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Posttraumatic stress disorder among survivors of critical illness: creation of a conceptual model addressing identification, prevention, and management

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Introduction

Quality of life is significantly impaired among survivors of critical illness [1–5]. Physical disability, psychiatric morbidity, and poor perceptions of overall health are common, and the varied nature of these impairments reflects the sweeping impact of the intensive care unit (ICU) experience. In recent years, considerable effort has been exerted to elucidate the epidemiology of psychiatric symptoms among ICU survivors, demonstrating evidence of substantial symptoms of depression, anxiety, and posttraumatic stress disorder (PTSD) [6–9]. Although symptoms of posttraumatic stress may be accompanied by symptoms of

Abstract Quality of life is frequently impaired among survivors of critical illness, and psychiatric morbidity is an important element contributing to poor quality of life in these patients. Among potential manifestations of psychiatric morbidity following critical illness, symptoms of posttraumatic stress are prevalent and intricately linked to the significant stressors present in the intensive care unit (ICU). As our understanding of the epidemiology of post-ICU posttraumatic stress disorder improves, so must our ability to identify those at highest risk for symptoms in the period of time following critical illness and our ability to implement strategies to prevent symptom development. In addition, a focus on strategies to address clinically apparent psychiatric morbidity will be essential. Much remains to be

understood about the identification, prevention, and management of this significant public health problem. This article addresses the importance of uniformity in future epidemiologic studies, proposes framing of risk factors into those likely to be modifiable versus non-modifiable, and provides an assessment of modifiable risk factors in the context of a novel conceptual model that offers insight into potential strategies to attenuate symptoms of posttraumatic stress among survivors of critical illness.

Keywords Stress disorders · Posttraumatic · Intensive care · Quality of life · Outcome assessment (health care)

depression and anxiety in individual patients, the unique features of these disorders emphasize the importance of understanding not only how they might interrelate for survivors of critical illness, but also how these disorders differ. Patients may manifest these different symptoms simultaneously, but prominence of posttraumatic stress symptoms such as hypervigilance, hyperarousal, or avoidant behaviors may inform the need for referral for PTSD-specific treatments such as trauma-focused cognitive behavioral therapy. Furthermore, it is possible that manifestations of post-ICU psychiatric morbidity differ by specific patient-level or ICU-level risk factors, including etiology of critical illness (e.g., trauma) and sedation use in the ICU.

In this article, we focus on PTSD given its prevalence and important relationship to critical illness. PTSD is characterized by having experienced a life-threatening (or perceived to be life-threatening) traumatic event and subsequently experiencing intrusive recollections of the event (e.g., intrusive thoughts or memories, nightmares), symptoms of hyperarousal (e.g., easy startling, hypervigilance), and avoidant behavior related to the traumatic event (e.g., avoiding thoughts, places, or situations that serve as reminders of the traumatic event). For many patients, critical illness represents a traumatic event that is a significant threat to life and is associated with a variety of stressors commonly present in the ICU environment, including endotracheal intubation and suctioning of the airway, invasive procedures for vascular access, periods of delirium, physical restraints, and significant impairment in mobility and the ability to communicate.

Several recent systematic reviews have described the prevalence of post-ICU PTSD and potential risk factors related to posttraumatic stress among survivors of critical illness. However, these reviews do not directly address the identification of post-traumatic stress symptoms following critical illness, nor do they use existing data to develop a conceptual model for prevention, identification, and management of symptoms of posttraumatic stress among ICU survivors. The practical application of knowledge gained from epidemiologic studies, as well as studies of measures to prevent and treat symptoms of posttraumatic stress, is an important next step. This article addresses the importance of uniformity in future epidemiologic studies, proposes framing of risk factors into those deemed to be modifiable versus non-modifiable, and provides an assessment of modifiable risk factors in the context of studies that offer insight into potential strategies to attenuate symptoms of posttraumatic stress among survivors of critical illness. In doing so, we hope to promote a conceptual model that will assist clinicians caring for critically ill patients and advance the conversation surrounding this significant public health problem.

Addressing the prevalence of PTSD and symptoms of PTSD among ICU survivors

In the past decade, five systematic reviews have addressed the prevalence of PTSD among ICU survivors [6, 10–13] (Table 1). Similar methodological concerns have been identified by each of these reviews, including variation in the timing of symptom evaluation as well as variation in the methods (e.g., self-report questionnaires versus diagnostic interviews) used to assess PTSD symptoms. Among standardized interviews, the structured clinical interview for DSM-IV (SCID) and clinician-administered PTSD scale (CAPS) are frequently utilized for the diagnosis of PTSD. Commonly used questionnaires allowing

assessment of symptoms of posttraumatic stress include the PTSD checklist-civilian version (PCL), the impact of events scale-revised (IES-R), and the posttraumatic symptom scale-10 (PTSS-10). The PCL has been validated among trauma-exposed populations and used in several assessments of post-ICU PTSD [14, 15], and the IES-R and PTSS-10 have been validated in survivors of critical illness [16, 17].

