Posttraumatic Stress Disorder in Critical Illness Survivors: A Metaanalysis

Ann M. Parker, MD1,2; Thiti Sricharoenchai, MD3; Sandeep Raparla, MD4; Kyle W. Schneck, BA5; O. Joseph Bienvenu, MD, PhD2,6; Dale M. Needham, FCA, MD, PhD1,2,7

Objective: To conduct a systematic review and metaanalysis of the prevalence, risk factors, and prevention/treatment strategies for posttraumatic stress disorder symptoms in critical illness survivors.

Data Sources: PubMed, Embase, CINAHL, PsycINFO, and Cochrane Library from inception through March 5, 2014.

Study Selection: Eligible studies met the following criteria: 1) adult general/nonspecialty ICU, 2) validated posttraumatic stress disorder instrument greater than or equal to 1 month post-ICU, and 3) sample size greater than or equal to 10 patients.

Data Extraction: Duplicate independent review and data abstraction from all eligible titles/abstracts/full-text articles.

Data Synthesis: The search identified 2,817 titles/abstracts, with 40 eligible articles on 36 unique cohorts (n = 4,260 patients). The Impact of Event Scale was the most common posttraumatic stress disorder instrument. Between 1 and 6 months post-ICU (six studies; n = 456), the pooled mean (95% CI) Impact of Event Scale score was 20 (17–24), and the pooled prevalences of clinically important posttraumatic stress disorder symptoms (95% CI) were 25% (18–34%) and 44% (36–52%) using Impact of Event Scale thresholds greater than or equal to 35 and greater than or equal to 20, respectively. Between 7 and 12 months post-ICU (five studies; n = 698), the pooled mean Impact of Event Scale score was 17 (9–24), and pooled prevalences of posttraumatic stress disorder symptoms were 17% (10–26%) and 34% (22–50%), respectively. ICU risk factors for posttraumatic stress disorder symptoms included benzodiazepine administration and post-ICU memories of frightening ICU experiences. Posttraumatic stress disorder symptoms were associated with worse quality of life. In European-based studies: 1) an ICU diary was associated with a significant reduction in posttraumatic stress disorder symptoms, 2) a self-help rehabilitation manual was associated with significant posttraumatic stress disorder symptom reduction at 2 months, but not 6 months; and 3) a nurse-led ICU follow-up clinic did not reduce posttraumatic stress disorder symptoms.

Conclusions: Clinically important posttraumatic stress disorder symptoms occurred in one fifth of critical illness survivors at 1-year follow-up, with higher prevalence in those who had comorbid psychopathology, received benzodiazepines, and had early memories of frightening ICU experiences. In European studies, ICU diaries reduced posttraumatic stress disorder symptoms. (Crit Care Med 2015; XX:00–00)

Key Words: critical care; critical illness; metaanalysis; posttraumatic stress disorders; review

As mortality from critical illness decreases, there is an ever-growing population of critical illness survivors who frequently experience long-lasting physical, cognitive, and mental health impairments (1–5). Posttraumatic stress disorder (PTSD) is one important mental health impairment related to life-threatening ICU experiences. According to the Diagnostic and Statistical Manual of Mental Disorders, 5th Edition, PTSD can be diagnosed if an individual is exposed to actual or threatened serious injury/death (e.g., critical illness and related ICU treatments) and subsequently develops the following symptoms which last more than 1 month and...
cause significant distress or changes in functionality: persistently reexperiencing the event and attempting to avoid trauma-related stimuli; new negative alterations in mood/cognition; and new/increased arousal/reactivity. Prior systematic reviews reported that substantial PTSD symptoms occurred in 5–63% of critical illness survivors and were associated with worse health-related quality of life (HRQOL) (6–9). Previously described risk factors for PTSD include younger age, sedation with benzodiazepines, and recall of frightening ICU experiences (6–8). PTSD in the general population is associated with greater physical disability (10–12).

