Abstract

Aim
To determine which factors relate to the development of posttraumatic stress disorder, in adult patients who are admitted to critical care units.

Background
Patient survival rates from critical care areas are improving each year and this has led to interest in the long term outcomes for patients who have been discharged from such environments. Patients typically require invasive and extensive treatment, which places a stress on physical and mental health. Prevalence estimates of posttraumatic stress disorder in the critical care discharge population vary from 5-63%, yet it remains unclear what the predisposing factors are.

Design. A systematised review

Method
Subject heading and keyword searches were conducted in MEDLINE, CINAHL, PsycINFO and ScienceDirect, with 23 articles identified that examined the relationship between critical care and the development of posttraumatic stress disorder.

Results
Three main themes were identified; Critical Care Factors, Patient Factors and Experience Factors. Eight key and 3 potential causative factors were found: younger age, female, previous psychiatric history, length of ICU stay, benzodiazepine sedation, use of stress hormones, delusional memory and traumatic memory, delirium, GCS score of ≤9 on admission & use of mechanical restraint

Conclusions
Posttraumatic stress reactions can be strongly related to the development and presence of traumatic and delusional memories. Younger patients may exclude themselves from research to avoid their traumatic thoughts. The role of prior psychiatric illness is unknown. Distinction between 'factual' and 'false' or delusional memory as occurs in the literature maybe unhelpful in understanding trauma reactions.

Relevance to clinical practice
There are around 38,000 occupied critical care beds each year in England. The scale of the issue is therefore substantial. Risk factors can be isolated from available evidence and provide a rudimentary risk assessment tool to inform practice development in this area.

Introduction and background

The classic premise of post-traumatic stress disorder (PTSD) as a reaction to warfare or natural disasters is challenged by a small but growing body of international evidence that suggests it can be developed following road traffic accidents, childbirth, domestic violence and sexual exploitation (Jones et al., 2001a; Holeva et al., 2002; Olde, et al., 2006; Weinert & Meller, 2007) and also medical illness. In a German study, the prevalence in medical populations (at 1 year follow up) has been estimated to be 4% of patients who have had a myocardial infarction, to 14% of patients diagnosed with cancer (Mehnert & Koch, 2007). This is in contrast to 0.37% in the general global population (WHO, 2001). In the critical care population Davydow et al. (2008) reported 19% prevalence. Such figures provide a rationale for the study of posttraumatic stress disorder in critical care survivors, who are reported to have higher prevalence rates of posttraumatic stress reactions than typically 'high-risk' populations (Davydow et al., 2008; Richardson et al., 2010). Knowledge of the risk factors could potentially inform selection of patients for follow post ICU discharge.

The International Classification of Diseases 10 (WHO, 1992) defines posttraumatic stress disorder as:

> Arises as a delayed or protracted response to a stressful event or situation (of either brief or long duration) of an exceptionally threatening or catastrophic nature, which is likely to cause pervasive distress in almost anyone...Typical features include episodes of repeated reliving of the trauma in intrusive memories ("flashbacks"), dreams or nightmares, occurring against the persisting background of a sense of "numbness" and emotional blunting, detachment from other people, unresponsiveness to surroundings, anhedonia, and avoidance of activities and situations reminiscent of the trauma. There is usually a state of autonomic hyperarousal with hypervigilance, an enhanced startle reaction, and insomnia. Anxiety and depression are commonly associated with the above symptoms and signs, and suicidal ideation is not infrequent. The onset follows the trauma with a

latency period that may range from a few weeks to months. The course is fluctuating but recovery can be expected in the majority of cases' (F43.1).

These symptoms must have occurred for more than 1 month following exposure to a trauma and be severe enough to cause 'clinically significant distress' and impairment of social or occupational functioning, negative alterations in cognition and mood', as well as an exclusion criteria for anyone whose symptoms or disturbance relate to the use of illicit substances, medication or other illness.

Patients are typically admitted to critical care environments, such as intensive care units or high dependency areas, due to life threatening illness, injury or for post-operative monitoring following major surgery. Patients usually have some level of organ dysfunction, resulting in often invasive and intensive treatment e.g. mechanical ventilation and extensive monitoring, usually by a single nurse (Adhikari et al., 2010). It is estimated that more than 130,000 patients are admitted to intensive care units each year, and that number is significantly higher if high dependency unit patients are also considered (Davydow et al., 2008). With more survivors come different challenges, as patients who previously may not have survived are returning to acute ward areas and eventually back into the community with potentially life altering deficits and increased levels of physical health needs (Kim et al., 2010). This has led to a shift in the body of research with an increasing demand for evidence that describes the problems and guides the management of post-discharge critical care patients in non-critical care settings (Angus & Carlet, 2003). Long-term outcomes were not considered to be relevant to intensivists, but a growing body of literature is increasingly stating that patients who are discharged from critical care areas are likely to face an increasing amount of problems with both their physical and psychological health such as depression,

anxiety and posttraumatic stress disorder (Hauer et al., 2009; Rattray et al., 2010; Peris, et al., 2011).

