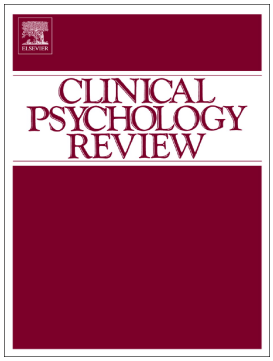

Early psychological interventions for posttraumatic stress, depression and anxiety after traumatic injury: A systematic review and meta-analysis

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Abstract

The psychological impacts of injury have significant long-term implications on injury recovery. This review examined the effectiveness of interventions delivered within three months of injury on the severity of posttraumatic stress disorder (PTSD), anxiety and depression symptoms. A systematic search of seven databases (PsycINFO, Medline, Web of Science, CINAHL, Embase, Scopus and Cochrane Library) identified 15,224 records; 212 full-text articles were retrieved; 26 studies were included in narrative synthesis, and 12 studies with lower risk of bias were included in meta-analyses. Prolonged exposure, and cognitive and behavioural interventions elicited improvements in PTSD, anxiety and depression symptoms; multidisciplinary interventions improved PTSD and depression symptoms; and education-based interventions had little impact on psychological symptoms. Studies comprising risk stratified or stepped care methods showed markedly greater population impact through better reach, implementation and adoption. Meta-analyses revealed small-medium reductions in PTSD symptoms over the first 12 months (SMD= 0.32 to 0.49) with clinically meaningful effects in 64% of studies; reduced depression symptoms at 0-3 (small effect; SMD = 0.34) and 6-12 months (medium effect; SMD = 0.60) postinjury, with clinically meaningful effects in 40% of studies; but no pooled effects on anxiety symptoms. Altogether, exposure- and CBT-based psychological interventions had the greatest impact on PTSD and depression symptoms postinjury when delivered within three months of injury, with risk-stratified, stepped care having greater population impact potential.

Keywords: Injury; accident; prevention; treatment; psychological

Abbreviations

BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; BDI-II = Beck Depression Inventory-II; CAPS = Clinician-Administered PTSD Scale; CBT = cognitive

behavioural therapy; CES-D = Center for Epidemiological Studies Depression Scale; CI = confidence interval; DASS-21 = Depression Anxiety and Stress Score; EMD = eye movement desensitisation; FE = fixed effects; HADS-A = Hospital Anxiety and Depression Scale, Anxiety subscale; HADS-D = Hospital Anxiety and Depression Scale, Depression subscale; IES = Impact of Events Scale; IES-R = Impact of Events Scale-Revised; mTBI = mild traumatic brain injury; MVC = motor vehicle collision; NHMRC = National Health and Medical Research Council; NICE = National Institute for Health and Care Excellence; NR = not reported; NS = not stated; PCL-C = PTSD Checklist-Civilian Version; PC-PTSD-Primary Care Post-Traumatic Stress Disorder Screening; PDS = Posttraumatic Diagnostic Scale; PHQ-9 = Patient Health Questionnaire-9 item Depression Screen; PRISMA = Preferred Reporting Items for Systematic Reviews and Meta-analyses; PSS-I = The PTSD Symptom Scale Interview; PSS-SR = The PTSD Symptom Scale-Self Report Version; PTSD = posttraumatic stress disorder; PTSS-10 = Posttraumatic Stress Syndrome questionnaire; RCT = randomised controlled trial; RE = random effects; RevMan = Review Manager; SD = standard deviation; SMD = standardised mean difference; STAI = the State-Trait Anxiety Inventory; SUDS = Subjective Units of Distress Score.

Introduction

Most people show remarkable resilience and recover well after injury; however, a significant minority develop psychological conditions including anxiety, depression and posttraumatic stress disorder (PTSD). For instance, within one year of traumatic injury, about a third of people meet the diagnostic criteria for PTSD and depression (Shih, Schell, Hambarsoomian, Belzberg, & Marshall, 2010; Sterling, Hendrikz, & Kenardy, 2011), and approximately one in five have a clinically poor trajectory for psychological outcomes (Bryant et al., 2010). A recent systematic review found that psychological distress symptoms are especially elevated after whiplash injury, spinal cord injury and acquired brain injury sustained in a motor vehicle collision (Craig et al., 2016). Several studies have shown that, once present, elevated psychological distress symptoms remain stable over the first two to three years post injury for a subset of injured people (Craig et al., 2016; Mayou & Bryant, 2002). Moreover, people who develop conditions like PTSD, depression or anxiety after injury typically have poorer long-term physical health, disability, and reduced participation in activities of daily living, including social and economic participation (Zatzick et al., 2008), highlighting the need to treat those at risk early.

After injury, psychological conditions may arise partly due to predisposing risk factors as well as trauma-related characteristics including high levels of acute distress, and difficulty coping with the consequences of the event (Bryant et al., 2010; Shih et al., 2010). In particular, the development of psychological distress symptoms within three months postinjury is one of the strongest determinants of disability 12 months postinjury (O'Donnell et al., 2013), more so than factors like injury severity, premorbid disability and acute pain severity. The frequent co-occurrence of anxiety, depression and PTSD symptoms after traumatic injury (Shalev, Freedman, Peri, & Brandes, 1998) is thought to indicate a generalised distress response to the trauma (Grant, Beck, Marques, Palyo, & Clapp, 2008;

Thompson, Berk, O'Donnell, Stafford, & Nordfjaern, 2015). However, it is notable that early symptoms of several psychological conditions (especially PTSD; Fishbain, Pulikal, Lewis, & Gao, 2016) increase the likelihood of other disabling outcomes like chronic pain (Liedl et al., 2010; Mayou & Bryant, 2002; Wiech & Tracey, 2009) through shared vulnerability mechanisms. Identifying those at risk of poor outcomes and implementing early interventions to improve injury recovery is therefore a high priority (Forneris et al., 2013).

The key goal of early intervention is to prevent or attenuate the severity of psychological sequelae of injury in those at greatest risk during the acute or sub-acute period. While implementing interventions early after injury is a high priority, it is not clear which early interventions are the most effective at reducing the severity and impact of psychological conditions, nor which intervention modalities offer the greatest potential for population impact. To date, most early interventions for psychological outcomes involve education, psychological therapy using cognitive behavioural therapy (CBT), prolonged exposure, and medical review and management (National Institute for Health and Care Excellence, 2005, 2011, 2016). International guidelines recommend physician or psychologist delivered trauma-focused CBT for those who present with PTSD symptoms within 3 months of a traumatic event (National Institute for Health and Care Excellence, 2005; Phoenix Australia - Centre for Posttraumatic Mental Health, 2013). Similarly, individual self-help interventions based on CBT, or group-based CBT, are recommended for people with mild to moderate depression who do not respond to first-line treatments (i.e. psychoeducation and active monitoring; National Institute for Health and Care Excellence, 2016). CBT-based self-help and guided psychoeducational groups are also the first-line recommended treatments for those whose anxiety symptoms persist despite education and encouragement of active monitoring strategies (National Institute for Health and Care Excellence, 2011). We note that these recommendations are specific to the early period post-injury, and that the theoretical

frameworks and treatment guidelines for chronic mental health conditions are likely to differ (e.g., recommending medications).

Only one previous systematic review examined the effectiveness of interventions implemented to prevent psychological distress following a motor vehicle crash (Guest, Tran, Gopinath, Cameron, & Craig, 2016). Three of the six CBT-based studies identified in that review brought about significant reductions in distress symptoms compared with waitlist control interventions. However, the studies identified in that review delivered interventions up to 18 months postinjury, and focused only on prevention of psychological symptoms in those who did not already have clinically elevated symptoms after transport injury. Therefore, the effects, and likely population-level impacts, of *early* interventions using psychological treatments (e.g., CBT or prolonged exposure) after traumatic injury remains to be critically examined.

The present systematic review examined the efficacy of early interventions delivered to adults within three months of traumatic injury on the severity of psychological symptoms. Traumatic injury was defined as unintentional traumatic damage to the bodily tissues, and did not include trauma with a primary psychological injury, or that was intentional. Where possible, we sought to identify the key features of successful interventions, and to examine the likely population impact of interventions based on the likely Reach, Effectiveness, Adoption, Implementation and Maintenance (RE-AIM) framework (Glasgow, Lichtenstein, & Marcus, 2003; Zatzick, 2012). Meta-analyses of studies considered to have lower risk of bias were conducted to determine the efficacy of early interventions (within and across intervention types) on PTSD, depression and anxiety symptoms.

Method

Search strategy

A systematic search of PsycINFO, Medline, Web of Science, CINAHL, Embase, Scopus and

Cochrane Library electronic databases was conducted in September 2016, and was updated in September 2017. Procedures outlined in the Preferred Reporting Items for Systematic-Reviews and Meta-analyses (PRISMA) were followed (see Figure 1; Moher, Liberati, Tetzlaff, & Altman, 2010). The search strategy included a combination of population, intervention and outcome keywords and Medical Subject Heading (MeSH) terms specific to early treatment to prevent chronic pain and secondary psychological outcomes following injury. Search terms included (but were not limited to): Motor vehicle accident/crash, work accident, injury, compensable injury (Population); Prevention, rehabilitation, cognitive behavioural therapy, cognitive training, psychological debriefing, CBT, psychological first aid, trauma-focused CBT, exposure therapy, cognitive therapy (Intervention); and Psychological distress, anxiety, depression, PTSD and posttraumatic stress. See Table A1 for all keywords and MeSH terms, and Table A2 for the Medline search strategy.

Trial authors and chief investigators of published protocols and registered trials on www.clinicaltrials.gov and www.anzctr.org.au were contacted to obtain any new published outcomes that may not have been indexed yet; however, none were available. A targeted search of Google Scholar was conducted for prominent study authors' research output, as well as a targeted search of the National Institute of Health and Care Excellence (NICE) grey literature database. Search outputs were managed using Endnote version X8.

Inclusion and exclusion criteria

The search was restricted to peer-reviewed papers that described original empirical research, written in English, and published between 1990 and September 2017, to ensure that included papers were consistent with the most recent treatment guidelines.

Population

Studies were included if the interventions were delivered to adults (i.e. ≥18 years old) who sustained unintentional musculoskeletal, soft tissue, orthopaedic or mild traumatic brain

injury in a transport, work or other incidents. Studies were excluded if the interventions were delivered to those who experienced trauma with no physical injury (e.g., primary psychological injury), or that resulted from intentional injury (e.g., suicidal/non-suicidal self-injury, sexual assault, physical assault, or domestic violence or from a military setting). Studies were also excluded if the interventions were delivered to those who sustained a spinal cord injury or moderate to severe traumatic brain injury as these catastrophic injuries may lead to a different trajectory of psychological outcomes and/or impact on the capacity to engage with psychological therapies, and therefore require tailored treatments specific to that population. Where studies included a range of trauma or injury types, or if they included some participants aged under 18 years old, they were retained if at least fifty percent of the population met the population inclusion criteria.

Intervention

Studies were included if the intervention comprised a psychological clinical framework, and may also have comprised education, uni-or multi-disciplinary rehabilitation (i.e., physician, physiotherapy, psychology, occupational therapy). Interventions must have sought to prevent the incidence, or reduce the severity and impact, of psychological conditions. Studies were excluded if the intervention was initiated more than three months postinjury (for all, or more than 50 percent of participants), focused on the management of chronic pre-existing psychological conditions, or if the study primarily evaluated pharmacological interventions; however, pharmacotherapy could be included as part of a broader multi-component intervention. Studies were excluded if the intervention was solely delivered within the first week postinjury, in accordance with recommendations for early interventions only if symptoms have not improved after active monitoring and education in the first four weeks (National Institute for Health and Care Excellence, 2005, 2011, 2016).

Classification of studies

Studies were classified according to the National Health and Medical Research Council (2009) levels of evidence. Studies were included if they compared an active intervention with a control group (i.e. active care, waitlist or usual care), with or without randomisation (i.e., Levels II, III-1 and III-3). Pre- and post-intervention comparisons of a single intervention group that evaluated clinical effectiveness were included (i.e., III-3, level IV cohort trials) to facilitate the compilation of all available evidence; however studies comprising anecdotal reports or case series with fewer than 10 participants were excluded. Systematic reviews and meta-analyses (i.e., Level I) were excluded.

Outcomes

Intervention studies had to include assessment of anxiety, depression, and/or PTSD symptoms or clinical diagnoses of those respective conditions.

Study selection

Titles and abstracts were independently screened by two reviewers against the inclusion criteria. Each reviewer assigned inclusion codes of yes, no or unsure. Full text articles were then obtained and assessed for eligibility. The reviewers compared the screening results and discussed any disagreements regarding study eligibility.

Data extraction

Two reviewers used a customised form to extract study information to enable the evaluation of study characteristics, heterogeneity, and likely population impact through reach, effectiveness, adoption and implementation (Kearns, Ressler, Zatzick, & Rothbaum, 2012). The following data were extracted: (1) study country; (2) cohort characteristics (including injury type, injury context, gender distributions and sample size at recruitment and outcome assessment); (3) study inclusion and exclusion criteria; (4) study design; (5) characteristics of the intervention and control groups; (6) details of the intervention(s) including timing postinjury, discipline of therapy/therapists, modality (e.g., individualised, group) and

intensity; (7) setting in which interventions were adopted; (8) who implemented the intervention (e.g., research staff or non-research clinicians); (9) timing of follow-up assessments; (10) primary and secondary outcomes; (11) measurement tools; (12) intervention effects on outcomes; (13) number (percent) of participants lost to follow up; (14) presence of missing data; (15) reporting of adverse events; (16) intervention acceptability and reach, including factors impacting on trial recruitment or effects; and (17) intervention requirements that may influence external generalisability of the intervention (e.g., computer or phone access, travel requirements).

Outcome data included means and standard deviations (SDs) for continuous data and the number of participants with the desired outcome for categorical data. The reviewers contacted study authors for additional data where necessary. Studies were classified according to the broad intervention domain, discipline, modality and/or goal, which included cognitive and behavioural interventions; education or information-based interventions; prolonged exposure and eye movement desensitisation (EMD) interventions; and multidisciplinary/collaborative care interventions.

Risk of bias assessment

As both randomised controlled trials (RCTs) and non-randomised studies were eligible and included risk of bias assessment was undertaken using a tailored tool based on the respective Cochrane Collaboration guidelines (Higgins et al., 2011; Sterne et al., 2016). Risk of bias was evaluated for the following domains: (1) *selection bias* (e.g., randomisation and stratification); (2) *performance bias* (e.g., blinding of participants and personnel); (3) *detection bias* (e.g., missing data and appropriate confounders); and (4) *reporting bias* (e.g., selective reporting); see Table A3 for the risk of bias framework. Two reviewers independently assessed each study for bias, which was coded as high, moderate, low or unclear/unknown. Where appropriate, the direction of bias was noted as favouring the

intervention/control, or unclear. Overall risk of bias ratings were determined qualitatively and some domains were weighted more heavily than others, as recommended by Higgins et al. (2011). For example, trial performance and detection and analysis were given more weight as studies with high risk of bias in these domains may be more likely to favour the intervention group. Each reviewer was blind to the assessment of the other reviewer. The reviewers cross-checked their final assessments and resolved any disagreements through discussion.

Grade of evidence

The evidence was evaluated according to the NHMRC (2009) levels of evidence with respect to the overall level of evidence, the consistency of evidence, and clinical impact.

Meta-analysis and data synthesis

Meta-analyses using Random Effects (RE) models were used to examine the outcomes of PTSD, depression, and anxiety symptoms using Review Manager (RevMan 5.3, Cochrane Collaboration). Comparisons were made based on follow-up time (i.e., outcomes at 0-3 months, 3-6 months and 6-12 months), and studies were classified according to intervention type: (a) cognitive and behavioural interventions (including CBT, cognitive therapy, interpersonal counselling and psychological debriefing); (b) prolonged exposure interventions; (c) multidisciplinary/collaborative care interventions; and (d) education or information-based interventions. Meta-analyses compared follow-up symptoms, and did not account for baseline means and SDs. If multiple assessments were reported during any period, the last assessment in that period was used. If a study examined two or more active treatment arms, the group that received the closest to usual care was selected as the control group.

As the tools used to measure PTSD, depression, and anxiety symptoms varied between studies, intervention effects were quantified as the standardised mean difference (SMD) between the intervention and control group at the respective follow-up time. Means and SDs were used to calculate the SMD for all outcomes. If variance was reported as standard errors

or confidence intervals (CI), the SD was calculated in RevMan. Values of $p < 0.05$ were considered statistically significant. If a study was included in the same meta-analysis more than once due to reporting multiple subscales, the sample size was distributed across subscales to prevent sample size inflation, consistent with previous reviews (Berryman et al., 2013). For instance, both the intrusion and avoidance subscales of the Impact of Events Scale were analysed in several studies.

Studies were excluded from the meta-analysis if they had high risk of bias, or if there was insufficient data reported (e.g., no indication of variability via SDs, standard errors or CIs), and the original data could not be obtained through contact with the author or substituted with values from other studies. This resulted in exclusion of three studies (Bisson, Shepherd, Joy, Probert, & Newcombe, 2004; Des Groseilliers, Marchand, Cordova, Ruzek, & Brunet, 2013; Zatzick et al., 2004). Heterogeneity was calculated and expressed as I^2, where values above 60% indicated substantial heterogeneity (Higgins et al., 2011). The Chi square test was used to determine heterogeneity where $p<0.10$ indicates significant heterogeneity (Higgins et al., 2011).

For studies with high or unknown risk of bias, and for secondary outcomes that were heterogeneous in nature and measurement, we calculated Hedges *g* and risk ratios (RR), and reported these findings in the narrative synthesis of results. Effects were only calculated where a significant effect was reported by the study ($p < 0.05$) and, where possible, adjusted for group differences at baseline (i.e., by subtracting the baseline effect size from the follow-up effect size; Durlak, 2009). When RRs were calculated, risk was expressed as the likelihood of the desired outcome (e.g., no PTSD diagnosis) after the intervention compared with pre-intervention, or after a control intervention. The probability of the desired outcome was calculated in accordance with the Cochrane guidelines, whereby the probability = 100 x (1 - *RR*). Effect estimates were interpreted as: <0.1 = very small effect, ≥.20 = small effect, ≥.50 =

medium effect, ≥.80 = large effect, ≥1.20 = very large effect and ≥2.0 = huge effect (Sawilowsky, 2009).

To determine whether intervention effects at 0-3 months, 3-6 months and 6-12 months post-treatment were likely to be clinically meaningful we reported the estimated magnitude of the group differences using the SMD from the RE models, which indicates the number standard deviations by which the groups differed. The estimations were then contextualised using the following validated clinical outcome measures, which were used by several of the included studies:

- PTSD Checklist: a change of 10-20 points is clinically meaningful (Weathers et al., 2014). Variability (SD) in PTSD symptoms postinjury on the PTSD checklist has been reported to be 14.86 at 12 months (Giummarra et al., 2017).
- Hospital Anxiety and Depression Scale: minimally important change in the HADS subscales is 1.5 points in a chronic obstructive pulmonary disease sample (Puhan, Frey, Büchi, & Schünemann, 2008). Variability on the anxiety subscale has been reported to be 3.76 to 4.40 12 months postinjury (Giummarra et al., 2017; O'Donnell et al., 2013), whereas variability on the depression subscale was 4.10 to 4.12 12 months postinjury (Giummarra et al., 2017; O'Donnell et al., 2013).

Finally, we determined early interventions had clinically meaningful effects by examining whether the reported symptoms in the intervention group were below the clinical "diagnostic" threshold for the respective scale, or had reduced to a meaningful degree in accordance with published scoring instructions for the respective scale. This approach is consistent with other studies that have examined the clinical significance of interventions (van Hooff et al., 2014).

Estimates of population impact

The population impact was estimated in accordance with the broad principles proposed by

(Koepsell, Zatzick, & Rivara, 2011); however, rather than examining a reduction in likely rates of illness, we examined the magnitude of symptom reductions and reach. Population impact analyses were specifically applied to findings from studies evaluating cognitive and behavioural therapies, prolonged exposure, multidisciplinary and collaborative care. Population impact was further stratified by the two broad methods through which interventions were delivered: risk stratified and stepped care interventions (e.g., interventions that comprise multiple modules and methods based on patient risk characteristics or symptoms) and standard interventions (e.g., interventions reflecting traditional one-on-one clinical therapy).

To evaluate population impact, we first calculated the proportion of the at-risk population who completed the interventions using the participant screening flow data reported in the respective studies (i.e., the percent of those identified to be at risk and eligible across all studies in the respective category who enrolled in the study, divided by the percent who completed the intervention). Second, pooled effect sizes were estimated for PTSD, depression and anxiety symptoms in RevMan 5.3 using RE analyses (see Figure A1). The SMD was then converted into likely differences in symptom severity based on published variance estimates for PTSD, depression and anxiety, summarised above, for the PCL-C and HADS to determine whether the effects would be clinically meaningful.

The likely population impact was then contextualised using data from the Australian setting for the number of annual injury hospitalisations (Pointer, 2015), and the proportion of patients who develop PTSD, major depressive episode or generalized anxiety disorder within 12 months of injury hospitalisation (Bryant et al., 2010). These numbers were used to estimate a "best case scenario" effect of early intervention on reductions in symptom severity if all of those who had the highest risk of developing PTSD, depression or anxiety were offered a risk stratified or standard intervention early postinjury.

