

Review Article

Relationship of symptoms associated with ICU-survivorship: An integrative literature review

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ABSTRACT

Background: The number of adults who survive a critical illness involving admission to an intensive care unit is increasing. These survivors have an increased risk of developing impairments in cognition, physical function and psychological health.

Objective: This integrative literature review examined the literature for studies exploring the relationships among two or more of the variables of interest, i.e. cognitive, physical, and psychological symptoms (depressive, anxiety, or posttraumatic stress) in intensive care unit survivors post-hospital discharge.

Methods: A literature search was conducted using PubMed, CINAHL and PsycINFO databases.

Findings: While all 13 studies included in the review explored some aspect of a relationship among the variables of interest, none explored associations among all three variables. Five studies explored physical function and psychological symptoms, four studies explored cognitive impairment and psychological symptoms and five studies explored the association among different psychological symptoms. Inconsistencies were found in the study designs, follow-up time frames, patient populations and measures used.

Conclusions: Further research using well-designed methodologies and standardized instruments is warranted. Gaining a better understanding of the relationships among these impairments has the potential to contribute to the development of screening guidelines, preventative strategies, and treatments.

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Implications for clinical practice

- Impairments in cognition, physical function, and psychological health are common in intensive care unit survivors and often co-occur.
- Intensive care unit survivors should be screened and treated for these impairments post-hospital discharge.
- This review highlights the need for further research studying relationships among these impairments with standardized instruments in a variety of populations.

Introduction

Intensive care unit (ICU) survivorship is a term applied to individuals who survive the experience of a critical illness but who, as part of their hospitalization, have been patients in an ICU setting (Turnbull et al., 2016). Reportedly, the number of adults who survive critical illness is on the rise (Kaukonen et al., 2014;

Zimmerman et al., 2013) with over 4.6 million adult hospital discharges involving admission to an ICU reported in 2011 alone (Barrett et al., 2014). Survivors of critical illness have an increased risk of negative psychophysiological outcomes post-hospital discharge that can include new or worsening impairments in cognition, physical function and/or psychological health (i.e. depression, anxiety, or posttraumatic stress [PTS]). Such worsening is now identified as postintensive care syndrome (PICS) (Needham et al., 2012), a condition that contributes to decreased health-

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related quality of life (HRQOL) (Herridge et al., 2011; McKinley et al., 2016; Wang et al., 2017).

Potential impairments of ICU survivorship

Cognitive impairment has been reported to affect over 70% of all ICU survivors (Girard et al., 2010; Jackson et al., 2010; Pandharipande et al., 2013). Such impairment may involve long-term (>12 months) deficits in global cognition and executive function (Girard et al., 2010; Pandharipande et al., 2013). The presence and duration of delirium in the ICU has been reported as the major risk factor for post-ICU cognitive impairment (Girard et al., 2010; Jackson et al., 2010; Pandharipande et al., 2013).

Physical impairments in ICU survivors may include generalized muscle weakness, known as ICU-acquired weakness (ICUAW), as well as deficits in physical and instrumental activities of daily living (ADLs) (Needham et al., 2012, pp. 503–504). Over one-third of ICU survivors have ICUAW at hospital discharge and while it may improve over time, there is the potential for it to persist for ≥ two years (Fan et al., 2014). Risk factors for ICUAW include increased ICU length of stay (Bienvenu et al., 2012; Needham et al., 2014), duration of mechanical ventilation (van der Schaaf et al., 2008), prolonged bedrest (Fan et al., 2014) and corticosteroid use (Needham et al., 2014).