Aim

This systematized review aims to determine which factors relate to the development of posttraumatic stress disorder, in adult patients who are admitted to critical care units.

Method

The process of literature searching that defines this paper as a 'systematized review' (Grant & Booth, 2011) follows a systematic process but without exclusion based on quality criteria. However, although systematized reviews do not have consistent quality standards, this review follows a comprehensive systematic process attempting to locate all relevant literature. The PICO (patient, intervention, comparison, outcome) framework informed the development of a focused search question (Bettany-Saltikov, 2012). Firstly the Patient group, intervention and outcome were defined:

- Patient group; Adult patients
- Intervention: Admission to critical care setting
- No comparison
- Outcome: Development of PTSD following discharge.

This led to the search question: What are the causative factors for posttraumatic stress disorder following admission to a critical care unit for adult patients?

Search Strategy

The databases MEDLINE (1946-2013), CINAHL (1937-2013), PsycINFO (1967-2013) and Science Direct (1937-2013) were selected as their content is diverse in physical health related research. Subject headings and key word searches were conducted using terms related to: critical care, posttraumatic stress disorder, cause

and experience (See Table 1). Searches were completed on 8th Nov 2013 and updated 8th Jan 2015.

INSERT table 1 here

Inclusion & Exclusion Criteria

The search strategy was informed by the formulated search question. Therefore, adult (18+) patients who experience PTSD as a medical diagnosis were included. English language was also an inclusion criterion. Studies which were excluded were those that focused on:

- family members or health professionals
- children.
- acute stress disorder
- prevalence studies
- other mental disorders eg anxiety/depression.
- PTSD following traumatic (life) events e.g. veterans or natural disaster.

A number of key research papers were identified prior to conducting the initial scoping search, to determine whether the selected key terms were suitably sensitive to identify these papers. In particular, the PsychINFO database differed in their key word categories due to the nature of their psychological based literature, requiring the addition of 'client' as well as 'patient'.

Grey literature from The Royal College of Psychiatrists, PTSD Resolution, MIND, the Society for Critical Care Medicine and the Intensive Care Society failed to provide any relevant guidance on the management of posttraumatic stress disorder relating to medical intervention or critical care admission.

Results

A total of 284 articles were yielded in the initial scoping search, which was reduced to 123 following the removal of duplicate studies. Sixty eight articles were retrieved and 23 of these met the inclusion criteria.

The 23 identified articles were subject to data extraction (see table 2) and review before identifying core themes. Three core themes were identified; Critical Care Factors, Patient Factors and Experience Factors. Table 3 shows the key predictor variables identified within each theme.

INSERT TABLE 2 HERE

Patient follow up ranged from 2 months to 8 years, although most studies followed up at several time points within the first 12 months post-ICU discharge.

INSERT TABLE 3 HERE

Findings and discussion

Critical care factors

Critical Care factors relate to the events and interventions that may occur throughout a patient's admission to a critical care unit. Longer length of stay is correlated with PTSD symptomology with the longest stay and follow up (Kapfhammer et al., 2004a; Rattray et al., 2005; Davydow et al., 2009). However longer hospital admission may account for this rather than ICU admissions and may be the true PTSD predictor (Boer et al., 2007). Nevertheless, ongoing practical and psychological support has been found to be needed at 6 month follow up where average quality of life scores were significantly below the Australian norms (Aitken et al., 2012). It is possible that length of stay is a proxy for patient acuity, as patients with ARDS have a higher mortality rate (43%) than other type of ICU patients (Zambon & Vincent, 2008). It may be more conservative to align with the idea of an exposure-response relationship between longer intensive care stays and the incidence of posttraumatic outcome (Rattray et al, 2005). A unique study, Peris et al. (2011) found that being admitted to intensive care with a Glasgow coma scale score of 9 or below was the only indicative factor for a significant IES score at 12 months post ICU discharge.

Sedation practices and the presence of delirium arose as potential moderators in the critical care and posttraumatic stress symptomology relationship. Girard et al. (2007) found that cumulative lorazepam dose significantly predicted PTSD symptomology, with every 10 milligram increase in lorazepam administered, PTSS-10 score increased by 0.39 points.