Results

The search yielded 15,224 records. After the removal of 3,537 duplicates, 11,687 records remained and 11,475 did not meet the inclusion criteria after screening the titles and abstracts. The reference lists of 27 systematic reviews were screened, and chief investigators and authors of 48 published protocols and registered trials were contacted. Two hundred and twelve full text articles were assessed for eligibility, and 183 did not meet the inclusion criteria. Twenty-nine papers, reporting on 26 studies, were included for data extraction, and 12 studies were included in meta-analyses.

Three papers were published prior to 2000, 12 between 2000 and 2010, and 14 from 2010 to September 2017. Study characteristics, including cohort information, intervention details and outcome measures are described in Table 1. Study inclusion and exclusion criteria are provided in Table A5. To our knowledge, only seven studies were registered, including the studies by Bell et al. (2008; NCT00483444), Mouthaan et al. (2013; ISRCTN57754429), O'Donnell et al. (2012; ACTRN081605), Rothbaum et al. (2012; NCT00895518), Shalev et al. (2012; 2016; NCT00146900), Silverberg et al. (2013; NCT00893347) and Wu et al. (2017; ACTRN12613000203752)

Population

Of the 26 included studies, six were conducted in the USA, six in Australia and the remaining 14 were conducted in nine other countries. Participants were predominantly recruited from hospital emergency departments or trauma centres (22 studies), three studies recruited participants from a PTSD service and one recruited participants from multiple sources. Studies most commonly recruited participants with a range of injury mechanisms and causes (22 studies). Four studies recruited people who had sustained mild traumatic brain injury in a range of circumstances including motor vehicle crashes, falls, non-sexual assaults, bicycle accidents and sporting accidents.

Across all studies 1,747 (56.7%) men and 1,332 (43.3%) women participated. Although the percentage of men varied from 42.7% in prolonged exposure interventions to 60.0% in the multidisciplinary interventions, there was no significant difference in the proportion of males in each study sample across all intervention types ($F(3,25) = 1.83$, $p = 0.17$, participant sex was not reported in one study) or between risk stratified/stepped care and standard interventions ($F(1,22) = 1.25$, $p = 0.28$), see Figure A2.

The majority of studies only recruited participants aged 16 to 70 and while nine studies did not set an upper age limit, inspection of the variability of aged showed that 95% of participants were between 24 and 50 years of age; see Figure A3. Nearly all studies (19 studies, 73.1%) indicated that participants were only eligible if they were proficient in the native language of the respective country (14 English, 2 German and 3 Dutch, Norwegian or Hebrew/Arabic). Six studies (23.1%) explicitly only included those who lived locally; however it was likely that most interventions involving face-to-face therapy were implicitly limited to those who lived reasonably close to the treatment centre.

Just under half of the studies (n = 12, 46.2%) explicitly targeted injured people with acute distress or partial/full PTSD criteria. Fourteen (53.8%) studies excluded people with a prior mental health condition or suicidality/intentional injury, 15 (57.7%) excluded those with pre-existing or acquired brain injury, disease or cognitive impairment, and eight (30.8%) excluded those with drug or alcohol problems.

Interventions

Study and intervention design

All but one study adopted an RCT design, with one study implementing a case series design. Shalev et al. (2012) compared three treatment groups (cognitive therapy, prolonged exposure and pharmacotherapy) with two control groups (waitlist control and placebo medication). All other studies compared a single intervention to a waitlist, control or usual

care group. For most participants, interventions were initiated between 12 hours and 10 weeks postinjury, and the majority (20 studies) were initiated within one month of injury. The intensity of psychological interventions varied from a single exposure to 12 weekly cognitive therapy sessions with three monthly booster sessions according to individual need.

One paper (Bryant, Moulds, & Nixon, 2003b) combined the cohorts from two previous studies (Bryant, Harvey, Dang, Sackville, & Basten, 1998; Bryant, Sackville, Dang, Moulds, & Guthrie, 1999), Des Groseilliers et al. (2013) reported a three-year follow-up on a previously reported study (Brunet, Des Groseilliers, Cordova, & Ruzek, 2013), and Shalev et al. (2016) reported a three-year follow-up on a previous study that included depression data not previously reported (Shalev et al., 2012).

The setting in which interventions were trialled was not explicitly described in the majority of studies, especially those delivering CBT and prolonged exposure. In several interventions, CBT and/or coordinated care were initiated in the inpatient setting (Tecic et al., 2011; Zatzick et al., 2013; Zatzick et al., 2015; Zatzick et al., 2004), and the trials by Zatzick et al. involved collaborative care with healthcare providers in the primary care and community rehabilitation settings. Most interventions were delivered by a clinical psychologist, social worker or nurse who was trained and supervised to deliver the intervention. Only a handful of studies specifically used research staff to deliver the interventions, with most appearing to use providers working in a clinical setting.

There were four key intervention designs: cognitive and behavioural interventions (13 studies); prolonged exposure or EMD interventions (4 studies); multidisciplinary or collaborative care interventions (6 studies); and education or information-based interventions (3 studies). Further descriptions of the interventions, including timing and modality, are provided in Table 1.

The most common interventions had a CBT framework, including CBT (n = 9),

Cognitive Therapy (n = 2) and Interpersonal Counselling (n = 1). These were all delivered face-to-face and individually, except for one study that included the participant's significant other (Brunet et al., 2013), one study that provided CBT in a self-directed manner purely via electronic and printed resources using the internet or a computer (Mouthaan et al., 2013), and three studies that provided printed resources and self-help information, with telephone support as needed (Bell et al., 2008; Bugg, Turpin, Mason, & Scholes, 2009; Scholes, Turpin, & Mason, 2007). CBT interventions typically involved a combination of psychoeducation, muscle relaxation, cognitive restructuring and prolonged exposure (described in greater detail below), and often included structured homework activities. In one intervention, the program involved a flexible modular CBT program that allowed clinicians to target individual symptom profiles (i.e., anxiety, depression and PTSD; O'Donnell et al., 2012). Several CBT-based interventions involved stepped care to ensure that people with persistent, recurrent and/or clinically elevated symptoms received higher-intensity care, which was monitored using a decision support tool (Zatzick et al., 2015). Two studies delivered cognitive therapy interventions (Ehlers et al., 2003; Shalev et al., 2012). Ehlers et al. (2003) developed a cognitive therapy program as a tailored form of CBT for PTSD to modify excessively negative appraisals, correct autobiographical memory disturbances (e.g., related to the trauma), and extinguish problematic behavioural and cognitive strategies.

Three studies specifically evaluated prolonged exposure that was delivered as either a stand-alone treatment, or together with anxiety. Prolonged or graded exposure therapy aims to achieve fear extinction through repeatedly confronting memories and reminders of a traumatic event (Foa, 2011). Over time, prolonged exposure enables one to habituate to potentially threatening stimuli, and normalises emotional processing. This intervention is based on the notion that PTSD arises partly due to a failure to extinguish fear after trauma. Several of the CBT interventions that focused on PTSD comprised components of exposure and habituation

therapy (e.g., Bisson et al., 2004; Bryant et al., 1998; Tecic et al., 2011; Wu, Li, & Cho, 2014). One study evaluated psychological debriefing (Conlon, Fahy, & Conroy, 1999), and one used EMD, which involves bringing to mind an image of a traumatic event while tracking sensory stimuli across left/right space (e.g., the therapist's index finger, or auditory or tactile stimuli) (Kutz, Resnik, & Dekel, 2008).

Five studies involved multidisciplinary and collaborative care interventions that comprised elements of case management, allied health involvement, pharmacotherapy and psychotherapy including components of CBT and motivational interviewing. One of these studies examined the involvement of an in-reach rehabilitation team during the acute phase (Wu et al., 2017). The aim was to supplement ward-based therapy by providing physiotherapy and occupational therapy. The teams also encouraged multidisciplinary assessments in a variety of areas, including mobility, mood and cognition, in a timely manner. Another study implemented a multidisciplinary outpatient follow-up program involving individual contacts and psychoeducational group sessions (Vikane et al., 2017).

Two interventions involved multidisciplinary and collaborative care (e.g., across in- and out-patient settings; Zatzick et al., 2013; Zatzick et al., 2015). These interventions were delivered using tailored, individualised approaches using case managers trained to use motivational interviewing and decision support tools. Changes in treatment were decided through case conferencing. Motivational interviewing is a style of behaviour change counselling that was developed for clients with high-risk behaviours (e.g., substance abuse), and aims to coach the client towards behaviour change and self-management. The collaborative care interventions by Zatzick and colleagues included motivational interviewing for those who were admitted with a positive blood alcohol reading to address risky behaviours associated with alcohol use (Zatzick et al., 2013; Zatzick et al., 2015). One other intervention involved motivational interviewing-based telephone counselling (Bell et al.,

2008).

Behavioural Activation Psychotherapy was delivered in some of the CBT interventions (Zatzick et al., 2013; Zatzick et al., 2015), which involved pleasant activity scheduling, targeting sadness related to loss of pre-injury function, and avoidance of postinjury anxiety. Zatzick et al. (2015) also provided participants with a laptop computer and smart-phone application that contained trauma recovery websites and resource recommendations. Participants were encouraged to use the computer for personal use.

Participant recruitment and adherence

Studies employing risk stratification and stepped care had very high recruitment rates, randomizing 871 (73.3%) of 1,221 potential participants who were screened and identified to be eligible, and retaining 766 (87.9%) of those participants to intervention completion. Moreover, completion rates were very high and similar for both the intervention (340/396, 85.9%) and control (426/475, 89.7%) groups. However, within the risk stratification studies, only about 50% of people recruited expressed interest in receiving the full psychological treatment and/or showed adequate readiness for CBT (O'Donnell et al., 2012; Zatzick et al., 2015). Moreover, compliance with psychological therapies and medications was reported to be poor (e.g., of only 35 (58.3%) participants who showed CBT readiness of whom 23.3% received one or more CBT session and two received all five sessions, and of 44 (77.3%) who showed medication readiness only 45% adhered to their prescribed medications; Zatzick et al., 2015). In another study only 25 (26.9%) participants showed adequate CBT readiness, of whom only nine (36.0%) received four or more CBT sessions (Zatzick et al., 2013).

While recruitment rates were not available for several studies that comprised standard intervention delivery methods (i.e., without risk stratification or stepped care), the reach was clearly poorer in standard interventions than in studies using risk stratification. For standard interventions only 2,215 (38.1%) of 5,810 eligible persons were recruited and randomized, or

whom only 782 (72.5%) participants completed the intervention and 946 (83.3%) participants completed the control condition, see Figure A4. For standard CBT interventions, 1,146 (40.1%) of 2,860 people who were eligible in 10 studies were randomized to the intervention (n = 516) and control (n = 594) groups, of whom 395 (71.6%) participants completed the intervention, and 516 (86.9%) completed the control condition. For standard prolonged exposure interventions, 293 (43.6%) of 672 eligible participants were recruited and randomized to the intervention (n = 132) and control (n = 161) groups, of whom 104 (78.8%) completed the intervention and 147 (91.3%) completed the control condition. For the education interventions, 798 (30.8%) out of 2,588 potential participants were recruited and randomized to the intervention (n = 387) and control (n = 411) groups, of whom 255 (65.9%) completed the intervention and 297 (72.3%) completed the control condition.

Altogether, people who were less likely to enrol or to drop out after commencement were male, younger, sustained intentional injury (e.g. assault), had a more severe injury (e.g., a longer stay in ICU) and reported more comorbidities (O'Donnell et al., 2012; Scholes et al., 2007; Tecic et al., 2011; Zatzick et al., 2004).

Resources required to receive the interventions

Three types of resources were identified to be necessary for participation in most interventions: literacy, technology, and geographic proximity or travel. While the nature of homework activities was not described sufficiently in most studies, we anticipate that the face-to-face CBT, prolonged exposure, collaborative care and education interventions require a minimum of primary school level literacy to be accessible and effective. Seven interventions required participants to have a telephone, three studies required access to an audio player for exposure-related homework, and two required access to a computer, smart phone and the internet. The location of the setting in which the interventions were conducted was not explicitly disclosed in most studies, however it is likely that, at a minimum, the face-

to-face interventions required participants to be in close proximity to, or be able to travel to, a psychology or outpatient clinic (22 studies). One study noted that geographical distance was a barrier for potential participants who had been admitted to a major trauma service at a metropolitan hospital but resided outside of metropolitan areas (O'Donnell et al., 2012). Finally, interventions that included pharmacological treatments would require (a) absence of contraindications and/or tolerance for the medication, and (b) willingness and capacity to purchase the medications.

Outcomes

Each study examined between one (18 studies) and four (one study) primary outcomes. The timing of outcome assessments ranged from one month to four years postinjury. In some studies, follow-up periods were specified relative to the time since commencing or completing the treatment, and not time postinjury. PTSD symptoms or diagnosis were reported as primary outcomes in 21 studies, and secondary outcomes in seven studies. Depression symptoms or diagnoses were primary outcomes in seven studies, and secondary outcomes in 14 studies. Anxiety symptoms or diagnoses were primary outcomes in six studies, and secondary outcomes in 11 studies. While the paper by Bryant et al. (2003b) followed up participants from two previous studies (Bryant et al., 1998; Bryant et al., 1999) that had measured PTSD, depression and anxiety symptoms, the four year follow-up paper only reported on PTSD symptoms. Moreover, while Shalev et al. (2016) reported a three year follow up from the previous paper (Shalev et al., 2012), it reported depression symptoms that had not been described in the first paper.

The most common tool used to measure PTSD symptoms was the Clinician-Administered PTSD Scale (CAPS; Blake et al., 1995), followed by the Impact of Event Scale (IES; Horowitz, Wilner, & Alvarez, 1979) or IES -Revised (IES-R; Weiss & Marmar, 1997) and the PTSD Checklist-Civilian Version (PCL-C; Weathers & Ford, 1996). Other tools

included the Posttraumatic Diagnostic Scale (PDS; Foa, 1995), the PTSD Symptom Scale Interview (PSS-I; Foa, Riggs, Dancu, & Rothbaum, 1993), the PTSD Symptom Scale-Self Report Version (PSS-SR; Foa, Cashman, Jaycox, & Perry, 1997), and the Primary Care Post-Traumatic Stress Disorder screening (Ebell, 2007). A composite measure of PTSD symptoms was used by Bell et al. (2008), based on the Head Injury Symptom Checklist (McLean, Dikmen, & Temkin, 1993) that also took into account any functional areas that were affected by head injury symptoms.

The Beck Depression Inventory (BDI; Beck, Ward, Mendelson, Mock, & Erbaugh, 1961) was most commonly used to measure depressive symptoms, followed by the Hospital Anxiety and Depression Scale Depression Subscale (HADS-D; Zigmond & Snaith, 1983), Patient Health Questionnaire-9 item Depression Screen (PHQ-9; Kroenke, Spitzer, & Williams, 2001), the Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996), the Center for Epidemiological Studies Depression Scale (CES-D; Radloff, 1977) and the Depression Anxiety Stress Scale 21 (DASS: Lovibond & Lovibond, 1995)

Tools used to measure anxiety symptoms included the Hospital Anxiety and Depression Scale Anxiety subscale (HADS-A; Zigmond & Snaith, 1983), the State-Trait Anxiety Inventory (STAI; Spielberger, Gorsuch, Lushene, Vagg, & Jacobs, 1983), the Beck Anxiety Inventory (BAI; Beck & Steer, 1993) and the Depression Anxiety Stress Scale 21 (DASS: Lovibond & Lovibond, 1995)

Risk of bias assessment

Risk of bias judgements for each paper are summarised in Table 2. Seven papers (24%) were considered to have low risk of bias, eleven (38%) had moderate risk of bias and 11 (38%) had high risk of bias. Poor selection methods, lack of adjustment for confounding factors and inadequate analysis were the main sources of bias, see Figure 2. While inadequate blinding of personnel was a key source of bias, we acknowledge that it is rarely possible to fully blind

participants and clinicians to active psychological interventions.

Narrative synthesis

Cognitive and behavioural interventions

Interventions delivering CBT had small (Bisson et al., 2004), large (Bryant et al., 1998; Bryant, Moulds, Guthrie, & Nixon, 2003a; Bryant et al., 2003b) and very large (Bryant et al., 1998; Bryant et al., 2003a) effects on PTSD symptoms at six months, 13 months and four years postinjury, see specific effect sizes in Table 3. One CBT intervention also had large effects on anxiety and depression at 6 months postinjury (Bryant et al., 1998). It should be noted that three of these studies were considered to have a high risk of bias due to inadequate handling of missing data and patient attrition (Bryant et al., 1998; Bryant et al., 2003a; Bryant et al., 2003b).

A two session dyadic intervention comprising motivational interviewing and psychoeducation had small (Brunet et al., 2013) and medium (Des Groseilliers et al., 2013) effects on PTSD symptoms at 3 months and 2 years postinjury, respectively. Both of these papers, reporting on the same study, had a moderate risk of bias with analyses failing to account for attrition and missing data. Specifically, in the two year follow up study by Des Groseilliers et al. (2013), the last available observation of participants who were lost to follow up were carried forward. This may have favoured the intervention group, particularly given that the meta-analysis showed that longer-term effects of psychological treatments were small. Pirente (2007) found no effect of CBT on depression or anxiety symptoms but reported an effect of time, whereby both the intervention and control groups improved at 12 months postinjury. This study was considered to have a high risk of bias due to inadequate reporting of blinding procedures and missing data, failure to conduct intention to treat analyses or to accommodate group differences in confounding characteristics at baseline. For injured persons with mTBI, provision of CBT in addition to a concussion clinic had no impact on

anxiety or depression (Silverberg et al., 2013).

Providing early CBT at a personalised frequency (vs early short term CBT only) had greater effects on reducing the likelihood of developing a psychological condition (Tecic et al., 2011). However, the results of this study must be interpreted with caution, due to high risk of bias from high attrition, and unclear reporting of how the data were coded and analysed, especially the calculation of PTSD symptoms. While brief CBT, comprising four sessions, had large effects on depression and anxiety at 6 months postinjury (Wu et al., 2014) this study was underpowered and participants were excluded from analyses if they had used other interventions rather than analysing the data using an intention-to-treat approach.

Interpersonal counselling (Holmes et al., 2007) and CBT delivered online (Mouthaan et al., 2013) had no effects on depression, anxiety or PTSD symptoms. A single psychological debriefing session also failed to have a significant effect on PTSD symptoms at 3 months postinjury (Conlon et al., 1999). A stepped care model (comprising flexible, modular CBT with structured homework activities) had medium and large effects on PTSD at 6 and 12 months post injury, respectively (O'Donnell et al., 2012). This intervention also had effects on anxiety that were large at 6 months, and medium at 12 months, and large to very large effects on depression at 6 and 12 months, respectively. It is worth noting, however, that this study had a moderate risk of bias due to protocol deviation, lack of participant blinding and inadequate treatment of missing data and confounders.

One of the studies that evaluated cognitive therapy found a large effect on PTSD symptoms at 5 months, and a small effect at 9 months postinjury (Shalev et al., 2012). Similarly, Ehlers (2003) found that cognitive therapy had large to very large effects on PTSD and anxiety symptoms at 3 months and 9 months post-treatment, but this did not differ when compared with self-help or repeated clinical assessment without therapeutic input (Ehlers et al., 2003). Cognitive therapy had large effects on depression symptoms at 3 and 9 months

compared to self-help. When compared with repeated clinical assessments, cognitive therapy had large effects at 3 months, and small to medium effects at 9 months.

Prolonged exposure and EMD interventions

Three studies evaluated prolonged exposure interventions, and all had significant effects on PTSD. One intervention had large and small effects on PTSD symptoms at 5 and 9 months, respectively (Shalev et al., 2012), and a medium effect on depression symptoms at 5 months. These effects were not sustained at three years post-intervention (Shalev et al., 2016). Another study had large to very large effects on PTSD and anxiety at 6 months (Bryant et al., 1999), and the magnitude of the effects was similar regardless of whether the prolonged exposure was delivered alone or combined with anxiety management. However, the study by Bryant et al. (1999) had a high risk of bias due to insufficient explanation of the intervention, recruitment bias and inappropriate analysis. Rothbaum et al. (2012) reported small effects of prolonged exposure on PTSD outcomes at 1 and 3 months postinjury, and on depression outcomes at 1 month.

The study by Kutz et al. (2008) evaluated the effectiveness of EMD, and found that 59% of participants experienced immediate relief from EMD and 24% experienced substantial relief at 6 months posttreatment. This study specifically recruited people whose acute stress symptoms had not subsided after several days, and the study was considered to have a high risk of bias due to the recruitment approach, lack of randomisation and participant blinding, and the reporting of weak and incomplete analyses.