Though questionnaires and interviews are often used in combination to evaluate symptoms of PTSD, many studies rely on one method of assessment and prevalence estimates vary depending on the measurement tool used. Jackson et al. [10] reviewed 16 studies, ten of which used brief screening tools as their sole measure of PTSD symptoms while the remaining six studies utilized both questionnaires and structured interviews. The studies assessing posttraumatic symptoms via questionnaire alone reported a prevalence of symptoms ranging from 5 to 51 % while those using a combination of questions and structured interviews reported a prevalence of PTSD between 10 and 44 %. The review by Griffiths et al. [11] evaluated 30 studies: two used structured interviews alone, 19 used questionnaires alone, and the remaining nine used a combination of both. The reported prevalence of posttraumatic stress symptoms was 5-64 % when assessments were performed with questionnaires, and the prevalence of PTSD was 0-64 % when standardized interviews were employed. A systematic review of psychiatric morbidity among survivors of acute respiratory distress syndrome (ARDS) by Davydow et al. [6] assessed six observational studies with measures of posttraumatic stress symptoms. Of these, half used only questionnaires while the remaining half used a combination of questionnaires and structured interviews. Prevalence of psychiatrist-diagnosed PTSD declined from 44 % at the time of hospital discharge to 25 and 24 % at 5- and 8-year follow-up, respectively. Studies using questionnaire assessments reported a prevalence of clinically important posttraumatic symptoms ranging from 21 to 35 %. A systematic review by Davydow et al. [12] evaluating PTSD in general ICU survivors included 15 studies, identifying three that used structured interviews and 12 that only used self-report questionnaires. The prevalence of clinicianascertained post-ICU PTSD was 10-39 %, and the prevalence of questionnaire-ascertained PTSD symptoms was 8–51 %. The most recent systematic review conducted by Wade et al. [13] included 26 papers with only two reported as having used some form of structured interview. Those using structured interviews identified prevalence estimates of 10-19 %; prevalence of PTSD symptoms gathered from questionnaires ranged from 0 to 75 %.

The difficulty inherent in comparing estimates across studies using varying methods of assessment for symptoms of posttraumatic stress should encourage efforts to pursue uniformity in symptom evaluation for future studies. Of the available questionnaires, consistent

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References	Inclusion/exclusion criteria for articles	Articles reviewed	Prevalence of PTSD or PTSD symptoms
Jackson et al. [10]	Inclusion criteria: Studies must (1) evaluate the association between medical ICU hospitalization and PTSD [either the diagnostic entity called PTSD or posttraumatic stress symptoms (PTSS)], and (2) employ qualitative and/or objective measures of PTSD or PTSS	16	Questionnaire-assessed symptoms of PTSD: 5–51 %
	<i>Exclusion criteria</i> : (1) Investigations published in a language other than English, (2) unpublished studies and abstracts, and (3) studies consisting entirely of physical trauma and/or surgical ICU patients		PTSD in studies using structured interviews: 10–44 %
Griffiths et al. [11]	<i>Inclusion criteria</i> : (1) Studies of adult ICU survivors (defined as a population consisting of entirely medical and/or surgical patients >16 years old), (2) patients experienced ICU length of stay ≥24 h, and (3) measurement of PTSD prevalence after ICU discharge	30	Diagnosed by standardized clinical interview: 0–64 %
	<i>Exclusion criteria</i> : Studies without either an English title or abstract		Diagnosed by self-report measure: 5–64 % ^a
Davydow et al. [6]	<i>Inclusion criteria</i> : (1) Studies reporting data on psychiatric morbidity at least once after intensive care treatment of ALI/ARDS	6	Questionnaire-ascertained "clinically significant" PTSD symptoms: 21–35 %
	<i>Exclusion criteria</i> : (1) Studies dealing with neonatal or pediatric intensive care, (2) studies reporting only QOL data, and (3) case reports and review articles		Psychiatrist-diagnosed PTSD at hospital discharge: 44 %, at 5 years: 25 %, and at 8 years: 24 %
Davydow et al. [12]	Inclusion criteria: (1) Study population composed of adult ICU survivors, and (2) PTSD assessments conducted using validated measures at >1 month following ICU discharge	15	Questionnaire-ascertained "clinically significant" PTSD symptoms: 22 %
	<i>Exclusion criteria</i> : (1) Studies focusing solely on survivors of ALI/ARDS or of specialty ICUs (i.e., trauma/surgical, coronary, or neurological ICUs), and (2) abstracts, case reports, and review articles		Clinician-diagnosed PTSD: 19 %
Wade et al. [13]	Inclusion criteria: (1) Studies of adult mixed- diagnosis ICU patients receiving intensive care for >24 h in general, medical, or surgical ICUs, including patients receiving mechanical ventilation and (2) studies that used reliable, validated questionnaires or interviews for PTSD	26	PTSD diagnosed by standardized clinical interview: 10–19 %
	<i>Exclusion criteria</i> : (1) Studies focusing solely ICU subgroups such as patients with ARDS or pancreatitis, (2) studies using single-item measures or questionnaires not validated for PTSD, (3) studies with a sample size smaller than 30, (4) conference papers or abstracts, (5) investigations published in a language other than English, (6) studies published pre-1997, and (7) studies set in neonatal or pediatric ICUs		Possible/likely PTSD or some symptoms of PTSD by self-report measure: 0–75 % ^a

Table 1 Summary of systematic reviews assessing prevalence of posttraumatic stress disorder among survivors of critical illness

ICU intensive care unit, PTSD posttraumatic stress disorder, ALI/ARDS acute lung injury/acute respiratory distress syndrome, QOL quality of life

Includes estimates from study subpopulations (control groups and/or treatment or case groups)

utilization of those that have been validated for assessment of posttraumatic stress symptoms (i.e., PCL, IES-R, and PTSS-10) may improve the ability to compare estimates of PTSD prevalence. Furthermore, care should be taken in the language used to describe findings based upon questionnaire-based assessments. Though symptoms of PTSD can be readily assessed, the diagnosis of PTSD from 24 to 88 % of enrolled patients [13]. Loss to follow-

cannot be made via questionnaire alone. Finally, problems obtaining adequate follow-up among survivors of critical illness may impact prevalence estimates. Among the noncross-sectional studies assessed in the systematic review by Wade et al., reported follow-up rates (proportion of those enrolled who completed PTSD follow-up) ranged up is a concern in assessing the prevalence of any phenomenon, but may be particularly problematic in assessing PTSD since avoidant behavior, a key characteristic of PTSD, might cause some ICU survivors to avoid participating in long-term follow-up. Thus, many of the cited studies may underestimate the true prevalence of PTSD.