Psychological health concerns reported in ICU survivors include symptoms of depression, anxiety, and PTS. Depressive symptoms have been reported in 31% of survivors three months post-ICU discharge (Davydow et al., 2013) while anxiety symptoms have been reported in 38% of ICU survivors at three months after the onset of critical illness (Stevenson et al., 2013). Symptoms of PTS have been reported in 13.5% of ICU survivors six months post-hospital discharge (Elliott et al., 2016). Risk factors associated with depressive symptoms may include prior depression or other psychiatric history (Dowdy et al., 2009; Paparrigopoulos et al., 2014) and lower level of education (Bienvenu et al., 2012). Risk factors associated with post-discharge anxiety symptoms range from whether or not an individual has survived a trauma or head injury (Ringdal et al., 2009) or is an acute lung injury (ALI) survivor (Hopkins et al., 2010). Possible risk factors of PTS symptoms include younger age and female sex (Asimakopoulou and Madianos, 2014) and recall of traumatic events (Wintermann et al., 2015).

While some negative sequelae of ICU survivorship may improve over time, others may persist for years (Needham et al., 2012). Seeking to gain a better understanding of PICS as a syndrome, we sought to examine the literature for studies that explored relationships among two or more of the variables of interest, i.e. cognitive, physical, and psychological (i.e. depression, anxiety, and/or PTS) symptoms. We anticipated that insights gleaned from such a review would provide the foundation for future research focused on PICS. Enhancing our understanding of the relationships among these symptoms has the potential to facilitate development of preventative strategies, screening guidelines, and treatment modalities.

Literature review

Method

A title and abstract search was conducted in PubMed, CINAHL, and PsycINFO databases. Search terms included “critical illness”, “critical care”, or “intensive care” AND “physical impairment”, “cognitive impairment”, “functional impairment”, “depression”, “anxiety”, “post-traumatic stress”, or “posttraumatic stress”. Databases were searched from January 2008 to January 2018 to explore the current state of the science. Exclusion criteria included studies

published in a language other than English, dissertations, and studies involving children and cardiac surgery survivors. Studies involving cardiac surgery survivors were excluded due to the possible confounding effect of cardiac surgery and cardiopulmonary bypass on post-discharge outcomes (Selnes et al., 2012). Abstracts were reviewed and articles were selected for inclusion if the studies examined an association among two or more of the variables of interest. Out of 95 articles retrieved, 10 met the inclusion criteria for our literature review. An examination of the reference lists revealed three additional articles that met the inclusion criteria (see Fig. 1). A narrative analysis was performed in an effort to synthesize studies addressing associations among the variables, thus aiding in the development of hypotheses that would be foundational for future research (Baumeister and Leary, 1997; Cronin