Multidisciplinary/collaborative care interventions

Stepped and collaborative care interventions involving case management, and increased clinician involvement as needed, delivered a combination of brief motivational interviewing, evidence-based pharmacotherapy and psychotherapy. The study by Zatzick et al. (2004) found collaborative care brought about a significant but small reduction in the likelihood of

having PTSD symptoms at 12 months postinjury. Likewise, Zatzick et al. (2013) found small effects on PTSD symptoms 6, 9 and 12 months postinjury, and a small effect on depression at 6 months. The same stepped collaborative care model with the addition of information technology enhanced tools and interventions had small effects on PTSD symptoms at 3 and 6 months postinjury, and no effects on depression (Zatzick et al., 2015). Although the first intervention by Zatzick et al. (2001) had large and medium effects on PSTD and depression symptoms, respectively, at 1 month postinjury, the group differences favoured the control group at 4 months. This study was a pilot study, and was deemed to have a moderate risk of bias due to small sample size and lack of detail on how missing data were handled. The intervention by Vikane et al. (2017) had no significant effects on anxiety or depression 12 months postinjury. Similarly, the intervention by Wu et al. (2017) had no significant effects on depression or anxiety, or posttraumatic stress. However, a time by group interaction was trending towards significance for depression and anxiety, whereby the intervention group demonstrated a trend towards improvement in the period from discharge to follow-up, whereas the control group may have worsened over this time.

Education or information-based interventions

Self-help interventions in the form of a CBT-based booklet, information on traumatic stress and recovery strategies or a writing exercise did not influence PTSD, anxiety or depression outcomes (Bugg et al., 2009; Scholes et al., 2007). An intervention that provided information and reassurance via brief telephone counselling had a small effect on posttraumatic symptoms in patients with mTBI (Bell et al., 2008). This study was deemed to have a moderate risk of bias with selective reporting.

Intervention timing and effect sizes

Overall the majority of the studies that had medium to large effects on PTSD, depression and anxiety symptoms were implemented within the first four weeks postinjury, see Figure A5.

Of the 23 interventions targeting PTSD, seven studies had medium to very large effects. Six of those interventions were implemented within the first four weeks postinjury, and comprised CBT (Bryant et al., 1998; Bryant et al., 2003a; Bryant et al., 2003b; O'Donnell et al., 2012) and prolonged exposure treatment paradigms (Bryant et al., 1999; Shalev et al., 2012). Nineteen studies measured depression as an outcome, and six interventions that had medium to very large effects. Five of those studies were implemented within the first four weeks postinjury and comprised CBT (Bryant et al., 1998; O'Donnell et al., 2012; Wu et al., 2014), prolonged exposure (Shalev et al., 2012) and collaborative care (Zatzick et al., 2001). Fourteen studies measured anxiety as an outcome, and four studies had medium to very large effects. Each of those interventions were implemented within the first four weeks postinjury, and comprised CBT (Bryant et al., 1998; O'Donnell et al., 2012; Wu et al., 2014), prolonged exposure (Bryant et al., 1999) or collaborative care (Zatzick et al., 2001).

Grade of evidence

Considering the findings from all studies together, evidence is considered *good* regarding the effectiveness of multidisciplinary and collaborative care, *satisfactory* to *good* for prolonged exposure, *satisfactory* for cognitive and behavioural therapies, and *poor* for education-focused interventions, see Table 4. There was *good* consistency and *good* clinical impacts on PTSD symptoms; however, consistency and clinical impacts were generally *poor* (or not measured) for depression and anxiety symptoms.

Meta-analyses

Posttraumatic Stress Disorder (PTSD)

The pooled results revealed significant heterogeneity at 0-3 months ($\chi^2 = 14.71$, $p = 0.04$; $I^2 = 52\%$), 3-6 months ($\chi^2 = 20.86$, $p = 0.008$; $I^2 = 62\%$) and 6-12 months post-intervention ($\chi^2 = 22.72$, $p < 0.001$; $I^2 = 82\%$). There were significant effects of early interventions on PTSD symptoms at 0-3 months (eight studies, N = 1033; SMD = -0.32, 95% CI: -0.51, -0.13, $p =$

0.001), 3-6 months (8 studies, N = 954; SMD= -0.39, 95% CI: -0.63, -0.15, p = 0.001), and 6-12 months post-intervention (five studies, N = 700; SMD= -0.49, 95% CI: -0.90, -0.08, p = 0.02), see Figure 3. The pooled effects were small up to 3 months and 6 months post-intervention , and medium at 6-12 months post-intervention.

At 0-3 months post-intervention, significant effects were specifically observed for the multidisciplinary and collaborative care interventions (SMD = -0.26, 95% CI: -0.47, -0.05, p = 0.01), but not for cognitive and behavioural (95% CI: -1.16, 0.00), prolonged exposure (95% CI: -0.59, 0.08) or education-based interventions (95% CI: -0.38, 0.33). By 3-6 months, significant effects were specifically observed for cognitive and behavioural (SMD = -0.44, 95% CI: -0.85, -0.04, p = 0.03) and prolonged exposure interventions (SMD = -0.83, 95% CI: -1.18, -0.47, p < 0.001), but not for multidisciplinary and collaborative care (95% CI: -0.70, 0.08) or education-based interventions (95% CI: -0.39, 0.40). By 6-12 months, significant effects were only evident for multidisciplinary and collaborative care interventions (SMD = -0.30, 95% CI: -0.58, -0.03, p = 0.03), and not for cognitive and behavioural (95% CI: -1.81, 0.20) or prolonged exposure interventions (95% CI: -0.51, 0.24).

Depression

The pooled results revealed significant heterogeneity at 0-3 months (χ^2 = 18.30, p = 0.01; I^2= 62%), 3-6 months (χ^2 = 31.50, p < 0.001; I^2 = 81%) and 6-12 months (χ^2 = 25.40, p < 0.001; I^2 =88%). There were significant effects on depression symptoms at 0-3 months (eight studies, N = 991; SMD = -0.34, 95% CI: -0.56, -0.11, p = 0.003), and 6-12 months post-intervention (four studies, N = 591; SMD = -0.60, 95% CI: -1.16, -0.04, p = 0.04), but not at 3-6 months (seven studies, N = 819; SMD= -0.25, 95% CI: -0.61, 0.11, p = 0.17), see Figure 4. The effects were medium to large at 3-6 months post-intervention, but only small to medium when measured at 0-3 and 6-12 months post-intervention.

Effects at 0-3 months were specifically observed for prolonged exposure interventions

(SMD= -0.46, 95% CI: -0.80, -0.12, p = 0.008), and not for cognitive and behavioural (95% CI: -1.52, 0.12), multidisciplinary and collaborative care (95% CI: -0.42, -0.00) or education-based interventions (95% CI: -0.36, 0.36). While the pooled results at 6-12 months were significant, there were no significant effects for specific intervention types, highlighting that effects were very small.

Anxiety

Heterogeneity was notably higher for the anxiety outcomes than the PTSD and depression symptom analyses, ranging from 74-89% (0-3 months: χ^2 = 11.90, p = 0.008; I^2 = 75%; 3-6 months: χ^2 = 11.71, p = 0.008; I^2 = 74%; 6-12 months; χ^2 =18.69, p < 0.001; I^2 =89%). Early interventions had no significant effect on anxiety outcomes at 0-3 months (four studies, N = 497; SMD = -0.24, 95% CI: -0.67, 0.19, p = 0.27), 3-6 months (four studies, N = 465; SMD= -0.39, 95% CI: -0.85, 0.07, p = 0.09) or 6-12 months (three studies, N = 384; SMD = -0.58, 95% CI: -1.47, 0.32, p = 0.21), see Figure 5.

Clinically meaningful effects (excluding studies with high risk of bias)

Given typical variability in PTSD, depression and anxiety symptoms in the first 12 months after traumatic injury, and the magnitude of change considered to be clinically meaningful on the PTSD checklist and the HADS, we examined whether the pooled effects for each intervention type achieved greater effects in the intervention group compared with the control group, see Figure 6.

The reductions in symptoms for the intervention group compared with the control group were clinically meaningful (i.e., >10 point change on the PTSD checklist) for cognitive and behavioural interventions at 6-12 months post-treatment only. None of the pooled effects for the other intervention types showed clinically meaningful reductions in PTSD symptoms; however, seven of the 11 studies examining PTSD symptoms reported that participants in the intervention groups had, on average, clinically meaningful reductions in PTSD symptom

severity at 0-3 months (Brunet et al., 2013; Ehlers et al., 2003; Rothbaum et al., 2012); 3-6 months (Bryant et al., 2003a; O'Donnell et al., 2012; Shalev et al., 2012; Zatzick et al., 2013) and 6-12 months (Ehlers et al., 2003; O'Donnell et al., 2012; Shalev et al., 2012; Zatzick et al., 2013), see Table A4. However, the control groups also had clinically meaningful PTSD symptom reductions in two studies (Brunet et al., 2013; Shalev et al., 2012). This supports the fact that, to varying degrees, PTSD symptoms may attenuate regardless of intervention postinjury.

The pooled effects showed clinically meaningful reductions in depression symptoms (i.e., >1.50 point change on the HADS-depression subscale) for the cognitive and behavioural (all follow-up time-points), and prolonged exposure interventions (at 0-3 months post-intervention only, although this was the only time at which depression was measured in a prolonged exposure study). Participants in the intervention groups also had, on average, clinically meaningful depression symptom reductions four of the 10 studies that measured depression at 0-3 month (Ehlers et al., 2003; Rothbaum et al., 2012), 3-6 month (O'Donnell et al., 2012; Zatzick et al., 2013) and 6-12 months (Ehlers et al., 2003; O'Donnell et al., 2012). The pooled effects showed clinically meaningful reductions in anxiety symptoms for the intervention group (i.e., >1.50 point change on the HADS-Anxiety subscale) for the cognitive and behavioural interventions only (3-6 month and 6-12 month post-intervention). Participants in the intervention groups also had clinically meaningful anxiety reductions in two of the six studies that measured anxiety at 0-3 month (Ehlers et al., 2003); 3-6 month (O'Donnell et al., 2012) and 6-12 month follow ups (Ehlers et al., 2003; O'Donnell et al., 2012).

The pooled effects did not show clinically meaningful reductions in symptoms for the multidisciplinary and coordinated care or education-based; however, some caution should be observed given the small number of studies.

Estimated population impact

Using annual Australian injury hospitalisation admissions (N = 382,023) and the prevalence of PTSD (9.7%), depression (17.3%) and anxiety (9.0%) after hospitalised injury, Figure 7 shows that the population impact of risk stratified psychological interventions far exceeds that of standard methods for delivering cognitive, behavioural or prolonged exposure interventions. First, the risk stratified interventions demonstrate markedly higher potential impact through higher recruitment rates (85.9% versus 67.1%) and intervention completion rates (85.9%versus 76.1%) resulting in 73.7% of those at risk being likely to complete a risk stratified intervention compared with 51.1% of those enrolled in standard psychological interventions. Moreover, people receiving risk stratified interventions would be expected to consistently achieve small to medium symptom reductions that are clinically meaningful for depression and anxiety, and that are similar in magnitude to the effects achieved in standard interventions. Both stratified and standard interventions showed only small to medium effects on PTSD symptoms that were not clinically meaningful.

Discussion

This systematic review and meta-analysis examined the efficacy and effectiveness of early interventions delivered within the first three months after unintentional traumatic injury (e.g., musculoskeletal, soft tissue, orthopaedic or mild traumatic brain injury), in preventing or reducing the incidence and severity of PTSD, depression and anxiety after injury. Twenty-six studies described in 29 papers were identified, and 12 were included in meta-analyses. Considering the results from all studies, interventions implemented within the first four weeks comprising CBT, prolonged exposure, and collaborative care had the largest effects on PTSD, depression and anxiety symptoms. The collaborative care interventions had significant but small effects on PTSD symptoms, and limited effects on depression symptoms. Only one study examined EMD, which reported relief from acute stress symptoms for more than half of

those who received the treatment. Interventions focused on education had small effects on PTSD symptoms, and no effects on anxiety and depression. When considering treatment reach, effectiveness, implementation and adoption it was apparent that interventions comprising risk stratified, stepped and/or collaborative care had much greater potential for population impact than standard CBT or prolonged exposure interventions. These findings are consistent with a previous empirical comparison of one collaborative care and one CBT-based intervention that showed that collaborative care had a 9.5-fold greater reduction in PTSD, despite having smaller effect sizes (Zatzick, Koepsell, & Rivara, 2009).

The meta-analyses revealed significant effects of early intervention on PTSD symptoms over the first 12 months post-treatment, weak effects on depression symptoms, and no effects on anxiety symptoms. Specifically, the cognitive and behavioural interventions had small to medium effects on PTSD symptoms at 0-3, 3-6 and 6-12 months post-intervention, with *clinically* significant effects at 6-12 months post-intervention only. Prolonged exposure interventions had large effects that approached clinical significance on PTSD symptoms 3-6 months post-intervention, and medium effects on depression symptoms that were clinically significant at 0-3 months post-intervention only. Multidisciplinary and collaborative care interventions had small effects on PTSD symptoms at 0-3 months and 6-12 months, but not at 3-6 months where usual care had a larger effect than collaborative care in one study (Zatzick et al., 2001).

With respect to the overall grade of evidence, there was satisfactory support for the effectiveness of CBT-based interventions on PTSD, depression and anxiety, but some inconsistency with some studies showing minimal and very small clinical impacts, and others showing very large clinical impacts. Prolonged exposure showed good evidence of effects on PTSD symptoms with only small levels of inconsistency, good evidence but high inconsistency of clinical impacts on depression symptoms, and poor evidence to support

effects on anxiety symptoms. There is a good level of evidence to support collaborative care interventions for PTSD and depression, but no evidence to support education-based interventions.

Overall, most treatments for PTSD were effective for PTSD symptoms, but had inconsistent effects on anxiety and depression symptoms. While this may suggest that symptom-specific treatment may be required to address anxiety and depression (Bisson et al., 2004), it was apparent that when treatment occurred within a broad cognitive framework depression symptoms were reduced (e.g., Bryant et al., 1998; Ehlers et al., 2003; O'Donnell et al., 2012). It is not known from the present studies whether immediate treatment effects on depression are enduring, or whether ongoing treatment would be required.

While the provision of information and resources about psychological conditions after injury were considered helpful by those who could and did read them, these interventions alone did not improve PTSD symptoms (Scholes et al., 2007). While providing educational resources to 'at risk' patients may not directly impact on psychological outcomes, it may nonetheless provide an opportunity for health providers to discuss their clients' psychological expectations after injury and increase help-seeking or treatment engagement at a later date (O'Donnell, Bryant, Creamer, & Carty, 2008). Brief and/or stand-alone treatments such as debriefing (Conlon et al., 1999), brief supportive counselling (Bryant et al., 1998), and interventions conducted in the absence of clinical engagement (e.g., writing about the trauma) (Bugg et al., 2009) or via an online portal (Mouthaan et al., 2013), had little effect on psychological symptoms. Brief CBT was only effective if patients had the opportunity to attend follow up sessions (Tecic et al., 2011), and had little impact on PTSD symptoms (Wu et al., 2014).

Interventions delivered within the first four weeks post-intervention had the largest effects. It was notable, however, that many studies failed to bring about clinically significant

effects. This may be due to the fact that the vast majority of patients show excellent resilience and recover well after traumatic injury (Schnyder, Moergeli, Klaghofer, & Buddeberg, 2001), even after a diagnosis with acute distress disorder (Bryant, 2011).

Enhancing the population impact of early intervention

Interventions comprising stepped or collaborative care (i.e., tailored to patient risks and needs), and standard clinical methods showed fairly similar levels of effectiveness (with effects on PTSD being slightly better in standard care, but effects on anxiety slightly better in stepped care). However, the stepped care interventions were overall likely to bring about larger population impacts than standard interventions as they: (a) reached approximately 1.5 the number of patients at risk of poor psychological recovery from traumatic injury, with higher recruitment and intervention completion rates; (b) were acceptable to those who are normally excluded explicitly or implicitly from interventions (e.g., older patients, those with drug and alcohol problems, language barriers, remoteness issues); (c) have broader demonstration of implementation and adoption in clinical settings, including trauma system, outpatients and community health and rehabilitation providers; and (d) bring about significant symptom reduction compared with usual care that is clinically significant for anxiety and depression symptoms. Stepped care interventions therefore show superior acceptability for the trauma population, while maintaining significant and meaningful effectiveness, and thereby demonstrated good evidence for likely adoption and implementation of these interventions.

Most standard interventions, however, represented only a subset of the trauma population, and were largely limited to those who were middle aged, female (i.e., 43.3% were females compared with 31.6% of those with hospitalised injuries; Pointer, 2015), proficient in the language of the country of residence, and were not suitable for people with comorbid mental health, drug and alcohol problems, or conditions involving impaired cognition. These standard interventions may, therefore, be considered to be primarily valid, available,

acceptable and effective for those who are young adults or middle aged, female, have proficiency in the native language, live near metropolitan psychology providers, and do not have significant pre-existing mental health (including drug and alcohol) comorbidities or cognitive impairments.

As help seeking and referral to psychological services postinjury most often occurs once chronicity is established (Bolduc et al., 2015) effective and proactive implementation of *early* intervention requires specific strategies to facilitate screening, referral and patient engagement. Given that the largest effects were found in studies commencing within four weeks post-injury, screening for vulnerability should ideally occur within the first two to four weeks postinjury, with continued monitoring to identify those who have persistent or emerging symptoms or distress that may require intervention (for screening recommendations see O'Donnell et al., 2008). It is important to note, however, that high levels of distress immediately after injury is common, and can be a normal and adaptive reaction to the trauma that will dissipate with time. Indeed, most of the studies in this review found a reduction in distress-related symptoms over time, regardless of whether an intervention was received. Therefore, it is important that screening focuses on identifying emerging or persistent symptoms to enable provision of interventions that are flexible in their delivery method, tailored to risk factors, and stepped up over time in accordance with treatment readiness.

A range of predisposing (e.g. age, sex, residential location), enabling (e.g. access to insurance and availability of transport) and need (e.g. PTSD symptom severity, preference to manage symptoms independently) factors were found to impact on recruitment, compliance and efficacy of treatment across studies (Andersen, 1995). For instance, people with lower baseline anxiety and depression levels responded better to self-help CBT (Wu et al., 2014). Moreover, women were more likely to engage in psychological therapies, be compliant with recommended interventions, and to have superior outcomes than men (Zatzick et al., 2001).

These findings were consistent with the conclusions from a recent systematic review of the barriers to engaging with mental health service utilization in adult trauma survivors (Kantor, Knefel, & Lueger-Schuster, 2017). Proactive implementation of early psychological interventions therefore requires careful consideration of these characteristics in order to achieve maximum therapeutic impacts postinjury. Furthermore, for the delivery of CBT-based psychological treatments, assessment of readiness for therapy (e.g., evaluating level of engagement and clinical, crisis and logistical barriers; Trusz, Wagner, Russo, Love, & Zatzick, 2011) should be undertaken to ensure that barriers to therapy engagement are identified, and adequately addressed to maximise treatment engagement and therapeutic impact. A case coordinator may then be beneficial to facilitate problem solving (e.g. supporting transport, or literacy issues), and increase patient readiness (e.g., through motivational interviewing). The four studies that included case coordination involved frequent in person and telephone-based outreach mechanisms by a clinician with masters or doctorate level training (Zatzick et al., 2013; Zatzick et al., 2015; Zatzick et al., 2004; Zatzick et al., 2001). The most intensive period of case coordination occurred in the first 4-6 months post injury, and the use of internet-based resources markedly reduced the intensity of case coordination while maintaining the same level of treatment effects. The case coordination approach has been found to increase engagement and adherence through addressing barriers to therapy.

Successful interventions tended to comprise between four and six sessions, with flexibility for additional support or interventions as required. All interventions were psychologist-led and those with the largest effects were delivered face-to-face by a single psychologist. Interventions that comprised collaborative care, stepped care and/or modular therapy ensured that fundamental recovery needs were met before stepping up to manage psychosocial risk factors. These models had the capacity to tailor the therapy to individual

participant characteristics, and ensured that participants were ready for more complex therapies. To facilitate the provision of targeted care throughout the first 12 months postinjury, it would be necessary to implement mechanisms that enable ongoing monitoring of emerging psychosocial risks and treatment needs over time. Zatzick, et al. (2015) trialled an intervention that incorporated a computerised decision support tool to facilitate client progress monitoring. This tool helped to facilitate real-time workflow through integrated screening and intervention recommendation procedures that assisted decision making to escalate intervention complexity and content. Case conferencing was then used to evaluate treatment-related decision-making. These proactive decision-making processes were integrated into the community-based model of care and case coordination.

Limitations and future directions

It is worth considering a number of limitations of this review when seeking to use the evidence to inform policy or practice change. First, the majority of studies included had moderate to high risk of bias. This is important given that several study designs disproportionately favoured the active intervention in their analysis and reporting of results. Therefore, there remains a need for more high quality interventions to determine the effect of early interventions on psychological conditions after injury. Second, many studies had insufficient follow-up periods, with several studies only assessing outcomes at one to four months post-treatment, which limits our capacity to determine the long-term impacts of early intervention. Third, while it is necessary to address the significant impacts of injury on pain, function and psychological wellbeing, very few interventions identified in this review concurrently targeted pain management, or evaluated the co-occurrences of pain and psychological symptoms. Given that pain and psychological conditions are highly comorbid (Edwards, Dworkin, Sullivan, Turk, & Wasan, 2016), with several theoretical models implicating shared vulnerability mechanisms for the development of persistent pain and PTSD

after injury (Fishbain et al., 2016), future interventions must take into consideration other potentially mechanistically related symptoms.