Estimates from the national comorbidity survey replication (NCS-R), a longitudinal investigation of the prevalence of various psychiatric disorders among the general US population, suggest a lifetime prevalence of PTSD among American adults of 6.8 % [18]. In comparison, estimates of post-ICU PTSD fall within the range of PTSD prevalence seen after the occurrence of natural disasters [19]. Furthermore, studies focused on longitudinal assessments of posttraumatic stress among ICU survivors provide evidence of symptom persistence over time. A recent single-center study utilizing the PCL to assess post-ICU PTSD symptoms among medical-surgical patients found a prevalence of 16 % at 3 months post-ICU and 15 % at 12 months post-ICU [15]. A multicenter study evaluating patients following mechanical ventilation for acute lung injury used the IES-R and demonstrated a point prevalence of PTSD symptoms of 23 % at 12-month follow-up and 24 % at 24-month follow-up [20]. There is substantial evidence to suggest that post-ICU PTSD is common, and even more concerning is the evidence that the impact of critical illness on mental health may last for years.

Creation of a conceptual model addressing PTSD among ICU survivors

To begin to address the burden of psychiatric morbidity among survivors of critical illness, clinicians must be able to recognize symptoms characteristic of PTSD (Table 2). In addition, they must be able to identify patients at high risk of posttraumatic stress in the post-ICU period. Numerous factors have been associated with increased risk of PTSD following critical illness. While some risk factors are not modifiable during an episode of critical illness, they remain important as potential indicators of those at high risk for post-ICU PTSD. Identification of these individuals should begin at the time of ICU admission, taking into consideration factors that arrive with the patient. Other risk factors arise during a patient's ICU stay. These factors differ in that they may serve as targets for intervention both during and after critical illness. Thus, in a conceptual model of post-ICU PTSD it is important to differentiate between non-modifiable and modifiable risk factors in order to encourage early recognition of those at high risk (for non-modifiable factors) and allow efforts to address intra-ICU events that may accentuate or attenuate the risk of subsequent symptoms of posttraumatic stress (for modifiable factors). Importantly, an understanding of risk factors facilitates potential

strategies that may attenuate the risk of symptom development (Fig. 1).

Non-modifiable risk factors associated with post-ICU PTSD

Evidence of psychological distress or mental illness in the time period prior to ICU admission has been strongly associated with increased risk of PTSD after survival of critical illness [20-24], and this important risk factor should be noted by clinicians in order to identify survivors of critical illness who are at highest risk for adverse outcomes. For example, a recent longitudinal evaluation of PTSD symptoms after acute lung injury (ALI) identified a significant and independent association between pre-ALI depressive illness and post-ALI PTSD (hazards odds ratio 1.96, 95 % CI 1.06–3.64, P = 0.03) [20]. Survivors of traumatic injury also represent a unique patient population with a high risk of post-ICU psychological distress [25, 26]. Among other non-modifiable, patient-specific variables, both younger age and female sex have been suggested as potential risk factors for symptoms of posttraumatic stress, but with inconsistent results across studies [13]. Theoretical considerations would suggest severity of illness as an important potential precipitant of future mental health disorders, but it has not been found to be predictive of post-ICU PTSD [12, 13]. Exploration of the role of genetic factors in the occurrence of post-ICU PTSD has provided interesting insights into non-modifiable factors that inform the potential pathogenesis of PTSD among survivors of critical illness. An investigation of post-cardiac surgery patients requiring ICU treatment demonstrated increased symptoms of PTSD among individuals homozygous for a singlenucleotide polymorphism of the glucocorticoid receptor gene [27]. Another recent study of medical-surgical ICU patients revealed an association between homozygosity for a single-nucleotide polymorphism of the corticotrophin-releasing hormone binding protein and decreased post-ICU PTSD symptoms [28]. Although genetic polymorphisms are not modifiable, they may offer future targets to assist in identification of those at highest risk.

Modifiable risk factors and potential strategies to attenuate post-ICU PTSD

For many patients, extreme agitation is a significant component of the ICU experience and higher levels of agitation in the ICU have been identified as a predictor of PTSD-related symptoms [29]. Agitation can negatively affect both patient and staff safety, and attempts to minimize patient self-harm often rely on the use of physical restraints. The use of physical restraints has also been associated with greater risk of PTSD; however, the

by having a life-threatening traumatic event (real or perceived), followed by intrusive				
egin within 3 months of the traumatic event				
Differentiating PTSD from depression in the post-ICU period may be difficult, as symptoms may be shared. However, key to the diagnosis of PTSD is the presence of intrusive recollections of a traumatic event and avoidant behaviors related to the event				
r flashbacks related to the traumatic event ce iccentrating olems anger eping ionally numb wing or talking about the traumatic event				

Table 2 Posttraumatic stress disorder and symptoms of posttraumatic stress

ICU intensive care unit. PTSD posttraumatic stress disorder

Symptoms of posttraumatic stress may be assessed by questionnaire, but PTSD is diagnosed by clinician assessment



ICU Intensive Care Unit; PTSD Posttraumatic stress disorder; PTSS Posttraumatic stress symptoms; CBT Cognitive-behavioral therapy

Fig. 1 A conceptual model for post-ICU PTSD: identification, prevention, and diagnosis and treatment. ICU intensive care unit, PTSD posttraumatic stress disorder, PTSS posttraumatic stress symptoms, CBT cognitive behavioral therapy

correlation between physical restraint and agitation makes this association complex [30].