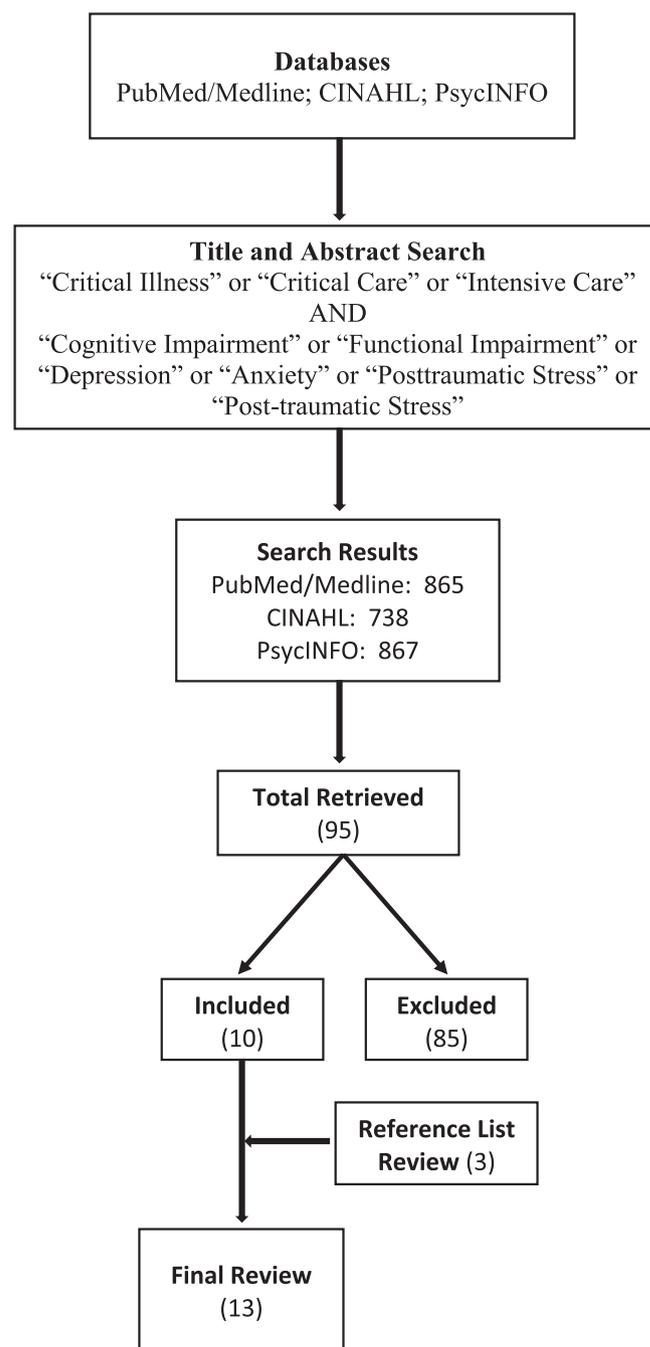


Fig. 1. Literature search and selection flow diagram.

et al., 2008). Each study was summarized to include study aims, ICU survivor characteristics, follow-up time frames, and instruments utilized.

Results

Of the 13 studies included, each explored some aspect of a relationship among the variables of interest. However, none of the studies explored associations among all three variables of interest. Relationships examined included the association of physical impairment and psychological symptoms, cognitive impairment and psychological symptoms, and relationships among different psychological symptoms. Populations included survivors of ALI and/or acute respiratory distress syndrome (ARDS) as well as medical/surgical ICU survivors.

Physical impairment and psychological symptoms

In a secondary analysis of a single-ICU, longitudinal descriptive study, Choi et al. (2016) examined associations among physical impairment and symptoms of depression and anxiety in ICU survivors who received mechanical ventilation ($n = 47$). Follow-up occurred at two weeks, two months, and four months post-ICU discharge. A majority of the participants were reported to have a risk for clinical depression at all time points (range of 64.3–72%). The highest anxiety scores were reported at two weeks post-ICU. In addition, most participants were reported to have moderate to high care needs (range 65.5–92.1%). While trends of higher depressive and anxiety symptoms were noted in those with moderate or high care needs, neither trend was statistically significant.

A multicenter, prospective cohort study of ALI survivors was conducted with follow-up at three, six, 12, and 24 months after ALI onset. Three publications from this study addressing associations among variables that met our search criteria were extant in the literature. In the most recent publication, Bienvenu et al. (2015) examined symptoms of anxiety, depression and PTS, as well as physical impairment, in ICU survivors of ALI ($n = 186$) over the four time points. Anxiety symptoms were reported in 56% of participants while depressive symptoms were reported in 46% of participants in at least one follow-up with 35% of participants having PTS symptoms in at least one follow-up. Anxiety and depressive symptoms, anxiety and PTS symptoms, and depression and PTS symptoms were reported as significantly associated ($p \leq 0.001$) at all time points. Improved physical functioning at 24 months was significantly associated with remission of anxiety ($p = 0.02$) and PTS symptoms ($p = 0.02$) but not with depressive symptoms.

The second report from this study (Stevenson et al., 2013) addressed anxiety symptoms, physical impairment, and HRQOL at the three month timepoint only ($n = 152$). At three-months post-ALI onset, 38% of participants were reported to have a positive screening for anxiety symptoms that were associated with the number of instrumental ADL dependencies ($p = 0.004$) but not the number of physical ADL dependencies. In the third reported study, Bienvenu et al. (2012) examined depressive symptoms and physical impairment in ICU survivors at all four timepoints post ALI-onset ($n = 186$). The authors reported that 14–22% of participants met the criteria for both depressive symptoms and physical impairment at each follow-up, noting that depressive symptoms and physical impairment were significantly related to each other at each follow-up ($p < 0.001$ at three months, six months and 24 months; $p < 0.05$ at 12 months).