The burden of PTSD symptoms in critical illness survivors has gained increasing recognition in the past 5 years, with the number of studies published on this topic more than doubling compared with the preceding 5-year interval (7). Furthermore, there is increasing homogeneity between studies regarding the instruments used for and timing of PTSD symptom assessment post-ICU. Such consistencies in study design provide new opportunities for pooling data on prevalence and severity of PTSD symptoms across studies. In addition, over the past 5 years, evidence has emerged regarding interventions for prevention and treatment of PTSD symptoms in critical illness survivors (13, 14).

Given this background, our objectives were to evaluate the prevalence of PTSD symptoms in general critical illness survivors via metaanalysis and to perform a systematic review of the literature to synthesize the following: 1) patient-specific and ICU-related risk factors for PTSD symptoms; 2) associations between PTSD and HRQOL; and 3) effectiveness of prevention and treatment interventions for PTSD symptoms.

**MATERIALS AND METHODS**

**Search Strategy**

We searched five electronic databases (PubMed, Embase, CINAHL, PsycINFO, and Cochrane Library) from inception through March 5, 2014, to identify eligible studies (Fig. 1). We combined controlled vocabulary (MeSH and Emtree) and keyword terms and phrases to define the concepts of PTSD, psychometrics, critical care, and respiratory distress. These terms were “exploded” when applicable. The search strategy was not limited by language of publication. Detailed search strategies for each database are presented in Supplemental Digital File—Search Strategy (Supplemental Digital Content 1, http://links.lww.com/CCM/B193). A manual search of the reference lists from all relevant review articles was performed.

**Study Selection**

For inclusion in the systematic review, articles were required to meet the following criteria: 1) study population consisting of adult critical illness survivors, 2) PTSD assessment conducted using a validated measure, and 3) PTSD assessment conducted greater than or equal to 1 month post-ICU discharge while patients were in their home environment. Articles were excluded from the review if the study population met any of the following:
The effects model, respectively, with a random intercept for study. IES score were pooled using a binomial and linear random-effects model. PTSD assessments, we report pooled PTSD prevalences across two time frames after critical illness: 1–6 months and 7–12 months. Given variability among studies in the timing of PTSD assessment, PTSD assessment instrument (and scoring method), point prevalence of clinically important PTSD symptoms (i.e., PTSD symptom score above a predefined threshold), potential PTSD risk factors, and associations between PTSD symptoms and HRQOL. Authors of eligible studies were contacted for additional information or clarifications, when necessary.

Data Abstraction

Two reviewers independently abstracted data from each eligible article, with any differences resolved by consensus among abstractors in consultation with an independent coauthor (D.M.N.). The following were abstracted from each eligible study: design and population, baseline cohort characteristics, inclusion/exclusion criteria, proportion of patients with pre-existing psychiatric illness, timing of and sample size(s) at each PTSD assessment, PTSD assessment instrument (and scoring method), point prevalence of clinically important PTSD symptoms (i.e., PTSD symptom score above a predefined threshold), potential PTSD risk factors, and associations between PTSD symptoms and HRQOL. Authors of eligible studies were contacted for additional information or clarifications, when necessary.

Risk of Bias Assessment

Risk of bias assessment for included studies was conducted using the Cochrane Risk of Bias (15) for randomized controlled trials (RCTs) and the Newcastle Ottawa Scale (16) for observational studies.

Statistical Analysis

The Impact of Event Scale (IES) was the most common instrument used for measuring PTSD symptoms. For studies using the IES, we abstracted the following data (or requested these data from study authors when not reported): 1) point prevalence of clinically important PTSD symptoms as indicated by an IES score greater than or equal to 20 and greater than or equal to 35 (most commonly used thresholds) and 2) mean (SD) IES score. Given variability among studies in the timing of PTSD assessments, we report pooled PTSD prevalences across two time frames after critical illness: 1–6 months and 7–12 months. IES-measured PTSD symptom prevalence and mean IES score were pooled using a binomial and linear random-effects model, respectively, with a random intercept for study. The F statistic was used to evaluate between-study statistical heterogeneity; when the F was greater than 50%, indicating substantial heterogeneity, a sensitivity analysis was performed in which any study with qualitative evidence of heterogeneity was removed and the metaanalysis repeated. We could not assess publication bias due to the small number of studies.

