Published in final edited form as:

Gen Hosp Psychiatry. 2013 ; 35(3): 226–232. doi:10.1016/j.genhosppsych.2012.12.005.

A Longitudinal Investigation of Posttraumatic Stress and Depressive Symptoms over the Course of the Year Following Medical-Surgical Intensive Care Unit Admission

Dimitry S. Davydow, M.D., M.P.H.¹, Douglas Zatzick, M.D.¹, Catherine L. Hough, M.D., M.Sc.², and Wayne J. Katon, M.D.¹

¹Department of Psychiatry and Behavioral Sciences, University of Washington, Seattle, WA, USA

²Department of Medicine, University of Washington, Seattle, WA, USA

Abstract

Objective—To identify risk factors for posttraumatic stress disorder (PTSD) and depressive symptoms after medical-surgical intensive care unit (ICU) admission.

Method—This longitudinal investigation included 150 medical-surgical ICU patients. We assessed acute stress and post-ICU PTSD symptoms with the PTSD Checklist-civilian version and post-ICU depressive symptoms with the Patient Health Questionnaire-9. Mixed-model linear regression ascertained associations between patient and clinical characteristics and repeated measures of post-ICU PTSD and depressive symptoms.

Results—The prevalences of substantial PTSD and depressive symptoms were 16% and 31% at 3 months post-ICU and 15% and 17% at 12 months post-ICU, respectively. In-hospital substantial acute stress symptoms (beta: 16.9, 95% Confidence Interval [95%CI]: 11.4, 22.4) were independently associated with increased post-ICU PTSD symptoms. Lifetime history of major depression (beta: 2.2, 95%CI: 0.1, 4.2), greater prior trauma exposure (beta: 0.5, 95%CI: 0.2, 0.9) and in-hospital substantial acute stress symptoms (beta: 3.5, 95%CI: 0.8, 6.2) were independently associated with increased post-ICU depressive symptoms.

Conclusions—In-hospital acute stress symptoms may represent a modifiable risk factor for psychiatric morbidity in ICU survivors. Early interventions for at-risk ICU survivors may improve longer-term psychiatric outcomes.

Keywords

posttraumatic stress disorder; depression; critical care; intensive care; outcome assessment (health care)

© 2012 Elsevier Inc. All rights reserved.

Address for Correspondence: Dimitry S. Davydow, M.D., M.P.H., Department of Psychiatry and Behavioral Sciences, University of Washington School of Medicine, Box 359911, Harborview Medical Center, 325 Ninth Ave, Seattle, WA 98104, Phone: (206)-744-4534, Fax: (206)-744-3236, ddavydo1@u.washington.edu.

All authors have had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis.

Disclosures: Drs. Davydow, Zatzick, and Hough have no relevant conflicts of interest to disclose. Dr. Katon discloses that he has received honoraria in the last 12 months for CME lectures funded indirectly by Lilly, Forest and Pfizer.

Publisher's Disclaimer: This is a PDF file of an unedited manuscript that has been accepted for publication. As a service to our customers we are providing this early version of the manuscript. The manuscript will undergo copyediting, typesetting, and review of the resulting proof before it is published in its final citable form. Please note that during the production process errors may be discovered which could affect the content, and all legal disclaimers that apply to the journal pertain.

INTRODUCTION

Each year, millions of Americans survive hospitalizations in intensive care units (ICUs) for the treatment of critical illnesses [1]. As advances in critical care medicine decrease mortality, patient-centered outcomes such as emotional well-being are of increasing importance [2]. Critical illnesses expose patients to enormous stressors such as respiratory insufficiency, pain, and delirium [3], and are by definition life-threatening experiences. Furthermore, survivors may face considerable physical limitations during recovery [4–6]. Therefore, posttraumatic stress disorder (PTSD) and major depression are a potential risk for ICU survivors that may markedly affect subsequent quality of life [3, 4, 7].

Three systematic reviews of 24 cohort studies of general ICU and acute respiratory distress syndrome survivors have found that 22% and 28% of patients surviving critical illnesses may have substantial PTSD and depressive symptoms, respectively [3, 4, 7]. PTSD and major depression following critical illnesses are important public health problems since both disorders are independently associated with increased physical symptom burden, adverse medical outcomes and increased health care costs [8–12], and may also impair patients' ability to participate in their often prolonged post-ICU rehabilitation, thereby promoting enduring disability [2, 5]. Furthermore, in a nationwide US study of traumatic injury survivors in which approximately 50% of patients required ICU admission, substantial PTSD and depressive symptoms independently contributed to the inability to return to work 12 months after hospitalization [13].

Despite evidence about mental health disorders adversely affecting functioning and quality of life after hospitalization, there are few studies in non-injured populations examining whether specific critical illness-related exposures are independently associated with increased risk of subsequent PTSD and/or major depression. Prior studies have suggested that critical illnesses and their treatments may increase risk for adverse mental health outcomes [14–17]. However, very few studies of post-critical illness psychiatric disorders were appropriately designed to test this hypothesis. For instance, only three have examined the contribution of premorbid psychiatric symptoms using a standardized measure [5, 18, 19]. One of these studies, a longitudinal investigation of depressive symptoms in older survivors of severe sepsis, found no associations between severe sepsis itself or any of its treatment-related exposures with increased risk of subsequent substantial depressive symptoms after adjusting for pre-sepsis substantial depressive symptoms [5]. Ascertaining and understanding potential risk factors for PTSD and/or major depression following critical illnesses is crucial since psychiatric morbidity in the aftermath of an ICU admission could be a modifiable contributor to functional decline in these patients.

