baseline characteristics of participants who dropped out of the study versus those who completed the study. A higher proportion of participants who dropped out of the study had experienced a prior trauma, and a slightly higher proportion were female, compared to participants who were followed up. Participants who dropped out of the study also had higher peritraumatic dissociation (PDEQ) scores and slightly higher peritraumatic distress (PDI) scores, but a lower mean Injury Severity Score, than participants who stayed in the study.

Table 4.1. Baseline Characteristics of Participants Who Dropped Out Versus Those Who Completed the Study (N = 23)

Baseline variable	Participants who dropped out (*n* = 4)	Participants who completed the study (*n* = 19)
Female, *n* (%)	2 (50%)	7 (37%)
Age, *M* (*SD*)	36.0 (10.7)	36.8 (11.5)
Years in education, *M* (*SD*)	15.8 (4.3)	16.3 (4.1)
Previous mental health problem, *n* (%)	0 (0%)	1 (5%)
Prior trauma, *n* (%)	4/4 (100%)	11/19 (58%)
Perceived life threat		
Self, *M* (*SD*)	4.0 (2.2)	4.7 (3.3)
Other, *M* (*SD*)	2.5 (3.0)	1.9 (2.8)
PDEQ score, *M* (*SD*)	25.8 (8.2)	18.2 (8.2)
PDI score, *M* (*SD*)	19.3 (6.6)	14.8 (10.3)
ISS, *M* (*SD*)	1.3 (1.9)	2.4 (2.5)
Admitted to ward, *n* (%)	2 (50%)	9 (47%)

Completion rate of the primary outcome measure

19 out of 23 participants (83%) were followed up at one week. All 19 completed the Intrusion Diary and returned it in the post. Table 4.2 shows a comparison between the Intrusion Diary and alternative potential primary outcome measures with regards to completion rate and participant preference.

Table 4.2. Comparison of Potential Primary Outcome Measures on Completion Rate and Participant Preference (N = 19)

Outcome measure	Completion rate (*n* = 19)	Rated as preferred method of recording intrusions (*n* = 17)[a]
Intrusion diary, no. of intrusions	19/19 (100%)	12/17 (71%)
Telephone interviews		3/17 (18%)
Intrusion Interview, no. of intrusions	19/19 (100%)	
CAPS Re-experiencing subscale	19/19 (100%)	
Online/postal questionnaires		2/17 (12%)
Intrusion Questionnaire, no. of intrusions	17/19 (89%)	
IES-R Intrusion subscale	18/19 (95%)	

[a] Data were missing for two participants.

For participants who did not drop out of the study, completion rates for all methods of assessing outcome were high (89% and above). The majority of participants (71%) rated the Intrusion Diary as their preferred method of recording their intrusions, over the

telephone interview and online/postal questionnaires. Reasons provided were that the diary was more convenient (e.g. "very quick and easy to have with you and fill in at the exact time you have an intrusion", "I can do the diary… in my own time anywhere") and more accurate (e.g. "I filled in the diary on the day of the intrusion so therefore believe it is most accurate", "minimises the risk of losing memory of the intrusions", "most precise way").

Results from the Intrusion Questionnaire were not included in further analyses, as the Intrusion Questionnaire assessed the same constructs as the Intrusion Interview, but had a lower completion rate.

Intervention and control procedures

Refinements were made during the course of the study to improve the intervention and control procedures (described in the section "Procedural changes made during the study"). Tables 4.3 and 4.4 show the results on key baseline and outcome measures for the simple cognitive task intervention condition, with and without the "intense" reactivation cue, and the usual care control condition, with and without the "hotspots of the accident" form, for the 19 participants who completed the study.

A comparison of the total simple cognitive task group and the total usual care group indicated that most baseline measures were balanced between the two groups, with a few notable exceptions. A higher proportion of participants in the simple cognitive task group than the usual care group were women, non-White British and had experienced a prior trauma, although only the difference in prior trauma was statistically significant. Injury severity score appeared to be slightly lower for the simple cognitive task group than the usual care group, although the difference was not statistically significant.

Mean outcome scores on the Intrusion Diary and Intrusion Interview for the total groups indicated a greater number of intrusive memories in the simple cognitive task group than the usual care group. This effect was in the opposite direction to that predicted, although the difference did not quite reach statistical significance. Results for the Intrusion Diary and Intrusion Interview were similar but not identical, suggesting that retrospective report of the number of intrusions differed slightly from diary-based assessment. Scores on secondary outcome measures assessing distress of intrusive memories and clinical symptom severity (CAPS, IES-R, BAI and BDI) indicated no differences between the groups. Further, quality of life rating (EQ-5D) was slightly higher in the simple cognitive task group than the usual care group, but not quite significantly.

Table 4.3. Baseline Measures for the Intervention and Control Groups (N = 19)

Baseline variable	Simple cognitive task (with "intense" reactivation) (*n* = 5)	Simple cognitive task (without "intense" reactivation) (*n* = 4)	Usual care (with hotspots form) (*n* = 8)	Usual care (without hotspots form) (*n* = 2)	Simple cognitive task (total) (*n* = 9)	Usual care (total) (*n* = 10)	Between-groups analysis[a]
Gender (female), *n* (%)	3 (60%)	1 (25%)	1 (13%)	2 (100%)	4 (44%)	3 (30%)	χ^2= .425, *p* =.650
Age (years), *M* (SD)	35.6 (12.5)	37.5 (11.7)	38.4 (13.5)	32.0 (4.24)	36.44 (11.42)	37.10 (12.27)	*t* =.120, *p* = .906
Years in education, *M* (SD)	17.6 (2.9)	18.0 (3.5)	14.4 (4.9)	17.5 (3.5)	17.78 (2.95)	15.00 (4.64)	*t* = 1.877, *p* = .078
White British, *n* (%)	3 (60%)	2 (50%)	8 (100%)	2 (100%)	5 (56%)	10 (100%)	χ^2= 5.630, *p* = .060
Vehicle							χ^2= 2.153, *p* =.541
Car/van, *n* (%)	3 (60%)	0 (0%)	3 (38%)	1 (50%)	3 (33%)	4 (40%)	
Motorcycle, *n* (%)	0 (0%)	2 (50%)	2 (25%)	0 (0%)	2 (22%)	2 (20%)	
Bicycle, *n* (%)	2 (40%)	2 (50%)	3 (38%)	1 (50%)	4 (44%)	4 (40%)	
Mental health problem							
Current, *n* (%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	0 (0%)	N/A
Previous, *n* (%)	1 (20%)	0 (0%)	0 (0%)	0 (0%)	1 (11%)	0 (0%)	χ^2= 1.173, *p* =.474
Family history, *n* (%)	3 (60%)	0 (0%)	1 (13%)	0 (0%)	3 (33%)	1 (10%)	χ^2= 1.552, *p* =.303
Prior trauma, *n* (%)	5 (100%)	3 (75%)	3 (38%)	0 (0%)	8 (89%)	3 (30%)	χ^2= 6.739, *p* =.020
Opiates given, *n* (%)	2 (40%)	1 (25%)	3 (38%)	1 (50%)	3 (33%)	4 (40%)	χ^2= .090, *p* = 1.00
PLT – self, *M* (SD)	5.00 (4.30)	4.75 (1.26)	4.50 (3.66)	5.00 (4.24)	4.89 (3.14)	4.60 (3.53)	*t* =.187, *p* = .854
PLT – other, *M* (SD)	3.20 (3.11)	0.50 (0.57)	1.00 (2.45)	5.50 (3.54)	2.00 (2.65)	1.90 (3.11)	*U* = 38.00, *z* = -.608, *p* = .604
PDEQ, *M* (SD)	20.20 (13.01)	13.75 (0.96)	18.38 (7.63)	21.50 (3.54)	17.33 (9.82)	19.00 (6.96)	*U* = 34.00, *z* = -.905, *p* = .400
PDI, *M* (SD	21.60 (13.89)	7.25 (0.96)	11.75 (7.27)	25.50 (3.54)	15.22 (12.41)	14.50 (8.72)	*U* = 41.50, *z* = -.288, *p* = .780
ISS, *M* (SD)	1.40 (0.89)	1.50 (1.73)	3.25 (3.24)	3.00 (2.83)	1.44 (1.24)	3.20 (3.01)	*t* = 1.692, *p* = .116
Admitted to ward, *n* (%)	2 (40%)	2 (50%)	4 (50%)	1 (50%)	4 (44%)	5 (50%)	χ^2= .059, *p* = 1.00

Note. PLT = perceived life threat; PDEQ = Peritraumatic Dissociative Experiences Questionnaire; PDI = Peritraumatic Distress Inventory; ISS = Injury Severity Score. [a] *t*-test was used for continuous data, Mann Whitney U test for continuous data that were not normally distributed, χ^2 test for frequency data, and Fisher's Exact test for frequency data where > 20% of expected frequencies were ≤ 5.

Table 4.4. Outcome Measures for the Intervention and Control Groups (N = 19)

Outcome variable	Simple cognitive task (with "intense" reactivation) (*n* = 5)	Simple cognitive task (without "intense" reactivation) (*n* = 4)	Usual care (with hotspots form) (*n* = 8)	Usual care (without hotspots form) (*n* = 2)	Simple cognitive task (total) (*n* = 9)	Usual care (total) (*n* = 10)	Between-groups analysis[a]
Intrusion Diary (No. of intrusions)	12.60 (13.72)	7.75 (4.65)	3.63 (4.84)	6.50 (7.78)	10.44 (10.43)	4.20 (5.14)	*U* = 23.00, *z* = -1.81, *p* = .071
Intrusion Interview							
No. of intrusions	11.80 (10.35)	7.75 (4.65)	3.38 (4.50)	18.50 (23.33)	10.00 (8.14)	6.40 (10.81)	*U* = 22.50, *z* = -1.85, *p* = .064
Vividness (0-100)	81.00 (13.42)	52.25 (41.23)	40.00 (42.85)	63.00 (2.83)	68.22 (30.94)	44.60 (39.02)	*U* = 25.50, *z* = -1.62, *p* = .106
Distress (0-100)	48.00 (31.14)	31.25 (32.76)	25.88 (35.36)	57.00 (33.94)	40.56 (31.07)	32.10 (35.68)	*U* = 36.00, *z* = -.740, *p* = .459
Nowness (0-100)	26.00 (26.08)	25.00 (37.86)	23.75 (33.78)	42.00 (25.46)	25.56 (29.63)	27.40 (31.92)	*U* = 44.50, *z* = -.043, *p* = .965
CAPS Re-experiencing	15.00 (8.37)	8.50 (7.33)	7.63 (9.35)	17.00 (12.73)	12.11 (8.18)	9.50 (10.08)	*t* = 0.615, *p* = .546
CAPS Total	37.00 (20.63)	11.25 (6.34)	22.12 (19.58)	46.50 (44.55)	25.56 (20.30)	27.00 (25.00)	*U* = 43.00, *z* = -.163, *p* = .870
EQ-5D-5L (0-100)	74.00 (12.94)	82.50 (9.57)	65.63 (19.96)	52.50 (31.82)	77.8 (11.7)	63.0 (21.3)	*t* = 1.842, *p* = .083
	n = 5	*n* = 4	*n* = 7	*n* = 2	*n* = 9	*n* = 9	
IES-R Intrusion*	13.20 (7.69)	5.00 (3.37)	8.00 (8.25)	14.00 (14.14)	9.56 (7.25)	9.33 (9.11)	*U* = 38.00, *z* = -.222, *p* = .825
IES-R Total*	31.00 (20.83)	9.00 (6.16)	18.57 (19.05)	34.50 (36.06)	21.22 (19.12)	22.11 (22.00)	*U* = 39.00, *z* = -.133, *p* = .895
BAI*	16.80 (13.52)	2.50 (3.79)	7.14 (9.10)	17.00 (22.63)	10.44 (12.39)	9.33 (12.04)	*U* = 36.00, *z* = -.403, *p* = .687
BDI-II*	12.80 (11.69)	2.25 (2.63)	6.43 (6.70)	20.50 (21.92)	8.11 (10.09)	9.56 (11.50)	*U* = 37.50, *z* = -.267, *p* = .790

Note. CAPS = Clinician-Administered PTSD Scale; EQ-5D-5L = EuroQoL-5D-5L; IES-R = Impact of Event Scale-Revised; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory-II.

[a] *t*-test was used for normally-distributed data, Mann Whitney U test for data that were not normally distributed.

Correlations between baseline and outcome measures

As an additional exploratory analysis, partial correlations were calculated to examine the relationship between the key baseline variables thought to predict post-traumatic stress symptoms and the main outcome variables, controlling for condition (see Table 4.5). Gender, perceived life threat (PLT) to self, peritraumatic dissociation (PDEQ score) and peritraumatic distress (PDI score) were most strongly correlated with the number of intrusions and other post-traumatic stress symptoms.

Table 4.5. Spearman's Correlations Between Main Baseline and Outcome Measures (N = 19)

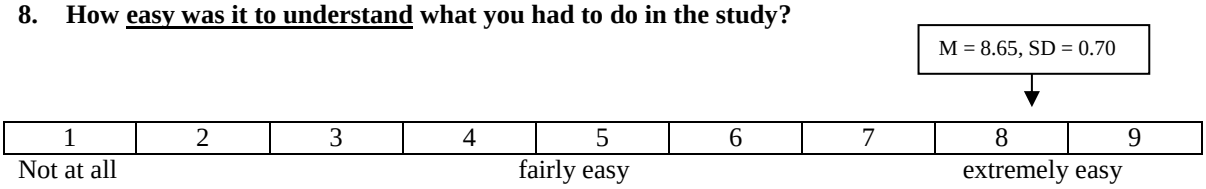
Baseline measure	Outcome measure				
	Intrusion diary - number of intrusions	CAPS re-experiencing score	CAPS total score	IES-R intrusion score	IES-R total score
Age	-.315	.038	.114	-.167	-.057
Years in education	-.046	.125	-.005	-.086	-.023
Gender	.490*	.807***	.662***	.706***	.707***
White British	-.097	.028	.013	-.086	-.015
Prior mental health problem	.111	-.401	-.434	-.304	-.435
Family history of mental health problem	.250	-.050	-.109	.054	-.044
Prior trauma	.046	.041	-.021	.133	.108
Opiate medication administered	-.207	-.218	-.350	-.278	-.255
PLT to self	.645***	.613**	.380	.627**	.565*
PLT to other	.392	.516*	.509*	.522*	.537*
PDEQ score	.836***	.541*	.440	.705***	.638**
PDI score	.687***	.624**	.529*	.703***	.476

* $p < .05$, ** $p < .01$, *** $p <. 005$.

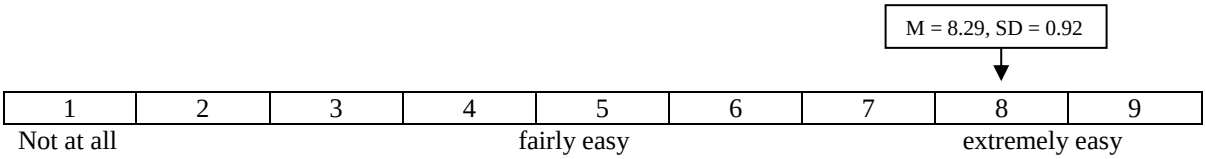
Participant experience

Figure 4.6 shows means and standard deviations of participants' ratings on the Feedback Questionnaire regarding their experience of completing the study. Results are shown for the 17 participants who completed the questionnaire. Participants' responses indicated that they found the study extremely easy to understand and take part in, and minimally difficult, distressing, or burdensome on their time. Table 4.7 shows participants' comments to free response questions on the Feedback Questionnaire regarding their experience of completing the study. Full details are provided in Appendix 4.8.

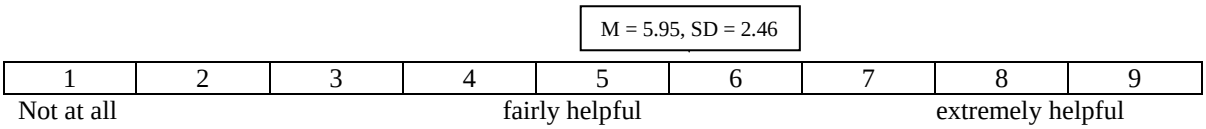
8. How <u>easy was it to understand</u> what you had to do in the study?



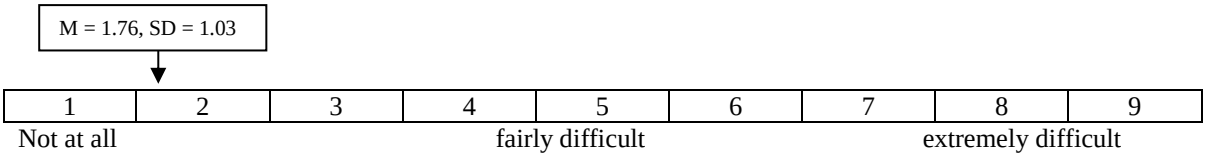
9. How <u>easy</u> did you find taking part in the study?



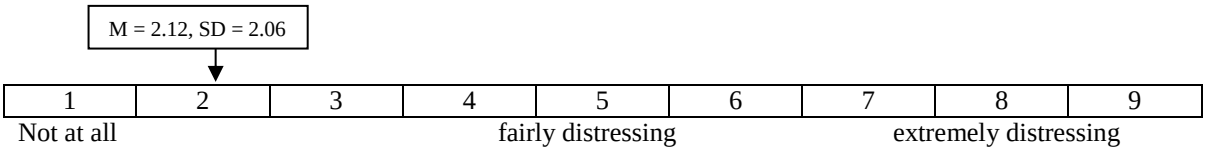
10. How <u>helpful</u> did you find taking part in the study?



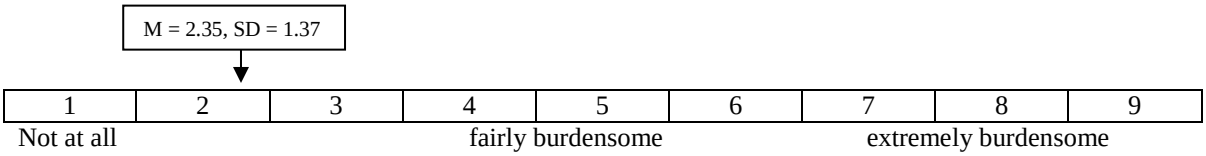
11. How <u>difficult</u> did you find taking part in the study?



12. How <u>distressing</u> did you find taking part in the study?



13. How much was the study a <u>burden on your time</u>?



14. How happy were you to be asked at random to either complete a computer task or not?

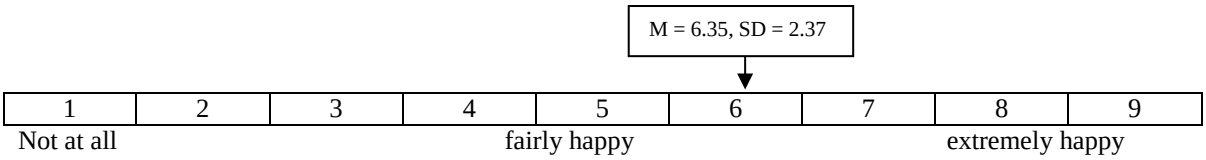


Figure 4.5. Means and standard deviations of participant ratings on the Feedback Questionnaire.

Table 4.6. Themes and Examples of Participants' Verbatim Responses on the Feedback Questionnaire (N = 17)

Feedback question	Themes in participants' responses	Examples of responses (verbatim)
What was positive about taking part in the study? (*n* = 16)	Contributing to research	"Feeling like I was making a difference" "Being able to contribute to a scientific study"
	Processing the trauma	"Able to focus on understanding the intrusions through writing down the images" "It helped me acknowledge what I was thinking and feeling instead of constantly negating it. "It felt better to write things down" "I could record them and bring them up with my partner i.e. talk them over" "Was good to reflect on the accident to slow down, and to realise I had been through a lot"
	Convenience of the study	"Easy to take part" "Being able to choose the time to take part in the telephone interview"
What was difficult about taking part in the study? (*n* = 16)	Filling in the diary	"Making sure I remembered to fill in the diary." "Distinguishing a 'intrusion' from a simple memory." "Having to face some of the moments of the accident"
	Nothing	"Nothing difficult" "I didn't find it difficult to take part." "Every part of the study was clear and concise."
	Circumstances	"Was admitted to hospital" "Filling it in whilst staying in hospital" "Noting intrusions at work without people wondering what I was filling in"

Table 4.6 continued.

Feedback question	Themes in participants' responses	Examples of responses (verbatim)
What could have improved your experience of taking part in the study e.g. made it easier or less of a burden? (*n* = 15)	Method of recording intrusions	"A more readily-available mechanism to enter the diary (e.g. Mobile phone app, or online diary accessible via the internet)" "Being able to give more descriptive answers in the diary." "Making the diary have more boxes to fill in that had simple answers e.g. a scale /10"
	Not difficult/burdensome	"It was not a burden, it was good to have something to focus on" "Nothing I have been asked to do has felt like a burden"
What could have improved how we contacted you in the week after the accident to make it easier to complete the study? (*n* = 13)	Contact was fine	"Nothing" "Contact was fine, not too pushy/laid back" "Text reminders were good" "Contact was unintrusive and always polite" "I think you have done all you can! I may not have taken part if I had to come back into the JR to complete the study"
	Additional support	"Possibly a call mid week to see if I was completing the diary." "Possibly could have been contacted by email also - e.g. reminder email every other day as well as text in case people use email more than text"
Do you have any other comments about the study? (*n* = 14)	Method of assessment	"I think I've answered a lot of the questions in the online questionnaire when speaking to the researcher on the phone on the seventh day, so this was a bit redundant and (unnecessarily) time-consuming."
	Positive experience	"All fine, very polite and outstanding attitude at a time of stress" "I found it enjoyable and therapeutic to be a part of the study. Thanks" "Writing the diary was very helpful for me processing the information following the car accident"

Expectancy of study effect on intrusions

Participants were asked to rate how much they predicted that what they had been asked to do in the emergency department would increase or decrease their intrusions of the accident, on a scale of -10 (*extreme decrease*) to 10 (*extreme increase*). There was no significant difference in expectancy ratings between the intervention (n = 9, M = 0.44, SD = 2.88) and control (n = 8, M = 0.13, SD = 2.47) groups (Mann-Whitney U = 34.5, p = 0.89).

Discussion: Implications for the randomised controlled study

Recruitment rate

The recruitment rate was successfully increased from a mean of 0.83 participants per week in the first feasibility and piloting study to a mean of 1.7 participants per week (i.e. approximately doubled) in this study. This suggested that a recruitment rate of approximately 2 participants per week would be feasible in the randomised controlled study, using a similar recruitment strategy. Therefore it would be possible to recruit the required sample of 72 participants to the randomised controlled study over a period of 9 months.

Eligibility criteria

Only seven out of 10 participants (70%) in the previous study were able to complete the simple cognitive task procedure in line with the protocol, whereas all 23 eligible participants (100%) completed the procedure in this study, indicating that the eligibility criteria were suitable. Therefore the eligibility criteria used in this second study were maintained in the randomised controlled study.

Randomisation

Part way through the study, an imbalance between the two groups on the Peritraumatic Distress Inventory (PDI) score (a key predictor of PTSD symptoms) was identified. Consequently, the method of allocating participants to the intervention or control condition was changed from alternate allocation to manual minimisation based on PDI score. In the main randomised controlled study this problem would be unlikely to occur, as a computerised method of minimisation would be used to balance the two groups

on key baseline variables. Minimisation variables selected were age and gender (key demographic variables) and perceived life threat to self (which was significantly correlated with the number of intrusive memories in this study: $r = .645$, $p < .005$). Perceived life threat to self was selected over peritraumatic dissociation (PDEQ score) and peritraumatic distress (PDI score) (which were also significantly correlated with the number of intrusive memories) as it consisted of a simple rating that could be used easily in the randomisation programme, given that the time available to input randomisation details would be limited.

Drop-out rate

Four out of 23 participants (17%) dropped out in this study, compared to two out of 10 participants (20%) in the previous study. Whilst this overall figure does not reflect a great reduction from the first study, the drop-out rate reduced as the study progressed, from 26% in the first half of the study to 9% in the second half of the study. This is attributed to a number improvements made during the study, which are described below. Further, the 17% drop-out rate in this study remains comparably lower than that of a recent trial of an early psychological intervention after trauma, initiated in a hospital ED, which found a loss to follow-up rate of 26% over one month and 34% over three months (Rothbaum et al., 2012) (although it is acknowledged that this study had a shorter follow-up period of one week).

Whilst numbers were too small to compare statistically, it appeared that participants who dropped out of the study were more likely to be female and to have experienced a prior trauma, and had higher peritraumatic dissociation and peritraumatic distress scores, than participants who completed the study. These factors are all predictors of PTSD (Ozer et al., 2003; Brewin et al., 2000), suggesting that participants with a higher risk of PTSD were more likely to drop out of the study: an unfortunate potential attrition bias in the study results. Whilst these findings do not lead to specific changes that might reduce drop-out in the randomised controlled study, it will be important to take into account that those who drop out might have more severe PTSD symptoms when interpreting the results of the randomised controlled trial, particularly if drop-out is not balanced between the two groups.

A number of developments emerged during this study that were thought to be responsible for the reduction in drop-out rate as the study progressed:

1) The memory reactivation cue in the simple cognitive task condition (asking participants to close their eyes and picture the worst moments of the accident for 30 seconds) was changed to a less intense reactivation cue (briefly noting down the worst moments of the accident).
2) A stricter criterion was used for ensuring that patients were only approached about the study if they were in a settled environment.
3) The inclusion criteria were assessed more rigorously to ensure that participants were only included in the study if they demonstrated clearly that they were willing and able to complete the study procedures, including follow-up assessments.

These improvements were carried forward into the randomised controlled study. In line with the second half of this study, the estimated drop-out rate for the randomised controlled study was projected to be approximately 10%.

Completion rate of the primary outcome measure

19 out of 23 participants (83%) returned the Intrusion Diary after one week. This reflects a marked improvement from the overall 10% return rate in the first feasibility and piloting study. This suggests the amendments made to improve the completion rate e.g. simplifying the intrusion diary and giving participants daily reminders to fill it in, were effective. These amendments were continued into the randomised controlled study.

The completion rate of the one-week telephone interview was the same as for the Intrusion Diary (83%), whilst the completion rate of the online questionnaires was slightly lower (78%). Seventy-one percent of participants rated the Intrusion Diary as their preferred method of assessing intrusions, over the telephone interview and online questionnaires. Taken together, these results suggest that the Intrusion Diary, delivered in its amended form, will be a suitable primary outcome measure for the randomised controlled study.

Intervention and control procedures

The main refinements made to the intervention and control procedures during the course of this study were: a) reducing the "intensity" of the memory reactivation cue in the simple cognitive task condition from asking participants to close their eyes and picture the worst moments of the accident for 30 seconds to briefly noting down the worst moments of the accident, and b) removing the "worst moments of the accident" form (which was

part of the intervention) from the control condition, as this had been included in the baseline assessment in error. Whilst it was difficult to evaluate the potential impact of these change due to the small number of participants, identifying and amending these procedural issues was considered an important step before proceeding to the randomised controlled study.

The main outcome results for the study showed a higher number of intrusive memories in the simple cognitive task group (M = 10.4, SD = 10.4) than the usual care control group (M = 4.2, SD = 5.1), although the difference was not statistically significant. This result was in the opposite direction to that predicted. This may have partly reflected the potential problems that were identified with the intervention and control procedures and rectified during the course of the study. Further, the large standard deviations for the values in each group and the small sample size made it difficult to interpret the mean values reliably.

The results indicated no difference between the two groups in the vividness and distress of intrusions, or in the severity of post-traumatic stress symptoms. Further, quality of life was higher in the simple cognitive task group (M = 77.8, SD = 11.7) than in the usual care group (M = 63.0, SD = 21.3), although not quite significantly (t (21) = 1.842, p = .083). These results indicate that whilst the simple cognitive task group had more intrusions than the usual care group, they did not experience greater distress.

Participant experience

Participants' ratings on the Feedback Questionnaire indicated that the study was extremely easy to understand and take part in, and minimally difficult, distressing or burdensome on their time. Participant ratings also indicated that they were happy to be randomised to either completing the simple cognitive task or not. These findings suggest that in general the study procedures were acceptable for participants.

Participants' comments on free response questions about their experience of the study indicated a number of positive aspects, such as the convenience of the study, contributing to research, polite and un-intrusive contact from the researcher, and finding the study enjoyable and beneficial. Interestingly a number of participants reported that writing down the content of their intrusions in the diary felt helpful for processing the trauma. This raised the possibility that writing the content of intrusions may have influenced the primary outcome (the number of intrusive memories in the first week).

Consequently, the Intrusion Diary was amended for the randomised controlled study by omitting the requirement for participants to write down the content of their intrusions, and instead simply tick a box for each intrusion they had.

Participants' comments also indicated a number of challenges associated with the study, such as remembering to fill in the diary, distinguishing intrusions from normal memories, filling in the diary whilst at work or in hospital, and an overlap in the content of the telephone interview and online questionnaires. Improvement suggestions included allowing more space in the diary to record information about intrusions, and using a mobile phone app or online diary to record intrusions, making an additional mid-week reminder call, and using email as well as text reminders.

Based on this feedback, a few amendments were introduced for the randomised controlled study:

1) Participants would receive a daily reminder to fill in their intrusion diary by a method of their choice e.g. text or email.
2) The Intrusion Diary was amended to include examples of participant's own intrusions, to help distinguish an intrusion from a normal memory.
3) The Intrusion Diary was simplified to a tick-box format to make it easier for participants to fill it in at work or in hospital (or other tricky environments).
4) The Intrusion Questionnaire (administered online) was omitted, as it replicated items in the Intrusion Interview (administered over the phone).

Some improvement suggestions were not taken forward:

1) The Intrusion Diary was not expanded to allow more space for describing intrusion content, for the reason mentioned earlier that writing the content of intrusions may have been therapeutic for some participants.
2) The Intrusion Diary was not adapted to a mobile phone app or online form, as the completion rate of the amended paper diary was high, and there was not sufficient reason to pilot an alternative format.
3) An additional mid-week phone call was not added to the protocol, as the results indicated that participants who were contacted the day after the accident remained compliant with the protocol, whereas participants who could not be contacted the day after the accident were those who dropped out.

Expectancy of study effect on intrusions

There was no difference between the intervention and control groups in participants' ratings of their expectation of the effect of the study on the number of intrusions they had in the week after the accident. Moreover, ratings in both groups were close to 0, suggesting no strong bias that either condition would have an effect.

Other observations

The initial design of the randomised controlled study (see Chapter 2) involved the clinician-administered outcome measures being carried out by a research nurse, who was blind to the participant's group allocation. Within this study, a number of participants had to be contacted out of working hours (e.g. evenings and weekends) to carry out clinician-administered measures over the telephone. As it would not be possible to guarantee that a research nurse would be available to conduct telephone interviews out of working hours, alternative methods of reducing bias in outcome assessment were considered, such as using self-report measures only.

Summary

This second feasibility and piloting study was conducted to improve a number of key procedures from the first feasibility and piloting study, namely a) the recruitment rate, b) the participant eligibility criteria, b) the drop-out rate, and d) the completion rate of the primary outcome measure (a pen-and-paper Intrusion Diary). The results showed successful improvements in the recruitment rate (from approximately one to two participants per week), eligibility criteria (e.g. improving the proportion of participants able to complete the simple cognitive task intervention from 70% to 100%), drop-out rate (from 20% to 17% overall, but to only 9% in the second half of this study), and the completion rate of the primary outcome measure (from 10% to 83%).

Further, this study tested and refined the procedures for both the simple cognitive task intervention and usual care control condition, and assessed participants' experience of taking part in the study. The results highlighted a number of key refinements to improve the randomised controlled study: 1) using a less "intense" reactivation cue than asking participants to close their eyes and picture the worst moments of the accident in the simple cognitive task intervention, 2) omitting the "worst moments of the accident" form from the

baseline assessment in the control condition (which was a part of the memory reactivation cue in the intervention condition, and therefore not congruent with a “usual care” control), and 3) amending the Intrusion Diary further to simplify the format and clarify the instructions.

Having made improvements to the key procedures, the next step was to proceed to the main randomised controlled study.

CHAPTER 5. Randomised Controlled Study - Method: A simple cognitive task intervention to reduce the occurrence of intrusive memories after a road traffic accident

Overview and aims

Previous work in this thesis has a) developed a design for a randomised controlled study to test the simple cognitive task intervention after real-world trauma (a road traffic accident) by adapting Holmes et al.'s (2009) laboratory procedure for use in a hospital emergency department (Chapter 2), and b) piloted the main procedures for the randomised controlled study in the emergency department (Chapters 3 and 4). This chapter describes the method for the main randomised controlled study, as part of the "Evaluation" stage of this research (see Figure 5.1). The aims and method described in this chapter were set out in the approved study protocol (Protocol Version 4.0 10/01/14)) and clinical trial registration (SCARTA trial, ClinicalTrials.gov Identifier: NCT02080351; Appendix 5.1) prior to commencing the study.

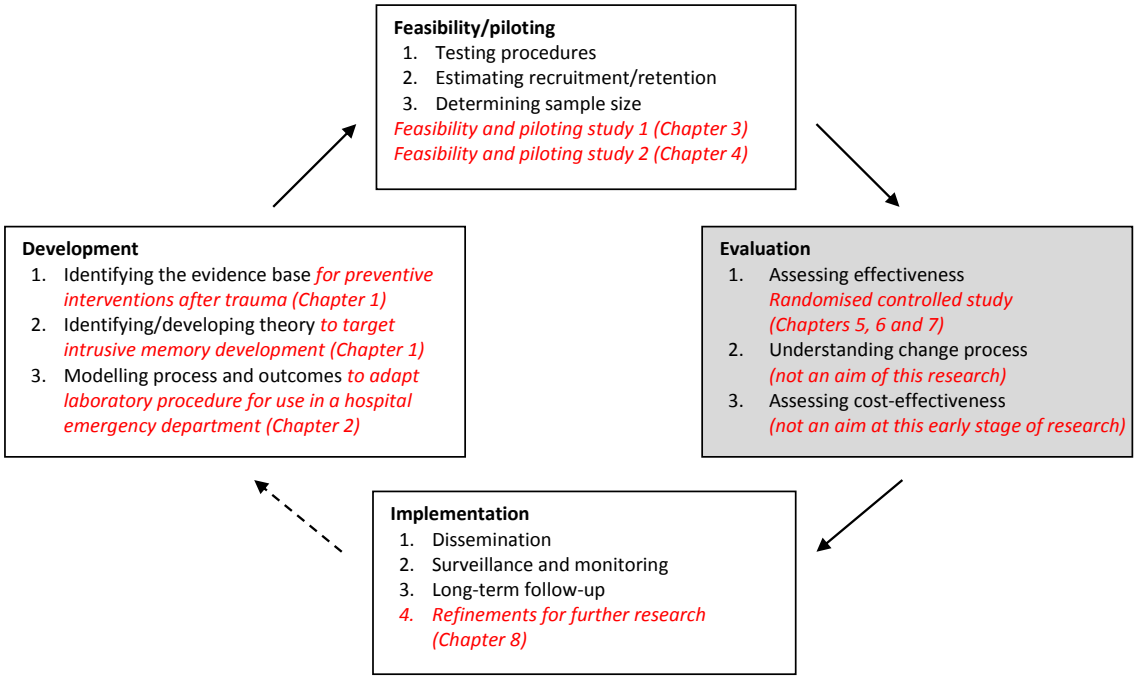


Figure 5.1. Key stages in this research to develop and evaluate a novel preventive intervention after trauma, based on the MRC Complex Interventions Guidance (2008). Adaptations for this research are shown in red italics.

Primary aim

To determine if a simple cognitive task intervention (a memory reactivation cue followed by playing the computer game Tetris), compared to usual care in the emergency department with a simple activity diary, could reduce the number of intrusive memories in the week after a road traffic accident (assessed using an Intrusion Diary).

Secondary aims

To determine if a simple cognitive task intervention (a memory reactivation cue followed by playing the computer game Tetris), compared to usual care in the emergency department with a simple activity diary, could reduce post-traumatic stress symptoms (PDS and IES-R scores), anxiety (HADS-A score), and depression (HADS-D score) at one week and one month after a road traffic accident.

Additional aim

To assess participants' experience of taking part in the study, to inform refinements for further research.

Results for the primary and secondary aims are reported in Chapter 6. Results for the additional aim regarding participant feedback are reported in Chapter 7.

Changes implemented following Feasibility and Piloting Study 2

In light of the outcomes and observations from the second feasibility and piloting study (Chapter 4), a number of changes were made to the planned procedure for the randomised controlled study. The purpose of these changes was to simplify the study procedure, reduce the burden on participants, minimise participant drop-out, and minimise the potential impact of assessor bias on outcome. These changes were approved by the NRES Research Ethics Committee before commencement of the study (see Amendment 4 approval letter dated 27/01/14, Appendix 5.2).

Primary outcome measure: Intrusion Diary

Participant feedback in the second feasibility and piloting study indicated that some participants found it helpful or therapeutic to write down the content of their intrusive

memories. This raised the possibility that any beneficial effect of filling in the intrusion diary might confound or mask the effect of the simple cognitive task intervention relative to the control condition. Therefore the diary was simplified to a tick-box only format, whereby participants were asked simply to tick a box for each intrusive memory they had (on the correct day and time of day), instead of writing a brief description of the memory.

Secondary outcome measures

In the second feasibility and piloting study, participants completed a variety of secondary outcome measures over the telephone (Intrusion Interview, CAPS, EQ-5D) and online (Intrusion Questionnaire, Impact of Events Scale-Revised, Beck Anxiety Inventory, Beck Depression Inventory, Work and Social Adjustment Scale, Feedback Questionnaire). Participant feedback indicated that some of the items in the online questionnaire felt redundant, as they repeated information that had been gathered by telephone. Whilst participant ratings indicated that they did not find the study burdensome (M = 2.35 on a 9-point Likert scale with ratings from 1 [*not at all burdensome*] to 9 [*extremely burdensome*]), outcome measures took approximately 30-60 minutes to complete in total and overall 17% of the sample was lost to follow-up. To reduce the length of time it would take for participants to complete outcome measures, and potentially minimise drop-out, the number of measures was reduced, and some measures were replaced with shorter measures to assess the same outcomes. Measures were selected to assess only key outcomes following trauma (post-traumatic stress symptoms, anxiety and depression) in line with the early-phase nature of the trial, rather than wider outcomes (e.g. quality of life), which may are more relevant in a late-phase trial.

The following changes were made:

a) The Intrusion Interview (Hackmann et al., 2004) and Intrusion Questionnaire (Hackmann et al., 2004) were omitted, as the results of the second feasibility and piloting study indicated that these were redundant.

b) The Work and Social Adjustment Scale (WSAS; Mundt et al., 2002) and EuroQoL-5D (EQ-5D-5L; Kind, 1996) were omitted, as these measures assessed wider outcomes of functioning and quality of life, which were not considered essential in this early-stage trial.

c) The 21-item Beck Anxiety Inventory (BAI; A. T. Beck et al., 1988) and 21-item Beck Depression Inventory (BDI-II; A. T. Beck et al., 1996) were replaced with the shorter 14-item Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith,

1983). As a brief measure of anxiety and depression symptoms, the HADS was considered particularly suitable for this study, as it has been validated in general medical patients (see Bjelland, Dahl, Haug, & Neckelmann, 2002 for a review).

d) The Clinician-Administered PTSD Scale (CAPS), a clinician-rated interview to assess PTSD symptoms and diagnosis, was replaced with the Posttraumatic Diagnostic Scale (PDS; Foa et al., 1997), a briefer self-report measure. First, this simplified the procedure by enabling participants to complete all outcome measures by post or online in their own time, rather than having to arrange a time to speak to a researcher on the telephone. Second, this reduced the potential impact of assessor bias on outcome, as all outcome measures would be self-report measures completed remotely.

Simple cognitive task intervention – memory reactivation cue

In the randomised controlled study, participants were asked to think back very briefly to the accident and briefly tell the researcher any images of the worst moments that popped back to mind, which the researcher noted down for them on the "Hotspots of the accident" form (Appendix 3.5). The purpose of this cue was to reactivate the memory of the accident just prior to playing Tetris. There was no instruction to close their eyes and picture the worst moments.

Usual care with activity diary

In the control condition, participants were asked to complete a simple pen-and-paper activity diary (see Appendix 3.6) for a similar duration of time to the simple cognitive task used in the intervention condition, as a "foil" cognitive activity.

Sample size

An earlier power calculation was used to determine a sample size estimate of 76 (see Chapter 2). This sample size included an estimated drop-out rate of 14%, based on a previous randomised controlled trial recruiting road traffic accident patients from the John Radcliffe Hospital ED (Hobbs et al., 1996). However, the results of the second feasibility and piloting study showed an approximate 10% loss to follow-up rate in the second half of the study; therefore the required sample size was adjusted to 72 to reflect this.

Method of randomised controlled study

Design

An open (unblinded), parallel randomised controlled design was used, in which participants were randomised to one of two groups: 1) a simple cognitive task intervention (a memory reactivation cue followed by playing the computer game Tetris) in addition to usual care in the emergency department or 2) usual care in the emergency department with a simple activity diary.