The generalisability of this review may be limited, given the review design. For instance, studies were only included if they treated psychological conditions secondary to traumatic injury and interventions for a primary psychological injury in the absence of physical injury were excluded. While interventions provided for primary psychological injury may be effective for those who have sustained a physical injury, and vice versa, the conclusions from this review may not generalise to those without physical injury. This review only included studies published in English, which may have limited several sources of evidence from culturally and linguistically diverse settings. Finally, while this review focused only on the effectiveness of early psychological interventions on mental health outcomes, it may be that some patients will benefit from other concurrent treatments. Further studies that use population sampling methods are required to enable the comparison of outcomes with those of the broader population, and to better understand the external validity and generalisability of early interventions for mental health postinjury (Kearns et al., 2012; Zatzick & Galea, 2007).

Conclusions

Given that approximately one in five people have a poor psychological trajectory up to six years postinjury (Bryant et al., 2015; Bryant et al., 2010), implementing systematic strategies for proactive delivery of early interventions may bring about marked population benefit through improved mental health postinjury. The findings from this review show strong support for the use of psychological treatments—including CBT, prolonged exposure, cognitive therapy—especially when the intervention comprises stepped or collaborative care. Although effects were generally smaller for the collaborative care interventions, the population reach, implementation and adoption potential of these models suggests that such interventions will

yield the greatest population impact.

Tables

Appendices

timing, using recommendations by Sawilowsky (2009).

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Table 1 Intervention study characteristics.

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
Cognitive and behavioural interventions							
Bisson et al. (2004)	Mixed physical; mixed (e.g. MVC, assault) (142, 75%); United Kingdom	RCT	IG: CBT (psycho-education, challenge cognitive distortions, image habituation training, with exposure components) CG: Usual care	T: 5w M: Individual face-to-face F: 4 x 1hr x weekly S: NR I: Research Psychologist	• Audio player • Literacy (written material provided) • Travel (NR)	13m	Primary (P): PTSD symptoms (IES) Secondary (S): Anxiety (HADS-A), depression (HADS-D), clinician-rated PTSD (CAPS)
Brunet et al. (2013) Des Groseilliers et al. (2013)	Mixed physical; mixed (MVC, work accident, leisure accident, physical assault) (74; 54%); Canada	RCT	IG: Dyadic CBT intervention with motivational interviewing CG: Waitlist	T: mean 26d (SD = 8.27) M: Face-to-face with patient and their significant other F: 2 x 75-90mins x fortnightly S: Hospital I: social worker or nurse trained &	• Metropolitan location • Significant other to attend therapy • Travel (NR)	3m 2y	P: PTSD symptoms (IES-R) S: PTSD diagnosis (CAPS)

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
				supervised by clinical psychologist			
Bryant et al. (1998)	Mixed; mixed (MVC or industrial accident) (24; 42%); New South Wales, Australia	RCT	IG: CBT with in vivo exposure CG: Supportive counselling	T: > 10d M: Individual face-to-face F:5 x 1.5hr x weekly S: NR I: clinical psychologist	• Literacy (diary of mood & problems) • Travel (NR)	6m	P: PTSD (IES), depression (BDI) and anxiety (STAI) symptoms S: None
Bryant et al. (2003a)	mTBI; mixed (MVC or nonsexual assault) (24; 33%); New South Wales, Australia	RCT	IG: CBT CG: Supportive counselling	T: < 2w M: Individual face-to-face F: 5 x 1.5h x weekly S: NR I: Clinical Psychologist	• Travel (NR) • Written homework (NR)	6m	P: PTSD symptoms (IES and CAPS) S: Depression (BDI), anxiety (BAI)
Bryant et al. (2003b) *	Mixed; mixed (MVC or nonsexual assault) (80; NR); New South Wales, Australia	RCT	IG: CBT CG: Supportive counselling	T: < 2w M: Individual face-to-face F: 5 x 1.5h x weekly S: NR I: 4 Clinical Psychologists	• Travel (NR) • Written homework (NR)	4y	P: PTSD symptoms (CAPS-II) S: None

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
Conlon et al. (1999)	Mixed physical; MVC (40; 48%); Ireland	RCT	IG: Psychological debriefing + information leaflet CG: Monitoring	T: 7d M: Individual, face-to-face F: 1 x 30min session S: NR I: NR	• Literacy (leaflet provided) • Travel (NR)	3m	P: PTSD symptoms (IES and CAPS-II) S: None
Ehlers et al. (2003)	Mixed physical; MVC (85; NS); England	RCT	IG: Cognitive therapy CG: Self-help booklet; Repeated assessment	T : ~ 7w M : Individual face-to-face F: 2-12 (mean 9) x 60-90mins x weekly, 0-3 booster sessions x monthly S: NR I: NR	• Literacy (leaflet & self-help booklet; symptom diary) • Telephone • Travel (NR)	9m	P: PTSD symptoms (PDS and CAPS) S:Anxiety (BAI), depression (BDI)
Holmes et al. (2007)	Mixed physical; mixed (MVC, falls or collisions, non-accidental injury) (90; 70%); Australia	RCT	IG: Interpersonal counselling CG: Treatment as usual	T: 2w (<3M) M: Individual, face-to-face F: Variable up to 3m S: NR I: Clinical Psychologists	• Travel (NR) • Homework (NR)	6m	P: Depression (BDI), anxiety (HADS-A), PTSD symptoms (PCL) S: None
Mouthaan et al. (2013)	Mixed physical; mixed (e.g.	RCT	IG: *Trauma TIPS*, 6-step self-guided internet-	T: 1w M: web-based, self-directed	• Internet • Literacy (written material	12m	P: PTSD symptoms

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
	MVC, work-related accident, fall, physical abuse) (300; 36%); Netherlands		based CBT CG: Usual care	F: variable over 1m S: Participant's home I: Research Group Psychotrauma	) • Audio/video material		(clinician) (CAPS) S: Anxiety (HADS-A), depression (HADS-D), self-reported PTSD (IES-R)
O'Donnell et al. (2012)	Mixed physical; mixed (MVC, falls, assaults, work-related accidents) (46; 61%); Australia	RCT	IG: Flexible modular CBT CG: Usual care	T : 4w M : Individual face-to-face F : 4 x 90mins then 6 x 90mins if elevated anxiety and depression S: Inner city clinic I: Clinical Psychologist	• Literacy (structured homework) • Travel	12m	P: PTSD (CAPS), anxiety (HADS-A) and depression (BDI) symptoms S: PTSD diagnosis (CAPS), major depression (MINI), anxiety disorder (MINI)
Pirente	Mixed	RCT	IG: Early	T: not	• Homew	12m	P: None

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
et al. (2007)	physical; mixed (MVC, cycling accident, collapse, pedestrian accident, industrial accident, sport/leisure accident) (130, 50%); Germany		onset CBT CG: Treatment as usual	stated; on hospital surgical ward M:Individual, face-to-face F: variable, up to 8 x 1hr x 3/weekly S: NR I: Research psychologists	ork (NR) • Travel (NR)		S: Depression (BDI), anxiety (STAI)
Silverberg et al. (2013)	Mild TBI; Mixed (MVC, fall, cycling accident, sporting accident) (28, 39%); Canada	RCT	IG: CBT+ treatment as usual CG: Treatment as usual	T: Up to 6w M: Individual, face-to-face F: 1 x 3h session + 50min x 1d x 6w S: concussion clinic I: Clinical Psychologists	• Travel • Literacy (written material, homework)	3m	P: None S: Anxiety (HADS-A), depression (HADS-D)
Tecic et al. (2011)	Mixed physical; MVC (113; 77%); Germany	RCT	IG: Short-term inpatient + Long-term tailored CBT (support/stabilise,	T: NS, inpatient M: Individual face-to-face F: up to 8 x 50mins	• Written homework (NR) • Travel	18m	P: Depression (BDI), anxiety (STAI) and

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
			counselling, cognitive reorganisation, imagination, exposure, relaxation) CG: Short-term CBT only	delivered inpatient setting + up to 6 x 50mins delivered in outpatient setting over 6 months S: outpatient psychology clinic I: Psychotherapists			PTSD (IES-R) symptoms S: None
Wu et al. (2014)	Mixed physical; MVC (53; 68%); China	RCT	IG: Brief CBT (psychoeducation, modify cognitive distortions, habituation training, exposure incl. homework) CG: Self-help CBT booklet + phone contact	T: 1-3m (completed) M: Individual face-to-face F: 4 x 1.5h x weekly S: NR I: Clinical psychologists	• Literacy (reading aloud, self-help book) • Audio player • Telephone (weekly calls) • Travel (NR)	6m	P: PTSD (IES-R), depression (HADS-D) and anxiety (HADS-A) symptoms S: None
Prolonged exposure or EMD interventions							
Bryant et al. (1999)	Mixed; mixed (MVC or nonsexua	RCT	IG: Prolonged Exposure; Prolonged	T: < 2w M: Individual face-to-face	• Literacy (diary of mood &	6m	P: PTSD (IES), depressi

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
	l assault) (66; 40%); New South Wales, Australia		Exposure +Anxiety management CG: Supportive counselling	F: 5 x 1.5h x weekly S: NR I: Clinical psychologists	problems) • Travel (NR)		on (BDI) and anxiety (STAI) symptoms (self-report) S: PTSD symptoms (clinician) (CAPS Form 2)
Kutz et al. (2008)	Mixed physical; Road, work, home or nature-related accidents (86; 44%); Israel	Cohort	IG: Modified EMD protocol (using alternative vibrotactile stimulation) CG: None	T: Up to 4m M: Individual, face-to-face F: Single session S: General hospital setting I: NR	• Vibration stimulus • Travel (NR)	6m	P: Distress level (SUDS score) S: None
Rothbaum et al. (2012)	Mixed physical; mixed (e.g. MVC, sexual assault, nonsexual assault) (137;	RCT	IG: Modified Prolonged Exposure CG: Assessment only	T: 12h (SD = 12.9) M: Individual face-to-face F: 3 x 1h x weekly S: ? Emergency department	• Literacy for homework (NR) • Travel (NR)	3m	P: PTSD (PDS and PSS-I) S: Depression (BDI-II)

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
	35%); America			I: Psychologist or social worker			
Shalev et al. (2012) Shalev et al. (2016)	Mixed physical; mixed (e.g. MVC, work accidents, terrorist attack) (242; 44%); Israel	RCT	IG: Prolonged Exposure vs Cognitive Therapy vs Pharmacotherapy CG: Waitlist; Placebo pharmacotherapy	T: mean 29d (SD = 5.71) M: Individual face-to-face F: 12 x 1.5h x weekly Pharma 20mg/d x 12w S: NR I: Clinical Psychologist	• Literacy for homework (NR) • No SSRI contra-indications • Travel (NR)	9m 3y	P: PTSD clinical diagnosis (CAPS) S: PTSD symptoms (PSS-SR)
Multidisciplinary/collaborative care interventions							
Vikane et al. (2017)	TBI; Mixed (e.g. MVC, fall, assault, sporting injury); (151; 61%); Norway	RCT	IG: Multidisciplinary outpatient treatment program CG: GP follow-up after multidisciplinary examination	T: ~2m D: Multidisciplinary M: Individual and group, face-to-face F: 1 year of individual contact including 4x group sessions S: Outpatient department of	• Travel	12m	P: None S: RTW, Anxiety and depression symptoms (HADS), PTSD symptoms (PTSS-10)

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
				neurosurgery I: multidisciplinary clinicians			
Wu et al. (2017)	Mixed physical; MVC (220; 68%); Australia	RCT	IG: Rehabilitation services + ward-based therapy using an in-reach team CG: Usual care (Ward-based therapy)	T: ~5days D: Multidisciplinary M: Individual, face-to-face F: 2 x sessions per day S: Inpatient rehabilitation service I: Multidisciplinary team, including physiotherapist and occupational therapist	• None (during inpatient stay)	3m or 6m (depending on injury severity)	P: None S: Depression and anxiety symptoms (DASS-21) and PTSD (PC-PTSD)
Zatzick et al. (2001)	Mixed physical; mixed (MVC, assault)(34; i-50%, c-75%); America	RCT	IG: Collaborative care CG: Usual care	T: mean 3-5d M: Individual, face-to-face, telephone, multidisciplinary F: Variable S: Inpatient,	• Travel	4m	P: PTSD (PCL-C) and depression (CES-D) symptoms S: None

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
				primary care, community rehabilitation I: Researcher, multi-disciplinary clinicians			
Zatzick et al. (2004)	Mixed physical; mixed (MVC, assault, work-related injury) (120; 35%); America	RCT	IG: Collaborative care (CC) comprising pharma, CBT (incl. graded exposure), Motivational interviewing (if alcohol risk) and case conferencing CG: Usual care	T: Up to 3m M: Individual, face-to-face, multidisciplinary F: Variable up to 12 months S: Inpatient, primary care outpatient, specialty mental health & community services I: Clinical case manager, multi-disciplinary clinicians	• Travel for therapy and rehabilitation • Telephone • Medication purchase • Homework (NR)	12m	P: PTSD symptoms (PCL-C) S: None
Zatzick et al. (2013)	Mixed physical; mixed	RCT	IG: Stepped collaborative care	T: > 13d M: Individual	• Travel for therapy	12m	P: PTSD sympto

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
	(intentional and unintentional) (207; 52%); America		CG: Usual care	face-to-face, telephone, multidisciplinary F: Variable over 12 months S: Inpatient, primary care outpatient, specialty mental health & community services I: Clinical case manager, multi-disciplinary clinicians	and rehabilitation • Telephone • Medication purchases • Homework (NR)		ms (PCL-C and CAPS) S: Depression symptoms (PHQ-9)
Zatzick et al. (2015)	Mixed physical; mixed (intentional and unintentional) (121; 64%); America	RCT	IG: Technology-enhanced stepped collaborative care CG: Usual care	T: NS, inpatient M: Individual face-to-face, web-based, multidisciplinary F: Variable over 6 months S: Inpatient, primary care	• Travel for therapy and rehabilitation • Telephone • Medication purchases • Homework (NR)	6m	P: PTSD symptoms (PCL-C) S: Depression symptoms (PHQ-9)

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
				outpatient, specialty mental health & community services I: Clinical case manager, multi-disciplinary clinicians	• Computer or smartphone • internet access • Literacy (computer resources)		
Education or information-focused interventions							
Bell et al. (2008)	mTBI; Mixed (e.g. MVC, Assault, Sporting injury, fall); (366; 64%); America	RCT	IG: scheduled telephone contact (provide information and reassurance on recovery and plan symptom management + booklet on concussion and brain injury CG: Usual care (some also received booklet)	T: 2d M: individual, telephone I: 5 calls (2d, 2w, 4w, 8w, 12w) S: NS I: Research co-ordinator with some clinical training	• Telephone • Literacy (handout materials)	6m	P: Post-Traumatic Symptoms composite (Head Injury Symptoms); general health composite (physical function-SF12, satisfaction, emotion – depression, anxiety/

Study (year)	Injury type; injury context (n, % male); country	Trial type	Intervention (IG) and Control (CG) description	Intervention timing > injury (T), discipline (D), modality (M) & frequency (F), Setting (S) and implementation (I)	Intervention participation requirement [+]	Follow up length	Outcome measures and tools
							panic, mental health-SF12)
Bugg et al. (2009)	Mixed physical; mixed (MVC, Assault, Work injury) (148; 28%); England	RCT	IG: Self-help booklet from (Scholes et al., 2007) + writing on 3 consecutive days CG: Self-help booklet only	T: 5-6w M: Individual, 1 face-to-face + 2X telephone, F: 3 x 20min x 3 consecutive days S: NS I: Researcher	• Telephone • Literacy (writing and reading written materials – age 9 level) • Travel for one session	6m	P: PTSD symptoms (PDS) S: Anxiety (HADS-A), depression (HADS-D)
Scholes et al. (2007)	Mixed physical; mixed (MVC, work injury, assault) (347; 55%); England	RCT	IG: Self-help booklet based on cognitive-behavioural strategies CG: Control	T: < 1m M: printed material F: single mail-out S: NS I: Researcher	• Literacy (writing and reading written materials – age 9 level)	6m	P: PTSD symptoms (PDS) S: Anxiety (HADS-A), depression (HADS-D), QoL

Abbreviations: BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; BDI-II = Beck Depression Inventory- II; CAPS = Clinician-Administered PTSD Scale; CBT = cognitive behavioural therapy; CES-D = Center for Epidemiological Studies Depression Scale; DASS-21- Depression Anxiety and Stress Score; EMD = eye movement desensitisation; HADS-A = Hospital Anxiety and Depression Scale, Anxiety subscale; HADS-D = Hospital Anxiety and Depression Scale, Depression subscale; IES = Impact of Events Scale; IES-R = Impact of Events Scale- Revised; mTBI = mild traumatic brain injury; MVC = motor vehicle collision; NR = not reported; NS = not stated; PCL-C = PTSD Checklist- Civilian Version; PC-PTSD- Primary Care Post-Traumatic Stress Disorder Screening; PDS = Posttraumatic Diagnostic Scale; PHQ-9 = Patient Health Questionnaire- 9 item Depression Screen; PSS-I = The PTSD Symptom Scale Interview; PSS-SR = The PTSD Symptom Scale-

Self Report Version; PTSD = posttraumatic stress disorder; PTSS-10 = Posttraumatic Stress Syndrome questionnaire; RCT = randomised controlled trial; SD = standard deviation; STAI = the State-Trait Anxiety Inventory; SUDS- Subjective Units of Distress Score.
* Follow up of Bryant et al. (1998) and Bryant et al. (1999) study samples.
+ The intervention requirements may have been provided by the participant or the intervention, but would be necessary to implement the intervention in a non-research setting.
Time is indicated in days (d), weeks (w), months (m) and years (y).

Table 2 Risk of bias judgements for each study.
(THIS TABLE SHOULD BE PRINTED IN COLOUR)

	Risk of bias					
Study	**OVERALL direction**	**Participant selection**	**Trial performance**	**Detection and analysis**	**Selective reporting**	**OVERALL rating**
Bell et al. (2008)	U	+	+	+	+	+
Bisson et al. (2004)	U	-	-	-	-	-
Brunet et al. (2013)	U	-	+	+	-	+
Bryant et al. (1998)	U	+	+	+	-	+
Bryant et al. (1999)	I	+	+	+	-	+
Bryant et al. (2003a)	U	-	?	+	-	+
Bryant et al. (2003b)	I	+	+	+	-	+
Bugg et al. (2009)	U	-	+	+	-	+
Conlon et al. (1999)	U	+	+	+	-	+
Des Groseilliers et al. (2013)	I	-	+	+	+	+
Ehlers et al. (2003)	U	-	?	+	-	+
Holmes et al. (2007)	I	-	+	+	-	+
Kutz et al. (2008)	I	+	+	+	?	+
Mouthaan et al. (2013)	U	-	-	+	-	-
O'Donnell et al. (2012)	U	-	+	+	-	+
Pirente et al. (2007)	C	+	+	+	+	+
Rothbaum et al. (2012)	U	-	-	-	-	-
Scholes et al. (2007)	U	-	?	+	-	+
Shalev et al. (2012)	U	-	+	-	+	+
Shalev et al. (2016)	U	-	+	-	+	+
Silverberg et al. (2013)	U	+	-	+	-	+
Tecic et al. (2011)	U	-	+	+	-	+
Vikane et al. (2017)	U	+	+	-	+	+
Wu et al. (2014)	I	+	+	+	+	+
Wu et al. (2017)	U	+	+	+	-	+
Zatzick et al. (2001)	U	+	+	+	-	+
Zatzick et al. (2004)	U	+	+	-	-	+
Zatzick et al. (2013)	U	-	-	-	-	-
Zatzick et al. (2015)	C	-	+	-	-	-

Note. Risk of bias was evaluated in relation to the following domains: selection bias (e.g., randomisation and stratification), performance bias (e.g., blinding of participants and personnel), detection bias (e.g., missing data and appropriate confounders) and reporting bias (e.g., selective reporting). Red indicates high risk of bias, orange indicates moderate risk of bias, green indicates low risk of bias and yellow indicates unknown risk of bias. U, Unknown/Not Applicable; I, Favoured intervention; C, Favoured comparison.

Table 3 Intervention study findings.