Using a cross-sectional design, van der Schaaf et al. (2009) examined physical impairment, depression, anxiety, PTS and HRQOL in ICU survivors one year after ICU discharge ($n = 746$). Mild physical dysfunction was present in 22% of respondents and

severe physical dysfunction was present in 32% of respondents. Symptoms of depression and anxiety were reported in 14% of respondents while symptoms of PTS were reported in 18% of respondents. Symptoms of depression and PTS were reported as significantly associated with poor physical status ($p < 0.000$).

Cognitive impairment and psychological symptoms

In a multicenter, prospective cohort study of medical/surgical ICU survivors ($n = 136$), Duggan et al. (2017) examined whether executive dysfunction at three months post-ICU discharge was associated with depressive symptoms and/or HRQOL at 12 months post-ICU discharge. At three months post-ICU discharge, perceived executive dysfunction was found in 26% of participants while 27% of participants were found to have objectively measured executive dysfunction. At 12 months post-ICU discharge, 31% of participants were reported as having depressive symptoms. Perceived executive dysfunction was found to be significantly associated with higher depression scores ($p = 0.015$) at 12 months. However, the same association was not found with objectively measured executive dysfunction.

Relationships among cognitive function, depression, anxiety, PTS, and HRQOL at 12 months post-hospital discharge were examined in a multicenter, prospective cohort study ($n = 102$) of ICU survivors with ALI (Mikkelsen et al., 2012). Objectively measured cognitive impairment was reported in 55% of participants. Symptoms of moderate to severe depression were found in 36% of participants while symptoms of moderate to severe anxiety were found in 62% of participants. PTS screening was positive in 39% of participants. Further, 42% of survivors had significant symptoms in two or more of these domains (depression, anxiety, and PTS). Cognitive impairment was reported to be significantly associated with symptoms of anxiety ($p = 0.04$) but not with depression or PTS.

Hopkins et al. (2010) conducted a single-center, prospective cohort study to explore risk factors, including cognitive impairment, for symptoms of depression and anxiety one and two years after hospital discharge in ICU survivors of ARDS ($n = 74$). They reported that 16% of participants at one-year post-hospital discharge and 23% of participants at two years post-hospital discharge had moderate to severe depressive symptoms while 24% at one-year post-hospital discharge and 23% at two years had moderate to severe anxiety symptoms. In addition, 46% of participants were found to be cognitively impaired at one-year post-hospital discharge and 47% at two years post-hospital discharge. At one-year post hospital discharge, cognitive impairment was not found to be a significant predictor of depression; however, it was a significant predictor of depression at two years post-hospital discharge ($p < 0.0001$). Cognitive impairment was not found to significantly predict anxiety symptoms.

In a cross-sectional telephone study, Mikkelsen et al. (2009) assessed the association of cognitive impairment, symptoms of anxiety and depression, and HRQOL in self-reported ARDS survivors one month to 20 years post-ARDS onset ($n = 79$). Cognitive impairment in at least one domain was reported in 56% of participants with memory and executive functioning being the domains most commonly affected. Moderate to severe symptoms of anxiety and depression were reported in 48% and 34% of participants, respectively. The authors reported a significant association between cognitive impairment and anxiety ($p = 0.008$), but not between cognitive impairment and depression.

Psychological symptoms

Some studies examined the relationship of various psychological symptoms. Elliott et al. (2016) explored factors associated with

symptoms of PTS at six months post-hospital discharge, including symptoms of depression and anxiety, with a prospective, survey-based study of adult ICU survivors ($n = 222$). Symptoms of PTS were reported in 13.5% of participants while 30% and 23% of participants were reported to have symptoms of depression and anxiety, respectively. The authors reported that increased PTS symptoms were significantly associated with depressive, but not anxiety, symptoms ($p < 0.005$).

