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Prediction of Cognitive Sequelae and Ecological Validity in Critically-Ill Adult Patients

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Prediction of Cognitive Sequelae and Ecological Validity in Critical Illness

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ABSTRACT

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Survivors of critical illness have a high prevalence of long-term cognitive and psychiatric morbidity and poor quality of life years after hospital discharge. Data are lacking regarding whether cognitive screening tests predict which critically ill patients may be at risk to develop long-term cognitive sequelae and whether cognitive sequelae predict the patients everyday functioning. This study sought to determine whether cognitive screening tests, including the Mini-Mental State Examination (MMSE) and Mini-Cog, predict long-term cognitive sequelae and everyday functioning in survivors of critical illness 6-month post-hospital discharge. A second purpose was to investigate whether cognitive sequelae are associated with poor everyday functioning in critically ill survivors. Finally, the relationship between cognitive sequelae and quality of life was assessed. Survivors of critical illness had a high rate of cognitive impairments at hospital discharge, as well as long-term cognitive and psychiatric sequelae, deficits in everyday functioning, and reduced quality of life at 6-month follow-up. The MMSE and Mini-Cog did not predict long-term cognitive sequelae or everyday functioning at 6-months.

Cognitive sequelae were not associated with poor everyday functioning; however, impaired attention, memory, and mental processing speed predicted problems with managing home/transportation, and impaired attention predicted problems in health and safety, social adjustment, and memory/orientation. Cognitive sequelae were associated with reduced quality of life in the role physical domain. Altogether, these findings lend additional knowledge to the literature regarding cognitive and psychiatric sequelae, everyday functioning, and reduced quality of life in critically ill patients, and may have clinical implications for the critical care providers, patients, and caregivers. Given the large population of survivors of critical illness each year, strategies aimed at recognizing, preventing and treating these morbidities are important research and public health concerns. Investigations into the clinical and economic burden of these morbidities and methods to mitigate them, including patient screening and referral to appropriate mental health and rehabilitation services, are warranted.

Keywords: Cognitive sequelae, depression, everyday functioning, critical illness, psychiatric disorders, quality of life.

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Patients admitted to the Intensive Care Unit (ICU) present with a variety of diagnoses, many of whom require invasive and life sustaining treatments. Recent development and advances in critical care have led to improved treatment and increased survival of large numbers of critically ill patients (Numa, 2001). Each day in the United States, approximately 55,000 patients are treated in ICU (Schmitz, Lantin, & White, 1998). ICU treatment is associated with high costs of approximately $11,000 (United States dollars) per patient-day (Dasta, McLaughlin, Mody, & Piech, 2005). Although investigations of the effects of critical illness on the central nervous system are limited, there is an increasing research on long-term neurological outcomes in critically ill patients. Current data suggest a high prevalence of neurological dysfunction in critically ill patients admitted to medical/surgical (e.g., non-neurological) ICUs, which appear to be associated with mortality and long-term morbidity. Neurological dysfunction during and following critical illness includes delirium, encephalopathy, sensory processing deficits, neuromuscular dysfunction, and cognitive and psychiatric sequelae that range in severity and persist for years following the illness. Survivors of critical illness are at increased risk to develop cognitive impairments, psychiatric disorders, impaired everyday function, and reduced quality of life (Herridge et al., 2003; Hopkins, Weaver et al., 2005; Hopkins et al., 1999; Jackson et al., 2003; Orme et al., 2003; Rothenhausler, Ehrentraut, Stoll, Schelling, & Kapfhammer, 2001; Weinert, Gross, Kangas, Bury, & Marinelli, 1997).

Prevalence of Cognitive Sequelae in ICU Survivors

Cognitive impairments may develop *de novo* from critical illness and/or its treatment. As many as 40% of critically ill adult patients require mechanical ventilation, representing

approximately 33% of all patients admitted to ICUs (Esteban et al., 2002; Young, 1995). To date, 15 cohorts (Adhikari et al., 2009; Christie et al., 2006; Duning et al., 2010; Hopkins, Jackson, & Wallace, 2005; Hopkins, Weaver, Chan, & Orme, 2004; Hopkins et al., 1999; Jackson et al., in press; Jackson et al., 2003; C. Jones, Griffiths, Slater, Benjamin, & Wilson, 2006; Marquis et al., 2000; Mikkelsen et al., 2009; Rothenhausler et al., 2001; Suchyta, Hopkins, White, Jephson, & Morris, 2004; Sukantarat, Burgess, Williamson, & Brett, 2005; van der Schaaf et al., 2008) comprising more than 950 patients have examined cognitive outcomes following critical illness. The populations include nine studies (Adhikari et al., 2009; Christie et al., 2006; Hopkins et al., 2004; Hopkins, Weaver et al., 2005; Hopkins et al., 1999; Jackson et al., in press; Mikkelsen et al., 2009; Rothenhausler et al., 2001; Suchyta et al., 2004) in patients with ARDS, one study (Hopkins, Weaver et al., 2005) in patients with respiratory failure, four studies (Duning et al., 2010; Jackson et al., 2003; C. Jones et al., 2006; van der Schaaf et al., 2008) in medical ICU patients, and one study (Sukantarat et al., 2005) in general ICU patients. Potential mechanisms or risk factors for the development of cognitive impairments include hypoxia (Hopkins, Gale, & Weaver, 2006; Hopkins et al., 1999), sedatives or analgesics (Starr & Whalley, 1994), hypotension (Hopkins et al., 2004), delirium (Griffiths & Jones, 2007; Jackson, Gordon, Hart, Hopkins, & Ely, 2004), hypoglycemia (Duning et al., 2010), and hyperglycemia (Marquis et al., 2000).

Cognitive Sequelae in Patients with Acute Respiratory Distress Syndrome

Acute respiratory distress syndrome (ARDS) is characterized by inflammation of the lung parenchyma that leads to impaired gas exchange and resultant hypoxia along with systemic release of inflammatory mediators. The inflammatory mediators result in inflammation and hypoxemia and can lead to multiple organ failure. A less severe form of ARDS is acute lung

injury (ALI) which may be a precursor to ARDS (Bernard et al., 1994). There are approximately 200,000 cases of ARDS/ALI per year in the United States, with an ICU mortality rate of 39% (Rubenfeld et al., 2005). Patients with ARDS frequently develop neurological injury (i.e., neuropathy), lesions, generalized brain atrophy, and hippocampal atrophy, as well as significant cognitive impairments including impaired memory, attention, mental processing speed, and executive function (Hopkins et al., 2006; Jackson et al., 2009). Among specific ICU populations such as ARDS, cognitive impairments occur in 78% of patients at hospital discharge and 45% at one and two years (Hopkins, Weaver et al., 2005), and 25% at 6 years (Rothenhausler et al., 2001). The most common cognitive domains affected are impaired memory and executive dysfunction (Hopkins & Jackson, 2009). For example, a retrospective, self-referred group of 79 ARDS patients were administered cognitive tests over the telephone, of whom 24% had impaired memory and 29% impaired executive function (Christie et al., 2004).

Cognitive impairments have been demonstrated years after discharge from the ICU. A retrospective study in 46 ARDS survivors found 24% of patients had cognitive impairments 6 years and 46% were not able to return to full-time employment, all of whom had cognitive impairments (Rothenhausler et al., 2001). A second study found ARDS patients had impairments in memory, attention, executive, and motor function 6.5 years after leaving the hospital (Suchyta et al., 2004). A prospective study using a memory questionnaire a median of 22 months after ICU discharge found 8% patients had moderate to severe and 20% had mild memory impairments (Adhikari et al., 2009). The prevalence of memory impairments in ARDS survivors declined over time with 13% of patients reporting impaired memory 5 years after ICU discharge (Herridge et al., 2006).

Cognitive Sequelae in other Critically Ill Populations

Several studies provide information regarding cognitive outcomes in medical critically ill populations. In mechanically ventilated patients, 32% had impairments in psychomotor speed, visual and working memory, verbal fluency, and visuo-construction at 6-month follow-up (Jackson et al., 2003). A prospective cohort of respiratory-failure patients found 91% of patients had cognitive impairments at hospital discharge and 41% had cognitive impairments at 6 months (Hopkins, Jackson et al., 2005). Similarly, 35% of medical critically ill patients had impaired executive function, including psychomotor problems and impulsivity and global decline in intellectual function (Sukantarat et al., 2005). A study of 30 non-delirious medical critically ill patients assessed in the ICU, 100% had significant deficits in executive function (i.e., strategic thinking and problem solving) and 67% in memory (C. Jones et al., 2006). At one-week post-ICU discharge, 87% of these patients continued to exhibit deficits in problem-solving skills, of whom 20% could not solve any of the problems, and 50% had memory deficits. At the 2-month follow-up, 50% had deficits in problem-solving skills, while 31% had memory deficits (C. Jones et al., 2006).

Cognitive impairments observed in ICU survivors are not only prevalent, but are often quite severe. For example, ARDS patients with cognitive sequelae (global measure of cognitive function) fell below the 6th percentile of the normal distribution of cognitive functioning, displaying marked deficits in various domains, including memory, executive functioning, and mental processing speed (Hopkins, Weaver et al., 2005). The observed impairments do not impact all domains equally, and deficits in some areas may recover more completely than others.

Despite differences in methods making across-study comparisons difficult, current data indicate that cognitive impairments are prevalent and pervasive in survivors of critical illness at

hospital discharge (e.g., Adhikari et al., 2009; Christie et al., 2004; Duning et al., 2010; Ernest et al., 2006; Herridge et al., 2006; Hopkins, Jackson et al., 2005; Hopkins et al., 2004; Hopkins, Weaver et al., 2005; Hopkins et al., 1999; Jackson et al., 2003; Marquis et al., 2000; Mikkelsen et al., 2009; Rothenhausler et al., 2001; Selnes et al., 2001; Suchyta et al., 2004; Sukantarat et al., 2005). Further, a recent longitudinal cohort study in older adults without premorbid cognitive impairments or dementia found that individuals who underwent acute care or critical illness hospitalization had a greater decline in cognitive function and incident dementia compared to individuals who were not hospitalized (Ehlenbach et al., 2010). This finding suggests that that acute or critical illness may cause an abrupt decline in cognitive function that is not due to premorbid cognitive problems. Thus, factors associated with acute or critical illness may be causally related to cognitive decline in older critically ill patients (Ehlenbach et al., 2010). The cognitive impairments following critical illness occur in a variety of cognitive domains and appear to improve during the first 6 to 12 months post-hospital discharge. However, many patients continue to experience significant chronic cognitive impairments, years after ICU discharge (Rothenhausler et al., 2001).

Lack of Early Identification of Cognitive Sequelae

Data are lacking regarding the use of cognitive screening tests to identify which critically ill patients may be at risk to develop long-term cognitive sequelae. In addition, fatigue and low tolerance for activities that require sustained attention may make the use of comprehensive neuropsychological test batteries problematic, especially in the period immediately following ICU discharge, as they require several hours to administer. Therefore, comprehensive neuropsychological test batteries may not be practical in the evaluation of cognitive function immediately following acute critical illness. However, early detection and identification of

cognitive impairments may 1) increase physician awareness of the potential for cognitive impairments after ICU hospitalization; 2) direct research at the contributing risk factors and mechanisms of cognitive impairments; 3) expedite neuropsychological evaluation; 4) guide the development of rehabilitation strategies; and 5) facilitate referral for cognitive rehabilitation (Borson, Scanlan, Brush, Vitaliano, & Dokmak, 2000), which are shown to improve cognitive function in patients with acquired brain injury (Ho & Bennett, 1997; Sohlberg, Ehlhardt, & Kennedy, 2005) and stroke (Michel & Mateer, 2006).

Despite a consensus among neurologists, psychiatrists, and other specialists regarding the importance of early identification of cognitive impairment (O' Connor et al., 1988; Petersen et al., 2001), there is limited recognition of cognitive impairments in ICU populations. Limited recognition of cognitive impairments is due in part to ICU clinicians lack of knowledge regarding effects of critical illness on cognitive function, time constraints, lack of neuropsychologists in critical care settings, perception of limited treatment options, and length of comprehensive neuropsychological test batteries (Boise, Camicioli, Morgan, Rose, & Congleton, 1999). Failure to identify cognitive impairments can have severe implications for patients everyday outcomes (Hopkins, Weaver et al., 2005). Given these concerns, brief cognitive screening tests that could be used to identify critically ill patients at risk to develop cognitive impairments are important.

Cognitive screening tests have been used in other populations to predict which patients are at risk for developing cognitive impairments. Data from traumatic brain injury (Drake, McDonald, Magnus, Gray, & Gottshall, 2006; Oh, Seo, Lee, & Song, 2006) and Alzheimer's disease (Heun, Papassotiropoulos, & Jennssen, 1998; McDowell, Kristjansson, Hill, & Hebert, 1997; Perneczky et al., 2006) suggest that cognitive screening tests are reliable and valid tools

that can be used to predict patients at risk for cognitive impairments. However, these tests have not been applied in critically ill patients, raising questions as to whether cognitive screening tests are reliable and valid ways to predict cognitive impairments in this population.

What are Cognitive Screening Tests?

While comprehensive neuropsychological tests are the gold standard for assessing cognitive function, many populations who are too ill or cognitive impaired often are not able to maintain attention for a brief period of time, especially during or immediately following ICU hospitalization. A comprehensive neuropsychological test battery often requires several hours to administer. Further, comprehensive neuropsychological testing is expensive and requires trained neuropsychologists who are often not available in acute medical settings. Therefore, brief cognitive screening tests are needed to assess cognitive function in critically ill populations.

Cognitive screening tests are quantitative instruments that assess global cognitive functioning and are used to detect cognitive impairments. Cognitive screening tests appropriate for use in the critical care setting must be brief, easy to administer, applicable to a large age range, and minimally affected by demographic variables (e.g., education, sex, and age), with a high sensitivity and specificity (Lorentz, Scanlan, & Borson, 2002). Despite some variability in the sensitivity and specificity of cognitive screening tests, they are generally adequate for screening cognitive function. Cognitive screening tests with good reliability and validity may be used to stratify patients with regard to severity of cognitive impairments (Brummel-Smith, 2000).