Study (year)	Final N	% loss to follow-up	Results for primary outcome	Results for secondary outcome
Cognitive and behavioural interventions				
Bisson et al. (2004)	116	24	PTSD symptoms: 13m (hedges *g* = 0.34)	Anxiety: ns Depression: ns Clinician PTSD: ns
Brunet et al. (2013) Des Groseilliers et al. (2013)	66 (3M) 46 (2Y)	11 (3m) 38 (2y)	PTSD symptoms: 3m (hedges *g* = 0.39) 2y (hedges *g* = 0.48)	None
Bryant et al. (1998)	24	NR	PTSD Intrusion 6m (hedges *g* = 0.89) PTSD Avoidance 6m (hedges *g* = 1.32) Anxiety (State) 6m (hedges *g* = 0.80) Depression 6m (hedges *g* = 0.94)	None
Bryant et al. (2003a)	24	0	PTSD Intrusion symptoms 0w (hedges *g* = 1.89) 6m (hedges *g* = 1.34) PTSD Avoidance symptoms 0w (hedges *g* = 2.24) 6m (hedges *g* = 1.55)	Depression: ns Anxiety: ns
Bryant et al. (2003b)*	41	36	PTSD Clinician Avoidance[#] 4y (hedges *g* = 0.91) PTSD Clinician Arousal[#] 4y (hedges *g* = 0.92)	None
Conlon et al. (1999)	40	8	PTSD symptoms (self-report): ns PTSD symptoms (clinician): ns	None
Ehlers et al. (2003)	78	8	(a) CT vs Self-Help booklet PTSD Self-Report Frequency Symptoms: 3m (hedges *g* = 1.05) 9m (hedges *g* = 1.17) PTSD Self-Report Distress Symptoms: 3m (hedges *g* = 1.20) 9m (hedges *g* = 1.14) PTSD Clinician Frequency Symptoms: 3m (hedges *g* = 0.90)	(a) CT vs Self-Help booklet Anxiety: 3m (hedges *g* = 1.18) 9m (hedges *g* = 1.27) Depression: 3m (hedges *g* = 1.16) 9m (hedges *g* = 1.04) (b) CT vs Repeated Assessment Anxiety: 3m (hedges *g* = 1.10)

Study (year)	Final N	% loss to follow-up	Results for primary outcome	Results for secondary outcome
			9m (hedges g = 0.94) PTSD Clinician Intensity Symptoms: 3m (hedges g = 1.00) 9m (hedges g = 0.90) (b) CT vs Repeated Assessment PTSD Self-Report Frequency Symptoms: 3m (hedges g = 1.22) 9m (hedges g = 0.91) PTSD Self-Report Distress Symptoms: 3m (hedges g = 1.29) 9m (hedges g = 1.04) PTSD Clinician Frequency Symptoms: 3m (hedges g = 1.13) 9m (hedges g = 0.74) PTSD Clinician Intensity Symptoms: 3m (hedges g = 1.21) 9m (hedges g = 0.70)	9m (hedges g = 0.93) Depression: 3m (hedges g = 1.02) 9m (hedges g = 0.46)
Holmes et al. (2007)	77	3M- 6% 6M- 8%	Depression: ns Anxiety: ns PTSD symptoms: ns	None
Mouthaan et al. (2013)	139	30	PTSD symptoms: ns	Anxiety: ns Depression: ns Self-report PTSD: ns
O'Donnell et al. (2012)	34	26	PTSD Symptoms 6m (hedges g = 0.53) 12m (hedges g = 0.91) Anxiety symptoms 6m (hedges g = 1.10) 12m (hedges g = 0.58) Depression symptoms 6m (hedges g = 1.99) 12m (hedges g = 1.54)	PTSD diagnosis‡ 6m: RR = 2.02, p<.05 12m: RR = 1.88, p<.05 Major depression diagnosis‡ 12m: RR = 1.78, p<.05 Anxiety disorder: ns
Pirente et al. (2007)	92	29	None	Depression: ns Anxiety: ns
Silverberg et al. (2013)	24	14%	None	Anxiety: ns Depression: ns
Tecic et al. (2011)	46	59	Presence of a psychological disorder‡	None

Study (year)	Final N	% loss to follow-up	Results for primary outcome	Results for secondary outcome
			12M: RR = 1.27, p = .03 Anxiety: ns Depression: ns PTSD: ns	
Wu et al. (2014)	43	28	PTSD: ns Depression: 6m (hedges *g* = 1.08) Anxiety 6m (hedges *g* =1.12)	None
Prolonged Exposure or EMD interventions				
Bryant et al. (1999)	41	38	**(a) PE+AM V SC** PTSD intrusion 0w (hedges *g* = 1.11) 6m (hedges *g* = 1.01) PTSD Avoidance 0w (hedges *g* = 1.85) 6m (hedges *g* = 2.06) Anxiety 0w (hedges *g* = 0.94) 6m (hedges *g* = 1.39) Depression : ns **(b) PE V SC** PTSD Intrusion 0w (hedges *g* = 1.76) 6m (hedges *g* = 0.79) PTSD Avoidance 0w (hedges *g* = 2.30) 6m (hedges *g* = 1.95) Anxiety 0w (hedges *g* = 0.58) 6m (hedges *g* = 0.89) Depression: ns	**(a) PE+AM V SC** PTSD (clinician) Frequency[#] 0w (hedges *g* = 0.78) 6m (hedges *g* = 1.03) PTSD (clinician) Intensity[#] 0w (hedges *g* = 0.79) 6m (hedges *g* = 1.15) **(b) PE V SC** PTSD (clinician) Frequency[#] 0w (hedges *g* = 1.00) 6m (hedges *g* = 1.21) PTSD (clinician) Intensity[#] 0w (hedges *g* = 1.04) 6m (hedges *g* = 1.51)
Kutz et al. (2008)	86	0	Results from injury group: Distress level: Immediate relief (n= 27, 59%) Hedges *g*= 5.7 Substantial relief (n= 11, 24%) Hedges *g*= 2.97 No relief (n= 8, 17%) ns	None
Rothbaum et al. (2012)	91	34	PTSD symptoms 4w (hedges *g* = 0.37) 12w (hedges *g* = 0.31)	Depression 4w (hedges *g* = 0.24)
Shalev et al. (2012)	180	26	PTSD diagnosis[‡] (PE vs WL control) 5m: RR = 1.88 PTSD diagnosis[‡] (CT vs	PTSD clinician symptoms (PE vs WL) 5m (hedges *g*= 0.93) 9m (hedges *g*= 0.24)

Study (year)	Final N	% loss to follow-up	Results for primary outcome	Results for secondary outcome
			WL control) 5m: RR = 1.95 NOTE: Omission of T2 (9m) revealed no significant effect of group (esp. delayed intervention) between baseline and 9m.	PTSD self-reported symptoms (PE vs WL) 5m (hedges *g*= 0.87) 9m (hedges *g*= 0.20) PTSD clinician symptoms (CT vs WL) 5m (hedges *g*= 0.90) 9m (hedges *g*= 0.13) PTSD self-reported symptoms (CT vs WL) 5m (hedges *g*= 0.78) 9m (hedges *g*= 0.23)
Shalev et al. (2016)	180	26	None	Depression symptoms (PE vs Declined intervention) 5m (hedges *g*= 0.52) (CT vs Declined intervention) 5m (hedges *g*= 0.60) [§]
Multidisciplinary/collaborative care interventions				
Vikane et al. (2017)	151	17%	RTW: RR 0.85 None	Posttraumatic stress: ns Anxiety: ns Depression: ns
Wu et al. (2017)	214	3%	None	Psychological status: ns
Zatzick et al. (2001)	26	25	PTSD symptoms 1m (hedges *g* = 0.99) 4m (hedges *g* = 1.75) Depression symptoms 1m (hedges *g* = 0.58) 4m (hedges *g* = 1.44)	None
Zatzick et al. (2004)	33	28%	PTSD symptoms: 6m: ns 12m: RR: 1.06	None
Zatzick et al. (2013)	167	i-16; c-22	Clinician PTSD symptoms[#]: 6m (hedges *g* = 0.25) 12m (hedges *g* = 0.15) Self-report PTSD symptoms: 6m (hedges *g* = 0.28) 9m (hedges *g* = 0.15) 12m (hedges *g* = 0.14)	Depression: 6m (hedges *g*= 0.31)
Zatzick et al. (2015)	105	13	PTSD symptoms: 3m (hedges *g* = 0.19) 6m (hedges *g* = 0.20)	Depression: ns

Study (year)	Final N	% loss to follow-up	Results for primary outcome	Results for secondary outcome
Education or information based interventions				
Bell et al. (2008)	313	14	PTS composite# 6m (hedges g = 0.28) General health composite: ns	None
Bugg et al. (2009)	51	65%	PTSD symptoms: ns	Anxiety: ns Depression: ns
Scholes et al. (2007)	166	52	PTSD symptoms: ns	Anxiety: ns Depression: ns

Abbreviations: AM = active monitoring; CT = cognitive therapy; NR = not reported; NS = not significant; PCS = post-concussion syndrome; PE = prolonged exposure; PTSD = posttraumatic stress disorder; QoL = quality of life; RR = risk ratio; RTW = return to work; SC = supportive counselling.

* Follow up of Bryant et al. 1998 and Bryant et al. 1999 study samples

Hedges g not adjusted for baseline scores when baseline data were not reported

‡ Risk ratios indicates likelihood of positive outcomes (i.e., RTW, or not having mental health diagnosis/symptoms for intervention group vs control group)

§5m results from 2012 study published in 2016 paper but with alternate comparison

Time is indicated in weeks (w), months (m) and years (y).

Table 4 Grade of evidence for the effectiveness of early interventions on PTSD, depression and anxiety symptoms in accordance with the NHMRC (2009) Evidence Statement.

		Grade of evidence				
Outcome	**Intervention type**	**Evidence Base** [+]		**Consistency** [++]		**Clinical Impact** [+++]
PTSD	CBT	C		B		A – C
symptoms	PE	C		B		A – D
	Multidisciplinary and CC	B		B		A – D
	Education	N/A		B		N/A
Depression	CBT	C		D		A – N/A
symptoms	PE	B		D		C – D
	Multidisciplinary and CC	B		D		D
	Education	N/A		A		N/A
Anxiety	CBT	C		D		A – N/A
symptoms	PE	D		A		C – N/A
	Multidisciplinary and CC	N/A		N/A		N/A
	Education	N/A		A		N/A

Abbreviations: ROB = overall Risk of Bias, CC = collaborative care.
Grades indicate: A = Excellent, B = Good, C = Satisfactory and D = Poor.
[+] Evidence base grades: A = several level II studies with low ROB; B = 1 to 2 level II studies with low ROB; C = 1-2 level II studies with moderate ROB, D = level I to III with high ROB, N/A = not measured, or no effects
[++] Consistency grades: A = all studies consistent, B = most studies consistent and inconsistency may be explained, C = some inconsistency reflecting genuine uncertainty around clinical question, D = evidence is inconsistent, N/A = not measured;
[+++] Clinical impact grades: A = very large, B = substantial, C = moderate, D = slight/restricted, N/A = no impact or not measured.

Table A1 Search strategy, population, intervention and outcome keywords and Medical Subject Heading terms (MeSH).

	Keywords and MeSH terms
Population Key words	Motor vehicle accident; motor vehicle crash; work accident; injury; compensable injury
	OR
Population MeSH terms	Accidents, traffic; Accidents, occupational; Musculoskeletal Pain; Musculoskeletal diseases; Wounds and Injuries; Trauma; Acute Post-Traumatic Stress Disorder; General Surgery /orthopaedics
	AND
Intervention Keywords	Prevention; rehabilitation; progressive goal attainment program; cognitive functional therapy; acceptance and commitment therapy; cognitive behavioural therapy; cognitive behavioral therapy; EMDR; cognitive training; psychological debriefing; CBT; psychological first aid; trauma-focused CBT; exposure therapy; cognitive therapy
	OR
Intervention MeSH terms	Health Services for Persons with Disabilities; Community Health Services; mental Health Services; Physical and Rehabilitation Medicine; Rehabilitation /Occupational therapy /vocational /primary prevention /secondary prevention /Therapies, investigational; Pain Clinics; Education; Health Occupations /Allied Health Occupations /Psychology, Medical /Physical and Rehabilitation medicine /Psychiatric Rehabilitation; Telerehabilitation
	AND
Outcome Keywords	Pain; interference; fear of pain; kinesiophobia; psychological distress; anxiety; depression; PTSD; posttraumatic stress; (fear AND pain)
Outcome MeSH terms	Return to Work; Pain; Depression; Depressive Disorder; Mental Disorders /Trauma and Stressor Related Disorders /anxiety disorders /Dissociative disorders /somatoform disorders; Stress disorders, Post-traumatic; Stress disorders, Traumatic; Sick leave; Insurance, Disability

Table A2 Medline search strategy 22nd of September 2016 (rerun 11th September 2017).

1. (Motor vehicle accident or motor vehicle crash or work accident or injury or compensable injury).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading]
2. Accidents, Traffic/ or Accidents/ or Accidents, Occupational/
3. Musculoskeletal Diseases/ or Musculoskeletal Pain/
4. "Wounds and Injuries"/
5. Stress Disorders, Traumatic, Acute/
6. general surgery/ or orthopedics/
7. 1 or 2 or 3 or 4 or 5 or 6
8. (((prevention or rehabilitation or progressive goal attainment program or WISE or cognitive functional therapy or acceptance) and commitment therapy) or cognitive behavioural therapy or cognitive behavioral therapy or EMDR or cognitive training or psychological debriefing or CBT or psychological first aid or trauma-focussed CBT or exposure therapy or cognitive therapy).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading]
9. health services/ or community health services/
10. Health Services for Persons with Disabilities/ or Mental Health Services/
11. (Physical and rehabilitation medicine).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading]
12. rehabilitation/ or occupational therapy/ or rehabilitation, vocational/ or telerehabilitation/ or secondary prevention/ or therapies, investigational/
13. Pain Clinics/
14. Education/
15. health occupations/ or allied health occupations/ or psychology, medical/
16. Psychiatric Rehabilitation/
17. Telerehabilitation/
18. Primary Prevention/
19. 8 or 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18
20. (pain or interference or fear of pain or kinesiophobia or psychological distress or anxiety or depression or PTSD or posttraumatic stress or (fear and pain)).mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading]
21. Return to Work/
22. Pain/
23. Depressive Disorder/
24. Depression/
25. mental disorders/ or anxiety disorders/ or dissociative disorders/ or somatoform disorders/ or "trauma and stressor related disorders"/
26. Stress Disorders, Post-Traumatic/

27. Stress Disorders, Traumatic/
28. Sick Leave/
29. Insurance, Disability/
30. 20 or 21 or 22 or 23 or 24 or 25 or 26 or 27 or 28 or 29
31. 7 and 19 and 30
32. limit 31 to (english language and humans and yr="1990 -Current")
33. limit 32 to (abstracts and human and english language)
34. ("motor vehicle accident" or "motor vehicle crash" or "work accident" or "compensable injury").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading]
35. injury.mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading]
36. 34 or 35
37. 2 or 3 or 4 or 5 or 6 or 34
38. 19 and 30 and 37
39. limit 38 to (human and english language and yr="1990 -Current")
40. (prevention or rehabilitation or "progressive goal attainment program" or WISE or "cognitive functional therapy" or "acceptance and commitment therapy" or "cognitive behavioural therapy" or "cognitive behavioral therapy" or EMDR or "cognitive training" or "psychological debriefing" or CBT or "psychological first aid" or "trauma-focussed CBT" or "exposure therapy" or "cognitive therapy").mp. [mp=title, abstract, heading word, drug trade name, original title, device manufacturer, drug manufacturer, device trade name, keyword, floating subheading]
41. 9 or 10 or 11 or 12 or 13 or 14 or 15 or 16 or 17 or 18 or 40
42. 30 and 37 and 41
43. limit 42 to (human and english language and yr="1990 -Current")
44. limit 43 to abstracts

Table A3 Risk of bias assessment criteria.

ROB Domain/construct (SPSS Variable name)		For non-randomised trials	For RCTs
SELECTION BIAS			
	Recruitment	• Did participant characteristics noted after recruitment and enrolment influence inclusion/exclusion (e.g., retrospective allocation to groups based on an effect of intervention) • Is start of intervention/Follow-up timing consistent across participants • Were adjustment techniques used to adjust for selection biases (e.g., modelling missing participants, time factors). *Note these methods are not often used.*	As per non-randomised trials • Was appropriate randomisation undertaken (fully randomised = no ROB, partial/pseudo-randomized = possible ROB) • Was group allocation concealed from the researchers?
	Notes	Add notes/details that affected bias judgement	
	Judgement	Across sources of potential bias was there low, moderate or high risk of bias.	
	Direction	Did the bias favour intervention/comparator	
TRIAL PERFORMANCE			
	Intervention defined	• Were interventions well defined (whether individualised or manualised)? • Were co-interventions balanced across groups (e.g., usual care, medical management). • Were other treatments outside study recorded and reported?	As per non-randomised trials
	Personnel blinded?	Blinding of participants and personnel in relation to assessments and intervention delivery: • Were participants/ personnel blinded to the expected effects of the intervention? Could the outcome measure have been influenced by knowledge of the intervention received?	• Were participants/personnel blinded to group allocation?
	Assessors/Analysists blinded?	Blinding of participants and personnel in relation to outcome assessments and analysis: • Were outcome assessors blinded to participant group? NOTE Outcome assessor could be participant, or a therapist/researcher, depending on who administered outcome assessment. • Were analyses blinded (e.g., group A vs group B)? *Usually won't be clear*.	As per non-randomised trials
	Deviations from protocol	• Were there deviations from the intervention beyond those that may arise from duty of care/ethics? • Was the intervention implemented as intended? • Were these compliance/implementation factors considered in analyses (e.g., , inverse probability weighting or instrumental variable estimation)	As per non-randomised trials
	Notes	Add notes/details that affected bias judgement	
	Judgement	Across sources of potential bias was there low, moderate or high risk of bias.	
	Direction	Did the bias favour intervention/comparator	
DETECTION			
	Measurement	• Were methods of outcome assessment comparable across groups? • Were there systematic errors in measurement of outcomes between groups? • Were tools validated and appropriate?	As per non-randomised trials
	Missing Data	• Did participants show low compliance (e.g., imperfect compliance, cessation of intervention/withdrawal, crossovers to the comparator intervention and switches to another active intervention)? Was attrition reported in relation to the group/intervention effects (e.g., lack of efficacy, side-effects – if yes, = high risk) or did reasons differ between groups.	As per non-randomised trials

		• Were outcome data available for all, or nearly all participants? If data is missing from more than 10% of participants at FU may not be confident of findings. • Were participants excluded because of drop-out or partial missing data (e.g., list-wise deletion) or did they analyse as per intention to treat – e.g., multilevel modelling) • Was there differential dropout/missing data for the intervention group c.f. the comparator • Were the analyses/results robust to missing data (e.g., sensitivity analyses conducted)	
	Analysis Appropriate	• Were analysis techniques appropriate (e.g., to control for confounding).	As per non-randomised trials
	Confounders Measured	• Were confounding factors measured? • Were confounders measured with valid/reliable tools/variables	As per non-randomised trials
	Confounders Used	• Were appropriate confounders controlled for? • Were inappropriate confounders controlled for? (introducing bias)	As per non-randomised trials
	Notes	Add notes/details that affected bias judgement Give details of confounders or any other issues relating to measurement	
	Judgement	Across sources of potential bias was there low, moderate or high risk of bias.	
	Direction	Did the bias favour intervention/comparator	
REPORTING OUTCOMES			
	Selective Reporting?	Were results likely to have been selectively reported and/or interpreted because there were • Multiple outcome measurements within the outcome domain. • Multiple analyses of intervention-related outcome relationships • Multiple sub-groups	As per non-randomised trials
	Notes	Add notes/details that affected bias judgement	
	Judgement	Across sources of potential bias was there low, moderate or high risk of bias.	
	Direction	Did the bias favour intervention/comparator	
OVERALL			

Table A4 Clinically meaningful effects of studies included in the meta analyses (i.e., whether the intervention group had a meaningful reduction in symptoms, or were clinically sub-threshold at follow-up).