Participants

Participants were patients presenting to the John Radcliffe Hospital Emergency Department (ED) after a road traffic accident. Patients were included in the study if they met the following eligibility criteria:

Inclusion criteria

- Aged 18 or over
- Experienced or witnessed a road traffic accident (as a driver, passenger, motorcyclist, cyclist or pedestrian)
- Met the DSM-IV criterion A1 for PTSD ("experienced, witnessed, or confronted with actual or threatened death or serious injury")
- Seen in the ED within 6 hours of leaving the scene of the accident
- Report memory of the accident
- Alert and orientated, GCS = 15
- Fluent in written and spoken English
- Have sufficient physical mobility to play a computer game on the intervention platform (a Nintendo DS) at the point of taking informed consent
- Willing and able to provide informed consent and complete study procedures
- Willing and able to be contacted following discharge to complete follow-up assessments

Exclusion criteria

- Loss of consciousness of > 5 minutes
- Current intoxication

- Report a history of severe mental illness
- Current substance abuse or neurological condition
- Currently suicidal

The final sample of 71 participants consisted of 34 men and 37 women with a mean age of 39.66 years (*SD* 16.32). Further demographic information for the simple cognitive task and control groups is given in the study results in Chapter 6.

Materials and measures

Baseline measures

a) Self-report measures

Socio-demographic details. Demographic information, such as age, gender, education, marital status, employment status, and ethnicity were recorded (see Appendix 5.3). These factors have been found to be weak but significant predictors of PTSD symptoms (Brewin, Andrews & Valentine, 2000).

Clinical history form. Participants were asked to record any current physical health problems, current or past mental health problems, family history of mental health problems, and experience of previous traumas, as well as any current medication (see Appendix 3.1). Psychiatric history and prior trauma have been found to predict PTSD symptoms with small but consistent effect sizes (Brewin, Andrews & Valentine, 2000; Ozer et al., 2003).

Perceived life threat. Participants were asked to rate "to what extent did you feel your life was in danger?" and "to what extent did you feel that someone else's life was in danger?" each on a 10-point Likert scale from 0 (*not at all*) to 10 (*extremely*). This rating was based on ratings of perceived life threat used in previous prospective studies following trauma, which have shown an association between perceived life threat at the time of the trauma and later PTSD (e.g. E. B. Blanchard et al., 1995; Dunmore, Clark, & Ehlers, 1999; Heir et al., 2009; Holbrook et al., 2011) (see Appendix 3.2).

Peritraumatic Dissociative Experiences Questionnaire (PDEQ; Marmar et al., 1997). The PDEQ is a widely used 10-item self-report questionnaire assessing dissociative symptoms at the time of a traumatic event. Items are rated on a 5-point Likert scale from 1 (*not at all true*) to 5 (*extremely true*), and summed to give a total score (see Appendix 4.1). The measure has good reliability and validity (Marmar et al., 1998) and has been found to

predict later PTSD in patients recruited from a hospital emergency department (Birmes et al., 2003).

Peritraumatic Distress Inventory (PDI; Brunet et al., 2001). This 13-item measure assesses the extent to which participants experienced a number of emotional reactions during a traumatic event (see Appendix 3.4). Items are rated on a 5-point scale from 0 (*not at all*) to 4 (*extremely*), and ratings are summed to give a total score. The PDI has been found to be internally consistent, with good reliability and validity. PDI score has been found to predict the development of PTSD symptoms in road traffic accident patients admitted to an intensive care unit (e.g. Nishi et al., 2010).

b) Information from medical notes and Electronic Patient Record (EPR)[9]

Number of previous Emergency Department attendances in the last year. The number of times the participant had attended the ED within the last year was recorded from the EPR.

Brought in by ambulance. Whether or not the patient was brought in by ambulance was recorded from their ambulance record or notes on the EPR.

Details of the accident. Role in the accident (driver or passenger), vehicle type (car, van, bus, lorry, motorcycle, bicycle, pedestrian), and a brief description of the accident were recorded from ambulance/ED case notes. Timings of the accident were taken from ambulance records (time of call, time of arrival at the scene of the accident, time of leaving the scene of the accident, and time of arrival at the ED). If the patient was not brought in by ambulance or if the above timings were not recorded in the patient's ambulance notes, a) the time of the accident was taken from the ED case notes (if recorded) or the participant was asked verbally and b) the time of arrival at the ED was taken from the EPR.

Medication administered following the accident. The type, dose and timing of any medication administered in the ambulance or ED was recorded. In addition, whether or not the participant received any opiate medication was recorded, as this has been associated with later PTSD (Bryant, Creamer, O'Donnell, Silove, & McFarlane, 2009).

[9] The Electronic Patient Record (EPR) is computer system used by the John Radcliffe Hospital Emergency Department to register patients presenting to the department and record their clinical management.

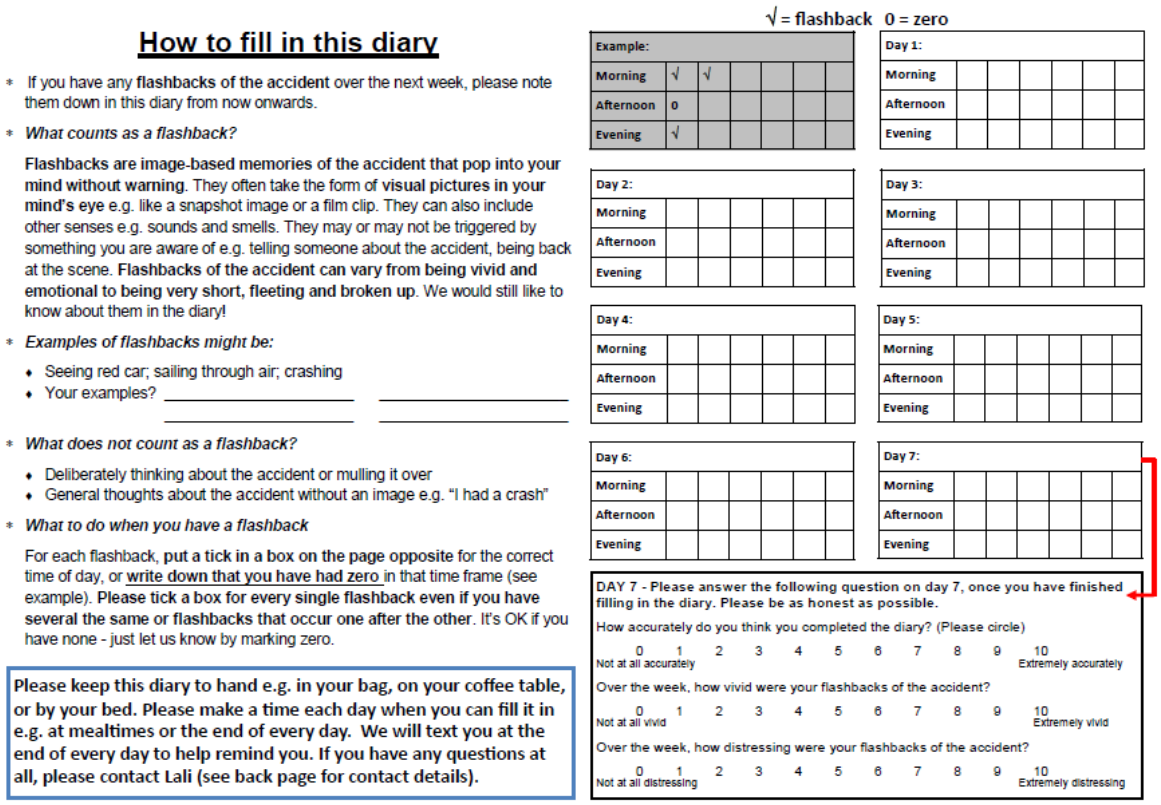
Heart rate. The earliest recording of participants' heart rate after presentation to the ED was taken from their medical records. If there was no record of heart rate in the ED notes, the last recording from the participant's ambulance record was used. Heart rate at emergency admission has been found to predict a diagnosis of PTSD at one month in road traffic accident survivors (Coronas et al., 2011).

Inpatient admission and time in hospital. Admission as an inpatient was recorded, as well as the ward the participant was admitted to (if relevant).

Injury Severity Score (ISS; Baker et al., 1974). The ISS is a widely used measure of the overall severity of physical injury. Injury severity in road traffic accident survivors has been found to predict later PTSD (Coronas et al,. 2011). The ISS was calculated using the Abbreviated Injury Scale 2005 Update 2008 (Association for the Advancement of Automotive Medicine, 2008) from information regarding participants' injuries recorded in their ED case notes and on the EPR. All ratings were checked by an ED Research Nurse trained in ISS scoring. There was 100% agreement in ratings.

Primary outcome measure

Intrusion Diary (adapted from Holmes et al., 2009; Holmes, James, et al., 2010). This simple pen-and-paper diary was used to assess the number of intrusive memories participants experienced in the week after the accident. The term "flashbacks" was used in the diary to describe intrusive memories of the accident, and defined as "image-based memories of the accident that pop into your mind without warning" (see Figure 5.2). Participants were asked to record each intrusive memory of the accident by ticking a box to show which day and time of day (morning, afternoon or evening) the intrusion occurred. At the end of the week, participants were asked to rate how accurately they thought they had completed the diary, and how vivid and distressing their intrusive memories had been over the week, each on a scale of 0 (*not at all*) to 10 (*extremely*). The full version of the Intrusion Diary is given in Appendix 5.4.



How to fill in this diary

* If you have any **flashbacks of the accident** over the next week, please note them down in this diary from now onwards.
* ***What counts as a flashback?***

  Flashbacks are image-based memories of the accident that pop into your mind without warning. They often take the form of **visual pictures in your mind's eye** e.g. like a snapshot image or a film clip. They can also include other senses e.g. sounds and smells. They may or may not be triggered by something you are aware of e.g. telling someone about the accident, being back at the scene. **Flashbacks of the accident can vary from being vivid and emotional to being very short, fleeting and broken up**. We would still like to know about them in the diary!
* ***Examples of flashbacks might be:***
  - Seeing red car; sailing through air; crashing
  - Your examples? _____ _____ _____ _____
* ***What does not count as a flashback?***
  - Deliberately thinking about the accident or mulling it over
  - General thoughts about the accident without an image e.g. "I had a crash"
* ***What to do when you have a flashback***

  For each flashback, **put a tick in a box on the page opposite** for the correct time of day, or **write down that you have had zero** in that time frame (see example). **Please tick a box for every single flashback even if you have several the same or flashbacks that occur one after the other**. It's OK if you have none - just let us know by marking zero.

Please keep this diary to hand e.g. in your bag, on your coffee table, or by your bed. Please make a time each day when you can fill it in e.g. at mealtimes or the end of every day. We will text you at the end of every day to help remind you. If you have any questions at all, please contact Lali (see back page for contact details).

√ = flashback 0 = zero

Example:						
Morning	√	√				
Afternoon	0					
Evening	√					

Day 1:						
Morning						
Afternoon						
Evening						

Day 2:						
Morning						
Afternoon						
Evening						

Day 3:						
Morning						
Afternoon						
Evening						

Day 4:						
Morning						
Afternoon						
Evening						

Day 5:						
Morning						
Afternoon						
Evening						

Day 6:						
Morning						
Afternoon						
Evening						

Day 7:						
Morning						
Afternoon						
Evening						

DAY 7 - Please answer the following question on day 7, once you have finished filling in the diary. Please be as honest as possible.

How accurately do you think you completed the diary? (Please circle)

0 1 2 3 4 5 6 7 8 9 10
Not at all accurately — Extremely accurately

Over the week, how vivid were your flashbacks of the accident?

0 1 2 3 4 5 6 7 8 9 10
Not at all vivid — Extremely vivid

Over the week, how distressing were your flashbacks of the accident?

0 1 2 3 4 5 6 7 8 9 10
Not at all distressing — Extremely distressing

Figure 5.2. Key pages from the Intrusion Diary (the primary outcome measure) used in the randomised controlled study.

Secondary outcome measures

a) Post-traumatic stress symptomatology

Impact of Events Scale-Revised (IES-R; Weiss & Marmer, 1997). The IES-R is a 22-item self-report questionnaire assessing the subjective distress caused by a traumatic event. Respondents rate how distressing each item has been for them during the past seven days on a 5-point scale from 0 (*not at all*) to 4 (*extremely*). Items are summed to give a total score (ranging 0 to 88), as well as PTSD symptom subscales scores for intrusions (7 items), avoidance (8 items), and hyperarousal (7 items). The measure shows high internal consistency ($\alpha = 0.96$) and high agreement with other measures of post-traumatic stress symptomatology e.g. the PTSD Checklist ($r = 0.84$) (Creamer, Bell, & Failla, 2003). The Impact of Events Scale is one of the most widely-used measures of trauma-related distress. It has been validated in road traffic accident survivors (J. G. Beck et al., 2008), used within the first week after an accident (e.g. Bryant & Harvey, 1996), and used as an outcome measure in previous randomised controlled trials of interventions after trauma (Bryant et al., 2008; Mouthaan et al., 2013). Further, the measure has been used in

experimental studies of cognitive task interventions after a trauma film (Holmes et al., 2009; Krans et al., 2013), suggesting that it is a useful translational outcome measure. In this study, participants were asked to rate items with respect to their recent road traffic accident, in relation to how things were before the accident (see Appendix 4.3).

Posttraumatic Diagnostic Scale (Foa et al., 1997). The PDS is a 49-item self-report questionnaire assessing post-traumatic stress symptoms related to the DSM-IV criteria for PTSD. As part of the PDS, respondents rate how often each of 17 symptoms bothered them in the last week or month, on the following 4-point scale: 0 (*not at all or only one time*), 1 (*once a week or less/once in a whil*e), 2 (*2 to 4 times a week/half the time*) and 3 (*5 or more times a week/almost always*). Ratings are used to provide a measure of the severity of PTSD symptoms (summed total for the 17 symptoms) as well as to aid in the diagnosis of PTSD (although it is not intended to be a replacement for a structured diagnostic interview). The PDS displays high internal consistency ($\alpha = .92$ for the symptom severity score), high test-retest reliability (e.g. 87% agreement between two time points with regards to diagnostic status) and satisfactory agreement with clinician-administered diagnostic interviews such as the CAPS (Foa et al., 1997).

The PDS has been used to assess post-traumatic stress symptoms within the first few weeks after a road traffic accident (Ehring, Ehlers, & Glucksman, 2006; Steel, Mahmood, & Holmes, 2008), and as an outcome measure in previous trials of early interventions after trauma (e.g. Rothbaum et al., 2012). In this study, participants were asked to complete the PDS at one week follow-up (using the one week instructions) and one month follow-up (using the one month instructions), with reference to their recent road traffic accident. Scores were used to provide an indication of the frequency of PTSD symptoms (total symptom severity and re-experiencing, avoidance and hyperarousal subscales) at one week and one month after the accident, and to indicate whether or not the symptoms endorsed were in line with the DSM-IV diagnostic criteria for PTSD.

b) Anxiety and depression

Hospital Anxiety and Depression Scale (HADS; Zigmond & Snaith, 1983). This widely-used 14-item questionnaire assesses symptoms of anxiety (7 items) and depression (7 items). Items are rated on a severity scale of 0 to 3 and summed to give total scores for anxiety (HADS-A) and depression (HADS-D). The measure has good internal consistency (HADS-A $\alpha = .68$ to .93, HADS-D $\alpha = .67$ to .90) and good concurrent validity (e.g.

correlations between HADS-A and State-Trait Anxiety Inventory of .64 to .81; correlations between HADS-D and Beck Depression Inventory of .71 to .73). The HADS has been validated in somatic patients, psychiatric patients and the general population (Bjelland et al., 2002). Here the measure was used to assess the severity of anxiety and depression symptoms at one week and one month after the road traffic accident.

Measures assessing post-traumatic risk factors

a) Additional questions at one week follow-up (Appendix 5.5)

Treatment since the last session. A single questionnaire item asked participants to indicate whether or not they had received any treatment since the last session (e.g. medication or psychological treatment), and if so to give brief details.

Playing Tetris in the week after the accident. Participants in the simple cognitive task condition only were asked to rate how much of the time they had imagined playing Tetris, and how much of the time they had played Tetris, when they had had an intrusive memory in the week after the accident. Each item was rated on a 9-point scale from 1 (*none of the time*) to 9 (*every time*).

b) *Additional questions at one month follow-up* (Appendix 5.6)

Treatment since the last session. As above.

Computer game play. Participants were asked to indicate whether or not they had played any computer games based on visual puzzles, such as the computer game Tetris, since the accident, and if so for how long.

Stressful life events. Participants were asked to indicate whether or not they had experienced any additional stressful life events since the accident, and if so to give brief details. Life stress following a traumatic event has been found to be one of the strongest predictors of PTSD symptoms (Brewin, Andrews & Valentine, 2000).

Other post-traumatic factors. Participants were asked to rate each of the following items on a scale from 1 (*not at all*) to 9 (*a great deal*): dwelling on memories of the accident (rumination); trying to push memories of the accident out of your mind (thought suppression); social support from family and friends following the accident; and positive effects of the accident. Rumination and thought suppression have been found to be cognitive predictors of PTSD in road traffic accident survivors (Ehlers et al., 1998), and

social support has been found to be one of the strongest predictors of PTSD across samples (Brewin et al., 2000; Ozer et al., 2003).

Participant experience of the study

Feedback Questionnaire. This questionnaire, administered at one month follow up, was designed to assess participant's experience of taking part in the study (see Appendix 5.7). Items assessed: how happy participants were to be offered something to do whilst waiting in the emergency department (rated on a 9-point scale from 1 [*not at all*] to 9 [*extremely happy*]); how much they predicted that what they were asked to do in the emergency department would increase or decrease their intrusive memories of the accident (rated on a 21-point scale from -10 [*extreme decrease*] to +10 [*extreme increase*]); how easy they found taking part in the study and how distressing or burdensome they found taking part in the study (both rated on a 9-point scale from 1 [*not at all*] to 9 [*extremely*]); suggestions for improving the study; and any other comments about the study (both free response items). Participants in the intervention condition were asked to complete a number of additional items regarding their experience of playing Tetris in the emergency department. Each of the following items was rated a 9-point scale from 1 (*not at all*) to 9 (*extremely*): how easy they found playing Tetris; how helpful they found playing Tetris; how distressing or burdensome they found playing Tetris; how willing they would be to play Tetris if they had a traumatic accident in the future; and how likely they would be to suggest playing Tetris if a friend had a similar accident. Finally, they were asked for any suggestions for improving using Tetris game play as something that might help after a traumatic event and for any other comments about using Tetris after a traumatic event (both free response items).

Tetris computer game

The computer game Tetris DS was played on a Nintendo DS XL: a hand-held gaming device with a screen size of 85 mm by 64 mm.

Figure 5.3 shows the timing that each measure was administered in the randomised controlled study.

	Emergency Department	One week follow-up	One month follow-up
Baseline measures			
Self-report measures			
Socio-Demographic Details	X		
Clinical History Form	X		
Perceived Life Threat	X		
PDEQ	X		
PDI	X		
Information from medical notes (e.g. details of the accident, medication, heart rate)	X		
ISS	X		
Simple cognitive task intervention			
Hotspots of the accident form	X		
Control			
Activity diary	X		
Outcome measures			
Intrusion Diary		X	
IES-R		X	X
PDS		X	X
HADS		X	X
Additional questions at one week follow-up		X	
Additional questions at one month follow-up			X
Feedback Questionnaire			X

Figure 5.3. Timing of measures in the randomised controlled study: within the emergency department, at one week follow-up and at one month follow-up.

Procedure

Figure 5.4 shows the procedure for the main randomised controlled study.

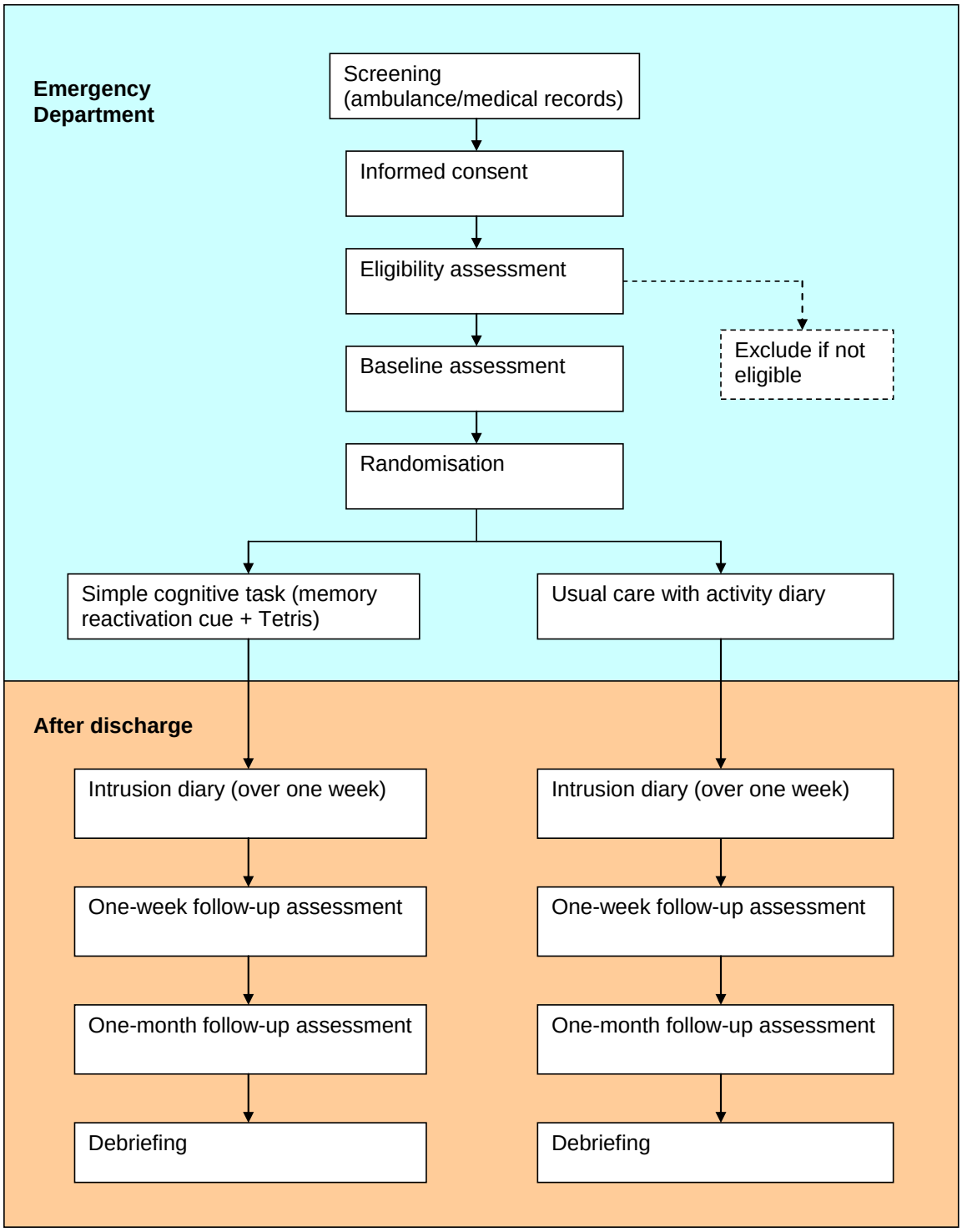


Figure 5.4. Diagram of the procedure for the randomised controlled study.

Screening. Patients were screened based on information from the ED online patient database ("FirstNet"[10]) and their ambulance and ED notes. Screening aimed to determine if patients met the following subset of inclusion criteria: aged 18 or over; experienced or witnessed a road traffic accident meeting the DSM-IV A1 criterion for PTSD; report memory of the accident; alert and orientated, GCS = 15; fluent in English; have sufficient physical mobility to use a hand-held gaming device (e.g. able to sit upright, use of both arms). If these criteria were met, a member of the ED staff asked the patient for verbal consent to speak to the researcher.

Informed consent. Participants were approached by the researcher during a settled time whilst they were waiting in the ED and provided with an information sheet about the study (see Appendix 5.8). They were given time to read this, ask questions, and consider whether or not they wished to participate. Those who decided to take part signed a consent form to indicate their decision (see Appendix 5.9).

Eligibility assessment. Participants were asked a series of questions to assess any remaining eligibility criteria, such as a reported history of severe mental illness, current substance abuse or a current neurological condition. Participants who no longer met eligibility criteria were excluded from the study.

Baseline assessment. Eligible participants completed the baseline measures in their own time. The researcher was present to assist with any queries. The researcher recorded additional baseline information from participants' medical notes.

Randomisation. Participants were randomised to the simple cognitive task or control group using a web-based randomisation system[11], accessed from computers at the emergency department. To ensure allocation concealment until the point of randomisation, the programme was accessed only after participants had completed the relevant baseline

[10] "FirstNet" is part of the Electronic Patient Record (EPR) system used by the John Radcliffe Hospital Emergency Department to register patients presenting to the department and record their clinical management.

[11] The randomisation system was written by the clinical trials software development team in the Oxford Cognitive Health and Neurosciences Clinical Trials Unit (OCHNCTU) and hosted by the Medical Sciences Information Management Unit (IMSU). The deployed software was fully validated using a combination of automated tests and manual checks, and the algorithms used were independently checked by statisticians at Oxford's Centre for Statistical Medicine (CSM). Randomisation was carried out using the minimisation method outlined by S. J. Pocock and Simon (1975), with a small random component to ensure that allocations remained unpredictable. Minimisation was based on gender (male/female), age (younger=18-30, middle=31-50, older=51+), and perceived life threat to self (low=0-4, high=5-10).

measures. Baseline scores were input to reveal the participant's group allocation. Appendix 5.10 shows screenshots for the randomisation system.

Simple cognitive task intervention. The researcher explained to the participant that they would be asked to play a computer game for approximately 20 minutes, and made any adjustments to help them remain comfortable and able to concentrate for this time e.g. adjusting their bed and pulling the curtain across. Participants were asked to think back to the accident for a moment and very briefly tell the researcher the worst moments of the accident that popped back to mind (typically two to three moments), which the researcher noted down on the "Hotspots of the accident" form (Appendix 3.5).

The researcher then demonstrated how to play the computer game Tetris on a Nintendo DS XL, and participants were given a chance to practice until they understood how to play the game. Participants were asked to play Tetris for approximately 20 minutes, but for as long as they wished. If a break was taken part way through the 20-minute period (e.g. due to interruption by staff or participant discomfort), participants were asked to briefly look at the "Hotspots of the accident" form again before resuming Tetris, and the timing of the break was recorded.

At the end of the 20-minute period, the researcher explained that 20 minutes was over, but that they were welcome to keep playing if they wanted to. All participants were told that over the next week, if they had an intrusive memory of the accident, they had the option of either playing Tetris (by downloading it on their phone or playing it online for free), or imagining playing Tetris (by closing their eyes and imagining the shapes), after recording an intrusive memory in their Intrusion Diary (see below).

Usual care with simple activity diary. Participants were asked to fill in a simple pen-and-paper record of the activities they did in the emergency department (see Activity Diary, Appendix 3.6). They were asked to note down briefly each activity in a few words (e.g. "talking with family", "reading"), and for how long they did each activity. They were left to fill in the activity diary for approximately 20 minutes, to provide a foil activity for a similar duration to the simple cognitive task intervention. Activity diaries were subsequently reviewed by the study researcher and an independent cognitive science researcher to rate whether participants engaged in any visuospatial activities during the 20-minute period, and if so for how long (results are given in Chapter 6).

Intrusion Diary. Before finishing the study in the ED, all participants were given instructions on how to fill in the Intrusion Diary over the next week, and a stamped addressed envelope to post back the diary in one week's time (but were also given the

option of collecting the diary from them if easier). Participants were contacted the day after the accident to check that they still had the diary and envelope, and understood how to fill in the diary. They were given a daily reminder between 6pm and 8pm by text (or by phone/email if preferred) to fill in the diary. One week after the accident, participants were contacted by telephone/email to remind them to return the diary in the post (or arrange a time to collect it from them). If participants were unable to return their original diary for any reason, they were asked to fill in and return a copy (any cases where this occurred was documented).

One week and one month follow-up assessments. Outcome measures were completed either online or in paper form by post, depending on participant preference. Online questionnaires were completed using Qualtrics software, whereby participants were emailed a secure link to access the questionnaires. Participants were contacted by telephone on the day to remind them to fill in the outcome measures.

Debriefing. Once their one month outcome measures were received, participants were debriefed about the study by telephone, and were able to ask any questions. They were sent a £30 store voucher in the post to thank them for their time, and a final email or letter with details of the research group website (where the results of the study would be available). Where participants' one month PDS symptom profiles were in line with the diagnostic criteria for PTSD, participants were not informed that their scores indicated potential psychological problems, but the final email or letter included advice to contact their GP in the first instance if they were concerned about their mood, and information about accessing local support and health services.

Participant safety. A risk management plan was created to specify that any participants who spontaneously reported suicidal ideation or intent during the one-week or one-month follow-up period would be advised to seek help (e.g. from their GP/emergency services). If a participant was thought to be at immediate risk and refusing to seek help, the appropriate services (e.g. their GP or emergency services) would be contacted, even without the participant's consent. These events would be recorded.

Statistical analysis plan

Statistical analyses were conducted using Statistical Package for the Social Sciences (SPSS) Version 20. Continuous variables were tested for normality by examining histograms and statistics of skewness and kurtosis. Values of larger than +/-1 for skewness and +/-3 for kurtosis indicated departure from normality (Stuart J. Pocock, Assmann, Enos, & Kasten, 2002). Where the distribution of the data suggested that a parametric test was not appropriate, data were either transformed or analysed using the equivalent non-parametric test. Given that this was a preliminary study of efficacy, and that the attrition rate was expected to be relatively low, per protocol analyses were conducted in addition to intention-to-treat analyses (see below). Corrections for multiple comparisons for the primary and secondary efficacy analyses were not applied, as it was considered preferable to make a type I error (i.e. incorrectly detect a difference that was not present) than a type II error (i.e. incorrectly reject a difference if one was present) in this early-phase trial.

Primary analysis

The primary efficacy analysis was a *t*-test of the difference in the number of intrusive memories recorded in the week after the accident (assessed using the Intrusion Diary) between the intervention and control groups, using an intention to treat analysis.

Secondary analyses

The secondary efficacy analyses were between-groups tests (*t*-tests and ANCOVAs as appropriate) carried out on a) the IES-R total and subscale scores, PDS symptom severity and subscale scores, HADS-A score and HADS-D score at one week and one month follow-up, using both the intention to treat population and the per protocol population and b) the number of intrusive memories recorded in the Intrusion Diary, using the per protocol population.

The difference in incidence of possible PTSD at one month (a dichotomous variable), assessed using the PDS, was tested using logistic regression. The percentage of participants with PDS scores consistent with possible PTSD at one month was calculated for each group, and the odds ratio (with 95% confidence interval) for the intervention compared to the control condition was calculated.

Intention to treat analysis

An intention to treat analysis includes all randomised participants in the groups to which they were randomly allocated. This conservative analysis approach is used in clinical trials to overcome bias due to non-compliance and missing outcomes (Gupta, 2011). In this study, multiple imputation was used to estimate missing values. Multiple imputation is a widely used method for managing missing data in clinical trials, and has been used in previous trials of preventative interventions after trauma (e.g. Mouthaan et al., 2013; Rothbaum et al., 2012). In SPSS, 5 data sets were generated for each missing value for one week follow-up data, and 10 data sets for each missing value for one month follow-up data, in line with the recommendation that the number of data sets approximately corresponds to the percentage of missing data (Bodner, 2008). Treatment group and key predictor variables (age, gender, and perceived life threat to self) were included as auxiliary variables (Sterne et al., 2009). Estimates were pooled in line with guidelines for multiple imputation (Rubin, 2004).

Per protocol analysis

The per protocol population was: a) all participants who received an adequate "dose" of the simple cognitive task intervention (if they were in the intervention group), defined as a memory reactivation cue followed by playing Tetris for at least one uninterrupted period of 10 minutes, and b) who completed the outcome measures for one week follow-up ("follow-up 1") and one month follow-up ("follow-up 2") within sufficient time to meaningfully relate to that time point, defined as under one month for follow-up 1 (to assess acute stress symptoms) and one month or more for follow-up 2 (to assess post-traumatic stress symptoms) (American Psychiatric Association, 2013).

Covariates

Covariates were not included in the primary efficacy analysis, for the following reasons. First, randomisation was expected to result in groups that were balanced on key baseline variables (Stuart J. Pocock et al., 2002). Second, the strength of the correlations between baseline variables and the primary outcome (the number of flashbacks) was unknown, hence a priori selection of baseline covariates might have reduced the power of the analysis if covariates were not prognostic of outcome (Kahan, Jairath, Dore, & Morris, 2014).

Secondary efficacy analyses, however, were run with and without adjustment for covariates. Covariate selection was based on the European Medicines Agency guideline on adjustment for baseline covariates in clinical trials (Committee for Medicinal Products for Human Use, 2015), which recommends adjustment for stratification variables (in this case age, gender and perceived life threat to self) and baseline factors known a priori to be strongly, or at least moderately, associated with outcome (in this case peritraumatic dissociation[12], assessed using the Peritraumatic Dissociative Experiences Questionnaire).

Comparison with wider population of road traffic accident admissions to the emergency department over the study period

Audit data were obtained from the Oxford University Hospitals NHS Trust Information Systems Team regarding patients aged 18 and over admitted to the Emergency Department during the period the study was conducted (March 2014 to January 2015). Summary statistics (broken down by month) were obtained for age, gender, numbers brought in by ambulance, and numbers presenting to the "majors" and "resuscitation" sections of the emergency department. These data were compared with corresponding summary statistics for the study sample, to provide an indication of how representative the study sample was of the wider population of road traffic accident patients presenting to the emergency department during the study period. Differences between the two groups were tested using t-tests for continuous data and Chi-square tests for categorical data (e.g. age, numbers brought in by ambulance and numbers presenting to the "majors" and "resuscitation" sections of the emergency department).

The results of the analyses are described in the next chapter.

[12] Peritraumatic dissociation was the only variable assessed at baseline that has been shown to be at least moderately associated with post-traumatic stress disorder symptoms in a previous meta-analysis (Ozer et al., 2003), indicated by an effect size of $r \geq .3$ (Cohen, 1988).

CHAPTER 6. Randomised Controlled Study – Results: A simple cognitive task intervention to reduce the occurrence of intrusive memories after a road traffic accident

Introduction

As described in Chapter 5, the "Evaluation" stage of the development of the simple cognitive task intervention involved conducting a randomised controlled study in the emergency department (see Figure 5.1, Chapter 5). The main aims of the randomised controlled study were to determine if the simple cognitive task intervention (a memory reactivation cue followed by playing the computer game Tetris), compared to usual care in the emergency department with a simple activity diary, could:

a) reduce the number of intrusive memories in the week after a road traffic accident (assessed using an Intrusion Diary) (*the primary aim*), and

b) reduce post-traumatic stress symptoms (PDS and IES-R scores), anxiety (HADS-A score) and depression (HADS-D score) at one week and one month after a road traffic accident (*secondary aims*).

This chapter presents the main results of the randomised controlled study. For clarity, the chapter is divided into three sections:

A. FLOW DIAGRAM AND STUDY SAMPLE: This section reports the progress of patients through the study and details of the randomised study sample, including demographic and baseline characteristics.

B. MAIN EFFICACY ANALYSES: This section presents the results of the pre-planned efficacy analyses to test the primary and secondary aims of the study (as above).

C. EXPLORATORY ANALYSES: This section describes a number of exploratory analyses that were conducted to examine differences between the intervention and control groups, and investigate possible moderators of the intervention effect.

A: FLOW DIAGRAM AND STUDY SAMPLE

CONSORT flow diagram

Figure 6.1 shows a flow diagram of the progress of patients through the randomised controlled study, based on the CONSORT[13] flow diagram (Schulz, Altman, Moher, & Group, 2010). The diagram summarises the phases of enrolment, group allocation, one week follow-up, one month follow-up, and data analyses. Only one participant allocated to the intervention group did not receive the full allocated intervention, as after 3 minutes of playing Tetris they were moved by staff to a different bay, and subsequently fell asleep. The loss to follow-up rate at one week was 3/37 (8%) in the intervention group and 1/34 (3%) in the control group, and at one month was 6/37 (16%) in the intervention group and 3/34 (9%) in the control group.

Intention to treat analyses included the whole sample. Per protocol analyses excluded participants who did not play Tetris for at least 10 minutes uninterrupted (intervention group only) and did not complete outcome measures within less than one month after the accident for one week follow-up or at one month or more for one month follow-up (see Chapter 5 for details of the intention to treat and per protocol analyses).

Over an 11-month period, 645 patients were screened for eligibility based on a subset of the eligibility criteria (see Chapter 5). The reasons that patients did not meet screening criteria (n = 505) are detailed in Table 6.1. The main reasons were that patients could not be seen within 6 hours of leaving the scene of the accident (e.g. the accident occurred a few days ago), or that they had insufficient physical mobility to play a computer game on the intervention platform (a Nintendo DS XL) (e.g. they had injured their arm or wrist). Of the 140 patients who met the screening criteria and were approached about the study, 67 (48%) declined to participate. Table 6.2 shows the reasons that patients declined to participate in the study. The main reasons were that they were not feeling well enough or wanted to leave the emergency department as soon as they were discharged. Of the 73 patients who consented to take part in the study and were assessed for the full set of eligibility criteria, two were excluded as they did not meet the eligibility criteria. Reasons for exclusion are shown in Table 6.3.

[13] The "Consolidated Standards of Reporting Trials" (CONSORT) group has produced an evidence-based, minimum set of recommendations for the transparent reporting of randomised controlled trials.

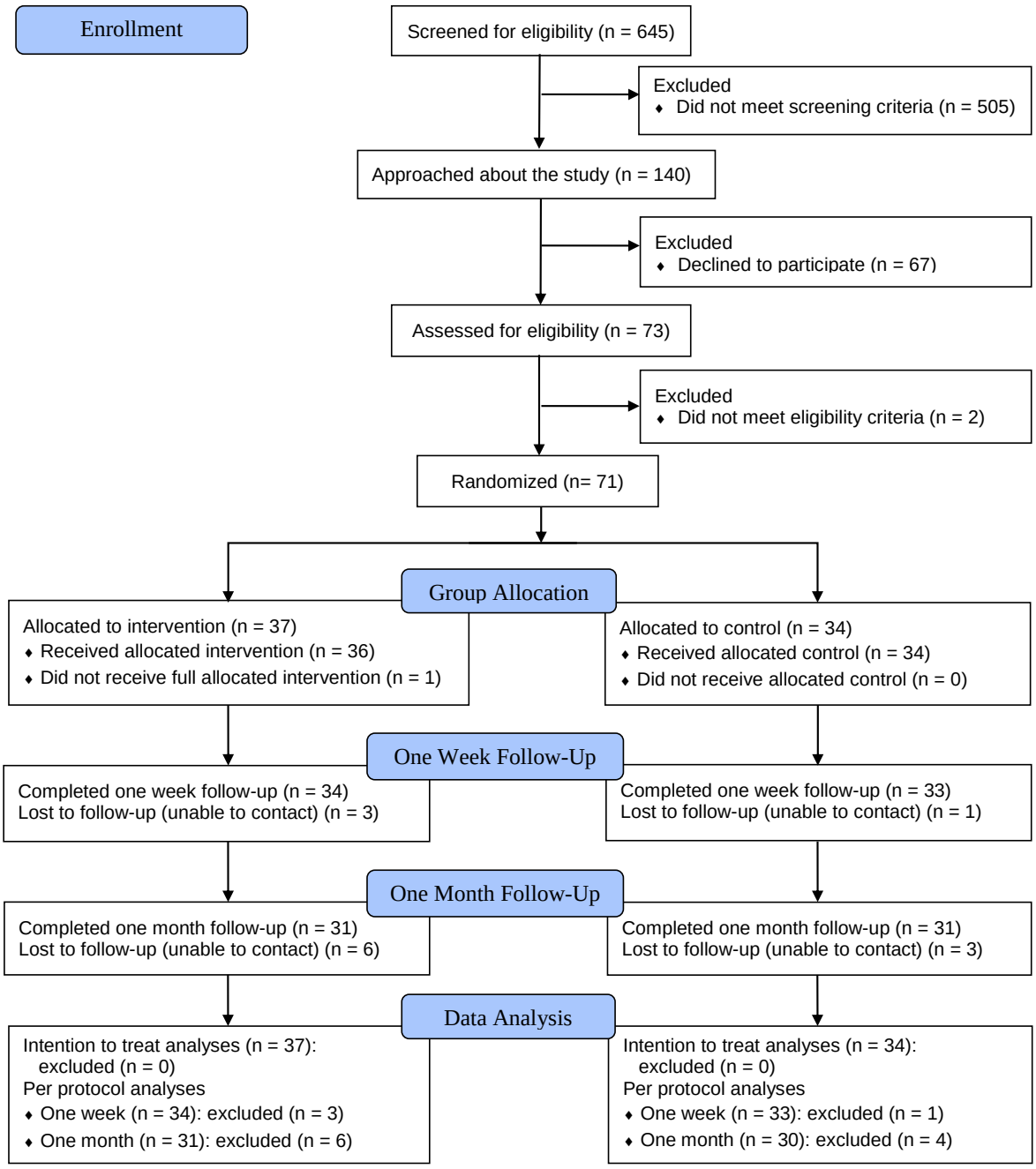


Figure 6.1. CONSORT flow diagram for patients in the randomised controlled study

Table 6.1. Reasons Patients Did Not Meet Screening Criteria (n = 505)

Reason patient did not meet screening criteria	*n*
Could not be seen within 6 hours of leaving scene of accident	166
Insufficient physical mobility to play computer game	108
Under 18	53
Did not meet DSM-IV criterion A1	39
No memory of accident	24
GCS < 15	21
Not fluent in English	14
Neurological condition	11
Loss of consciousness > 5 mins	6
Intoxicated	4
History of severe mental illness	3
Suicidal	2
Substance abuse	1
Not able to complete study procedures (no glasses; deaf; unable to look at computer screen due to migraine; drowsy from medication; insufficient time to be seen before discharge)	53
TOTAL	505

Table 6.2. Reasons Patients Declined to Participate (n = 67)

Reason patient declined to participate	*n*
Not feeling up to it/not well enough	13
Due to be discharged soon, want to leave ED ASAP	10
Did not give verbal consent to be approached by researcher	10
Too tired	6
Would rather not/not for me	6
Don’t have time	5
In pain	4
Headache	3
Did not want to fill in questionnaires	3
Did not want to play a computer game	3
Worried about family member	2
Did not wish to disclose any personal information	1
Too distressed	1
TOTAL	67

Table 6.3. Reasons Patients Did Not Meet Eligibility Criteria (n = 2)

Reasons patient did not meet eligibility criteria	*n*
Not sufficiently fluent in English	1
Neurological condition	1
TOTAL	2

Randomised study sample

A final sample of 71 eligible participants was recruited to the study, consisting of 34 men and 37 women, with a mean age of 39.66 years (*SD* 16.32). Further demographic details are provided in Table 6.5.