RESULTS

Description of Search and Study Characteristics

The authors identified 4,205 citations and reviewed 2,817 unique titles and abstracts (after de-duplication of identified citations) and 712 full-text articles, with 40 publications on 36 unique cohorts meeting eligibility criteria (Fig. 1). The 40 publications included seven RCTs (13, 17–22), four cross-sectional studies (23–26), and 29 prospective cohort studies (Supplemental Table 1, Supplemental Digital Content 2, http://links.lww.com/CCM/B194) (14, 18, 25–54), with at least one PTSD assessment completed for 4,260 patients, with most assessments occurring between 3 and 12 months after critical illness (Supplemental Table 2, Supplemental Digital Content 3, http://links.lww.com/CCM/B195). The studies were conducted predominantly in the United Kingdom (13, 20, 22, 24, 27, 33, 34, 39, 42–44, 47, 51, 53) and United States (21, 29, 30, 41, 52, 54).

Risk of Bias Assessment

Risk of bias assessment of the included RCTs demonstrated that randomized sequence generation and allocation concealment were adequate in most studies (Supplemental Table 3, Supplemental Digital Content 4, http://links.lww.com/CCM/B196). Double-blinding was feasible in only one RCT. Assessment of observational studies demonstrated that most adequately addressed selection, comparability of groups and outcomes (Supplemental Table 4, Supplemental Digital Content 5, http://links.lww.com/CCM/B197).

Measures and Prevalence of PTSD

In two studies, PTSD symptoms were assessed using a semistructured psychiatric interview (25, 50). The remaining publications used questionnaires, including most commonly: the IES (16 publications) (17, 22–24, 32–34, 36–39, 46, 47, 49, 51, 53), the IES-Revised (IES-R) (seven publications) (14, 18, 19, 28, 35, 40, 45), and the Posttraumatic Symptom Scale (PTSS)-10 (six publications) (18, 21, 25, 31, 52, 54). The assessments were conducted in-person, by telephone, and by mail in 15 (13, 21, 22, 32–35, 41, 42, 44, 45, 47, 50, 51, 53, 54), 15 (13, 14, 19, 26, 28–31, 33, 35, 40–43, 45, 49), and 11 studies (17, 19, 20, 23, 24, 27, 35–39, 46, 48), respectively (two studies did not report how data were collected) (25, 52).

In all studies in this review, the point prevalence of PTSD symptoms ranged from 4% to 62% (Fig. 2). The IES (potential score range, 0–75) was the most commonly used instrument to assess PTSD symptoms, with higher scores indicating greater intrusion and avoidance symptoms. Via metaanalysis of six studies (n = 456) that used the IES at 1–6 months post-ICU, the pooled mean (95% CI) score was 20 (17–24; F = 78%), and the pooled prevalence (95% CI) of clinically important PTSD symptoms was 25% (18–34%; F = 68%) and 44% (36–52%; F = 62%) using IES thresholds greater than or equal to 35 and 45.
greater than or equal to 20, respectively (22, 33, 34, 36–38, 46, 51, 53). In 698 patients (five studies), at 7–12 months post-ICU, the pooled mean IES score was 17 (9–24; \( F = 97\% \)), and pooled prevalences of PTSD symptoms were 17% (10–26%; \( F = 85\% \)) and 34% (22–50%; \( F = 93\% \)) (23, 34, 36–38, 46, 49, 51).