Outcome	Outcome period (months)	Study	Tool used	Clinical threshold Criteria		
				Criteria	Notes	Judgement
PTSD	0-3 m	Brunet, Des Groseilliers, Cordova, and Ruzek (2013)	IES-R	<33 points (Weiss & Marmar, 1997)	IG & CG below clinical threshold, but IG was significantly lower	Clinically meaningful
PTSD	0-3 m	Ehlers et al. (2003)	PDS CAPS	PDS: ≤10- mild, ≥11 and ≤20- moderate, ≥21 and ≤35- moderate to severe, ≥36- severe (Foa, 2017) CAPS: ≤45. Remission ≤20 and a response is a drop of 10 or more (Weathers, Keane, & Davidson, 2001)	IG (CT): mild symptoms CG (SH): moderate symptoms CG (RA) = moderate to severe (PDS)	Clinically meaningful
PTSD	0-3 m	Mouthaan et al. (2013)	n/a	n/a	n/a	No significant effects
PTSD	0-3m (1m)	Rothbaum et al. (2012)	PDS	PDS: ≤10- mild, ≥11 and ≤20- moderate, ≥21 and ≤35- moderate to severe, ≥36- severe (Foa, 2017)	IG: moderate symptoms CG: moderate-severe symptoms	clinically meaningful
PTSD	0-3m (1m)	Zatzick et al. (2001)	PCL-C	10-20 point change is meaningful (Monson et al., 2008), and cut off of 45 (Andrykowski, Cordova, Studts, &	IG & CG: <10 point reduction, Note: both groups below clinical threshold at baseline	Not clinically meaningful

Outcome	Outcome period (months)	Study	Tool used	Criteria	Clinical threshold Criteria	
					Notes	Judgement
				Miller, 1998; Blanchard, Jones-Alexander, Buckley, & Forneris, 1996)	and follow-up.	
PTSD	0-3m (3m)	Zatzick et al. (2013)-	n/a	n/a	n/a	No significant effects
PTSD	0-3m (3m)	Zatzick et al. (2015)	PCL-C	10-20 point change is meaningful (Monson et al., 2008), and cut off of 45 (Andrykowski et al., 1998; Blanchard et al., 1996)	IG & CG: <10-point reduction, but symptoms below clinical threshold at FU	Not clinically meaningful
PTSD	0-3m (3m)	Scholes, Turpin, and Mason (2007)	n/a	n/a	n/a	No significant effects
PTSD	3-6m (6m)	Bryant, Moulds, Guthrie, and Nixon (2003)	IES CAPS	IES: <26 (Horowitz, Wilner, & Alvarez, 1979) CAPS: ≤45. Remission ≤20 and a response is a drop of 10 or more (Weathers et al., 2001)	IG: point reduction >2 SDs & below clinical threshold (IES)	Clinically meaningful
PTSD	3-6m	Mouthaan et al. (2013)	n/a	n/a	n/a	No significant effects
PTSD	3-6m (6m)	O'Donnell et al. (2012)	CAPS	CAPS: ≤45. Remission ≤20 and a response is a drop of 10 or more (Weathers et al., 2001)	IG: ≥20 point reduction CG : ≥20 point reduction	Clinically meaningful
PTSD	3-6m (5m)	Shalev et al. (2012)	CAPS PSS-R	CAPS: ≤45. Remission ≤20	IGs (PE and CT): ≥20	Clinically meaningful

Outcome	Outcome period (months)	Study	Tool used	Criteria	Clinical threshold Criteria	
					Notes	Judgement
				and a response is a drop of 10 or more (Weathers et al., 2001); PSS-R: Cut off score of 14 (Coffey, Gudmundsdottir, Beck, Palyo, & Miller, 2006)	point reduction, and <clinical threshold CG (WL): ≥20 point reduction, but > clinical threshold (CAPS)	
PTSD	3-6m (4m)	Zatzick et al. (2001)	PCL-C	10-20 point change is meaningful (Monson et al., 2008), and cut off of 45 (Andrykowski et al., 1998; Blanchard et al., 1996)	IG & CG: increased symptoms from baseline and earlier assessment time.	Not clinically meaningful
PTSD	3-6m (6m)	Zatzick et al. (2013)	PCL-C CAPS	10-20 point change is meaningful (Monson et al., 2008), and cut off of 45 (Andrykowski et al., 1998; Blanchard et al., 1996)	IG (CC): ≥10 point reduction (PCL-C and CAPS) at 6m CG (UC): <10 point reduction (PCL-C) at 3m & 6m	Clinically meaningful
PTSD	3-6m (6m)	Zatzick et al. (2015)	PCL-C	10-20 point change is meaningful (Monson et al., 2008), and cut off of 45 (Andrykowski et al., 1998; Blanchard et al., 1996)	IG (CC): 4 point reduction, but move from >45 to <45 CG (UC): < 10 point reduction	Not clinically meaningful
PTSD	3-6m	Scholes et al. (2007)	n/a	n/a	n/a	No significant

Outcome	Outcome period (months)	Study	Tool used	Criteria	Clinical threshold Criteria	
					Notes	Judgement
						effects
PTSD	6-12m (9m)	Ehlers et al. (2003)	PDS CAPS	PDS: ≤10- mild, ≥11 and ≤20- moderate, ≥21 and ≤35- moderate to severe, ≥36- severe (Foa, 2017) CAPS: ≤45. Remission ≤20 and a response is a drop of 10 or more (Weathers et al., 2001)	IG (CT) mild symptoms CG (SH & RA) moderate symptoms (PDS)	Clinically meaningful
PTSD	6-12m	Mouthaan et al. (2013)	n/a	n/a	n/a	No significant effects
PTSD	6-12m (12m)	O'Donnell et al. (2012)	CAPS	CAPS: ≤45. Remission ≤20 and a response is a drop of 10 or more (Weathers et al., 2001)	IG >20 point reduction CG < 20) point reduction	Clinically meaningful
PTSD	6-12m (9m)	Shalev et al. (2012)	CAPS PSS-R	CAPS: ≤45. Remission ≤20 and a response is a drop of 10 or more (Weathers et al., 2001) PSS-R: Cut off score of 14 (Coffey et al., 2006)	All groups <14 (PSS-R) & <45 (CAPS), but IG had lowest scores	Clinically meaningful
PTSD	6-12m (12m)	Zatzick et al. (2013)	PCL-C CAPS	10-20 point change is meaningful (Monson et al., 2008), and cut off of 45 (Andrykowski et al., 1998; Blanchard et al.,	IG: >10 point reduction (PCL-C) CG: <10 point reduction (PCL-C) IG & CG	Clinically meaningful

Outcome	Outcome period (months)	Study	Tool used	Criteria	Clinical threshold Criteria	
					Notes	Judgement
				1996)	both reduced for CAPS, but greater reduction for IG	
Depression	0-3m	Silverberg et al. (2013)	n/a	n/a	n/a	No significant effects
Depression	0-3m	Mouthaan et al. (2013)	n/a	n/a	n/a	No significant effects
Depression	0-3m (3m)	Ehlers et al. (2003)	BDI	0–9 (minimal), 10–18 (mild), 19–29 (moderate), 30–63 (severe) (Beck, Steer, & Carbin, 1988)	IG: mild to minimal CG: moderate to mild	Clinically meaningful
Depression	0-3m (3m)	Rothbaum et al. (2012)	BDI-II	0-13 (minimal), 14-19 (mild), 20-28 (moderate), 29-63 (severe) (Beck, Steer, & Brown, 1996)	IG: mild range CG: moderate range	Clinically meaningful
Depression	0-3m (3m)	Zatzick et al. (2015)	PHQ-9	Cut off between 8 and 11 (Manea, Gilbody, & McMillan, 2012)	IG & CG > 11	Not clinically meaningful
Depression	0-3m	Zatzick et al. (2013)	n/a	n/a	n/a	No significant effects
Depression	0-3m (1m)	(Zatzick et al., 2001)	CES-D	16+ cut off (McDowell & Newell, 1996)	IG & CG > 16	Not clinically meaningful
Depression	0-3m	Scholes et al. (2007)	n/a	n/a	n/a	No significant effects
Depression	3-6m	Bryant et al. (2003)	n/a	n/a	n/a	No significant effects
Depressio	3-6m	Mouthaan	n/a	n/a	n/a	No

Outcome	Outcome period (months)	Study	Tool used	Criteria	Clinical threshold Criteria	
					Notes	Judgement
n		et al. (2013)				significant effects
Depression	3-6m (6m)	O'Donnell et al. (2012)	BDI	0–9 (minimal), 10–18 (mild), 19–29 (moderate), 30–63 (severe) (Beck et al., 1988)	IG change: severe to mild	Clinically meaningful
Depression	3-6m (4m)	Zatzick et al. (2001)	CES-D	16+ cut off (McDowell & Newell, 1996)	IG & CG > 16 and CG < IG	Not clinically meaningful
Depression	3-6m (6m)	Zatzick et al. (2013)	PHQ-9	Cut off between 8 and 11 (Manea et al., 2012)	IG between 8 and 11, and 6 month mean above	Clinically meaningful
Depression	3-6m	Zatzick et al. (2015)	n/a	n/a	n/a	No significant effects
Depression	3-6m	Scholes et al. (2007)	n/a	n/a	n/a	No significant effects
Depression	6-12m (9m)	Ehlers et al. (2003)	BDI	0–9 (minimal), 10–18 (mild), 19–29 (moderate), 30–63 (severe) (Beck et al., 1988)	IG change: mild to minimal. CG change: moderate to mild.	Clinically meaningful
Depression	6-12m	Mouthaan et al. (2013)	n/a	n/a	n/a	No significant effects
Depression	6-12m (12m)	O'Donnell et al. (2012)	BDI	0–9 (minimal), 10–18 (mild), 19–29 (moderate), 30–63 (severe) (Beck et al., 1988)	IG had mild symptoms (down from severe at baseline) CG had elevated symptoms	Clinically meaningful
Depression	6-12m	Zatzick et al. (2013)	n/a	n/a	n/a	No significant effects
Anxiety	0-3m	Ehlers et al.	BAI	Cut off of 12	CT < 12	Clinically

Outcome	Outcome period (months)	Study	Tool used	Criteria	Clinical threshold Criteria	
					Notes	Judgement
	(3m)	(2003)		(Foa et al., 1999)	SH and RA groups > 12	meaningful
Anxiety	0-3m	Mouthaan et al. (2013)	n/a	n/a	n/a	No significant effects
Anxiety	0-3m	Silverberg et al. (2013)	n/a	n/a	n/a	No significant effects
Anxiety	0-3m	Scholes et al. (2007)	n/a	n/a	n/a	No significant effects
Anxiety	3-6m	Bryant et al. (2003)	n/a	n/a	n/a	No significant effects
Anxiety	3-6m	Mouthaan et al. (2013)	n/a	n/a	n/a	No significant effects
Anxiety	3-6m (6m)	O'Donnell et al. (2012)	HADS-A	Cut off of 11 (Zigmond & Snaith, 1983)	IG < 11 CG > 11	Clinically meaningful
Anxiety	3-6m	Scholes et al. (2007)	n/a	n/a	n/a	No significant effects
Anxiety	6-12m (9m)	Ehlers et al. (2003)	BAI	Cut off of 12 (Foa et al., 1999)	IG (CT group) <12 CGs (SH and RA) > 12	Clinically meaningful
Anxiety	6-12m	Mouthaan et al. (2013)	n/a	n/a	n/a	No significant effects
Anxiety	6-12m (12m)	O'Donnell et al. (2012)	HADS-A	Cut off of 11 (Zigmond & Snaith, 1983)	IG (CBT) < 11 CG exactly 11	Clinically meaningful

Abbreviations: BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; BDI-II = Beck Depression Inventory- II; CAPS = Clinician-Administered PTSD Scale; CBT = cognitive behavioural therapy; CC = Collaborative Care; CES-D = Center for Epidemiological Studies Depression Scale; CG = Control Group; CT = Cognitive therapy; HADS-A = Hospital Anxiety and Depression Scale, Anxiety subscale; IES = Impact of Events Scale; IES-R = Impact of Events Scale- Revised; IG = Intervention Group; PCL-C = PTSD Checklist- Civilian Version; PDS = Posttraumatic Diagnostic Scale; PHQ-9 = Patient Health Questionnaire- 9 item Depression Screen; PSS-R = The PTSD Symptom Scale- Self Report Version; PTSD = posttraumatic stress disorder; RA = repeated assessments; SH = self-help booklet; UC = Usual care.

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Table A5 Inclusion and exclusion criteria for individual studies.

Study (year) [study number]	Inclusion criteria	Exclusion criteria
Cognitive and behavioural interventions		
Bisson, Shepherd, Joy, Probert, and Newcombe (2004) [1]	Sustained a physical injury, local resident, acute distress, 16-70y	Pre-existing mental health conditions, physical disability, illness or cognitive deficit
Brunet et al. (2013) [2] Des Groseilliers et al. (2013) [3]	< 10d since life threatening event causing traumatic reaction	Lack of English or French language proficiency; TBI; history of psychosis, AOD dependence, bipolar disorder or mental retardation; clinical depression in past 2y; taking psychotropic medication; sustained severe injury; reside outside Montreal Canada area; no significant other; no study appointment made within 30d post-trauma
Bryant et al. (1998) [4]	< 2w since sustaining an injury in a MVA or workplace accident; met ASD criteria on admission; 18-60y; English language proficiency	Suicidal ideation; psychosis, mental health condition; substance abuse; TBI
Bryant et al. (2003) [5]	< 2w since traumatic MVC or assault; mTBI; 18-60y; English language proficiency	None reported
Bryant et al. (2003)* [6]	< 2w since traumatic MVC or assault; 18-60y; English language proficiency; ASD diagnosis	Suicidal ideation; psychosis, mental health condition; substance abuse; TBI
Conlon et al. (1999) [7]	16-65y	Head injury; hospital admission
Ehlers et al. (2003) [8]	< 6mths since ED attendance for MVC ; 18-65y, met diagnostic criteria for moderate-severe PTSD	LOC > 15mins post MVC; have no memory of accident; history of psychosis; current AOD dependence; borderline personality disorder; severe depression; lack of English language proficiency
Holmes et al. (2007) [9]	≥18y; major physical trauma, ceased narcotic analgesics	Head injury; injury due to self-harm; psychotic illness

Mouthaan et al. (2013) [10]	Experienced a potentially traumatic event ; 18+y, Dutch language proficiency	Injury caused by self-harm, organic brain condition, psychotic disorder, depression; moderate/severe TBI, not resident of the Netherlands
O'Donnell et al. (2012) [11]	< 24h since injury requiring hospital admission ; 18-70y ; English language proficiency	Moderate/severe TBI; psychosis, suicidality
Pirente et al. (2007) [12]	2+ injuries with AIS score > 5; 18-70y; mental orientation	severe TBI; attempted suicide, receipt of psychotherapy prior to current trauma; crime-related injury; lack of German language proficiency; denied participation
Silverberg et al. (2013) [13]	Incurred head trauma within 6w of study entry; met American Congress of Rehabilitation criteria for MTBI; subjectively reported ≥1 symptom attributable to head trauma; 18-65y; English proficient; at risk for chronic PCS	"Mild-complicated" TBI; self-reported history of neurological disorder (including MTBI within past 6m); ≥3 grade whiplash injury; current use of medications with major sedative or cognitive side effects
Tecic et al. (2011) [14]	18-65y; sustained at least 2 injuries with combined AIS score > 4 in a MVC	Lack of German language proficiency; history of mental health conditions, addiction or suicidality
Wu et al. (2014) [15]	Sustained an injury requiring ED attendance; local resident; 18+y, persistent psychological distress > 1m post MVC	Pre-existing major mental health condition, cognitive deficit
Prolonged exposure or EMD interventions		
Bryant, Sackville, Dang, Moulds, and Guthrie (1999) [16]	< 2w since sustaining an injury in a MVA or workplace accident; met ASD criteria on admission; 18-60y; English language proficiency	Suicidal ideation; psychosis, mental health condition; substance abuse; TBI
Kutz, Resnik, and Dekel (2008) [17]	Intrusive acute stress symptoms had not subsided for several days; symptoms consisted of re-experiencing the traumatic event (mentally; physical sensation; intense preoccupation with the event)	SUDS score ≤5; acute grief; severe protracted dissociative responses

Rothbaum et al. (2012) [18]	ED presentation < 72h post trauma; 18-65y; met PTSD diagnostic criteria; English language proficiency; alert; retained memory of traumatic event	LOC > 5mins; intoxicated
Shalev et al. (2012) [19] Shalev et al. (2016) [20]	18-70y; local resident, acute PTSD symptoms (with or without dissociation)	Sustained an injury requiring > 7d hospital admission; unconscious on admission; medical condition preventing ability to consent; lack of Hebrew, Arabic or English language proficiency
Multidisciplinary/collaborative care interventions		
Vikane et al. (2017) [21]	16-55 years; Admitted to Dept of Neurosurgery for TBI; ICD-10 diagnosed S06.0-S06.9 with sustained symptoms 6-8 weeks post mTBI; hospitalised for >5h	Major psychiatric diseases or previous head trauma that impacted working skills; unemployment within the last six months; lack of Norwegian language skills; out of work diagnosed with substance abuse
Wu et al. (2017) [22]	Admitted to participating hospital; >18yrs; sustained injuries related to road trauma	LOS <5 days; receiving palliative care; unable to be followed up
Zatzick et al. (2001) [23]	14-65y; English language proficiency	Sustained an injury with AIS > 5
Zatzick et al. (2004) [24]	English-speaking survivors of intentional or unintentional injuries; >18y; live within 50 miles of trauma centre, symptomatic PTSD or depression	Severe injuries that prevent participation; self-inflicted injuries; active psychosis; incarcerated; recent history of violence
Zatzick et al. (2013) [25]	Sustained an injury requiring hospital admission; 18+y; English language proficiency	Required immediate psychiatric intervention; incarcerated; not local resident; history of violence
Zatzick et al. (2015) [26]	Sustained an injury requiring hospital admission for> 24h; 14+y; elevated PTSD symptoms	Required immediate psychiatric intervention; incarcerated; not local resident; history of violence
Education or information-focused interventions		
Bell et al. (2008) [27]	ED admission < 48h post injury; GCS 13-15; LOC < 30min; self-reported/witnessed confusion < 24h; English language proficiency; permanent residence	< 16y; intracranial abnormality; ICU admission; serious non-extremity injury; neurological disease; terminal disease; pre-existing mental health condition; sexual assault; > 2d hospitalisation for head injury in past 2y; AOD misuse; prisoners; in custody.

Bugg et al. (2009) [28]	18-65y; scored >50 on the ASDS; sustained injury through road traffic accident (RTA), occupational injury or assault	Non-English speaking
Scholes et al. (2007) [29]	Sustained an injury due to MVC, workplace accident or assault; 16-65y	Lack of English language proficiency

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Author disclosure statements

Statement 1: Role of Funding Sources

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Statement 2: Contributors

MJG: conception and development of the protocol and search strategy, screening and assessment of studies, quality assessment, analysis and interpretation of the data, writing and paper review.

AL: meta-analysis, interpretation of the data, writing of the paper.

GD: data extraction, quality assessment, meta-analysis and interpretation of the data, paper review.

BC: conception and development of the protocol and search strategy, literature search, screening and assessment of studies, data extraction, paper review.

BG: conception and development of the protocol, paper review.

Statement 3: Conflict of Interest

All authors declare that they have no conflict of interest.

Author biography

Dr Giummarra is a Research Fellow in the Pre-hospital, Emergency and Trauma Group in the Department of Epidemiology and Preventive Medicine and Institute for Safety, Compensation and Recovery Research, Monash University. She completed honours in psychology at the University of Melbourne (2002), and a PhD in Psychological Sciences at Monash University (2011). Dr Giummarra has nearly 50 peer-reviewed publications, was the 2017 Australian Pain Society "Rising Star" award recipient, and has received fellowships from the NHMRC (Early Career Fellowship, 2012-16) and ARC (Discovery Early Career Research Award, 2017-20). Her research investigates pain and mental health after injury, and the social context of pain and suffering. Dr Giummarra is currently working with the Victorian Transport Accident Commission to investigate the role of compensation system experience in chronic pain and function after injury, and the potential to reduce the incidence and impact of pain and mental health conditions through early intervention.

Figure Captions

Figure 1. Study inclusion based on the Preferred Reporting Items for Systematic-Reviews and Meta-analyses.

Figure 2. Risk of bias judgements for all papers.
Notes: risk of bias criteria of defining the intervention, blinding of personnel, assessors/analysts and deviations from protocol contributed to the overall "trial performance" assessment; measurement, missing data analytic approach and confounders contributed to the "detection and analysis" assessment.
(THIS FIGURE SHOULD BE PRINTED IN COLOUR)

Figure 3. Forest plots comparing intervention and control groups on PTSD outcomes measured 0-3 months, 3-6 months and 6-12 months post-intervention.
Abbreviations: CI, confidence interval; IV, inverse variance; df, degrees of freedom; Random, random-effect model; SD, standard deviation. *Notes:* Meta-analyses do not take baseline means and SDs into account. Sample size has been halved for Bryant, Moulds, Guthrie, and Nixon (2003) to account for the inclusion of the Intrusion (top row) and Avoidance (second row) subscales of the Impact of Events Scale. SDs were calculated for Mouthaan et al. (2013), Zatzick et al. (2013) and Zatzick et al. (2015) using CIs in RevMan. IES-R results used in meta-analysis for Mouthaan et al. (2013) at 3, 6 and 12 months. PDS was used in meta-analysis at 1 month for Rothbaum et al. (2012) and SDs were calculated from the standard error of the mean in RevMan. Used PDS frequency scale results for Ehlers et al. (2003) and self-help group was used as a control. Used total CAPS score, Prolonged Exposure as intervention group and waitlist as control for Shalev et al. (2012). Used 3, 6 and 12 month PCL-C data for Zatzick et al. (2013) and 3 and 6 month data for Zatzick et al. (2015).

Figure 4. Forest plots comparing intervention and control groups on depression outcomes measured at 0-3 months, 3-6 months and 6-12 months post-intervention.
Abbreviations: CI, confidence interval; IV, inverse variance; df, degrees of freedom; Random, random-effect model; SD, standard deviation. *Notes:* Meta-analyses do not take baseline means and SDs into account. SDs were calculated for Mouthaan et al. (2013), Zatzick et al. (2013) and Zatzick et al. (2015) using Cis in RevMan. 3, 6 and 12 month data used for Mouthaan et al. (2013). SDs were calculated for Rothbaum et al. (2012) from the standard error of the mean in RevMan. Self-help group used as control group for Ehlers et al. (2003). Used 3, 6 and 12 month data for Zatzick et al. (2013) and 3 and 6 month data for Zatzick et al. (2015).