Comparison with wider population of road traffic accident admissions to the Emergency Department over the study period

Table 6.4 shows a comparison of the study sample (*n* = 71) with the wider population of all road traffic accident patients aged 18 and over who presented to the Emergency Department during the 11-month period study was being conducted (*n* = 2298). The two samples were compared on available emergency department data from the Trust Information Systems Team (age, gender, numbers brought in by ambulance, and numbers admitted to the "majors" or "resuscitation" sections of the emergency department). Chapter 5 provides details of how these data were obtained.

Whilst the mean age of the study sample was comparable to that of the wider population, there was a significantly higher proportion of females in the study sample than in the wider population of road traffic accident patients presenting to the emergency department. There was also a significantly higher proportion of patients in the study sample who were brought in by ambulance, and seen in the resuscitation or majors area over the minors area, than in the wider population.

Table 6.4. Comparison of Study Sample (n = 71) and Wider Population of Road Traffic Accident Admissions to the Emergency Department Over the Study Period (n = 2298)

	Study sample (n = 71)	Wider population (n = 2298)	t-test / χ^2 test
Age, *M* (*SD*)	39.66 (16.32)	38.17 (17.04)	$t(2367) = 0.727$, $p = .468$
Gender, female, *n* (%)	37 (52.1%)	903 (39.3%)	$\chi^2(2369) = 4.663$, $p = .031$
Brought in by ambulance, *n* (%)	54 (76.1%)	1175 (51.1%)	$\chi^2(2369) = 17.149$, $p < .001$
Location in ED			$\chi^2(2369) = 21.315$, $p < .001$
Resuscitation, *n* (%)	14 (19.7%)	229 (10.0%)	
Majors, *n* (%)	26 (36.6%)	475 (20.7%)	
Minors/Other, *n* (%)	31 (43.7%)	1594 (67.4%)	

Demographic information

Demographic information for the intervention and control groups is given in Table 6.5. The results of between-groups comparisons indicated no significant differences between the two groups on any demographic variables at the .05 level[14].

[14] Correction for multiple comparisons was not applied, as it was considered preferable to make a type I error (i.e. incorrectly detect a difference that was not present) than a type II error (i.e. incorrectly reject a difference if one was present) in this early stage trial.

Table 6.5. Demographic Information for Intervention and Control Groups (N = 71)

Demographic variable	Simple cognitive task (*n* = 37)	Control (*n* = 34)	Between-groups analysis[a]
Gender, female, *n* (%)	20 (54.1%)	17 (50.0%)	$\chi^2(71) = 0.117$, $p = .733$
Age in years, *M* (*SD*)	38.91 (16.09)	40.47 (16.77)	$t(69) = 0397$, $p = .693$
Range	18 - 77	20 - 85	
Years in education, *M* (*SD*)	15.89 (3.34)	15.18 (3.21)	$t(69) = 0.920$, $p = .362$
Non-White British, *n* (%)	9 (24.3%)	6 (17.6%)	$\chi^2(71) = 0.474$, $p = .491$
Marital status			
Single, *n* (%)	18 (48.6%)	17 (50.0%)	Fisher's Exact $p = .891$
Married or cohabiting, *n* (%)	17 (45.9%)	14 (41.2%)	
Divorced, *n* (%)	2 (5.4%)	2 (5.9%)	
Widowed, *n* (%)	0 (0%)	1 (2.9%)	
Employment status			
Employed, *n* (%)	26 (70.3%)	24 (70.6%)	Fisher's Exact $p = .896$
Unemployed, *n* (%)	0 (0%)	1 (2.9%)	
Student, *n* (%)	7 (18.9%)	5 (14.7%)	
Retired, *n* (%)	4 (10.8%)	4 (11.8%)	

[a] *t*-test was used for continuous data, χ^2 test for frequency data, and Fisher's Exact test for frequency data where > 20% of expected frequencies were ≤ 5.

Baseline characteristics

Table 6.6 shows a comparison of baseline variables between the intervention and control groups. There were no significant differences between the two groups on any baseline variables at the .05 level, with the exception of a higher percentage of participants that were passengers in the accident (as opposed to drivers) in the control group (18.2%) than the intervention group (0%). Importantly, perceived life threat to self, peritraumatic dissociation (PDEQ score) and peritraumatic distress (PDI score), which were found to be the main peritraumatic risk factors for PTSD symptoms in a meta-analysis (Ozer et al., 2003), were balanced between the two groups.

Table 6.6. Baseline Characteristics for Intervention and Control Groups (N = 71)

Baseline variable	Simple cognitive task (*n* = 37)	Control (*n* = 34)	Between-groups analysis[a]
Details of the accident			
Vehicle			Fisher's Exact *p* = .209
Car/van/bus, *n* (%)	19 (51.4%)	17 (50%)	
Motorcyclist, *n* (%)	6 (16.2%)	5 (14.7%)	
Cyclist, *n* (%)	12 (32.4%)	8 (23.5%)	
Pedestrian, *n* (%)	0 (0%)	4 (11.8%)	
Driver status (for car/van/bus/motorcycle)[b]			Fisher's Exact *p* = .041
Driver, *n* (%)	25 (100%)	18 (81.8%)	
Passenger, *n* (%)	0 (0%)	4 (18.2%)	
Brought in by ambulance, *n* (%)	29 (78.4%)	25 (73.5%)	$\chi^2(1,71) = 0.229$, *p* = .632
Location in ED			$\chi^2(2,71) = 1.584$, *p* = .451
Resuscitation, *n* (%)	8 (21.6%)	6 (17.6%)	
Majors, *n* (%)	11 (27.9%)	15 (44.1%)	
Minors/Other, *n* (%)	18 (48.6%)	13 (38.2%)	
Time since accident (hrs:mins), *M* (*SD*)	3:12 (1:09)	3:31 (1:07)	*t*(69) = 1.203, *p* = .233
Peritraumatic variables			
Perceived Life Threat			
Self, *M* (*SD*)	5.19 (3.20)	5.56 (3.23)	*t*(69) = 0.484, *p* = .630
Other, *M* (*SD*)	2.22 (3.25)	3.56 (3.99)	*t*(69) = 1.398, *p* = .166
PDEQ score, *M* (*SD*)	19.86 (8.02)	19.18 (8.40)	*t*(69) = 0.387, *p* = .700
PDI score, *M* (*SD*)	18.70 (10.36)	16.59 (10.34)	*t*(69) = 0.860, *p* = .393
ISS, *M* (*SD*)	1.46 (2.34)	1.97 (2.10)	*t*(69) = 0.755, *p* = .453
0	8 (21.6%)	8 (23.5%)	Fisher's Exact *p* = .100
1	22 (59.5%)	12 (35.3%)	
2-5	6 (16.2%)	13 (38.2%)	
6 and over	1 (2.7%)	1 (2.9%)	
Heart rate, M (SD)[c]	75.11 (12.44)	76.57 (10.48)	t(69) = 0.511, *p* = .611
Opiate medication administered after the accident, *n* (%)	8 (21.6%)	9 (26.5%)	χ^2 (1,71) = 0.229, *p* = .632
Admitted as inpatient, *n* (%)	10 (27.0%)	10 (29.4%)	χ^2 (1,71) = 0.050, *p* = .823

Table 6.6. continued

Baseline variable	Simple cognitive task (n = 37)	Control (n = 34)	Between-groups analysis[a]
Pre-trauma variables			
Clinical History Form[d]			
Current mental health problem, *n* (%)	3 (8.3%)	4 (11.8%)	Fisher's Exact p = .706
Previous mental health problem, *n* (%)	4 (11.1%)	2 (5.9%)	Fisher's Exact p = .674
Family history of mental health problem, *n* (%)	10 (27.8%)	7 (20.6%)	χ^2 (1,71) = 0.492, p = .483
Prior trauma, *n* (%)	28 (77.8%)	24 (70.6%)	χ^2 (1,71) = 0.473, p = .492
Number of previous ED attendances in last year			χ^2 (1,71) = 0.599, p = .439
0, *n* (%)	31 (83.8%)	26 (76.5%)	
1 - 4, *n* (%)	6 (16.2%)	8 (23.5%)	

Note. PDEQ = Peritraumatic Dissociative Experiences Questionnaire; PDI = Peritraumatic Distress Inventory; ISS = Injury Severity Score.
[a] *t*-test was used for continuous data, χ^2 test for frequency data, and Fisher's Exact test for frequency data where > 20% of expected frequencies were ≤ 5.
[b] n = 25 in the simple cognitive task group, n = 22 in the control group
[c] n = 30 in the control group (heart rate recording was missing for 4 participants)
[d] n = 33 in the control group (one participant did not complete Clinical History Form)

B: MAIN EFFICACY ANALYSES

Primary outcome: the number of intrusive memories in the week after the accident

The primary efficacy analysis was an unadjusted intention-to-treat analysis[15] (*t*-test) of the difference in the number of intrusive memories in the week after the accident (recorded in an Intrusion Diary) between the simple cognitive task intervention group and the control group. The result showed that, as predicted, the number of intrusive memories was significantly lower in the simple cognitive task group than in the control group, with a medium effect size[16]: pooled t = 2.800, p = .005, d = 0.665, 95% CI [0.184, 1.141].

[15] The intention to treat analysis included all participants randomised to the simple cognitive task (n = 37) and control (n = 34) groups. Missing values were estimated using multiple imputation (see Chapter 5 p. 5.26).

[16] Effect sizes were interpreted as follows: d = 0.2 as a small effect, d = 0.5 as a medium effect and d = 0.8 as a strong effect (Cohen, 1988).

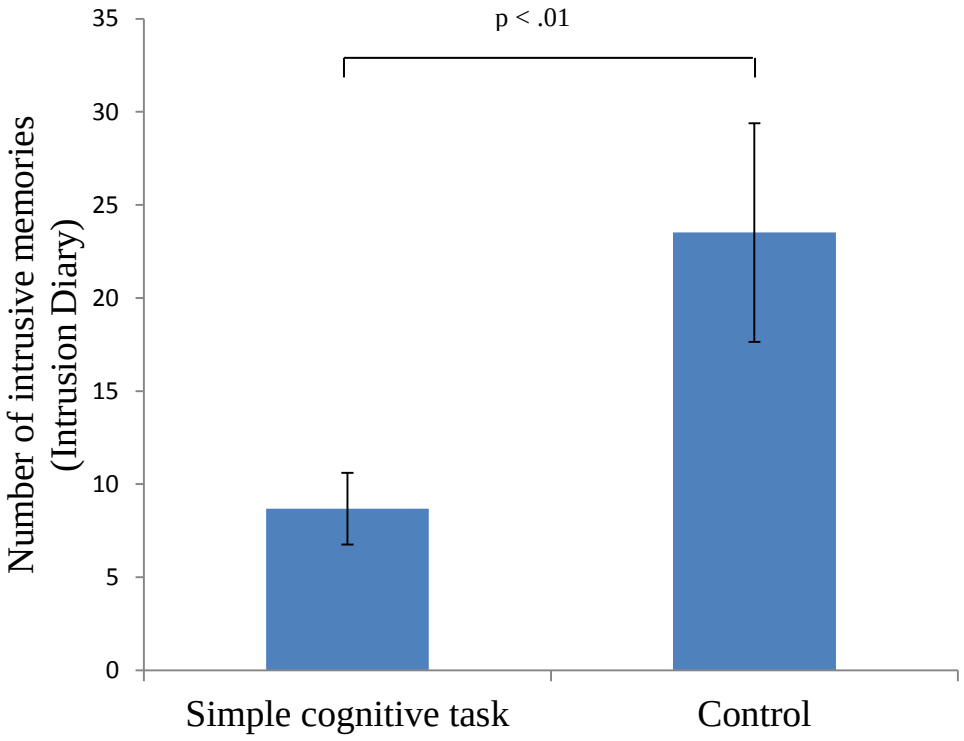


Figure 6.2. Mean number of intrusive memories in the week after the accident (recorded in an Intrusion Diary) in the simple cognitive task and control groups. Error bars show the standard error of the mean.

Figure 6.2 illustrates that participants in the simple cognitive task intervention group recorded approximately one third of the number of intrusive memories (n = 34, M = 8.68, SD = 11.22) recorded by participants in the control group (n = 33, M = 23.52, SD = 33.73). When the intention-to-treat analysis was conducted with adjustment for baseline covariates[17] (using an ANCOVA), the result showed a stronger effect size than for the unadjusted intention-to-treat analysis: pooled t = 3.156, p = .002, d = 0.750, 95% CI [0.256, 1.230]. Finally the result of the per protocol analysis of the primary outcome showed a similar effect size to the unadjusted intention-to-treat analysis: $t(65)$ = 2.733, p = .008, d = 0.678, 95% CI [0.22, 1.42]. Participant ratings of accuracy of diary completion (0-10) were high and did not differ significantly between the intervention (M = 8.5, SD = 1.3) and control (M = 8.0, SD= 1.9) groups.

[17] Covariates included in the analysis were age, gender, perceived life threat to self and peritraumatic dissociation (see Chapter 5).

Secondary outcomes

As for the primary outcome, the difference between the simple cognitive task and control groups on each of the secondary outcome measures was analysed using a) an unadjusted intention to treat analysis (*t*-test), b) an intention to treat analysis with adjustment for baseline covariates (ANCOVA) and c) a per protocol analysis (*t*-test). Results are presented for the secondary outcomes at one week, followed by the secondary outcomes at one month. All continuous outcomes were transformed with the exception of the one week IES-Intrusion subscale score and the one week PDS-Reexperiencing subscale score.

One week* s*econdary outcomes

Table 6.7 shows the means and standard deviations of one week secondary outcomes (vividness and distress of intrusive memories in the Intrusion Diary, IES-R subscale and total scores, PDS subscales and total scores and HADS anxiety and depression scores) for the simple cognitive task intervention and control groups. Results of the intention-to-treat *t*-test, intention-to-treat ANCOVA (with adjustment for covariates), per protocol *t*-test and intention to treat effect size (with 95% CI), are shown for each variable. Figure 6.3 shows bar charts of the results for the IES-R, PDS and HADS.

The results show that the simple cognitive task group, compared to the control group, had significantly lower scores on the IES-Intrusion subscale (pooled $t = 2.251$, $p = .024$, $d = 0.535$, 95% CI [0.059, 1.007]), and lower scores on the PDS-Reexperiencing subscale that did not quite reach significance (pooled $t = 1.891$, $p = .059$, $d = 0.449$, 95% CI [-0.024, 0.919]). Both of these differences showed medium effect sizes. The results were similar across the unadjusted intention-to-treat analysis, adjusted intention-to-treat analysis and per protocol analysis.

Table 6.7. Comparison of One Week Secondary Outcomes Measures (Intrusion Diary, IES-R, PDS and HADS) Between the Intervention and Control Groups

One week secondary outcome measure	Simple cognitive task (*n* = 34) *M* (*SD*)	Control (*n* = 33) *M* (*SD*)	Intention to treat *t* (*p*)	Adjusted intention to treat *t* (*p*)	Per protocol *t (p)*	Effect size *d* [95% CI][a]
Intrusion diary						
Vividness[b]	5.12 (3.28)	6.00 (2.44)	n/a	n/a	1.115 (.271)	0.300 [-0.231, 0.828]
Distress[b]	3.48 (2.77)	4.61 (3.13)	n/a	n/a	1.417 (.162)	0.381 [-0.152, 0.911]
IES-R scores (distress caused by the accident)						
Intrusion	7.26 (5.29)	10.73 (7.42)	2.251 (.024)	2.621 (.009)	2.205 (.031)	0.535 [0.059, 1.007]
Avoidance	7.50 (7.16)	8.06 (8.07)	0.256 (.798)	0.159 (.874)	0.154 (.878)	0.037 [-0.429, 0.503]
Hyperarousal	5.06 (5.54)	7.00 (7.60)	0.958 (.338)	1.340 (.181)	1.025 (.309)	0.228 [-0.240, 0.694]
Total	19.82 (16.66)	25.79 (21.40)	1.112 (.266)	1.320 (.190)	1.228 (.224)	0.264 [-0.205, 0.731]
PDS scores (frequency of ASD symptoms)						
Re-experiencing	4.03 (2.50)	5.64 (3.94)	1.891 (.059)	1.910 (.058)	1.987 (.052)	0.449 [-0.024, 0.919]
Avoidance	4.15 (3.89)	4.27 (5.09)	0.072 (.943)	0.254 (.799)	0.028 (.977)	0.017 [-0.449, 0.483]
Hyperarousal	3.06 (2.80)	4.36 (4.11)	1.197 (.233)	1.415 (.158)	1.268 (.209)	0.280 [-0.189, 0.747]
Total Symptom Severity	11.24 (8.26)	14.27 (11.90)	0.856 (.393)	1.420 (.159)	1.213 (.229)	0.203 [-0.265, 0.669]
HADS scores						
Anxiety	5.03 (3.93)	5.67 (5.00)	0.234 (.815)	0.257 (.798)	0.183 (.855)	0.056 [-0.410, 0.522]
Depression	3.00 (2.76)	4.21 (4.13)	0.945 (.345	1.010 (.313)	1.048 (.299)	0.225 [-0.243, 0.691]

Note. IES-R = Impact of Events Scale-Revised; PDS = Posttraumatic Diagnostic Scale; HADS = Hospital Anxiety and Depression Scale; n/a = not applicable (missing values could not be imputed as the variable was not rated for participants with 0 intrusive memories)

[a] Cohen's *d* = t [Sqrt(1/*n*1 + 1/*n*2)], 95% CI calculated using http://www.latrobe.edu.au/psy/research/cognitive-and-developmental-psychology/

[b] *n* = 25 in the simple cognitive task group, *n* = 31 in the control group, as variable could not be rated for participants with 0 intrusive memories. Effect sizes were calculated from the per protocol analysis

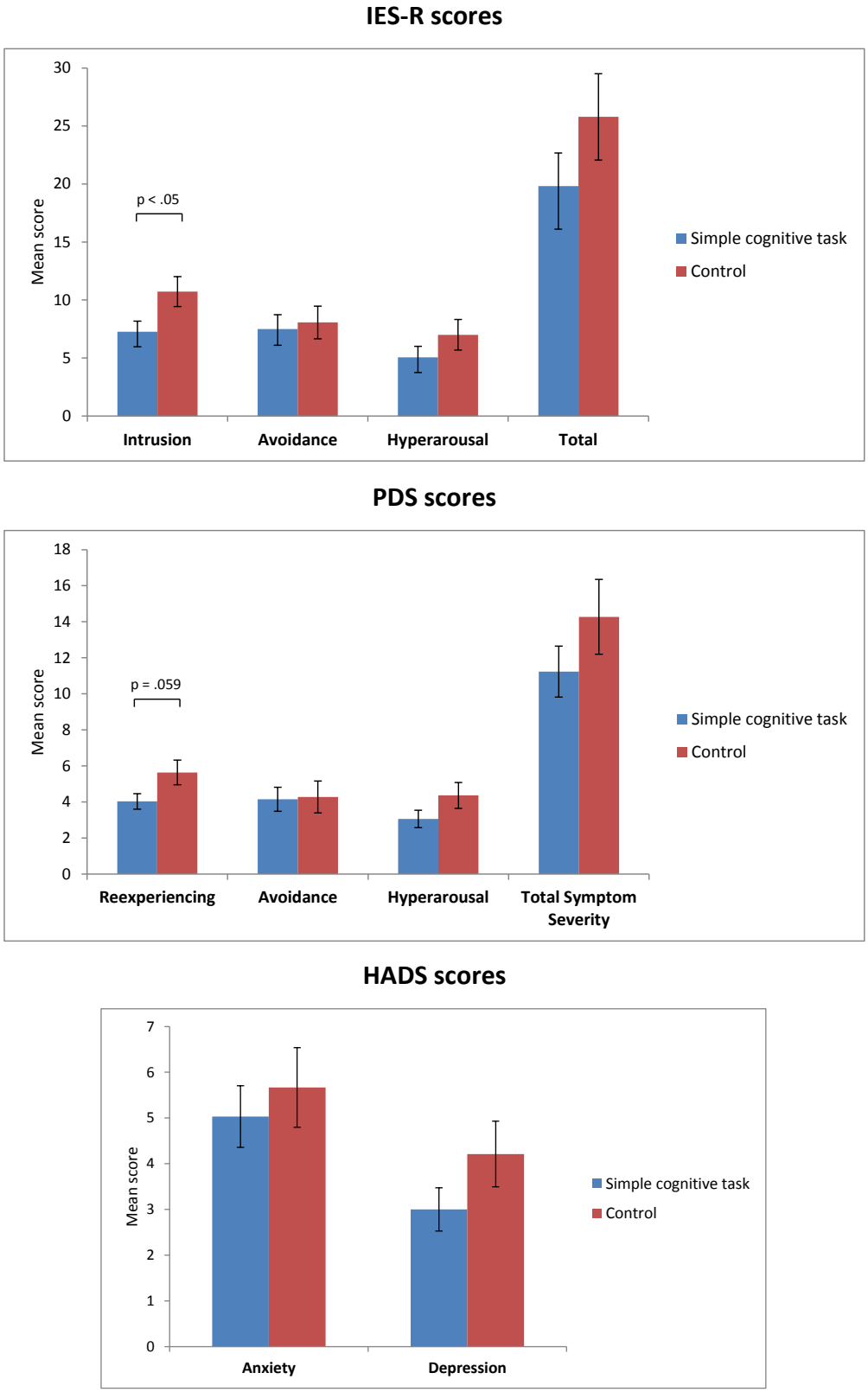


Figure 6.3. Bar charts of one week secondary outcome measures (IES-R, PDS and HADS) for the intervention and control groups. Results indicate a significant difference in IES-R Intrusion subscale score, and a trend difference in PDS Re-experiencing symptoms score.

One month secondary outcomes

Table 6.8 shows the means and standard deviations of one month secondary outcome scores (IES-R subscale and total scores, PDS subscales and total scores and HADS anxiety and depression scores) for the simple cognitive task intervention and control groups. Results of the unadjusted intention-to-treat analysis, adjusted intention-to-treat analysis, per protocol analyses and intention-to-treat effect size (with 95% CI) are shown for each variable. Figure 6.4 shows bar charts of these results.

There were no significant differences between the simple cognitive task intervention and control groups on any one month secondary outcome variables. However, there were small effect sizes (indicated by $d = 0.2$ or above) for the difference in IES-R intrusion symptoms (pooled $t = 0.926$, $p = .354$, $d = 0.220$, 95% CI [-0.248, 0.686]) and PDS Reexperiencing symptoms (pooled $t = 0.927$, $p = .354$, $d = 0.220$, 95% CI [-0.248, 0.686]) between the intervention and control groups.

One month PTSD symptoms

Table 6.9 shows the number and percentage of participants in the intervention and control groups with PDS scores consistent with the DSM-IV criteria for PTSD, the result of the intention to treat logistic regression, and the odds ratio of the difference for each variable. There was no significant difference between the two groups in the percentage of participants with PDS scores consistent with all criteria for PTSD, or for any individual PTSD criteria.

Table 6.8. Comparison of One Month Secondary Outcome Measures (IES-R, PDS and HADS) Between the Intervention and Control Groups

One month secondary outcome measure	Simple cognitive task (n = 31) M (SD)	Control (n = 31) M (SD)	Intention to treat t (p)	Adjusted intention to treat t (p)	Per protocol t (p)[a]	Effects size d [95% CI][b]
IES-R scores (distress caused by the event)						
Intrusion	5.26 (4.77)	6.94 (6.86)	0.926 (.354)	1.023 (.307)	0.518 (.606)	0.220 [-0.248, 0.686]
Avoidance	4.90 (6.05)	5.03 (6.96)	0.006 (.995)	0.059 (.953)	0.471 (.639)	0.001 [-0.465, 0.467]
Hyperarousal	4.06 (4.70)	5.16 (6.53)	0.592 (.554)	0.687 (.492)	0.253 (.801)	0.141 [-0.326, 0.627]
Total	14.23 (14.09)	17.13 (19.53)	0.461 (.645)	0.509 (.611)	0.134 (.894)	0.110 [-0.356, 0.576]
PDS scores (frequency of PTSD symptoms)						
Re-experiencing	3.26 (2.73)	3.74 (3.22)	0.927 (.354)	1.072 (.284)	0.660 (.512)	0.220 [-0.248, 0.686]
Avoidance	3.58 (4.20)	2.97 (4.48)	0.765 (.445)	0.673 (.501)	1.166 (.248)	0.182 [-0.285, 0.648]
Hyperarousal	2.77 (3.04)	3.45 (3.90)	0.791 (.429)	0.790 (.429)	0.345 (.732)	0.188 [-0.279, 0.694]
Total Symptom Severity	9.61 (8.82)	10.16 (10.99)	0.122 (.903)	0.418 (.676)	0.014 (.989)	0.029 [-0.437, 0.495]
HADS scores						
Anxiety	4.84 (4.39)	4.94 (4.77)	0.436 (.663)	0.319 (.750)	0.008 (.994)	0.104 [-0.362, 0.570]
Depression	2.68 (2.70)	3.32 (4.07)	0.087 (.931)	0.031 (.893)	0.268 (.790)	0.021 [-0.445, 0.487]

Note. IES-R = Impact of Events Scale-Revised; PDS = Posttraumatic Diagnostic Scale; HADS = Hospital Anxiety and Depression Scale

[a] For the per protocol analysis, n = 31 in the simple cognitive task group and n = 30 in the control group as one participant did not meet the protocol requirement that outcome measures were completed at least one month after the accident (this participant completed their one month outcome measures three days early in error)

[b] Cohen's d = t [Sqrt(1/n1 + 1/n2)], 95% CI calculated using http://www.latrobe.edu.au/psy/research/cognitive-and-developmental-psychology/

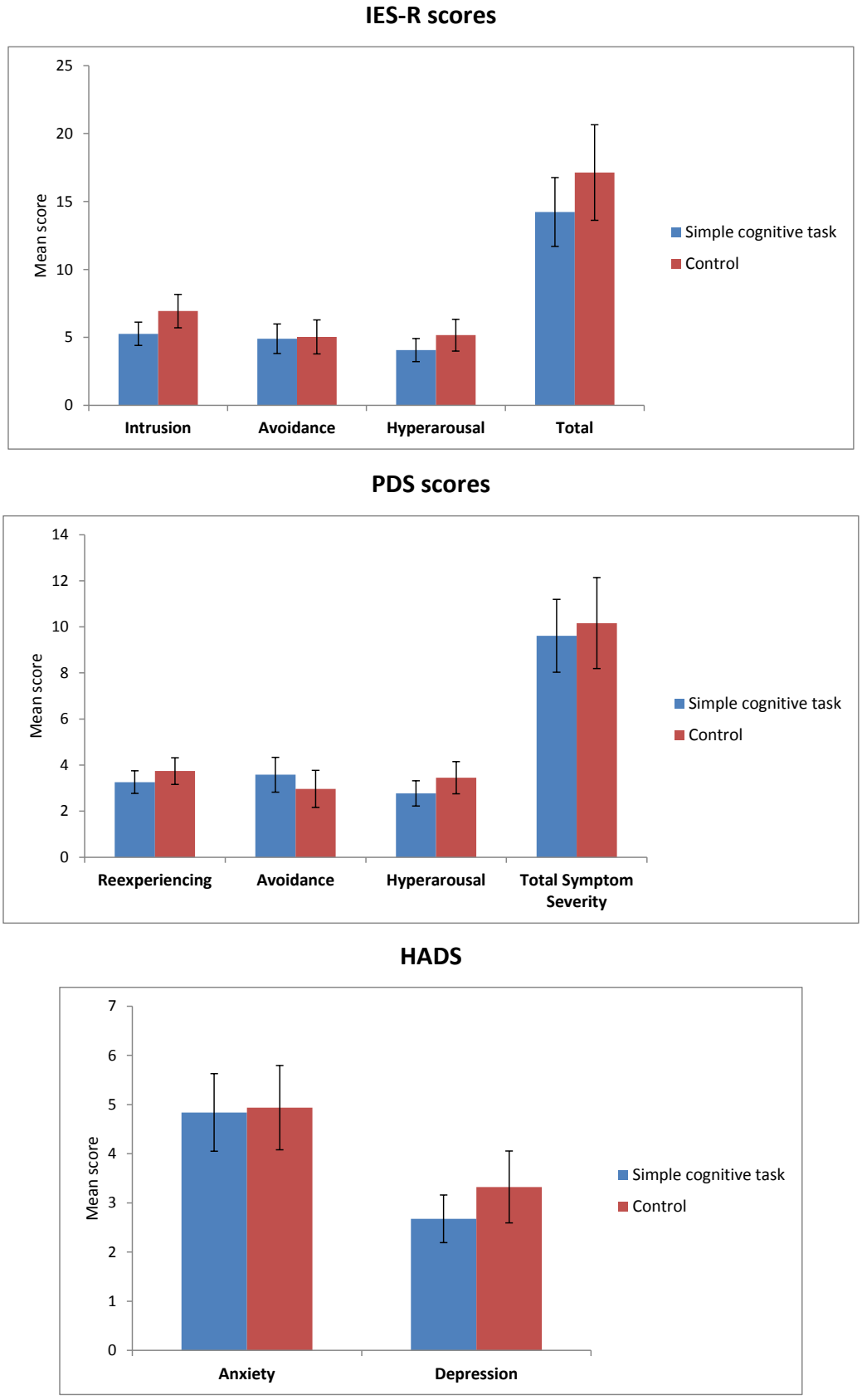


Figure 6.4. Bar charts of one month secondary outcome measures (IES-R, PDS and HADS) for the intervention and control groups. Results indicate no significant difference between the two groups.

Table 6.9. Comparison of PTSD Symptoms at One Month Between the Intervention and Control Groups: PDS Scores Consistent with DSM-IV Criteria for PTSD

PDS scores consistent with DSM-IV criteria for PTSD	Simple cognitive task (*n* = 31) *n* (%)	Control (*n* = 31) *n* (%)	Intention to treat *B* (*p*)	Odds ratio for intention to treat [95% CI]
All criteria for PTSD	4 (12.9%)	3 (9.7%)	0.476 (.534)	1.610 [0.359, 7.226]
Criterion A1: Traumatic event[a]	31 (100%)	31 (100%)		
Criterion A2: Fear, helplessness, horror[b]	25 (80.6%)	26 (83.9%)	0.084 (.900)	0.919 [0.245, 3.443]
Criterion B: Reexperiencing	25 (80.6%)	29 (93.5%)	1.442 (.082)	0.237 [0.047, 1.203]
Criterion C: Avoidance	10 (32.3%)	5 (16.1%)	0.967 (.130)	2.631 [0.751, 9.216]
Criterion D: Hyperarousal	17 (54.8%)	17 (54.8%)	0.038 (.943)	0.963 [0.336, 2.759]
Criterion E: Duration[c]	31 (100%)	30 (96.8%)	0.088 (.939)	0.916 [0.094, 8.969]
Criterion F: Impairment	15 (48.4%)	17 (54.8%)	0.323 (.544)	0.724 [0.254, 2.062]

Note. PTSD = Post-traumatic stress disorder; PDS = Posttraumatic Diagnostic Scale; DSM-IV = Diagnostic and Statistical Manual for Mental Disorders (4th Edition)

[a] All participants were assessed to meet criterion A1 as part of the eligibility assessment in the Emergency Department

[b] Corresponding PDS items were administered at one week follow-up

[c] Criterion E was inferred from length of time after the accident that one month PDS was completed. Consequently, one participant in the control group did not meet this criterion as they completed their one month outcome measures three days early in error.

C: EXPLORATORY ANALYSES

Exploratory analyses were conducted to a) investigate further the pattern and correlates of intrusive memories in the first week after the accident, including their time course over the first seven days, b) further explore differences in secondary outcomes, c) examine participants' hotspots of the accident, d) examine responses on the activity diary (control condition only), e) shed light on possible moderators of the intervention effect, and f) compare post-traumatic risk factors between the intervention and control groups.

Intrusive memories in the week after the accident

Distribution of the total number of intrusive memories

Figure 6.5 shows a boxplot of the total number of intrusive memories recorded in the Intrusion Diary in the week after the accident for the intervention and control groups. The overall distribution of data was lower in the simple cognitive task group than the control group, and that the control group contained four outliers with high numbers of intrusive memories in the week after the accident. Figure 6.6 shows a histogram of the total number of intrusive memories in the week after the accident for the intervention and control groups. A notable observation is the high percentage of participants in the simple cognitive task group who recorded no intrusive memories in the week after the accident.

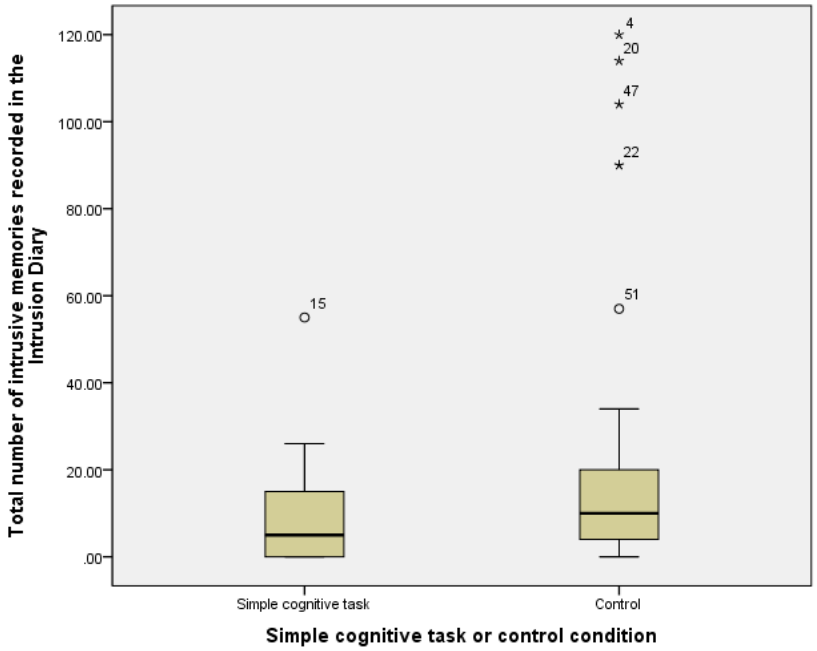


Figure 6.5. Boxplot of the number of intrusive memories in the week after the accident (recorded in the Intrusion Diary) for the intervention and control groups.

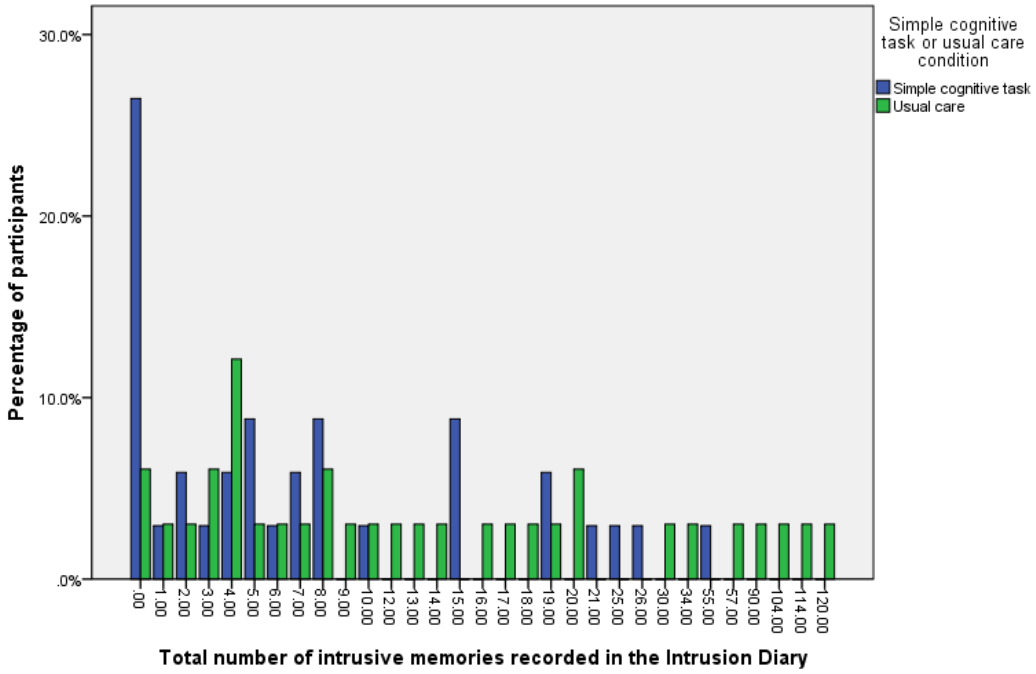


Figure 6.6. Histogram of the total number of intrusive memories in the week after the accident for the intervention and control groups.

Total number of intrusive memories as a categorical variable

To examine the difference between the intervention and control groups when the total number of intrusive memories was analysed as a binary categorical variable, a series of chi-square tests were conducted to compare the percentage of participants in each group with 0 intrusive memories (versus 1 or more), 0-1 intrusive memories (versus 2 or more), 0-2 intrusive memories (versus 3 or more) and so on (see Table 6.10). The results indicate that a significantly higher percentage of participants in the simple cognitive task group than the control group had two or fewer flashbacks, but this difference was no longer significant for three or fewer flashbacks.

Table 6.10. Comparison of Total Number of Intrusive Memories as a Categorical Variable Between the Intervention and Control Groups (N = 71)

Total number of intrusive memories in the week after the accident	Simple cognitive task (*n* = 34) Number of people (% out of 34)	Control (*n* = 33) Number of people (% out of 33)	χ^2 (*p*)	Odds ratio
0	9 (26.5%)	2 (6.1%)	5.084 (.045)	5.580
0-1	10 (29.4%)	3 (9.1%)	4.422 (.035)	4.167
0-2	12 (35.3%)	4 (12.1%)	4.947 (.026)	3.955
0-3	13 (38.2%)	6 (18.2%)	3.315 (.069)	2.786
0-4	15 (44.1%)	10 (30.3%)	1.366 (.242)	1.816

Time course of the number of intrusive memories over the first seven days

The time course of the number of intrusive memories over the first seven days after the accident was examined using a number of non-linear time series analyses[18] (similar to James et al., 2015). The first analysis examined the time course of the distribution of the number of intrusive memories on each of the first seven days after the accident for the intervention and control groups (see Figure 6.7). Overall, the distribution of the number of intrusive memories was lower in the simple cognitive task than the control group. The slope of the line indicates that there was an overall decrease in the number of intrusive memories in the simple cognitive task group from day 1 to day 7, whilst this reduction was not apparent in the control group. Both groups showed a slight increase in the number of intrusive memories on day 2, which appears more marked in the control group than the simple cognitive task group.

[18] The time series analyses were conducted with Professor Michael Bonsall, Professor of Mathematical Biology, University of Oxford. His input is gratefully acknowledged.

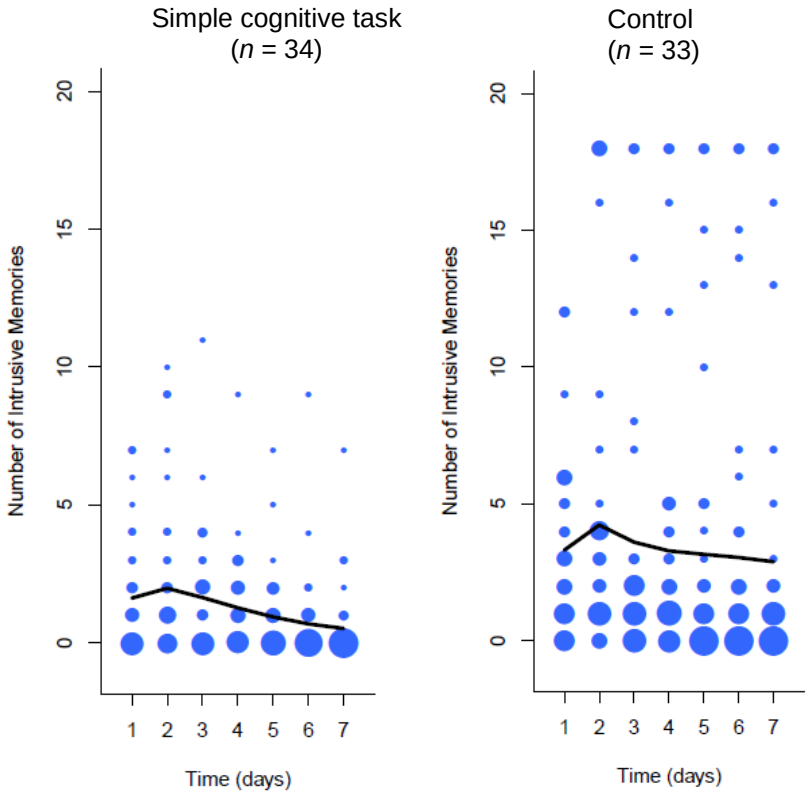


Figure 6.7. Time course graphs showing the distribution of the number of intrusive memories recorded it the Intrusion Diary on each of the first seven days after the road traffic accident in the simple cognitive task and control groups. The size of the circles represents the number of participants that recorded the indicated number of intrusive memories. The solid lines show the results of a generalised additive model to summarise the number of intrusive memories per day.