In sensitivity analyses, two studies (33, 53) at 1–6 months and one study at 7–12 months (49) with qualitative evidence of heterogeneity were removed from the metaanalysis, demonstrating similar results. At 1- to 6-month follow-up, based on four studies (\( n = 385 \)), the pooled mean (95% CI) IES score was 21 (19–22; \( I^2 = 0\%) \), and the pooled prevalence (95% CI) of clinically important PTSD symptoms was 24% (20–29%); \( I^2 = 0\% \) and 46% (41–52%; \( I^2 = 14\% \)), using IES thresholds greater than or equal to 35 and greater than or equal to 20, respectively (22, 33, 34, 36–38, 46, 51). At 7–12 months, the pooled mean IES score for four studies (\( n = 529 \)) was 19 (16–22) (\( I^2 = 75\% \)), and the pooled prevalence of PTSD symptoms was 22% (18–27%) (\( I^2 = 36\% \)) and 43% (35–51%) (\( I^2 = 63\% \)), respectively (23, 34, 36–38, 46, 51).

### Risk Factors for PTSD

Age was not associated with PTSD symptoms in nine of 16 studies (Supplemental Table 5, Supplemental Digital Content 6, http://links.lww.com/CCM/B198) (14, 24, 26, 27, 29, 30, 34, 35, 38, 40, 43, 45–48, 50, 54). Sex was not associated with PTSD symptoms in 13 of 18 studies (13, 14, 26, 27, 29, 32, 34, 35, 38–41, 43, 45, 46, 48, 49, 54). Pre-ICU psychopathology was associated with PTSD symptoms in five of nine studies (14, 25–27, 30, 42, 43, 50, 53). The four studies that did not report an association between pre-ICU psychopathology and PTSD symptoms tended to be smaller (\( n < 60 \)) (14, 50, 53) or assessed only pre-ICU depression versus all pre-ICU psychopathology (30). Sedation in the ICU was evaluated for associations with PTSD symptoms. Greater PTSD symptoms were associated with receipt of benzodiazepines in two of four studies (14, 31, 34, 40) and higher total dose of benzodiazepines in one of two studies (31, 54), but not with duration of benzodiazepines in one study (30). Daily interruption of sedation (21), light versus deep sedation (19), an analgesia-based sedation protocol (31), and a no-sedation (only bolus doses of morphine) protocol (18) were not associated with an increase in PTSD symptoms. Duration of delirium or any ICU delirium was not associated with PTSD symptoms in two of two studies (30, 54).

Corticosteroids administered in the ICU had no association with PTSD symptoms in two studies with sample sizes of less than 100 (14, 29). One of these studies reported fewer PTSD symptoms in individuals homozygous for the corticotrophin-releasing hormone-binding protein (CRHBP) T/T allele, a gene involved in the hypothalamic-pituitary-adrenal (HPA) axis; corticosteroid exposure differed according to CRHBP genotype (29).

Severity of illness and ICU length of stay (LOS) were not significantly associated with PTSD symptoms in 11 of 12 studies (14, 29, 34, 35, 38, 43, 46–48, 50, 54) and 12 of 14 studies (14, 24, 27, 34, 35, 37, 40, 43, 45–48, 50, 54), respectively. ICU admission diagnosis was not associated with PTSD symptoms in seven of seven studies (14, 27, 37, 43, 45, 48, 53) nor were mechanical ventilation or mechanical ventilation duration in five of eight studies (14, 30, 37, 38, 40, 43, 45, 50, 54).

Early post-ICU memories of frightening ICU experiences (e.g., hallucinations, paranoid delusions, and nightmares) were associated with PTSD symptoms in 10 of 12 studies (13, 17, 22, 31, 34, 40–42, 45, 49, 51, 53, 54). Post-ICU psychopathology (e.g., anxiety, depression, and substance abuse) was associated with PTSD symptoms in four of four studies (40, 50, 52, 53).