However, they found that the other sedative drugs used such as morphine, fentanyl, propofol and midazolam did not significantly predict PTSS-10 scores. Jones et al. (2007) examined the relationship between sedative administration, the development of clinical delirium and posttraumatic stress symptomology following ICU discharge and found that higher level of benzodiazepine administration resulted in greater prevalence of delirium related to the use of a combination of benzodiazepines. It may be plausible to state that patients who require more sedation may be demonstrating more signs of agitation, which is a clinical symptom of delirium and therefore disease acuity, may be the true underlying factor (Sessler et al., 2002). Therefore the underlying relationship behind sedation levels and posttraumatic stress disorder may be the presence of delirium. Jones et al. (2007) found that patients who were mechanically restrained experienced longer periods of agitation, and were significantly more likely to experience later PTSD symptomology. But as only one of the patients who had to be restrained actually recalled this at follow up, this may suggest that it is the presence of agitation and delirium that are clinically important.

Another critical care factor in the development of PTSD is the exogenous administration and role of stress hormones and hormone deregulation. Patients in intensive care are frequently treated with inotropic medication and vasopressors (adrenaline/noradrenaline), which stimulate the sympathetic nervous system to maintain sufficient cardiac output (Gillie et al., 2005). Other drugs e.g. hydrocortisone are used to stimulate the hypothalamus, pituitary glands and adrenal sections (HPA axis) that can be become deregulated during periods of critical illness (Dellinger et al., 2008). Schelling et al. (2001) conducted a double blind randomised controlled trial, in which 20 patients were either treated with hydrocortisone (cortisol) (n=9) or a placebo control (n=11). They found that patients who received hydrocortisone recovered more quickly, required less inotropic support in the intra-intensive

care period and were less likely to receive a diagnosis of posttraumatic stress disorder at 2.5-years post discharge. In addition, serum cortisol (hydrocortisone component) levels were lower in the patients with posttraumatic stress disorder throughout their intensive care stay. In an RCT with 91 ICU patients, Shelling et al. (2004) found that by administering stress doses of hydrocortisone, PTSS-10 scores at a 6 month follow-up were reduced. Similarly, Hauer et al. (2009) suggest that pathologically lower basal serum cortisol levels were associated with later increase incidence of chronic stress and a diagnosis of posttraumatic stress disorder.

Schelling et al (2001) proposed that hydrocortisone regulates the systemic inflammatory response which is frequently experienced by patients who are in a critical illness state. The mechanism of action, through which the administration of stress hormones is thought to lead to a higher incidence of posttraumatic stress symptomology, is via the facilitation of memory creation. Schelling (2002) suggests that stress hormones, particularly catecholamines and glucocorticoids (adrenaline and noradrenaline) facilitate the consolidation of emotional memory, discussed within the Experience Factors.

Patient factors

The next theme relates to patient factors; the demographic characteristics of the patients involved in each of the research studies. Age and gender have both been examined in relation to the development of posttraumatic stress disorder, with all indicating similar trends. People who are older (over 50) appear to be less likely to report symptoms of PTSD than younger people who score more highly on various PTSD scores at follow up (Scragg et al., 2001; Rattray et al., 2005; Boer et al., 2007; Girard et al., 2007; Wallen et al., 2008). Boer et al. (2007) found that non-responders were significantly younger than responders, perhaps

demonstrating the 'avoidant' component of posttraumatic stress disorder; if younger patients are experiencing more symptoms then they may be excluding themselves when approached to participate in research to avoid triggering the trauma they potentially experienced whilst in critical care. This may also be the case when considering gender differences in the prevalence of posttraumatic stress disorder with four studies indicating that women were more likely to develop posttraumatic stress reactions (Scragg et al., 2001; Girard et al, 2007; Samuelson et al., 2007). Although not supported by Rhodes et al. (2002) there appears to be a general trend in relation to the factors that lead to the development of posttraumatic stress symptomology; being younger (below aged 50) and female.

Another patient related factor that was found to link to the development of posttraumatic stress reactions was having previously experienced psychiatric illness. Having a pre ICU diagnosis of depression and alcohol dependence predicted higher scores on the Posttraumatic Stress Disorder Checklist (Davydow et al., 2008; Davydow et al. 2009). Jubran et al. (2010) found that all their participants who were diagnosed with posttraumatic stress disorder by structured clinical interview, had experienced a previous psychiatric illness, compared with 31% (n=72) of those who had no diagnosable PTSD. However, as this statistic suggests, previous psychiatric illness is not a reliable prediction variable, as 69% of the participants who had no evidence of posttraumatic stress disorder had previously experienced psychiatric illness. Not all of the included literature screened for previous psychiatric illness, but 6 studies excluded this patient group from inclusion in their study (Jones et al., 2001b; Schelling et al., 2001; Kapfhammer et al., 2004a; Kapfhammer et al., 2004b; Capuzzo et al., 2005; Jones et al., 2007). This exclusion criteria was found to be common across studies examining posttraumatic stress disorder, with the suggestion that post ICU follow up could measure pre ICU trauma in patient groups who had sustained non-accidental injury or had a

particularly traumatic history rather than the trauma of a critical care setting (Davydow et al., 2008). It may be more helpful to determine the role of prior psychiatric illness in the development of later posttraumatic stress reactions by controlling for presence of these factors within a sample. Davydow et al. (2009) categorised the presenting complaint of their sample, controlling for patients who were admitted due to non-accidental self-injury (attempted suicide/self-harm), accidental injury (road traffic accident) or general medical condition (ARDS), therefore allowing for control and comparison in later regression analyses. It is difficult to assess the degree to which previous psychiatric illness impacts on the later development of PTSD due to the common practice of excluding these groups from research samples, and it will not be made clearer until further research is conducted with appropriate variable control.