In addition to the utilization of physical restraints, medications are frequently administered to critically ill patients in order to control agitation and treat anxiety and discomfort. Much attention has been focused on the types of medications provided to ICU patients and the duration receipt of midazolam [29] and total dose of lorazepam

of medication use as they relate to risk of post-ICU PTSD. Particular interest has been placed on the role of benzodiazepines given the evidence of an association between these medications and the development of ICU delirium [31] and concerns about a potential relationship between ICU delirium and psychological morbidity [23]. Both

en associated with

[32] administered in the ICU have been found to be associated with greater risk of post-ICU PTSD. Opiates are also commonly prescribed in the ICU, and higher doses of opiates have been associated with an increased risk of PTSD symptoms [20]. However, associations between these specific medications and psychological distress among survivors of critical illness have not been uniformly apparent in investigations of post-ICU PTSD [12, 13], likely reflecting the difficulty in estimating the effects of medications that are often provided in the context of agitation and anxiety. To further complicate this relationship, preexisting psychological issues, a well-established risk factor for post-ICU PTSD, have been associated with receipt of sedative medications in the ICU [30].

The connection between medication administration and ICU delirium might suggest that minimization of sedation could reduce the occurrence of ICU delirium and potentially influence symptoms of posttraumatic stress. If minimization of sedation allows more days of wakefulness in the absence of delirium [33], judicious administration of sedatives may also be able to attenuate symptoms of posttraumatic stress. A study of long-term psychological outcomes offers some insight into a possible impact of this strategy on the risk of post-ICU PTSD [34]. Investigators compared mechanically ventilated patients receiving daily, protocol-driven sedation interruptions [35] to patients receiving sedation interruption at the discretion of their medical team. Assessment of psychological function occurred at a minimum of 6 months after hospital discharge. Patients in the intervention arm demonstrated a significant reduction in PTSD symptoms compared to those in the control arm (total IES-R 11.2 ± 14.9 in the intervention group versus 27.3 ± 19.2 in the control group; difference, 16.1; P = 0.02). Clinical interviews were also performed and only individuals in the control group received a diagnosis of PTSD based upon DSM-IV criteria (n = 6 of 19 versus 0 of 13 in intervention arm; P = 0.06). Although comparison of PTSD diagnosis between groups did not reach statistical significance, these results were based upon a small sample size [34]. The impact of sedation interruption or minimizing sedation on post-ICU PTSD risk remains unclear, but potential benefits of minimizing sedation seem to outweigh the potential harms [36–38]. The possibility of post-ICU PTSD symptom reduction is promising and provides yet another reason for physicians to minimizing sedation by employing a goaldirected approach to sedation [39].

Alternative sedation strategies may offer an opportunity to attenuate post-ICU PTSD symptoms but are not the only in-hospital mechanism by which providers might influence long-term outcomes. Significant levels of distress immediately following critical illness may represent another target for intervention. High levels of anxiety and depression in the immediate post-ICU period appear to influence the presence of psychological distress in the months after hospital discharge [40], and negative perceptions of the ICU experience at the time of hospital

discharge have been associated with subsequent anxiety and depression [29]. Furthermore, acute stress symptoms (PTSD symptoms less than 1 month after the acute stressor) have been linked to increased severity of post-ICU PTSD and depression [15]. Efforts to address these symptoms need not wait until after hospital discharge, and investigations focusing on early intervention offer encouraging results. In a single-center observational study, clinical psychologists provided a variety of services to patients while still in the ICU, including counseling, psychological support, education, and strategies focused on coping with psychological distress [41]. Those not experiencing interaction with the clinical psychologists served as a "control arm". Comparison of these groups at 12 months after ICU discharge demonstrated significant reductions in scores on the IES-R among the psychological intervention group (32.1 ± 14.2) in the control group versus 27.2 ± 9.2 in the intervention group; P = 0.01) [41]. While this investigation focused on traumatically injured patients, these results suggest that survivors of critical illness may benefit from efforts to identify evidence of acute stress and provide psychological support prior to ICU or hospital discharge.

In addition to confronting psychological distress in the immediate aftermath of critical illness, continued efforts to address recall of the ICU experience over time are also important. Descriptions of patient memories reveal recollections of discomfort related to common elements of ICU care [42] and reports of pain, anxiety, and fear are common [43]. Frightening hallucinations and paranoid delusions that occur during a patient's ICU stay, likely in the context of delirium, may continue to haunt individuals well after their critical illness has resolved [44]. Though the presence of factual memories does not obviate the risk of post-ICU symptoms of PTSD [45], evidence suggests that so-called delusional memories (i.e., memories of hallucinatory experiences and/or delusional events or thoughts during the ICU admission) place patients at higher risk of developing PTSD-related symptoms [30, 46, 47]. Minimizing the occurrence of delusional memories in the ICU poses a significant clinical challenge, and the limitations of current management strategies suggest that patients will continue to experience troubling recollections of the ICU. However, interventions focused on improving patient understanding of events occurring during critical illness have provided promising results.

Specifically, two investigations have focused on the role of diaries in the ICU as a method to reduce symptoms of post-ICU PTSD among survivors [48, 49]. Jones et al. [48] conducted a randomized trial involving creation of diaries with text and photographs, written in large part by the patient's bedside nurses but also including entries from family members and other healthcare providers. One month post-ICU, patients were either provided with their diaries and an explanation of the diary's contents or were required to wait, receiving the diary at 3-month follow-up.