The present study is a longitudinal investigation of potential risk factors for PTSD and depressive symptom severity over the course of the year following medical-surgical ICU admission. We hypothesized that in-hospital acute stress symptoms and a prior history of major depression would be more potent predictors of PTSD or depressive symptom severity in the aftermath of a medical-surgical ICU admission than critical illness or ICU treatment-related exposures.

METHODS

Study Setting, Participants, and Procedures

The current investigation took place at Harborview Medical Center (HMC) in Seattle, WA. HMC is an urban, public medical center operated by the University of Washington (UW). Between September 2010 and August 2011, we prospectively recruited 150 patients admitted to any of the ICUs at HMC. Key exclusion criteria for the study were: 1) initial

admission diagnosis of traumatic injury; 2) pre-existing cognitive impairment or dementia diagnosis noted in the medical record; 3) communication/language barrier; 4) ICU length of stay (LOS) ≥ 24 hours; 5) pre-existing medical illness with life-expectancy of < 12 months; and 6) admission for a suicide attempt. The study protocol was approved by the UW Institutional Review Board (IRB), and all participants provided informed consent prior to enrollment.

Study research assistants identified potentially eligible subjects through review of HMC's electronic admission records. Subjects eligible for enrollment were approached for study consent prior to transfer from the ICU to the general medical-surgical ward. Because the UW IRB did not allow surrogate consent for participation in the study, if the patient was unable to provide consent due to ongoing delirium and/or cognitive impairment, consent was not obtained, and they were re-approached once their delirium and/or cognitive impairment had resolved. Cognitive impairment was assessed using a cutoff score of ≥ 3 errors on the Six-Item Cognitive Screen [20]. The area under the receiver operating characteristic curve for the Six-Item Cognitive Screen using cognitive impairment as the gold standard was 0.86 for a community-based sample compared to the Community Screening Instrument for Dementia and 0.91 for a clinical sample a battery including the Mini-Mental State Examination and the Consortium for Establishment of Registry for Alzheimer Disease battery [20].

Enrolled patients were administered an in-person interview prior to hospital discharge and were re-interviewed via telephone at 3 and 12 months post-ICU.

Measurements and Assessments

PTSD Symptoms—Severity of PTSD symptoms at 3 and 12-months post-discharge from the ICU was assessed with the PTSD Checklist-civilian version (PCL-C) [21]. The PCL-C includes questions regarding 5 symptoms in the intrusive symptom cluster, 7 symptoms in the avoidant symptom cluster, and 5 symptoms in the arousal symptom cluster, and symptom severity is rated on a 5 point Likert scale [21]. Substantial PTSD symptoms can be ascertained with the PCL-C by following an algorithm that considers a score of 3 or more on at least 1 intrusive symptom, 3 avoidant symptoms, and 2 arousal symptoms as consistent with DSM diagnostic criteria [21].

Depressive Symptoms—Severity of depressive symptoms at 3 and 12-month post-discharge from the ICU was assessed with the Patient Health Questionnaire-9 (PHQ-9) [22]. We defined substantial depressive symptoms as a PHQ-9 score ≥ 10 . The PHQ-9 threshold score of 10 or more for a probable case of major depression has been found to have high sensitivity (88%) and specificity (88%) for the diagnosis of major depression compared to structured psychiatric interview [22].

Patient and ICU-related Characteristics—Baseline patient characteristics and ICU clinical factors were obtained through medical record review and in-person interview with the patient. Medical record-obtained characteristics included demographics (e.g., age, sex, race); ICU admission diagnosis; baseline medical comorbidity information to compute a Charlson Comorbidity Score [23]; illness severity measures at ICU admission (e.g., systolic blood pressure, temperature, white blood cell count) to compute a Simplified Acute Physiology Score II (SAPS II) [24], a measure of acute illness severity that has been validated for in-hospital mortality prediction; ICU and hospital LOS; requirements for mechanical ventilation and duration of ventilation; requirement for major surgery and number of surgeries; number of blood product transfusions; days of exposure (both in-ICU and on medical-surgical ward) to benzodiazepine, opioid, antipsychotic, and antidepressant

medications; requirements for physical restraint and days restrained; presence of delirium in-ICU per nursing documented assessment using the Confusion Assessment Method-ICU (CAM-ICU) [24]; and presence of confusion/disorientation/difficulty following commands in nursing documentation. We defined probable delirium as a documented positive CAM-ICU assessment in the ICU or nursing documented presence of confusion/disorientation/difficulty following commands at any point during the hospitalization.

Additional patient characteristics obtained from the baseline interviews included demographics not obtained from medical records (e.g., marital/partnered status, education); assessment of prior trauma exposure with the National Comorbidity Survey-Replication Trauma History Screen [26]; lifetime history of major depression with the Mini International Neuropsychiatric Interview (MINI) major depressive episode module [27]; alcohol use in the prior year with the Alcohol Use Disorders Identification Test (AUDIT), with baseline problem drinking defined as an AUDIT score ≥ 8 [28]; drug use in the prior year with the Drug Abuse Screening Test-10 (DAST-10), with baseline problem drug use defined as a DAST-10 score ≥ 3 [29]; and substantial acute stress symptoms (defined as symptoms consistent with PTSD that are present for less than 1 month after occurrence of a traumatic stressor) with the PCL-C utilizing the same algorithm used to ascertain substantial PTSD symptoms [21].