To explore further the change in the number of intrusive memories over time in the two groups, probability distributions for the predicted number of intrusive memories on Day 2 and Day 7 (using Poisson distributions) were examined for the intervention and control groups (see Figure 6.8)[19]. The graphs indicate a notably higher predicted likelihood of having fewer intrusive memories (e.g. 60% probability of 0 intrusive memories) on Day 7 than Day 2 in the simple cognitive task group, whereas there was little difference in the predicted likelihood of the number of intrusive memories between Day 2 and Day 7 in the control group.

[19] Day 2 was selected as this was the first full day for which all participants recorded intrusive memories, and therefore offered a better comparison than Day 1, which was not a full day for all participants as many participants had the accident part way through the day.

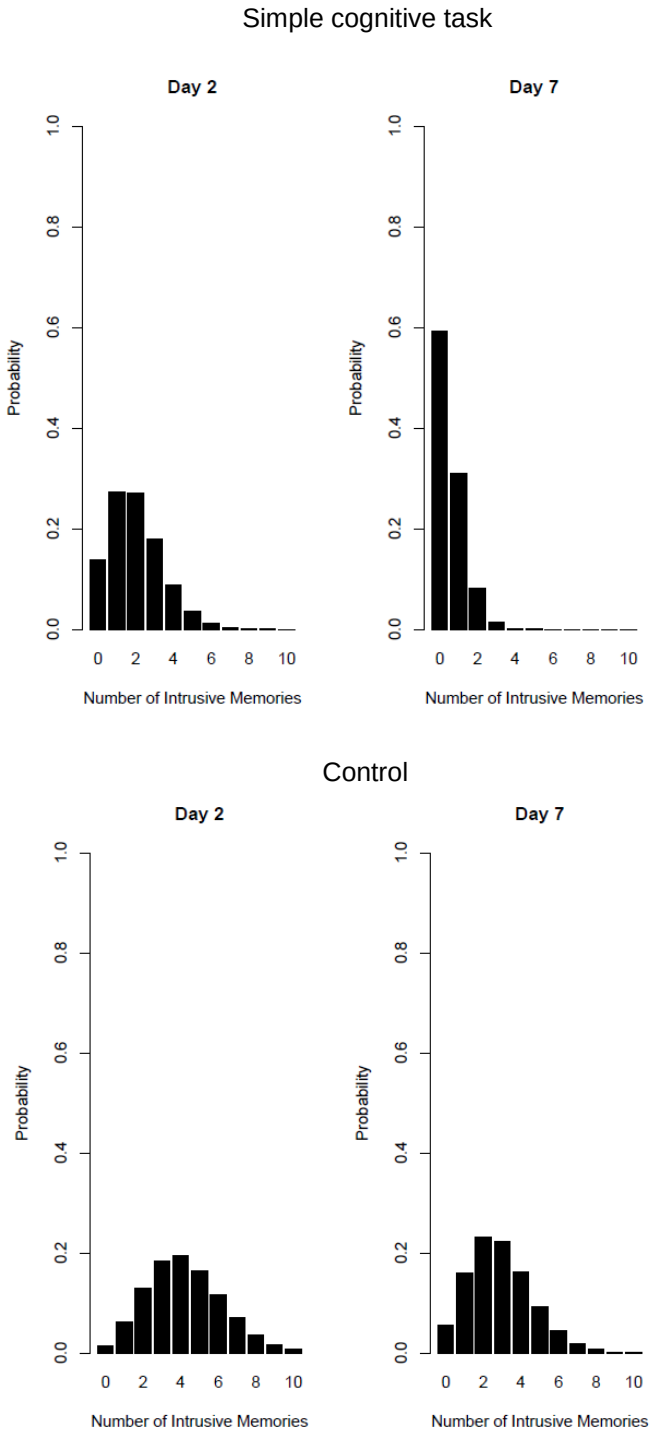


Figure 6.8. Probability distributions of the number of intrusive memories on Day 2 and Day 7 for the intervention (above) and control (below) groups.

Given that perceived life threat was hypothesized to be a key baseline predictor of post-traumatic stress symptoms, the next set of analyses examined the time course of the number of intrusive memories for participants with low (rating of 0 to 4) and high (rating

of 5 to 10) scores on the Perceived Life Threat to Self rating in the intervention and control groups (see Figure 6.9). Again, probability distributions on Day 2 and Day 7 were examined to assess the predicted likelihood of the number of intrusive memories in each of the four groups (see Figure 6.10).

Figure 6.9 indicates that, regardless of perceived life threat, the distribution of the number of intrusive memories was lower for participants in the simple cognitive group than the control group. However, the solid regression lines indicate a more rapid decrease in the number of intrusive memories over the seven days in participants with low than high perceived life threat in the intervention group, whilst this difference was not apparent in the control group. The probability distributions on Figure 6.10 show that in the simple cognitive group, participants with low perceived life threat had a more marked increase in the probability of having fewer intrusive memories at Day 7 than Day 2 (e.g. approximately a 95% probability of having 0 intrusive memories on Day 7), than participants with high perceived life threat (e.g. approximately a 40% probability of having 0 intrusive memories on Day 7). In the control group, there was little difference between participants with low and high perceived life threat in the change in probability of the number of intrusive memories from Day 2 to Day 7.

Baseline characteristics associated with the number of intrusive memories

As the number of intrusive memories in the week after a trauma has not been used as a primary outcome in previous intervention trials, it was interesting to examine which participant demographic and baseline characteristics were associated with this outcome. Partial correlations were calculated between each demographic/baseline variable and the number of intrusive memories in the week after the accident, controlling for group (intervention or control). The only variable that was significantly correlated with the number of intrusive memories in the week after the accident (controlling for group) was peritraumatic dissociation (PDEQ score): $r = .368$, $p = .003$.

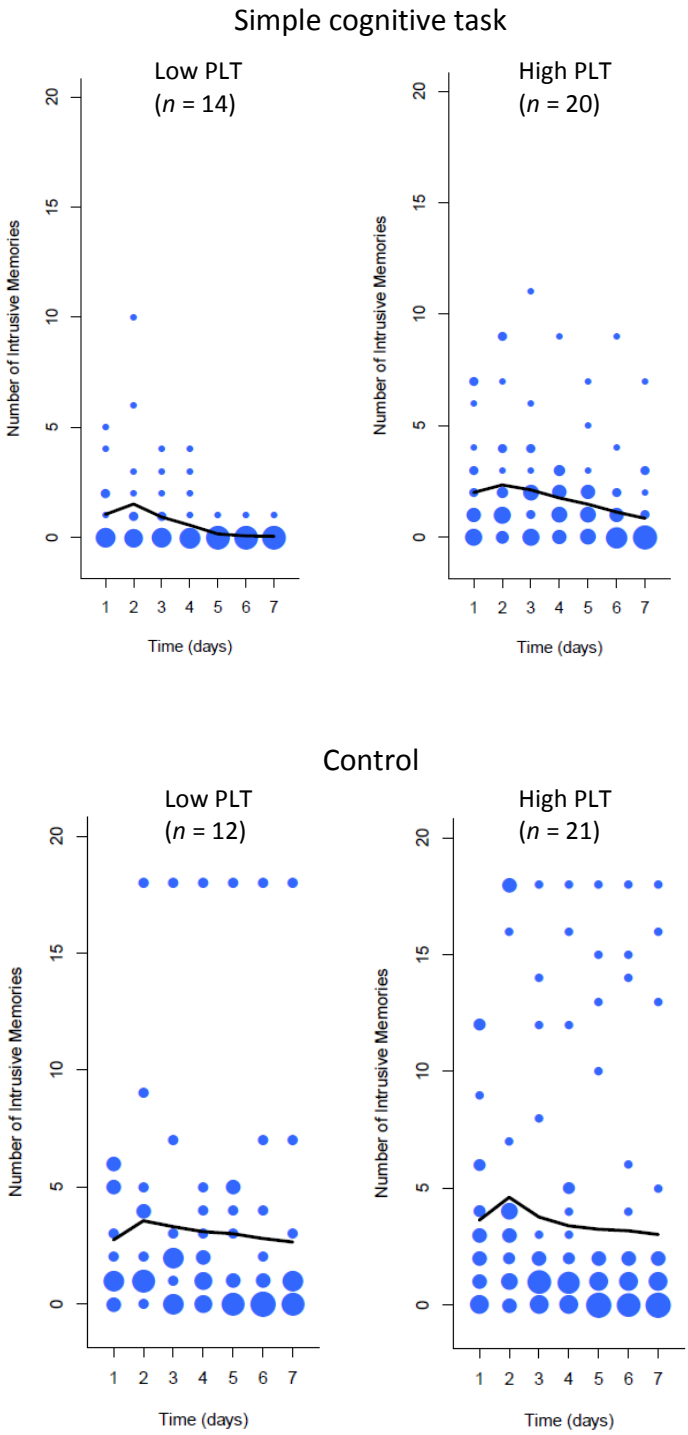


Figure 6.9. Time course graphs of the number of intrusive memories recorded in the Intrusion Diary over first seven days after the accident for participants with low (left hand side) and high (right hand side) perceived life threat in the simple cognitive task and control groups. The size of the circles represents the number of participants that recorded the indicated number of intrusive memories. The solid lines show the results of a generalised additive model to summarise the number of intrusive memories per day.

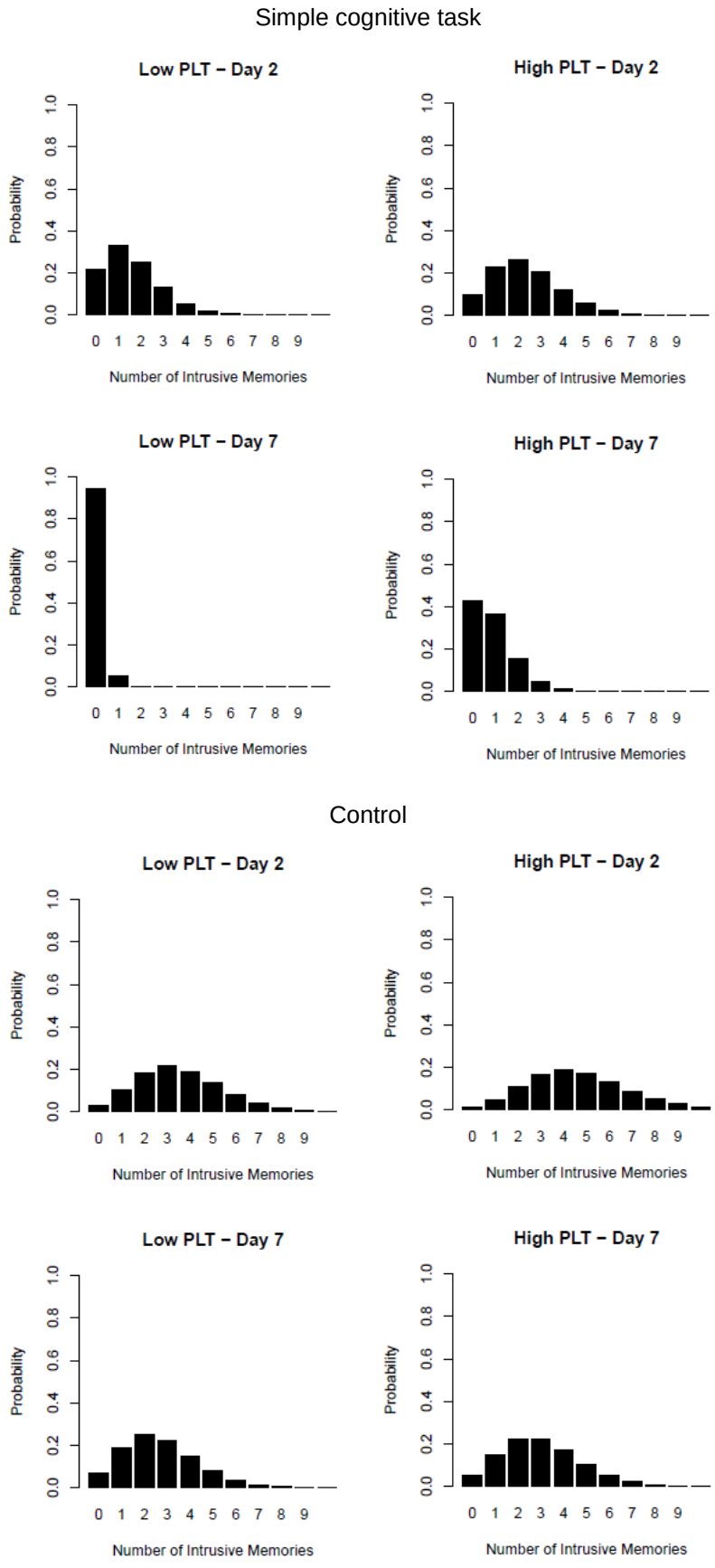


Figure 6.10. Probability distributions of the number of intrusive memories on Day 2 and Day 7 for participants with high and low perceived life threat in the intervention (above) and control (below) groups.

Exploratory analyses of secondary outcomes

Two sets of exploratory analyses on the secondary outcome measures were conducted. The first examined differences between the two groups on all outcome measures (one week and one month) for the subsample of participants meeting criterion A2 for PTSD (bringing the sample in line with that of a recent early intervention trial (Rothbaum et al., 2012). The second examined one month outcome measures for the subsample of participants with high perceived life threat, who were thought to be at great risk of PTSD symptoms.

Outcomes for participants with PDS scores consistent with DSM-IV criterion A2 for PTSD

A randomised controlled trial of a preventive intervention after trauma (Rothbaum et al., 2012), published after the start of this study, included patients who met the DSM-IV criterion A for PTSD, implying that participants met both criterion A1 ("the person experienced, witnessed, or was confronted with an event or events that involved actual or threatened death or serious injury, or a threat to the physical integrity of self or others") and criterion A2 ("the person's response involved intense fear, helplessness, or horror"). In this study, criterion A2 was not included as an eligibility criterion, given that its value as a necessary diagnostic criterion for PTSD has been questioned (e.g. Karam, 2010)[20]. However, in this study items from the PDS were used to assess criterion A2 one week after the accident. Therefore the primary and secondary efficacy analyses were conducted for the subgroup of participants with PDS scores consistent with Criterion A2, to examine the pattern of results when the sample was brought in line with that of Rothbaum et al. (2012).

Table 6.11 indicates that there were significant differences between the intervention and control groups in the number of intrusive memories in the week after the accident (recorded in the Intrusion Diary), and IES-Intrusion score and PDS-Reexperiencing score at one week after the accident. Reassuringly, this pattern of results was similar to that found for the full sample.

[20] Criterion A2 was subsequently excluded from the DSM-5 diagnostic criteria for PTSD (APA, 2013) whilst this study was in progress.

Table 6.11. Comparison of Outcomes Between Intervention and Control Groups for Participants with PDS Scores Consistent with DSM-IV Criterion A2 for PTSD

Outcome variable	Simple cognitive task *M* (*SD*)	Control *M* (*SD*)	*t*-test	Effect size[a]
	n = 27	*n* = 27	*t* (*p*)	*d* [95% CI]
Primary outcome measure				
Intrusion diary, number of intrusive memories	9.93 (12.05)	23.67 (31.84)	2.553 (.014)	0.571 [0.024, 1.113]
Secondary outcome measures, one week				
Intrusion diary				
Vividness[b]	5.67 (3.28)	5.93 (2.38)	0.305 (.762)	0.091 [-0.443, 0.624]
Distress[b]	3.86 (2.87)	4.85 (3.17)	1.123 (.267)	0.327 [-0.249, 0.899]
IES-R scores				
Intrusion	7.63 (5.29)	11.81 (7.16)	2.443 (.018)	0.664 [0.113, 1.209]
Avoidance	8.26 (7.37)	8.44 (8.50)	0.236 (.814)	0.023 [-0.511, 0.556]
Hyperarousal	5.37 (5.66)	7.81 (7.84)	1.212 (.231)	0.357 [-0.182, 0.893]
Total	21.26 (16.80)	28.07 (21.96)	1.211 (.231)	0.348 [-0.191, 0.884]
PDS scores				
Re-experiencing	4.26 (2.43)	6.41 (3.88)	2.441 (.019)	0.664 [0.113, 1.209]
Avoidance	4.41 (3.85)	4.85 (5.46)	0.073 (.942)	0.020 [-0.514, 0.553]
Hyperarousal	3.15 (2.71)	4.93 (4.28)	1.823 (.075)	0.497 [-0.048, 1.036]
Total Symptom Severity	11.81 (7.94)	16.19 (12.27)	1.518 (.135)	0.424 [-0.118, 0.992]
HADS scores				
Anxiety	5.30 (3.92)	6.22 (5.24)	0.241 (.811)	0.199 [-0.337, 0.733]
Depression	3.33 (2.67)	4.48 (4.29)	0.637 (.527)	0.322 [-0.217, 0.857]
Secondary outcome measures, one month	*n* = 25	*n* = 26	*t* (*p*)	*d* [95% CI]
IES-R scores				
Intrusion	5.76 (4.89)	7.31 (7.20)	0.401 (.690)	0.252 [-0.301, 0.802]
Avoidance	5.20 (5.99)	5.35 (7.46)	0.435 (.665)	0.022 [-0.527, 0.571]
Hyperarousal	4.40 (4.96)	5.46 (6.97)	0.246 (.807)	0.175 [-0.376, 0.724]
Total	15.36 (14.29)	18.12 (20.85)	0.083 (.934)	0.154 [-0.397, 0.703]
PDS scores				
Re-experiencing	3.48 (2.74)	3.88 (3.36)	0.694 (.491)	0.130 [-0.420, 0.679]
Avoidance	3.88 (3.40)	3.08 (4.59)	0.870 (.389)	0.198 [-0.353, 0.747]
Hyperarousal	2.96 (3.13)	3.73 (4.05)	0.560 (.578)	0.213 [-0.339, 0.763]
Total Symptom Severity	10.32 (8.94)	10.69 (11.38)	0.125 (.901)	0.036 [-0.513, 0.585]
HADS scores				
Anxiety	5.04 (4.17)	5.19 (4.98)	0.091 (.928)	0.033 [-0.516, 0.582]
Depression	2.72 (2.59)	3.42 (4.18)	0.030 (.926)	0.201 [-0.350, 0.750]

Note. PTSD = Post-traumatic stress disorder; DSM-IV = Diagnostic and Statistical Manual for Mental Disorders (4th Edition); IES-R = Impact of Events Scale-Revised; PDS = Posttraumatic Diagnostic Scale; HADS = Hospital Anxiety and Depression Scale. [a] Cohen's *d* calculated from means and pooled standard deviation, 95% CI calculated using http://www.latrobe.edu.au/psy/research/cognitive-and-developmental-psychology/. [b] *n* = 21 in the simple cognitive task group, as variable was not rated for participants with 0 intrusive memories

One month secondary outcomes for participants with high perceived life threat

Results of the main secondary efficacy analyses for one month outcomes found no significant differences between the two groups. However, the study was not powered to detect a difference in PTSD symptomatology at this time point. One exploratory hypothesis was that there may be a more marked difference between the two groups for participants at higher risk of PTSD symptoms. Perceived life threat was one of the strongest predictors of PTSD symptoms in a meta-analysis (Ozer et al., 2003). In this study, high perceived life threat was defined as a score of 5 to 10 on the "Perceived Life Threat to Self" rating, in line with the minimisation categories used at randomisation.

Table 6.12 shows the means and standard deviations of one month post-traumatic stress symptom scores (IES-R and PDS) for participants with low and high perceived life threat in the intervention and control groups.

Table 6.12. Comparison of Outcomes Between Intervention and Control Groups for Participants with High Perceived Life Threat (N = 38)

Outcome variable	Simple cognitive task (n = 19) M (SD)	Control (n = 19) M (SD)	t (p)	Effect size d [95% CI][a]
IES-R scores (distress caused by the accident)				
Intrusion	6.53 (5.31)	9.05 (7.69)	0.984 (.698)	0.319 [-0.299, 0.933]
Avoidance	5.32 (6.70)	7.21 (8.00)	0.933 (.357)	0.303 [-0.315, 0.917]
Hyperarousal	5.21 (5.37)	6.89 (7.69)	0.447 (.658)	0.145 [-0.469, 0.757]
Total	17.05 (16.05)	23.16 (22.60)	0.837 (.408)	0.272 [-0.345, 0.886]
PDS scores (frequency of PTSD symptoms)				
Re-experiencing	4.26 (2.70)	4.37 (3.68)	0.530 (.603)[b]	0.034 [-0.602, 0.670]
Avoidance	3.89 (4.54)	4.00 (5.43)	0.278 (.783)	0.090 [-0.523, 0.702]
Hyperarousal	3.42 (3.32)	4.47 (4.49)	0.822 (.417)	0.267 [-0.350, 0.881]
Total	11.58 (9.66)	12.84 (13.09)	0.186 (.853)	0.060 [-0.553, 0.672]
HADS scores				
Anxiety	5.16 (4.44)	6.05 (5.21)	0.659 (.514)	0.214 [-0.402, 0.827]
Depression	2.79 (2.57)	4.47 (4.67)	1.377 (.180)[c]	0.447 [-0.176, 1.065]

Note. IES-R = Impact of Events Scale-Revised; PDS = Posttraumatic Diagnostic Scale; HADS = Hospital Anxiety and Depression Scale

[a] Cohen's *d* calculated from means and pooled standard deviation, 95% CI calculated using http://www.latrobe.edu.au/psy/research/cognitive-and-developmental-psychology/

[b] Mann-Whitney U test used: value indicates the z score

Whilst mean scores on all one month outcomes were lower in the simple cognitive task group than the control group, none of the differences were significant at the 0.05 level. However, examination of the effect sizes for the differences shows that there were weak effect sizes (indicated by a cohen's *d* value of approximately 0.2 or above) for IES-Hyperarousal, PDS-Avoidance and PDS-Total, and a moderate effect size for HADS-Depression score. Visual inspection shows that the effect sizes were stronger for the subsample of participants with high perceived life threat than for the whole sample (see Table 6.8).

Hotspots of the accident

"Hotspots" are the parts of a traumatic experience that are described as the worst moments, and typically overlap with the content of intrusive memories (Holmes, Grey & Young, 2005). Table 6.13 shows examples of hotspots and the mean number of hotspots described by participants in the simple cognitive task and control groups. For participants in the simple cognitive task group, the worst moments were noted down by the researcher on the "hotspots of the accident" form as part of the memory reactivation cue and copied onto the Intrusion Diary. For participants in the control group (who did not complete the "hotspots of the accident" form), worst moments were noted down straight onto the Intrusion Diary. A table showing full details of the hotspots described by each participant is given in Appendix 6.1.

Table 6.13 shows an overlap in the content of hotspots of the accident in the intervention and control groups, as well as a similar number of hotspots in the two groups. Hotspots in both groups were predominantly vivid, sensory descriptions of moments of the accident.

Table 6.13. "Hotspots" of the Accident in the Intervention and Control Groups (N = 71)

	Simple cognitive task *n* = 37	Control *n* = 34
Examples of hotspots	Flash of airbag Hearing sirens Seeing smoke – being trapped Hitting the bus Losing control of the bike Blood streaming/dripping Catapulting forward Dust and smoke, debris everywhere Smell burning rubber Windscreen smashing, darkness	Bang of airbags – white Hearing bang – noise of crash Seeing van indicator lights Truck coming towards me – impact Losing control of steering Blood dripping on yellow raincoat Car spinning Curled up on all fours Being dragged Sparkly rain (glass)
Number of hotspots per person, *M* (*SD*)	2.38 (1.01)	2.32 (1.04)
Range	1 - 6	1 - 5

Activity diary in the control group

Participants in the control group (*n* = 34) were left to complete a simple activity diary (adapted from Porcheret et al., 2012) for approximately 20 minutes, to provide a foil activity to parallel the period during which participants in the intervention group completed the simple cognitive task. The mean duration of the diary completion period was 22.4 minutes (SD = 15.1). The mean number of activities recorded in the diary was 8.3 (range 3 to 21). Table 6.14 shows examples of activities recorded in participants' activity diaries.

Table 6.14. Examples of Activities Recorded in a Simple Activity Diary by Participants in the Control Group

Example of activity	Length of time (in minutes)
Spoke to family	4
Scan of chest + abdomen	4
Bought coffee	2
Spoke to triage nurse	4
Went for a smoke outside	5
Texting	1
Given painkiller for head pain	6
Nurse sorted out drip	4

Only one participant in the control group recorded playing a visuospatial computer game during their time in the emergency department. This participant recorded playing the game "Candy Crush" on their mobile phone for 20 minutes; however, this was recorded to occur before the participant took part in the research study. Ratings of the activity diary by the study researcher and an independent cognitive science researcher indicated showed 100% agreement that no participants in the control group completed a visuospatial activity during the time they were left with the diary.

Possible moderators of intervention effect

Experience of Tetris play and primary outcome

Similar to James et al. (2015: supplementary materials), a number of exploratory analyses were conducted to examine the relationship between the number of intrusive memories recorded in the Intrusion Diary and the following factors related to Tetris play: a) duration of Tetris play, including any breaks taken, b) how easy/distressing participants found playing Tetris, and c) previous experience of playing Tetris. Results are shown for participants in the simple cognitive task group who completed the Intrusion Diary (n = 34). This aimed to shed light on possible mechanisms/moderators of the intervention effect, based on the available data.

a) Duration of Tetris play

The mean total duration of Tetris play (excluding practice time; N = 37) was 18.5 minutes (SD = 4.2). Table 6.15 indicates that a longer duration of uninterrupted Tetris play was associated with fewer intrusive memories in the week after the accident for those who returned the intrusion diary (N = 34).

Table 6.15. Spearman's Correlations Between Duration of Tetris Play and Number of Intrusive Memories (N = 34)

Variable related to duration of Tetris play (in mins)	Correlation coefficient with the number of intrusive memories recorded in the Intrusion Diary
Total duration of Tetris practice + Tetris play	-.113
Total duration of Tetris play (excluding practice)	-.189
Longest uninterrupted period of Tetris play	-.375*

*Correlation is significant at the .05 level (two-tailed).

Table 6.16. Number of Intrusive Memories for Participants who Did vs. Did Not Take a Break During Tetris Play (N = 34)

Tetris play variable	Number of intrusive memories recorded in the Intrusion Diary, *M* (*SD*)	
	Yes *n* = 7	No *n* = 27
Took a break during Tetris play?	15.29 (18.91)	6.96 (7.91)

7 out of 37 participants (19%) took a brief break during gameplay. Table 6.16 indicates that for participants who returned the intrusion diary ($N = 34$), those who took a break during Tetris play had more intrusive memories in the week after the accident than those who did not. However, this difference was not significant (Mann-Whitney $U = 64.00$, $p = .206$). No participants took more than one break during Tetris play, and the main reasons for taking a break were interruptions by emergency department staff or the participant feeling tired.

b) Ratings of ease, helpfulness and difficulty of Tetris play

To examine whether participants' experience of playing Tetris was associated with the primary outcome, Spearman's correlation coefficients were calculated for the relationship between ratings of how easy, helpful and difficult participants found playing Tetris and the number of intrusive memories they recorded in the Intrusion Diary in the week after the accident. There were no significant correlations between participants' ratings of how easy ($r = .020$, $p = .914$), helpful ($r = .323$, $p = .076$) or distressing ($r = .141$, $p = .448$) they found playing Tetris and the number of intrusive memories they recorded in the Intrusion Diary. However, it was interesting to note a moderate positive correlation between how helpful participants found playing Tetris and the number of intrusive memories they recorded, indicating that those who found playing Tetris more helpful recorded a greater number of intrusions. This finding implies that participants' subjective experience of playing Tetris may be unrelated to the effect of the intervention on the number of intrusive memories.

c) Previous experience of playing Tetris

Of the 37 participants allocated to the simple cognitive task group, 33 (89%) had played Tetris before. To examine whether previous experience of playing Tetris was related to the number of intrusive memories in the week after the accident, the mean and

standard deviation of the number of intrusive memories was calculated for those participants who completed the Intrusion Diary who had (n = 31) and had not (n = 3) played Tetris before. The mean number of intrusive memories for participants who had played Tetris before was 9.52 (*SD* 11.41), and for participants who had not played Tetris before was 0.

Retrospective ratings of expectancy of study effect on primary outcome

As part of the feedback questionnaire completed at the end of the study (and therefore a retrospective measure only of expectation/demand), participants were asked to rate how much they predicted that what they had been asked to do in the emergency department would increase or decrease their intrusive memories of the accident, on a 21-point linear scale from -10 (*extreme decrease*) to 10 (*extreme increase*). Whilst both means were low in magnitude, there was a significant difference in expectancy ratings between the intervention (n = 31, M = -1.48, SD = 4.66) and control (n = 31, M = 1.35, SD = 2.79) groups at the 5% level (Mann-Whitney U = 313.00, p = 0.017).

Therefore Spearman's correlations between the expectancy rating and the number of intrusive memories recorded in the Intrusion Diary were calculated for the two groups, to examine whether expectation of the study effect was associated with the primary outcome. The correlation was not significant in the intervention group (n = 31, r = -0.155, p = 0.405) or the control group (n = 31, r = .272, p = .139). This suggests that participants' prediction of the effect of the study intervention on outcome was not related to the number of intrusive memories they recorded in the week after the accident; however, their expectancy rating may have been influenced by their outcome or actual performance given that it was completed at the end of the study.

Comparison of post-trauma risk factors

A number of post-trauma factors thought to be associated with the development of post-traumatic stress symptoms were assessed at one month follow-up, to examine whether there were any differences between the two groups. Table 6.17 shows the results for the differences between the two groups on these variables.

Table 6.17. Comparison of Post-Traumatic Risk Factors for PTSD (Assessed at One Month Follow-Up) Between the Intervention and Control Groups (N = 62)

Post-trauma variable	Simple cognitive task (*n* = 31)	Control (*n* = 31)	Between-group difference
Variables with Yes/No response	*n* (%)	*n* (%)	χ^2 (*p*)
Played computer games based on visual puzzles	13 (41.9%)	4 (12.9%)	6.565 (.010)
Received treatment in relation to the accident	12 (38.7%)	14 (45.2%)	0.265 (.607)
Experienced additional stressful life events since the accident	9 (29.0%)	16 (51.6%)	3.284 (.070)
Variables rated on a 9-point scale from 1 (*not at all*) to 9 (*a great deal*)	*M* (*SD*)	*M* (*SD*)	*t* (*p*)
Dwelt on memories of the accident (rumination)	3.52 (1.77)	3.52 (2.22)	0.305 (.761)
Pushed memories of the accident out of mind (thought suppression)	3.03 (2.42)	2.23 (2.09)	1.650 (.104)
Had support from family and friends (social support)	7.90 (1.66)	6.90 (2.50)	1.592 (.111) [a]
Accident had some positive effects on life	3.81 (2.63)	3.61 (2.57)	0.294 (.770)

[a] Value indicates z-score result of Mann-Whitney U test

As expected, the proportion of participants who played computer games based on visual puzzles in the month after the accident was higher in the simple cognitive task group than the control group. However, participants reported playing a variety of different computer games, including Scrabble, Solitaire, Tetris, Temple Run, Candy Crush, Nongrams, Minecraft, Bubble Witch 2, and Reversee. No other differences in post-trauma factors between the two groups were statistically significant at the 0.05 level; however, it was notable that a higher proportion of participants in the control group than in the simple cognitive task group reported experiencing additional stressful life events since the accident.

Discussion

Here, the main findings of the randomised controlled study are discussed. A more general discussion of the implications of the findings, limitations of the study and ideas for future research is provided in Chapter 8.

A. Flow diagram and study sample

Recruitment, adherence and attrition

In this study, 645 patients were screened over an 11-month period, to yield a total sample of 71 participants. The average recruitment rate was approximately 1.5 participants per week, which was slightly lower than that estimated from piloting (1.7 participants per week). However, a good final sample size was achieved, in line with that estimated by the power calculation.

Adherence to the simple cognitive task intervention was high. All except one participant allocated to the intervention condition completed the memory reactivation cue (very briefly thinking back to the accident and briefly telling the researcher the worst moments) followed by playing Tetris for a minimum of 10 minutes uninterrupted. The participant that did not adhere to the full intervention only played Tetris 3 minutes before being interrupted by staff to move to a different bay, and subsequently falling asleep.

Participant attrition was relatively low for the whole sample, with only 5.6% drop-out at one week follow-up and 12.7% drop-out at one month follow-up. This compares well with the 26% drop-out at one month in a recent trial of an early intervention after trauma, Rothbaum et al., (2012). No adverse effects (i.e., negative reactions to the treatment procedures, such as significantly increased distress or suicidality) were reported by participants or observed in either the intervention or control groups.

Representativeness of the study sample

Whilst there was an even gender split the study sample (52% female), there was in fact a lower proportion of females in the wider population of road traffic accident patients presenting to the emergency department during the study period (39%). This may reflect that a higher proportion of female than male patients met the eligibility criteria for the study, or that female patients were more willing than male patients to participate in the study. A greater proportion of patients in the study sample than in the wider population were brought in by ambulance, and seen in the resuscitation or majors area over the minors area, indicating that they had experienced more severe accidents or injuries. This would seem consistent with the eligibility criterion that the road traffic accident met the DSM-IV criterion A1 for PTSD (“experienced, witnessed, or confronted with actual or threatened death or serious injury”).

Demographic and baseline variables

The results indicated that the intervention and control groups were well balanced with regards to demographic information and baseline characteristics. The only variable found to differ significantly between the two groups was the proportion of participants in vehicle accidents that were passengers (0% in the intervention group and 18.2% in the control group). However, this variable was not thought to be a critical prognostic factor.

It was interesting to note that the age of participants ranged up to 77 in the simple cognitive task condition and 85 in the control condition, indicating that even older patients were willing and able to complete the computer game intervention. The average length of time between participants leaving the scene of the accident and taking part in the study was approximately 3 hours, highlighting the very early nature of this intervention approach, even in contrast to other early intervention studies (e.g. an average of 12 hours post-trauma in Rothbaum et al., 2012).

Participant scores on measures of perceived life threat and peritraumatic distress (assessed using the PDI) were comparable to those of previous prospective studies of hospitalised road traffic accident patients (Blanchard et al., 1995; Nishi et al., 2010). The mean score on a measure of peritraumatic dissociation (the PDEQ) was similar to that of hospital assault survivors who did not develop later PTSD (Birmes et al., 2003), suggesting that the severity of dissociation in the current sample was consistent with low risk of PTSD. Indicators of injury severity (such as the Injury Severity Score and admission to hospital) suggested that the study sample was comparable to a previous prospective study of post-traumatic stress symptoms in hospitalised road traffic accident patients (Ehlers et al., 1998).

B. Main efficacy analyses

The main aims of this randomised controlled study were to determine if a simple cognitive task intervention (a memory reactivation cue followed by playing the computer game Tetris), compared to usual care in the emergency department with a simple activity diary, could a) reduce the number of intrusive memories (as assessed using an intrusion diary) in the week after a road traffic accident (the primary outcome), and b) reduce post-traumatic stress symptoms (PDS and IES-R scores), anxiety (HADS-A score) and depression (HADS-D score) at one week and one month after a road traffic accident (secondary outcomes).

Primary outcome

The result of the primary efficacy analysis (an intention to treat analysis) showed that participants in the simple cognitive task intervention group recorded significantly fewer intrusive memories in the week after the road traffic accident than participants in the control group (t = 2.800, p = .005, d = 0.665, 95% CI [0.184, 1.141]), and on average recorded approximately one third of the number of intrusive memories (a mean of 8.86 in the simple cognitive task group and 23.52 in the control group; see Figure 6.2. p.6.11).

This result was not only in the predicted direction, but also found a "medium" effect size of d = 0.665, which was close to the estimated effect size of d = 0.7. This is an exciting and encouraging result, given that this study took a first step in translating findings from previous laboratory-based research (e.g. showing an effect size of d = 0.91; Holmes et al., 2009) to a real-world, clinical setting.

Whilst the primary outcome measure, a simple tick-box Intrusion Diary which participants completed in the week after the accident, was not a validated clinical measure of intrusion symptoms, it was adapted from the Intrusion Diary used in preceding laboratory studies and had high clinical relevance at a surface level, similar to thought records used in cognitive behavioural therapy. Further, there were strong positive correlations in this study between the number of intrusive memories recorded in the diary and clinical measures of intrusion symptoms (IES-R intrusion subscale score and PDS Reexperiencing symptoms score) at one week. This provides initial support for the clinical validity of the Intrusion Diary, but clearly further studies are needed to test its reliability and validity.

One week secondary outcomes

Results of the secondary efficacy analyses for outcomes one week after the accident showed that participants in the simple cognitive task group had significantly lower scores on a clinical measure of the distress caused by intrusion symptoms (the intrusion subscale of the Impact of Events Scale-Revised; t = 2.251, p = .024, d = 0.535, 95% CI [0.059, 1.007]), and lower scores that did not quite reach significance at the 0.05 level on a clinical measure of the frequency of intrusion symptoms (the re-experiencing subscale of the Posttraumatic Diagnostic Scale; t = 1.891, p = .059, d = 0.449, 95% CI [-0.024, 0.919]). The effect size for both of these variables was in the "medium" range. Given that the study was not powered to detect a difference between the groups on these

clinical measures of intrusion symptoms, these findings are very encouraging, as they suggest that the simple cognitive task intervention might reduce not only the number of intrusive memories, but also clinically-relevant intrusion symptoms, in the week after the accident.

No other secondary outcomes at one week (i.e. other post-traumatic stress symptoms of avoidance and hyperarousal, anxiety, depression or qualities of intrusive memories such as vividness and distress) showed significant differences between the two groups. This is perhaps unsurprising, given that the simple cognitive task intervention was hypothesised to selectively target the occurrence of intrusive memories. However, there were small effects (indicated by *d* of 0.2 or above; Cohen, 1988) for the reduction in the vividness and distress of intrusive memories, hyperarousal symptoms (severity and frequency), total post-traumatic stress symptoms (severity and frequency) and depression symptoms in the simple cognitive task group compared to the control group. This suggests that the reduction in the occurrence of intrusive memories may have had associated effects on other outcomes at one week, but larger studies would be needed to test this hypothesis.

One month secondary outcomes

Results of the secondary efficacy analyses for one month outcomes indicated no significant differences between the two groups on any measures of post-traumatic stress symptoms, anxiety or depression (see Table 6.8). Again, this result was not surprising given that the study was not powered to detect differences in one month outcomes between the two groups. However, a small effect size of $d = 0.220$ was found for the reduction in intrusion symptoms (IES-Intrusion and PDS-Reexperiencing scores) in the simple cognitive task group relative to the control group, and mean scores for the total severity of PTSD symptoms (IES-R and PDS total scores) at one month were in the expected direction (see Table 6.8). This suggests that a larger study might have sufficient power to detect a difference in intrusion symptoms at one month between the two groups. Based on the effect size of $d = 0.220$, a sample of 652 participants (326 in each group) would be needed to detect a significant difference at the 0.05 level in intrusion symptoms at one month between the two groups.

When only participants with high perceived life threat (indicating higher risk for PTSD symptoms) were compared, the effect size for the difference in intrusion symptoms (IES-R intrusion score) at one month between the two groups was slightly stronger

(d = 0.319). Based on this effect size, a total sample of 312 participants who were at higher risk of PTSD symptoms would be needed to detect a treatment effect.

One month PTSD criteria

There was no significant difference between the simple cognitive task and control groups in the percentage of participants with scores on the Posttraumatic Diagnostic Scale (PDS) that were consistent with a DSM-IV diagnosis of PTSD. The figures for the percentages of participants in the simple cognitive task (12.9%) and control (9.7%) groups with a symptom profile consistent with PTSD were substantially lower than that found in a previous prospective study of road traffic accident patients recruited from the John Radcliffe Hospital Emergency Department (23.1%; Ehlers et al., 1998). This was despite similar injury severity in the two samples (e.g. 20% with bone injuries in Ehlers et al. compared to 23.9 % in this sample; 26% admitted to hospital in Ehlers et al. compared to 28% in this study), and a similar method of assessing PTSD symptoms (Ehlers et al. (1998) used the Post-traumatic Symptom Scale (PSS), which was the predecessor to the Posttraumatic Diagnostic Scale (PDS) used in this study). Interestingly, PDS symptom severity scores were very similar to those of a previous prospective study of PTSD symptoms after road traffic accidents (Ehring, Ehlers & Glucksman, 2008). For example, the mean one month PDS symptom severity score in the control group in this study was 10.16 (*SD* 10.99), compared to 10.63 (*SD* 11.32) in Ehring et al. (2008). This suggests the low proportion of participants with symptom profiles consistent with a DSM-IV diagnosis of PTSD may have reflected something specific to assessment of the diagnostic criteria for PTSD, such as low levels of functional impairment.

C. Exploratory analyses

Primary outcome: the number of intrusive memories

A notable finding was that there was significantly higher proportion of participants in the simple cognitive task group than the control group who had no intrusive memories in the first week after the road traffic accident (26.5% compared to 6.1%).