Experience factors

Experience factors relate to memory and delusions. The role of memory in critical care literature has been discussed widely (Davydow et al., 2008). Traumatic memories are categorised in the literature as being related to factual remembering of events during intensive care admission (Jones et al., 2001b). Hauer et al. (2009) provided a comprehensive list of traumatic memory categories, which were based on the Intensive Care Experience Questionnaire (ICE-Q) (Rattray et al., 2004), including feelings of anxiety/panic, respiratory distress, pain and nightmares/hallucinations. It has been suggested that delusional memory were events in the intensive care unit that were misinterpreted by the patient, therefore distorted and 'false' in some way, for example being intubated; traumatic memory may relate to remembering the procedure, feeling helpless and breathless, compared to delusional memory which may involve interpreting this action as violent, being suffocated or being under attack by the health professional (Jones et al., 2007). The main distinction between the

two types is the element of truth and perception, as the term 'traumatic' may also accurately describe the nature of the delusional memories and this experience should not be denied as a traumatic experience. However, this is a distinction used throughout this body of literature.

The number of 'adverse events' in Intensive Care increased, such as experiencing pain, anxiety of respiratory distress affecting outcome, with 2 or more resulting in significantly higher PTSS-10 and PTSS-14 scores (Kapfhammer et al., 2004b; Granja et al., 2008). Traumatic memories seem to have an exposure-response relationship with more traumatic memories equaling more intense posttraumatic reactions (Schelling, 2002; Girard et al, 2007). Although not statistically significant, three participants in Schelling et al. (2001) were found to have 3 or more categories of traumatic memories and received diagnoses of posttraumatic stress disorder and Hauer et al. (2009) found that patients who retrospectively reported more stress (Stress symptom inventory) had more categories of traumatic memory and a 'stronger trend' (p = 0.07) towards a higher incidence of PTSD, as assessed by psychiatrist interview. Boer et al. (2007) suggests that patients who reported more traumatic memories from their ICU stay earned higher scores on PTSS-10 and that this was the single strongest predictor of PTSD outcome in their sample. Traumatic memories could relate to the traumatic nature of invasive patient treatment in the ICU e.g. intubation and ventilation (Shaw et al., 2009; Davydow et al., 2009). Although, as previously stated this may relate more to patient acuity rather than the effect of the specific interventions.

Schelling et al. (2001) proposed an alternate mechanism of action between traumatic memory and the development of PTSD; as the number of traumatic memories significantly increased, so did serum cortisol when patients with 3 or more traumatic memories were compared with patients with no or one category of traumatic memory. Posttraumatic distress disorder is

characterised by a chronic persistence of stress symptoms including re-experiencing and increased psychological arousal that places the sufferer in a constant 'stress state' (WHO, 1992). Schelling et al. (2001) propose a 'desensitisation hypothesis' that suggests PTSD sufferers become desensitised to the effect of their natural cortisol secretions and therefore the body has to up-regulate the production of cortisol to achieve a physiological reaction. There is a large body of research that has examined the role of stress hormones (cortisol) in the production and recall of memory, with cortisol now being known to facilitate memory formation but inhibit delayed retrieval (Wolf et al., 2004). This research can be extrapolated to explain how the exogenous administration of hydrocortisone (cortisol) in the intensive care unit will facilitate the production and consolidation of memory during critical illness, at a time when traumatic events are occurring; as well as how once posttraumatic stress symptomology has begun and the chronic stress reaction is over-stimulating the cortisol response, this will impair the process of memory retrieval and cause potential distress.