There is a growing consensus regarding the importance of using cognitive screening tests as part of routine primary care of the elderly (Brodaty, Howarth, Mant, & Kurrle, 1994; Doraiswamy, 1996; Gambert, 1997; Knopman, 1998). The Mini-Mental Status Examination

(MMSE) is widely considered the gold standard (King, DiLuna, Cicchetti, Tsevat, & Roberts, 2006), which assesses a range of cognitive abilities including orientation, memory, and attention (M. F. Folstein, Folstein, & McHugh, 1975). The MMSE has been used for over 30 years (M. F. Folstein et al., 1975) and is recommended by the National Institute of Neurologic and Communicative Disorders and Stroke and the Alzheimer's disease and Related Disorders Association for diagnosis of Alzheimer's disease (McKhann et al., 1984). The Committee on Research of the American Neuropsychiatric Association states that brief cognitive screening tests, including the MMSE, can detect dementia with "reasonable accuracy" (Boustani, Peterson, Hanson, Harris, & Lohr, 2003; Malloy et al., 1997). Other commonly used cognitive screening tests include the Mini-Cog (Borson et al., 2000), Short-Portable Mental Status Questionnaire (SPMSQ; Denny, Kuchibhatla, & Cohen, 2006), and Six-item Screener (SIS; Boustani et al., 2006). Data suggest that the overall diagnostic accuracy may be improved by combining data from several cognitive screening tests (Fischer, Hannay, Loring, & Lezak, 2004; Tuokko & Hadjistavropoulos, 1998).

Comparison of Cognitive Screening Tests

The sensitivity and specificity of the MMSE have been compared to other cognitive screening tests in elderly and dementia populations. Perneczky and colleagues (2006) compared the MMSE to the Clinical Dementia Rating (CDR) and found the MMSE was a good surrogate measure for the CDR for the staging of dementia in Alzheimer's disease. A study that compared the MMSE, Syndrom-Kurztest, and clock drawing test in elderly patients found strong positive correlations between these measures and the diagnosis of dementia (Koch, Gurtler, & Szecsey, 2005). One investigation found the SIS had a better sensitivity and specificity than the Mini-Cog in detecting cognitive impairments in patients 65 years and older (Wilber, Lofgren, Mager,

Blanda, & Gerson, 2005). Alternatively, the Mini-Cog is reported to be one of the best screening tests for the detection of dementia (Brodaty, Low, Gibson, & Burns, 2006). The Mini-Cog is simple, brief, has good sensitivity, costs minimally, requires minimal testing and training time, and performs as well as or better than the MMSE in identifying cognitive impairments (Borson et al., 2000; Borson, Scanlan, Watanabe, Tu, & Lessig, 2005; Scanlan & Borson, 2001).

A study using cognitive screening tests to determine cognitive status at hospital discharge and follow-up in critically ill patients found the mean MMSE scores among patients who did not complete follow-up were below the impairment cutoff score of 24, and significantly lower than the mean scores of the patients who completed follow-up (Jackson et al., 2003). However, the MMSE was not used to predict patient cognitive impairments in this study. No study to date has used cognitive screening tests to predict long-term cognitive sequelae in critically ill populations. The primary purpose of the current study was to determine whether cognitive screening tests predict long-term cognitive sequelae or impairments in specific cognitive domains 6 months after hospital discharge in survivors of critical illness.

Cognitive Sequelae and Ecological Validity

Critically ill patients frequently experience new functional limitations, reflecting a decline in their everyday functioning and development of a new baseline level of functioning (Karlawish & Clark, 2003). Ecological validity is the extent to which inferences can be drawn regarding the patients' behaviors or ability to function in a variety of real-world settings on everyday tasks and their relationship with cognitive impairments as measured by neuropsychological tests (J. E. Franzen & Wilhelm, 1996). Thus, ecological validity addresses the question "does cognitive functioning predict the patient's ability to carry out everyday

tasks?" Tests that predict real world functioning or everyday functioning are described as ecologically valid (Brewer, 2000).

In addition to predicting long-term cognitive sequelae in critically ill patients (primary study purpose), another important question is whether cognitive impairments are related to the patients' everyday functioning post-hospital discharge. That is, can survivors of critical illness resume their previous level of everyday functioning and perform tasks such as self-care, making a grocery list, shopping, looking up telephone numbers, managing medications, managing money, and returning to work? Research in a variety of patient populations suggests there is an association between cognitive test performance and everyday functioning. For example, deficits in working memory are associated with difficulties managing finances in older patients (Earnst et al., 2001) and global neuropsychological performance is associated with difficulties managing finances following traumatic brain injury (Hoskin, Jackson, & Crowe, 2005). Measures of everyday functioning extend knowledge of patient outcomes beyond that of cognitive function by adding assessment of everyday skills and abilities, which may be adversely affected by cognitive impairments.

Everyday functioning is assessed from two different perspectives: basic activities of daily living (ADLs) and instrumental activities of daily living (IADLs). Basic ADLs include self-care such as bathing dressing, feeding, toileting, grooming, and self-transfer (Kane & Kane, 1981). IADLs involve more complex tasks such as shopping, managing medications, cooking, household chores, communication, and managing money, finances, and transportation (Kane & Kane, 1981; Lawton & Brody, 1969). While ADLs are fundamental to independence, the IADL scales assess the higher functional abilities that are required for independent living at home and in the community (Gallo & Paveza, 2005). Everyday functioning assessed on the IADLs is

central to the patients' return to independent living and to cope with the demands of everyday life (McColl et al., 1999).

Self-report or informant-based measures of IADLs are the most commonly used methods for assessing everyday functioning. These measures are easy and practical to administer and provide insight regarding the patient's everyday functioning. Self-report or informant-based measures of IADLs such as the Lawton Instrumental Activities of Daily Living (Lawton IADL; Lawton, 1988; Lawton & Brody, 1969; Lawton, Moss, Fulcomer, & Kleban, 1982) and Functional Activities Questionnaire (FAQ; Pfeffer, Kurosaki, Harrah, Chance, & Filos, 1982) have been used to assess everyday outcomes in patients with Alzheimer's disease (Farias, Harrell, Neumann, & Houtz, 2003; Porter et al., 2003) and rheumatoid arthritis (Kauppi, Hartikainen, Kautiainen, Laiho, & Sulkava, 2005). The FAQ has been used to assess everyday functioning in a trauma ICU population (Jackson et al., 2007). Several studies have compared the FAQ and Lawton IADL. Elderly community dwelling individuals FAQ score correlated .72 with their Lawton IADL score and .83 with a neurologist's global rating on a Scale of Functional Capacity (Pfeffer et al., 1982). The FAQ predicts mental status better than the Lawton IADL; the FAQ correlated .76 with the Mental Function Index (Pfeffer et al., 1982) and -.60 with the Cognitive Capacity Screening Examination (Senanarong et al., 2004).

In addition to assessing everyday functioning with self-report or informant-based questionnaires (Blessed, Tomlinson, & Roth, 1968; Fillenbaum, 1985; Lawton & Brody, 1969; Pfeffer et al., 1982), everyday functioning can be measured using direct assessment or performance-based assessment (Karagiozis, Gray, Sacco, Shapiro, & Kawas, 1998; Loeb, 1996; Loewenstein et al., 1989). Performance-based assessment provides an objective assessment of everyday skills, such as using the telephone, preparing a meal, managing medication, writing a

check, and managing money. The Independent Living Scales (ILS) is a performance-based measure of everyday functioning and requires individuals to perform various tasks, creating a "direct, more objective assessment of functioning in daily life" (Loeb, 1996, p. 1). The ILS has been used to assess everyday functioning in a variety of populations, including schizophrenia (Revheim & Medalia, 2004; Revheim et al., 2006) and dementia (Davis, Martin-Cook, Hynan, & Weiner, 2006; Martin-Cook, Davis, Hynan, & Weiner, 2005). There are no studies that compare questionnaire-based assessment of everyday functioning (i.e., Lawton IADL and FAQ) with objective measures such as the ILS.

Recent investigations have examined the impact of critical illness on everyday functioning. Everyday functioning of 817 adult ICU patients with prolonged mechanical ventilation were significantly below than that of the normal healthy general population and declined from premorbid levels, with 78% of patients requiring caregiver support at two-month after hospital discharge (Quality of Life After Mechanical Ventilation in the Elderly Study Investigators, 2002). Chelluri and colleagues (2004) found 57% of survivors of critical illness required caregiver assistance one year later. The odds of being dependent upon a caregiver at one-year were higher in older patients and in those who were dependent in IADLs prior to hospitalization. Among middle-aged trauma ICU survivors, 22% had impairments in everyday functioning, including managing financial or business affairs, and traveling or making travel arrangements (Jackson et al., 2007). The rate of return to work in ARDS survivors ranges from 33% (Hopkins, Jackson et al., 2005) to 51% (Herridge et al., 2003; Rothenhausler et al., 2001) with a high of 58% (Jackson et al., 2007), suggesting poor everyday functioning in this population. Reasons for inability to return to work include persistent fatigue and weakness, poor

everyday functioning, work-related stress, voluntary retirement, need for job retraining (Herridge et al., 2003), depression (Adhikari et al., 2009), and cognitive impairments (Jackson et al., 2007).

While functional morbidity in critically ill survivors is increasingly recognized, the extent to which everyday functioning is associated with cognitive impairments needs to be elucidated in order to understand the full impact of cognitive impairments in ICU survivors. Data are lacking regarding the relationships between the specific domains of everyday functioning (e.g., financial management) and specific cognitive domains (e.g., executive function) in survivors of critical illness. The second purpose of the current study was to assess whether cognitive impairments predict everyday functioning, as measured by the Lawton IADL, FAQ, and the ILS, in survivors of critical illness.

Psychiatric Sequelae and Quality of Life

Psychiatric sequelae following critical illness and ICU treatment are increasingly recognized. The prevalence of depression and anxiety in ICU survivors ranges from 10% to 58% (Adhikari et al., 2009; Angus et al., 2001; Herridge et al., 2003; Hopkins, Weaver et al., 2005; Hopkins et al., 1999; Kapfhammer, Rothenhausler, Krauseneck, Stoll, & Schelling, 2004; McCartney & Boland, 1994; Mikkelsen et al., 2009; Milisen et al., 2001; Orme et al., 2003; Skodol, 1999; Szokol & Vender, 2001; Weinert et al., 1997). Further, depression and anxiety are associated with cognitive impairments in ARDS patients (Rothenhausler et al., 2001). A review of 14 studies found that the median point prevalence of clinically significant depression among ICU survivors was 28% (range 17% to 43%) and premorbid depression was a risk factor for post-ICU depression (Davydow, Gifford, Desai, Bienvenu, & Needham, 2009). Predictors of depression at 1 year were alcohol dependence, female gender and younger age; where as predictors of anxiety at 1 year were ratio of arterial oxygen tension to inspired oxygen fraction

and duration of mechanical ventilation (Hopkins, Key, Suchyta, Weaver, & Orme Jr., 2010). Predictors of depression at 2 years were depression and cognitive sequelae at 1 year; whereas predictors of anxiety at 2 years was anxiety at 1 year (Hopkins et al., 2010).

A number of studies have examined relationships between life-threatening critical illnesses and the development posttraumatic stress disorder (PTSD). Kapfhammer and colleagues (2004) found that 44% of critically ill patients developed PTSD at hospital discharge with 24% had PTSD symptoms 8 or more years later. Further, 14% of medical ICU patients with mechanical ventilation developed symptoms of PTSD (Girard et al., 2007). A recent review of 15 studies found the median point prevalence of clinically significant PTSD symptoms among general ICU survivors was 22% (Davydow, Gifford, Desai, Needham, & Bienvenu, 2008).

Quality of life is an evaluation of health status associated with biological/physiological, mental, cognitive, physical, and social functions, and health perceptions (Weinert et al., 1997). The Medical Outcome Study 36-Item Short Form Health Survey (SF-36; Stewart, Hays, & Ware, 1988; Ware, 1993; Ware, Kosinski, & Keller, 1994) has been used extensively in assessing quality of life of critically ill patients (e.g., Dowdy et al., 2005; Hopkins et al., 2004; Mikkelsen et al., 2009). A meta-analysis found ARDS survivors had lower quality of life compared with matched, normal controls 66 months after ICU discharge (Dowdy et al., 2005). Psychiatric morbidity is associated with decreased quality of life (Davydow, Desai, Needham, & Bienvenu, 2008; Davydow et al., 2009; Davydow, Gifford et al., 2008; Hopkins et al., 2004; Kapfhammer et al., 2004; Schelling et al., 1998).

Conflicting findings exist regarding the relationships between cognitive impairment and quality of life. For example, decreased quality of life was not associated with cognitive impairments in ARDS survivors (Hopkins, Weaver et al., 2005) or with executive dysfunction in

medical ICU patients (Sukantarat et al., 2005). Conversely, ARDS survivors with cognitive impairment had lower quality of life compared to ARDS survivors without cognitive impairment (Christie et al., 2006). Likewise, survivors of ALI (Rothenhausler et al., 2001) and ARDS (Mikkelsen et al., 2009) with cognitive impairments have lower quality of life compared to individuals without cognitive impairment; however, both groups' quality of life was substantially lower than healthy controls (Mikkelsen et al., 2009; Rothenhausler et al., 2001). Relatively little is known regarding the specific impact of cognitive impairments secondary to critical illness on the specific quality of life domains (e.g., mental, physical, and social function). The third purpose of the current study was to better characterize the relationship between cognitive sequelae and quality of life in survivors of critical illness.

Study Purposes

The purposes of this study were threefold. The primary purpose of the study was to determine whether cognitive screening tests (MMSE and Mini-Cog) predict cognitive sequelae and everyday functioning in survivors of critical illness 6-month post-hospital discharge. Further, we sought to determine whether the MMSE predict long-term cognitive sequelae better than the Mini-Cog. The second purpose of this study was to determine whether long-term cognitive sequelae are associated with problems in everyday functioning (Lawton IADL, FAQ, and ILS) in critically ill survivors. Additionally, we assessed whether impairments in a specific cognitive domains (e.g., memory, executive dysfunction, etc.) predict everyday functioning in a related functional domain (e.g., financial management). The third purpose of the current study was to assess the relationship between cognitive sequelae and quality of life in survivors of critical illness.