Figure 5. Forest plots comparing intervention and control groups on anxiety outcomes measured at 0-3 months, 3-6 months and 6-12 months post-intervention.
Abbreviations: CI, confidence interval; IV, inverse variance; df, degrees of freedom; Random, random-effect model; SD, standard deviation. *Notes:* Meta-analyses do not take baseline means and SDs into account. SDs were calculated for Mouthaan et al. (2013) using CIs at 3, 6 and 12 months in RevMan. Used PDS frequency scale results for Ehlers et al. (2003) and self-help group was used as a control. High risk controls used as control group for Scholes, Turpin, and Mason (2007).

Figure 6. Summary of the magnitude of effects on (a) PTSD, (b) depression and (c) anxiety from studies included in the meta-analyses compared with a threshold for clinically meaningful change.

Figure 7. Estimated population impact of risk stratified compared with standard psychological interventions on PTSD, depression and anxiety symptoms.
Abbreviations: HADS = Hospital Anxiety and Depression Checklist, PCL = PTSD Checklist, SMD = standardized mean difference.
[+] All hospitalisations for injury from 2012-13 financial reported in AIHW report by Pointer, 2015).
[++] Based on proportion meeting clinical criteria for each condition from Bryant et al., (2010).
[+++] Percent of "at risk" population likely to complete psychological therapy: 73.7% (stratified intervention) or 51.1% (standard intervention) based on the recruitment and completion rates from studies evaluating CBT, PE and multidisciplinary or collaborative care (excluding studies evaluating educational, debriefing and EMDR interventions).
[++++] See Forest plots in Figure A7, based on sample sizes for the stratified interventions (N = 991 (PTSD), N = 991 (Depression) and N = 73 (Anxiety)) and non-stratified interventions (N = 1328 (PTSD), N = 1191 (Depression) and N = 1054 (Anxiety).

Highlights

- Early intervention is recommended to prevent or reduce psychological conditions postinjury
- Early interventions effectively reduced PTSD and depression symptom severity
- CBT-based therapy, with prolonged exposure, is likely to have the greatest clinical impact
- Interventions with stepped or collaborative care will have the greatest population impact

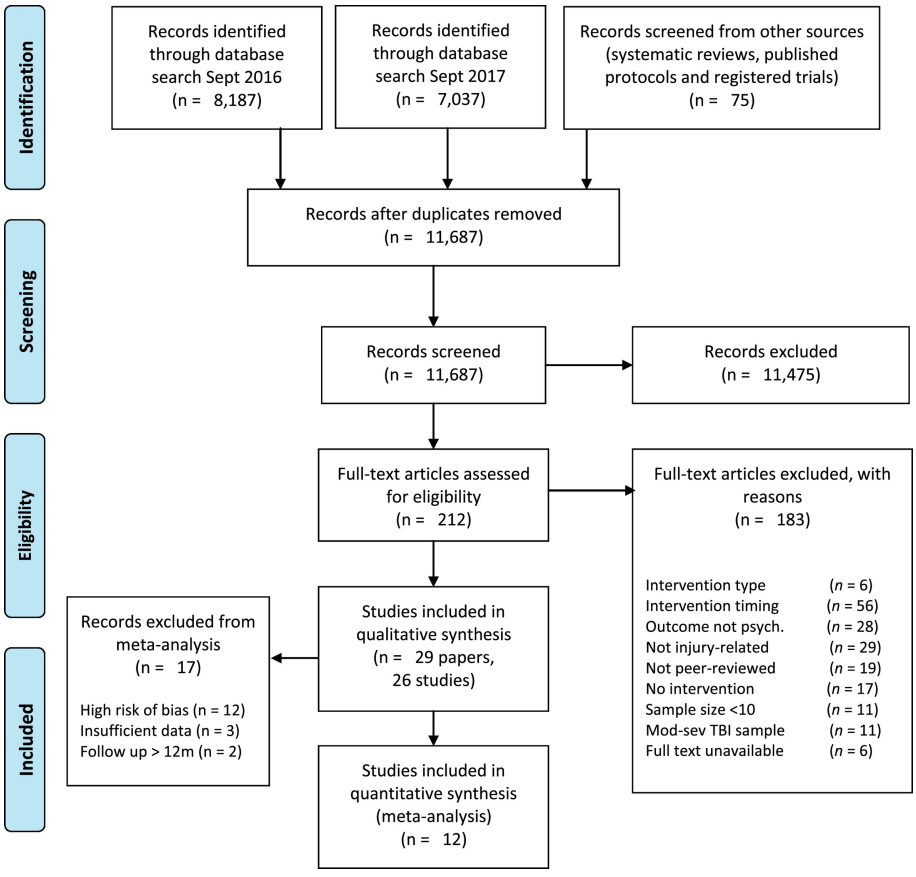

Identification
Screening
Eligibility
Included
Records identified through database search Sept 2016 (n = 8,187)
Records identified through database search Sept 2017 (n = 7,037)
Records screened from other sources (systematic reviews, published protocols and registered trials) (n = 75)
Records after duplicates removed (n = 11,687)
Records screened (n = 11,687)
Records excluded (n = 11,475)
Full-text articles assessed for eligibility (n = 212)
Full-text articles excluded, with reasons (n = 183)
Intervention type (n = 6)
Intervention timing (n = 56)
Outcome not psych. (n = 28)
Not injury-related (n = 29)
Not peer-reviewed (n = 19)
No intervention (n = 17)
Sample size <10 (n = 11)
Mod-sev TBI sample (n = 11)
Full text unavailable (n = 6)
Studies included in qualitative synthesis (n = 29 papers, 26 studies)
Records excluded from meta-analysis (n = 17)
High risk of bias (n = 12)
Insufficient data (n = 3)
Follow up > 12m (n = 2)
Studies included in quantitative synthesis (meta-analysis) (n = 12)

Figure 1

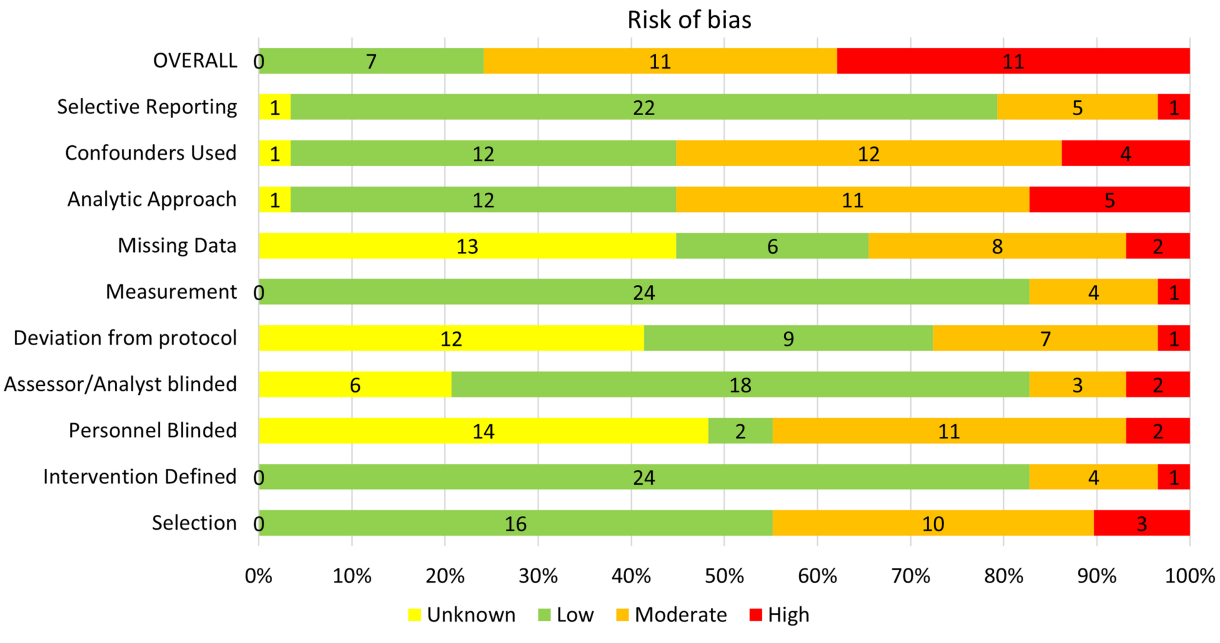
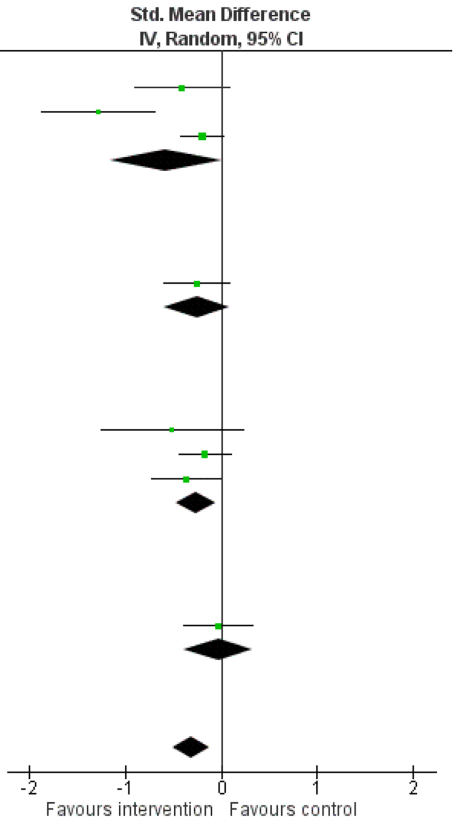

Risk of bias
OVERALL
Selective Reporting
Confounders Used
Analytic Approach
Missing Data
Measurement
Deviation from protocol
Assessor/Analyst blinded
Personnel Blinded
Intervention Defined
Selection
0 7 11 11
1 22 5 1
1 12 12 4
1 12 11 5
13 6 8 2
0 24 4 1
12 9 7 1
6 18 3 2
14 2 11 2
0 24 4 1
0 16 10 3
0% 10% 20% 30% 40% 50% 60% 70% 80% 90% 100%
Unknown
Low
Moderate
High

Figure 2

0-3 months

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
1.3.1 Cognitive and behavioural interventions								
Brunet et al. 2013	22.7	18.9	34	30.3	18	32	9.7%	-0.41 [-0.89, 0.08]
Ehlers et al. 2003	8.3	9.8	28	19.9	7.8	25	7.4%	-1.28 [-1.88, -0.69]
Mouthaan et al. 2013	9.7	10.6	151	11.8	10.5	149	19.0%	-0.20 [-0.43, 0.03]
Subtotal (95% CI)			**213**			**206**	**36.1%**	**-0.58 [-1.16, 0.00]**
Heterogeneity: Tau² = 0.21; Chi² = 11.16, df = 2 (P = 0.004); I² = 82%								
Test for overall effect: Z = 1.95 (P = 0.05)								
1.3.2 Prolonged exposure interventions								
Rothbaum et al. 2012	18.9	19.4	69	23.8	18.9	68	14.4%	-0.25 [-0.59, 0.08]
Subtotal (95% CI)			**69**			**68**	**14.4%**	**-0.25 [-0.59, 0.08]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 1.48 (P = 0.14)								
1.3.3 Multidisciplinary/collaborative care interventions								
Zatzick et al. 2001	33.1	11	14	39.9	14.5	15	5.3%	-0.51 [-1.25, 0.23]
Zatzick et al. 2013	45.9	15.4	104	48.6	15.9	103	17.0%	-0.17 [-0.44, 0.10]
Zatzick et al. 2015	41.2	14.1	60	46.4	14.5	61	13.6%	-0.36 [-0.72, -0.00]
Subtotal (95% CI)			**178**			**179**	**35.9%**	**-0.26 [-0.47, -0.05]**
Heterogeneity: Tau² = 0.00; Chi² = 1.14, df = 2 (P = 0.56); I² = 0%								
Test for overall effect: Z = 2.47 (P = 0.01)								
1.3.4 Education or information-based interventions								
Scholes et al. 2007	18.2	12.2	58	18.5	11.4	62	13.6%	-0.03 [-0.38, 0.33]
Subtotal (95% CI)			**58**			**62**	**13.6%**	**-0.03 [-0.38, 0.33]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.14 (P = 0.89)								
Total (95% CI)			**518**			**515**	**100.0%**	**-0.32 [-0.51, -0.13]**
Heterogeneity: Tau² = 0.04; Chi² = 14.71, df = 7 (P = 0.04); I² = 52%								
Test for overall effect: Z = 3.24 (P = 0.001)								
Test for subgroup differences: Chi² = 2.73, df = 3 (P = 0.43), I² = 0%								



3-6 months

Study or Subgroup	Experimental Mean	SD	Total	Control Mean	SD	Total	Weight	Std. Mean Difference IV, Random, 95% CI
2.3.1 Cognitive and behavioural interventions								
Bryant et al. 2003	11.3	9.8	6	20.2	9.7	6	3.4%	-0.84 [-2.05, 0.36]
Bryant et al. 2003	7.3	7.2	6	15.7	10.5	6	3.4%	-0.86 [-2.07, 0.35]
Mouthaan et al. 2013	8.2	8.7	151	9.8	10.5	149	18.2%	-0.17 [-0.39, 0.06]
O'Donnell et al. 2012	32	21	22	52.5	33.1	20	8.8%	-0.73 [-1.36, -0.11]
Subtotal (95% CI)			**185**			**181**	**33.6%**	**-0.44 [-0.85, -0.04]**
Heterogeneity: Tau² = 0.06; Chi² = 4.70, df = 3 (P = 0.20); I² = 36%								
Test for overall effect: Z = 2.15 (P = 0.03)								
2.3.2 Prolonged exposure interventions								
Shalev et al. 2012	28.6	25	56	50.6	27.5	79	14.7%	-0.83 [-1.18, -0.47]
Subtotal (95% CI)			**56**			**79**	**14.7%**	**-0.83 [-1.18, -0.47]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 4.54 (P < 0.00001)								
2.3.3 Multidisciplinary/collaborative care interventions								
Zatzick et al. 2001	42.5	18.2	12	36.1	11.7	14	6.6%	0.41 [-0.37, 1.19]
Zatzick et al. 2013	40.6	17	104	49.9	16.9	103	16.8%	-0.55 [-0.82, -0.27]
Zatzick et al. 2015	42.2	14.7	60	47.6	14.5	61	14.6%	-0.37 [-0.73, -0.01]
Subtotal (95% CI)			**176**			**178**	**38.0%**	**-0.31 [-0.70, 0.08]**
Heterogeneity: Tau² = 0.07; Chi² = 5.25, df = 2 (P = 0.07); I² = 62%								
Test for overall effect: Z = 1.56 (P = 0.12)								
2.3.4 Education or information-based interventions								
Scholes et al. 2007	14.8	11.9	49	14.7	12.1	50	13.7%	0.01 [-0.39, 0.40]
Subtotal (95% CI)			**49**			**50**	**13.7%**	**0.01 [-0.39, 0.40]**
Heterogeneity: Not applicable								
Test for overall effect: Z = 0.04 (P = 0.97)								
Total (95% CI)			**466**			**488**	**100.0%**	**-0.39 [-0.63, -0.15]**
Heterogeneity: Tau² = 0.07; Chi² = 20.86, df = 8 (P = 0.008); I² = 62%								
Test for overall effect: Z = 3.17 (P = 0.001)								
Test for subgroup differences: Chi² = 9.82, df = 3 (P = 0.02), I² = 69.4%								

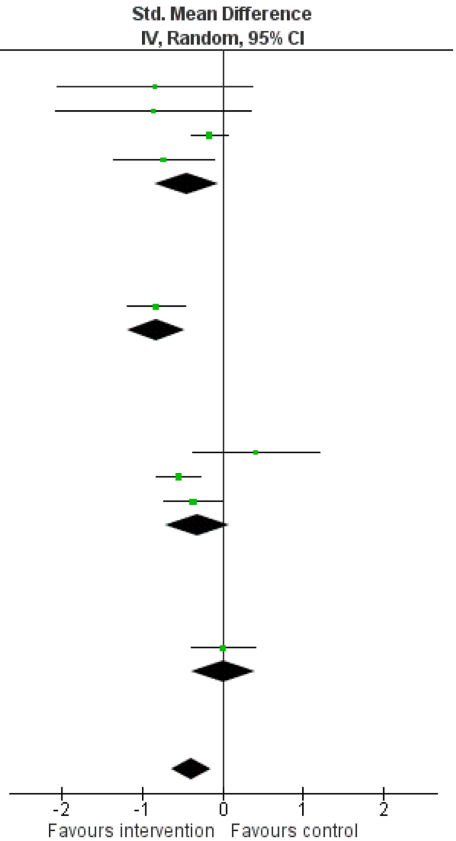


Figure 3A

6 – 12 months

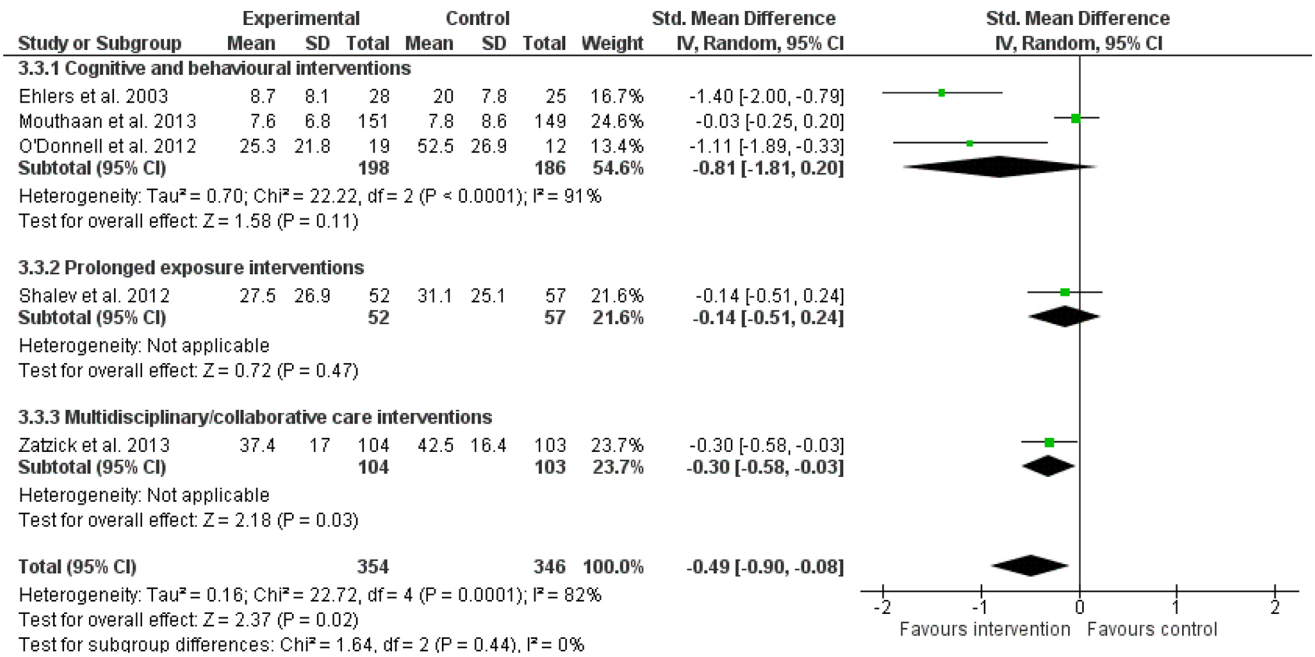
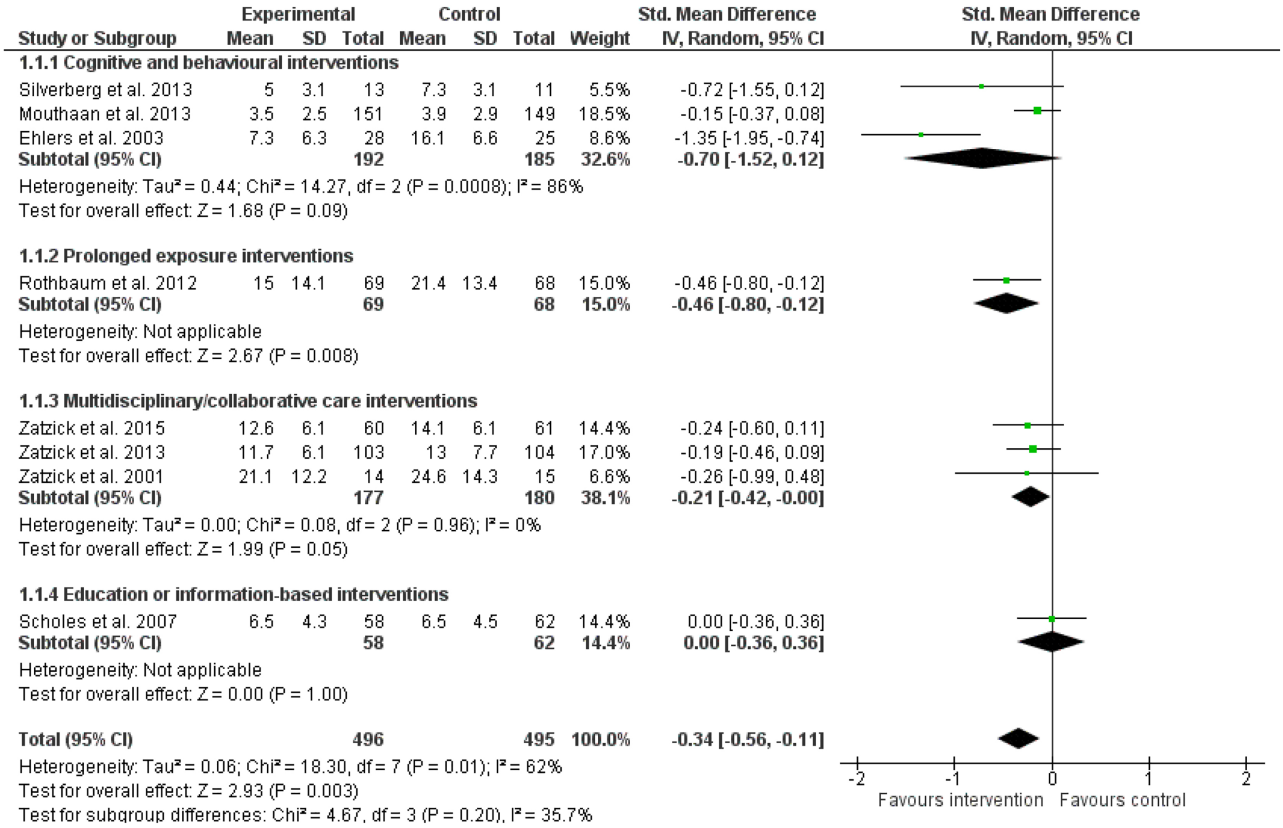