The presence of delusional recall was identified as a potential influential factor in the development of posttraumatic reactions. Rattray et al. (2005) found that a lack of 'factual' recall predisposed patients to experience a poorer emotional outcome, but not specifically posttraumatic reactions, a trend common across several pieces of research, which stated that the increased prevalence of delusional memory and reduced ability for factual recall led to greater incidence of posttraumatic reactions (Capuzzo et al., 2005; Jones et al., 2007; Granja, 2008; Weinhart & Sprenkle, 2008; Rattray et al., 2010). However, it should be noted that in the presence of no delusional recall posttraumatic reactions still occur, and having factual recall alone is not a protective factor (Granja et al., 2008). Granja et al. (2008) findings suggest that patients with mixed recall for factual and delusional memories predicts greater PTSS-14 scores. Rattray et al. (2010) propose that patients who are less aware of their

surroundings (heavily sedated) experienced more 'blurring' in their memory and recalled more frightening experiences, which may partially explain the significance of delusional memories. Jones et al (2007) proposed that intensive care patients experience a 'hypnogogic state' throughout their admission, which is described as the time between sleeping and wakefulness. This altered state of consciousness may facilitate the distortion of external stimuli and the internal interpretation of events, which may lead to the development of delusional recall.

This evidence shows a clear relationship between the role of memory, whether it is traumatic or delusional in nature, and the later development of posttraumatic stress reactions. It is apparent that the interventions and experiences that are common in critical care settings are often remembered by patients, despite the fact that they may be under the influence of various sedative medications. Further to this, the impairment of memory by such medication and the amnesic nature of posttraumatic stress disorder appear to exacerbate the traumatic symptomology that may be experienced following hospital discharge.

Limitations of Reviewed Literature

Research examining posttraumatic stress disorder is inherently inhibited by the nature of the disorder, in that sufferers are avoidant of stimuli that may relate to their trauma (Jackson et al., 2007). This presents a particular problem for researchers who wish to explore posttraumatic stress reactions, as participants are perhaps more likely to opt out of research that seeks to examine their symptoms to prevent further episodes of re-experiencing and act in concordance with the avoidant characteristic of the disorder (Rattray et al., 2005). This may result in a volunteer bias where a skewed sample of patients who are acutely re-experiencing ICU related trauma are recruited, which may explain the wide prevalence of

estimates of posttraumatic stress disorder in critical care and other population groups (Davydow et al., 2008).

Further complications arise due to the issue of mortality rates in critical care patients, with research estimates of 20-50% mortality within 6 months of hospital discharge following critical care treatment (Kim et al., 2010). All but 4 studies in this review followed up patients within 12 months of ICU/hospital discharge, which again can result in a sample bias, as a large portion of a critical care research sample can be expected to be lost in the immediate 6 months after discharge. This was found to be particularly evident in 3 of the included studies who reported attrition rates of between 43% and 80% (Girard et al., 2007; Jubran et al., 2010; Rattray et al., 2010), although some studies only report the attrition rates of included samples, rather than from the potential pool of participants who may have been lost to follow up or who died before recruitment (either in ICU or before hospital discharge).

Sixteen of the included studies utilised prospective cohort methods and some reported significant attrition rates of between 43% and 85% that were due to death, refusal of participation or lost to follow up (Girard et al., 2007; Jubran et al., 2010; Rattray et al., 2010). Attrition biases are particularly problematic when sample sizes are already initially small and participants are to be prospectively followed, compared with cross sectional studies, which have fewer problems with attrition (Parahoo, 2006). Seven of the included studies examined data from less than 50 participants which is comparatively small compared with Davydow et al. (2009) who had the largest sample consisting of 1906 ICU survivors recruited from 69 hospitals across the USA. Four studies had reasonable sample sizes of between 200-300 participants (Jones et al., 2007; Samuelson et al., 2007; Weinert & Sprenkle, 2008; Peris et al., 2011). Despite this, Wallen et al. (2008) conducted post hoc analyses that suggested a

sample size of 500 would have been required to detect significant differences in gender in their study, and that a larger sample (n=100) would have yielded more independent predictors of PTSD. Research examining the underlying processes of posttraumatic stress reactions in the critical care population is a relatively new field, with all of the included studies in this review having been published in the last 13 years.

A limitation of the current research is the reliance on screening tools and questionnaires in the assessment of posttraumatic stress symptomology in the critical care population. Only 6 studies employed structured clinical interviews, in which patients are assessed in relation to the applicable diagnostic criteria (Jones et al., 2001a; Schelling et al., 2001; Hauer et al., 2009; Kapfhammer et al., 2004a; Rattray et al., 2005; Jubran et al., 2010). Seventeen studies relied on screening tools, such as the Posttraumatic Symptom Scale 10 or Impact of Events Scale, which are limited in their capacity to confirm a diagnosis. Screening tools are designed to identify disease/disorder characteristics that indicate a comprehensive assessment is required, but criticisms of screening tools focus on their lack of a meaningful description of pathologies (Jull, 2002). Therefore a number of nursing and social factors that may be relevant have not been studied, for example factors such as visits of relatives or if the nurses provided feelings of security which could theoretically impact on the long term outcome in relation to PTSD following critical care.

Recommendations

A number of research and practice recommendations can be drawn from the reviewed literature.