Study Hypotheses

Hypothesis 1a. Low scores on cognitive screening tests (MMSE and Mini-Cog) will predict long-term cognitive sequelae at 6-month follow-up. Further, the Mini-Cog will better predict long-term cognitive sequelae compared to the MMSE, due to its higher sensitivity and specificity.

Hypothesis 1b. Low scores on the MMSE and Mini-Cog will predict impairments in specific cognitive domains (e.g., memory and executive function).

Hypothesis 2a. Low scores on cognitive screening tests (MMSE and Mini-Cog) will predict everyday functioning (e.g., Lawton IADL, FAQ, and ILS Full Scale Score) at 6-month follow-up.

Hypothesis 2b. Long-term cognitive sequelae at 6 months will predict everyday functioning as measured by the Lawton IADL, FAQ, and ILS Full-Scale scores at 6-month follow-up.

Hypothesis 2c. Impairments in specific cognitive domains (e.g., memory and executive function) at 6-month follow-up will predict everyday functioning on the ILS subscale scores (i.e., Memory/Orientation, Managing Money, Managing Home and Transportation, Health and Safety, and Social Adjustment).

Hypothesis 3. Long-term cognitive sequelae will predict poor quality of life.

Method

Participants

Consecutive critically ill patients were recruited from the Shock Trauma Intensive Care Unit and Respiratory ICU at LDS Hospital and Intermountain Medical Center in Salt Lake City for this prospective outcome study to assess cognitive functioning, psychiatric functioning,

quality of life, and everyday functioning. Mechanical ventilator management, including the use of sedatives, narcotics, and paralytic medications, was carried out using clinical protocols as part of the patient's routine clinical care (Morris et al., 1994; Thompson et al., 1994).

Study inclusion criteria were mechanical ventilation $\geq$ 48 hours and participant age 18 to 85 years. Study exclusion criteria were (a) disease states that were irreversible (e.g., liver failure, malignancy, AIDS) and in which six-month survival is unlikely, (b) central nervous system damage (CNS) due to injury or CNS disease (e.g., traumatic brain injury or cognitive impairment), (c) comorbid disorders with known cognitive effects including chronic obstructive pulmonary disease, chronic heart failure, cervical spinal cord injury, disease malignancy, and chronic renal failure, (d) a psychotic disorder (e.g., schizophrenia and bipolar disorder), (e) preexisting cognitive impairment, (f) non-English-speaking, (g) primary residence greater than 200 miles from the study site, and (h) informed consent could not be obtained. Approval of this study was obtained from the institutional review boards at Intermountain Medical Center and Brigham Young University. Written informed consent was obtained prior to hospital discharge.

An unavoidable reality of studying patients with unanticipated acute critical illnesses is that evaluation of pre-ICU cognitive, psychiatric, everyday functioning, and quality of life is not possible as it is not possible to determine who will become critically ill. Patients with a history of dementia or other cognitive impairments based on medical records review were excluded from the study. In order to determine if unknown pre-existing cognitive impairments were present, patients were administered the Modified Blessed Dementia Rating Scale (MBDRS; Blessed et al., 1968). Patients were considered to have preexisting cognitive impairments if their MBDRS score was > 3 (Blessed et al., 1968; Inouye, Viscoli, Horwitz, Hurst, & Tinetti, 1993). The preexisting cognitive impairments were presumably of mild to moderate severity as we excluded

patients with dementia or known premorbid cognitive impairments. Patients were not excluded from the study on the basis of their MBDRS scores.

From August 2007 to December 2008, consecutive critically ill patients were evaluated for eligibility in our prospective outcome study. Figure 1 shows the study flow diagram. Of 319 patients screened for the study, 226 patients met exclusion criteria including pre-existing CNS disease (n = 136), disease states that were irreversible (n = 43), comorbid disease with known cognitive effects (n = 14), residence > 200 miles from study site (n = 13), non-English speaking (n = 10), pre-existing psychiatric disorder with psychosis (n = 6), and pre-existing cognitive impairments (n = 4). Eleven patients declined the study and 12 patients were transferred to another long-term care facility without obtaining consent, resulting in 70 ICU survivors who were enrolled in the study. Of the 70 patients, 10 patients died between hospital discharge and six month follow-up. The cause of death was respiratory failure (n = 5), cardiac arrest (n = 2), gastrointestinal complications (n = 1), multiple organ failure (n = 1), and withdrawn support after ICU readmission (n = 1). Three patients declined the follow-up (e.g., too busy or not interested) and four patients could not be contacted, despite efforts to contact the patient, patient's identified family member(s) or significant other by telephone and letter, resulting in 7 patients lost to follow-up. A total of 53 patients completed 6-month follow-up assessments.

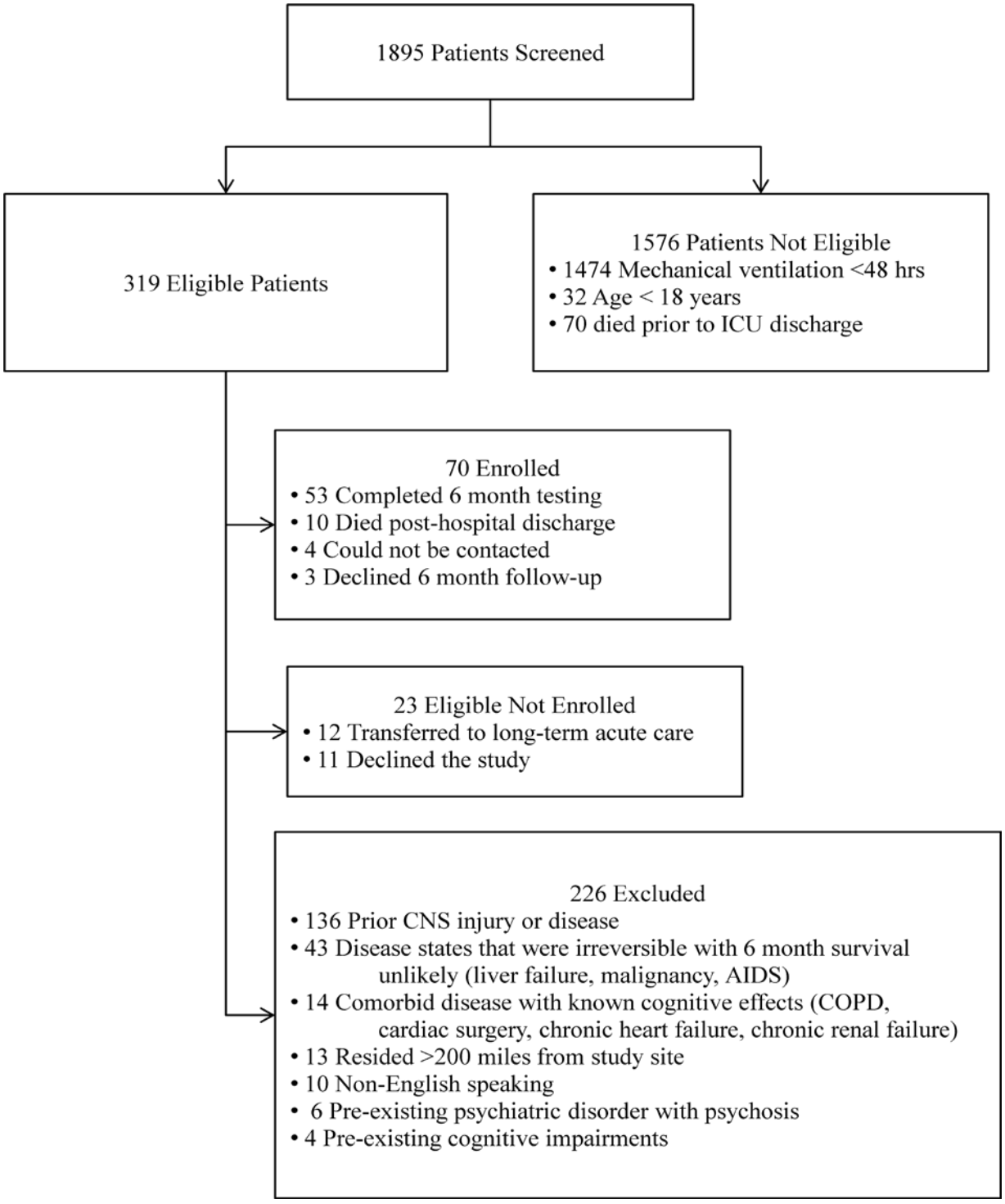

Figure 1. Study flow diagram

AIDS = Acquired Immune Deficiency Syndrome
CNS = Central Nervous System
COPD = Chronic Obstructive Pulmonary Disease

The 6-month follow-up rate was 76% (n = 53). Excluding patients who died during the first 6 months following hospital discharge, the follow-up rate was 88% (n = 53). The 6-month follow-up evaluation consisted of measures of cognitive functioning, psychiatric functioning, everyday functioning, and quality of life was completed in a single 3- to 4-hour period. Patients who completed the 6-month follow-up evaluation were reimbursed $50 for their time and travel expenses.

Demographic and medical data were collected prospectively as part of routine clinical care, including length of stay, ventilator data, and the Acute Physiologic and Chronic Health Evaluation II (APACHE II) score (Knaus, Draper, Wagner, & Zimmerman, 1985). The APACHE II is a severity of disease classification system which scores a patient's age, previous health status, initial routine physiological measurements, admission type (medical or surgical) and the diagnosis. The score range from 0 to 71, with high scores indicating increased illness severity and risk of death (Knaus et al., 1985).

Hospital Discharge Assessment

Cognitive screening tests were administered just prior to hospital discharge if patients were oriented to person, place and time. The following measures were administered: history or current alcohol dependence (Rapid Alcohol Problems; Cherpitel, 1995), history or current substance abuse (DAST-20; Gavin, Ross, & Skinner, 1989; Staley & el-Guebaly, 1990), and the MMSE and the Mini-Cog. The MMSE and Mini-Cog were counterbalanced to control for order effects. Detailed test descriptions are provided in Appendix.

Cognitive Tests

Standardized cognitive tests administered at 6-month post-hospital discharge assessed attention/concentration, motor, language, memory and learning, mental processing speed,

executive function. The reading subtest of the Wide Range Achievement Test-3 (Wilkinson, 1993) was used to estimate the patients' premorbid intellectual abilities, while the Wechsler Abbreviated Scale of Intelligence (WASI; Wechsler, 1999) was used to assess the patients' current intellectual abilities. The cognitive tests included the Trail Making Test Parts A and B (Reitan & Wolfson, 1993), Hayling Sentence Completion Test (Burgess & Shallice, 1997), Hand Dynamometer Test (Reitan & Davison, 1974), Grooved Pegboard Test (Matthew & Klove, 1964), Finger Tapping Test (Halstead, 1947), Logical Memory subtest (Wechsler, 1997), California Verbal Learning Test-II (CVLT-II; delay recall trial; Delis, Kramer, Kaplan, & Ober, 2000), Rey-Osterrieth Complex Figure Test (ROCFT; 30-minute delayed recall trials; Rey, 1941), Stroop Test-Golden Version (Interference trial; Golden, 1978), and Digit Symbol subtest (Wechsler, 1981). Detailed test descriptions are provided in Appendix.

Raw scores were transformed to demographically corrected T-scores (i.e., age, gender, education, and ethnicity) which have a mean of 50 and standard deviation of 10 for the Trail Making Test Parts A and B, Hand Dynamometer Test (each hand), Grooved Pegboard Test (each hand), Finger Tapping Test (each hand), and Digit Symbol subtest (Heaton, Miller, Taylor, & Grant, 2004). *T* scores were also calculated using normative data for the Parts A and B from the Hayling Sentence Completion Test (Burgess & Shallice, 1997), long-delay free-recall trial from the CVLT-II (Delis et al., 2000), 30-minute delay trials from the Logical Memory subtest (Wechsler, 1997), 30-minute delayed trials from the ROCFT (Meyers & Meyers, 1995), and Interference trial from the Stroop Test-Golden Version (Golden, 1978).

A priori the presence of cognitive sequelae was defined as scores on 2 or more neuropsychological tests that were greater than 1.5 standard deviations (*SD*) or one test score that was greater than 2 *SD* below the normative population mean. This definition of cognitive

sequelae was similar to those used in previous studies following critical illness (Hopkins, Weaver et al., 2005; Jackson et al., 2003).

A priori the presence of cognitive impairments was defined as scores on one or more neuropsychological tests in each cognitive domain (i.e., memory, mental processing speed, attention, motor speed, language, and executive function) that are greater than 1.5 standard deviations (*SD*) below the normative population mean. This definition of cognitive impairment was similar to those used in standard neuropsychological evaluations (Heaton et al., 2004).

Everyday Functioning

Everyday functioning was assessed at 6 months using the Lawton IADL (Lawton & Brody, 1969), FAQ (Pfeffer et al., 1982), and the performance-based ILS (Loeb, 1996). The Lawton IADL is a widely used self-report or informant-report questionnaire that assesses shopping, managing transportation, climbing stairs, managing finances, doing housework, using the telephone, doing the laundry, managing medications, walking outdoors, driving, holding down a paying job, and preparing meals (Lawton & Brody, 1969). The Lawton items are scored as 0 (completely dependent), 1 (need some assistance), and 2 points (independent), and then summed to form a total score that ranges from 0 (cannot perform any of the functions independently) to 16 (able to perform all the functions independently). A total score ≤ 15 indicates impairments in one or more areas of everyday functioning with lower scores indicate worse performance (Lawton, 1988).

The FAQ is self-report or informant-report instrument assessing the ability to perform 10 high-level skills used in everyday functioning, including shopping, preparing meals, handling finances, and understanding current events (Pfeffer et al., 1982). Each item is scored on a 3-point Likert scale (0 = independent; 3 = dependent) of increasing caregiver dependence. The scores

range from 0 to 30, with a higher scores indicating worse everyday functioning. A score of 9 or greater indicates impaired functioning or dependence in everyday activities (Pfeffer et al., 1982).