Statistical Analysis

We present descriptive data as means and standard deviations (SDs) or proportions. To examine if there were significant differences between patients who completed 12-month follow-up and those that did not, we used one-way analysis of variance for continuous baseline and clinical variables and χ^2 -tests or Fisher's Exact tests for categorical variables.

In order to examine potential risk factors for PTSD and depressive symptom severity over the course of the year post-discharge from the ICU, we conducted two series of mixed-model linear regression analyses. The dependent variables were the repeated measures of PTSD symptom severity for the first series of analyses and the repeated measures of depressive symptom severity in the second series of analyses. Initially, we tested the associations of our hypothesized independent variables with our outcomes of interest without adjustment. We then added two groups of potential confounding variables to the regression models all chosen *a priori* because they have been found to be important in critical illness-related research [3, 6, 7, 30]: 1) demographics and baseline clinical characteristics (age, sex, race, education, marital/partnered status, lifetime history of major depression [in PTSD models], number of prior traumatic event exposures, problem drinking, problem drug use and Charlson score); and 2) clinical characteristics of the ICU admission (SAPS II score, duration of mechanical ventilation, number of surgeries, number of blood product transfusions, days physically restrained, presence of probable delirium during the hospitalization, days of exposure to benzodiazepines, opioids, antipsychotics, and antidepressants, and substantial acute stress symptoms [in depression models]). Continuous clinical variables that were non-normally distributed (i.e., duration of mechanical ventilation, number of surgeries, number of blood product transfusions, days physically restrained, and days of exposure to benzodiazepines, opioids, antipsychotics, and antidepressants), were included as categorical variables in our final regression model. We implemented our regression analyses using *xtmixed* in STATA 11.2 (Stata Corporation, College Station, TX).

We used two-sided significance tests for all analyses with statistical significance set at a *P* value of 0.05. Analyses were performed with appropriate components of the IBM SPSS Statistics 18 (SPSS Inc., Chicago, IL) and STATA 11.2 statistical software programs.

RESULTS

Of the 150 patients enrolled in the study, 120 (80%) completed a 12-month telephone follow-up interview (Figure 1). Table 1 presents the baseline and clinical characteristics of patients who did and did not complete 12-month follow-up. Baseline interviews were completed at a mean of 11.1 days after hospital admission (SD: 9.5). Patients' mean age at hospitalization was 48.2 years (SD: 13.7), and they had experienced a mean of 4.2 traumatic events (SD: 2.8) over their lifetime. Nearly half required mechanical ventilation during their ICU admission with a mean duration of 2.3 days (SD: 6.3, median: 2.0 days, interquartile range: 1.0, 4.0). The prevalence of probable delirium during the course of hospitalization was 51% and nearly half of patients were physically restrained during their hospitalization. At baseline, 29% met criteria for lifetime history of major depression based on the MINI, and 15% had substantial acute stress symptoms. Patients who did not complete follow-up were more likely to have substantial acute stress symptoms during their hospitalization.

Figure 2 illustrates the 3 and 12-month prevalences of post-ICU substantial PTSD and depressive symptoms. At 3 months post-discharge from the ICU (mean: 88.8 days, SD: 28.0), 16% (95% Confidence Interval [95% CI]: 10%, 23%) of patients had substantial PTSD symptoms and 31% (95% CI: 23%, 39%) had substantial depressive symptoms. Among patients with substantial PTSD symptoms at 3 months post-discharge from the ICU, 71% reported that these symptoms were related to memories of events that occurred while in the ICU. One year after ICU admission (mean: 356.4 days, SD: 29.2), the prevalence of substantial depressive symptoms had decreased to 17% (95% CI: 10%, 23%) while the prevalence of substantial PTSD symptoms was 15% (95% CI: 9%, 21%). Over two-fifths of patients with substantial PTSD symptoms at 12-months post-discharge from the ICU reported that these symptoms were related to memories of in-ICU events.

In unadjusted analyses, substantial acute stress symptoms during the hospitalization were associated with a 20 point higher PCL-C score (95% CI: 15.3, 24.9) over the course of the year following the ICU admission. A lifetime history of major depression was associated with a nearly 4 point higher post-ICU PHQ-9 score (95% CI: 1.6, 5.5) in unadjusted analyses.

After adjusting for baseline patient characteristics, substantial acute stress symptoms were associated with a 17 point higher post-ICU PCL-C score (95% CI: 12.1, 22.4) (Table 2). In addition, exposure to a greater number of lifetime traumatic events was also associated with a higher mean post-ICU PCL-C score (beta: 0.6, 95% CI: 0.04, 1.2). In the final model that adjusted for both patient and in-hospital clinical characteristics of the ICU admission, substantial acute stress symptoms remained the most potent factor associated with greater severity of PTSD symptoms over the course of the year after the ICU admission (beta: 16.9, 95% CI: 11.4, 22.4). No other baseline patient characteristics or clinical factors were found to be associated with greater post-ICU PTSD symptom severity in our final model.