Research

- Future research examining the underlying processes of potential predictor variables that have a small inconclusive evidence base e.g. GCS scores, delirium and the use of mechanical restraint.

- Researchers should aim to improve the statistical power of studies by having wider participant inclusion criteria, but with controls to limit the effect of possible demographic or patient factors e.g. previous psychiatric diagnosis.

- Future research should seek to describe the experience of patients in critical care environments using qualitative methods, for example to determine what it is about critical care environments patients find traumatic, how relationships with others or presence of visitors affects their experience. This will help to educate and inform the practice of health care professionals and improve the quality of advice that can be offered to patients and visitors to minimise the psychological stress of critical care settings.

Practice

Use of Sedative Agents

- From the literature reviewed there is some indication that:

  - lighter sedation practices, in particular with benzodiadepines could improve both physical and psychological outcomes

  - minimum use of lorazepam and midazolam improves clinical outcomes in adult patients who are mechanically ventilated

  - alternative sedative agents such as propofol may be less harmful in relation to longer-term outcomes for critical care patients

Conclusion

Patient factors such as being aged 65 or over and male appear to be protective against the development of posttraumatic stress symptomology. Having a previous psychiatric diagnosis was a risk factor, although this remains unclear in respect to the underlying causes and how this increases risk. Critical care treatment factors such as the role of mechanical restraint; Glasgow Coma Scale scores and delirium were weak predictors only being indicated in single studies (Jones, 2007a; Girard et al., 2007; Peris et al., 2011). However, treatment factors

such as amount and type of sedatives administered were identified by a number of studies as predictive factors (Jones et al., 2007; Girard et al., 2007). It remains unclear, however, what the mechanism of action sedatives play in the development of posttraumatic stress symptomology, although it has been suggested that agitation and the presence of unacknowledged delirium could be potential underlying causes. Length of stay greater than 5 days appears to be a significant predictor variable predictive of posttraumatic stress reactions. The role and administration of stress hormones and how they modulate the inflammatory response, as well as their interaction with memory formation has been an identified determinant of posttraumatic reactions in critical care patients within this review, although a large body of evidence does exist outside of this paper, that extensively explores the function of stress hormones and their role in different posttraumatic stress disorder populations (Schelling et al., 2001; Schelling et al., 2004; Hauer et al., 2009).

Delusional and traumatic memory were inextricably linked with the development of posttraumatic symptomology with the root of trauma within a critical care setting centering on the experiences of patients. The evidence clearly shows that having a greater recall of traumatic events or delusional recall of the critical care period predicted a poorer outcome, as measured by several posttraumatic screening tools. This effect was seen to be evident across several time points, from 1-week (Schelling, 2002) to 8 years post critical care discharge (Kapfhammer et al., 2004b).

Relevance to practice

This literature review has revealed a number of important findings in relation to the development of posttraumatic stress disorder following admission to a critical care environment. Eight key causative and 3 potential risk factors identified are:

1. Younger than 50 years of age
2. Female
3. Previous psychiatric illness
4. Length of stay in ICU more than 5 days
5. Sedatives: benzodiazepine use
6. Administration of stress hormones
7. Delusional memory (at follow up)
8. Traumatic memory (at follow up)
   a. delirium
   b. GCS score of ≤9 on admission
   c. use of mechanical restraint should also be kept in mind as potential risk factors.

This list can be used as a rudimentary screening tool by ICU staff. This knowledge can help nurses be mindful of the potential effect of their interventions and could help nurses identify those at most risk. If ICU nurses have a way of reporting this in a concise way in clinical notes, there is the potential for further exploration at follow up appointments for patients at risk. This could also inform practice development projects in implementing helpful interventions such as critical care diaries (Jones et al., 2010). Given that there were 3,184 occupied critical care beds in England alone in December 2014, the scale of the issue is substantial (NHS, 2015).

Summary: What does this paper contribute to the wider global community?

- Identification of 8 key and 3 potential identifiable risk factors for PTSD in the critical care population
- It highlights the importance and significance of the mental health implications of interventions in critical care environments

- Knowledge with the potential for practice development interventions for PTSD to be recognized in critical care populations which can contribute to a decrease the global disease burden

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Table 1 Combinations of subject headings and keywords

Subject headings		Keywords
Critical Care	**OR**	critical care
	OR	Intensive care
Intensive Care Units	**OR**	intensive care unit
	OR	ICU
	AND	
Stress Disorders, Post-Traumatic	OR	Post traumatic stress
	OR	Post traumatic stress disorder
	OR	Posttraumatic stress syndrome
	AND	
Patient Attitudes	OR	Cause
Life Experiences	OR	Experience
	OR	?etiology