The ILS is used to assess competency in Memory / Orientation, Managing Money, Managing Home and Transportation, Health and Safety, and Social Adjustment, as well as two overall subscales of Problem Solving and Performance / Information (Loeb, 1996). The Performance / Information subscale reflects actual knowledge or skills used to perform tasks; for example, using a telephone book or making change. The Problem Solving subscale evaluates abstract reasoning and judgment required for living (e.g., "What would you do if your lights and television went out simultaneously?" and "What would you do if you unintentionally lost ten pounds in a month?") Lower scores indicate worse everyday functioning. Scores of 20 to 39 suggest maximum (full-time) supervision for daily living (i.e., inpatient hospitalization or nursing home setting), scores of 40 to 49 suggest moderate supervision, and scores of 50 to 63 suggest minimal supervision or independent living (Loeb, 1996). Detailed test descriptions are provided in Appendix.

Psychiatric Functioning

Psychiatric functioning was assessed at six months using the Beck Depression Inventory-II (BDI-II; Beck, Steer, & Brown, 1996) and the Beck Anxiety Inventory (BAI; Beck & Steer, 1993). Beck Depression Inventory-II scores of 0-13 indicate *minimal*, 14-19 mild, 20-28 *moderate*, and 29-63 *severe* depression. Beck Anxiety Inventory scores of 0-9 indicate *minimal,* 10-16 *mild*, 17-29 *moderate*, and 30-63 *severe* anxiety.

The Posttraumatic Diagnostic Scale (PDS) is a self-report 49-item scale that is used to assist with the diagnosis of PTSD and provide a means of quantifying the severity of PTSD symptoms (Foa, 1995). The PDS has six subscales: exposure to a traumatic event, re-

experiencing symptoms, avoidance symptoms, symptom duration, and the level of impairment of functioning. The PDS assessment parallels DSM-IV diagnostic criteria for a PTSD diagnosis (Foa, 1995). The PDS has been used with combat veterans, survivors of sexual assault, accident victims (Hunsley & Mash, 2008), and medically ill patients (R. C. Jones, Harding, Chung, & Campbell, 2009).

The Outcome Questionnaire (OQ-45.2), a measure of general distress, was used to assess the patients' global psychological functioning, including how they feel, how they get along with others, and how they are doing in important life tasks (Lambert et al., 2004). The items on the OQ-45.2 assess commonly occurring problems across a wide variety of psychological disorders, as well as personally and socially relevant characteristics that may affect quality of life. The OQ-45.2 consists of three domains: Symptoms Distress (subjective distress), Interpersonal Relations (satisfaction and problems in interpersonal relations), and Social Role (level of dissatisfaction, conflict, distress and inadequacy in tasks related to employment, family roles, and leisure life) (Lambert et al., 2004). The OQ-45.2 provides a total score and three domain scores; the Total Score ranges from 0 to 180, the Symptom Distress subscale scores 0 to 100, the Interpersonal Relations subscale scores 0 to 44, and the Social Role subscale scores 0 to 36, with higher scores indicating greater distress.

The OQ-45.2 is used to: 1) measure current level of distress; 2) measure outcome or ongoing treatment response (administered before and after treatment); and 3) improve quality of patient care (Lambert et al., 2004). For the purposes of our study, the OQ-45.2 was used to assess the patients' current level of distress at 6-month follow-up. The OQ-45.2 Total Scores of > 63 indicates the presence of significant symptom distress, interpersonal difficulties, and difficulties in social roles. The OQ-45.2 Symptom Distress subscale score of > 36 indicates presence of

significant intrapsychic distress (subjective discomfort); the Interpersonal Relationship subscale score of > 15 indicates presence of significant interpersonal problems; and the Social Role subscale score of > 12 indicates significant difficulties fulfilling workplace, student, or home duties. Only one study has used the OQ-45.2 in a medical population (James et al., 2010). In this study, the OQ-45.2 was used to measure overall changes in psychological function at two time points (at admission and discharge) in an inpatient physical rehabilitation population (James et al., 2010). The inpatients had psychological improvement over the course of physical rehabilitation compared to their initial OQ-45.2 scores. Detailed descriptions of the BDI-II, BAI, PDS, and OQ45.2 are provided in Appendix.

Quality of Life

The Medical Outcome Study 36-Item Short Form Health Survey (SF-36; Stewart et al., 1988; Ware, 1993; Ware et al., 1994) was administered at 6-month follow-up to assess health-related quality of life. The eight domains of the SF-36 (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health) are clustered to form two higher order domains, the physical and mental health scores. Each domain is scored from 0 to 100, with higher scores indicating better quality of life (Ware, 1993). Detailed descriptions of the SF-36 are provided in Appendix.

Statistical Analyses

All statistically analyses were carried out using SPSS 17.0 for Windows. Descriptive statistics were carried out for demographic (i.e., age, sex, education, MBDRS scores, RAPS scores, DAST-20 scores) and medical, cognitive screening, IQ, neuropsychological, psychiatric, everyday functioning, and quality-of-life data. Impairments on cognitive screening tests at hospital discharge were reported as the percent of patients who scored below each test's cutoff

score. Cognitive and psychiatric sequelae were reported as percent of patients with sequelae at 6-month follow-up. Sensitivity, specificity, and predictive values of the MMSE and Mini-Cog were calculated.

Independent *t*-tests were conducted to determine if there were significant differences for demographic and medical data comparing: 1) critically ill survivors and patients who died after hospital discharge; 2) patients who completed follow-up and those who lost to follow-up; and 3) patients with cognitive sequelae compared to patients without cognitive sequelae. Independent *t*-tests were also conducted to compare the cognitive screening test scores for patients who completed 6-month follow-up compared to those who died after hospital discharge (prior to 6 month follow-up). The patient's premorbid intelligence (WRAT-3 Reading subtest scores) was compared to the WASI Full-Scale IQ scores using paired-sample *t*-tests. One-sample *t* tests were used to compare the OQ.45.2 and SF-36 scores with respective data from normal, community dwelling adults for patients who completed 6-month follow-up.

Hypothesis 1a. Low scores on cognitive screening tests (MMSE and Mini-Cog) will predict long-term cognitive sequelae at 6-month follow-up. Further, the Mini-Cog will better predict long-term cognitive sequelae compared to the MMSE, due to its higher sensitivity and specificity.

Bivariate stepwise logistic regression analyses were carried out to predict cognitive sequelae using MMSE cutoff scores < 24 (*scores below cutoff*) and Mini-Cog cutoff scores (*scores below cutoff*). Covariates included in the analyses were age, gender, education, estimated premorbid IQ, ICU length of stay, APACHE II scores, duration of mechanical ventilation, depression scores, and anxiety scores. The analysis was repeated using the MMSE < 27 scores (*scores below cutoff*) in one analysis, and the MMSE scores in another analysis. Because the

distribution of data was positively skewed, a logarithmic transformation was used for MMSE scores. Odds ratios were obtained. A two-tailed .05 alpha level of significance level was used.

Bivariate stepwise logistic regression analyses were carried out to predict cognitive sequelae using continuous MMSE scores and Mini-Cog scores. Covariates included in the analyses were age, gender, education, estimated premorbid IQ, ICU length of stay, APACHE II scores, duration of mechanical ventilation, depression scores, and anxiety scores. Because the distribution of data was positively skewed, a logarithmic transformation was used for MMSE scores. Odds ratios were obtained. A two-tailed .05 alpha level of significance level was used.

Hypothesis 1b. Low scores on the MMSE and Mini-Cog will predict impairments in specific cognitive domains (e.g., memory and executive function).

Five separate stepwise logistic regression analyses were carried out using the MMSE < 24 cutoff score (*scores below cutoff*) and Mini-Cog cutoff score (*scores below cutoff*) to predict impairments in specific cognitive domains (*impaired or not impaired*). Each cognitive domain was analyzed in separate analyses (i.e., memory, executive function, mental processing speed, language, and attention). Covariates included in the analysis were age, gender, education, estimated premorbid IQ, ICU length of stay, APACHE II scores, duration of mechanical ventilation, depression scores, and anxiety scores. The analyses were repeated using the predictor variable MMSE < 27 cutoff score (*scores below cutoff*). Preliminary assumption testing was conducted to check for normality, linearity, outliers, homoscedasticity, and multicollinearity, with no violations noted. Odds ratios were obtained. A two-tailed .05 alpha level of significance level was used.

Eight separate stepwise multiple regression analyses were carried out using the MMSE continuous scores and Mini-Cog continuous scores to predict cognitive test scores (e.g., CVLT-

II Long-Delay Free Recall, WMS-III Logical Memory II, ROCFT Long Delay, HSCT Box C, Trail-Making Test Part B, WAIS-R Digit Symbol, COWA, and SCWT Interference scores). Because the distribution of data was positively skewed, a logarithmic transformation was used for MMSE scores. Covariates included in the regression analysis were age, gender, education, estimated premorbid intelligence, ICU length of stay, APACHE II scores, duration of mechanical ventilation, depression scores, and anxiety scores. Preliminary assumption testing was conducted to check for normality, linearity, outliers, homoscedasticity, and multicollinearity, with no violations noted. A two-tailed .05 alpha level of significance level was used.

Hypothesis 2a. Low scores on cognitive screening tests (MMSE and Mini-Cog) will predict everyday functioning (e.g., Lawton IADL, FAQ, and ILS Full Scale Score) at 6-month follow-up.

To predict everyday functioning, three separate stepwise multiple regression analyses were carried out for the following dependent variables: Lawton IADL, FAQ, and ILS Full Scale scores. The predictor variables were MMSE < 24 cutoff score (*scores below cutoff* or *normal*) and Mini-Cog cutoff score (*scores below cutoff* or *normal).* Covariates included in the analyses were age, gender, education, estimated premorbid IQ, ICU length of stay, APACHE II scores, duration of mechanical ventilation, depression scores, and anxiety scores. The analyses were repeated using the predictor variable MMSE < 27 cutoff scores (*scores below cutoff* or *normal*). Preliminary assumption testing was conducted to check for normality, linearity, outliers, homoscedasticity, and multicollinearity, with no violations noted. A two-tailed .05 alpha level of significance level was used.

Hypothesis 2b. Long-term cognitive sequelae at 6 months will predict everyday functioning as measured by the Lawton IADL, FAQ, and ILS Full-Scale scores at 6-month follow-up.

To predict everyday functioning, three separate stepwise multiple regression analyses were carried out for the following dependent variables: Lawton IADL, FAQ, and ILS Full Scale scores. The predictor variable was presence or absence of cognitive sequelae at 6 months. Covariates used in the analyses were age, gender, education, estimated premorbid IQ, ICU length of stay, APACHE II scores, duration of mechanical ventilation, depression scores, and anxiety scores. Preliminary assumption testing was conducted to check for normality, linearity, outliers, homoscedasticity, and multicollinearity, with no violations noted. A two-tailed .05 alpha level of significance level was used.

Hypothesis 2c. Impairments in specific cognitive domains (e.g., memory and executive function) at 6-month follow-up will predict everyday functioning on the ILS subscale scores (i.e., Memory/Orientation, Managing Money, Managing Home and Transportation, Health and Safety, and Social Adjustment).

Five stepwise multiple regression analyses were conducted for the following dependent variables: Memory/Orientation, Managing Money, Managing Home and Transportation, Health and Safety, and Social Adjustment. The predictor variables were impaired cognitive domains (*normal* or *impaired*), including memory, mental processing speed, attention, language, and executive function. Covariates used in the regression analyses were age, gender, education, estimated premorbid IQ, ICU length of stay, APACHE II scores, duration of mechanical ventilation, depression scores, and anxiety scores. Preliminary assumption testing was conducted

to check for normality, linearity, outliers, homoscedasticity, and multicollinearity, with no violations noted. A two-tailed .05 alpha level of significance level was used.

Eight stepwise multiple regression analyses were conducted for the following dependent variables: Memory/Orientation, Managing Money, Managing Home and Transportation, Health and Safety, and Social Adjustment scores. The predictor variables were each of the cognitive test continuous scores, including the CVLT-II Long-Delay Free Recall, WMS-III Logical Memory II, ROCFT Long Delay, HSCT Box C, Trail-Making Test Part B, COWA, WAIS-R Digit Symbol, and Stroop Inteference scores. Covariates used in the regression analyses were age, gender, education, estimated premorbid IQ, ICU length of stay, APACHE II scores, duration of mechanical ventilation, depression scores, and anxiety scores. Preliminary assumption testing was conducted to check for normality, linearity, outliers, homoscedasticity, and multicollinearity, with no violations noted. A two-tailed .05 alpha level of significance level was used.

Hypothesis 3. Long-term cognitive sequelae will predict poor quality of life.

Eight separate stepwise multiple regression analyses were carried out in which the SF-36 domain scores (Physical Functioning, Role-Physical, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, and Mental Health) were entered as separate dependent variables in each analysis. The predictor variable was presence or absence of cognitive sequelae at six months. Covariates used in the analyses were age, gender, education, estimated premorbid IQ, ICU length of stay, APACHE II scores, duration of mechanical ventilation, depression scores, and anxiety scores. Preliminary assumption testing was conducted to check for normality, linearity, outliers, homoscedasticity, and multicollinearity, with no violations noted. A two-tailed .05 alpha level of significance level was used.

Results

Descriptive Statistics

Descriptive statistics for demographic and medical data for the 70 critically ill patients are shown in Table 1. There were 35 females and 35 males with a mean age of 54.4 ± 17.3 years (range 21 to 85) and a mean education level of 13.3 ± 2.2 years (range 10 to 20). Primary etiologies for ICU admission were sepsis (n = 27), trauma (n = 14), pneumonia (n = 9), post-operative complications (n = 5), respiratory disease (n = 4), cardiovascular disease (n = 3), gastrointestinal disease (n = 3), renal disease/failure (n = 3), liver failure (n = 1), and cancer (n = 1). Only one patient had preexisting cognitive impairments identified by the MBDRS, 2 patients had a history of drug abuse, and 8 patients had a history of alcohol dependence (Table 1).

There was no difference in the MMSE scores for patients who completed 6-month follow-up (24.4 ± 3.8) compared to patients who died post-hospital discharge (24 ± 3.6: t = .32, p = .75). Similarly, there was no difference in the Mini-Cog scores for patients who completed follow-up (1.98 ± 1.1) compared to patients who died post-hospital discharge (1.9 ± 1.1; t = .21, p = .83).