Comparison of these groups revealed that at the 3-month evaluation, patients who received their diaries earlier were less likely to be diagnosed with PTSD [48]. Second, in a single-center study of medical-surgical ICU patients, Garrouste-Orgeas et al. [49] assessed the influence of ICU diaries on symptoms of post-ICU posttraumatic stress among both patients and their family members. Diaries written by family members, nurses, and physicians were provided to survivors at the time of ICU discharge and diaries were provided to relatives of non-survivors. For both patients and relatives, levels of posttraumatic symptoms as measured by the IES-R were lower at 12-month follow-up, when compared to pre- and postdiary controls [49]. ICU diaries have also been associated with reductions in related post-ICU psychiatric morbidities, including depressive and anxiety symptoms [50]. These investigations suggest that introduction and processing of factual information may be of significant benefit for survivors of critical illness.

Future directions for identification and management of post-ICU PTSD

Although the prevalence of and risk factors for PTSD after critical illness have been assessed in many studies, few have evaluated feasible ways to screen patients during or after critical illness for symptoms of posttraumatic stress [51, 52]. Importantly, screening tools developed for patient assessment should also be evaluated for post-ICU PTSD among family members of critically ill patients, another population with significant risk for psychiatric morbidity [53–55]. The development of screening tools to identify those at high risk for PTSD in the post-ICU setting represents an opportunity for future investigation and will be of increasing utility as additional studies investigate interventions focused on mitigating the development of post-ICU PTSD via effective and scalable interventions.

PTSD in the general population suggest that a variety of to be common among ICU survivors and symptoms of

interventions may be beneficial, including cognitive behavioral therapy (particularly exposure-based therapies such as trauma-focused cognitive behavioral therapy) and pharmacologic treatment [56]. However, there is little information to inform best practices for long-term management of PTSD among ICU survivors and it is unknown if one or more of the aforementioned treatment strategies may be better suited to these patients. Recent investigations of coping and mindfulness techniques as approaches to managing psychological stress following ICU discharge have provided promising results [57, 58]. Qualitative evaluations of coping skills employed by medical professionals affected by the ICU environment may also provide insights into approaches to attenuate the development of PTSD [59]. These techniques may serve as important strategies to improve quality of life for a significant number of patients who survive critical illness, but until they can be further evaluated and implemented on a broader scale, patients will continue to rely on their outpatient providers for care in the post-ICU period. After hospital discharge, patients often return to providers who may be unfamiliar with the psychological distress that can follow treatment in the ICU. Primary care providers often manage mental health disorders [60], and education regarding the common occurrence of PTSD after critical illness may help these providers recognize posttraumatic stress symptoms early so that effective treatment and appropriate referrals to specialists can be implemented. Patients at particularly high risk for post-ICU PTSD may benefit from care in clinics dedicated to the management of the myriad physical and psychological complications that occur among survivors of critical illness. This may include individuals with preexisting psychiatric illness or those who exhibit evidence of early post-ICU psychiatric symptoms.

Summarv

Current practice guidelines for the management of Although prevalence estimates vary widely, PTSD appears

Table 3 Posttraumatic stress disorder among ICU survivors: important insights and implications for clinical care

PTSD is common following critical illness and symptoms may persists for months

Recognition of non-modifiable risk factors is important to identify those at high risk of post-ICU PTSD

Preexisting psychiatric illness should serve as a prompt to ensure close follow-up for psychiatric morbidity in the peri-ICU period Minimizing sedation in the ICU and addressing early post-ICU distress may attenuate subsequent symptoms of posttraumatic stress Physicians should target lighter levels of sedation in the ICU

PTSD symptoms <1 month after the acute stressor should alert clinicians to those at high risk of severe psychiatric morbidity Efforts to educate and counsel patients about the ICU experience can reduce psychiatric morbidity

Psychological support in the ICU may benefit high-risk patients

Introduction of ICU diaries into routine clinical care may improve clinical outcomes for patients and their family members Future research is needed to inform best practices for identification and management of PTSD among ICU survivors There is need for a validated screening tool to identify those with significant psychiatric symptoms after ICU discharge Providers who care for patients after ICU discharge should be aware of common symptoms of PTSD Studies evaluating coping strategies and mindfulness techniques as interventions for post-ICU psychiatric morbidity are promising

ICU intensive care unit, PTSD posttraumatic stress disorder

posttraumatic stress can persist for many months after recovery from critical illness. With the assistance of a conceptual model that integrates known risk factors and current evidence regarding potential strategies to reduce symptoms of posttraumatic stress (Fig. 1), the important implications for clinical practice can be appreciated (Table 3). Additional study is necessary to improve understanding of salient risk factors, as is ongoing effort to develop methods of screening to identify patients at high risk for post-ICU PTSD. Until reliable and validated screening tools are developed, physicians should be aware of the potential risk factors for PTSD among ICU survivors. These may include non-modifiable risk factors that are present prior to ICU admission, such as preexisting psychiatric conditions or traumatic injury. Modifiable risk factors that exist during the patient's ICU stay may include frightening hallucinations, paranoid delusions, and episodes of extreme agitation. Medications administered in the ICU, particularly benzodiazepines, may

play a significant role in pathogenesis of post-ICU PTSD, and minimizing sedatives seems to reduce the occurrence of PTSD symptoms without evidence of patient harm. Modifiable risk factors occurring in the early post-ICU period are also important. Psychological distress manifested by anxiety and/or acute stress symptoms is an important marker of post-ICU PTSD risk, warranting attention from providers caring for these patients before they are discharged from the hospital. Finally, the positive impact of interventions to provide patients with coping skills in the aftermath of critical illness and to enhance patient understanding of traumatic events offers promise for improving long-term management of PTSD among ICU survivors.