When we adjusted for baseline patient characteristics, lifetime history of major depression was associated with a nearly 3 point higher post-ICU PHQ-9 score (95% CI: 1.0, 4.8) (Table 3). In addition, exposure to a greater number of lifetime traumatic events was also associated with a higher mean post-ICU PHQ-9 score (beta: 0.6, 95% CI: 0.3, 0.9). After adjusting for patient characteristics and clinical factors of the ICU admission, lifetime history of major depression (beta: 2.2, 95% CI: 0.1, 4.2), exposure to a greater number of lifetime traumatic events (beta: 0.6, 95% CI: 0.2, 0.9), and substantial acute stress symptoms during the hospitalization (beta: 3.5, 95% CI: 0.8, 6.2) were all independently associated with greater severity of depressive symptoms over the course of the year after the ICU admission.

DISCUSSION

In this longitudinal investigation of PTSD and depressive symptoms in medical-surgical ICU survivors, we highlight several key features of psychiatric morbidity in this population, including the identification of potentially modifiable risk factors for these adverse outcomes. We found that acute stress symptoms while in the hospital had a potent independent association with increased severity of not only PTSD symptoms, but also depressive symptoms over the course of the year post-ICU. Importantly, since in-hospital acute stress symptoms were associated with loss to follow-up at 12 months, the association we found is likely an underestimate.

High levels of patient distress prior to hospital discharge represent a potential risk factor for longer-term adverse mental health outcomes following ICU admission that may be modifiable if distressed patients are identified and receive evidence-based treatments early [31]. Interventions that combine screening and increased exposure to evidence-based treatments have improved mental health outcomes for patients hospitalized for traumatic injuries [32, 33], and they warrant dissemination to medical-surgical ICUs. Moreover, the primary care providers of patients surviving medical-surgical ICU admissions at heightened risk for psychiatric morbidity should be made aware of the potential for these adverse outcomes as part of optimal transition of care from inpatient to outpatient care settings, thereby facilitating screening and early intervention efforts.

Furthermore, the 1-year post-ICU prevalences of substantial PTSD and depressive symptoms in our cohort were considerably higher than the 1-year prevalences of PTSD and major depression found in the National Comorbidity Survey Replication [34]. Also, to our knowledge, this study is the first investigation of non-injured ICU survivors to include assessment of prior traumatic event exposure, which represents a potent risk factor for PTSD following an acute stressor [35], and a possible moderator of stress-response gene polymorphisms associated with risk of major depression [36].

Nearly three-quarters of the patients in our cohort with substantial PTSD symptoms at 3 months post-discharge from the ICU reported that their symptoms were related to memories of in-ICU events, a proportion that remained at over 40% nine months later. Prior studies have found that early post-ICU memories of frightening and/or traumatic in-ICU experiences were associated with both PTSD and depressive symptoms post-discharge from the ICU [3, 6]. Evidence is emerging that diaries compiled by ICU staff and patients' families that document the ICU experience and are reviewed with, and given to, patients after hospital discharge may reduce acute distress and subsequent PTSD symptoms by re-integrating fragmented memories of in-ICU traumatic and/or psychotic experiences [37, 38]. These interventions, along with others that target PTSD and depressive symptoms in medical-surgical ICU survivors, require further investigation.

Unlike the findings of prior studies in this area [3, 6, 16], we did not find that in-hospital exposure to benzodiazepines was independently associated with greater severity of PTSD or depressive symptoms over the course of the year following medical-surgical ICU admission. Although our inability to find an association between benzodiazepine exposure and post-ICU psychiatric morbidity could be due to ascertaining this exposure as duration of categorical exposure versus maximum daily doses of exposure, it is important to note that prior studies of post-critical illness psychiatric morbidity which identified benzodiazepines as a potential risk factor for these outcomes did not control for patient history of major depression [3, 6]. A recent longitudinal study of potential risk factors for substantial depressive symptoms in survivors of acute respiratory distress syndrome (ARDS) which used medical record diagnosis of depression as a measure of premorbid depression did not

find an independent association between maximum daily doses of benzodiazepine exposure and post-ARDS substantial depressive symptoms [4]. In addition, premorbid depression and anxiety has been associated with receiving more benzodiazepines in-ICU [39], suggesting that exposure to greater amounts of benzodiazepines in-ICU may be a marker for premorbid psychiatric illness or acute distress more broadly rather than a risk factor in-and-of-itself.

In line with prior work from members of our group [5], we found that the lifetime prevalence of major depression pre-dating ICU admission in this cohort was quite high. The high prevalence of major depression prior to ICU admission in our cohort suggests that additional study is warranted to examine if major depression is a potentially modifiable risk factor for critical illnesses, particularly given an emerging body of evidence suggesting a bidirectional relationship between depression and chronic medical illnesses [40]. Also, prior major depression has been found to be a potential risk factor for ICU admission in patients with diabetes [41], further supporting the need for additional research in this area.

Our study has several limitations. Since we were unable to obtain surrogate consent from patients who were persistently delirious and therefore could not include them in our study, we could not effectively evaluate whether prolonged delirium was associated with psychiatric morbidity post-discharge from the ICU. However, requiring patients to pass a validated cognitive screen prior to providing consent for study participation likely minimized the possibility that our assessment of in-hospital substantial acute stress symptoms was confounded by residual hyperactive delirium. Information on prior traumatic event exposure, lifetime major depression history and pre-ICU substance use may be subject to recall bias since this data was obtained from patients while they were still in the hospital, and is therefore retrospective in nature. Since we assessed PTSD and depressive symptoms with questionnaires, we could not make diagnoses of PTSD and/or major depression. Also, although the questionnaires we used to assess PTSD and depressive symptoms have not been specifically validated for use in medical-surgical ICU survivors, they have been used in many relevant populations such as family members of medical-surgical ICU patients [42, 43]. Further, our study was conducted in a single center serving a safety net population, and therefore our results may not be generalizable to the entire population of medical-surgical ICU survivors. Finally, the possibility of residual confounding remains as in any observational study.