Table 2. Matrix of Included Literature

Author (Year)	Methodology	Diagnostic Tool	Sample	Themes	Main Findings
Aitken et al 2012	Prospective cohort study	Kessler psychological distress scale PTSD civilian checklist SF-36	Initial=123 discharged form Australian hospital ICU 1 month= 93, 6 months= 88	PTSD symptoms Psychological distress Health and social care support	All participants required ongoing support six months after discharge from hospital. Self-efficacy above average reported and reduced illness perception approx. half required support services such as accommodation and home modifications. Approx. 20% reported post-traumatic stress symptoms, approx. Half the participants reported psychological distress. Average quality of life scores were significantly below the Australian norms both one and six months post discharge.
Boer, K. R. et al. (2007)	Cohort Study	APACHE Impact Events Scale Revised PTSS -10	107 peritonitis patients	Length of Critical Care Stay Traumatic Memory Age	Those patients who remained longer in ICU scored higher on PTSD measures Strongest factor for prediction of future PTSD younger age was related to higher scores on PTSS-10
Capuzzo, M. et al. (2005)	Prospective Cohort Study	Impact of Events Scale	84 completed IES at 1 week post-discharge, 63 at 3 months post-discharge	Delusional Memory	In patients with PTSD related symptoms, fewer factual memories were recorded
Davydow, D. S. et al. (2009)	Multi-centre Prospective Cohort Study	Post traumatic Stress Disorder Checklist	1906 ICU survivors from 69 hospitals across USA. Telephone interview 12 months post discharge	Length of Critical Care Stay Traumatic Memory Pre-morbid Psychiatric Diagnosis Educational Status	Length of Stay > 5 days resulted in symptoms of predicted PTSD at 12 months Having Pulmonary Arterial Catheter led to greater PTSD symptoms. Proposed that this may be a proxy for illness severity Pre ICU depression, alcohol abuse dependence predicted symptoms suggestive of PTSD University education or higher was a protective factor against developing PTSD symptomology
Girard, T. et al. (2007)	Prospective Cohort Study	APACHE II PTSS-10	43 ICU patients followed up 6 months post ICU discharge	Delirium	Length of measurable delirium was not a predictive factor of PTSD
				Traumatic Memory	More traumatic memoires resulted in higher PTSS scores
				Sedation Practice	Higher cumulative amount of Lorazepam correlated with higher PTSS-10 score
				Age	PTSS-10 scores significantly reduced in patients aged over 50
				Gender	Women more likely than men
Granja, C. (2008)	Multi-centre longitudinal cohort study	PTSS-14	935 patients were included from 9 Portuguese Intensive Care Units with 313 final respondents at 6 month follow up	Delusional Memory Traumatic Memory	Factual memories were not a protective factor. Combination of real and delusional memories predicted greater incidence of PTSD Number of 'adverse experiences' significantly predicted higher PTSS-14 scores

Table 2. Matrix of Included Literature continued…

Author (Year)	Methodology	Diagnostic Tool	Sample	Themes	Main Findings
Hauer, D. et al. (2009)	Longitudinal Cohort Study	Psychiatrist Interview – DSM Criteria	33 long term ARDS survivors 7.5 years post ICU	Stress Hormones Traumatic Memory	Patients with an increased number of traumatic memories from the ICU show significantly lower basal serum cortisol levels and an increased incidence of chronic stress symptoms and PTSD Those with more category traumatic memories experienced more PTSD symptoms
Jones, C. (2007)	Multi-centre Prospective Cohort Study	APACHE, CAM ICU PTSS 14 Posttraumatic diagnostic Scale (PDS)	238 ICU patients from 5 hospitals across Europe, 3 months post discharge	Sedation Practice Mechanical Restraint	More sedatives (more than one) associated with higher incidence of posttraumatic stress disorder
Jones, C. (2001b)	Case series Cohort	Semi-structured Interview Impact of Events Scale	45 patients were interviewed at 2 weeks post-ICU discharge and 30 patients at 8 weeks	Delusional Memory	Having only delusional recall was linked to high level of PTSD symptoms
Jubran, A. et al. (2010)	Longitudinal Cohort Study	PTSS-10 Structure Interview - Psychologist	72 patients were studied one week after weaning and 41 patients were studied again three months later	Pre-morbid Psychiatric Diagnosis	All those diagnosed with PTSD had episodes of pre-morbid psychiatric illness.
Kapfhammer, H. P. et al. (2004a)	Longitudinal Cohort Study	Structured Clinical Interview (DSM Criteria) PTSS 10	46 ARDS survivors interviewed 8 years post ICU	Length of Critical Care Stay	Length of stay was significantly correlated with receiving a full diagnosis of PTSD Patients who had to be physically restrained were more likely to have symptoms of PTSD, despite only 1 patient being able to recall being restrained
Kapfhammer, H. P. (2004b)	Retrospective, cohort, case-controlled analyses	PTSS 10	46 patients who were admitted to hospital from 1985 to 1995 and who survived an episode of ARDS were followed up at 8 years post-discharge	Traumatic Memory	Increase in 'adverse events' such as pain, respiratory distress or anxiety increased the risk of developing PTSD. Having 2 or more adverse events led to higher incidence of PTSD compared with having 1 adverse event
Peris, A. et al (2011)	Comparative Groups Design	Impact Events Scale Revised	209 patients 12 months post ICU	GCS Score	Patients who are admitted with reduced consciousness are more likely to experience symptoms of PTSD
Rattray, J. E. et al. (2005)	Prospective Longitudinal Study	Impact of Events Scale (IES) Intensive Care Experience Questionnaire – Structured Interview	80/255 ICU patients interviewed at discharge, 6 and 12 month intervals	Length of Critical Care Stay	Longer ICU stay was linked with higher intrusion scores on the IES measure
				Delusional Memory	Lack of factual recall predisposed patients to poorer emotional outcome
				Age	Patients who were younger experienced higher intrusion and avoidance scores on IES
Rattray, J. et al. (2010)	Multi-centre longitudinal cohort study	Impact of Events Scale Intensive Care Experience Questionnaire, HADS	103 participants recruited from six ICUs in one Critical Care Network in the UK. Followed up at ICU discharge, hospital discharge, 2 and 6 months	Delusional Memory	Patients who were less aware of their surroundings, had blurred memories and had more frightening memories and these patients also tended to have higher scores on the subscales of both the HADS and IES