The results of the time course analyses of the number of intrusive memories over the first seven days after the road traffic accident suggest that participants in the simple cognitive task group showed overall lower numbers of intrusive memories across the seven

days, as well as accelerated recovery from intrusive memories over the seven days, compared to participants in the control group. A notable observation was that a number of participants in the control group had consistently high numbers of intrusive memories across the seven days, indicating a possible "resistance" to recovery, whereas this was not seen in the simple cognitive task group. This implies that the intervention may have protected against having consistently high numbers of intrusive memories, and aided recovery in those who might otherwise have shown resistance. Another interesting observation was the increase in the number of intrusive memories on Day 2 in both groups (although more marked in the control group). This may reflect that not all participants recorded a full day of intrusive memories on Day 1, as the accident occurred part way through the day for many participants, or alternatively may reflect a real increase in the number of intrusive memories on Day 2 after the first night's sleep, once memories have been further consolidated (Stickgold, 2005).

The results of the time series analyses for participants with low and high perceived life threat in the intervention and control groups again highlighted the limited recovery from intrusive memories for participants in the control group with both low and high perceived life threat (possibly reflecting the participants who recorded consistently high numbers of intrusive memories across the seven days, even in the low perceived life threat group), whereas in the intervention group, recovery over time was more marked for participants with low than high perceived life threat. This suggests that participants with low perceived life threat (indicating low risk of post-traumatic stress symptoms following trauma) responded better to the intervention than those at higher risk of post-traumatic stress symptoms. One hypothesis is that participants with a less severe subjective reaction to the trauma were better able to attend to and engage with the intervention, although these possible mechanisms/moderators of the intervention effect were not assessed in this study.

Given that the number of intrusive memories has not been used as a primary outcome in previous intervention trials, this study explored which baseline characteristics were associated with the primary outcome. Only peritraumatic dissociation (assessed using the PDEQ) was significantly correlated with the number of intrusive memories in the week after the accident, controlling for group allocation. This correlation is consistent with the literature concerning risk factors for PTSD, which indicates that peritraumatic dissociation is one of the strongest predictors of PTSD symptoms (Ozer et al., 2003). Contrary to the PTSD literature, however, perceived life threat and peritraumatic distress were not

significantly correlation with the number of intrusive memories, suggesting that these may not be as important prognostic factors for early post-traumatic stress symptoms as for later PTSD. This raises the possibility that peritraumatic dissociation would have been a more suitable baseline variable to use for balancing the two groups at randomisation than perceived life threat to self.

Hotspots of the accident

The number of worst moments of the accident (or "hotspots") that participants identified in the emergency department were similar in the two groups (mean 2.3, range 1-6 in the intervention group; mean 2.3 range 1-5 in the control group), but low in comparison to a previous study examining hotspots in mixed-trauma patients with PTSD (mean 6.1, range 2-11; Holmes, Grey & Young, 2005). The content of participants' hotspots was very similar in the two groups, and predominantly described vivid sensory moments of the accident e.g. "flash of airbag", "blood streaming/dripping", "smell burning rubber", "windscreen smashing", "catapulting forward", and "seeing van indicator lights" (see Appendix 6.1 for details of all participant hotspots). A comparison with the hotspots described by people who had experienced a road traffic accident in Holmes, Grey & Young (2005) indicated a great deal of overlap with regards to the content and strong sensory nature e.g. "lying on ground", "car hits me", "head hitting pavement", "twisting of bike and body at impact", "sounds of glass shattering" and "screaming and flowing of blood".

Activity diary (control condition only)

Participants in the control condition recorded a variety of activities on the simple activity diary, which was a foil task given to them for a similar duration to the simple cognitive task intervention. Examples of recorded activities were "spoke to family", "scan of chest + abdomen", "bought coffee", "nurse sorted out drip", and "texting". Rating of the activities by the study researcher and an independent cognitive science researcher indicated that no participants in the control condition completed any visuospatial activities (similar to the simple cognitive task intervention, and therefore that might confound the study results) during the period they were left to complete the activity diary.

Tetris play (intervention group only)

A striking finding was that 89% of patients allocated to the intervention condition had played the computer game Tetris before, highlighting the popularity of this game. Further, participants' ratings of how easy, helpful or distressing they found playing the game were not related to how many intrusive memories they recorded in the week after the accident, indicating that outcome was not simply moderated by participants' subjective experience of the game. Interestingly, the longest uninterrupted period of Tetris play was significantly negatively correlated with the number of intrusive memories in the week after the accident, suggesting that participants who played Tetris for longer without interruption had better outcomes.

Expectancy of the study effect

One possible explanation for the difference in the number of intrusive memories between the two groups was a demand effect, whereby participants in the intervention group expected to have fewer intrusive memories than those in the control group. Expectancy ratings (rated from -10 indicating an expected extreme decrease in intrusive memories to +10 indicating an expected extreme increase in intrusive memories) indicated that there was a significant difference between the two groups (mean of -1.48 in the simple cognitive task group compared to 1.35 in the control group). However, the expectancy rating was not correlated with the number of intrusive memories in either group, suggesting that expectancy did not account for the difference in outcome.

Summary

In summary, this randomised controlled study succeeded in providing a first test of the simple cognitive task intervention in a hospital emergency department setting with road traffic accident patients. 71 participants were recruited over an 11-month period: study adherence was high and drop-out was low. The intervention and control groups were well balanced on demographic variables and key baseline characteristics. The main findings were in line with prediction: participants in the simple cognitive task intervention group had significantly fewer intrusive memories (recorded in an Intrusion Diary), and significantly lower clinical intrusion symptom scores (assessed using the IES-R), in the first week after the accident than participants in the control group. Whilst there were no

significant differences in one month outcomes, effect sizes allowed an estimation of sample sizes for future trials. This was the first study to show that it was possible to deliver a simple cognitive task intervention involving computer game play in a hospital emergency department setting, and to extend findings from previous laboratory studies (e.g. Holmes et al., 2009) to a clinical setting. The implications of these findings, as well as a discussion of limitations of the study and ideas for potential further research, are included in the general discussion in Chapter 8.

CHAPTER 7. Randomised Controlled Study - Participant Feedback: A simple cognitive task intervention to reduce the occurrence of intrusive memories after a road traffic accident

Introduction

An additional aim of the randomised controlled study was to assess participants' experience of taking part in the study, in order to inform refinements for further research (see Protocol 4.0, Appendix 5.1). Assessing patient views has been proposed as an important outcome in clinical trials (Nelson et al., 2013), and is part of a wider agenda to promote the interests of patients and the public in UK health research (National Institute for Health Research, 2013). Participant experience was assessed using a Feedback Questionnaire (Appendix 5.6), which was completed online or by post at the end of the study (at one month follow-up; see Chapter 5).

This chapter describes the results of participants' ratings and free responses on the Feedback Questionnaire regarding their experience of playing Tetris in the emergency department (for participants in the simple cognitive task intervention group only) and their experience of taking part in the study (all participants).

Results

Sample of participants who completed the Feedback Questionnaire

The overall completion rate of the Feedback Questionnaire was 87%. Table 7.1 shows key demographic information and accident details for participants who completed the Feedback Questionnaire in the simple cognitive task group (n = 31 out of 37; 84%) and the control group (n = 31 out of 34; 91%). There were no significant differences between the two groups on any of these variables.

Table 7.1. Demographic Information and Accident Details for Participants Who Completed the Feedback Questionnaire (N = 62)

Demographic variable	Simple cognitive task (*n* = 31)	Control (*n* = 31)
Gender, female, *n* (%)	18 (58%)	17 (55%)
Age in years, *M* (*SD*)	39.5 (15.6)	41.8 (16.9)
Range	19 - 77	20 - 85
Years in education, *M* (*SD*)	16.3 (3.3)	15.3 (3.3)
Ethnicity, non-White British, *n* (%)	8 (26%)	6 (19%)
Vehicle type		
Car/van/bus, *n* (%)	16 (52%)	16 (52%)
Motorcyclist, *n* (%)	4 (13%)	3 (10%)
Cyclist, *n* (%)	11 (35%)	8 (26%)
Pedestrian, *n* (%)	0 (0%)	4 (13%)
Location in ED		
Resuscitation, *n* (%)	8 (26%)	6 (19 %)
Majors, *n* (%)	9 (29%)	14 (45%)
Minors/other, *n* (%)	14 (45%)	11 (36%)

Ratings of participant experience of playing Tetris in the emergency department

Figure 7.1 shows boxplots of participant ratings for how easy, helpful, and distressing/burdensome they found playing Tetris after the road traffic accident, for participants in the intervention group only (*n* = 31). Each item was rated on a 9-point scale from 1 (*not at all*) to 9 (*extremely*). The results indicate that on average, participants in the intervention condition found playing Tetris very easy (median = 7) and very helpful (median = 7), and minimally distressing or burdensome (median = 1). Only one participant rated playing Tetris after the road traffic accident to be more than "fairly distressing" (indicated by a rating of above 5). This participant reported in the emergency department that they had found playing Tetris more stressful than they would normally. Interestingly, this same participant reported during debriefing (at one month follow-up) that they only had one intrusive memory in the week after the accident, which they found surprising given that they had experienced a lot of intrusive memories following previous traumatic events. Thus, any distress from playing Tetris in the emergency department did not seem to be associated with later PTSD symptomatology.

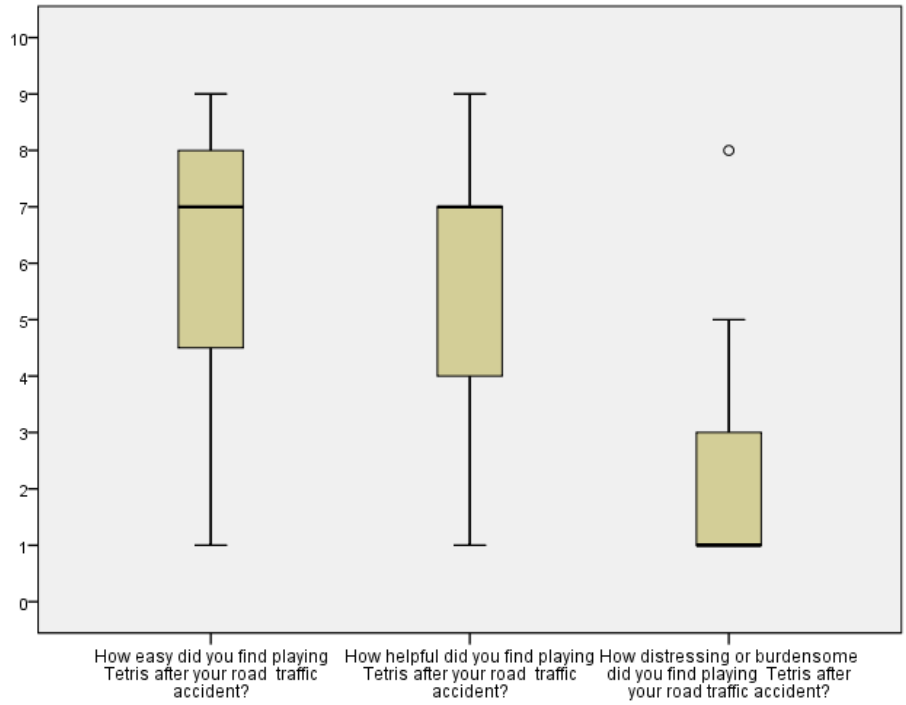


Figure 7.1. Boxplots of participant ratings for how easy, helpful, and distressing/ burdensome they found playing Tetris in the emergency department (intervention group only). Thick horizontal lines represent the median, boxes represent the interquartile range and vertical lines represent the range of values. The circle represents an outlying value.

Figure 7.2 shows boxplots of participant ratings for how willing they would be to play Tetris again after a traumatic event if it was offered to them as something that would help (rated on a 9-point scale from 1 [*extremely unwilling*] to 9 [*extremely willing*]) and how confident they would be in suggesting playing Tetris to a friend if they had a similar accident (rated on a 9-point scale from 1 [*extremely unconfident*] to 9 [*extremely confident*]). The results indicate that most participants would be willing to play Tetris again after a traumatic event (median = 7), and that on average participants would be confident in suggesting playing Tetris to a friend after a similar accident (median = 6).

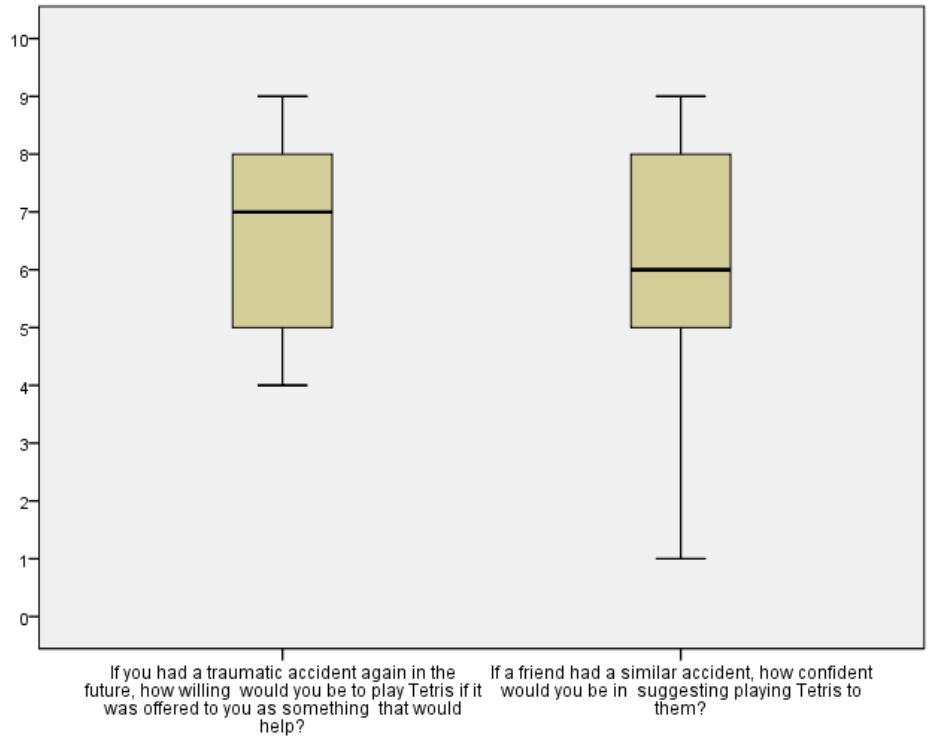


Figure 7.2. Boxplots of participant ratings for willingness to play Tetris again after a traumatic accident and confidence in suggesting playing Tetris to a friend after an accident (intervention group only). Thick horizontal lines represent the median, boxes represent the interquartile range and vertical lines represent the range of values.

Free response questions regarding participant experience of playing Tetris in the emergency department

Two free response questions were used to assess participants' experience of playing Tetris in the emergency department: the first asked about suggestions for improving using Tetris after a traumatic event and the second asked for any other comments.

Thirteen out of 31 participants in the intervention group gave comments regarding suggestions for improving using Tetris as something that might help after a traumatic event. Sixteen out of 31 participants gave additional comments about using Tetris after a traumatic event. Tables 7.2 and 7.3 show possible themes in participants' responses, and examples of participants' responses, on these two items. Full details of participants' comments on the Feedback Questionnaire are given in Appendix 7.1.

Table 7.2. Comments Regarding Suggestions for Improving Using Tetris After a Traumatic Event (Intervention Group Only, N =13)

Feedback Questionnaire item	Themes in participant comments	Examples of participant comments
Do you have any suggestions for improving using Tetris as something that might help after a traumatic event?	How Tetris was helpful (3 participants)	"It has been the visualisation of Tetris that was helpful - possibly after finishing playing" "I find playing Tetris quite relaxing in general"
	Improvement suggestions (4 participants)	"Found screen small, moving neck and head and sore chest was uncomfortable… Maybe larger screen would help" "Supply hospitals with some hand held Tetris consoles so that patients have the choice to play them when they're waiting"
	No suggestions (6 participants)	"No" "None"

Table 7.3. Other Comments About Using Tetris After A Traumatic Event (Intervention Group Only, N = 16)

Feedback Questionnaire item	Themes in participant comments	Examples of participant comments
Do you have any other comments about using Tetris as something that might help after a traumatic event?	Beneficial effects (6 participants)	"I think that playing Tetris helped focus my mind and bring some "normality" back to my head. I didn't dwell on the accident too much while I was in hospital. Playing Tetris seemed a bit strange at the time, but looking back it has been a help." "It certainly took my mind off of it at a time when I probably would have sat brooding and feeling very sorry for myself"
	Other games (2 participants)	"Sudoku in the head for people that cannot use their hands because of the injury" "Other simple games can be possibly benificial also, but obviously you wouldn't give a car racing game to someone who has just had a car crash"
	Possible mechanism (3 participants)	"I can see that the idea of fitting shapes and 'compartmentalising' things may be useful" "It seems logical that having something to occupy the mind whilst waiting in a hospital environment reduces the tendency to dwell upon the incident"
	Negative associations (3 participants)	"I wonder if I were to be reminded of Tetris, some time in the future, would it bring back memories of the accident, through association?" "I don't know if it is just me but the images of falling objects just after falling off a bike was a bit stressful. Maybe some colouring thing or musical game would have been better..."
	No comments (2 participants)	"No" "None"

Ratings of participant experience of taking part in the study

Table 7.4 shows the means and standard deviations for participant ratings of how happy they were to be offered something to do whilst waiting in the emergency department, how easy they found taking part in the study, and how distressing or burdensome they found taking part in the study, for both the simple cognitive task group (n = 31) and the control group (n = 31). Each item was rated on a 9-point scale from 1 (*not at all*) to 9 (*extremely*).

Table 7.4. Feedback Questionnaire Ratings Regarding their Experience of Taking Part in the Study for the Intervention and Control Groups (N = 62)

Feedback Questionnaire rating	Simple cognitive task (n = 31)	Control (n = 31)
How happy were you to be offered something to do whilst you were waiting in the emergency department after your accident?	7.10 (1.72)	6.00 (2.16)
How easy did you find taking part in the study?	7.55 (1.71)	7.19 (2.06)
How distressing or burdensome did you find taking part in the study?	2.52 (1.88)	2.10 (1.38)

Note. Values refer to the mean (and standard deviation) of participant ratings.

The results in Table 7.4 indicate that in both groups, participants were happy to be offered something to do whilst waiting in the emergency department, and found taking part in the study very easy and minimally distressing or burdensome. The results of between-groups comparisons of ratings indicated that participants in the simple cognitive task group retrospectively rated that they were happier to be offered something to do whilst waiting in the emergency department than were participants in the control group ($t(60) = 2.212$, $p = .031$, $d = 0.563$). There was no significant difference between the intervention and control groups in how easy (Mann-Whitney U = 438.5, $z = 0.620$, $p = .535$, $d = 0.190$) or distressing/burdensome (Mann-Whitney U = 434.0, $z = 0.698$, $p = .485$, $d = 0.255$) participants found taking part in the study.

Free response questions regarding participant experience of taking part in the study

Two free response items were used to assess participants' views regarding the study in general: the first asked how the study could be improved if it was rolled out on a larger scale and the second asked for any other comments about the study or their experience of taking part. Twelve out of 31 participants in the intervention group, and 20 out of 31 participants in the control group, gave comments regarding how the study could be improved. Eleven out of 31 participants in the intervention group, and 18 out of 31 participants in the control group, gave additional comments about the study. Tables 7.5 and 7.6 shows the main possible themes in participant comments, and examples of their comments, on these two items (see Appendix 7.1 for full details).

Other spontaneous feedback during the study

During the time in the emergency department, and during the debriefing telephone call at one month, some participants made other comments about the study that offered useful feedback. For example, after playing Tetris in the emergency department, nine participants in the intervention group commented that they had found it fun, enjoyable or calming, whilst three participants commented that they had found it stressful or frustrating, and one participant reported that they had a headache from concentrating. Some comments during debriefing offered further insight into how participants experienced the intervention in the context of the emergency department environment. One participant commented that it was helpful to "have your mind taken off it at a time when you're running the whole thing through your mind - when you're on your own, "a vulnerable time", after the ambulance crew have left you" and another commented that it was a "different approach in the emergency department to being asked about medical symptoms. Playing Tetris focused me away from my symptoms and pain." This bears similarities to comments in the Feedback Questionnaire (see Table 7.3).

Only one participant in the control group commented on their experience of completing the simple activity diary (a foil task). They reported "it made me aware of time passing and I found it slightly disturbing to answer how long things took - I had no idea. It emphasized something negative about the experience." No other participants in the control group made similar comments, and it is noted that some participants in the intervention group identified negative aspects of the intervention (see Table 7.3).

Table 7.5. Comments Regarding How the Study Could be Improved (Intervention Group N = 12; Control Group N = 21)

Feedback Questionnaire item	Themes in participant comments	Examples of participant comments (by group)
If we were to roll out the study on a larger scale, how could we improve the study?	Questionnaire suggestions (3 participants in the simple cognitive task group; 5 in the control group)	"You could add to the diary how long someone played Tetris per day and how often it was directly played after a flashback." *(simple cognitive task)* "Possibly provide opportunity to explain some answers in more depth, i.e. one of the questions asked about positive impact of accident - for me personally it means I have started to wear a cycle helmet." *(control)*
	Design suggestions (2 participants in the simple cognitive task group; 2 in the control group)	"Make the gender field not mandatory or add a "prefer not to say" option" *(simple cognitive task)* "I haven't tried completing this on a mobile device only a PC, this should be considered if not already possible." *(simple cognitive task)* "Need to reduce number of questions and repetition" *(control)*
	Alternative tasks to Tetris (2 participants in the simple cognitive task group)	"Maybe a different game such as Flow Free could be used as well as Tetris" "Maybe have more alternatives to computerised versions, bearing in mind age of participants i.e. won't all be into computer games"
	Dissatisfaction (2 in the control condition)	"Explain that the study will take more time than originally explained" "Offer to help people after the accident"
	No improvement suggestions (5 in the simple cognitive task group; 7 in the control group)	"From my experience the study was done very professionally from start to finish… I can't think of any way it could be improved" *(simple cognitive task)* "I think it's fine the way it is" *(control)*
	Unsure (3 participants in the control group)	"Don't know" "Not sure"

Table 7.6. Additional Comments About the Study or The Experience of Taking Part (Intervention Group N = 11; Control Group N = 18)

Feedback Questionnaire item	Themes in participant comments	Examples of participant comments (by group)
Do you have any other comments about the study or your experience of taking part in the study?	Beneficial effects of taking part in the study (2 participants in the simple cognitive task group; 3 in the control group)	"Overall having something to do was useful" *(simple cognitive task)* "In answering some of the quesions it has underlined for me how lucky we were both in terms of the accident itself and the outcome for us." *(control)*
	Beneficial effects of playing Tetris (2 simple cognitive task)	"Playing Tetris has helped me deal with my accident in a way I don't think I appreciated at the time."
	Positives of the study (2 simple cognitive task; 1 control)	"Very helpful staff" *(simple cognitive task)* "Support and instruction was good" *(control)*
	Happy to take part (1 participant in the simple cognitive task group; 6 in the control group)	"I'm just glad to feel part of something and hopefully the resauts of this study can benifit many people in years to come" *(simple cognitive task)* "I was happy to take part and welcomed the opportunity" *(control)*
	Difficult aspects of the study (2 in the simple cognitive task group; 1 in the control group)	"Straight after the accident it was difficult for me to differentiate between flashbacks and just thinking about the accident" *(simple cognitive task)* "It has provided sharp reminders of the incident - and my failings" *(control)*
	Design queries (3 participants in the control group)	"I would question its validity as the questionairre acted as a prompt to remind me of the accident."
	No comments (1 in the simple cognitive task group; 3 in the control group)	"None" *(simple cognitive task)* "No" *(control)*

Discussion

An additional aim of the randomised controlled study was to assess participants' experience of playing Tetris in the emergency department (in the intervention group only), and participants' experience of taking part in the study (all participants), to inform improvements to the study for further research.

Playing Tetris as part of an intervention after real-world trauma

A key finding was that, on average, participants in the intervention group rated playing Tetris after the road traffic accident to be very easy, very helpful, and minimally distressing (see Figure 7.1). Moreover, the majority rated that they would be willing to play Tetris again after a traumatic accident, and on average would feel confident in suggesting playing Tetris to a friend if they had a similar accident. Whilst participants' experience of playing Tetris clearly varied, more participants spontaneously reported finding the game enjoyable or relaxing rather than stressful or frustrating. Together, these results suggest that playing Tetris after the road traffic accident was well tolerated by participants and considered an acceptable part of the intervention, which is very reassuring for future development of the intervention. Whilst participants' experience of the memory reactivation cue (briefly thinking back to the accident and briefly telling the researcher the worst moments) was not assessed in the Feedback Questionnaire, it was notable that no participants in the intervention group commented on any negative experiences associated with this part of the procedure, and no participants became overly distressed during it.

Encouragingly, participants' comments about playing Tetris indicated that they found a variety of aspects of the game beneficial, including finding it relaxing, finding it a helpful distraction away from their thoughts about the accident and their physical pain, finding that it brought back some "normality" after the accident, and visualising the game after leaving the emergency department. Further, two participants commented that playing Tetris helped in a way they had not appreciated at the time of the accident. These comments suggest that, contrary to potentially viewing the computer game as a trivial activity after a traumatic event, many participants valued playing Tetris as part of a therapeutic intervention in the emergency department. The implications of this for patient care in emergency settings are considered further in the general discussion (Chapter 8).

One helpful improvement suggestion for further research was to play the game on a larger screen, as one participant found the small gaming device (a Nintendo DS XL)

uncomfortable to use. Participants also suggested the use of other computer games (such as Flow Free[21]) or alternatives to computerised games (such as Sudoku), which may be interesting avenues to explore in further studies. A few participants in the intervention group (three out of 31) identified possible negative associations between Tetris and the accident, such as potentially remembering the accident if they were reminded of Tetris in the future; possible "side effects" may be something to assess in future studies.

Experience of the study in general

Participants in both groups rated the study to be very easy and minimally distressing or burdensome to take part in, which is again encouraging for developing this research further. Interestingly, participants in the intervention group rated that they were happier to be offered something to do in the emergency department than participants in the control group (although both groups rated highly on this item), suggesting that the intervention procedure was retrospectively viewed more positively by participants than the control procedure.

With regards to improvement suggestions about the study, a number of participants gave useful comments for improving the Intrusion Diary, such as adding information about Tetris play in the week after the accident, assessing the number of intrusive memories that were not distressing, and improving the reliability of the measure. Future studies would benefit from considering further amendments to the Intrusion Diary. A large number of participants felt the study did not require any improvements, and only two participants (both in the control group) made comments indicating general dissatisfaction with the study (although neither participant indicated distress caused by the study during debriefing).

Other comments highlighted participants' experience of the benefits of taking part in research (e.g. benefitting others in the future) and positive aspects of the study itself (e.g. helpful staff and good support and instruction). With regards to difficult aspects of the study, one participant commented on the challenge of distinguishing between intrusive memories and normal thoughts about the accident, particularly in the first few days when the accident was in mind a great deal of the time. Future studies might provide participants with more help concerning this distinction.

[21] Big Duck Games LLC, 7 December 2014.

General limitations and other future directions

One limitation to the Feedback Questionnaires was that there was no explicit question for participants in the intervention group regarding their experience of the memory reactivation cue, or for participants in the control condition regarding their experience of completing the activity diary (which paralleled the time during which participants in the intervention condition completed the simple cognitive task). Further studies may benefit from using a more detailed feedback questionnaire.

Participant experience was assessed in this study using a brief online/postal feedback questionnaire, whereas interview-based feedback may offer fuller qualitative information. Further, participants responses were not formally analysed using qualitative methodologies such as grounded theory (Glaser & Strauss, 1967) or interpretative phenomenological analysis (J. A. Smith & Osborn, 2003). Future studies might use more detailed participant interviews, ideally conducted by someone external to the study, such as a patient or member of the public who might bring an alternative patient-centred perspective to the study (see National Institute for Health Research, 2014).

The next and final chapter presents a general discussion of the findings from this research.

CHAPTER 8. General discussion

Overview of the thesis

The overarching aim of this research was to develop and evaluate a simple cognitive task intervention (a memory reactivation cue followed by playing the computer game "Tetris") as a novel preventive intervention to reduce the occurrence of intrusive memories after a psychological trauma. Previous laboratory studies with healthy participants found that playing Tetris after an experimental trauma (viewing a film with traumatic content) reduced the frequency of intrusive memories of the film over the following week (Holmes et al., 2009; Holmes, James, et al., 2010), and also reduced scores on clinical measures of post-traumatic stress symptoms (Holmes et al., 2009). This research translated previous laboratory studies to a clinical setting, in a hospital emergency department with patients who had experienced a road traffic accident.

The research consisted of a series of stages, based on the MRC guidelines for the development and evaluation of complex interventions (Medical Research Council, 2008). Stage 1 involved identifying the current evidence base for preventive interventions after trauma, and drawing on theory from clinical and experimental psychology to propose a novel intervention to target specifically the development of intrusive memories in the first week after a trauma (Chapter 1). This stage followed with adapting the laboratory procedure used by Holmes et al. (2009) to design a randomised controlled trial in a hospital emergency department (ED; Chapter 2). Stage 2 involved piloting and refining the procedure in the emergency department through two "feasibility and piloting" studies with patients who had experienced a road traffic accident (Chapters 3 and 4). Stage 3 involved conducting a randomised controlled study to test of the efficacy of the simple cognitive task intervention, compared to usual care with a simple activity diary "foil" task, in reducing intrusive memories in the week after a road traffic accident. Stage 4 involved reviewing the main findings of the research to identify possible refinements for further development of the intervention (discussed here in Chapter 8: see Figure 8.1).

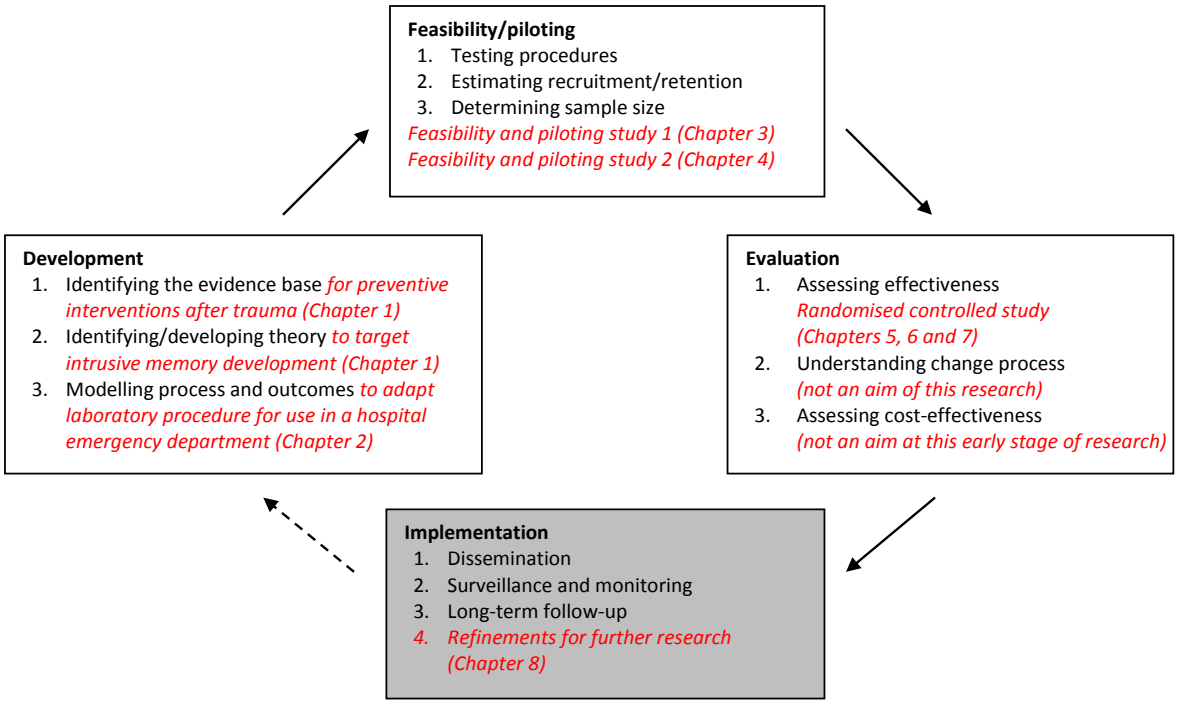


Figure 8.1. Stages in this research to develop and evaluate a novel preventive intervention after trauma, based on the MRC Complex Interventions Guidance (2008). Adaptations for this research are shown in red italics.

Main findings of the thesis

Development

A review of the evidence base for preventive interventions after trauma (Chapter 1) indicated a lack of preventive interventions that: a) could be delivered in the immediate aftermath of trauma (i.e. within the first few hours and days), b) could be offered universally to all trauma survivors, regardless of whether or not they exhibited acute stress symptoms, c) were low-intensity in nature, and d) targeted specific processes known to be important in the development of early post-traumatic symptoms as well as later PTSD.

Chapter 1 went on to discuss theory from clinical psychology indicating that intrusive memories in the week after a traumatic event might be a suitable target for a preventive intervention after trauma, as not only are intrusive memories distressing in their own right, but early intrusive memories may predict later post-traumatic stress disorder. Finally, Chapter 1 reviewed relevant experimental psychology literature showing that specific cognitive tasks that tax working memory (in particular visuospatial cognitive

tasks) can interfere with intrusive image-based memories, and that completing these tasks four hours after an experimentally-induced trauma (before memories of the trauma are hypothesised to have consolidated; Nader, Schafe, & LeDoux, 2000) can reduce the frequency of intrusive memories over the following week.

Feasibility and Piloting Study 1

The initial feasibility and piloting study in the emergency department (n = 10; see Chapter 3) tested key procedures for the randomised controlled study, namely the recruitment of road traffic accident patients, delivery of the simple cognitive task intervention, and completion of the primary outcome measure (a pen-and-paper Intrusion Diary). Results regarding recruitment and delivery of the simple cognitive task intervention showed: a) a recruitment rate of approximately one participant per week, b) 62.5% of road traffic accident patients approached about the study were willing to complete the simple cognitive task intervention, and c) 70% of participants were able to complete the intervention with a minimum of 10 minutes of Tetris play. Amendments were made to the recruitment strategy (e.g. increasing the time that the researcher was available in the emergency department) and eligibility criteria (e.g. ensuring participants had sufficient physical mobility to play Tetris at the point of taking informed consent) to improve these outcomes.

Results regarding the completion rate of the Intrusion Diary (the primary outcome measure) for the first eight participants indicated a clear problem (0% return rate). Based on participant responses on a feedback questionnaire, a number of amendments were made to help improve the completion rate, including simplifying the diary format and sending participants a daily reminder to fill it in. These amendments were implemented for the last two participants with encouraging results (50% return rate). Two out of 10 participants (20%) were lost to follow up, which was a slightly higher drop-out rate than estimated.

Feasibility and Piloting Study 2

A second feasibility and piloting study (n = 23; see Chapter 4) was conducted in the emergency department to implement refinements from the previous study and test the procedures for both the intervention and control conditions (as the initial pilot study only tested the intervention procedure). A serial piloting approach was taken, whereby minor

changes were implemented during the course of the study in response to accumulating outcome data, observational data, and participant responses on a feedback questionnaire.

The results showed improvements in: a) the recruitment rate (from approximately one participant per week to approximately two participants per week), b) the eligibility criteria (such that the proportion of participants able to complete the simple cognitive task intervention increased from 70% to 100%), c) the drop-out rate (a reduction from 20% to 17% overall, but only 9% in the second half of the study), and d) the completion rate of the Intrusion Diary (from 10% to 83%).

Refinements were made during the course of the pilot study to improve the intervention and control procedures (such as reducing the intensity of the memory reactivation cue in the intervention condition and removing a procedure from the control condition that was not congruent with usual care). The Intrusion Diary was refined further to simplify the format and clarify the instructions in response to participant feedback.

Main Evaluation

The design of the main study in this research was an open (unblinded), parallel two-group randomised controlled trial (n = 71; ClinicalTrials.gov Identifier NCT02080351) to test the simple cognitive task intervention in patients waiting in a hospital emergency department after a road traffic accident (see Chapter 5, 6 and 7). Participants were randomly allocated to one of two groups using an online randomisation system[22]: 1) a simple cognitive task intervention (a memory reactivation cue followed by playing the computer game Tetris) in addition to usual care in the emergency department (see Figure 8.2) or 2) usual care in the emergency department with a simple activity diary (a foil task with a similar duration to the simple cognitive task intervention). The primary outcome was the number of intrusive memories participants recorded in the week after a road traffic accident (using an Intrusion Diary), and secondary outcomes were post-traumatic stress symptoms (PDS and IES-R scores), anxiety (HADS-A score) and depression (HADS-D score) at one week and one month after a road traffic accident.

[22] The online randomisation programme was developed by Oxford Cognitive Health and Neurosciences Clinical Trials Unit (OCHNCTU) and accessed from the emergency department after participants had completed the relevant baseline measures to ensure allocation concealment until the point of randomisation.

Participants' experience of taking part in the study was assessed using a Feedback Questionnaire, to inform refinements for further research.

Figure 8.2. Example of someone playing Tetris in the emergency department. This image has been used with written consent from the individual.

Study participants

Thirty-seven participants were allocated to the intervention group and 34 to the control group. Only one participant in the intervention group did not adhere to the full intervention, as they only played Tetris for 3 minutes instead of the required minimum of 10 minutes uninterrupted play (due to being moved to a different bay by staff, and subsequently falling asleep). Attrition was relatively low, with 5.6% drop-out at one week and 12.7% drop-out at one month (compared to 26% drop-out at one month in a recent trial of an early intervention after trauma; Rothbaum et al., 2012).

Randomisation resulted in intervention and control groups that were balanced on demographic characteristics and key prognostic factors for PTSD (perceived life threat, dissociation and distress at the time of the accident).

Primary outcome

The completion rate of the Intrusion Diary was high (94%). The result of the primary efficacy analysis (an intention to treat analysis) showed that participants in the simple cognitive task group recorded significantly fewer intrusive memories in the week after the accident than participants in the control group (t = 2.800, p = .005, d = 0.665, 95% CI [0.184, 1.141]), and on average recorded approximately one third of the number of intrusive memories (a mean of 8.86 in the simple cognitive task group and 23.52 in the control group; see Figure 6.2., Chapter 6).

This result was not only in the predicted direction, but also found a medium effect size[23] of d = 0.665, which was close to the estimated effect size of d = 0.7. This is an exciting and encouraging result, given that this study is a first step in translating findings from previous laboratory-based research (e.g. showing an effect size of d = 0.91; Holmes et al., 2009) to a clinical setting after real-world trauma.

This outcome indicates that the study was sufficiently powered to detect a treatment effect. This is likely to reflect an adequate sample size as well as the benefits of extensive piloting in the emergency department, which helped to achieve high completion rates, low drop-out, and rigorous adherence to the study protocol, thereby minimising noise in the implementation of the randomised controlled study.

Secondary outcomes

The results of the secondary efficacy analyses showed that participants in the simple cognitive task group had significantly lower scores on a clinical measure of the distress caused by intrusion symptoms (the intrusion subscale of the Impact of Event Scale-Revised; t = 2.251, p = .024, d = 0.535, 95% CI [0.059, 1.007]), and lower scores that did not quite reach significance at the 0.05 level on a clinical measure of the frequency of intrusion symptoms (the re-experiencing subscale of the Posttraumatic Diagnostic Scale; t = 1.891, p = .059, d = 0.449, 95% CI [-0.024, 0.919]). The effect size for both of these measures was in the medium range.

No other secondary outcomes at one week or one month (e.g. other post-traumatic stress symptoms, anxiety or depression) showed significant differences between the two

[23] Effect sizes were interpreted as follows: d = 0.2 as a small effect, d = 0.5 as a medium effect and d = 0.8 as a strong effect (Cohen, 1988).

groups. This is perhaps unsurprising, given that the simple cognitive task intervention was hypothesised to target selectively the occurrence of intrusive memories. However, small effect sizes in the predicted direction were found for the vividness and distress of intrusive memories in the first week, hyperarousal symptoms, total post-traumatic stress symptoms, and depression at one week, and intrusion symptoms at one month. Figure 8.3 shows aggregated results for the intention to treat analyses of the primary outcome measure and key secondary outcome measures in the randomised controlled study.[24]

Key exploratory findings regarding outcome

A notable exploratory finding from the randomised controlled study was that a significantly higher proportion of participants in the simple cognitive task group than the control group had 0 intrusive memories in the first week after the road traffic accident (26.5% compared to 6.1%). Further, a time course analysis of the number of intrusive memories per day in the first week after the accident indicated that whilst the number of intrusive memories decreased over the seven days in the intervention group (to approximately a 60% probability of having 0 intrusive memories at day 7), the number of intrusive memories remained relatively consistent over the seven days in the control group (with approximately a 5% probability of having 0 intrusive memories at day 7). Interestingly, participants in the intervention group with low perceived life threat (thought to be at lower risk of PTSD symptoms; Ozer et al., 2003) showed a more rapid decline in the number of intrusive memories over the seven days than those with high perceived life threat, whilst there was a less marked difference between participants with low and high perceived life threat in the control group.

[24] The same pattern of results across the primary and secondary outcome measures (i.e. a significant reduction only in the number of intrusive memories and one week intrusion symptoms in the simple cognitive task group compared to the control group) was found when the efficacy analyses were conducted with adjustment for baseline covariates and using the per protocol population.