Figure 3B

0-3 months



3-6 months

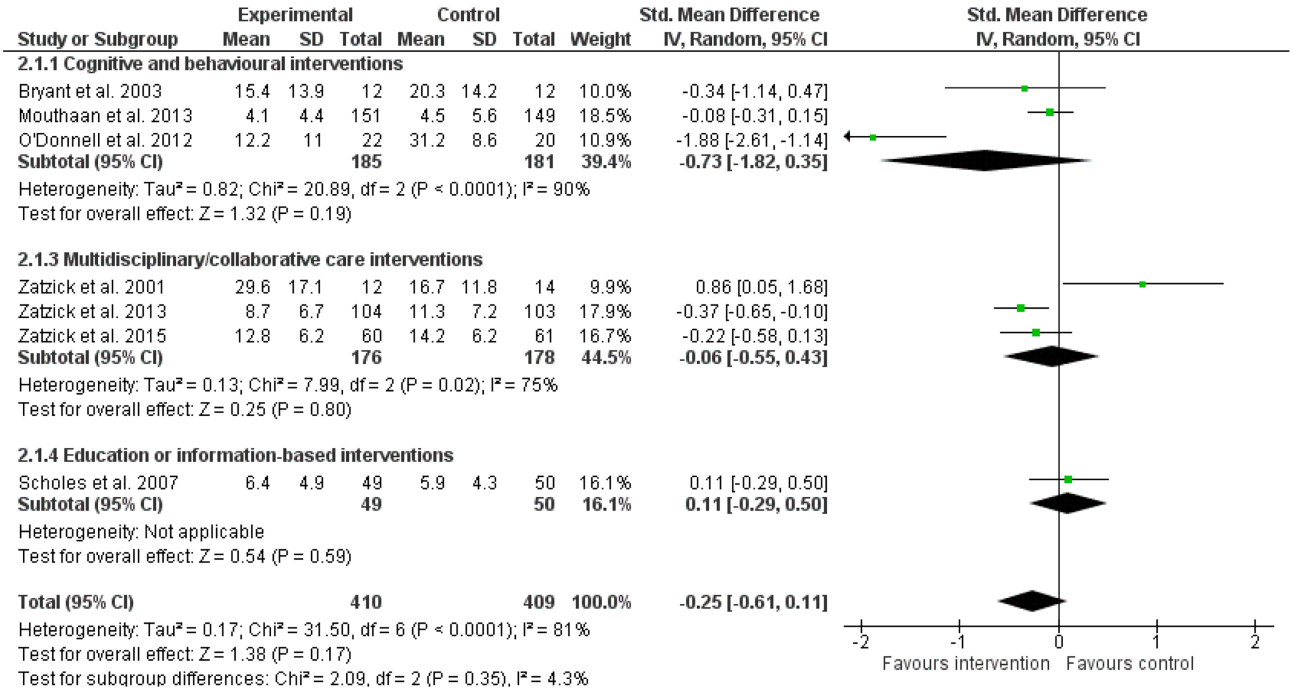


Figure 4A

6 – 12 months

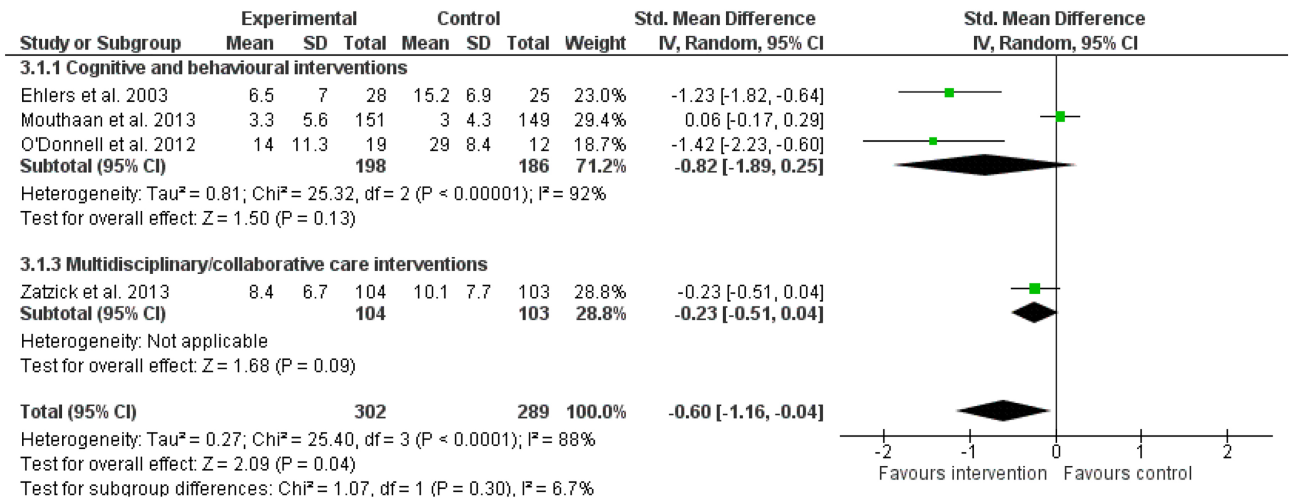
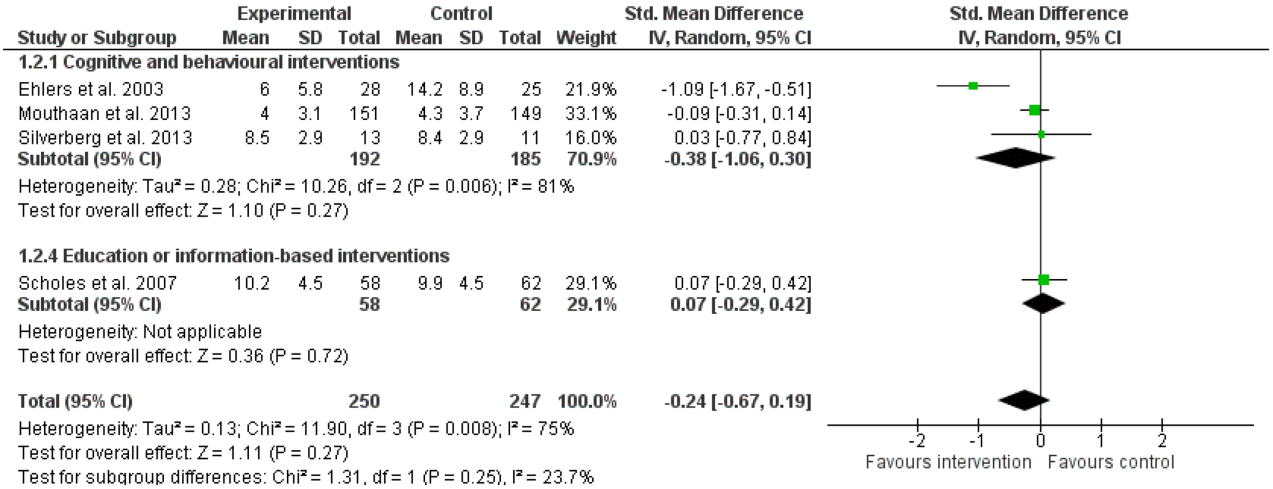
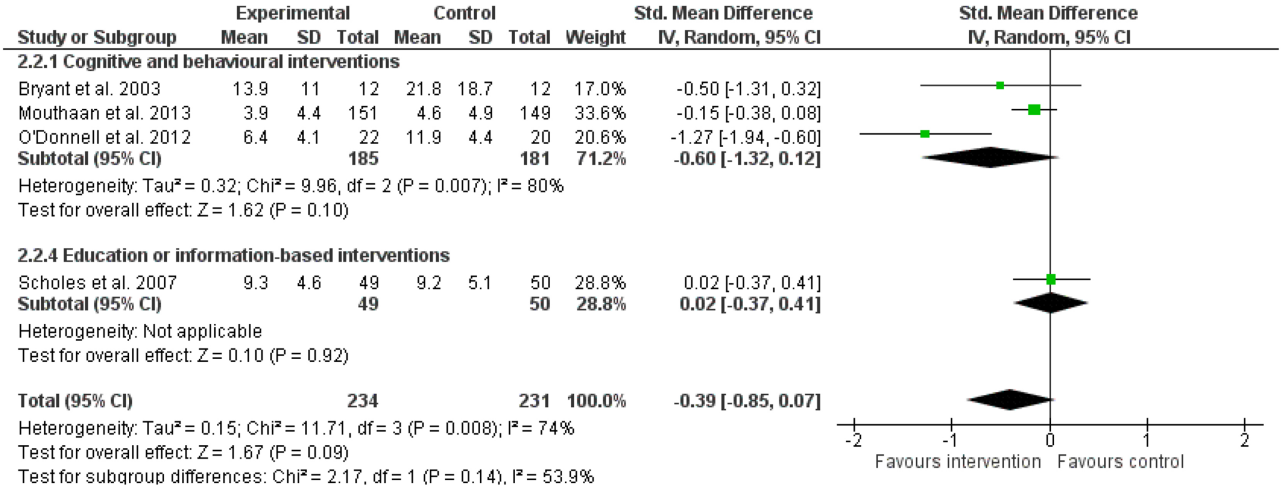


Figure 4B

0-3 months



3-6 months



6 – 12 months

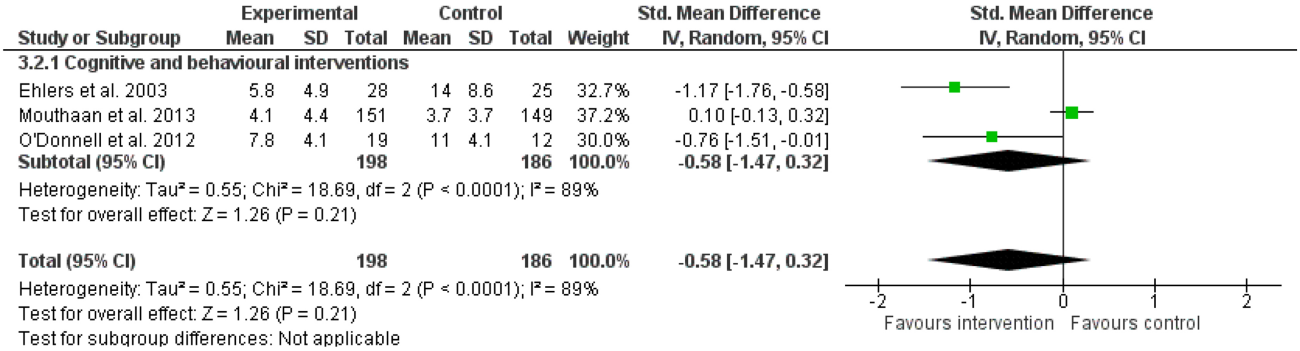


Figure 5

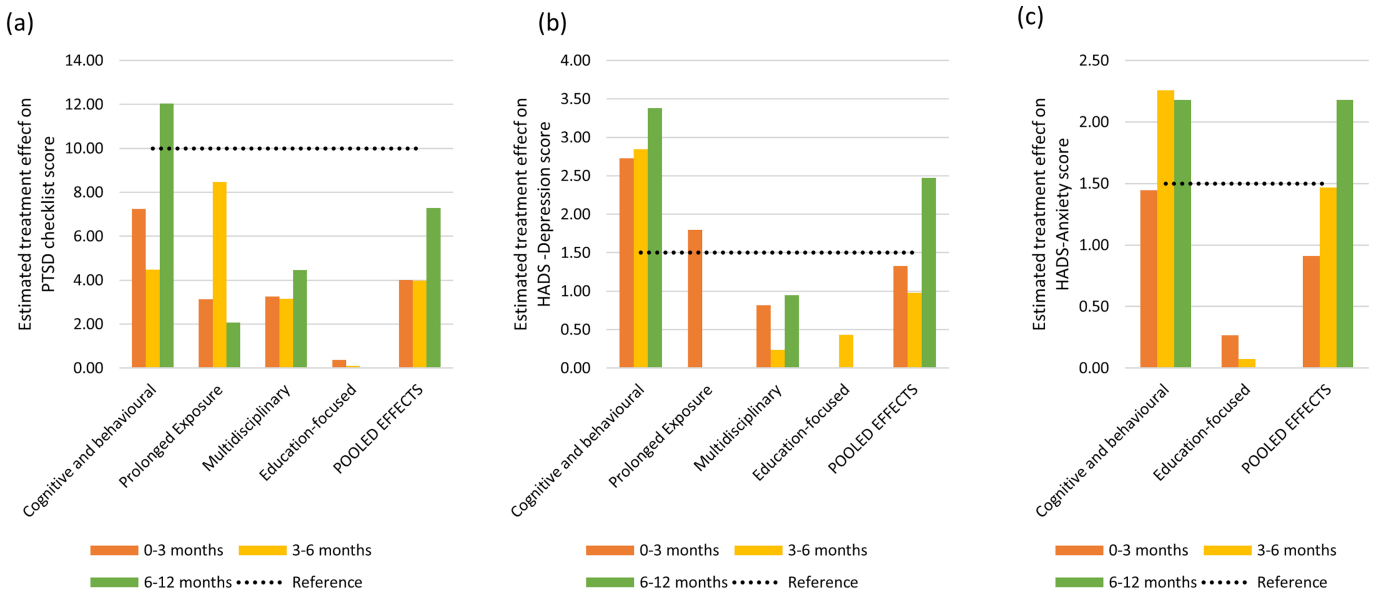

(a)
Estimated treatment effecf on PTSD checklist score
14.00
12.00
10.00
8.00
6.00
4.00
2.00
0.00
Cognitive and behavioural
Prolonged Exposure
Multidisciplinary
Education-focused
POOLED EFFECTS
0-3 months
3-6 months
6-12 months
Reference
(b)
Estimated treatment effecf on HADS -Depression score
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
0.00
Cognitive and behavioural
Prolonged Exposure
Multidisciplinary
Education-focused
POOLED EFFECTS
0-3 months
3-6 months
6-12 months
Reference
(c)
Estimated treatment effecf on HADS-Anxiety score
2.50
2.00
1.50
1.00
0.50
0.00
Cognitive and behavioural
Education-focused
POOLED EFFECTS
0-3 months
3-6 months
6-12 months
Reference

Figure 6

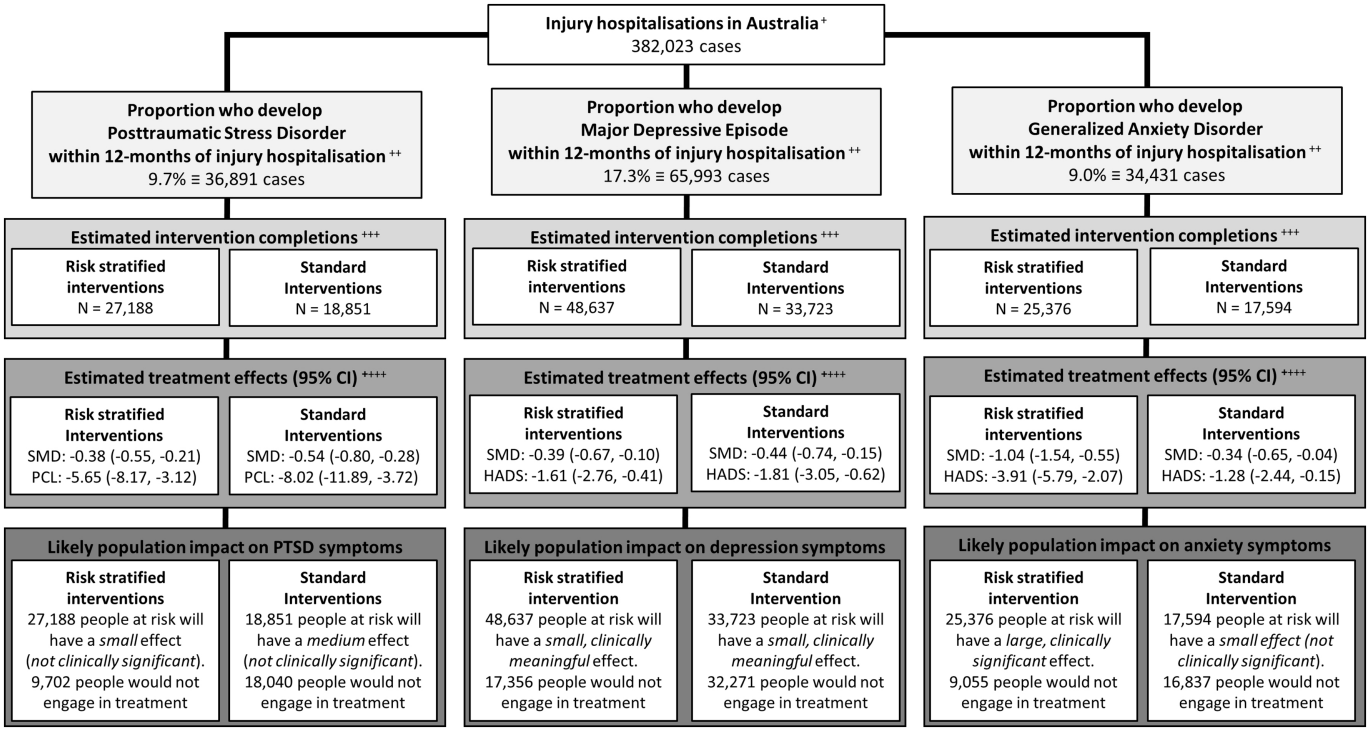

Injury hospitalisations in Australia +
382,023 cases
Proportion who develop Posttraumatic Stress Disorder within 12-months of injury hospitalisation ++
9.7% ≡ 36,891 cases
Proportion who develop Major Depressive Episode within 12-months of injury hospitalisation ++
17.3% ≡ 65,993 cases
Proportion who develop Generalized Anxiety Disorder within 12-months of injury hospitalisation ++
9.0% ≡ 34,431 cases
Estimated intervention completions +++
Risk stratified interventions N = 27,188
Standard Interventions N = 18,851
Estimated intervention completions +++
Risk stratified interventions N = 48,637
Standard Interventions N = 33,723
Estimated intervention completions +++
Risk stratified interventions N = 25,376
Standard Interventions N = 17,594
Estimated treatment effects (95% CI) ++++
Risk stratified Interventions SMD: -0.38 (-0.55, -0.21) PCL: -5.65 (-8.17, -3.12)
Standard Interventions SMD: -0.54 (-0.80, -0.28) PCL: -8.02 (-11.89, -3.72)
Estimated treatment effects (95% CI) ++++
Risk stratified interventions SMD: -0.39 (-0.67, -0.10) HADS: -1.61 (-2.76, -0.41)
Standard Interventions SMD: -0.44 (-0.74, -0.15) HADS: -1.81 (-3.05, -0.62)
Estimated treatment effects (95% CI) ++++
Risk stratified interventions SMD: -1.04 (-1.54, -0.55) HADS: -3.91 (-5.79, -2.07)
Standard Interventions SMD: -0.34 (-0.65, -0.04) HADS: -1.28 (-2.44, -0.15)
Likely population impact on PTSD symptoms
Risk stratified interventions 27,188 people at risk will have a small effect (not clinically significant). 9,702 people would not engage in treatment
Standard Interventions 18,851 people at risk will have a medium effect (not clinically significant). 18,040 people would not engage in treatment
Likely population impact on depression symptoms
Risk stratified intervention 48,637 people at risk will have a small, clinically meaningful effect. 17,356 people would not engage in treatment
Standard Intervention 33,723 people at risk will have a small, clinically meaningful effect. 32,271 people would not engage in treatment
Likely population impact on anxiety symptoms
Risk stratified intervention 25,376 people at risk will have a large, clinically significant effect. 9,055 people would not engage in treatment
Standard Intervention 17,594 people at risk will have a small effect (not clinically significant). 16,837 people would not engage in treatment

Figure 7