In conclusion, we found that medical-surgical ICU survivors have high rates of psychiatric illness before and after ICU admission. In addition to lifetime history of major depression and greater prior traumatic event exposure, we identified that a potentially modifiable factor, in-hospital substantial acute stress symptoms, was independently associated with greater severity of post-ICU PTSD and depressive symptoms. Efforts to incorporate screening of medical-surgical ICU survivors for PTSD and major depression into routine care following critical illnesses, as well as additional research into interventions that prevent or ameliorate psychiatric morbidity in this population, are especially important in light of the enormous toll that critical illnesses, PTSD and major depression take on patients, their families and society.

Acknowledgments

The authors thank Collin McFadden, B.A., and Jeffrey Love, B.A., for assistance with patient recruitment and data collection, and Jin Wang, Ph.D., for assistance with data cleaning.

Funding: This work was supported by grants KL2 TR000421, NRSA-T32/MH20021-12, R03 AA020146-02, R01 AA01602 and K24 MH086814-03 from the National Institutes of Health and grant ADAI-1009-2 from the University of Washington Alcohol and Drug Abuse Institute.

References

1. Iwashyna TJ. Survivorship will be the defining challenge of critical care in the 21st century. *Ann Intern Med.* 2010; 153:204–205. [PubMed: 20679565]
2. Needham DM, Feldman DR, Kho ME. The functional costs of ICU survivorship: collaborating to improve post-ICU disability. *Am J Respir Crit Care Med.* 2011; 183:962–964. [PubMed: 21498817]
3. Davydow DS, Gifford JM, Desai SV, Needham DM, Bienvenu OJ. Posttraumatic stress disorder in general intensive care unit survivors: a systematic review. *Gen Hosp Psychiatry.* 2008; 30:421–434. [PubMed: 18774425]
4. Bienvenu OJ, Colantuoni E, Mendez-Tellez PA, et al. Depressive symptoms and impaired physical function after acute lung injury: a 2-year longitudinal study. *Am J Respir Crit Care Med.* 2012; 185:517–524. [PubMed: 22161158]
5. Davydow DS, Hough CL, Langa KM, Iwashyna TJ. Symptoms of depression in survivors of severe sepsis: a prospective cohort study of older Americans. *Am J Geriatr Psychiatry.* 2012 Jun 15. [Epub ahead of print].
6. Davydow DS, Gifford JM, Desai SV, Bienvenu OJ, Needham DM. Depression in general intensive care unit survivors: a systematic review. *Intensive Care Med.* 2009; 35:796–809. [PubMed: 19165464]
7. Davydow DS, Desai SV, Needham DM, Bienvenu OJ. Psychiatric morbidity in survivors of the acute respiratory distress syndrome: a systematic review. *Psychosom Med.* 2008; 70:512–519. [PubMed: 18434495]
8. Edmonson D, Richardson S, Falzon L, et al. Posttraumatic stress disorder prevalence and risk of recurrence in acute coronary syndrome patients: a meta-analytic review. *PLoS One.* 2012; 7:38915. Epub 2012 Jun 20.
9. Katon WJ, Rutter C, Simon G, et al. The association of comorbid depression with mortality in patients with type 2 diabetes. *Diabetes Care.* 2005; 28:2668–2672. [PubMed: 16249537]
10. Walker EA, Katon W, Russo J, et al. Health care costs associated with posttraumatic stress disorder symptoms in women. *Arch Gen Psychiatry.* 2003; 60:369–374. [PubMed: 12695314]
11. Katon W, Lin E, Russo J, Unützer J. Increased medical costs of a population-based sample of depressed elderly patients. *Arch Gen Psychiatry.* 2003; 60:897–903. [PubMed: 12963671]
12. Katon W, Lin EH, Kroenke K. The association of depression and anxiety with medical symptom burden in patients with chronic medical illness. *Gen Hosp Psychiatry.* 2007; 29:147–155. [PubMed: 17336664]
13. Zatzick D, Jurkovich GJ, Rivara FP, et al. A national US study of posttraumatic stress disorder, depression, and work and functional outcomes after hospitalization for traumatic injury. *Ann Surg.* 2008; 248:429–437. [PubMed: 18791363]
14. Nelson BJ, Weinert CR, Bury CL, Marinelli WA, Gross CR. Intensive care unit drug use and subsequent quality of life in acute lung injury patients. *Crit Care Med.* 2000; 28:3626–3630. [PubMed: 11098964]
15. Hopkins RO, Key CW, Suchyta MR, Weaver LK, Orme JF Jr. Risk factors for depression and anxiety in survivors of acute respiratory distress syndrome. *Gen Hosp Psychiatry.* 2010; 32:147–155. [PubMed: 20302988]
16. Dowdy DW, Bienvenu OJ, Dinglas VD, et al. Are intensive care factors associated with depressive symptoms 6 months after acute lung injury? *Crit Care Med.* 2009; 37:1702–1707. [PubMed: 19357507]
17. Herridge MS, Tansey CM, Matté A, et al. Functional disability 5 years after acute respiratory distress syndrome. *N Engl J Med.* 2011; 364:1293–1304. [PubMed: 21470008]
18. Weinert C, Meller W. Epidemiology of depression and antidepressant therapy after acute respiratory failure. *Psychosomatics.* 2006; 47:399–407. [PubMed: 16959928]
19. Davydow DS, Hough CL, Russo JE, et al. The association between intensive care unit admission and subsequent depression in patients with diabetes. *Int J Geriatr Psychiatry.* 2012; 27:22–30. [PubMed: 21308790]