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References

- Davidson TA, Caldwell ES, Curtis JR, Hudson LD, Steinberg KP (1999) Reduced quality of life in survivors of acute respiratory distress syndrome compared with critically ill control patients. JAMA 281:354–360
- 2. Cuthbertson BH, Roughton S, Jenkinson D, Maclennan G, Vale L (2010) Quality of life in the five years after intensive care: a cohort study. Crit Care 14:R6
- Dowdy DW, Eid MP, Sedrakyan A, Mendez-Tellez PA, Pronovost PJ, Herridge MS, Needham DM (2005) Quality of life in adult survivors of critical illness: a systematic review of the literature. Intensive Care Med 31:611–620
- Hopkins RO, Weaver LK, Collingridge D, Parkinson RB, Chan KJ, Orme JF Jr (2005) Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. Am J Respir Crit Care Med 171:340–347
- Schmidt M, Zogheib E, Roze H, Repesse X, Lebreton G, Luyt CE, Trouillet JL, Brechot N, Nieszkowska A, Dupont H, Ouattara A, Leprince P, Chastre J, Combes A (2013) The PRESERVE mortality risk score and analysis of longterm outcomes after extracorporeal membrane oxygenation for severe acute respiratory distress syndrome. Intensive Care Med 39:1704–1713
- Davydow DS, Desai SV, Needham DM, Bienvenu OJ (2008) Psychiatric morbidity in survivors of the acute respiratory distress syndrome: a systematic review. Psychosom Med 70:512–519

- Davydow DS, Gifford JM, Desai SV, Bienvenu OJ, Needham DM (2009) Depression in general intensive care unit survivors: a systematic review. Intensive Care Med 35:796–809
- Adhikari NK, McAndrews MP, Tansey CM, Matte A, Pinto R, Cheung AM, Diaz-Granados N, Barr A, Herridge MS (2009) Self-reported symptoms of depression and memory dysfunction in survivors of ARDS. Chest 135:678–687
- Schelling G, Stoll C, Haller M, Briegel J, Manert W, Hummel T, Lenhart A, Heyduck M, Polasek J, Meier M, Preuss U, Bullinger M, Schuffel W, Peter K (1998) Health-related quality of life and posttraumatic stress disorder in survivors of the acute respiratory distress syndrome. Crit Care Med 26:651–659
- Jackson JC, Hart RP, Gordon SM, Hopkins RO, Girard TD, Ely EW (2007) Post-traumatic stress disorder and post-traumatic stress symptoms following critical illness in medical intensive care unit patients: assessing the magnitude of the problem. Crit Care 11:R27
- Griffiths J, Fortune G, Barber V, Young JD (2007) The prevalence of post traumatic stress disorder in survivors of ICU treatment: a systematic review. Intensive Care Med 33:1506–1518
- Davydow DS, Gifford JM, Desai SV, Needham DM, Bienvenu OJ (2008) Posttraumatic stress disorder in general intensive care unit survivors: a systematic review. Gen Hosp Psychiatry 30:421–434

- Wade D, Hardy R, Howell D, Mythen M (2013) Identifying clinical and acute psychological risk factors for PTSD after critical care: a systematic review. Minerva Anestesiol 79:944–963
- 14. Davydow DS, Zatzick DF, Rivara FP, Jurkovich GJ, Wang J, Roy-Byrne PP, Katon WJ, Hough CL, Kross EK, Fan MY, Joesch J, MacKenzie EJ (2009) Predictors of posttraumatic stress disorder and return to usual major activity in traumatically injured intensive care unit survivors. Gen Hosp Psychiatry 31:428–435
- 15. Davydow DS, Zatzick D, Hough CL, Katon WJ (2013) A longitudinal investigation of posttraumatic stress and depressive symptoms over the course of the year following medical-surgical intensive care unit admission. Gen Hosp Psychiatry 35:226–232
- Bienvenu OJ, Williams JB, Yang A, Hopkins RO, Needham DM (2013) Posttraumatic stress disorder in survivors of acute lung injury: evaluating the impact of event scalerevised. Chest 144:24–31
- 17. Stoll C, Kapfhammer HP, Rothenhausler HB, Haller M, Briegel J, Schmidt M, Krauseneck T, Durst K, Schelling G (1999) Sensitivity and specificity of a screening test to document traumatic experiences and to diagnose post-traumatic stress disorder in ARDS patients after intensive care treatment. Intensive Care Med 25:697–704