Using a national, multicenter prospective cohort study, Huang et al. (2016) studied symptoms of depression, anxiety, and PTS in ICU survivors of ARDS at six and 12 months after ARDS onset ($n = 613$). At six and 12-month follow-ups, the authors reported symptoms of depression, anxiety, and PTS in 36%, 42%, and 24% of participants, respectively. Symptoms of depression and anxiety ($p < 0.001$), anxiety and PTS ($p < 0.001$), and depression and PTS ($p < 0.001$) were reported as significantly associated at both six and 12 months.

A cross-sectional study by Paparrigopoulos et al. (2014) examined depressive and PTS symptoms in general ICU survivors at 18–24 months after ICU discharge ($n = 48$). The authors reported that 31% of participants had depressive symptoms and 25% had PTS symptoms. Further, it was reported that 17% had both depressive and PTS symptoms, which was reported as significantly associated ($p < 0.001$).

Using a retrospective, cross-sectional study Kowalczyk et al. (2013), examined depressive and anxiety symptoms in ICU survivors from two hospitals ($n = 186$). Participants were at least one-year post-ICU and some were \geq five years post-ICU. Depressive symptoms were reported in 27.4% of respondents while anxiety symptoms were reported in 34.4% of respondents. Symptoms of depression and anxiety were significantly associated ($p < 0.001$).

Discussion

While each study examined ICU survivorship using valid and reliable instruments, none of the studies explored associations among all three variables of interest. Additionally, findings were inconsistent. For example, among the four studies that examined the association of physical impairment and depressive symptoms, two did not find an association (Bienvenu et al., 2015; Choi et al., 2016) while two other studies reported a significant association (Bienvenu et al., 2012; van der Schaaf et al., 2009). Of the three studies that examined the association of physical impairment and symptoms of anxiety, two reported a significant association (Bienvenu et al., 2015; Stevenson et al., 2013) while one did not (Choi et al., 2016). Two studies examined physical impairment and symptoms of PTS, both reporting a significant association (Bienvenu et al., 2015; van der Schaaf et al., 2009). Similarly, findings varied among studies examining cognitive impairment and one or more psychological symptoms. Among the four studies that examined cognitive impairment and depressive symptoms, one study reported an association between perceived, but not objectively measured cognitive impairment and depression (Duggan et al., 2017). The remaining three studies only examined the relationship of objectively measured cognitive impairment with depression. Two studies by the same author did not find an association between cognitive impairment and depressive symptoms (Mikkelsen et al., 2009, 2012) while a different study reported cognitive impairment to be a predictor of depressive symptoms at two-years post-hospital discharge but not one-year post-hospital discharge (Hopkins et al., 2010). Meanwhile, three studies examined objective cognitive impairment and anxiety symptoms. Two of these studies (by the same author) reported a significant association (Mikkelsen et al., 2009, 2012) while the other did not (Hopkins et al., 2010). One study exam-

ined cognitive impairment and symptoms of PTS and reported no significant association (Mikkelsen et al., 2012). Findings were more consistent in the studies that explored the association of psychological symptoms. Depressive and anxiety symptoms were examined in three studies and all reported a significant association (Bienvenu et al., 2015; Huang et al., 2016; Kowalczyk et al., 2013). Depressive and PTS symptoms were examined in four studies, all reporting a significant association (Bienvenu et al., 2015; Elliott et al., 2016; Huang et al., 2016; Paparrigopoulos et al., 2014). Symptoms of anxiety and PTS were examined in three studies, with two reporting a significant association (Bienvenu et al., 2015; Huang et al., 2016) and one not reporting a significant association (Elliott et al., 2016). These disparate studies, in which researchers examined associations among some but not all PICS-related impairments while also reporting some associations among the variables studied, suggest that there is a window of opportunity for strengthening our understanding of these relationships through future research. That is, examining all three PICS-related impairments and their associations in a single study, rather than examining them as single or paired entities, has the potential to contribute to an enhanced understanding of PICS as a syndrome.