20. Callahan CM, Unverzagt FW, Hui SL, Perkins AJ, Hendrie HC. Six-item screener to identify cognitive impairment among potential subjects for clinical research. *Med Care*. 2002; 40:771–781. [PubMed: 12218768]
21. Weathers, FW.; Huska, JA.; Keane, TM. The PTSD Checklist – civilian version. Boston, MA: The National Center for PTSD, Boston VA Medical Center; 1991.
22. Kroenke K, Spitzer RL, Williams JB. The PHQ-9: validity of a brief depression severity measure. *J Gen Intern Med*. 2001; 16:606–613. [PubMed: 11556941]
23. Charlson ME, Pompei P, Ales KL. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J Chron Dis*. 1987; 40:373–383. [PubMed: 3558716]
24. Le Gall JR, Lemeshow S, Saulnier F. A new Simplified Acute Physiology Score (SAPS II) based on a European/North American Multicenter Study. *JAMA*. 1993; 270:2957–2963. [PubMed: 8254858]
25. Ely EW, Inouye SK, Bernard GR, et al. Delirium in mechanically ventilated patients: validity and reliability of the Confusion Assessment Method for the intensive care unit (CAM-ICU). *JAMA*. 2001; 286:2703–2710. [PubMed: 11730446]
26. Ramstad SM, Russo J, Zatzick DF. Is it an accident? Recurrent traumatic life events in level I trauma center patients compared to the general population. *J Trauma Stress*. 2004; 17:529–534. [PubMed: 15730072]
27. Sheehan DV, Lecrubier Y, Sheehan KH, et al. The Mini-International Neuropsychiatric Interview (M.I.N.I.): the development and validation of a structured diagnostic psychiatric interview for DSM-IV and ICD-10. *J Clin Psychiatry*. 1998; 59:S22–S33.
28. Babor, TF.; de la Fuente, JR.; Saunders, J.; Grant, M. Guidelines for use in primary health care. Geneva, CH: World Health Organization; 1992. The Alcohol Use Disorders Identification Test.
29. Skinner HA. The Drug Abuse Screening Test. *Addict Behav*. 1982; 7:363–367. [PubMed: 7183189]
30. Davydow DS, Zatzick DF, Rivara FP, et al. Predictors of posttraumatic stress disorder and return to usual major activity in traumatically injured intensive care unit survivors. *Gen Hosp Psychiatry*. 2009; 31:428–435. [PubMed: 19703636]
31. Shalev AY, Ankri Y, Israeli-Shalev Y, et al. Prevention of posttraumatic stress disorder by early treatment: results from the Jerusalem Trauma Outreach and Prevention Study. *Arch Gen Psychiatry*. 2012; 69:166–176. [PubMed: 21969418]
32. Zatzick D, Roy-Byrne P, Russo J, et al. A randomized effectiveness trial of stepped collaborative care for acutely injured trauma survivors. *Arch Gen Psychiatry*. 2004; 61:498–506. [PubMed: 15123495]
33. Zatzick D, Jurkovich G, Rivara F, et al. A randomized stepped care intervention trial targeting posttraumatic stress disorder for surgically hospitalized injury survivors. *Ann Surg*. In Press.
34. Kessler RC, Chui WT, Demler O, Merikangas KR, Walters EE. Prevalence, severity and comorbidity of 12-month DSM-IV disorders in the National Comorbidity Survey Replication. *Arch Gen Psychiatry*. 2005; 62:617–627. [PubMed: 15939839]
35. Zatzick DF, Kang SM, Müller HG, et al. Predicting posttraumatic distress in hospitalized trauma survivors with acute injuries. *Am J Psychiatry*. 2002; 159:941–946. [PubMed: 12042181]
36. Zimmermann P, Brückl T, Nocon A, et al. Interaction of FKBP5 gene variants and adverse life events in predicting depression onset: results from a 10-year prospective community study. *Am J Psychiatry*. 2011; 168:1107–1116. [PubMed: 21865530]
37. Jones C, Bäckman C, Capuzzo M, et al. Intensive care diaries reduce new onset post traumatic stress disorder following critical illness: a randomised, controlled trial. *Crit Care*. 2010; 14:R168. [PubMed: 20843344]
38. Garrouste-Orgeas M, Coquet I, Périer E, et al. Impact of an intensive care unit diary on psychological distress in patients and relatives. *Crit Care Med*. 2012; 40:2033–2040. [PubMed: 22584757]
39. Jones C, Bäckman C, Capuzzo M, et al. Precipitants of post-traumatic stress disorder following intensive care: a hypothesis generating study of diversity in care. *Intensive Care Med*. 2007; 33:978–985. [PubMed: 17384929]