### Interventions to Reduce PTSD Symptoms

An ICU diary was associated with a significant reduction in PTSD symptoms at 3- to 12-month follow-up in two studies.
(RCT, \( n = 352 \) and prospective study, \( n = 143 \)) \((13, 14)\), and a self-help rehabilitation manual was associated with a significant reduction at 2 months but not at 6 months (RCT, \( n = 126 \)) (Supplemental Table 5, Supplemental Digital Content 6, http://links.lww.com/CCM/B198) \((22)\). A nurse-led ICU follow-up clinic showed no benefit for PTSD symptoms in one RCT \((n = 286)\) \((20)\), and a pre-post study of a multidisciplinary follow-up clinic \((n = 258)\) found benefit for women, but not men \((32)\).

**Association Between PTSD and HRQOL**

Six of six studies evaluating the cross-sectional association between PTSD and HRQOL reported that greater PTSD symptoms were associated with worse mental HRQOL (Supplemental Table 6, Supplemental Digital Content 7, http://links.lww.com/CCM/B199) \((17, 23, 26, 36, 47, 54)\). There was no consistent association between PTSD symptoms and physical function.

**DISCUSSION**

This systematic review and metaanalysis of PTSD symptoms in critical illness survivors demonstrate that clinically important PTSD symptoms occur in one of five patients in the first 12 months post-ICU and are associated with worse HRQOL. Variables associated with PTSD symptoms in ICU survivors include benzodiazepines in the ICU, early memories of frightening ICU experiences, and pre-ICU comorbid psychopathology (Table 1). Severity of illness, admission diagnosis, and ICU LOS are consistently not associated with PTSD symptoms. ICU diaries are associated with a reduction in PTSD symptoms.

The pooled prevalence of clinically important PTSD symptoms \((\text{IES score } \geq 35)\) 1–6 and 7–12 months after ICU discharge was 24% and 22%, respectively. In a sensitivity analysis, two studies in the 1- to 6-month interval and one study in the 7- to 12-month interval were identified for removal from the metaanalysis due to heterogeneity. Unlike the other studies in the metaanalysis, one study \((33)\) removed at 1–6 months assessed PTSD symptoms using multiple instruments at the same time point in the setting of a relatively small sample size, and another study \((53)\) assessed PTSD symptoms relatively early \((2 \text{ mo postdischarge})\). The study removed at 7–12 months \((49)\) had two important distinctions that might account for its low prevalence estimates: 1) the IES was translated into Spanish and 2) there was a low proportion \((15\%)\) of patients with a primary diagnosis of respiratory failure. Statistical measures of heterogeneity improved after the sensitivity analysis with modest changes in the pooled results.

Compared with the 22% pooled prevalence of PTSD symptoms in critical illness survivors, the prevalence of PTSD symptoms following acute coronary syndromes was 12% in one recent metaanalysis including studies using similar PTSD instruments as in this review \((55)\). In a prospective cohort study of major traumatic injury patients, 23% had an IES score greater than or equal to 35 at 1-year follow-up \((56)\). Although different instruments with possibly stricter thresholds were used, the prevalence of clinically important PTSD symptoms in critical illness survivors in this metaanalysis was generally comparable to survivors war-time combat \((57, 58)\) \((11–31\%)\) and the World Trade Center attacks \((59, 60)\) \((11–23\%)\).

Establishing standardized assessments to measure PTSD symptoms in critical illness survivors is important, as highlighted by a comparison between the pooled prevalence of PTSD symptoms at 1-year post-ICU from this metaanalysis and the 7% estimate provided in a recent large \((n = 400)\) prospective study published after the systematic review \((61)\). Notably, the instrument used in the prospective cohort, the PTSD Checklist, was used by only two studies in the systematic review that also reported a lower prevalence of PTSD symptoms than the pooled prevalence from the metaanalysis \((19, 29, 30)\). Only two instruments have been validated against clinician diagnostic semistructured interviews in survivors of critical illness: the PTSS-10 \((\text{sensitivity } 77\% \text{ and specificity } 97\%)\) \((62)\) and IES-R \((\text{area under the receiving operating characteristic curve } [\text{AUROC}], 95\% [88–100\%])\) \((63, 64)\). A study in this review validated the PTSS-14 against the Posttraumatic Stress Diagnostic Scale \((\text{AUROC}, 82–95\%)\) \((33)\). The 36 unique cohorts in this systematic review used eight different questionnaires with substantial variability in scoring, follow-up periods, and risk factors assessed, making comparisons across studies difficult. The field could be advanced by use of common survey instruments validated against “gold standard” diagnostic instruments, with standardized follow-up time point(s), scoring methods and thresholds, and reporting of both continuous and binary \(i.e., \text{above threshold}\) PTSD symptom data \((1, 2, 65)\).