The survivors were younger and had lower mean FiO_2 levels (i.e., less ill) compared to patients who died post-hospital discharge (Table 2). No other demographic or medical variables differed between the groups.

Table 1

Patient demographic and medical data

Demographic and Medical Variables ($N = 70$)	*Mean* ± *SD* or *n* (%)	Range
Sex – male, *N* (%)	35 (50)	
Age – years	54.4 ± 17.3	21 to 85
Education level - years	13.3 ± 2.2	10 to 20
MBDRS > 3, *n* (%)	1 (1)	1 to 4
RAPS $4 \geq 1$, *n* (%)	8 (11)	0 to 4
DAST-20 > 5, *n* (%)	2 (3)	0 to 12
ICU Length of Stay (days)	15.4 ± 9.8	4 to 52
Hospital Length of Stay (days)	25.0 ± 16.2	5 to 103
Duration of Mechanical Ventilation (days)	8.8 ± 6.4	2 to 31.62
Maximum FiO_2 (%)	94.6 ± 13.7	50 to 100
Minimum PaO_2 mmHg	60.3 ± 16.5	35 to 130
APACHE II Score	25.4 ± 6.5	14 to 45
ICU Admission Diagnosis, *n* (%)		
Sepsis	27 (39)	
Trauma	14 (20)	
Pneumonia	9 (13)	
Post-operative Complications	5 (7)	
Respiratory Disease	4 (5)	
Cardiovascular Disease	3 (4)	
Gastrointestinal Disease	3 (4)	
Renal Disease/Failure	3 (4)	
Liver Failure	1 (2)	
Cancer	1 (2)	

Demographic and Medical Variables (N = 70)	*Mean* ± *SD* or *n* (%)	Range
Died after hospital discharge *n* (%)	10 (14.3)	
Declined Follow-up *n* (%)	3 (4)	
Lost to Follow-up *n* (%)	4 (6)	

APACHE II = Acute Physiology and Chronic Health Evaluation II
DAST-20 = Drug Abuse Screening Test-20
ICU = Intensive care unit
MBDRS = Modified Blessed Dementia Rating Scale
RAPS 4 = Rapid Alcohol Problems Screen 4

Table 2

Demographic and medical data for patients who survived compared to patients who died after hospital discharge

Characteristics	Survivors (n = 60)		Died before Follow-up (n = 10)		Survivors vs. Died before Follow-up	
	M±SD	Range	*M±SD*	Range	*t*	*p*
Duration MV (days)	9 ± 6.6	1.8 to 31.6	7.8 ± 4.4	2.1 to 17.5	-.54	.59
Hospital LOS (days)	25.3 ± 16.9	5 to 104	21.6 ± 9.5	7 to 35	-.68	.50
ICU LOS (days)	15.4 ± 9.9	4.6 to 51.6	15.5 ± 9.6	4.3 to 1.1	.03	.98
Maximum FiO_2 (%)	93.7 ± 14.6	50 to 100	100 ± 0	100 to 100	3.36	.01
Minimum PaO_2 mmHg	61.1 ± 17.5	35 to 130	55.7 ± 6.9	43.4 to 66.2	-.94	.35
APACHE II	24.9 ± 6.6	14 to 45	28.3 ± 5.8	21 to 41	1.55	.13
Age (years)	52.4 ± 17.3	21 to 85	65.4 ± 10.2	47 to 79	2.3	.03
Education (years)	13.4 ± 2.1	10 to 18	13.1 ± 2.6	12 to 20	-.36	.72
	n		*n*		χ^2	*p*
Sex (Male/Female)	30/30		5/5		300	.99

APACHE II = Acute Physiology and Chronic Health Evaluation II Score
FiO_2 = Fractional inspired concentration of oxygen
ICU = Intensive care unit.
LOS = Length of stay
MV = Mechanical ventilation
PaO_2 = Arterial oxygen tension

Patients who completed follow-up had higher education levels than patients who were lost to follow-up (Table 3). No other demographic or medical variable differed between patients who completed follow-up compared and those who were lost to follow-up. There was no difference on any demographic or medical variables comparing patients with and without cognitive sequelae (Table 4).

Table 3

Demographic and medical data comparing patients who completed follow-up with patients who were lost to follow-up

Characteristics	Completed Follow-up (n = 53)		Lost to Follow-up (n = 7)		Completed vs. Lost to Follow-up	
	M±SD	Range	*M±SD*	Range	*t*	*p*
Duration MV (days)	9.1 ± 6.7	1.8 to 31.6	8.6 ± 6.7	2.4 to 21.6	.16	.88
Hospital LOS (days)	26.2 ± 17.7	5 to 104	19 ± 7	10 to 28	1.06	.29
ICU LOS (days)	15.8 ± 10.2	4.6 to 51.6	11.7 ± 6.7	5.3 to 24.5	1.04	.30
Maximum FiO_2 (%)	93.6 ± 14.7	50 to 100	94.3 ± 15.1	60 to 100	-.12	.91
Minimum PaO_2 mmHg	60 ± 16.9	35 to 130	69 ± 21.6	43.5 to 109	-1.28	.21
APACHE II	25.4 ± 6.7	16 to 45	21.1 ± 4.5	14 to 28	1.61	.11
Age (years)	52.6 ± 16.2	21 to 84	50.4 ± 26.1	23 to 85	.22	.83
Education (years)	13.6 ± 2.1	10 to 18	11.7 ± .5	11 to 12	5.45	.01
	n		*n*		χ^2	*p*
Sex (Male/Female)	25/28		5/2		140.5	.23

APACHE II = Acute Physiology and Chronic Health Evaluation II Score
FiO_2 = Fractional inspired concentration of oxygen
ICU = Intensive care unit.
LOS = Length of stay
MV = mechanical ventilation
PaO_2 = Arterial oxygen tension

Table 4

Demographic and medical data for patients with long-term cognitive sequelae compared to patients without cognitive sequelae

Characteristics	Total Patients who Completed Follow-up (n = 53)		Cognitive Sequelae (n = 30)		No Cognitive Sequelae (n = 23)		Cognitive Sequelae vs. No Cognitive Sequelae	
	M±SD	Range	*M±SD*	Range	*M±SD*	Range	*t*	*p*
Duration MV (days)	9.1 ± 6.7	1.8 to 31.6	8.7 ± 7.4	1.8 to 31.6	9.6 ± 5.7	2.7 to 24	.49	.63
Hospital LOS (days)	26.2 ± 17.7	5 to 104	29.8 ± 22.1	5 to 104	21.6 ± 7.6	10 to 40	-1.89	.06
ICU LOS (days)	15.8 ± 10.2	4.6 to 51.6	16.5 ± 12.2	4.6 to 51.6	15.1 ± 7.0	5 to 30.2	-.52	.60
Maximum FiO_2 (%)	93.6 ± 14.7	50 to 100	93.7 ± 15.0	50 to 100	93.5 ± 14.7	60 to 100	-.05	.96
Minimum PaO_2 mmHg	60 ± 16.9	35 to 130	62.7 ± 20.0	35 to 130	56.4 ± 11.2	36 to 77.5	-1.36	.18
APACHE II	25.4 ± 6.7	16 to 45	24.7 ± 6.1	16 to 36	26.2 ± 7.5	17 to 45	.82	.42
Age (years)	52.6 ± 16.2	21 to 84	55.3 ± 16.1	24 to 82	49.2 ± 16.0	21 to 84	-1.38	.17
Education (years)	13.6 ± 2.1	10 to 18	13.4 ± 1.9	11 to 18	13.8 ± 2.4	10 to 18	.73	.47
	n		*n*		*n*		χ^2	*p*
Sex (Male/Female)	25/28		13/17		12/11		314.5	.53

APACHE II = Acute Physiology and Chronic Health Evaluation II Score
FiO_2 = Fractional inspired concentration of oxygen
ICU = Intensive care unit.
LOS = Length of stay
MV = mechanical ventilation
PaO_2 = Arterial oxygen tension

Cognitive screening tests. At hospital discharge, 45 (64%) patients had cognitive impairments on the MMSE (score < 27) with a mean score of 24.4 ± 3.65. Thirty-two (45%) patients had cognitive impairments on the Mini-Cog (word recall score = 0 word, or, recall 1 to 2 words with a clock drawing test score ≥ 1) with a mean score of 1.96 ± 1.10 (Figure 2). Twenty-seven (39%) patients were impaired on both the MMSE and Mini-Cog, while only 20 (28%) patients had scores in the normal range on both measures (Figure 2). MMSE scores did not differ between patients who completed 6-month follow-up (24.4 ± 3.8) and patients who died post-hospital discharge (24 ± 3.6; $t = .32$, $p = .75$). Similarly, Mini-Cog scores did not differ between patients who completed follow-up (1.98 ± 1.1) and patients who died post-hospital discharge (1.9 ± 1.10; $t = .21$, $p = .83$).

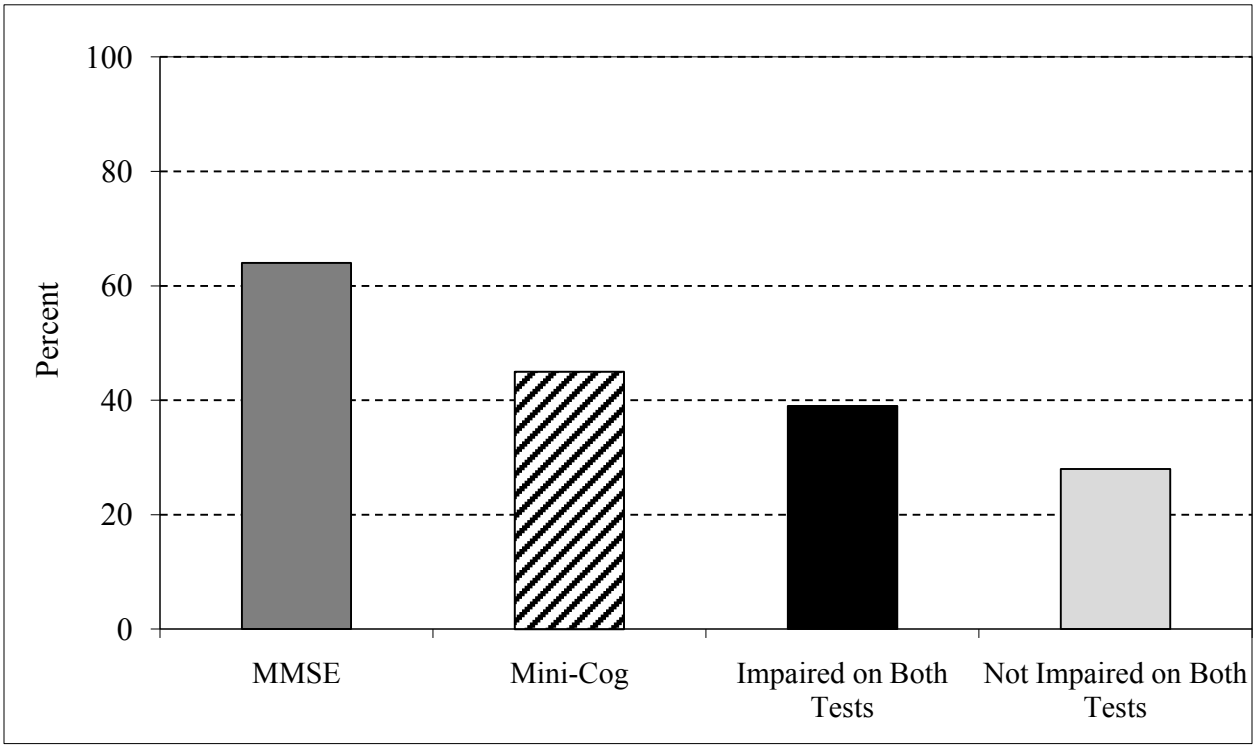

Figure 2. Percent of patients impaired on cognitive screening tests at hospital discharge.

The sensitivity, specificity, and predictive values for the MMSE and Mini-Cog are shown in Figure 3. The MMSE sensitivity was 60% and specificity was 35%, while the Mini-Cog sensitivity was 47% and specificity was 65%. The sensitivity (55%) and specificity (50%) did not improve when both tests were combined. The positive predictive values (the proportion of correctly identified true positives) for the MMSE and Mini-Cog were 55% and 64%, respectively. The negative predictive values (the proportion of correctly identified true negatives) for the MMSE and Mini-Cog were 40% and 48%, respectively.

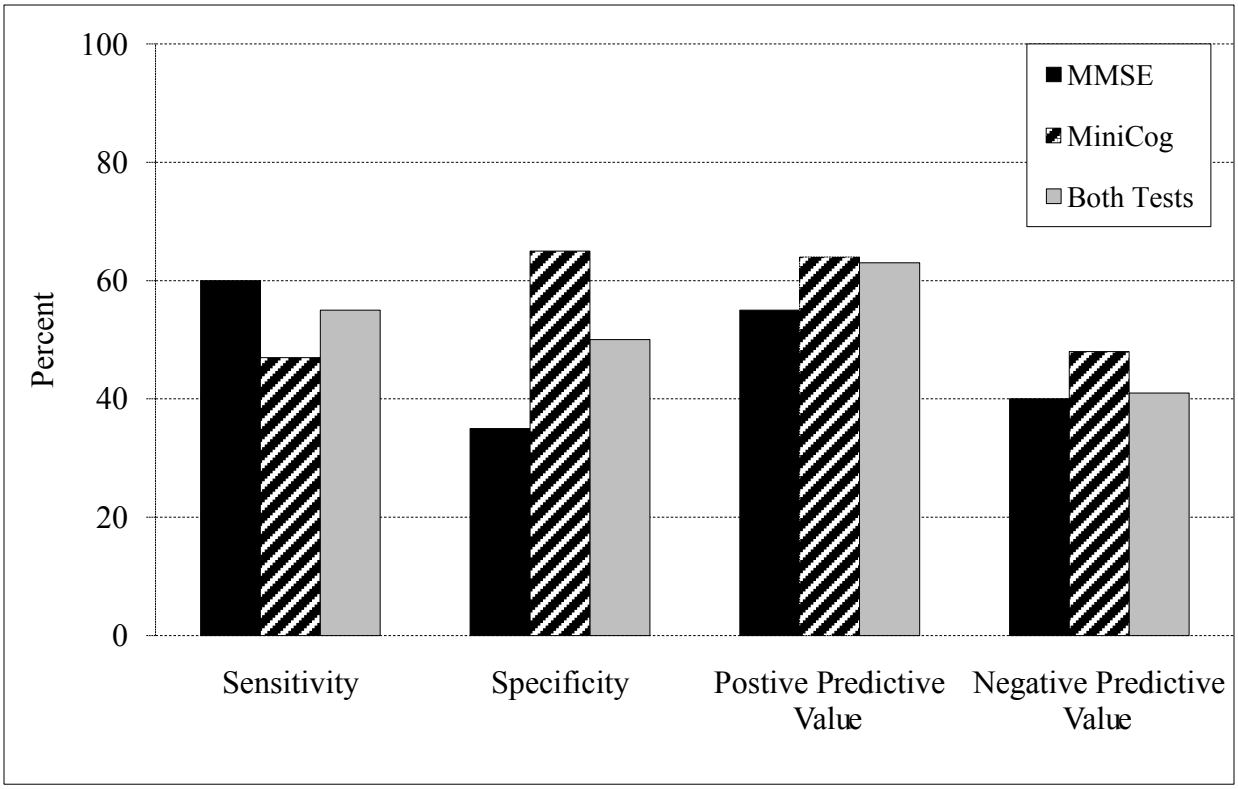

Figure 3. Sensitivity, specificity, and predictive values for the MMSE and Mini-Cog screening tests.