Limitations

The inconsistency in the study findings may be attributed to various study designs, follow-up time frames, types of patient populations and measures used. For example, there were eight prospective cohort studies (Bienvenu et al., 2012, 2015; Duggan et al., 2017; Elliott et al., 2016; Hopkins et al., 2010; Huang et al., 2016; Mikkelsen et al., 2012; Stevenson et al., 2013), three cross-sectional studies (Mikkelsen et al., 2009; Paparrigopoulos et al., 2014; van der Schaaf et al., 2009), one secondary analysis (Choi et al., 2016), and one retrospective study (Kowalczyk et al., 2013). Most studies assessed participants during the first year (Bienvenu et al., 2012, 2015; Choi et al., 2016; Duggan et al., 2017; Elliott et al., 2016; Hopkins et al., 2010; Huang et al., 2016; Kowalczyk et al., 2013; Mikkelsen et al., 2012; Stevenson et al., 2013; van der Schaaf et al., 2009); however, six studies examined participants at two years post-discharge or greater (Bienvenu et al., 2015, 2012; Hopkins et al., 2010; Kowalczyk et al., 2013; Mikkelsen et al., 2009; Paparrigopoulos et al., 2014). Finally, follow-up post-hospital/ICU discharge ranged from two weeks to five or more years. Additionally, there was a wide range of different instruments used among the studies to capture similar variables (see Table 1). This is most evident among the studies exploring physical function. Both the definition of physical impairment as well as the instruments used varied. Of the five studies examining physical function, four measured-by-count the number of physical and/or instrumental ADL dependencies (Bienvenu et al., 2015, 2012; Choi et al., 2016; Stevenson et al., 2013) while two utilized self-report measures (Bienvenu et al., 2015; van der Schaaf et al., 2009). Instruments used to assess psychological symptoms were also varied (see Table 1). For example, six instruments were used among the 12 studies examining depressive symptoms while four instruments were used among the 10 studies examining anxiety symptoms. Among the six studies examining symptoms of PTS, five different instruments were used. Measurement of cognitive function varied as well (see Table 1). Of the five studies examining cognition, three objectively measured cognitive function (Duggan et al., 2017; Hopkins et al., 2010; Mikkelsen et al., 2009) while one used a self-report instrument (Duggan et al., 2017). This lack of standardized instrument use makes it difficult to synthesize and/or generalize findings among the included studies.

Table 1
Study summaries.