- R. Merikangas KR. Walters EE (2005) Lifetime prevalence and age-of-onset distributions of DSM-IV disorders in the national comorbidity survey replication. Arch Gen Psychiatry 62:593-602
- 19. Galea S, Nandi A, Vlahov D (2005) The epidemiology of post-traumatic stress disorder after disasters. Epidemiol Rev 27.78 - 91
- 20. Bienvenu OJ, Gellar J, Althouse BM, Colantuoni E, Sricharoenchai T, Mendez-Tellez PA, Shanholtz C. Dennison CR, Pronovost PJ, Needham DM (2013) Post-traumatic stress disorder symptoms after acute lung injury: a 2-year prospective longitudinal study. Psychol Med 43:2657-2671
- 21. Cuthbertson BH, Hull A, Strachan M, Scott J (2004) Post-traumatic stress disorder after critical illness requiring general intensive care. Intensive Care Med 30:450-455
- 22. Nickel M, Leiberich P, Nickel C, Tritt K, Mitterlehner F, Rother W, Loew T (2004) The occurrence of posttraumatic stress disorder in patients following intensive care treatment: a crosssectional study in a random sample. J Intensive Care Med 19:285-290
- 23. Wade DM, Howell DC, Weinman JA, Hardy RJ, Mythen MG, Brewin CR, Borja-Boluda S, Matejowsky CF, Raine RA (2012) Investigating risk factors for psychological morbidity three months after intensive care: a prospective cohort study. Crit Care 16:R192
- 24. Jubran A, Lawm G, Duffner LA, Collins EG, Lanuza DM, Hoffman LA, Tobin MJ (2010) Post-traumatic stress disorder after weaning from prolonged mechanical ventilation. Intensive Care Med 36:2030-2037
- 25. Holbrook TL, Hoyt DB, Stein MB, Sieber WJ (2001) Perceived threat to life predicts posttraumatic stress disorder after major trauma: risk factors and functional outcome. J Trauma 51:287-292 (discussion 292-293)
- 26. O'Donnell ML, Creamer M, Holmes AC, Ellen S, McFarlane AC, Judson R, Silove D, Bryant RA (2010) Posttraumatic stress disorder after injury: does admission to intensive care unit increase risk? J Trauma 69:627-632
- 27. Hauer D, Weis F, Papassotiropoulos A, Schmoeckel M, Beiras-Fernandez A, Lieke J, Kaufmann I, Kirchhoff F Vogeser M, Roozendaal B, Briegel J, de Quervain D, Schelling G (2011) Relationship of a common polymorphism of the glucocorticoid receptor gene to traumatic memories and posttraumatic stress disorder in patients after intensive care therapy. Crit Care Med 39:643-650

- 18. Kessler RC, Berglund P, Demler O, Jin 28. Davydow DS, Kohen R, Hough CL, Tracy JH. Zatzick D. Katon WJ (2014) A pilot investigation of the association of genetic polymorphisms regulating corticotrophin-releasing hormone with posttraumatic stress and depressive symptoms in medical-surgical intensive care unit survivors. J Crit Care 29:101-106
 - 29. Samuelson KA, Lundberg D, Fridlund B (2007) Stressful memories and psychological distress in adult mechanically ventilated intensive care patients-a 2 month follow-up study. Acta Anaesthesiol Scand 51:671–678
 - 30. Jones C, Backman C, Capuzzo M, Flaatten H, Rylander C, Griffiths RD (2007) Precipitants of post-traumatic stress disorder following intensive care: a hypothesis generating study of diversity in care. Intensive Care Med 33:978-985
 - 31. Pandharipande P, Shintani A, Peterson J, Pun BT, Wilkinson GR, Dittus RS, Bernard GR, Ely EW (2006) Lorazepam is an independent risk factor for transitioning to delirium in intensive care unit patients. Anesthesiology 104:21-26
 - 32. Girard TD, Shintani AK, Jackson JC, Gordon SM, Pun BT, Henderson MS. Dittus RS, Bernard GR, Ely EW (2007) Risk factors for post-traumatic stress disorder symptoms following critical illness requiring mechanical ventilation: a prospective cohort study. Crit Care 11:R28
 - 33. Hager DN, Dinglas VD, Subhas S, Rowden AM, Neufeld KJ, Bienvenu OJ, Touradji P, Colantuoni E, Reddy DR, Brower RG, Needham DM (2013) Reducing deep sedation and delirium in acute lung injury patients: a quality improvement project. Crit Care Med 41:1435-1442
 - 34. Kress JP, Gehlbach B, Lacy M, Pliskin N, Pohlman AS, Hall JB (2003) The long-term psychological effects of daily sedative interruption on critically ill patients. Am J Respir Crit Care Med 168:1457-1461
 - 35. Kress JP, Pohlman AS, O'Connor MF, Hall JB (2000) Daily interruption of sedative infusions in critically ill patients undergoing mechanical ventilation. N Engl J Med 342:1471-1477
 - Treggiari MM, Romand JA, Yanez ND, 36. Deem SA, Goldberg J, Hudson L, Heidegger CP, Weiss NS (2009) Randomized trial of light versus deep sedation on mental health after critical illness. Crit Care Med 37:2527-2534

- 37. Girard TD, Kress JP, Fuchs BD, Thomason JW. Schweickert WD. Pun BT, Taichman DB, Dunn JG, Pohlman AS, Kinniry PA, Jackson JC, Canonico AE, Light RW, Shintani AK, Thompson JL, Gordon SM, Hall JB, Dittus RS, Bernard GR, Ely EW (2008) Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (awakening and breathing controlled trial): a randomised controlled trial. Lancet 371:126-134
- 38. Jackson JC, Girard TD, Gordon SM, Thompson JL, Shintani AK, Thomason JW, Pun BT, Canonico AE, Dunn JG, Bernard GR, Dittus RS, Ely EW (2010) Long-term cognitive and psychological outcomes in the awakening and breathing controlled trial. Am J Respir Crit Care Med 182:183-191
- 39. Barr J, Fraser GL, Puntillo K, Ely EW, Gelinas C, Dasta JF, Davidson JE, Devlin JW, Kress JP, Joffe AM, Coursin DB, Herr DL, Tung A, Robinson BR, Fontaine DK, Ramsay MA, Riker RR, Sessler CN, Pun B, Skrobik Y, Jaeschke R (2013) Clinical practice guidelines for the management of pain, agitation, and delirium in adult patients in the intensive care unit. Crit Care Med 41:263–306
- 40. Rattray JE, Johnston M, Wildsmith JA (2005) Predictors of emotional outcomes of intensive care. Anaesthesia 60:1085-1092
- 41. Peris A, Bonizzoli M, Iozzelli D, Migliaccio ML, Zagli G, Bacchereti A, Debolini M, Vannini E, Solaro M, Balzi I, Bendoni E, Bacchi I, Trevisan M, Giovannini V, Belloni L (2011) Early intra-intensive care unit psychological intervention promotes recovery from post traumatic stress disorders, anxiety and depression symptoms in critically ill patients. Crit Care 15:R41
- 42. van de Leur JP, van der Schans CP, Loef BG, Deelman BG, Geertzen JH, Zwaveling JH (2004) Discomfort and factual recollection in intensive care unit patients. Crit Care 8:R467-R473
- 43. Ethier C, Burry L, Martinez-Motta C, Tirgari S, Jiang D, McDonald E Granton J, Cook D, Mehta S (2011) Recall of intensive care unit stay in patients managed with a sedation protocol or a sedation protocol with daily sedative interruption: a pilot study. J Crit Care 26:127-132
- Zetterlund P, Plos K, Bergbom I, 44. Ringdal M (2012) Memories from intensive care unit persist for several years-a longitudinal prospective multi-centre study. Intensive Crit Care Nurs 28:159-167