Sensitivity = the proportion of actual positives which were correctly identified as such.
Specificity = the proportion of actual negatives which were correctly identified as such.
Positive Predictive Value = the proportion of patients with cognitive sequelae who were correctly identified.
Negative Predictive Value = the proportion of patients without cognitive sequelae who were correctly identified.

Long-term cognitive outcome. Survivors' estimated IQ scores (100.28 ± 13.56) on the WRAT-3 Reading subtest did not differ from their measured FSIQ (102 ± 12.41) of the WASI (*t* = -.95, df = 49, *p* = .35) at 6 month follow-up, indicating that general intellectual function did not decline from their estimated premorbid levels in our critically ill patients. Cognitive sequelae occurred in 57% (30 of 53) of our patients at 6-month follow-up. Table 5 shows the patient's intellectual and neuropsychological test scores at 6-months. Twenty patients (38%) had impaired memory, 19 (36%) executive functioning, 14 (26%) motor speed, 9 (17%) language, 4 (8%) attention, and 1 (2%) mental processing speed.

Table 5

Six-month neuropsychological data

Domain Assessed	Test	T-scores *Mean ± SD*	Range
Intelligence	Wechsler Abbreviated Scale of Intelligence		
	Verbal IQ	49.7 ± 10.0	32 to 68
	`Performance IQ	52.1 ± 8.7	35 to 79
	Full-Scale IQ	51.3 ± 8.3	34 to 72
Executive functioning	Trail Making Test		
	Part A	43.0 ± 10.6	21 to 75
	Part B	44.5 ± 9.4	26 to 66
	Hayling Sentence Completion Test		
	Response Suppression Score	48.7 ± 14.2	20 to 63
	Overall Scaled Score	45.1 ± 11.8	20 to 63
Motor	Hand Dynamometer Test		
	Dominant Hand	37.1 ± 9.5	10 to 55
	Non-dominant Hand	37.8 ± 8.3	16 to 51
	Grooved Pegboard Test		
	Dominant Hand	37.3 ± 13.2	7 to 67
	Non-dominant Hand	35.8 ± 10.3	13 to 62

Domain Assessed	Test	T-scores *Mean ± SD*	Range
	Finger Tapping Test		
	Dominant Hand	44.8 ± 11.0	18 to 68
	Non-dominant Hand	44.3 ± 11.1	18 to 70
Memory	Wechsler Memory Scale-III		
	Logical Memory I	57.5 ± 10.9	37 to 73
	Logical Memory II	52.8 ± 14.3	30 to 73
	California Verbal Learning Test-II		
	Long-delay Free Recall	48.9 ± 13.6	10 to 75
	ROCFT		
	30-min Delay Recall	41.2 ± 14.9	20 to 80
Language	Controlled Oral Word Association Test (FAS)	41.6 ± 8.9	13 to 67
	Wide-Range Assessment Test-3 Reading Score	50.2 ± 9.0	13 to 61
Attention	Golden Stroop Test		
	Color-Word Trial	46.0 ± 9.0	23 to 71
	Interference	49.0 ± 7.6	30 to 62
Processing speed	Weschler Adult Intelligence Scale-Revised		
	Digit Symbol	55.8 ± 11.1	33 to 80

Psychiatric functioning. Table 6 shows the patients psychiatric functioning at six-month follow-up. Ten (19%) patients had moderate to severe symptoms of depression and 16 (31%) had moderate to severe symptoms of anxiety. On the PDS, the mean number of PTSD symptoms (*re-experiencing, avoidance, and hyperarousal*) our 53 patients endorsed was 6 (± 4.8, range 0 to 17). Twenty five (47%) patients met partial-PTSD criteria (i.e., reached cut-off scores in one or two of the three basic PTSD symptoms: *re-experiencing, avoidance, and hyperarousal*). Thirty-seven (70%) of our 53 patients identified *life-threatening illness* (i.e., critical illness) as their significant primary traumatic event, and 9 (17%) of these patients met full PTSD criteria. Of 53 patients, 3 (6%) identified other primary traumatic events (e.g., combat, HIV positive, and

accident) with critical illness as their secondary traumatic event, but these 3 patients did not meet full criteria for PTSD. In addition, several patients reported experiencing other traumatic events, including motor-vehicle accidents (n = 8), death of a family member (n = 1), nonsexual assault (n = 1), combat (n = 1), and imprisonment (n = 1); however, none of these patients met full PTSD criteria. Therefore, of 53 patients, 9 (17%) met full PTSD criteria, all of whom identified critical illness as their significant primary traumatic events.

Table 6

Psychiatric functioning at 6-month follow-up

Psychological Domain	Questionnaire	*Mean ± SD* or *n* (%)	Range	% Impaired or Severity (*n*)
Depression	Beck Depression Inventory	11.7 ± 9.0	0 to 36	Mild: 13 (7) Moderate: 11 (6) Severe: 8 (4)
Anxiety	Beck Anxiety Inventory	11.2 ± 9.5	0 to 40	Mild: 25 (13) Moderate: 21 (11) Severe: 6 (3)
General Distress	Outcome Questionnaire-45.2			
	Total Score	45.8 ± 24.4	9 to 99	21 (11)
	Symptom Distress	28.4 ± 16.0	3 to 69	34 (18)
	Interpersonal Relations	8.4 ± 5.5	0 to 21	11 (6)
	Social Role	9.0 ± 4.4	1 to 18	21 (11)
Posttraumatic Stress Disorder	Posttraumatic Stress Diagnostic Scale			
	Symptom Severity Score	9.8 ± 9.3	0 to 41	Mild: 47 (25) Moderate: 25 (13) Moderate to Severe: 6 (3) Severe: 4 (2)
	Met PTSD Criteria (%)	9 (17)		

PTSD = Posttraumatic stress disorder

The results of the OQ-45.2 are shown in Table 6. Of the 53 patients, 18 (34%) had elevated scores on Symptom Distress, 6 (11%) on Interpersonal Relationship difficulties, 11 (21%) on Social Role Performance difficulties, and 11 (21%) on Total Score, indicating general psychological distress (Table 6). However, the mean OQ-45.2 scores at 6-months were not significantly different from data from normal community dwelling adults for the Total Score (t = .06, p = .95), Symptom Distress (t = 1.33, p = .19), and Social Role (t = -1.18, p = .25) (Figure 4). The Interpersonal Relations scores in survivors of critical illness at 6-months were significantly lower than those in normal population (t = -2.40, p = .02), indicating that patients had positive interpersonal relations (Figure 4).

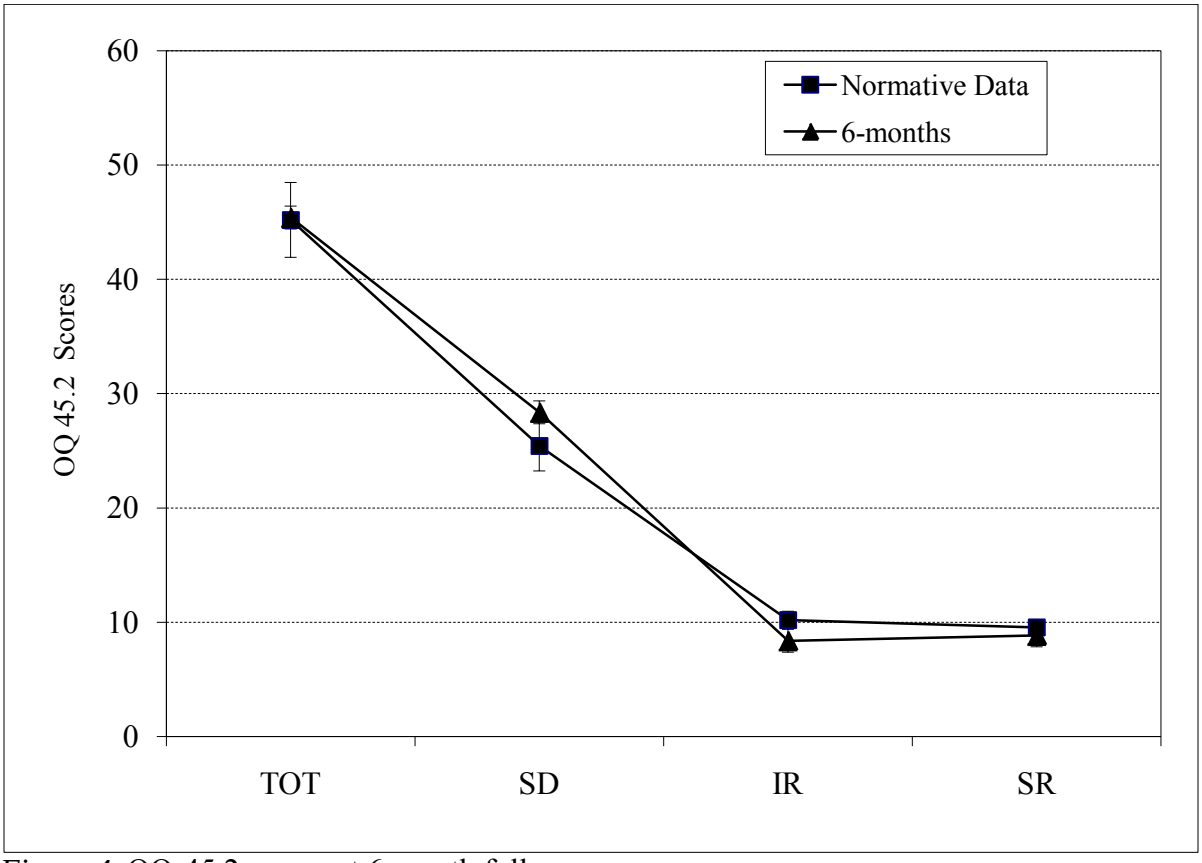

Figure 4. OQ-45.2 scores at 6-month follow-up.

IR = Interpersonal Relations
SD = Symptom Distress
SR = Social Role
TOT = Total Score

Everyday functioning. Table 7 shows the patient scores on measures of everyday functioning at 6-month follow-up. The mean Lawton IADL score for our patients was 13.7 ± 2.8 which is below the impairment cut-off score of ≤ 15. Notably, 32 (60%) patients reported difficulty on tasks of everyday functioning. The mean FAQ score was 5.8 ± 6.5 with 10 (19%) of scores fell below the impairment cut-point of > 8. The areas of greatest difficulty in everyday functioning on both the Lawton IADL and FAQ were medication management, mobility, home management, shopping, and financial management.

Table 7

Everyday functioning at 6-months in survivors of critical illness

Measures	*Mean ± SD*	Range
Lawton IADL raw scores	13.7 ± 2.8	5 to 16
Functional Activities Questionnaires raw scores	5.8 ± 6.5	0 to 28
Independent Living Scale		
Full-Scale Standard Score	102.5 ± 12^{+}	55 to 117
Problem Solving	52.2 ± 9.0*	20 to 64
Performance/Information	50.7 ± 8.2*	27 to 61
Memory/Orientation	54.5 ± 7.1*	31 to 60
Managing Money	49.9 ± 8.7*	24 to 61
Managing Home and Transportation	51.7 ± 6.1*	29 to 59
Health and Safety	52.3 ± 8.9*	26 to 63
Social Adjustment	46.9 ± 11.4*	22 to 59

$^{+}$ = Standard score with a *mean* of 100 and *SD* of 15.
* = T-scores with a *mean* of 50 and *SD* of 10.

Critically ill patients had moderate to severe deficits in everyday functioning on the ILS, indicating poor everyday functioning (Figure 5). Of the 53 patients, 10 (20%) had significant difficulty with Memory/Orientation, 20 (40%) Managing Money, 9 (18%) Managing Home and

Transportation, 15 (29%) Health and Safety, 27 (52%) Social Adjustment, 17 (34%) Problem Solving, and 18 (36%) had impairments in Performance/Information (Figure 5).