Author	Type of study	Population	Variables	Instruments	Major Study Findings
Mikkelsen et al. (2009)	Cross-sectional telephone	ICU with ARDS	Cognition Depression Anxiety HRQOL	NP test battery Zung Self-Rating Depression Scale (Zung, 1965) Beck Anxiety Inventory (Beck et al., 1988) Sickness Impact Profile (de Bruin et al., 1994) Medical Outcomes Study 36 Item Short Form (Ware and Sherbourne, 1992)	Significant association between cognitive impairment and anxiety. No association between cognitive impairment and depression. The mental health summary score (not the physical summary score) of the SF-36 was significantly associated with cognitive impairment.
van der Schaaf et al. (2009)	Single-ICU, Cross-sectional	Adult ICU	Physical function Depression Anxiety PTS HRQOL	Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983) Impact of Event Scale (Horowitz et al., 1979) Sickness Impact Profile 68 (de Bruin et al., 1994) Medical Outcomes Study 36 Item Short Form (Ware and Sherbourne, 1992)	Symptoms of depression and PTS were reported as significantly associated with poor physical status. SF-36 scores for Physical Function, Role Physical, and General Health scales were lower than the general population.
Hopkins et al. (2010)	Single-center, prospective cohort	ICU with ARDS	Cognition Depression Anxiety HRQOL	NP test battery Beck Depression Inventory (Beck et al., 1961) Beck Anxiety Inventory (Beck et al., 1988) Medical Outcomes Study 36 Item Short Form (Ware and Sherbourne, 1992)	Cognitive impairment was a significant predictor of depression at two years post-hospital discharge. Cognitive impairment was not found to significantly predict anxiety symptoms. SF-36 scores were significantly different over the course of follow-up.
Bienvenu et al. (2012)	Multicenter, prospective cohort	ICU with ALI	Physical function Depression	Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983)	Depressive symptoms and physical impairment significantly related at each follow-up. Remission of symptoms occurred in 39% of participants with significant depressive symptoms and in 54% of participants with physical impairment while recurrence occurred in 20% of patients with significant depressive symptoms and 14% of those with physical impairment over the course of the study.
Mikkelsen et al. (2012)	Multicenter, prospective cohort	ICU with ALI	Cognition Depression Anxiety PTS HRQOL	NP test battery Zung Self-Rating Depression Scale (Zung, 1965) Beck Anxiety Inventory (Beck et al., 1988) Post-Traumatic Symptom Scale-10 (Stoll et al., 1999) Health Utilities Index Mark 2 (Torrence et al., 1996)	Cognitive impairment significantly associated with symptoms of anxiety but not depression, PTS, or HRQOL. HRQOL was significantly worse in those with anxiety, depressive, and/or PTS symptoms than those without symptoms.
Kowalczyk et al. (2013)	Retrospective, cross-sectional	Medical-Surgical ICU	Depression Anxiety	Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983)	Symptoms of depression and anxiety significantly associated. Depressive symptoms were correlated with increased age, negative ICU-related memories, lower income, worse housing conditions, and unemployment while anxiety symptoms were correlated with negative ICU-related memories and lower income.
Stevenson et al. (2013)	Multicenter, prospective cohort	ICU with ALI	Physical function Anxiety HRQOL	Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983) Katz ADL scale (Katz, 1963) Lawton Instrumental ADL scale (Lawton and Brody, 1969) EQ-5D (The EuroQol Group, 1990) Medical Outcomes Study 36 Item Short Form (Ware and Sherbourne, 1992)	Anxiety symptoms associated with the number of instrumental ADL dependencies but not the number of physical ADL dependencies. Anxiety symptoms were reported as significantly associated with worse quality of life per the visual analog scale and utility score of the EQ-5D and the mental health and physical function domains of the SF-36.
Paparrigopoulos et al. (2014)	Single-ICU, Cross-sectional	Adult ICU	Depression PTS HRQOL	Center for Epidemiologic Studies for Depression (Radloff, 1977) Davidson Trauma Scale (Davidson et al., 1997) Medical Outcomes Study 36 Item Short Form (Ware and Sherbourne, 1992)	Depressive and PTS symptoms were significantly correlated. Older age and psychiatric history were significantly associated with higher CES-D scores and DTS scores were significantly associated with traumatic events during adulthood and psychiatric history.
Bienvenu et al. (2015)	Multicenter, prospective cohort	ICU with ALI	Physical function Depression Anxiety PTS	Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983) Impact of Event Scale-Revised (Weiss and Marmar, 1997) Medical Outcomes Study 36 Item Short Form (Ware and Sherbourne, 1992)	Anxiety and depressive symptoms, anxiety and PTS symptoms, and depression and PTS symptoms were significantly correlated. Better physical function significantly associated with remission of anxiety and PTS symptoms, but not with depressive symptoms.