40. Katon W. Clinical and health services relationships between major depression, depressive symptoms, and general medical illness. *Biol Psychiatry*. 2003; 54:216–226. [PubMed: 12893098]
41. Davydow DS, Russo JE, Ludman E, et al. The association of comorbid depression with intensive care unit admission in patients with diabetes: a prospective cohort study. *Psychosomatics*. 2011; 52:117–126. [PubMed: 21397103]
42. Gries CJ, Engelberg RA, Kross EK, et al. Predictors of symptoms of posttraumatic stress and depression in family members after patient death in the ICU. *Chest*. 2010; 137:280–287. [PubMed: 19762549]
43. Kross EK, Engelberg RA, Gries CJ, et al. ICU care associated with symptoms of depression and posttraumatic stress disorder among family members of patients who die in the ICU. *Chest*. 2011; 139:795–801. [PubMed: 20829335]

Figure 1. Study Flow Diagram

Abbreviations (in alphabetical order): HMC = Harborview Medical Center; ICU = intensive care unit.

Figure 2. Prevalences of substantial PTSD^a and depressive symptoms^b at three and twelve months following medical-surgical intensive care unit admission

^a Substantial PTSD symptoms are defined as meeting PTSD Checklist-Civilian Version algorithm-based criteria for the DSM diagnosis of PTSD.

^b Substantial depressive symptoms are defined as a PHQ-9 score ≥ 10 .

Table 1

Characteristics of participants who did and did not complete twelve month follow-up

Variables	Completed follow-up (n = 120)	No follow-up (n = 30)	Test Statistics ^a	P Value
Patient Baseline Characteristics				
Age	49.0 (14.6)	48.1 (13.5)	F = 0.09	0.76
Female	51 (42.5%)	10 (34.5%)	$\chi^2 = 0.62$	0.43
Non-white	30 (25.2%)	10 (32.5%)	$\chi^2 = 1.61$	0.20
< High school graduate	15 (12.6%)	6 (20.7%)	$\chi^2 = 1.29$	0.26
Married/Partnered	63 (52.5%)	11 (37.9%)	$\chi^2 = 1.98$	0.16
Charlson Comorbidity Score	1.6 (2.0)	1.9 (2.4)	F = 0.56	0.46
Prior history of major depression per interview	32 (26.9%)	11 (39.3%)	$\chi^2 = 1.75$	0.19
Lifetime number of traumatic event exposures	4.1 (2.8)	4.6 (2.9)	F = 0.62	0.43
AUDIT	3.6 (5.5)	5.5 (9.7)	F = 1.93	0.17
Problem drinking (AUDIT = 8)	14 (11.7%)	6 (20.7%)	$\chi^2 = 1.64$	0.20
DAST-10	0.8 (2.0)	1.2 (2.7)	F = 1.19	0.28
Problem Drug use (DAST-10 = 3)	14 (11.8%)	5 (17.2%)	$\chi^2 = 0.63$	0.43
Admission Clinical Characteristics				
Hospital LOS (days)	16.7 (12.1)	16.7 (10.9)	F = 0.001	0.99
ICU LOS (days)	7.5 (8.2)	5.5 (4.4)	F = 1.57	0.21
SAPS II	25.9 (15.3)	28.3 (15.9)	F = 0.60	0.44
Admission Diagnosis				
Cardiovascular	11 (9.2%)	0 (0%)		0.12
Pulmonary	18 (15.0%)	1 (3.4%)		0.12
Infectious Disease	31 (25.8%)	11 (37.9%)	$\chi^2 = 1.69$	0.19
Neurologic	33 (27.5%)	8 (27.6%)	$\chi^2 = 0.00$	0.99
Vascular Surgery	19 (15.8%)	3 (10.3%)		0.57
Gastrointestinal	14 (11.7%)	4 (13.8%)		0.75
Endocrine/Renal	5 (4.2%)	2 (6.9%)		0.62
Orthopedic	10 (8.3%)	1 (3.4%)		0.69
Oncologic	3 (2.5%)	2 (6.9%)		0.25
Other	3 (2.5%)	2 (6.9%)		0.25
Mechanically ventilated	56 (46.7%)	12 (41.4%)	$\chi^2 = 0.26$	0.61
MV duration (days)	2.5 (6.9)	1.0 (2.2)	F = 1.36	0.25
Number of surgeries	1.3 (2.1)	1.2 (1.5)	F = 0.02	0.89
Number of blood product transfusions	0.9 (3.8)	1.3 (5.2)	F = 0.28	0.60
Probable delirium	63 (52.5%)	13 (44.8%)	$\chi^2 = 0.55$	0.46
Restrained in hospital	60 (50.0%)	12 (41.4%)	$\chi^2 = 0.70$	0.40
Days restrained in hospital	2.6 (5.1)	1.6 (3.6)	F = 0.86	0.35
Total days received benzodiazepines	4.7 (7.6)	5.1 (6.8)	F = 0.06	0.80
Total days received opioids	12.9 (10.7)	14.0 (10.6)	F = 0.27	0.60
Total days received antipsychotics	1.4 (4.0)	2.1 (5.1)	F = 0.67	0.41

Variables	Completed follow-up (n = 120)	No follow-up (n = 30)	Test Statistics ^a	P Value
Total days received antidepressants	2.7 (6.3)	2.2 (6.6)	F = 0.18	0.67
PCL-C score at baseline interview	29.8 (11.7)	34.8 (14.0)	F = 3.89	0.05
Substantial acute stress symptoms	14 (11.7%)	9 (31.0%)	$\chi^2 = 6.71$	0.01

All values are mean $\pm$ SD or N (%) unless otherwise indicated.