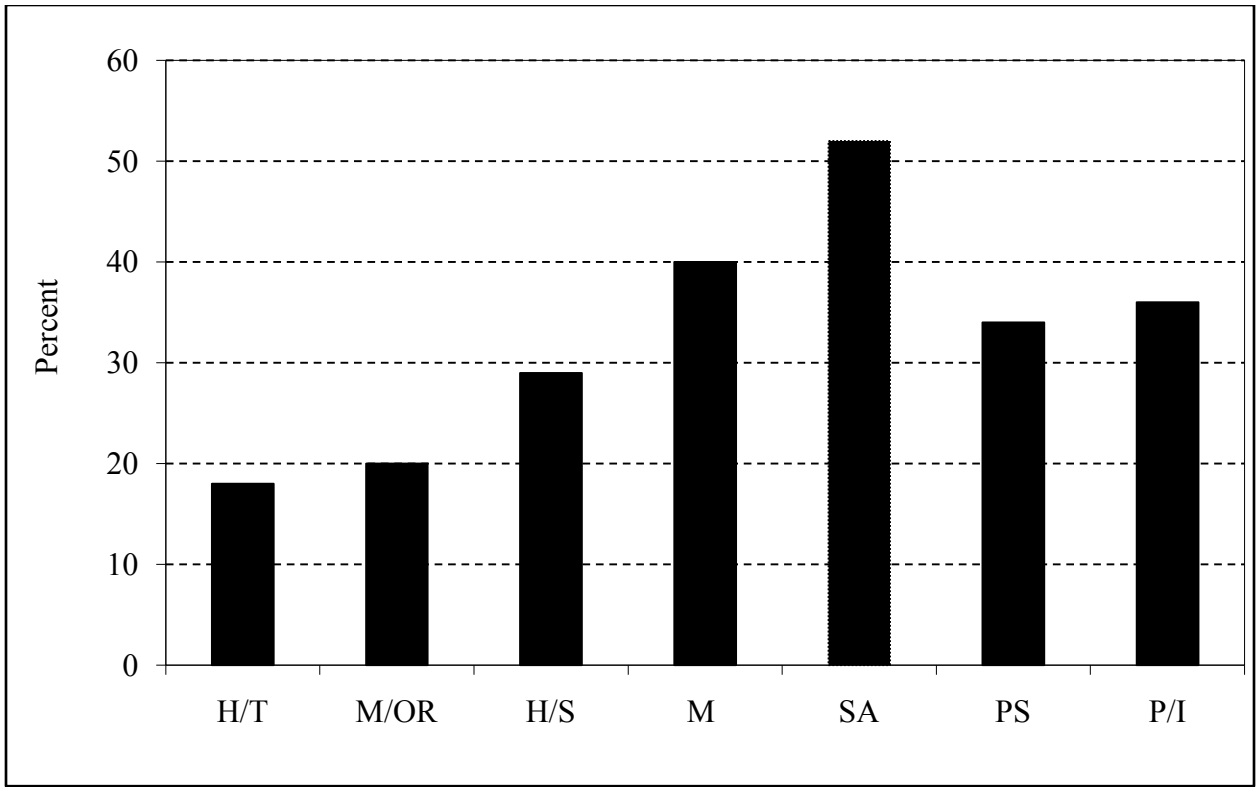

Figure 5. Percent critically ill patients who had moderate to severe deficits in everyday functioning on the ILS.

Subscales:
H/T: Managing Home and Transportation
M/OR: Memory/Orientation
H/S: Health and Safety
M: Managing Money
SA: Social Adjustment
Summary scales:
P/I: Performance/Information
PS: Problem Solving

Quality of life. The SF-36 scores were significantly lower than normal population data at 6-months for Physical Functioning (t = -9.01, p < .001), Social Functioning (t = -6.24, p < .001), Role Physical (t = -8.37, p < .001), Role Emotion (t = -2.99, p = .004), Bodily Pain (t = -4.35, p <

.001), Vitality (t = -4.96, p < .001), and General Health (t = -6.96, p < .001) (Figure 6). However, there was no difference in Mental Health scores for survivors of critical illness compared to normal population data (t = .20, p = .84) (Figure 6).

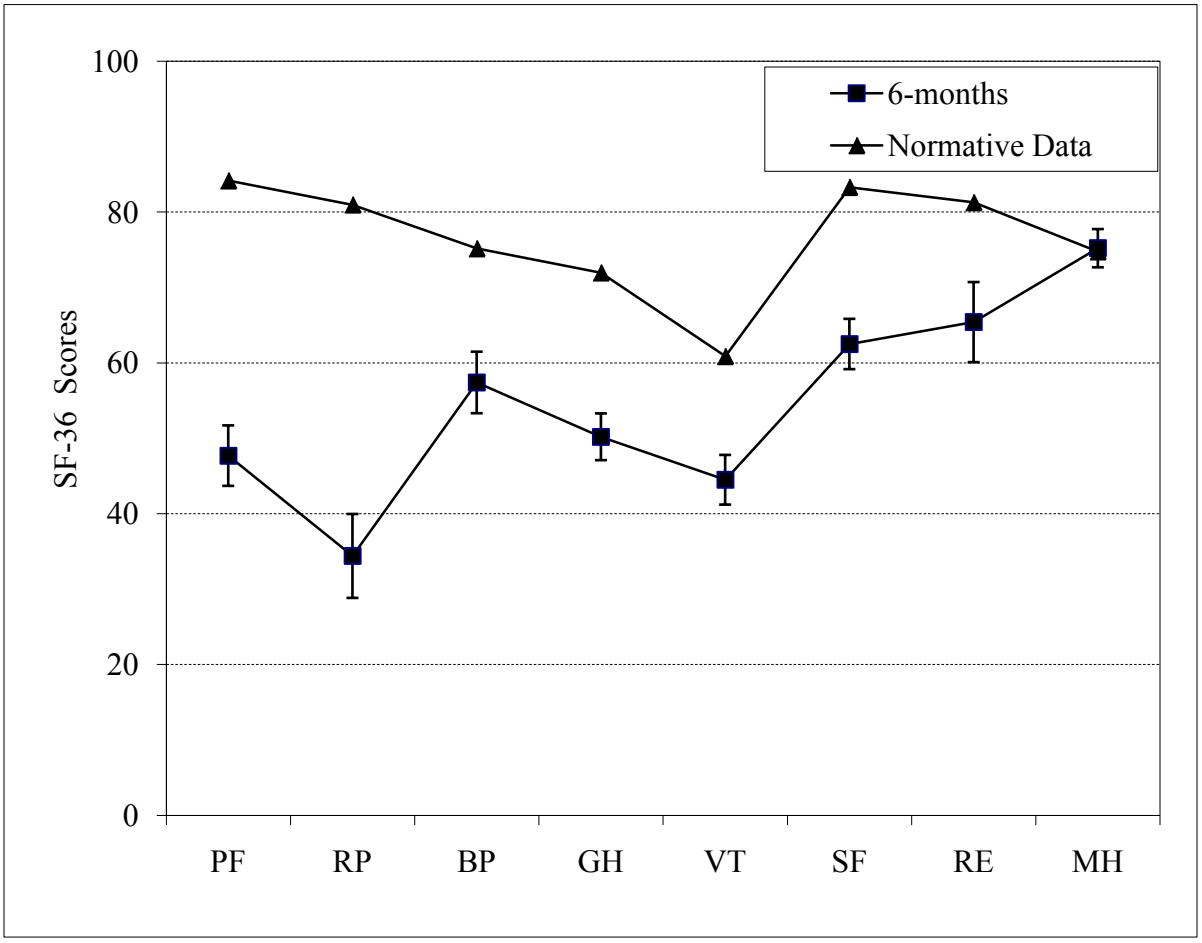

Figure 6. SF-36 scores at 6-month follow-up.

Data are presented as mean ± standard error and compared to normative data (Ware, 1993).
BP = Bodily Pain
GH = General Health
MH = Mental Health
PF = Physical Functioning
RE = Role Emotional
RP = Role Physical
SF = Social Functioning
VT = Vitality

Hypothesis 1a

Neither the MMSE scores < 24 (OR = 1.41, Wald χ^2 = 2.90, p = .24) nor Mini-Cog cutoff scores (OR = .84, Wald χ^2 = .45, p = .36) predicted cognitive sequelae at six-months. The analyses were repeated using the MMSE cutoff scores of < 27 (OR = 1.19, Wald χ^2 = 1.03, p = .13) and the results did not change. Further, neither the MMSE continuous scores (OR = 1.19, Wald χ^2 = 2.35, p = .13) nor the Mini-Cog continuous scores (OR = .50, Wald χ^2 = 2.30, p = .13) predicted cognitive sequelae at six-months.

Hypothesis 1b

The MMSE scores < 24 and Mini-Cog cutoff scores did not predict impairments in executive functioning (MMSE: OR = 1.41, Wald χ^2 = .133, p = .72; Mini-Cog: OR = .59, Wald χ^2 = .37, p = .54), memory (MMSE: OR = 1.27, Wald χ^2 = .06, p = .81; Mini-Cog: OR = .20, Wald χ^2 = 2.36, p = .13), mental processing speed (MMSE: OR = .01, Wald χ^2 = 1.40, p = .24; Mini-Cog: OR = .29, Wald χ^2 = 1.10, p = .29), language (MMSE: OR = 7.13, Wald χ^2 = 1.91, p = .17; Mini-Cog: OR = .12, Wald χ^2 = 2.55, p = .11), or attention (MMSE: OR = .01, Wald χ^2 = .01, p = .99; Mini-Cog: OR = .01, Wald χ^2 = .01, p = .99). The analyses were repeated using the MMSE cutoff score of < 27 and the results did not change.

The MMSE and Mini-Cog scores did not predict any cognitive test scores: CVLT-II Long-Delay Free Recall, WMS-III Logical Memory II, ROCFT Long Delay, HSCT Box C, Trail-Making Test Part B, WAIS-R Digit Symbol, COWA, and SCWT Interference scores (Table 8).

Table 8

Prediction of individual cognitive test scores using the MMSE and Mini-Cog continuous scores

Predictors	*B*	*β*	*t*	*p*	Bivariate *r*	Partial *r*
CVLT-II Long-Delay Free Recall						
MMSE continuous scores	-.46	-.14	-.83	.41	.02	-.12
Mini-Cog continuous scores	2.10	.19	1.11	.27	.12	.15
Model summary: R^2 = .13, R^2_{adj} = .08, $F(3, 49)$ = 2.31, p = .53						
WMS-III Logical Memory II						
MMSE continuous scores	-.24	-.09	-.55	.58	.09	-.08
Mini-Cog continuous scores	2.04	.22	1.34	.19	.24	.19
Model summary: R^2 = .18, R^2_{adj} = .13, $F(3, 49)$ = 3.39, p = .40						
ROCFT Long Delay						
MMSE continuous scores	-.18	-.05	-.28	.78	.16	-.04
Mini-Cog continuous scores	2.15	.24	1.49	.14	.22	.22
Model summary: R^2 = .19, R^2_{adj} = .14, $F(3, 49)$ = 3.52, p = .27						
HSCT Box C						
MMSE continuous scores	-.30	-.09	-.54	.59	.05	-.08
Mini-Cog continuous scores	-.02	0	-.01	.99	.11	-.01
Model summary: R^2 = .22, R^2_{adj} = .17, $F(3, 49)$ = 4.36, p = .81						
Trail-Making Test Part B						
MMSE continuous scores	.30	.12	.73	.47	.20	.11
Mini-Cog continuous scores	.77	.09	.54	.59	.18	.08
Model summary: R^2 = .12, R^2_{adj} = .06, $F(3, 49)$ = 1.99, p = .40						
WAIS-R Digit Symbol						
MMSE continuous scores	-.11	-.04	-.25	.81	-.14	-.04
Mini-Cog continuous scores	.56	.06	.35	.73	-.13	.05
Model summary: R^2 = .23, R^2_{adj} = .18, $F(3, 49)$ = 4.49, p = .94						
COWA						
MMSE continuous scores	.16	.08	.44	.66	.06	.07
Mini-Cog continuous scores	-.28	-.04	-.22	.83	.01	-.03
Model summary: R^2 = .01, R^2_{adj} = -.04, $F(3, 49)$ = .10, p = .91						

Predictors	*B*	*β*	*t*	*p*	Bivariate *r*	Partial *r*
SCWT Interference						
MMSE continuous scores	.42	.22	1.29	.20	.29	.19
Mini-Cog continuous scores	-.75	-.11	-.66	.51	.16	-.10
Model summary: R^2 = .26, R^2_{adj} = .21, $F(3, 49) = 5.05$, $p = .44$						

CVLT-II = California Verbal Learning Test-II
WMS-III = Wechsler Memory Scale-III,
ROCFT = Rey Osterrieth Complex Figure Test
HSCT = Hayling Sentence Completion Test
COWA = Controlled Oral Word Association
WAIS-R = Wechsler Adult Intelligence Scale-Revised
SCWT = Stroop Color-Word Test

Hypothesis 2a

The MMSE cutoff scores < 24 (*scores below cutoff*) and Mini-Cog cutoff scores (*scores below cutoff*) did not predict the Lawton IADL, FAQ, and ILS Full Scale scores (Table 9). The analyses were repeated using the MMSE cutoff scores of < 27 and the results did not change.

Table 9

*Prediction of everyday functioning (the Lawton IADL, Functional Activities Questionnaire, and Independent Living Scale Full Scale scores) using MMSE cutoff scores < 24 and Mini-Cog scores (*below cutoff*)*

Predictors	*B*	*β*	*t*	*p*	Bivariate *r*	Partial *r*
Lawton IADL						
MMSE < 24	1.02	.18	1.07	.29	-.03	.16
Mini-Cog (*below cutoff)*	-1.81	-.32	-1.93	.06	-.26	-.27
Model summary: R^2 = .17, R^2_{adj} = .12, $F(3, 49) = 3.20$, $p = .17$						
Functional Activities Questionnaire						
MMSE < 24	-1.25	-.09	-.57	.57	.05	-.08
Mini-Cog (*below cutoff)*	1.94	.15	.91	.37	.12	.13
Model summary: R^2 = .21, R^2_{adj} = .16, $F(3, 49) = 4.07$, $p = .66$						
Independent Living Scale (Full Scale)						
MMSE < 24	-7.15	-.21	-1.95	.06	-.42	-.28
Mini-Cog (*below cutoff)*	-2.30	-.09	-.63	.53	-.33	-.10
Model summary: R^2 = .37, R^2_{adj} = .32, $F(3, 49) = 4.36$, $p = .06$						

Hypothesis 2b

Long-term cognitive sequelae did not predict the Lawton IADL, FAQ, or ILS Full Scale scores (Table 10).