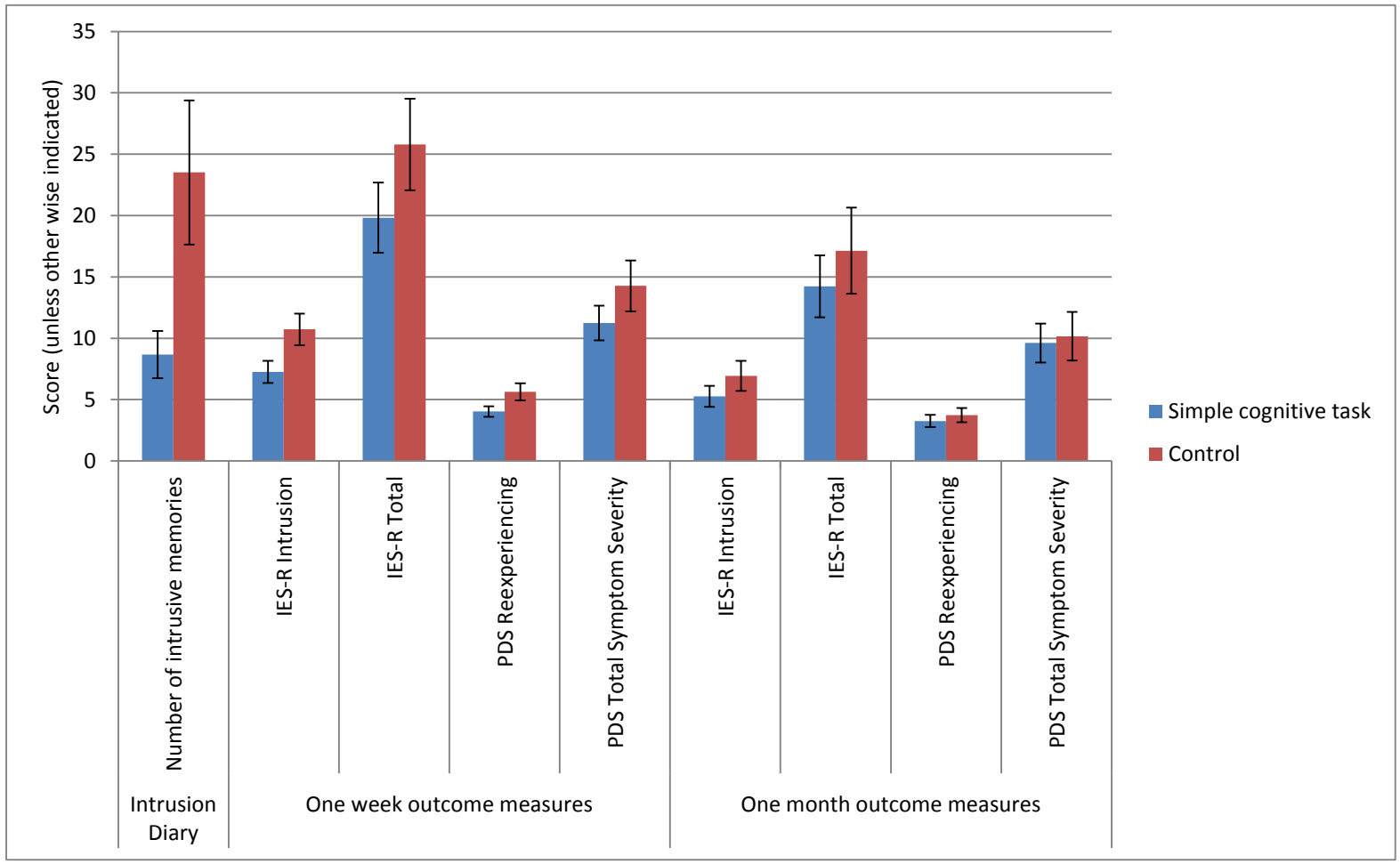


Figure 8.3. Graph to illustrate the pattern of results for key outcomes in the study, indicating early effects that diminish over time.

The examples noted in the Intrusion Diary of participants' worst moments of the accident, or "hotspots" (which were hypothesised to correspond to their intrusive memories; Holmes et al., 2005) were very similar in the two groups, and predominantly described vivid sensory moments of the accident e.g. "flash of airbag", "blood streaming/dripping", "smell burning rubber", "windscreen smashing", "catapulting forward", and "seeing van indicator lights".

Participant feedback

Participants' responses on a feedback questionnaire at the end of the study indicated that their experience of the study was predominantly positive. Critically, participants in the intervention condition rated playing Tetris in the emergency department to be easy, helpful and minimally distressing. Comments highlighted an unexpectedly wide range of positive reactions to playing Tetris in the emergency department, including finding the game calming, a helpful distraction from dwelling on the accident, a helpful distraction from pain and physical symptoms in an environment in which the main focus was on their physical symptoms, and finding that it brought back a sense of "normality" after the trauma. Only a few participants (four out of 37) commented on negative reactions to the intervention, such as finding the computer game frustrating or more stressful than usual.

Implications of the thesis

Translational research implications

This research took a first step in translating a simple cognitive task intervention (a memory reactivation cue followed by playing the computer game Tetris) from previous laboratory studies with healthy participants to a hospital setting with patients who had experienced a real-world road traffic accident. The first notable finding with translational research implications was that it was feasible to deliver the simple cognitive task intervention in a busy and distracting hospital emergency department environment. This finding is not to be underestimated, as it implies that the intervention (which involved playing a computer game for at least 10 minutes) has potential to be adapted and implemented flexibly in a variety of clinical settings, and is not only deliverable under controlled laboratory conditions.

The second notable point from a translational perspective was that findings from the randomised controlled study replicated those found in preceding laboratory studies, i.e. participants allocated to the simple cognitive task group had significantly fewer intrusive memories in the week after the accident (recorded in an Intrusion Diary), as well as significantly lower intrusion symptom scores on a clinical measure of PTSD symptomatology at one week (the IES-R intrusion subscale). Moreover, the effect on the number of intrusive memories remained robust (d = 0.66) even with translation to a "noisier" and less controlled hospital setting.

These results suggest that a simple cognitive task that taxes working memory can not only reduce intrusive memories of experimental trauma (a film with traumatic footage), but can also reduce intrusive memories of real-world traumatic experiences. This supports that the notion that the trauma film paradigm may be a useful experimental analogue for real-world trauma (Holmes & Bourne, 2008; Horowitz, 1969), and the view that intrusive memories may lie along a continuum with varying severity from intrusive autobiographical memories to "flashbacks" in PTSD (see Kvavilashvili, 2014).

This study combined experimental cognitive science with clinical psychology to take a first step in testing a novel preventive intervention to target intrusive memories after real-world psychological trauma. As such, it is part of an important translational research agenda that seeks to bridge the gap between basic science research and routine clinical practice in mental health (Engelhard, 2012; Holmes, Craske, & Graybiel, 2014).

Implications for patient recovery from trauma

Clinically, the study results implied that giving patients a simple cognitive task intervention soon after a traumatic road traffic accident (compared to usual care in the emergency department with a simple activity diary) accelerated their recovery from intrusive memories and clinical intrusion symptoms in the first week after the accident. This offers a potential means to reducing patient distress in the first week after a traumatic event - a period for which there is currently a lack of effective interventions.

The occurrence of intrusive memories in the first week after trauma has been found to predict the development of later PTSD (Creamer et al., 2004), suggesting that by reducing early intrusion symptoms, there may be potential to alleviate later post-traumatic distress. Whilst this study was not sufficiently powered to detect a

difference between the intervention and control groups in one month PTSD symptoms, the effect sizes for one month outcomes suggested that a larger study with 652 participants (or 312 participants at higher risk of PTSD symptoms) would be able to detect a difference between the two groups in clinical intrusion symptoms at one month. Further, even the small effect sizes found at one month follow-up may be worth pursuing, given the low-intensity and potential cost-effective nature of this intervention.

Exploratory findings from this study suggested that the simple cognitive task intervention might be more effective for patients who have a less severe subjective reaction to the trauma than those with a more severe subjective reaction, in this study indicated by low versus high perceived life threat. One possible hypothesis for this is that people who are more severely affected by the trauma (e.g. have high perceived life threat, high emotional distress and high dissociation) are less able to attend to the cognitive task intervention in the immediate aftermath, thereby minimising the extent to which it taxes their working memory resources and reduces subsequent intrusive memories (Engelhard et al., 2011; Holmes et al., 2004; Stuart et al., 2006).

An unexpected, but clinically salient, outcome from this study was the wide range of positive feedback from participants regarding their experience of playing Tetris in the emergency department. Participants described a number of beneficial effects of playing Tetris, and highlighted how much the intervention was valued at a difficult and vulnerable time. Therefore, perhaps contrary to what some might expect, the computer game was not viewed as a trivial part of the intervention. Testimonies from survivors of trauma have highlighted the perceived lack of support in the immediate aftermath of a traumatic event (National Institute for Health and Clinical Excellence, 2005). Further, a systematic synthesis of qualitative research regarding patient experience in the emergency department identified this as a time when patients are feeling vulnerable, stressed and fearful, perceive a “medical-technical” culture over “caring” behaviour in staff, and are often left alone for long periods of time, which is particularly distressing and frustrating if no family or friends are present (J. Gordon, Sheppard, & Anaf, 2010). Therefore, in addition to aiding recovery from early intrusive memories, this simple cognitive task intervention may provide something to offer trauma survivors to help alleviate feelings of anxiety, frustration and isolation in the immediate aftermath of trauma.

A final interesting observation from a patient perspective was the large proportion of patients that had played Tetris before (89% in the intervention group), and who reported

playing other similar visuospatial computer games, such as Candy Crush Saga, Free Flow, Bubble Witch and Minecraft. These types of computer games have become extremely popular in recent years through availability on smartphones and tablets (Shute, 2013, May 14), suggesting that they may offer an intervention approach with high ecological validity. Encouragingly, in this study even older participants (up to age 85) were willing (and indeed able) to play the computer game in the emergency department. Therefore, whilst it has been suggested that motivating traumatised individuals to play a computer game within 6 hours of a traumatic event may be a challenge (Dyregrov & Regel, 2011), results from this study would indicate otherwise.

Implications for interventions after trauma

Despite a wealth of research into preventive interventions for PTSD symptoms, there remains a lack of effective interventions that can be delivered in the immediate aftermath of a traumatic event, leading current clinical and organisational guidelines to recommend "watchful waiting" (National Institute for Health and Clinical Excellence, 2005) or psychological first aid (which involves no specific psychological intervention; North Atlantic Treaty Organization (NATO), 2008; World Health Organization, 2011) in this early period. However, professionals often feel drawn "to do something" in the immediate aftermath of trauma, even if it lacks an evidence base (Bell, 2013, May 12). The results of this research suggest that the simple cognitive task intervention may provide a theory-based intervention to offer trauma survivors in the immediate aftermath to aid recovery from intrusive memories in the first week. This is a first step towards developing a preventive intervention after trauma to address the current gap.

The simple cognitive task intervention was very brief (approximately 20 minutes), low intensity and easy to deliver (as only brief input was required from the researcher during the memory reactivation cue and to explain the instructions for the computer game), and very well tolerated by patients (most found it easy and minimally distressing). Further, it was delivered flexibly in different environments on a portable gaming device (or smartphone/PC in the week after the accident). Therefore the simple cognitive task has future potential as a highly practical and accessible intervention that could be used in a variety of trauma contexts, such as following mass disasters, in hospital or emergency service settings, or in even soldiers deployed to war zones. The low potential cost of this intervention (particularly in relation to alternative higher-intensity early interventions such

as trauma-focused cognitive behavioural therapy: e.g. Ehlers & Clark, 2000) is an important advantage, as disaster funding is often poor (e.g. Gheytanchi et al., 2007).

From the perspective of clinical emergency and trauma services (e.g. in the UK National Health Service, NHS), there is a real need for simple interventions that can be delivered in acute trauma settings. For example, in presenting this research to the "Injuries and Emergencies" specialty group for the local Clinical Research Network[25], clinical research staff suggested that this type of intervention would have high applicability in Intensive Care Units and with ambulance service staff, where they felt that immediate post-trauma interventions were lacking and much needed. A simple computer game intervention (which could potentially be "self-administered") may hold particular appeal for occupational groups with routine exposure to trauma but high levels of stigma over mental health problems, such as emergency service staff (e.g. Ross & Goldner, 2009). Future research will need to establish in what settings and for which groups this intervention approach might be appropriate.

Due to the brief and low-intensity nature of this intervention, it may possible in the future to embed it with minimal interference within existing organisational procedures after traumatic incidences. For example, local Fire and Rescue Services hold a group debriefing meeting for employees within a few days after any major incident (B. Jeffries, personal communication, June 2010), which may offer an opportunity to utilise such an intervention. At a population level, current consensus guidelines for organisational trauma response (e.g. Williams et al., 2009) recommend a stepped care model in which the first response to psychosocial needs is at the level of family, friends and the local community. This simple, low-intensity intervention may have potential in the future to be integrated within this model at an early stage, without requiring specialist "outsider" intervention, or to be recommended in the form of a simple psychological "prescription".

Finally, this study demonstrated that it was possible to incorporate clinical psychology provision within an emergency department environment, and suggested it may have a valuable role to play. Part of the success of the study reflected that the researcher was embedded within the emergency department for the period of the study, and became accepted as a part of the emergency department staff team, showing the potential for Clinical Psychologists to work in this environment. Previous research has identified the

[25] Thames Valley & South Midlands Clinical Research Network Injuries and Emergencies Specialty Research Meeting, 3rd July 2015, Transport Research Laboratory, Crowthorne, Berkshire UK.

lack of support for patient's emotional and psychosocial needs in the emergency department (Gordon, Sheppard & Anaf, 2010). A few research studies have examined clinical psychological interventions in acute hospital settings with encouraging results (e.g. Peris et al., 2011; Rothbaum et al., 2012), but this has not reached the stage of translation into clinical practice. As research in this area expands, there may be a case to develop a role for clinical psychology in emergency care in the future.

Strengths of this research

Two general strengths of this research are worth noting, as they are likely to have facilitated the success of the study. The first is the extensive piloting that took place in the emergency department prior to commencing the randomised controlled study. This allowed critical procedures to be refined, so that in the randomised controlled study recruitment ran smoothly, attrition was low, and the completion rate of the primary outcome measure was high. This highlights the value of rigorous pilot work in translational research. The second strength to note was that the researcher was physically based in the emergency department throughout the main studies in the research, and attended staff handover meetings and developed good relationships with the clinical team. Consequently the researcher became embedded as a member of the emergency department staff team, and this no doubt facilitated recruitment and the general smooth running of the study.

Limitations of this research

This section will discuss the main limitations in the design of the randomised controlled study with implications for its internal and external validity. One potential criticism is that participants with very severe injuries tended to be excluded from the study (e.g. as a result of being physically unable to play the computer game, or having sustained head injuries), potentially limiting the external validity of the study. However, this may well reflect the potential application of the intervention in clinical practice, as the intervention would be necessarily targeted at people who had sufficient physical ability and felt well enough to play a computer game, i.e. those potentially less severely affected by the trauma.

The primary outcome measure, an Intrusion Diary completed in the week after the road traffic accident, was not a validated clinical measure of intrusive memories, but

instead was selected on its translational strength given that it has been shown to be sensitive to the effect of cognitive task interventions in the laboratory (Holmes & Bourne, 2008). As such, its reliability and validity has not been assessed. Further, only self-report measures were used to assess PTSD symptoms, whereas a clinician-rated interview (such as the Clinician-Administered PTSD Scale, CAPS) might have increased the validity of the findings.

Selection of an optimal control condition was a challenge. Whilst "usual care" in the emergency department was initially selected, following piloting a simple activity diary foil task was introduced to parallel the period during which participants in the intervention group completed the simple cognitive task. Whilst this allowed a controlled comparison, as well as an assessment of what participants in the control condition were doing during that period, the effect of completing the activity diary on the primary outcome was unknown, raising the possibility that the procedure might have influenced the number of intrusive memories in the week after the accident.

Randomisation used a process of minimisation to balance the two groups on key demographic variables (age and gender) and a known predictor of PTSD symptoms (perceived life threat). However, the actual association between these variables and the primary outcome (the number of intrusive memoires in the week after the accident) was unknown, raising the possibility that other factors may have been more prognostically relevant. Further, allocation by perceived life threat was based on a somewhat arbitrary division of low (0 to 4) and high (5 to10) perceived life threat ratings. Nonetheless, the intervention and control groups were well balanced on all key baseline variables.

The randomised controlled study was unblinded, introducing the potential for bias in how participants in the two groups were treated (performance bias) or assessed at outcome (detection bias). However, measures were taken to minimise such bias, for example by using protocolised procedures with all participants and assessing outcome using self-report measures only. Expectancy ratings indicated that participants in the control condition predicted a slight increase in the number of intrusive memories, whilst participants in the intervention condition predicted a slight decrease in the number of intrusive memories; however, these ratings were taken retrospectively, so may have been biased by outcome, and reassuringly ratings were not correlated with the primary outcome in either group.

This early-phase study was primarily concerned with assessing the efficacy of the simple cognitive task intervention in reducing intrusive memories, and did not set out to

explore the potential mechanisms of the intervention. As well as completing the simple cognitive task in the emergency department, participants in the intervention group were instructed that they were welcome to play the computer game Tetris, or imagine playing it, if they had an intrusive memory in the week after the accident. The results indicated that uptake of this suggestion was variable, and some participants played other visuospatial computer games in the month after the accident. Therefore it was not possible to evaluate the relative impact of the simple cognitive task in the emergency department (during the hypothesised period of memory consolidation) and playing Tetris or other similar games after leaving the emergency department (which may have affected memory reconsolidation; James et al., 2015).

Finally, a number of potential risk factors influencing post-traumatic stress symptoms and other outcomes following the road traffic accident were not assessed in this study, such as visitation by family or friends in the emergency department (Lubomirsky et al., 2013) and posttraumatic cognitions (Ehlers et al., 1998; Kleim, Ehlers, & Glucksman, 2012).

Future directions of this research

Given that this research took a first step in translating the simple cognitive task intervention from the laboratory to real-world trauma, future trials are clearly needed to replicate and extend the study findings. Replications studies are likely to benefit from considering refinement to the primary outcome measure, such as using a measure with demonstrated reliability and validity (which may involve assessing the psychometric properties of the Intrusion Diary and refining it accordingly), or using alternative methods of assessing intrusive memory frequency, such as electronic diary methods (Kleim, Graham, Bryant, & Ehlers, 2013; Priebe et al., 2013). The use of a clinician-rated measure of PTSD symptoms, such as the Clinician-Administered PTSD Scale, would improve the validity of the findings. It would be advantageous to find ways of blinding the study, such as having outcome assessors who were unaware of the participant's group allocation (in a single blind study).

Future studies might be powered to detect an effect of the intervention on PTSD symptoms at one month. Based on the effect sizes found in this study, a sample of 652 participants would be required to detect a difference between the intervention and control groups in clinical intrusions symptoms (e.g. IES-R intrusion score) at one month. Another

possibility would be to limit the sample to patients with a higher risk of developing PTSD symptoms (e.g. those with high perceived life threat), in an attempt to increase the treatment signal. Based on the results of this study for participants with high perceived life threat only, a sample of 312 participants would be needed. Late-phase trials may benefit from assessing PTSD symptoms over a longer follow-up period (e.g. 6 months or 1 year), as well as looking at wider outcomes such as participants' work and social functioning, and their quality of life.

If further studies are successful in replicating the efficacy of the simple cognitive task intervention after real-world trauma, it will be interesting to examine factors that may moderate the intervention effect, such as the "dose" or duration of the intervention, or particular participant characteristics (e.g. mental imagery ability, subjective reaction to the trauma). Exploratory analyses in this study indicated some potentially relevant factors. For example, the maximum length of time for which participants played Tetris uninterrupted was negatively associated with the number of intrusive memories, suggesting that playing Tetris for a longer uninterrupted period was beneficial.

Further, participant feedback regarding the aspects of playing Tetris they found helpful pointed to factors such as reduced arousal ("calming effect"), attentional focus (finding the game absorbing and distracting), and enjoyment in the game. Another potential moderating factor to explore is the complexity of the game, as tasks that tax working memory to a moderate degree (rather than to a low or high degree) have been shown to be most effective in reducing the frequency of intrusive memories (Engelhard et al., 2011).

Another potential moderator to explore is subjective threat to life. Exploratory results in this study suggested that people with low perceived life threat showed a more rapid decline in the number of intrusive memories over the first seven days than those with high perceived life threat. General mental imagery ability (Morina, Leibold, & Ehring, 2013) and spatial configuration learning (Meyer et al., 2013) are other individual characteristics that might predict response to the intervention. Through exploring these potential moderators of the intervention effect, it may be possible to identify who may benefit most from this type of intervention, and how to optimise the effect of the intervention in the future.

Alongside clinical studies concerning the application of this intervention approach after real-world trauma, experimental studies are still needed to examine further the potential mechanisms of the intervention with relation to memory consolidation theory

(which was beyond the scope of this research) and to identify future potential applications. For example, recent laboratory studies have extended the intervention timing from the consolidation window (approximately the first 6 hours after trauma) to reconsolidation (by reactivating the trauma memory after it has consolidated), and tested the effect of the component parts of the intervention (the memory reactivation cue and playing Tetris; James et al. 2015), with implications for how the intervention might be used beyond the 6-hour time frame used in this study. Further, brain imaging studies are starting to offer insights into the neural correlates of intrusive memories (e.g. Clark et al., 2014).

An exciting avenue for further research is to explore alternative computer games that might have a similar effect to Tetris as part of a cognitive task intervention. Currently there are a large and expanding number of computer games based on visuospatial processing that are available as smartphone applications, and extremely popular (e.g. Candy Crush Saga, Bejewelled, Free Flow, Bubble Witch, and Minecraft). Having a variety of computer games to offer people based on individual preference is likely to increase the acceptability and uptake of this intervention approach.

Finally, the use of visuospatial cognitive tasks to disrupt distressing mental imagery has potential for a range of clinical applications outside trauma and post-traumatic stress disorder. For example, studies have begun to explore their use to reduce public speaking anxiety (Homer, Deeprose, & Andrade, 2015) and cravings (Skorka-Brown, Andrade, & May, 2014).

Conclusions of this thesis

This research developed and tested a simple cognitive task intervention (a memory reactivation cue followed by playing the computer game "Tetris") to reduce the occurrence of intrusive memories in the week after a road traffic accident. This involved: a) adapting the procedure used in previous laboratory studies with healthy participants (Holmes et al., 2009; Holmes et al., 2010) for use in a hospital emergency department with patients who had experienced a road traffic accident, b) piloting the key procedures in the emergency department, and c) conducting a randomised controlled study to provide a preliminary test of the efficacy of the intervention (a pre-registered clinical trial: ClinicalTrials.gov Identifier NCT02080351).

This research was the first to show that it was feasible to deliver a psychological intervention involving playing a computer game in a busy emergency department

environment in the immediate aftermath of a trauma (on average 3 to 4 hours after the accident). This highlights possibilities for new innovations in healthcare, using simple computerised interventions.

Critically, the results of the randomised controlled study showed a significant reduction in the number of intrusive memories in the first week after the accident (the primary outcome) in the simple cognitive task intervention group compared to the control group, with an effect size of $d = 0.67$. Notably, participants in the intervention group had approximately a third of the number of intrusive memories as those in the control group. Further, participants in the intervention group had significantly lower clinical intrusion symptom scores at one week than those in the control group. These encouraging results were the first to extend previous laboratory findings to a clinical setting. Whilst no significant differences were found between the two groups in PTSD symptoms at one month, small effect sizes were found in the predicted direction, suggesting that larger studies in the future might be sufficiently powered to detect an effect.

Further, patients in the randomised controlled study reported predominantly positive feedback about the intervention, and highlighted the value of being offered such an intervention after the road traffic accident. This indicates that there a much-needed role for psychological care in emergency settings. For example, one participant commented on a feedback questionnaire at one month follow-up, "I think that playing Tetris helped focus my mind and bring some "normality" back to my head. I didn't dwell on the accident too much while I was in hospital. Playing Tetris seemed a bit strange at the time, but looking back it has been a help. Thank you."

At present, we lack evidence-based preventive interventions for PTSD symptoms to offer trauma survivors in the immediate aftermath of traumatic events (Agorastos et al., 2011). This research provides a first step towards developing a simple, low-intensity, and acceptable preventive intervention with potential to address this gap. As this research was the first clinical test of the simple cognitive task intervention, further studies may help to refine the intervention, for example by exploring how to optimise the cognitive effect of the computer game or examining alternative computer tasks. Studies are also needed to replicate the findings, and to extend the research to other settings and populations, for example occupational groups exposed to trauma (such as emergency personnel or the military), where simple preventive interventions are much-needed. Crucially, the intervention may have particular value cross-culturally in the context of disaster aid, as it is both non-stigmatising and language-free. In line with the MRC

framework for the development of complex interventions (2008), evaluation of changes processes (e.g. mechanisms and moderators of the intervention effect) and determining cost-effectiveness are also important steps before this preventive approach may be implemented and evaluated in clinical practice.

CHAPTER 9. References

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CHAPTER 10. Appendices

APPENDIX 2.1 Training course certificates

Certificate of Attendance

is hereby granted to:

Lalitha Iyadurai

Randomised Controlled Trials Course:

A guide to design, analysis, interpretation and reporting

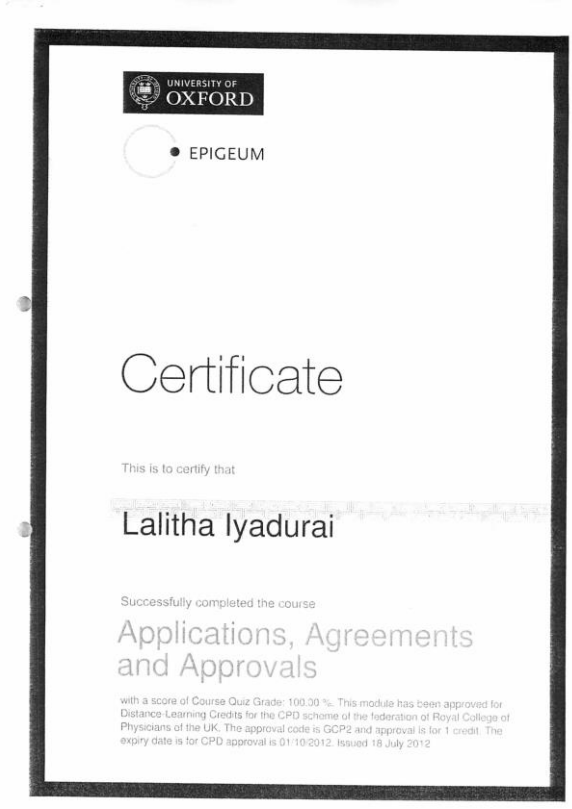
17th September– 21st September 2012

Oriel College, Oxford

Doug Altman, Director of CSM

C S M

Approved by the Federation of the Royal College of Physicians of the United Kingdom for 28 category 1 (external) CPD credits



UNIVERSITY OF OXFORD

EPIGEUM

Certificate

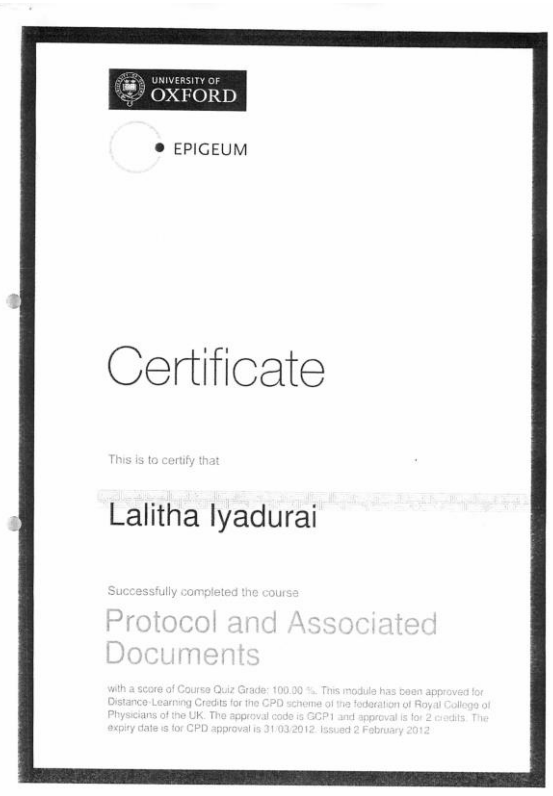
This is to certify that

Lalitha Iyadurai

Successfully completed the course

Applications, Agreements and Approvals

with a score of Course Quiz Grade: 100.00 %. This module has been approved for Distance-Learning Credits for the CPD scheme of the federation of Royal College of Physicians of the UK. The approval code is GCP2 and approval is for 1 credit. The expiry date is for CPD approval is 01/10/2012. Issued 18 July 2012



UNIVERSITY OF OXFORD

EPIGEUM

Certificate

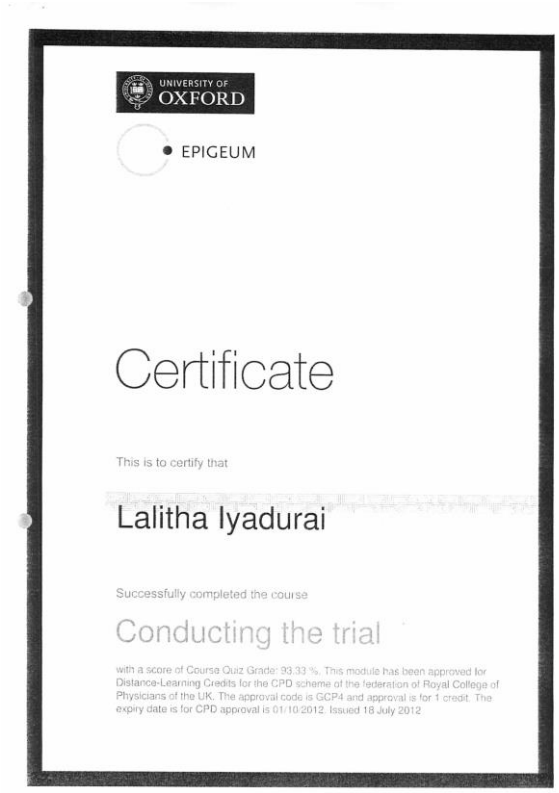
This is to certify that

Lalitha Iyadurai

Successfully completed the course

Protocol and Associated Documents

with a score of Course Quiz Grade: 100.00 %. This module has been approved for Distance-Learning Credits for the CPD scheme of the federation of Royal College of Physicians of the UK. The approval code is GCP1 and approval is for 2 credits. The expiry date is for CPD approval is 31/03/2012. Issued 2 February 2012



UNIVERSITY OF OXFORD

EPIGEUM

Certificate

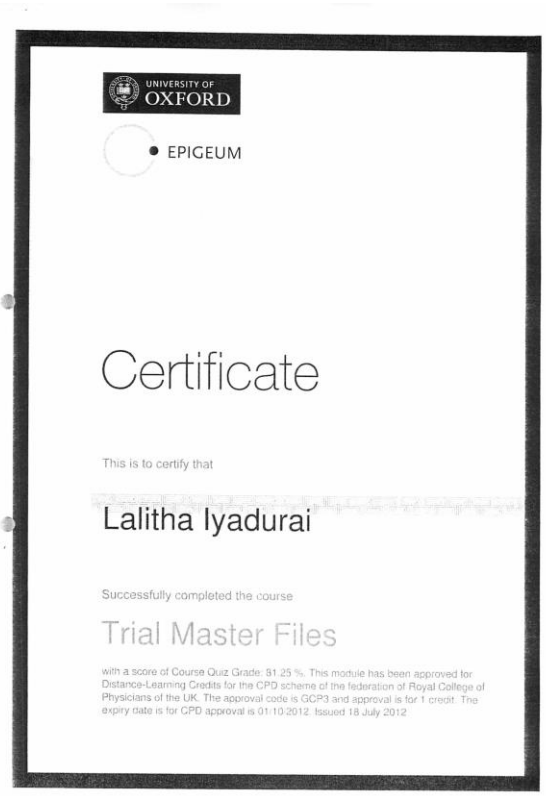
This is to certify that

Lalitha Iyadurai

Successfully completed the course

Conducting the trial

with a score of Course Quiz Grade: 33.33 %. This module has been approved for Distance-Learning Credits for the CPD scheme of the federation of Royal College of Physicians of the UK. The approval code is GCP4 and approval is for 1 credit. The expiry date is for CPD approval is 01/10/2012. Issued 18 July 2012



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EPIGEUM

Certificate

This is to certify that

Lalitha Iyadurai

Successfully completed the course

Trial Master Files

with a score of Course Quiz Grade: 81.25 %. This module has been approved for Distance-Learning Credits for the CPD scheme of the federation of Royal College of Physicians of the UK. The approval code is GCP3 and approval is for 1 credit. The expiry date is for CPD approval is 01/10/2012. Issued 18 July 2012

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EPIGEUM

Certificate

This is to certify that

Lalitha Iyadurai

Successfully completed the course

Safety Reporting

with a score of Course Quiz Grade: 85.71 %. This module has been approved for Distance-Learning Credits for the CPD scheme of the federation of Royal College of Physicians of the UK. The approval code is GCP5 and approval is for 2 credits. The expiry date is for CPD approval is 01/10/2012. Issued 19 July 2012

APPENDIX 2.2 Trial Management Group meeting agenda template

MRC Cognition and Brain Sciences Unit

Oxford University Hospitals NHS Trust

NHS National Institute for Health Research

SCARTA: A simple cognitive task after a road traffic accident

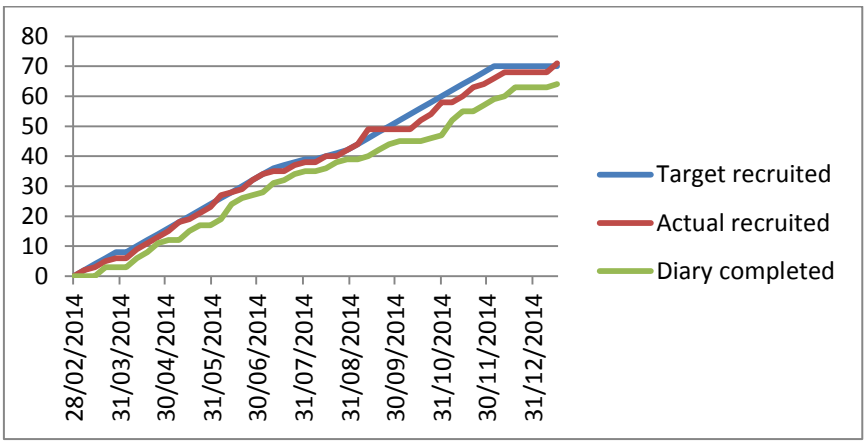
TRIAL MANAGEMENT GROUP MEETING

Date and time:
Location:
Present:
Apologies:

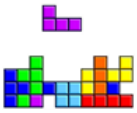
Agenda

1. **Participant recruitment**
2. **Participant attrition**
3. **Adherence to protocols**
4. **Safety reporting**
5. **Data monitoring**
6. **Data analysis**
7. **Any other business**
8. **Next TMG meeting**

Example recruitment graph



APPENDIX 2.3 Trial monitoring plan



Oxford University Hospitals NHS
NHS Trust

NHS
National Institute for
Health Research

SCARTA: A simple cognitive task after a road traffic accident

MONITORING PLAN

Chief Investigator (CI): Dr Lalitha Iyadurai
Main Supervisor: Prof Emily Holmes
Site: Emergency Department, John Radcliffe Hospital

1. General

Definition of source data
The source data in the trial are the:

- Paper questionnaires completed by participants in the Emergency Department (ED) and at one-week and one-month follow up (including the flashback record in the first week).
- Medical notes recorded by emergency service and ED staff.
- Online questionnaires completed by participants at one-week and one-month follow-up.
- Paper forms completed by the researcher in the Emergency Department (e.g. eligibility checklist, session 1 protocol, hotspots of the accident form) and at follow-up (e.g. follow-up protocol).
- The researcher's written notes on paper forms and in the SCARTA lab book.
- The participant contact log kept by the researcher.

Source data verification
Source data verification will occur in the following way:

1) Source data will be reviewed by the CI as it is entered into a participant's CRF, and any incomplete data queried.
2) Once a participant has completed the study, their CRF will be reviewed by the CI, who will verify that all data is present, or missing data accounted for, before signing off the CRF.
3) For the first few participants in the trial, their source data will be checked against the CRF by an investigator other than the one who completed the CRF.
4) Thereafter, source data will be checked against the CRF by an investigator other than the one who completed the CRF for the most recently recruited participant every 1-2 months.

Handling of protocol deviations

1) The CI and their Supervisor will be informed of protocol deviations at the earliest opportunity.
2) Protocol deviations will be raised at the Trial Management Group meetings.
3) The investigator reporting the protocol deviation will indicate on the "off study form" at the back of the CRF that a protocol deviation has occurred.
4) They will then complete a "Protocol deviation form" to be attached to the back of the CRF, and copy this information into the study "Protocol deviation log".

2. Central and onsite monitoring

Trial administration will be based at the University of Oxford Department of Psychiatry. Participants will be recruited at the John Radcliffe Hospital Emergency Department. Monitoring will therefore cover both these sites.

Participant recruitment
Participant recruitment (e.g. screening and eligibility) will be reviewed weekly at the Investigator meetings (e.g. CI, Supervisor and/or other investigators). The recruitment rate will be monitored and any problems identified and addressed.

Participant tracking
At the weekly Investigator meetings, the progress of any participants currently in the study will be reviewed.

Protocol adherence
Adherence to the protocol will be discussed at weekly Investigator meetings.
Once the CI and Research Nurses are trained in administering the protocol in the emergency department, another member of the investigator team will observe the protocol being administered approximately every 20 participants.

Completeness of data collection
Data will be checked for completeness as they are entered from source documents into the CRF and as they are entered into the database on an ongoing basis. This will be reviewed at the weekly Investigator meetings and any issues identified and addressed.

Database integrity
At the weekly Investigator meetings, it will be checked that the trial database is being saved correctly to create an audit trail (see 2.6 Database entry below).

Date checking
1) For the first few participants in the trial, their source data will be checked against the CRF by an investigator other than the one who completed the CRF, by reviewing the source data and checking scoring of questionnaires.
2) Thereafter, source data will be checked against the CRF by an investigator other than the one who completed the CRF for the most recently recruited participant every 1-2 months.
3) A randomly selected 10% of the study sample will have their CRFs checked against the database, again by a designated investigator who did not originally enter the data in to the database.

Database entry
In line with OCTUMI SOP CTU-015 (Database Design), an audit trail needs to be created to track database changes across time.
The SPSS database is designated "Read Only", and each time new data are entered, the file requires saving as a new database. To save databases chronologically, save in the following format:
date(ddmmyy).time(hhmm).initials.SCARTAdatabase
e.g. 030214.1600.LI.SCARTAdatabase

Storage of data
1) Participant packs containing anonymised source data (e.g. questionnnaires and investigator protocols) and CRFs will be stored in a locked filing cabinet at the Department of Psychiatry, and will only be accessible by study investigators.
2) All electronic files (e.g. database) will be stored on a secure Department of Psychiatry network, which can only be accessed by the research team.
3) Paperwork containing identifiable participant details (e.g. consent form, contact details form) will be stored in a locked filing cabinet at the Department of Psychiatry, separate from anonymised participant data.
4) At the end of the study, data will be archived in accordance with Departmental archiving guidance (see Archiving document).

Monitoring visits
Monitoring visits will be led by the CI with another member of the investigator team present (e.g. Supervisor). All monitoring visits will be recorded on the Monitoring Visit Log in the Investigator Site File (ISF).

Start of study
At the site initiation visit, the CI will check that:

1) The study team has appropriate qualifications and training, and are sufficiently familiar with the trial protocols and procedures as appropriate
2) The facilities and equipment are adequate and safe
3) The Investigator Site File and Trial Master File is in place in accordance with GCP guidelines and OCTUMI SOPs
4) The delegation log is completed and signed correctly
5) The correct approvals, e.g. ethics, R&D are in place
6) Informed consent procedures are appropriately delegated
7) Investigators are aware of the safety reporting procedures
8) Investigators are aware of their obligations to work in accordance with the regulations, the approved study protocol, and the applicable SOPs.
9) The appropriate SOPs are in place for all procedures relating to the study
10) The frequency and nature of monitoring visits will be agreed.

The CI will document the visit in the Site Initiation Visit Report.

Subsequent visits
Subsequent monitoring visits will occur every two months, at which point the CI will review:

1) Informed Consent procedures and documentation
2) Participant eligibility
3) Completeness of the primary endpoint
4) Adverse Events reporting
5) Study staff and facilities
6) The Investigator Site File and Trial Master File

The CI will then complete the Monitoring Visit Report, which will be filed in the ISF and TMF.

Investigator meetings
Investigator meetings will be held weekly, and will include the PI and at least one other member of the investigator team.

Trial management group meetings
Trial management group meetings will be held monthly at the first instance, and the frequency reviewed.

3. Safety reporting

1) The CI will discuss any Adverse Event with a clinical colleague on the investigator team as soon as possible after it is identified.
2) If a participant is identified to have probable PTSD at one month follow-up (indicated by scores on the PDS suggesting a diagnosis of PTSD), they will be sent/emailed information about accessing local support and health services, including advice to contact their GP in the first instance. This information will be included at the bottom of the final email thanking participants for taking part in the study – participants will not be informed that their scores indicated potential psychological problems.
3) If a participant spontaneously reports suicidal ideation or intent at follow up, they will be advised to seek help from their GP/emergency services (or CPN if relevant).
4) If a participant is at immediate risk and refusing to seek help, the appropriate services (e.g. emergency services or their GP) will be contacted even without their consent.
5) In all cases an incident report form will be completed and checked by another member of the investigator team. The original copy will be stored in the ISF and an anonymised copy will be stored in the participant pack.
6) All Adverse Events (including Serious Adverse Events) will be recorded in the participant CRF.
7) Any risk assessment or contact with the participant's GP/emergency services will be conducted in line with the SCARTA risk management guidance (see SCARTA Participant Risk Management Protocol 1.0).