Preexisting psychopathology was the only pre-ICU factor consistently associated with PTSD symptoms. Importantly, and also in line with prior reviews, the following ICU-related factors were consistently not associated with PTSD symptoms: severity of illness, admission diagnosis, ICU LOS, and mechanical ventilation.

In this systematic review, two ICU-related variables had important associations with PTSD: sedation and early memories of frightening ICU experiences. It is unclear if associations between benzodiazepine sedation and PTSD symptoms reflect a true causal relationship or whether patients with high in-ICU anxiety \(i.e., \text{independent risk factor for PTSD symptoms}\) simply receive higher doses of sedatives. Sedation may contribute to PTSD symptoms through delirium; however, of the two studies in this systematic review that evaluated the association between in-ICU delirium and later PTSD symptoms, neither found a significant association \((30, 54)\). Similarly, a longitudinal study of PTSD symptoms in acute respiratory distress syndrome \((\text{ARDS})\) survivors, excluded because it focused on a subpopulation of ICU survivors, did not demonstrate a relationship between duration of delirium and later PTSD symptoms \((66)\). The authors hypothesized that the study lacked statistical power to detect a difference in PTSD symptoms with the presence/absence of delirium because virtually all of the patients experienced in-ICU delirium \((66)\). Perhaps sedation contributes to PTSD symptoms not through the duration of delirium but through an increased recall of...
in-ICU nightmares/psychotic experiences that may have been enhanced by delirium (7, 42).

There are already several known benefits of interruption of sedation paired with spontaneous breathing trials (67–70). In this systematic review, interruption of sedation, light versus deep sedation, and analgesia-based sedation did not increase and, in fact, showed trends toward decreased PTSD symptoms. In a longitudinal study of ARDS survivors, high-dose opiates were associated with greater PTSD symptoms while the duration of exposure to opiates was associated with less PTSD symptoms, suggesting that sufficient pain control may be protective while excessive opiate dosing may contribute to sedation and subsequent PTSD symptoms (66).

Several reports involving PTSD symptoms in patients surviving specific illness (e.g., cardiac surgery, sepsis, and ARDS) as well as wartime combat have demonstrated that corticosteroids may protect against PTSD symptoms, perhaps by their role in consolidation of traumatic memories (66, 71–74). Although two studies (14, 29) in this review did not find a significant association between corticosteroids in the ICU and PTSD symptoms, one of these studies highlighted that individuals who were homozygous for the CRHBP T/T allele, a gene involved in the HPA axis, fewer PTSD symptoms (29). Another study, not included in this review because it focused exclusively on cardiac surgery patients, found that individuals homozygous for the BCl1 G allele, also involved in the HPA axis, had greater PTSD symptoms (75).

Since the publication of prior systematic reviews (6, 7, 9), there has been increasing focus on interventions to reduce clinically important PTSD symptoms. Two studies in this systematic review reported that patients receiving an ICU diary had fewer PTSD symptoms; this intervention has become standard care in some European ICUs (International ICU Diary Network, http://www.icu-diary.org). Another study taking place in a trauma ICU, and therefore not included in this systematic review of general critical illness survivors, found that an “early intra-ICU psychological intervention” was associated with less PTSD symptoms (76). A third promising intervention, a post-ICU discharge telephone-based coping skills intervention, has also shown benefits in reducing PTSD symptoms in a very small ($n = 7$) pilot study (77). Prolonged exposure therapy, the mainstay of treatment for PTSD in other populations (78, 79), has not been assessed in this population, and its feasibility and benefit remain uncertain.