- 45. Granja C, Gomes E, Amaro A, Ribeiro 52. Twigg E, Humphris G, Jones C, O, Jones C, Carneiro A, Costa-Pereira A (2008) Understanding posttraumatic stress disorder-related symptoms after critical care: the early illness amnesia hypothesis. Crit Care Med 36:2801-2809
- 46. Jones C, Skirrow P, Griffiths RD, Humphris GH, Ingleby S, Eddleston J, Waldmann C, Gager M (2003) Rehabilitation after critical illness: a randomized, controlled trial. Crit Care Med 31:2456-2461
- 47. Jones C, Griffiths RD, Humphris G, Skirrow PM (2001) Memory, delusions, and the development of acute posttraumatic stress disorder-related symptoms after intensive care. Crit Care Med 29:573-580
- 48. Jones C, Backman C, Capuzzo M, Egerod I, Flaatten H, Granja C, Rylander C, Griffiths RD (2010) Intensive care diaries reduce new onset post traumatic stress disorder following critical illness: a randomised, controlled trial. Crit Care 14:R168
- 49. Garrouste-Orgeas M, Coquet I, Perier A, Timsit JF, Pochard F, Lancrin F. Philippart F, Vesin A, Bruel C, Blel Y, Angeli S, Cousin N, Carlet J, Misset B (2012) Impact of an intensive care unit diary on psychological distress in patients and relatives. Crit Care Med 40:2033-2040
- 50. Knowles RE, Tarrier N (2009) Evaluation of the effect of prospective patient diaries on emotional well-being in intensive care unit survivors: a randomized controlled trial. Crit Care Med 37:184-191
- 51. Schandl A, Bottai M, Hellgren E, Sundin O, Sackey PV (2013) Developing an early screening instrument for predicting psychological morbidity after critical illness. Crit Care 17:R210

- Bramwell R. Griffiths RD (2008) Use of a screening questionnaire for posttraumatic stress disorder (PTSD) on a sample of UK ICU patients. Acta Anaesthesiol Scand 52:202-208
- 53. Azoulay E, Pochard F, Kentish-Barnes N, Chevret S, Aboab J, Adrie C, Annane D, Bleichner G, Bollaert PE, Darmon M, Fassier T, Galliot R, Garrouste-Orgeas M, Goulenok C, Goldgran-Toledano D, Hayon J, Jourdain M, Kaidomar M, Laplace C, Larche J, Liotier J, Papazian L, Poisson C, Reignier J, Saidi F, Schlemmer B (2005) Risk of post-traumatic stress symptoms in family members of intensive care unit patients. Am J Respir Crit Care Med 171:987-994
- 54. Colville G, Pierce C (2012) Patterns of post-traumatic stress symptoms in families after paediatric intensive care. Intensive Care Med 38:1523-1531
- 55. Azoulay E, Kouatchet A, Jaber S, Lambert J, Meziani F, Schmidt M, Schnell D, Mortaza S, Conseil M, Tchenio X, Herbecq P, Andrivet P, Guerot E, Lafabrie A, Perbet S, Camous L, Janssen-Langenstein R, Collet F, Messika J, Legriel S, Fabre X, Guisset O, Touati S, Kilani S, Alves M, Mercat A, Similowski T, Papazian L, Meert AP, Chevret S, Schlemmer B, Brochard L, Demoule A (2013) Noninvasive mechanical ventilation in patients having declined tracheal intubation. Intensive Care Med 39:292-301

- 56. Ursano RJ, Bell C, Eth S, Friedman M, Norwood A. Pfefferbaum B. Pvnoos JD, Zatzick DF, Benedek DM, McIntyre JS, Charles SC, Altshuler K, Cook I, Cross CD, Mellman L, Moench LA, Norquist G, Twemlow SW, Woods S, Yager J (2004) Practice guideline for the treatment of patients with acute stress disorder and posttraumatic stress disorder. Am J Psychiatry 161:3-31
- 57. Cox CE, Porter LS, Hough CL, White DB, Kahn JM, Carson SS, Tulsky JA, Keefe FJ (2012) Development and preliminary evaluation of a telephonebased coping skills training intervention for survivors of acute lung injury and their informal caregivers. Intensive Care Med 38:1289-1297
- 58. Cox CE, Porter LS, Buck PJ, Hoffa M, Jones D, Walton B, Hough CL, Greeson JM (2014) Development and preliminary evaluation of a telephonebased mindfulness training intervention for survivors of critical illness. Ann Am Thorac Soc 11:173-181
- 59. Mealer M, Jones J, Moss M (2012) A qualitative study of resilience and posttraumatic stress disorder in United States ICU nurses. Intensive Care Med 38:1445-1451
- 60. Possemato K (2011) The current state of intervention research for posttraumatic stress disorder within the primary care setting. J Clin Psychol Med Settings 18:268-280