Table 1 (continued)

Author	Type of study	Population	Variables	Instruments	Major Study Findings
Choi et al. 2016	Single-ICU, Secondary data analysis	Medical ICU	Physical function Depression Anxiety	Shortened Center for Epidemiologic Studies-Depression 10 items (Radloff, 1977) Shortened Profile of Mood States-Anxiety scale (tension anxiety subscale) (Usala and Hertzog, 1989) Katz ADL scale (Katz, 1963) Lawton Instrumental ADL scale (Lawton and Brody, 1969)	A trend of higher depressive and anxiety symptoms was noted in those with moderate to high care needs at all time points, but neither trend was statistically significant. Symptoms of depression and anxiety were not significantly associated with discharge destination (home versus non-home).
Elliott et al. (2016)	Single-ICU, Prospective, survey-based study	Adult ICU	Depression Anxiety PTS ICU experiences Sleep	Depression, Anxiety, and Stress Scales-21 (Lovibond and Lovibond, 1995) Posttraumatic Stress Disorder Checklist-Specific (U.S. Department of Veterans Affairs, 2014) Intensive Care Experience Questionnaire (Rattray et al., 2004) Insomnia Severity Index (Bastien et al., 2001) Richards-Campbell Sleep Questionnaire (Richards et al., 2000) Pittsburgh Sleep Quality Index (Buysse et al., 1989)	Higher PTS scores were significantly associated with stress, depressive symptoms, PSQI scores at 6 months, frightening experiences per the ICEQ, and higher pain intensity at enrollment.
Huang et al. (2016)	Multicenter, prospective cohort	ICU with ARDS	Depression Anxiety PTS	Hospital Anxiety and Depression Scale (Zigmond and Snaith, 1983) Impact of Event Scale-Revised (Weiss and Marmar, 1997)	Symptoms of depression and anxiety, anxiety and PTS, and depression and PTS significantly associated. Female sex, unemployment prior to hospital admission, and alcohol abuse were noted as significant risk factors for symptoms of depression, anxiety, and PTS. Younger age was also noted as a significant risk factor for anxiety and PTS and greater use of opioids in the ICU was also noted as a significant risk factor for depression and anxiety.
Duggan et al. (2017)	Multicenter, prospective cohort	Medical-Surgical ICU	Executive function Depression Mental HRQOL	Behavior Rating Inventory of Executive Function-Adult Trail Making Test B (Reitan, 1958) Beck Depression Inventory-II (Beck et al., 1996) Medical Outcomes Study 36 Item Short Form (Mental Component Score) (Ware and Sherbourne, 1992)	Perceived executive dysfunction and lower Mental Health Component Scores on the SF-36 were significantly associated with higher depressive symptom scores. Objectively measured executive dysfunction not associated with depressive symptoms.

Note: ADL refers to Activities of Daily Living, ALI refers to Acute Lung Injury, ARDS refers to Acute Respiratory Distress Syndrome, HRQOL refers to Health Related Quality of Life, ICU refers to Intensive Care Unit, NP refers to Neuropsychological, PSQI refers to Pittsburgh Sleep Quality Index, PTS refers to Posttraumatic Stress, SF-36 refers to Medical Outcomes Study 36 Item Short Form.

Implications for research and practice

Intensive care unit survivors are known to experience impairments in physical function, cognition and/or psychological health, known as PICS. However, few studies have examined the association among two or more of these variables and we found no study examining associations among all three variables. Findings were inconsistent and likely due to varying study designs, patient populations, follow-up time frames and instruments used. The inconsistency found in our results underscores the significance of research methodology in advancing the science of ICU survivorship. In an effort to understand the complex and often multiple problems experienced by ICU survivors, continued research is warranted. This would include addressing study limitations related to measuring cognitive status in ICU survivors. This discrepancy between self-report versus objectively measured cognitive status in the studies reported points to an area of needed research in capturing accurate cognitive status in this patient population. We suggest that using well-designed methodologies and standardized instruments in a variety of ICU survivor populations has the potential to contribute to the development of screening guidelines, preventative strategies, and treatments for this clinically meaningful condition.

Conflict of interest

None.

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Ethical approval details

Not applicable.

Ethical approval form

This manuscript is a literature review, therefore, Institutional Review Board approval was not required.

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