Abbreviations (in alphabetic order): AUDIT = Alcohol Use Disorders Identification Test; DAST-10 = Drug Abuse Screening Test=10; ICU = intensive care unit; LOS = length of stay; MV = mechanical ventilation; PCL-C = PTSD Checklist-civilian version; SAPS II = Simplified Acute Physiology Score II.

^aResults from Pearson χ^2 test with 1 degree of freedom, Fisher's Exact test or F-statistic with 148 degrees of freedom.

Table 2

Adjusted associations of patient and clinical characteristics with symptoms of posttraumatic stress disorder over the course of the year following medical-surgical intensive care unit admission^a

Variables	Adjusted for Patient Characteristics	Adjusted for Hospitalization Characteristics
β Coefficient (95% Confidence Interval)		
In-hospital substantial acute stress symptoms	17.3 (12.1, 22.4) [‡]	16.9 (11.4, 22.4) [‡]
Age	−0.1 (−0.2, 0.1)	−0.1 (−0.2, 0.1)
Male	−2.7 (−6.0, 0.6)	−2.2 (−5.8, 1.3)
Non-white	2.3 (−1.7, 6.2)	2.7 (−1.4, 6.9)
Education less than high school	−0.3 (−4.7, 5.3)	0.3 (−5.0, 5.6)
Married	−0.4 (−3.7, 3.0)	−0.3 (−3.0, 3.2)
Lifetime history of major depression	3.3 (−0.5, 7.1)	2.9 (−1.2, 7.0)
Problem drinking at baseline	2.4 (−2.8, 7.6)	2.7 (−3.0, 8.3)
Problem drug use at baseline	0.5 (−5.0, 5.9)	−0.2 (−6.0, 5.6)
Number of prior traumatic event exposures	0.6 (0.04, 1.2) [*]	0.6 (−0.1, 1.2)
Charlson Comorbidity Score	0.4 (−0.5, 1.2)	0.4 (−0.6, 1.4)
SAPS II		−0.03 (−0.2, 0.1)
Mechanically ventilated		1.5 (−5.3, 8.2)
Required major surgery		0.2 (−3.6, 4.0)
Required blood product transfusion		1.9 (−2.5, 6.4)
Probable delirium		1.0 (−3.5, 5.5)
Required physical restraints		−0.6 (−7.0, 5.7)
Required benzodiazepines		−2.2 (−6.7, 2.4)
Required opioids		4.5 (−15.3, 24.3)
Required antipsychotics		−1.0 (−6.0, 3.9)
Required antidepressants		2.5 (−1.7, 6.8)

Abbreviations (in alphabetic order): MV = mechanical ventilation; SAPS II = Simplified Acute Physiology Score II.

^aThe dependent variable of the mixed-model regression analyses above are the repeated measures of PTSD symptoms at 3 and 12 months following medical-surgical intensive care unit admission. The β coefficients can be interpreted as mean change in PCL-C scores.

^{*} P < 0.05

[†] P < 0.01

[‡] P < 0.001

Table 3

Adjusted associations of patient and clinical characteristics with symptoms of depression following medical-surgical intensive care unit admission^a

Variables	Adjusted for Patient Characteristics	Adjusted for Hospitalization Characteristics
		β Coefficient (95% Confidence Interval)
Lifetime history of major depression	2.9 (1.0, 4.8) [†]	2.2 (0.1, 4.2)*
Age	−0.03 (−0.1, 0.1)	−0.03 (−0.1, 0.1)
Male	−1.1 (−2.7, 0.6)	−1.1 (−2.9, 0.6)
Non-white	0.6 (−1.4, 2.5)	−0.003 (−2.1, 2.1)
Education less than high school	0.2 (−2.3, 2.7)	−0.3 (−2.9, 2.3)
Married	−1.3 (−3.0, 0.4)	−1.2 (−3.0, 0.5)
Problem drinking at baseline	0.3 (−2.3, 2.9)	−0.7 (−3.5, 2.1)
Problem drug use at baseline	1.0 (−1.7, 3.8)	0.8 (−2.1, 3.6)
Prior traumatic event exposure	0.6 (0.3, 0.9) [‡]	0.6 (0.2, 0.9) [†]
Charlson Comorbidity Score	0.03 (−0.4, 0.5)	−0.01 (−0.5, 0.5)
SAPS II		0.02 (−0.1, 0.1)
Mechanically ventilated		0.5 (−2.8, 3.8)
Required major surgery		−1.0 (−2.9, 0.8)
Required blood product transfusion		1.2 (−1.0, 3.4)
Probable delirium		0.3 (−1.9, 2.5)
Required physical restraints		−1.3 (−4.4, 1.8)
Required benzodiazepines		−0.3 (−2.5, 2.0)
Required opioids		3.6 (−6.1, 13.4)
Required antipsychotics		−0.4 (−2.8, 2.0)
Required antidepressants		−0.1 (−2.2, 2.0)
In-hospital substantial acute stress symptoms		3.5 (0.8, 6.2)*

Abbreviations (in alphabetic order): MV = mechanical ventilation; SAPS II = Simplified Acute Physiology Score II.

^aThe dependent variable of the mixed-model regression analyses above are the repeated measures of depressive symptoms at 3 and 12 months following medical-surgical intensive care unit admission. The β coefficients can be interpreted as mean change in PHQ-9 scores.