This systematic review has several important limitations. First, with the exception of one study, PTSD symptoms were assessed using questionnaires. Ideally, studies would use a clinician diagnostic semistructured interview, but this is not feasible in large multicenter studies. The heterogeneity of sample populations and PTSD symptom instruments makes direct comparison difficult. However, the use of metaanalysis to pool the results of the 11 studies using the IES for PTSD symptom assessment strengthens the assertion that PTSD symptoms are highly prevalent among general critical illness survivors. Additionally, our exclusion of studies focusing on patient populations with a specific illness may affect generalizability of our results. However, some specific ICU survivor populations (e.g., trauma or cardiac surgery patients) may, in fact, be distinct from other survivors in terms of their prevalence of PTSD symptoms.

### TABLE 1. Association of Posttraumatic Stress Disorder Symptoms in Critical Illness Survivors With Pre-ICU, ICU, and Post-ICU Factors and Interventions

<table>
<thead>
<tr>
<th>Risk Factors and Interventions</th>
<th>Association With Posttraumatic Stress Disorder Symptoms</th>
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<tbody>
<tr>
<td><strong>Pre-ICU factors</strong></td>
<td></td>
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<tr>
<td>Pre-ICU psychopathology</td>
<td>+ve</td>
</tr>
<tr>
<td>Age</td>
<td>NA</td>
</tr>
<tr>
<td>Sex</td>
<td>NA</td>
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<tr>
<td><strong>ICU factors</strong></td>
<td></td>
</tr>
<tr>
<td>Corticosteroids</td>
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<tr>
<td>Corticotrophin-releasing hormone-binding protein T/T allele</td>
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<td>Benzodiazepines</td>
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<td>Any</td>
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</tr>
<tr>
<td>Total dose</td>
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</tr>
<tr>
<td>Duration</td>
<td>NA</td>
</tr>
<tr>
<td><strong>Sedation strategy</strong></td>
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<td>Daily interruption of sedation</td>
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<tr>
<td>Light vs deep sedation</td>
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<td>Analgesia-based sedation</td>
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<td>Delirium</td>
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<tr>
<td>Severity of illness</td>
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<td>ICU length of stay</td>
<td>NA</td>
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<td>Admission diagnosis</td>
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<td>Mechanical ventilation</td>
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<td><strong>Post-ICU factors</strong></td>
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<td>Early post-ICU memories of frightening ICU experiences</td>
<td>+ve</td>
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<td>Post-ICU psychopathology</td>
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<tr>
<td><strong>Interventions</strong></td>
<td></td>
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<tr>
<td>ICU diary</td>
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<td>Self-help rehabilitation manual*</td>
<td>NA</td>
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<tr>
<td>ICU follow-up clinic</td>
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</tbody>
</table>

NA = no association, +ve = positive association, -ve = negative association.

*Associated with a significant reduction in posttraumatic stress disorder symptoms at 2 months but not at 6 months (randomized controlled trial, $n = 126$).
symptoms and possible risk factors. Finally, although care was taken to identify all potentially relevant studies for this systematic review, it is possible that some studies were inadvertently omitted.

CONCLUSIONS
In conclusion, PTSD symptoms occurred in one fifth of critical illness survivors over 1-year follow-up, with higher prevalences in those who had comorbid psychopathology, received benzodiazepines, and had early post-ICU memories of frightening ICU experiences. Given the association between PTSD symptoms and worse HRQOL, identification of risk factors is important to target patients for prevention/treatment interventions and motivate changes in ICU practices that are associated with subsequent PTSD symptoms. One such intervention, ICU diaries, reduced PTSD symptoms in European studies, but the generalizability of these results deserves further study.

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