APPENDIX 2.4 NRES Research Ethics Committee approval letter

Health Research Authority

NRES Committee South Central - Oxford C
Room 002
TEDCO Business Centre
Rolling Mill Road
Jarrow
NE32 3DT

Telephone: 0191 4283387
Facsimile: 0191 4283432

18 October 2012

Dr Lalitha Iyadurai
Department of Psychiatry
University of Oxford
Warneford Hospital
Oxford
OX3 7JX

Dear Dr Iyadurai

Study title:	**A simple cognitive task to reduce the build-up of flashbacks after a road traffic accident: a randomised controlled study in an emergency department.**
REC reference:	**12/SC/0485**
IRAS project number:	**96155**

Thank you for your letter of 15 October 2012, responding to the Committee's request for further information on the above research and submitting revised documentation.

The further information has been considered on behalf of the Committee by the Chair.

Confirmation of ethical opinion

On behalf of the Committee, I am pleased to confirm a favourable ethical opinion for the above research on the basis described in the application form, protocol and supporting documentation as revised, subject to the conditions specified below.

Ethical review of research sites

NHS sites

The favourable opinion applies to all NHS sites taking part in the study, subject to management permission being obtained from the NHS/HSC R&D office prior to the start of the study (see "Conditions of the favourable opinion" below).

Conditions of the favourable opinion

The favourable opinion is subject to the following conditions being met prior to the start of the study.

Management permission or approval must be obtained from each host organisation prior to the start of the study at the site concerned.

Management permission ("R&D approval") should be sought from all NHS organisations involved in the study in accordance with NHS research governance arrangements.

Guidance on applying for NHS permission for research is available in the Integrated Research Application System or at http://www.rdforum.nhs.uk.

Where a NHS organisation's role in the study is limited to identifying and referring potential participants to research sites ("participant identification centre"), guidance should be sought from the R&D office on the information it requires to give permission for this activity.

For non-NHS sites, site management permission should be obtained in accordance with the procedures of the relevant host organisation.

Sponsors are not required to notify the Committee of approvals from host organisations

It is the responsibility of the sponsor to ensure that all the conditions are complied with before the start of the study or its initiation at a particular site (as applicable).

Approved documents

The final list of documents reviewed and approved by the Committee is as follows:

Document	*Version*	*Date*
Covering Letter	Dr Lalitha Iyadurai	06 September 2012
Investigator CV	Dr Lalitha Iyadurai	20 August 2012
Investigator CV	Emily A Holmes	28 August 2012
Investigator CV	John Richard Geddes	06 September 2012
Investigator CV	Anna Christina de Ozorio Nobre	
Letter from Sponsor	Elaine Chick	20 August 2012
Other: Proof of Funding	Dr Mal Palin	03 February 2012
Other: Sample Flashback Record		
Other: Activity Diary	Version 1.0	12 October 2012
Participant Consent Form	Version 1.1	12 October 2012
Participant Information Sheet: Participant Summary	Version 1.0	12 October 2012
Participant Information Sheet	Version 1.1	12 October 2012
Protocol	1.0	10 August 2012
Questionnaire: Trauma Memory Questionnaire		
Questionnaire: Impact of Event Scale - Revised		
Questionnaire: Clinician-Administered PTSD Scale for DSM-IV (CAPS)		
Questionnaire: BAI		
Questionnaire: BDI-II		
Questionnaire: Work and Social Adjustment		
Questionnaire: EQ-5D		
Questionnaire: Socio-Demographic Details		
Questionnaire: Baseline Assessment		
Questionnaire: Cognitive Processing Questionnaire		
Questionnaire: Peritraumatic Distress Inventory		
Questionnaire: Posttraumatic Cognitions Inventory		
Questionnaire: Ongoing Life Stress/Treatment		
Questionnaire: Expectancy Questionnaire		
REC application	IRAS Version 3.4, 96155/354734/1/920	20 August 2012

Response to Request for Further Information	Dr Lalitha Iyadurai (University of Oxford)	15 October 2012

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

After ethical review

Reporting requirements

The attached document *"After ethical review – guidance for researchers"* gives detailed guidance on reporting requirements for studies with a favourable opinion, including:

- Notifying substantial amendments
- Adding new sites and investigators
- Notification of serious breaches of the protocol
- Progress and safety reports
- Notifying the end of the study

The NRES website also provides guidance on these topics, which is updated in the light of changes in reporting requirements or procedures.

Feedback

You are invited to give your view of the service that you have received from the National Research Ethics Service and the application procedure. If you wish to make your views known please use the feedback form available on the website.

Further information is available at National Research Ethics Service website > After Review

12/SC/0485	**Please quote this number on all correspondence**

With the Committee's best wishes for the success of this project.

Yours sincerely

S. Grimshaw

pp
Professor Nigel Wellman
Chair

Email: nrescommittee.southcentral-oxfordc@nhs.net

Enclosures: "After ethical review – guidance for researchers" *SL-AR2*

Copy to: *Ms Heather House, Oxford University Hospitals NHS Trust*

APPENDIX 3.1 Clinical history form

Clinical history form

Do you have any current physical health difficulties e.g. diabetes, heart problems?

Y / N

Details: _____

_____

_____

Are you receiving any current treatments/medications for these?

Y / N

Details: _____

_____

_____

Have you been treated for/diagnosed with any mental health problems e.g. depression, anxiety, post-traumatic stress disorder?

Y / N

Mental health problem	Past	Current
_____	☐	☐
_____	☐	☐
_____	☐	☐

If current, are you receiving any current treatments/medications for these e.g. psychological treatment, counselling, medication, alternative therapies?

Y / N

Details: _____

_____

_____

Has anyone in your close family been treated for/diagnosed with any mental health problems?

Mental health problem	Y / N Family member
_____	_____
_____	_____
_____	_____

Have you previously experienced or witnessed a stressful or traumatic event (not including the accident today)?

Road accident	Y / N	
Other serious accident	Y / N	
Natural disaster	Y / N	
Sexual assault	Y / N	
Non-sexual assault	Y / N	
War	Y / N	
Imprisonment	Y / N	
Torture	Y / N	
Life-threatening illness	Y / N	
Other	Y / N	_____

APPENDIX 3.2 Perceived life threat

DURING THE ROAD TRAFFIC ACCIDENT…

To what extent did you feel your life was in danger?

0	1	2	3	4	5	6	7	8	9	10
Not at all										Extremely

To what extent did you feel that someone else's life was in danger?

0	1	2	3	4	5	6	7	8	9	10
Not at all										Extremely

APPENDIX 3.3 State Dissociation Questionnaire

Page 2

DURING THE TRAUMATIC EVENT...

	This applied to me				
	Not at all	**A little**	**Moderately**	**Strongly**	**Very strongly**
1. I felt dazed, unable to take in what was happening.	0	1	2	3	4
2. The world around me seemed strange or unreal.	0	1	2	3	4
3. My body felt as if it was not really mine.	0	1	2	3	4
4. I felt emotionally numb.	0	1	2	3	4
5. I felt as if I was separate to my body and was watching it from outside.	0	1	2	3	4
6. I felt as if time was going faster or slower than it really was.	0	1	2	3	4
7. I felt as if I was living in a dream or a film, rather than in real life.	0	1	2	3	4
8. Things around me seemed too big or too small, or distorted in shape.	0	1	2	3	4
9. I felt distant from my emotions.	0	1	2	3	4

APPENDIX 3.4 Peritraumatic Distress Inventory

Peritraumatic Distress Inventory

Please rate the extent to which each item was experienced during and immediately after the road traffic accident.

	Not at all	Slightly	Somewhat	Very	Extremely
I felt helpless to do more	0	1	2	3	4
I felt sadness and grief	0	1	2	3	4
I felt frustrated or angry I could not do more	0	1	2	3	4
I felt afraid for my safety	0	1	2	3	4
I felt guilt that more was not done	0	1	2	3	4
I felt ashamed of my emotional reactions	0	1	2	3	4
I felt worried about the safety of others	0	1	2	3	4
I had the feeling I was about to lose control of my emotions	0	1	2	3	4
I had difficultly controlling my bowel and bladder	0	1	2	3	4
I was horrified by what happened	0	1	2	3	4
I had physical reactions like sweating, shaking and pounding heart	0	1	2	3	4
I felt I might pass out	0	1	2	3	4
I thought I might die	0	1	2	3	4

APPENDIX 3.5 Hotspots of the accident

Hotspots of the accident

Please **very briefly** note the worst moments of the accident for you e.g. "seeing headlights approaching" (just a couple of words is fine).

1. _____
2. _____
3. _____
4. _____
5. _____
6. _____

APPENDIX 3.6 Activity diary

Activity Diary

Please note down each activity you did in the emergency department (e.g. reading, talking, receiving treatment, crossword, texting, game) and how long you did it for. Please be as specific as possible e.g. if you played a game or did a puzzle, state what the game or puzzle was.

Activity	Length of time

APPENDIX 3.7 Tetris feedback questionnaire – feasibility and piloting study 1

TETRIS FEEDBACK QUESTIONNAIRE v1.0 02/01/13

This questionnaire asks you about your experience of playing the computer task Tetris in the emergency department. We very much value both positive and negative feedback, and your answers will be used to improve the study, so please answer these questions as honestly as possible.

1) **How happy were you to be offered something to do whilst waiting in the emergency department?**

1	2	3	4	5	6	7	8	9
Not at all				fairly happy				extremely happy

2) **How <u>trivial</u> did you find it being asked to play the computer task Tetris after your road traffic accident?**

1	2	3	4	5	6	7	8	9
Not at all				fairly trivial				extremely trivial

3) **How <u>enjoyable</u> did you find playing Tetris in the emergency department?**

1	2	3	4	5	6	7	8	9
Not at all				fairly enjoyable				extremely enjoyable

4) **How <u>helpful</u> did you find playing Tetris in the emergency department?**

1	2	3	4	5	6	7	8	9
Not at all				fairly helpful				extremely helpful

5) **How <u>distressing</u> did you find playing Tetris after your road traffic accident?**

1	2	3	4	5	6	7	8	9
Not at all				fairly distressing				extremely distressing

6) **How <u>easy</u> did you find playing Tetris after your road traffic accident?**

1	2	3	4	5	6	7	8	9
Not at all				fairly easy				extremely easy

7) **How <u>easy</u> did you find it <u>to concentrate</u> on playing Tetris after your road traffic accident?**

1	2	3	4	5	6	7	8	9
Not at all				fairly easy				extremely easy

PLEASE TURN OVER

8) **Do you think you would have been able to play Tetris for as long as an hour?**

   Y / N

9) **What is the maximum length of time you think you would have been able to play Tetris for?**

_____

10) **What was positive about playing Tetris in the emergency department?**

_____
_____
_____

11) **What was difficult about playing Tetris in the emergency department?**

_____
_____
_____

12) **What would improve your experience of playing Tetris in the emergency department?**

_____
_____
_____

13) **Any other comments?**

_____
_____
_____

Thank you for completing this questionnaire!

APPENDIX 3.8 Intrusion Diary version 1 – feasibility and piloting study 1

Thank you!!!

Thank you for completing the diary. Your participation is very much appreciated. The researcher will call you in one week to ask you about the diary and remind you to post it back in the envelope provided.

The researcher will call you on:

at:

If you have any questions or problems, please do not hesitate to contact me at lalitha.iyadurai@psych.ox.ac.uk

If you would like to discuss anything related to the study or your reactions to it, please do not hesitate to contact the responsible Investigator, Dr Lalitha Iyadurai at any point in the week after the film or beyond. Dr Iyadurai can be contacted at the University Department of Psychiatry Warneford Hospital, Warneford Lane, Oxford, OX3 7JX tel: 01865223923 or emailed at lalitha.iyadurai@psych.ox.ac.uk

PARTICIPANT DIARY

Participant ID:

Start date:

End date:

How to fill in this diary

❖If over the next week you have any **flashbacks of the road traffic accident**, please note them down in this diary.

❖Flashbacks are memories of the accident that pop into your mind without warning. They are vivid, emotional and often like visual pictures in your mind's eye e.g. like a snapshot image or a film clip. However, they can involve any senses e.g. sounds, smells and sensations in your body. Flashbacks of the accident can be very short/fleeting and broken up. We would still like to know about them in the diary!

❖For each flashback, put a tick in a box on pages 3 and 4 for the correct time of day, or **write down that you have had zero** in that time frame. Then for every single flashback you have had fill in the details of the content on pages 5, 6 and 7. **Please write an entry for each flashback even if you have several flashbacks that happen one after the other or the same flashback that happens a number of times.**

❖If you are sometimes unable to record details of the flashback, please make sure you at least tick a box to show that a flashback has happened.

PLEASE KEEP THIS DIARY – IT IS VITAL FOR THE STUDY. THANK YOU!!!!

Date / Day of flashback	What was the content of the flashback of the accident? (e.g. subject matter)	How distressing was the flashback? (0 = not at all, 10 = extremely)	How vivid was the flashback? (0 = cloudy and unclear, 10 = as vivid as experiencing it again)

Mark each flashback by ticking a box. Otherwise write '0' for that time frame.

Example Day	
Morning	0
Afternoon	0
Evening & Night	√

Day 1 Date:	
Morning	
Afternoon	
Evening & Night	

Day 2 Date:	
Morning	
Afternoon	
Evening & Night	

Day 3 Date:	
Morning	
Afternoon	
Evening & Night	

Please remember to fill in the content page (pages 5, 6 and 7) for each flashback indicated. Thank you

p3

Content Page

Date / Day of flashback	What was the content of the flashback of the accident? (e.g. subject matter)	How distressing was the flashback? (0 = not at all, 10 = extremely)	How vivid was the flashback? (0 = cloudy and unclear, 10 = as clear as experiencing it again)
Day 1 Evening	*The body between the tube and the platform, sound of child screaming*	*6*	*4*

p5

Day 4 Date:	
Morning	
Afternoon	
Evening & Night	

Day 5 Date:	
Morning	
Afternoon	
Evening & Night	

Day 6 Date:	
Morning	
Afternoon	
Evening & Night	

Day 7 Date:	
Morning	
Afternoon	
Evening & Night	

Please remember to fill in the content page (pages 5, 6 and 7) for each flashback indicated. Thank you

p4

Date / Day of flashback	What was the content of the flashback of the accident? (e.g. subject matter)	How distressing was the flashback? (0 = not at all, 10 = extremely)	How vivid was the flashback? (0 = cloudy and unclear, 10 = as vivid as experiencing it again)

p6

APPENDIX 3.9 Intrusion diary feedback questionnaire – feasibility and piloting study 1

FLASHBACK DIARY FEEDBACK QUESTIONNAIRE v1.0 02/01/13

This questionnaire asks you about your experience of filling in the flashback diary. We very much value both positive and negative feedback, and your answers will be used to improve the study, so please answer these questions as honestly as possible.

1) **How easy was it to <u>understand how</u> to fill in the flashback diary?**

1	2	3	4	5	6	7	8	9
Not at all				fairly easy				extremely easy

2) **How easy did you find it to fill in the flashback diary?**

1	2	3	4	5	6	7	8	9
Not at all				fairly easy				extremely easy

3) **How helpful did you find it to fill in the flashback diary?**

1	2	3	4	5	6	7	8	9
Not at all				fairly helpful				extremely helpful

4) **How distressing did you find it to fill in the flashback diary?**

1	2	3	4	5	6	7	8	9
Not at all				fairly distressing				extremely distressing

5) **How accurately do you think you filled in the flashback diary?**

1	2	3	4	5	6	7	8	9
Not at all accurately				fairly accurately				extremely accurately

6) **How true is the following: I have often been unable (or forgotten) to record my flashbacks of the accident in the diary?**

1	2	3	4	5	6	7	8	9
Not at all true				fairly true				extremely true

7) **How helpful was it to receive text reminders to fill in the flashback diary?**

1	2	3	4	5	6	7	8	9
Not at all				fairly helpful				extremely helpful

8) How annoying was it to receive text reminders to fill in the flashback diary?

1	2	3	4	5	6	7	8	9

Not at all fairly annoying extremely annoying

9) What was positive about completing the flashback diary in the week after your accident?

_____
_____
_____

10) What was difficult about completing the flashback diary in the week after your accident?

_____
_____
_____

11) What would improve your experience of completing the flashback diary over the week after your accident, or have made it easier?

_____
_____
_____

12) Do you have any other comments about the flashback diary?

_____
_____
_____

Thank you for completing this questionnaire!

APPENDIX 3.10 NRES Research Ethics Committee approval letter - Amendment 1

NHS
Health Research Authority
NRES Committee South Central - Oxford C
Room 002
TEDCO Business Centre
Rolling Mill Road
Jarrow
NE32 3DT

Tel: 0191 428 3564
Fax: 0191 428 3432

22 January 2013

Dr Lalitha Iyadurai
Department of Psychiatry
University of Oxford
Warneford Hospital
Oxford
OX3 7JX

Dear Dr Iyadurai

Study title: **A simple cognitive task to reduce the build-up of flashbacks after a road traffic accident: a randomised controlled study in an emergency department.**
REC reference: **12/SC/0485**
Protocol number: **N/A**
Amendment number: **N/A**
Amendment date: **04 January 2013**
IRAS project ID: **96155**

The above amendment was reviewed by the Sub-Committee in correspondence

Ethical opinion

The Sub-Committee did not raise any ethical issues

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Covering Letter	Dr Lalitha Iyadurai (University of Oxford)	08 January 2013
Notice of Substantial Amendment (non-CTIMPs)	N/A	04 January 2013
Questionnaire: Pilot Study Feedback Questionnaire	v1.0	02 January 2013
Computer Game Acceptability Questions	v1.0	02 January 2013
Participant Consent Form	v1.3	02 January 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

12/SC/0485:	**Please quote this number on all correspondence**

Yours sincerely

(pp)

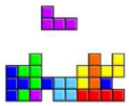
Professor Nigel Wellman
Chair

E-mail: nrescommittee.southcentral-oxfordc@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Joint Research Office, Oxford University Hospitals NHS Trust/University of Oxford*

APPENDIX 3.11 Emergency department staff poster



Oxford University Hospitals NHS
NHS Trust

SCARTA

A Simple Cognitive task After a Road Traffic Accident

SCARTA is a study to assess the effect of a simple computer task in the ED on the development of post-traumatic stress symptoms (flashbacks) after a road traffic accident.

This aims to inform new psychological treatments to prevent post-traumatic stress symptoms after a trauma.

Patient screening criteria

- Experienced or witnessed a road traffic accident (driver, passenger, motorcyclist, cyclist or pedestrian)
- Seen in ED within 6 hours of the accident
- Aged 18 or over
- Fluent in English

ED role *(as soon as possible after patient presents)*

Check patient is willing to speak to a researcher

Call: Dr Lali Iyadurai **Research Nurses**

OR

07534 009612 **01865 222003**

(Available 8 a.m. to 8 p.m. daily, including weekends)

APPENDIX 4.1 Peritraumatic Dissociative Experiences Questionnaire

Peritraumatic Dissociative Experiences Questionnaire – Self-Report Version

Please complete the items below by circling the choice that best describes your experiences and reactions *during the accident and immediately afterward*. If an item does not apply to your experience, please circle "Not at all true."

1. I had moments of losing track of what was going on – I "blanked out" or "spaced out" or in some way felt that I was not a part of what was going on.

1	**2**	**3**	**4**	**5**
Not at all true	Slightly true	Somewhat true	Very true	Extremely true

2. I found that I was on "automatic pilot" – I ended up doing things that I later realized I hadn't actively decided to do.

1	**2**	**3**	**4**	**5**
Not at all true	Slightly true	Somewhat true	Very true	Extremely true

3. My sense of time changed – things seemed to be going in slow motion.

1	**2**	**3**	**4**	**5**
Not at all true	Slightly true	Somewhat true	Very true	Extremely true

4. What was happening seemed unreal to me, like I was in a dream or watching a movie or play.

1	**2**	**3**	**4**	**5**
Not at all true	Slightly true	Somewhat true	Very true	Extremely true

5. I felt as though I were a spectator watching what was happening to me, as if I were floating above the scene or observing it as an outsider.

1	**2**	**3**	**4**	**5**
Not at all true	Slightly true	Somewhat true	Very true	Extremely true

6. There were moments when my sense of my own body seemed distorted or changed. I felt disconnected from my own body, or that it was unusually large or small.

1	**2**	**3**	**4**	**5**
Not at all true	Slightly true	Somewhat true	Very true	Extremely true

7. I felt as though things that were actually happening to others were happening to me – like I was being trapped when I really wasn't.

1	**2**	**3**	**4**	**5**
Not at all true	Slightly true	Somewhat true	Very true	Extremely true

8. I was surprised to find out afterward that a lot of things had happened at the time that I was not aware of, especially things I ordinarily would have noticed.

1	**2**	**3**	**4**	**5**
Not at all true	Slightly true	Somewhat true	Very true	Extremely true

9. I felt confused: that is, there were moments when I had difficulty making sense of what was happening.

1	**2**	**3**	**4**	**5**
Not at all true	Slightly true	Somewhat true	Very true	Extremely true

10. I felt disorientated; that is, there were moments when I felt uncertain about where I was or what time it was.

1	**2**	**3**	**4**	**5**
Not at all true	Slightly true	Somewhat true	Very true	Extremely true

APPENDIX 4.2 Intrusion Diary version 2 – feasibility and piloting study 2

Participant ID: ____

Thank you!!!

Thank you for helping us with this research project. Your help is very much appreciated. The researcher will call you in one week to ask you about the diary and remind you to post it back in the envelope provided. In the meantime, we will call / text you to support you with filling in the diary.

The researcher will call you on:

At:

We look forward to speaking to you then!

It is common to have questions about filling in this diary. If you have any questions or problems, please do not hesitate to contact me:

Dr Lali Iyadurai

07534 009612

scarta@psych.ox.ac.uk

SCARTA DIARY

Start date: .....

End date: .....

THANK YOU FOR FILLING IN THIS DIARY. PLEASE KEEP IT SAFE- IT IS VITAL FOR THE STUDY.

How to fill in this diary

- If you have any **flashbacks of the accident** over the next week, please note them down in this diary.
- **Flashbacks are memories of the accident that pop into your mind without warning**. They can be vivid and emotional, and are often like visual pictures in your mind's eye e.g. like a snapshot image or a film clip. However, they can involve any senses e.g. sounds, smells and sensations in your body. Flashbacks of the accident can be very short, fleeting and broken up. We would still like to know about them in the diary!
- For each flashback, put a tick in a box on the page opposite for the correct day, or write down that you have had zero for that day. Then **for every single flashback, write down a brief description to remind you what the flashback was of** e.g. if it was a flashback of a helicopter crash, write "image of helicopter crash". Please write an entry for each flashback even if you have several flashbacks that happen one after the other or the same flashback that happens a number of times.

  As an example, please note down your key moments of the accident, or any flashbacks you have already had.

EXAMPLE	Tick for each flashback	What was the flashback of?	Tick for each flashback	What was the flashback of?
	√	*Image of helicopter crash*		

- If you are sometimes unable to record details of the flashback, please make sure you at least tick a box to show that a flashback has happened.

Please keep this diary to hand, and make a time each day when you can fill it in. If you have any questions at all, please contact me (see back page for my contact details)

DAY	Tick for each flashback	What was the flashback of?	Tick for each flashback	What was the flashback of?
Day 1				
Day 2				
Day 3				
DAY 4				
Day 5				
Day 6				
Day 7				

APPENDIX 4.3 Impact of Event Scale – Revised

INSTRUCTIONS: Below is a list of difficulties people sometimes have after stressful life events. Please read each item, and then indicate how distressing each difficulty has been for you **DURING THE PAST 7 DAYS <u>with respect to this recent road traffic accident. (Please make your ratings in relation to how things were for you before this accident).</u>**

	Date completed: _____	Not at all	A little bit	Moderately	Quite a bit	Extremely
1	Any reminder brought back feelings about the accident	0	1	2	3	4
2	I had trouble staying asleep	0	1	2	3	4
3	Other things kept making me think about the accident	0	1	2	3	4
4	I felt irritable and angry	0	1	2	3	4
5	I avoided letting myself get upset when I thought about the accident or was reminded of the accident	0	1	2	3	4
6	I thought about the accident when I didn't mean to	0	1	2	3	4
7	I felt as if the accident hadn't happened or wasn't real	0	1	2	3	4
8	I stayed away from reminders about the accident	0	1	2	3	4
9	Pictures about the accident popped into my mind	0	1	2	3	4
10	I was jumpy and easily startled	0	1	2	3	4
11	I tried not to think about the accident	0	1	2	3	4
12	I was aware that I still had a lot of feelings about the accident , but I didn't deal with them	0	1	2	3	4
13	My feelings about the accident were kind of numb	0	1	2	3	4
14	I found myself acting or feeling like I was back at that time	0	1	2	3	4
15	I had trouble falling asleep	0	1	2	3	4
16	I had waves of strong feelings about the accident	0	1	2	3	4
17	I tried to remove the accident from my memory	0	1	2	3	4
18	I had trouble concentrating	0	1	2	3	4
19	Reminders of the accident caused me to have physical reactions, such as sweating, trouble breathing, nausea, or a pounding heart	0	1	2	3	4
20	I had dreams about the accident	0	1	2	3	4
21	I felt watchful and on guard	0	1	2	3	4
22	I tried not to talk about the accident	0	1	2	3	4

APPENDIX 4.4 Feedback Questionnaire – feasibility and piloting study 2

GENERAL STUDY FEEDBACK QUESTIONNAIRE

This questionnaire asks you about your experience of taking part in the study. We very much value both positive and negative feedback, and your answers will be used to improve the study, so please answer these questions as honestly as possible.

1) **How easy was it to understand what you were asked to do in the study?**

1	2	3	4	5	6	7	8	9
Not at all				fairly easy				extremely easy

2) **How easy did you find taking part in the study?**

1	2	3	4	5	6	7	8	9
Not at all				fairly easy				extremely easy

3) **How helpful did you find taking part in the study?**

1	2	3	4	5	6	7	8	9
Not at all				fairly helpful				extremely helpful

4) **How difficult did you find taking part in the study?**

1	2	3	4	5	6	7	8	9
Not at all				fairly difficult				extremely difficult

5) **How distressing did you find taking part in the study?**

1	2	3	4	5	6	7	8	9
Not at all				fairly distressing				extremely distressing

6) **How much was the study a burden on your time?**

1	2	3	4	5	6	7	8	9
Not at all				slightly burdensome				extremely burdensome

7) **How happy were you to be asked at random to either complete a computer task or not in the emergency department?**

1	2	3	4	5	6	7	8	9
Not at all				fairly happy				extremely happy

8) What was positive about taking part in the study?

_____
_____
_____

9) What was difficult about taking part in the study?

_____
_____
_____

10) How could we have improved your experience of taking part in the study e.g. made it easier or less of a burden?

_____
_____
_____

11) How could we have improved how we contacted you in the week after the accident to make it easier to complete the study?

_____
_____
_____

12) How would you prefer to tell us about your flashbacks in the week after the accident? Please rank 1, 2, 3 in order of preference.

☐ **Fill in the flashback diary**

☐ **Tell the researcher about them over the telephone after one week**

☐ **Fill in a questionnaire about them after one week (either online or by post)**

Reasons for choosing this order:

_____
_____
_____

13) Any other comments about the study

_____
_____
_____

Thank you for completing this questionnaire!

APPENDIX 4.5 NRES Research Ethics Committee approval letter - Amendment 2

Health Research Authority

NRES Committee South Central - Oxford C

Bristol REC Centre
Level 3, Block B
Whitefriars Building
Lewins Mead
Bristol
BS1 2NT
Tel: 01173421392

REISSUED DUE TO ADMIN ERROR
17 September 2013

04 June 2013

Dr Lalitha Iyadurai
Department of Psychiatry, University of Oxford
Warneford Hospital
Oxford
OX3 7JX

Dear Dr Iyadurai

Study title:	**A simple cognitive task to reduce the build-up of flashbacks after a road traffic accident: a randomised controlled study in an emergency department.**
REC reference:	**12/SC/0485**
Protocol number:	**N/A**
Amendment number:	**AM02**
Amendment date:	**10 May 2013**
IRAS project ID:	**96155**

The above amendment was reviewed on 27 May 2013 by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Participant Consent Form: Tracked Changes	3.0	10 May 2013
Participant Information Sheet: Tracked Changes	2.0	10 May 2013
Protocol	2.0	10 May 2013
Notice of Substantial Amendment (non-CTIMPs)		10 May 2013
Covering Letter		10 May 2013
SCARTA diary	1.0	10 May 2013
SCARTA diary: tips for filling in	1.0	10 May 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

12/SC/0485:	**Please quote this number on all correspondence**

Yours sincerely

P. P.

Professor Nigel Wellman
Chair

E-mail: nrescommittee.southcentral-oxfordc@nhs.net

Enclosures: List of names and professions of members who took part in the review

Copy to: Ms Heather House, University of Oxford

APPENDIX 4.6 NRES Research Ethics Committee approval letter - Amendment 3

NHS
Health Research Authority

NRES Committee South Central - Oxford C

Bristol REC Centre
Level 3, Block B
Whitefriars Building
Lewins Mead
Bristol
BS1 2NT

Tel: 01173421392

24 June 2013

Dr Lalitha Iyadurai
Department of Psychiatry, University of Oxford
Warneford Hospital
Oxford
OX3 7JX

Dear Dr Iyadurai

Study title:	**A simple cognitive task to reduce the build-up of flashbacks after a road traffic accident: a randomised controlled study in an emergency department.**
REC reference:	**12/SC/0485**
Protocol number:	**3.0**
Amendment number:	**Amendment 3**
Amendment date:	**04 June 2013**
IRAS project ID:	**96155**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Advertisement	1.0	04 June 2013
Protocol	3.0	04 June 2013
Notice of Substantial Amendment (non-CTIMPs)	n/a	04 June 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

12/SC/0485:	**Please quote this number on all correspondence**

Yours sincerely

P P

Professor Nigel Wellman
Chair

E-mail: nrescommittee.southcentral-oxfordc@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Ms Heather House*

SCARTA Research Study

Oxford University Hospitals NHS
NHS Trust

Have you just been involved in a road traffic accident?

Would you like something to do whilst you are waiting?

We are running a research study in the emergency department to find out about the impact of road traffic accidents. We hope this will help to develop better treatments to give people in the future after these sorts of events.

What will the study involve?
The study will involve:

- Filling in some questionnaires and possibly doing a computer task whilst you are waiting in the emergency department
- Keeping a diary of your memories of the accident over the next week
- Being contacted after you leave the emergency department and filling in some more questionnaires.

What to do if you would like to take part
If you think you might be interested in taking part in this study today, whilst you are waiting in the emergency department, please contact us now for more information. We will come and see you whilst you are waiting to tell you a bit more about the study.

Please contact: **The Research Nurses** **01865 222003**

Or: **Dr Lali Iyadurai** **07534 009612**

Or ask one of the staff to phone us.

APPENDIX 4.8 Comments on the Feedback Questionnaire – feasibility and piloting study 2

What was positive about taking part in the study?

Simple cognitive task group

1. Able to focus on understanding the flashbacks through writing down the images, thoughts, feelings. Good to talk to someone and feel that what had happened could be used constructively and that I was not alone.
2. Acknowledge the accident in a more analytical way.
3. Being able to talk about how I was feeling. Being able to choose the time to take part in the telephone interview.
4. Made me realise that my accident didn't affect me too much.
5. It helped me acknowledge what I was thinking and feeling instead of constantly negating it.
6. the thought it might help
7. Being able to contribute to a scientific study, especially in light of having an interest in psychology and having heard of this type of study before.
8. The study made it seem like someone cared how traumatic we found the accident.
9. Easy to take part

Usual care group

1. Feeling like I was making a difference
2. I could record them and bring them up with my partner i.e. talk them over
3. was good to reflect on the accident to slow down, and to realise I had been through a lot.
4. Although my personal experience negated most questions, it's good to know that studies of this nature are being conducted. I suppose it's just as important that I contribute to statistics gathered from the study as someone more detrimentally affected by road incidents, as it shows that it is possible not to be pshychologically scarred from a traumatic event.
5. Allowing me to remember the accident well
6. It felt better to write things down
7. Always a pleasure to help improve understanding and treatment of PTSD etc!

What was positive about taking part in the study?

Simple cognitive task group

1. More space in the diary to write more details information
2. Having to face some of the moments of the accident, but gradually getting used to them was good.
3. I didn't find it difficult to take part.
4. Making sure I remembered to fill in the diary.
5. Nothing really, although filling in the diary brought some sadness.
6. nothing difficult
7. Making sure the info I gave was a real account and not an imagined memory of the event.
8. Noting flashbacks at work without people wondering what I was filling in
9. Nothing

Usual care group

1. Nothing difficult
2. Was admitted to hospital
3. Nothing
4. Every part of the study was clear and concise.
5. Remembering the distressing part of the accident
6. Filling it in whilst staying in hospital
7. Distinguishing a 'flashback' from a simple memory. I spoke about the accident a lot so it was often in my mind intentionally.

What could have improved you experience of taking part in the study e.g. made it easier or less of a burden?

Simple cognitive task group

1. Perhaps doing things online as an option
2. A more readily-available mechanism to enter the diary (e.g. Mobile phone app, or online diary accessible via the internet)
3. When I agreed to do it I knew it would take some time, but nothing I have been asked to do has felt like a burden.

4. To be able to text my flashbacks straight away. I would still record it myself but would make it easier and less of a burden.
5. Nothing
6. unsure if anything coild make it easier as it wasn't difficult in first place
7. Probably the point I alluded to before. Being able to give more descriptive answers in the diary.
8. it seemed fine - taking notes was a necessary part of the study
9. Nothing

Usual care group

1. Maybe made a few questions easier to understand
2. It was not a burden, it was good to have something to focus on
3. first text was a few days after the incident, possibly to text from day 1 may remind some people, though in my case there was nothing new
4. No comments
5. Making the diary have more boxes to fill in that had simple answers - e.g. a scale /10
6. I don't feel it was a burden.

What could have improved how we contacted you in the week after the accident to make it easier to complete the study?

Simple cognitive task group

1. No change.
2. The contact was absolutely fine.
3. Possibly a call mid week to see if I was completing the diary.
4. Nothing
5. nothing contact was not intrusive
6. Nothing really
7. Nothing
8. Nothing

Usual care group

1. Contact was fine, not too pushy/laid back
2. N/A Text reminders were good
3. Contact was unintrusive and always polite.
4. Possibly could have been contacted by email also - e.g. reminder email every other day as well as text in case people use email more than text
5. I think you have done all you can! I may not have taken part if I had to come back into the JR to complete the study.

Do you have any other comments about the study?

Simple cognitive task group

1. I would like to say thank you to Lali for helping in this study and allowing the difficult experience I had to be of use to the research. Writing the diary was very helpful for me processing the information following the car accident. Helping me work through my emotions/thoughts in a constructive way.
2. I think i've answered a lot of the questions in the online questionnaire when speaking to the researcher on the phone on the seventh day, so this was a bit redundant and (unnecessarily) time-consuming.
3. No
4. No, I was happy with the study.
5. No, thank you
6. Nope
7. No
8. No
9. No

Usual care group

1. Record if injury is visible, as people are more likely to ask about it and may trigger more flashbacks; one item asks about things you found out about after the accident (PDEQ), which may be best answered the next day
2. all fine, very polite and outstanding attitude at a time of stress
3. None
4. I found it enjoyable and therapeutic to be a part of the study. Thanks
5. I hope it is very successful :)

APPENDIX 5.1 SCARTA clinical trial registration

Available at: https://clinicaltrials.gov/ct2/show/study/NCT02080351

ClinicalTrials.gov
A service of the U.S. National Institutes of Health

A Simple Cognitive Task to Reduce the Build-Up of Flashbacks After a Road Traffic Accident (SCARTA)

This study has been completed.
Sponsor: University of Oxford
Collaborators: Oxford University Hospitals NHS Trust
National Institute for Health Research, United Kingdom
Medical Research Council Cognition and Brain Sciences Unit
Information provided by (Responsible Party): University of Oxford
ClinicalTrials.gov Identifier: NCT02080351
First received: March 4, 2014
Last updated: May 29, 2015
Last verified: May 2015

Purpose

This research study is designed to investigate the effects of a simple cognitive task (a memory reactivation cue following by playing the computer game "Tetris") on flashbacks and other post-traumatic stress symptoms after a road traffic accident. Patients presenting to a hospital emergency department soon after a road traffic accident will be randomly allocated to either the simple cognitive task intervention or usual care. Participants will be followed up at one week and one month. It is predicted that participants given the simple cognitive task intervention will develop fewer flashbacks and less severe clinical symptoms than those who are not. This will inform the potential future development of a simple technique to prevent distressing psychological symptoms after a traumatic event.

Condition	Intervention
Post-traumatic Stress Disorders	Behavioral: Simple cognitive task

Study Type: Interventional

Study Design: Allocation: Randomized
Endpoint Classification: Efficacy Study
Intervention Model: Parallel Assignment
Masking: Open Label
Primary Purpose: Prevention

Official Title: A Simple Cognitive Task to Reduce the Build-Up of Flashbacks After a Road Traffic Accident: A Randomised Controlled Study in an Emergency Department

Further study details as provided by University of Oxford:

Primary Outcome Measures:

- Number of flashbacks recorded by participants in a Flashback Record in the week after the accident [Time Frame: Within one week after the accident (Flashback Record will be returned to a researcher at one week follow-up)] [Designated as safety issue: No]

Secondary Outcome Measures:

- Post-traumatic Stress Diagnostic Scale (PDS) [Time Frame: One week and one month follow-up] [Designated as safety issue: No]
- Impact of Event Scale - Revised (IES-R) [Time Frame: One week and one month follow-up] [Designated as safety issue: No]
- Hospital Anxiety and Depression Scale (HADS) [Time Frame: One week and one month follow-up] [Designated as safety issue: No]

Other Outcome Measures:

- Feedback Questionnaire [Time Frame: One month follow-up] [Designated as safety issue: No]

Enrollment: 71

Study Start Date: March 2014
Study Completion Date: March 2015
Primary Completion Date: January 2015 (Final data collection date for primary outcome measure)

Arms	Assigned Interventions

Experimental: Simple cognitive task A memory reactivation cue followed by playing the computer game "Tetris"	Behavioral: Simple cognitive task
No Intervention: Usual care Usual care in the emergency department	

Eligibility:
Ages Eligible for Study: 18 Years and older
Genders Eligible for Study: Both
Accepts Healthy Volunteers: No
Criteria

Inclusion Criteria:

- Aged 18 or over
- Experienced or witnessed a road traffic accident (as a driver, passenger, motorcyclist, cyclist or pedestrian)
- Met the Diagnostic and Statistical Manual of Mental Disorders, 4th Edition (DSM-IV) criterion A1 for Post-Traumatic Stress Disorder (PTSD) ("experienced, witnessed, or confronted with actual or threatened death or serious injury)
- Can be seen in the emergency department within 6 hours of leaving the scene of the accident
- Report memory of the accident
- Fluent in written and spoken English
- Alert and orientated, Glasgow Coma Scale score (GCS) = 15
- Have sufficient physical mobility to play a computer game on the intervention platform (a Nintendo DS) at the point of taking informed consent
- Willing and able to provide informed consent and complete study procedures
- Willing and able to be contacted following discharge to complete follow-up assessments

Exclusion Criteria:

- Loss of consciousness of > 5 minutes
- Current intoxication
- Report a history of severe mental illness
- Current substance abuse or neurological condition
- Currently suicidal

Locations:

Emergency Department, John Radcliffe Hospital
Oxford, Oxfordshire, United Kingdom, OX3 9DU

Sponsors and Collaborators:
University of Oxford
Oxford University Hospitals NHS Trust
National Institute for Health Research, United Kingdom
Medical Research Council Cognition and Brain Sciences Unit

Investigators:

Principal Investigator: Lalitha Iyadurai University of Oxford

Principal Investigator: Emily A Holmes MRC Cognition and Brain Sciences Unit, Cambridge

No publications provided

Responsible Party: University of Oxford

ClinicalTrials.gov Identifier: NCT02080351 History of Changes

Other Study ID Numbers: 12/SC/0485

Study First Received: March 4, 2014

Last Updated: May 29, 2015

Health Authority: United Kingdom: NHS Health Research Authority
United Kingdom: Oxford University Hospitals NHS Trust

ClinicalTrials.gov processed this record on July 29, 2015

APPENDIX 5.2 NRES Research Ethics Committee approval letter - Amendment 4

NHS
Health Research Authority

NRES Committee South Central - Oxford C

Bristol REC Centre
Level 3, Block B
Whitefriars Building
Lewins Mead
Bristol
BS1 2NT

Tel: 01173421387

27th January 2014

Dr Lalitha Iyadurai
Department of Psychiatry, University of Oxford
Warneford Hospital
Oxford
OX3 7JX

Dear Dr Iyadurai,

Study title:	**A simple cognitive task to reduce the build-up of flashbacks after a road traffic accident: a randomised controlled study in an emergency department.**
REC reference:	**12/SC/0485**
Protocol number:	**N/A**
Amendment number:	**Updates to Protocol, PIS, consent form & data collection methods. Addition of investigators, affiliation change for some investigators**
Amendment date:	**13 January 2014**
IRAS project ID:	**96155**

The above amendment was reviewed by the Sub-Committee in correspondence.

Ethical opinion

There were no ethical issues.