Table 2. Matrix of Included Literature continued…

Author (Year)	Methodology	Diagnostic Tool	Sample	Themes	Main Findings
Samuelson, K. A. M. et al. (2007)	Prospective Cohort Study	ICU Memory Tool ICU Stressful Experience Questionnaire Impact of Event Scale-R	226 patients who had been admitted to ICU for more than 24h at 5 days and 2 months post-discharge	Gender	Females were more likely to have higher IES-R scores
Schelling, G. (2002)	Retrospective comparative groups design Longitudinal Cohort Study	PTSS-10	148 ICU patients 6 months post ICU	Stress Hormones Traumatic Memories	Catecholamines and glucocorticoids facilitate memory consolidation of emotionally arousing material Recall of traumatic memories of pain, anxiety, respiratory distress and imminent threat of death were present at 1 week and 6 month follow up following ICU discharge
Schelling, G et al. (2004)	Randomised controlled trial	PTSS-10	91 ICU patients who underwent cardiac surgery	Stress Hormones	Stress doses of hydrocortisone in patients undergoing CS are associated with a lower intensity of chronic stress and PTSD symptoms at 6 months
Schelling, G. et al. (2001)	Prospective double-blind randomized controlled trial		20 patients interviewed 2.5 years post ICU	Stress Hormones Traumatic Memory	Receiving stress doses of hydrocortisone significantly reduced the incidence of PTSD at follow up. Patients with 3 categories of traumatic memory were all diagnosed with PTSD
Scragg, P. et al. (2001)	Cross sectional non-experimental design (Questionnaire)	PTSS-10 Psychiatrist Interview – DSM Criteria	80 patients who had been admitted and discharged from ICU	Age Gender	Patients under 65 then more likely to have PTSD symptoms Women were more likely to experience symptoms of PTSD compared with men in a 2:1 ratio
Shaw, R. J. et al. (2009)	Comparative Groups Design	PTSD: Trauma Symptom Checklist 33 Impact of Events Scale	20 adult pulmonary patients requiring ventilation in the ICU were compared with 20 patients who had NIV in HDU All had COPD and had respiratory failure	Traumatic Memory	Specific traumatic aspects of a patient's treatment, in this case the experience of intubation and mechanical ventilation, may be an additive risk factor for the development of PTSD
Wallen, K. et al. (2008)	Prospective Cohort Study	Impact of Events Scale - Revised	100 patients who had been admitted to ICU in Australian Hospital	Age	Patients who were under 65 were 5.6 times more likely to experience symptoms of PTSD
Weinert & Sprenkle (2008)	Longitudinal Cohort Study	Post-traumatic Stress Diagnostic Scale	Two hundred seventy-seven subjects requiring >36 h of mechanical ventilation were enrolled; 149 completed follow-up interviews 2 months later and 80 at 6 months.	Delusional Memory	Incidence of delirious memories was associated with more 're-experiencing'. However these did not remain at 6 months follow-up

Table 3. Key factors related to the development of PTSD symptomology

Critical Care Factors	Patient factors	Experience factors
Length of ICU stay	Age	Delusional memory
Sedation	Gender	Traumatic memory
Stress hormones	Previous psychiatric illness	
Delirium		
GCS score ≤9 on admission		
Mechanical restraint		