The members of the Committee taking part in the review gave a favourable ethical opinion of the amendment on the basis described in the notice of amendment form and supporting documentation.

Approved documents

The documents reviewed and approved at the meeting were:

Document	Version	Date
Questionnaire: Clinical History Form	2.0	20 December 2014
Questionnaire: Feedback Questionnaire	1.0	20 December 2013
Questionnaire: Perceived Life Threat	1.0	28 August 2012
Notice of Substantial Amendment (non-CTIMPs)	Updates to Protocol, PIS, consent form & data collection methods. Addition of	13 January 2014

NHS
Health Research Authority

	investigators, affiliation change for some investigators	
Questionnaire: Socio-Demographic Details	2.0	09 January 2014
Questionnaire: Additional questions at one week follow-up	1.0	09 January 2014
Investigator CV	Sally Beer	
Participant Consent Form: Consent Form	4.0	20 December 2013
Participant Information Sheet: PIS	3.0	09 January 2014
Questionnaire		
SCARTA: What happens next	1.0	20 December 2013
Investigator CV	Soubera Rymell	
Questionnaire: Peritraumatic Dissociative Experiences Questionnaire		
Questionnaire		
Hotspots of the accident	1.0	20 December 2013
Investigator CV	Laura Hoppitt	15 January 2014
Questionnaire: Hospital Anxiety and Depression Scale		
Questionnaire: Additional questions at one month follow-up	1.0	09 January 2014
Investigator CV	Karen Warnes	
Participant Information Sheet: Participant Summary	2.0	20 December 2013
Protocol	4.0	10 January 2014
Questionnaire: Posttraumatic diagnostic Scale		
Methods of contact	1.0	20 December 2013
Investigator CV	Alexis Espinosa	
Questionnaire: Flash Back Record	2.0	20 December 2013

Membership of the Committee

The members of the Committee who took part in the review are listed on the attached sheet.

R&D approval

All investigators and research collaborators in the NHS should notify the R&D office for the relevant NHS care organisation of this amendment and check whether it affects R&D approval of the research.

Statement of compliance

The Committee is constituted in accordance with the Governance Arrangements for Research Ethics Committees and complies fully with the Standard Operating Procedures for Research Ethics Committees in the UK.

We are pleased to welcome researchers and R & D staff at our NRES committee members' training days – see details at http://www.hra.nhs.uk/hra-training/

NHS
Health Research Authority

12/SC/0485:	Please quote this number on all correspondence

Yours sincerely

PP S Payne.

Professor Nigel Wellman
Chair

E-mail: nrescommittee.southcentral-oxfordc@nhs.net

Enclosures: *List of names and professions of members who took part in the review*

Copy to: *Ms Heather House, Oxford University Hospitals NHS Trust*

APPENDIX 5.3 Socio-demographic details form

SOCIO-DEMOGRAPHIC DETAILS

Age (in years):……..

Gender (please tick): □ Male
□ Female

Current employment status (please tick): □ Employed
□ Unemployed
□ Student
□ Retired

Marital status (please tick): □ Single
□ Married or cohabiting
□ Divorced or separated
□ Widowed

Years in education:…….....

Yearly family income (please tick): □ £0 – 19, 999
□ £20,000 – 29,999
□ £30,000 – 39,999
□ £40,000 – 49,999
□ £50,000 +

Ethnic group (please tick):

□ White British
□ Any Other White background (please specify) _____
□ Indian
□ Pakistani
□ Bangladeshi
□ Black Caribbean
□ Black African
□ Chinese
□ Mixed background (please specify) _____
□ Any Other background (please specify) _____

APPENDIX 5.4 Intrusion Diary version 3 – randomised controlled study

Participant ID: ____

Oxford University Hospitals NHS

Thank you!!!

Your help on this research project is very much appreciated.

The researcher will call you on:

Day 2: ..... To check that you are happy with the study and to answer any questions you may have

Day 8: ..... To remind you to post back the diary and fill in some questionnaires online (or by post)

It is common to have questions about filling in this diary. If you have any questions or problems, please do not hesitate to contact me:

Dr Lali Iyadurai

07534 009612

scarta@psych.ox.ac.uk

SCARTA DIARY

Start date (day 1): .....

End date (day 7): .....

THANK YOU FOR FILLING IN THIS DIARY. PLEASE KEEP IT SAFE- IT IS VITAL FOR THE STUDY.

Flashback Record Version 2.0 20/12/13

How to fill in this diary

- If you have any **flashbacks of the accident** over the next week, please note them down in this diary from now onwards.
- *What counts as a flashback?*

  Flashbacks are image-based memories of the accident that pop into your mind without warning. They often take the form of **visual pictures in your mind's eye** e.g. like a snapshot image or a film clip. They can also include other senses e.g. sounds and smells. They may or may not be triggered by something you are aware of e.g. telling someone about the accident, being back at the scene. **Flashbacks of the accident can vary from being vivid and emotional to being very short, fleeting and broken up**. We would still like to know about them in the diary!
- *Examples of flashbacks might be:*
  - Seeing red car; sailing through air; crashing
  - Your examples? _____ _____ _____ _____
- *What does not count as a flashback?*
  - Deliberately thinking about the accident or mulling it over
  - General thoughts about the accident without an image e.g. "I had a crash"
- *What to do when you have a flashback*

  For each flashback, **put a tick in a box on the page opposite** for the correct time of day, or **write down that you have had zero** in that time frame (see example). **Please tick a box for every single flashback even if you have several the same or flashbacks that occur one after the other**. It's OK if you have none - just let us know by marking zero.

Please keep this diary to hand e.g. in your bag, on your coffee table, or by your bed. Please make a time each day when you can fill it in e.g. at mealtimes or the end of every day. We will text you at the end of every day to help remind you. If you have any questions at all, please contact Lali (see back page for contact details).

√ = flashback 0 = zero

Example:						
Morning	√	√				
Afternoon	0					
Evening	√					

Day 1:						
Morning						
Afternoon						
Evening						

Day 2:						
Morning						
Afternoon						
Evening						

Day 3:						
Morning						
Afternoon						
Evening						

Day 4:						
Morning						
Afternoon						
Evening						

Day 5:						
Morning						
Afternoon						
Evening						

Day 6:						
Morning						
Afternoon						
Evening						

Day 7:						
Morning						
Afternoon						
Evening						

DAY 7 - Please answer the following question on day 7, once you have finished filling in the diary. Please be as honest as possible.

How accurately do you think you completed the diary? (Please circle)

0 (Not at all accurately) 1 2 3 4 5 6 7 8 9 10 (Extremely accurately)

Over the week, how vivid were your flashbacks of the accident?

0 (Not at all vivid) 1 2 3 4 5 6 7 8 9 10 (Extremely vivid)

Over the week, how distressing were your flashbacks of the accident?

0 (Not at all distressing) 1 2 3 4 5 6 7 8 9 10 (Extremely distressing)

APPENDIX 5.5 Additional questions at one week follow-up

Additional questions at one-week follow-up

Date completed: _____

Treatment

Since the last session (in the emergency department), have you received any treatment in relation to the accident e.g. medication or psychological treatment?

Y / N

If yes, please give details:

_____
_____
_____

Playing Tetris at home (for participants in the simple cognitive task condition only):

1) How much of the time when you had a flashback of the accident did you imagine playing Tetris?

1	2	3	4	5	6	7	8	9

none of the time half the time every time

2) How much of the time when you had a flashback of the accident did you play Tetris?

1	2	3	4	5	6	7	8	9

none of the time half the time every time

APPENDIX 5.6 Additional questions at one month follow-up

Additional questions at one-month follow-up

Computer game play

Since the accident, have you played any computer games based on visual puzzles, such as the computer game Tetris? Y / N

If yes, please indicate roughly how many minutes you have played these games/puzzles for altogether: _____ minutes

Treatment

Since the last session (one week after the accident), have you received any treatment in relation to the accident e.g. medication or psychological treatment? Y / N

If yes, please give details:
_____

Stressful life events

Since the accident, have you experienced any additional stressful life events e.g. relationship problems, bereavements, financial problems, work problems, health problems etc.? Y / N

If yes, please give details:
_____

Rumination and thought suppression

How often have you dwelt on memories of the accident or mulled over them?

1	2	3	4	5	6	7	8	9
Not at all				somewhat				a great deal

How often have you tried to push memories of the accident out of your mind when they occurred?

1	2	3	4	5	6	7	8	9
Not at all				somewhat				a great deal

Social support

How much do you feel you have had support from family and friends following the accident?

1	2	3	4	5	6	7	8	9
Not at all				somewhat				a great deal

Positive effects

To what extent do you feel the accident has had some positive effects on your life?

1	2	3	4	5	6	7	8	9
Not at all				somewhat				a great deal

APPENDIX 5.7 Feedback Questionnaire – randomised controlled study

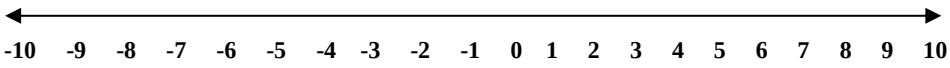
FEEDBACK QUESTIONNAIRE

This questionnaire asks you about your experience of taking part in the study. We very much value both positive and negative feedback, and your answers will be used to improve this research in the future, so please answer these questions as honestly as possible.

14) How happy were you to be offered something to do whilst you were waiting in the emergency department after your accident?

1	2	3	4	5	6	7	8	9
Not at all				fairly happy				extremely happy

15) How much do you predict that what we asked you to do in the emergency department would increase or decrease your flashbacks of the accident?
(Please circle a number)



extreme decrease **no effect** **extreme increase**

For participants who played the computer game Tetris only (shaded areas):

<u>The computer game Tetris</u>

1) How <u>easy</u> did you find playing Tetris after your road traffic accident?

1	2	3	4	5	6	7	8	9
Not at all				fairly easy				extremely easy

2) How <u>helpful</u> did you find playing Tetris after your road traffic accident?

1	2	3	4	5	6	7	8	9
Not at all				fairly helpful				extremely helpful

3) How <u>distressing</u> or <u>burdensome</u> did you find playing Tetris after your road traffic accident?

1	2	3	4	5	6	7	8	9
Not at all				fairly distressing/ burdensome				extremely distressing/ burdensome

4) If you had a traumatic accident again in the future, how willing would you be to play Tetris if it was offered to you as something that would help?

1	2	3	4	5	6	7	8	9
Extremely unwilling				unsure				extremely willing

5) If a friend had a similar accident, how confident would you be in suggesting playing Tetris to them?

1	2	3	4	5	6	7	8	9
Extremely unconfident				unsure				extremely confident

6) Do you have any suggestions for improving using Tetris as something that might help after a traumatic event? Please note, we will explain how this might help when we contact you again to debrief you about the study.

_____
_____

7) Do you have any other comments about using Tetris as something that might help after a traumatic event?

_____
_____

The study in general

16) How easy did you find taking part in the study?

1	2	3	4	5	6	7	8	9
Not at all				fairly easy				extremely easy

17) How distressing or burdensome did you find taking part in the study?

1	2	3	4	5	6	7	8	9
Not at all				fairly distressing/ burdensome				extremely distressing/ burdensome

18) If we were to roll out the study on a larger scale, how could we improve the study (over and above anything you have already mentioned)?

_____
_____

19) Do you have any other comments about the study or your experience of taking part in the study (over and above anything you have already mentioned)?

_____
_____

Thank you for completing this questionnaire!

APPENDIX 5.8 Participant information sheet

UNIVERSITY OF OXFORD
DEPARTMENT OF PSYCHIATRY
WARNEFORD HOSPITAL
OXFORD
OX3 7JX
TEL: (01865) 223923
FAX: (01865) 793101

Oxford University Hospitals NHS
NHS Trust

PARTICIPANT INFORMATION SHEET (Version 3.0 09/01/14)

Study Title: SCARTA - Simple cognitive activities after a road traffic accident
Chief Investigator: Dr Lalitha Iyadurai
REC Reference Number: 12/SC/0485

Introduction
You are being invited to take part in a research study. Before you decide, it is important for you to understand why the research is being done and what it will involve. Please take time to read this information carefully. Talk to others about the study if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you would like to take part.

Part 1 tells you the purpose of this study and what will happen to you if you take part. Part 2 gives you more detailed information about the conduct of the study. Thank you for reading this.

PART 1

What is the purpose of the study?
After a traumatic event, such as a road traffic accident, people may have upsetting, intrusive memories, called "flashbacks". We are carrying out research to examine how simple activities affect flashbacks and other symptoms after a road traffic accident. We hope that this research will lead to the development of new treatments after trauma in the future.

Who can take part?
We are looking for about 70 to 80 people aged 18 and over who have experienced or witnessed a road traffic accident and attended the emergency department immediately afterwards. To be able to take part, we would like you to be able to:

- Remember the accident
- Speak English fluently
- Be willing to be contacted by phone and email/post after 1 week and 1 month.

You are not suitable to take part if:

- You have physical injury that makes you unable to play a hand-held computer game
- You lost consciousness for more than 5 minutes
- You are currently intoxicated or suicidal
- You have a history of severe mental illness, drug or alcohol problems or a neurological condition (e.g. dementia, multiple sclerosis or other brain injury).

Do I have to take part?
No – it is up to you to decide whether or not to take part. If you do decide to take part you will be given this information sheet to keep and will be asked to sign a consent form. You will still be free to withdraw at any time and without giving a reason. A decision to withdraw at any time, or a decision not to take part, will not affect the standard of care you receive.

What would happen to me if I take part?
1) In the emergency department

- First, you will be asked a few questions to see if you are suitable to take part. Your responses to these questions will be kept confidential.
- If it looks like you may be suitable, we will ask you to provide written consent to participate. We will then ask you to complete some questionnaires about the road traffic accident and some brief questions about your personal history. These will take about 15 minutes, and can be

completed in your own time whilst you are waiting in the emergency department. The researcher will be available to answer questions.

- The researcher will record a few additional details from your clinical records, such as the severity of any injuries you have, and any medication you have been given in the emergency department.
- You will then be randomly assigned to either:
  1) being asked to note down the worst moments of the accident for 30 seconds (to bring back the memory), followed by completing a simple computer task for approximately 20 minutes, or
  2) filling in a record of the activities you have done in the emergency department and receiving standard care e.g. being monitored by staff in the emergency department. Which group you are allocated to will be determined by chance, rather like the toss of a coin, with an equal chance of being in one or the other of the groups. This is important so that the results of our study are not influenced by any bias from the researchers.
- You will then be given instructions on how to fill out a paper diary to record any flashbacks you have of the accident over the next week. You will be asked to fill this in every time you have a flashback. If we asked you to complete the computer task in the emergency department, we will give you the option of imagining the task (or completing it again) each time you have a flashback.

2) *Once you return home*

- In the first week after the accident, the researcher will contact you regularly by text, email or telephone to offer you support with filling in the diary.
- After one week, we will contact you by telephone, and ask you to return your flashback diary in the post, or we can arrange a time to collect it from you. We will also ask you to complete some questionnaires, either by post or online (using a secure webpage). These will take about 20 minutes. You can complete the questionnaires from home or wherever is convenient for you. If you have any problems we can try to help you with these.

- One month after the accident we will contact you again to complete a similar set of questionnaires by post or online, including questions about your feedback on the study. Finally, we will contact you by phone at one month to debrief you about the study and answer any remaining questions you may have.

Please note:

- You can decide to stop participating at any point.
- You need not answer questions that you do not wish to.
- Anything you tell us will be confidential. Your name will be removed from the information and it will not be possible to identify anyone from our reports on the study.

What are the possible risks of taking part?

We may ask you to note down the worst moments of the accident, and will also be asking you questions related to the accident and any past stressful events or difficulties with your mental health, which some people might find upsetting. If you do find this upsetting you may stop the study at any time without having to give a reason, and you would not have to answer any questions that you did not want to.

What are the possible benefits of taking part?

Many people find taking part in these studies interesting, and find it helpful to have to something to occupy themselves whilst waiting in the emergency department. If you have any severe problems when we follow you up, and would like to receive help, we may be able to signpost you to the appropriate local healthcare service for support.

Reimbursement

To thank you for your time, we will send you a £30 store voucher for completing the study.

What if something goes wrong?

Any complaint about the way you have been dealt with during the study or any possible harm you might suffer will be addressed. The detailed information on this is given in Part 2.

Will my taking part in the study be kept confidential?

Yes, your taking part in the study will be kept confidential. We will follow ethical and legal practice and all information about you will be handled in confidence. The details are included in Part 2.
If the information in Part 1 has interested you and you are considering participation, please read the additional information in Part 2 before making any decision.

PART 2

What if something goes wrong?
If you wish to complain about any aspect of the way in which you have been approached or treated during the course of this study, you should contact the Chief Investigator for the project: Dr Lalitha Iyadurai, University Department of Psychiatry, Warneford Hospital, Oxford OX3 7JX, tel: 01865 223923, email: scarta@psych.ox.ac.uk, or you may contact the University of Oxford Clinical Trials and Research Governance (CTRG) office on 01865 572224 or the head of CTRG, email ctrg@admin.ox.ac.uk. Given the nature of this study, it is highly unlikely that you will suffer harm by taking part. However, the University of Oxford, as Sponsor, has appropriate insurance in place in the unlikely event that you suffer any harm as a direct consequence of your participation in this trial.

Would information collected about me during this study be kept confidential?
All information that is collected about you during the course of the research would be kept confidential and would be accessible only to the research team and authorised outside parties (see below). All research data will be assigned a number, and will be stored without your name on them. We are obliged to keep all research data for a period of 10 years. After this time all data will be destroyed. If you decide to withdraw from the study part way through, we will not collect any further information from you, but will keep any information we have already collected anonymously until the end of the study. We may choose to quote something you have said word for word in a publication arising from this study. If we do this, we will first make sure that any identifying information is removed. If you have any high
levels of distress or suicidal ideation when we follow you up, we may wish to feed this back to your GP. However, we would discuss this with you first and would only disclose information of immediate relevance.

Responsible members of the University of Oxford or the Oxford University Hospitals NHS Trust may be given access to data for monitoring and/or audit of the study to ensure we are complying with regulations. All will have a duty of confidentiality to you as a research participant and nothing that could reveal your identity would be disclosed outside of the research site.

What would happen to the results of the research?
The results of the research will be written up for publication in scientific journals, and will contribute towards Dr Iyadurai's PhD thesis. Any research publication would not identify you individually. If you wish to obtain a copy of the published results, please inform the researcher. We would be delighted to send them to you when they are available. The results may be made available to other researchers but only through a protected database after removing all information that identifies individuals.

Who is organising and funding the research?
The study is sponsored by the University of Oxford. It is funded by the National Institute for Health Research.

Who has reviewed the study?
This study has received ethical approval from the NRES Committee South Central – Oxford C, Ref number: 12/SC/0485.

Contact for further information
If you have any further questions about this research, please feel free to speak to Dr Lalitha Iyadurai (NIHR Doctoral Research Fellow) on 01865 223923 or e-mail scarta@psych.ox.ac.uk.

Thank you for taking the time to read this information sheet and considering whether to take part in this research. You will be given a copy of this Information Sheet and a signed consent form to keep if you do take part.

APPENDIX 5.9 Consent form

UNIVERSITY OF OXFORD
DEPARTMENT OF PSYCHIATRY
WARNEFORD HOSPITAL
OXFORD
OX3 7JX
TEL: (01865) 223923
FAX: (01865) 793101

Oxford University Hospitals NHS
NHS Trust

CONSENT FORM (Version 4.0 20/12/13)

Study Title: SCARTA - Simple cognitive activities after a road traffic accident
Chief Investigator: Dr Lalitha Iyadurai
REC Reference Number: 12/SC/0485

[Please initial the box]

I confirm that I have read and understand the Information Sheet dated 09/01/14 (Version 3.0) for the above study. I have had the opportunity to consider the information, ask questions, and have had these answered satisfactorily. Specifically, I understand that the study involves:

- **Completing a flashback diary over the week after the accident and sending it in the post**
- **Being contacted in the week after the accident for support with filling in the diary**
- **Being contacted after 1 week and 1 month**
- **Completing online/postal questionnaires after 1 week and 1 month** ☐

I understand that my participation is voluntary and that I am free to withdraw at any time, without giving any reason, without my medical care or legal rights being affected. ☐

I am aware that data collected as part of my routine clinical care will be available to the study researchers. ☐

I am aware that all information will be kept strictly confidential except in the rare circumstances in which it is judged that I or someone else is at current risk of serious harm, and in which case my GP or other named health professional will be informed. ☐

I understand that data collected during the study may be looked at by authorised individuals from the University of Oxford or the Oxford University Hospitals NHS Trust where it is relevant to my taking part in this research. I permit these individuals access to my research records. ☐

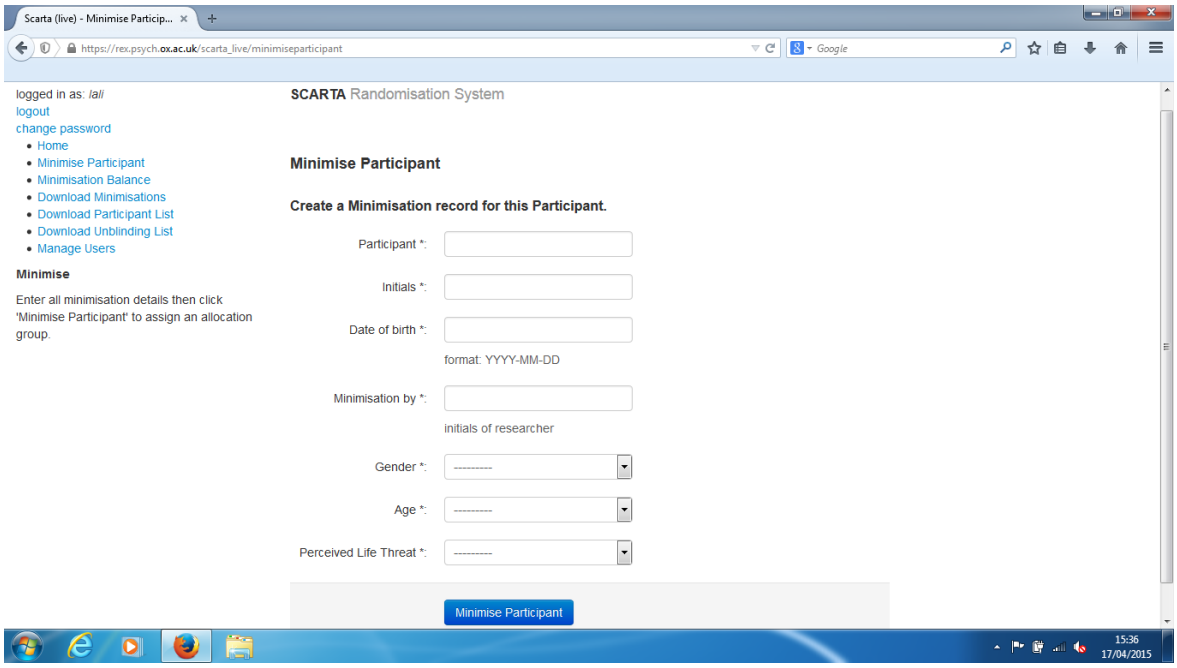
I am aware that the results may be made available to other researchers but only through a protected database after removing all information that identifies individuals. ☐

[*Optional*] I am willing to be contacted by the research team about future research studies. ☐

I agree to take part in the above study. ☐

Name of Participant	Date	Signature
_____	_____	_____
Name of Researcher taking consent	Date	Signature
_____	_____	_____

APPENDIX 5.10 Randomisation programme screenshot



APPENDIX 6.1 Hotspots of the accident for participants in the randomised controlled study

Simple cognitive task			Usual care		
Participant code	Hotspots	Number of hotspots	Participant code	Hotspots	Number of hotspots
SC-006	Seeing the curb Pain in ear Face down	3	SC-034	Flipping car Lorry close behind	2
SC-010	Seeing tree Flash of airbag	2	SC-052	Seeing the car Spitting tooth	2
SC-023	Bracing myself Rag doll	2	SC-068	Car sliding towards me	1
SC-047	Car not slowing down Spinning round Seeing airbags Other car on verge Parts on road Hearing sirens	6	SC-075	Seeing the tube	1
SC-081	Flying through air Screaming	2	SC-099	Hearing banging – noise of crash Sight of rock Losing control of steering & crash to tarmac* Sliding on road*	4
SC-109	Seeing car coming "what are you doing?" Inevitability	1	SC-121	Guy's face See him turning Car bonnet in front* Ambulance*	4
SC-132	Lying in road – seeing sky Seeing car moving Other car coming Trying to get up	4	SC-145	Seeing car in front of me Seeing similar car*	2
SC-150	Seeing smoke – being trapped Hedge coming towards me and tree	2	SC-166	Blood dripping Blood dripping on yellow raincoat Seeing guy who called ambulance	3
SC-184	Car close and accelerating – moment of impact Blurriness – seeing stuff go by People coming over	3	SC-178	Back end of lorry	1
SC-204	Smashing face Seeing car Seeing children	3	SC-215	Van approaching Curled up on all fours	2
SC-258	Hitting the bus Losing control of the bike	2	SC-227	Feet moving Seeing bloke's face – scared	2

SC-262	Back end going Airbag in my face Feeling impact Jostled around in car	4	SC-236	Van coming towards us Bang of airbags – white	2
SC-270	Losing control of car	1	SC-243	Van coming towards us Sitting in the car	2
SC-291	Seeing bike smashed up	1	SC-289	Lying on the ground Looking around at people Trying to brake	3
SC-317	Seeing other bike Sliding over road – heard helmet	2	SC-301	Feeling slow motion Car in rear-view mirror	2
SC-329	Seeing little girl in other car	1	SC-338	Fox Hitting tree Seeing car	3
SC-340	Lorry in mirror Woman screaming	2	SC-364	Car spinning	1
SC-355	Seeing girl look away – point of no return Girl being hysterical Impact – slow motion	3	SC-372	Seeing her car Finishing spinning Seeing smoke	3
SC-408	Fighting to keep it up (the scooter) Seeing people round me	2	SC-386	Seeing the car coming	1
SC-420	Car spinning Trapped inside	2	SC-393	Throwing up in bin Colleague driving Sitting on wall, hearing argument	3
SC-431	Seeing barrier Stopped – realising what had happened	2	SC-412	Impact noise* Car driving out of side road (trigger)*	1
SC-465	Feeling head banging Woman saying “it’s quite deep” Blood dripping Seeing car parked	4	SC-449	Being dragged	1
SC-477	Catapulting forward Seeing car pushing, sparks from exhaust Lying there, people watching	3	SC-454	Braking, not stopping Seeing car	2
SC-505	Car coming across	1	SC-483	Seeing red car Seeing driver	2
SC-514	Dust and smoke, debris everywhere Seeing car heading towards us Bang, airbags going off	3	SC-496	Truck coming towards me - impact Seeing foot out to one side	2
SC-533	Actual impact Seeing back of van	2	SC-522	Car coming towards us Airbags going off Smoke in the car	3

SC-551	Seeing the car stationary "I've got no time to stop" Smell burning rubber*	2	SC-546	Smell of car Lights flashing Bang of airbags Other car in ditch Broke screen*	5
SC-579	Seeing myself collide with other bike Seeing myself go over handlebars Collecting myself together afterwards	3	SC-567	Pavement, bin, going over Car driving away	2
SC-598	Seeing the gap between myself and the ground Losing control of the car	2	SC-580	Seeing van indicator lights Tingling in my mouth Stumbling to pavement The floor/asphault*	4
SC-607	Car coming across road at me Seeing smoke coming out of the airbag and smell	2	SC-611	Sliding Seeing steering wheel and bushes Looking back afterward Road sliding*	4
SC-630	Having difficulty breathing Image of van suddenly moving sideways – seeing mirror Image of corner of lorry	3	SC-624	Moment of falling down Lying on the floor	2
SC-669	Seeing the car Orange smudge	2	SC-648	Falling Standing up, leg shaking	2
SC-676	Actual impact Car flipping Windscreen smashing, darkness	3	SC-653	Car pulling straight out Landing on back on the road Flash and noise	3
SC-682	Truck indicator and truck coming out Massive jolt	2	SC-695	Sparkly rain (glass) Truck continuing to pull out	2
SC-703	Being on the ground and feeling along Seeing the sun	2			
SC-719	Car door opening Hitting the ground	2			
SC-726	Seeing road surface and light flying Blood streaming/dripping	2			
Mean (SD)		2.38 (1.01)	Mean (SD)		2.32 (1.04)

* Added to Intrusion Diary by participant

Note. In the simple cognitive task group, hotspots were noted down by the researcher on the "Hotspots of the accident" form as part of the memory reactivation cue, and then copied onto the participant's Intrusion Diary under "Your examples". In the usual care condition, hotspots were noted down directly onto the participant's Intrusion Diary under "Your examples".

APPENDIX 7.1. Comments on the Feedback Questionnaire from participants in the randomised controlled study

Participants

Respondents were 31 out of 37 participants allocated to the intervention group and 31 out of 34 participants allocated to the control group. Verbatim responses are shown in order of participant number for those who provided comments (participants who provided no comment are excluded).

Free response question 1. Do you have any suggestions for improving using Tetris as something that might help after a traumatic event? (*Intervention group only)*

1. No
2. I don't think I appreciated how it could help. It has been the visualisation of Tetrus that was helpful - possibly after finishing playing. Visualise playing?
3. No
4. found screen small, moving neck and head and sore chest was uncomfortable, despite position change etc. Maybe larger screen would help
5. Offering an alternative to Tetris Blitz. This version of Tetris can take some time to load, and bombards the user with free-to-play game mechanics which takes time to deal with upon opening the app, slowing down the time it takes to start playing. Tetris litz games also only last 2 minutes, with classic tetris, you can potentially play for as long as you feel necessary, rather than in 2 minute chunks.
6. Supply Hospitals with some hand held Tetris consols so that patents have the choice to play then when their waiting in wards to help them with any current worries, flashbacks etc.
7. tetris, or just talking is a good distraction after the accident.
8. I find playing tetris quite relaxing in general even in stressful situation not related to the accident.
9. Hard for me to answer this as my traffic accident was not traumatic
10. No
11. None
12. In a more comfortable environment with music
13. None

Free response question 2. Do you have any other comments about using Tetris as something that might help after a traumatic event? (*Intervention group only)*

1. I think that playing Tetris helped focus my mind and bring some "normality" back to my head. I didn't dwell on the accident to much while I was in hospital. Playing Tetris seemed a bit strange at the time, but looking back it has been a help. Thank You.
2. No
3. Every time I see the notepads/fridge magnets I think of the accident/hospital.
4. I can see that the idea of fitting shapes and 'compartmentalising' things may be useful - I'm not a very 'gamey' person when it comes to computerised things so for me don't think it did much - did like the fridge magnets and post its though, did use those
5. I wonder if I were to be reminded of Tetris, some time in the future, would it bring back memories of the accident, through association?
6. I don't know if it is just me but the images of falling objects just after falling off a bike was a bit stressful. Maybe some colouring thing or musical game would have been better...
7. Possible distraction - don't know
8. Sudoku in the head for people that cannot use their hands because of the injury (someone might need to assist to write in the numbers)
9. Other simple games can be possibly benificial also, but obviously you wouldn't give a car racing game to someone who has just had a car crash.

10. I think it helped a lot to distract my mind after accident by playing tetris. I was less worried about the cut in my head. My flashbacks decreased after a few days, which might not only have been an effect of playing tetris, but also being back to work. Ialso was less stressed about the accident when I figured out what happened
11. Unsure, personally I found it useful as a simple game to pass the time.
12. It certainly took my mind off of it at a time when I probably would have sat brooding and feeling very sorry for myself.
13. I had only one flashback and that was when I went to see the car. Iecoected to get a lot more flashbacks a shave had in past she had accidents.
14. Very relaxing
15. It seems logical that having something to occupy the mind whilst waiting in a hospital environment reduces the tendency to dwell upon the incident.
16. None

Free response question 3. If we were to roll out the study on a larger scale, how could we improve the study?

Intervention group

1. Make the gender field not mandatory and/or add a "prefer not to say" option. Which would probably mean not basing your assignment to treatment and control groups on gender. Which shouldn't matter, because random assignment without stratification by gendershould still provide a balance of genders in expectation - which is why we do it.
   So this isn't a case of putting participants' sensibilities ahead of experimental validity - though even if it *were*, a good research design should always prioritize th wellbeing of participants over design choices which would otherwise be expedient or convenient. Because it undermines the purpose of human research (be it social or medical) if you harm or distress people when doing it.
   I'd also strongly recommend thooughly reviewing every question you ask based on textbook survey criteria. What is this question meant to measure? Does it? Is the wording unambiguous? Could it be made clearer or streamlined?
   (I can't recall any specific examples, but I think some of he initial data capture forms from when we met in A&E had questions that were quite confusing and long-winded and could have been worded better).
2. Oh, and make these feedback boxes bigger than four lines deep! I hate scrolling to check I'm making sense sing a tiny scrollbar.
3. From my experience the study was done very professionally from start to finish. The online questionnaires have been easy to understand and fill in. I haven't felt pressured at any time and have been happy to help with the study. I can't think of any way i could be improved.
4. Maybe a different game such as Flow free could be used as well as Tetris (I am much better at this game and had never played tetris before and was rubbish at it.
5. see comments above - maybe have more alternatives to computerised versions, bearing in mind age of participants ie won't all be into computer games..
6. I think its great as it is!!!
7. Maybe you could add to the diary how often and how long someone played tetris per day and how often it was directly played after a flashback. I think that varied for me a lot. Sometimes I just played a short (2 min) game or played for an hour even after nt having a flashback.
8. I haven't tried completing this on a mobile device only a PC, this should be considered if not already possible.
9. It was fine
10. Nothing at all
11. Presumably you take into account the severity of the RTA/injuries as you assess the responses. I can imagine that my responses could have been very different if my injuries were significant and/or the nature of the accident had been more dramatic

12. I had a back injury from my accident which meant I have not really been able to have a normal life since so many of the questions about the impact of the accident on my life were a little difficult as I have not been at work, not been socialising or to bein with sleeping well, however that has not been to do with any mental aspects of the accident it has been purely physical. I wasn't sure how to answer these questions.

Control group

1. None
2. Offer to help people after the accident
3. Possibly provide opportunity to explain some answers in more depth, ie. one of the questions asked about positive impact of accident - for me personally it means I have started to wear a cycle helmet.
4. By teaching bikers to be aware of trucks carrying rubble and the real fact that an accident could be waiting to happen.Ie to be wary of trucks especially if they are in front on the road.When driving.
5. I was in a biks accident and actually a lot if the emotional aftermath was brought up when I got back on my bike which wan't for about 3 Weeks later, and I'm not sure that the study does enough to capture data about triggers for emotional responses. Up unil I got back on the bike, I would have answered very differently
6. Develop a more reliable questionnaire
7. None
8. Don't know
9. Wouldn't change anything
10. I think it's fine the way it is
11. Perhaps ask the number of times flashbacks or unsought memories of the accident that were not distressing or unsettling occurred
12. Not sure
13. I think the study was very good and probably does not need improving
14. Explain that the study will take more time than originally explained
15. I have no background in surveys to work from, so I'm really not able to offer a reliable opinion. Sorry.
16. I reckon people that sustain physical injuries as a result of their accident are more likely to have flashbacks. Maybe have a section in one of the questionnaires that describes what injuries (if any) were sustained. I think it could also be useful to d the survey with loved ones to the person involved as they are affected by the trauma too. I noticed my sister and mother being particularly absent minded like myself during their care of me due to the stress getting to them too.
17. By making it less repetitive
18. Need to reduce number of questions and repetition (thought it may affect accuracy). Categorize traumatic experiences. E.g. into types and degree of injuries.This would have an impact on respondents but would help understand the different types traumatic exeriences better.
19. It works fine how it is I think!
20. I think it's already very easy and pretty straight forward!
21. Nothing to add.

Free response question 4. Do you have any other comments about the study or your experience of taking part in the study?

Intervention group

1. I'm sorry it took me so long to fill in this last questionnaire!
2. Playing Tetris has helped me deal with my accident in a way I don't think I appreciated at the time. I will suggest this to family and friends. Thank You.
3. I contact was useful as a reminder
4. I found it interesting to take part in the study and I think the distraction of being asked to take part in something helped as a distraction and reduced my distress and shock after the fall.
5. Difficultly answering the questions honestly and correctly

6. I'm just glad to feel part of something and hopefully the resauts of this study can benifit many people in years to come.
7. Overall having something to do, think about was useful. I had been given drugs, so trying to concentrate and stay awake was not easy. I was in the Army for 24 years so maybe I could handle a traumatic experience better than the average average person coul.
8. Especially at the beginning straight after the accident it was difficult for me to differentiate between flashback and just think about the accident. I sometimes had the feeling I force myself to think about it. The feeling/picture of falling on the stree with my head kept popping up in my head (especially when I checked my cut in the mirrow at home). So it wasn't a flashback out of the blue, but it appeard in my thoughts quite quickly.
9. None
10. Assume playing Tetris was fundamental to only having one flashback. Still found myself nervous when driving especially on slip roads
11. Very helpful staff

Control group

1. I wonder about the heterogeneity in incidents classified as RTAs by reception staff. Are the responses after such diverse experiences comparable?
2. It has helped to an extent to keep me pro active and increase my confidence.
3. The study has helped me to identify how the accident affected me personally by making me review areas of my life that have been affected and has helped me try and move forward for example my appearance, enjoyment of activities. I maybe hadn't realised tha the accident had altered me in that way but reviewing the questionnaire helped identify this. The accident and hospital experience was quite scary but somehow taking the questionnaire almost made you able to focus on what happened and realised why you wee feeling that way.
4. I would question its validity as the questionairre acted as a prompt to remind me of the accident. However, if that was its intention then there are no validity issues.
5. Thank you
6. No
7. Support and instruction was good
8. I was very happy to take part in the study.
9. I was happy to take part and welcomed the opportunity
10. No
11. I have been very happy to help
12. No
13. Only that I'm pleased to have been able to help, though I can't really say how much help I've been able to offer, not having experienced the symptoms of PTSD that the survey described.
14. People with injuries I think are more likely to think about the accident more frequently as they are constantly reminded either by physical pain, disability to be able to do normal things, or visits to doctors etc where they have to recount the accident sveral times over.
15. It has provided sharp reminders of the incident - and my failings.
16. Happy to help and will be keen to read the results and implications for care
17. I just wanted to add that another way that I have been affected by the accident is during driving again.... When I am driving towards a similar bend I sometimes have the feeling that my car is sliding out of control but its not! This makes me literally fel sick when it happens. Then I get the same flashback as I always do which is seing the road as I lost control of the car just before impact of the ditch and field.
18. It's good to know that there is an attempt to improve people's experiences with a view to having a positive effect on their recovery.
    In terms of my experience, the act of taking part in the study has had a positive effect. In answering some of the quesions it has underlined for me how lucky we were both in terms of the accident itself and the outcome for us. Things could have been so much worse, and both my husband and I are aware of how much worse the result could have been both physically and mentaly.

APPENDIX 8.1. Publications, presentations and public communication during this DPhil

Publications

Holmes, E. A, **Iyadurai, L.**, Jacob, G., & Hales, S. (2015). Mental imagery in psychological disorders: An opportunity for treatment innovation. *Emerging Trends in the Social and Behavioural Sciences.*

Hales, S., Blackwell, S. E., Di Simplicio, M., **Iyadurai, L.**, Young, K., & Holmes, E. A. (2015). Imagery-based behavioural assessment. In G. P. Brown & D. A. Clark (Eds.), *Cognitive Behavioural Assessment, Diagnosis and Case Formulation.* New York: Guilford Press.

Clark, I. A., James, E. L., **Iyadurai, L.**, & Holmes, E. A. (2015). Mental imagery in psychopathology: From the lab to the clinic. In D. Berntsen & L. Watson (Eds.), *Clinical Perspectives on Autobiographical Memory.* Cambridge: Cambridge University Press.

Iyadurai, L., Holmes, E.A., & Sandberg, A. (2010) Why we should treat but not erase trauma memories. *British Journal of Psychiatry.* http://bjp.rcpsych.org/cgi/eletters/197/5/414-b

Holmes, E.A., Sandberg, A., & **Iyadurai, L.** (2010). Erasing trauma memories: Is this what the science suggests or even what we want to do? *British Journal of Psychiatry* 197, 414-415.

Publications in preparation

Iyadurai, L., Nobre, A. C., Geddes, J. & Holmes, E. A. *Pilot randomised controlled trial of a simple cognitive task to reduce the occurrence of early intrusive memories after a road traffic accident.* Manuscript in preparation.

Iyadurai, L., Hales, S., & Holmes, E. A. *Using a Simple Imagery-Competing Task within CBT to Treat Intrusive Imagery: A Case Study.* Manuscript in preparation.

Oral presentations

Iyadurai, L. (2014, December). *Tetris after trauma.* Presented at the Experimental Psychopathology Meeting, Cumberland Lodge, Windsor.

Iyadurai, L. & James, E. (2013, March). *Imagery and memory: A simple cognitive task ("Tetris") to reduce flashbacks after a trauma.* Presented at Maddingley Hall Imagery Meeting, Cambridge.

Poster presentations

Iyadurai, L., Nobre, A. C., Geddes, J. & Holmes, E. A. (2012, June). *Can we prevent flashbacks after trauma? A plan to test a simple cognitive task in A&E.* Presented at Merton College Graduate Day, Oxford.

Public communication

Nixon, R. Playing Tetris may treat PTSD flashbacks. *LiveScience.com,* 2012. Thursday 25th April: 3:36:51 PM ET. [online] Available at http://www.msnbc.msn.com/id/47176735/ns/technology_and_science-science/#.T5khA3bLKqk