Table 10

*Prediction of everyday functioning (the Lawton IADL, Functional Activities Questionnaire, and Independent Living Scale Full Scale scores) with cognitive sequelae (*presence or absence*)*

Predictors	*B*	*β*	*t*	*p*	Bivariate *r*	Partial *r*
Lawton IADL	-.66	-.12	-.86	.40	-.16	-.12
Model summary: $R^2 = .12$, $R^2_{adj} = .08$, $F(2, 49) = 3.18$, $p = .40$						
Functional Activities Questionnaire	2.74	.21	1.63	.11	.27	.23
Model summary: $R^2 = .24$, $R^2_{adj} = .21$, $F(2, 49) = 7.34$, $p = .11$						
Independent Living Scale (Full Scale)	-3.58	-.15	-1.13	.27	-.28	-.17
Model summary: $R^2 = .28$, $R^2_{adj} = .23$, $F(2, 49) = 5.88$, $p = .27$						

Hypothesis 2c

I**LS Memory/Orientation.** Impaired attention significantly predicted poor Memory/Orientation scores (Table 11). This model accounted for 52% of the variability in Memory/Orientation. Memory, mental processing speed, language, and executive function did not predict Memory/Orientation scores.

ILS Managing Home/Transportation. Impaired attention, mental processing speed, and memory significantly predicted poor Managing Home/Transportation scores (Table 11). This model accounted for 41% of the variability in Managing Home/Transportation. Language and executive function did not predict Managing Home/Transportation scores.

ILS Health and Safety. Impaired attention significantly predicted poor Health and Safety scores (Table 11). This model accounted for 35% of the variability in Health and Safety. Memory, mental processing speed, language, and executive function did not predict Health and Safety scores.

ILS Social Adjustment. Impaired attention significantly predicted poor Social Adjustment scores (Table 11). This model accounted for 50% of the variability in Social Adjustment. Memory, mental processing speed, language, and executive function did not predict Social Adjustment scores.

ILS Managing Money. Memory, mental processing speed, attention, language, and executive function did not predict Managing Money scores.

Table 11

*Prediction of ILS subscale scores by cognitive domain (*normal or impaired*)*

Predictors	*B*	*β*	*t*	*p*	Bivariate *r*	Partial *r*
Memory/Orientation						
Attention	-14.01	-.57	-3.93	.001	-.68	-.53
Model summary: $R^2 = .52$, $R^2_{adj} = .43$, $F(7, 46) = 5.96$, $p = .001$						
Managing Home/Transportation						
Attention	-6.27	-.29	-1.99	.04	-.35	-.30
Mental Processing Speed	-5.66	-.28	-2.22	.03	-.27	-.33
Memory	-3.93	-.31	-2.22	.03	-.47	-.33
Model summary: $R^2 = .41$, $R^2_{adj} = .32$, $F(6, 56) = 4.58$, $p = .001$						
Health and Safety						
Attention	-16.39	-.54	-3.68	.001	-.56	-.50
Model summary: $R^2 = .35$, $R^2_{adj} = .27$, $F(5, 47) = 4.36$, $p = .003$						
Social Adjustment						
Attention	-14.86	-.38	-2.88	.006	-.45	-.41
Model summary: $R^2 = .50$, $R^2_{adj} = .43$, $F(6, 47) = 6.69$, $p = .001$						

Impairments in any cognitive test scores (CVLT-II Long-Delay Free Recall, WMS-III Logical Memory II, ROCFT Long Delay, HSCT Box C, Trail-Making Test Part B, COWA, WAIS-R Digit Symbol, and Stroop Interference scores) did not predict ILS Memory/Orientation, Managing Money, Managing Home and Transportation, Health and Safety, and Social Adjustment (Table 12).

Table 12

Prediction of ILS subscale scores by individual cognitive test scores

Predictors	*B*	*β*	*t*	*p*	Bivariate *r*	Partial *r*
Memory/Orientation						
CVLT-II Long-Delay Free Recall	-.03	-.05	-.27	.79	.11	-.05
WMS-III Logical Memory II	.13	~.21	1.06	.29	.22	.18
ROCFT Long Delay	.06	.12	.71	.49	.22	.12
HSCT Box C	.02	.03	.20	.85	.30	.03
Trail-Making Test Part B	-.06	-.07	-.48	.63	.12	-.08
COWA	-.19	-.22	-1.44	.16	-.08	-.24
WAIS-R Digit Symbol	.08	.13	.71	.48	-.03	.12
SCWT Interference	.18	.20	1.19	.24	.42	.20
Model summary: $R^2 = .38$, $R^2_{adj} = .20$, $F(10, 42) = 2.13$, $p = .54$						
Managing Money						
CVLT-II Long-Delay Free Recall	-.19	-.28	-1.6	.12	.12	-.26
WMS-III Logical Memory II	.32	.40	2.07	.06	.37	.33
ROCFT Long Delay	.13	.22	1.26	.22	.36	.21
HSCT Box C	.01	.01	.07	.95	.15	.01
Trail-Making Test Part B	.20	.20	1.40	.17	.18	.23
COWA	-.11	-.10	-.66	.51	.03	-.11
WAIS-R Digit Symbol	-.12	-.15	-.89	.38	.06	-.15
SCWT Interference	.19	.17	1.08	.29	.25	.18
Model summary: $R^2 = .35$, $R^2_{adj} = .19$, $F(10, 42) = 2.16$, $p = .12$						

Predictors	*B*	*β*	*t*	*p*	Bivariate *r*	Partial *r*
Managing Home/Transportation	-.12	-.24	-1.50	.14	.08	-.19
CVLT-II Long-Delay Free Recall	.19	.32	1.71	.10	.24	.211
WMS-III Logical Memory II	.07	.16	.89	.38	.28	.11
ROCFT Long Delay	.09	.19	1.32	.19	.16	.16
HSCT Box C	.07	.16	.89	.38	.28	.11
Trail-Making Test Part B	-.02	-.02	-.15	.88	.03	-.02
COWA	-.08	-.14	-.87	.39	.12	-.11
WAIS-R Digit Symbol	-.19	.23	-1.57	.13	-.01	-.19
SCWT Interference						
Model summary: R^2 = .44, R^2_{adj} = .31, $F(10, 42) = 2.26$, $p = .06$						
Health and Safety						
CVLT-II Long-Delay Free Recall	.11	.17	.96	.34	.31	.16
WMS-III Logical Memory II	.17	.21	1.09	.29	.28	.18
ROCFT Long Delay	.60	.10	.56	.58	.27	.09
HSCT Box C	.1	.16	1.02	.32	.32	.17
Trail-Making Test Part B	.19	.21	1.42	.16	.25	.23
COWA	-.08	-.07	-.46	.65	-.01	-.08
WAIS-R Digit Symbol	-.16	-.20	-1.19	.24	-.08	-.19
SCWT Interference	.18	.16	.99	.33	.29	.16
Model summary: R^2 = .31, R^2_{adj} = .16, $F(8, 44) = 2.04$, $p = .07$						
Social Adjustment						
CVLT-II Long-Delay Free Recall	.10	.12	.83	.41	.37	.14
WMS-III Logical Memory II	.19	.20	1.15	.26	.31	.19
ROCFT Long Delay	-.01	-.01	-.04	.97	.34	-.01
HSCT Box C	.21	.15	1.13	.27	.45	.34
Trail-Making Test Part B	-.01	-.01	-.06	.95	.15	-.01
COWA	.50	.04	.29	.78	.17	.05
WAIS-R Digit Symbol	-.01	-.01	-.02	.99	.06	-.01
SCWT Interference	.21	.15	1.13	.27	.29	.19
Model summary: R^2 = .53, R^2_{adj} = .41, $F(9, 43) = 2.14$, $p = .08$						

CVLT-II = California Verbal Learning Test-II
WMS-III = Wechsler Memory Scale-III,
ROCFT = Rey Osterrieth Complex Figure Test
HSCT = Hayling Sentence Completion Test
COWA = Controlled Oral Word Association
WAIS-R = Wechsler Adult Intelligence Scale-Revised
SCWT = Stroop Color-Word Test

Hypothesis 3

Long-term cognitive sequelae significantly predicted Role-Physical scores (Table 13). This model accounted for 20% variability in Role-Physical scores. Long-term cognitive sequelae did not predict Physical Functioning, Bodily Pain, General Health, Vitality, Social Functioning, Role-Emotional, or Mental Health scores (Table 13).

Table 13

*Prediction of quality of life with cognitive sequelae (*presence or absence*)*

SF-36	*B*	β	*t*	*p*	Bivariate *r*	Partial *r*
General Health	-1.47	-.03	-.27	.79	-.15	-.04
Model summary: $R^2 = .36$, $R^2_{adj} = .31$, $F(3, 50) = 3.18$, $p = .79$						
Physical Functioning	-8.72	-.15	-1.04	.30	-.15	-.15
Model summary: $R^2 = .02$, $R^2_{adj} = .01$, $F(1, 52) = 1.09$, $p = .30$						
Role-Physical	-23.55	-.29	-2.19	.03	-.32	-.30
Model summary: $R^2 = .20$, $R^2_{adj} = .16$, $F(2, 51) = 5.75$, $p = .03$						
Role-Emotional	-4.41	-.06	-.47	.64	-.16	-.07
Model summary: $R^2 = .33$, $R^2_{adj} = .29$, $F(3, 50) = 7.70$, $p = .64$						
Social Functioning	-3.78	-.08	-.62	.54	-.1	-.09
Model summary: $R^2 = .31$, $R^2_{adj} = .26$, $F(3, 50) = 6.78$, $p = .54$						
Bodily Pain	-3.45	-.06	-.48	.63	-.18	-.07
Model summary: $R^2 = .33$, $R^2_{adj} = .29$, $F(3, 53) = 7.50$, $p = .63$						
Vitality	-6.10	-.13	-.99	.33	-.18	-.14
Model summary: $R^2 = .23$, $R^2_{adj} = .20$, $F(2, 51) = 7.12$, $p = .33$						
Mental Health	-4.46	-.13	-1.31	.20	-.24	-.19
Model summary: $R^2 = .59$, $R^2_{adj} = .56$, $F(3, 50) = 21.83$, $p = .20$						

SF-36 = Medical Outcome Study 36-Item Short Form Health Survey

Discussion

Our critically patients had a high rate of cognitive impairments on the MMSE (64%) and on the Mini-Cog (45%) at hospital discharge. Our patients' mean MMSE score of 24.4 at hospital discharge is similar to the mean MMSE score in mechanically ventilated medical ICU patients who completed follow-up (24.4), but higher than the patients who did not complete follow-up (20.4) (Jackson et al., 2003). The rate of impairments on the MMSE of 67% (64%)??? in our patients is higher than in similar critically ill patients (27%) who were assessed 3 to 7 days post-ICU discharge (van der Schaaf et al., 2008). The between-study difference are likely due to the fact that the patients in the van der Schaaf and colleagues' study were less ill than our patients (APACHE II score 16 *vs*. 26) and the MMSE was administered several days later than in our patients, which may have allowed for additional time for cognitive performance to improve (van der Schaaf et al., 2008). The mean MMSE score for our patients was lower than that of an ARDS patient whose MMSE score at hospital discharge was 30, notwithstanding this patient had significant cognitive impairments one and 3.5 years after ICU discharge (Jackson et al., 2009). The rate of cognitive impairments at hospital discharge in ARDS patients was significantly higher (73%) (Hopkins, Weaver et al., 2005) than in our patients assessed using cognitive screening tests (64% on the MMSE and 45% on the Mini-Cog). The reason for the higher rate of cognitive impairments at hospital discharge in the Hopkins and colleagues' (2005) study is likely due to the differences in how cognitive function was assessed, that is, a comprehensive neuropsychological test battery instead of cognitive screening tests.

Our critically ill patients had a high rate (57%) of long-term cognitive sequelae (6 months). These findings are striking because the survivors' premorbid IQ was within normal limits (mean WRAT Reading subtest score 100), they were middle aged (mean age 54 years),

well educated (mean education 13.3 years). Further, only 1 patient had undetected pre-existing cognitive impairments on the MBDRS, suggesting the preexisting cognitive impairments do not explain long-term cognitive impairments in our patients. Among mechanically ventilated general medical ICU survivors, approximately a third or more demonstrate moderate to severe cognitive impairment 6 months after discharge (Jackson et al., 2003). Among medical and surgical ICU cohorts, including those with specific conditions such as sepsis and ARDS, rates of impairment (25% to 78%) are extremely variable in part due to methods used to assess cognitive function and timing of the assessments after ICU discharge (Hopkins & Brett, 2005; Hopkins & Jackson, 2006). In specific populations, notably very ill patients with ARDS, the prevalence of cognitive sequelae is particularly high and persistent, with 46% of patients at 1 year (Hopkins et al., 1999) and 25% of patients at 6 years having cognitive impairments (Rothenhausler et al., 2001).

Cognitive impairments in our critically ill patients occur in multiple cognitive domains with impaired memory being the most frequently observed deficit (38%), followed by executive function (36%), motor speed (26%), language (17%), attention (8%), and mental processing speed (2%). The impaired cognitive domains in our critically ill patients are similar to those reported in other ICU survivors (Hopkins & Jackson, 2009) and following carbon monoxide poisoning (Hopkins & Woon, 2006; Weaver et al., 2002). Although the cognitive domains that are impaired include many aspects of cognition, the predominant deficits occur in memory and executive functioning which is mediated by the frontal and temporal lobes. The frontal and temporal lobes have known susceptibility to hypoxemia, which is implicated in the pathophysiology of ICU-related cognitive impairments (Hopkins et al., 1999). A recent study reported that a critically ill patient with severe hypoxemia had generalized brain atrophy,

including frontal and temporal lobe atrophy on quantitative brain MRI along with concomitant impairments in memory and executive functioning (Jackson et al., 2009).

Prediction of Long-term Cognitive Sequelae

To our knowledge, this is the first study that examined whether the two well-known cognitive screening tools, the MMSE or Mini-Cog, predict long-term cognitive sequelae in survivors of critical illness. Neither the MMSE (cutoff scores < 24, cutoff scores < 27, and continuous scores) nor the Mini-Cog (continuous scores and scores below cutoff) predicted cognitive sequelae at 6 months. In other words, the MMSE and Mini-Cog did not differentiate critically ill patients with cognitive sequelae from patients without cognitive sequelae. Furthermore, the MMSE and Mini-Cog did not predict impairments in any cognitive domain (e.g., memory, executive function, etc.) In spite of the usefulness of the MMSE and Mini-Cog in diagnostic screening in other populations (Boustani et al., 2003; Brodaty et al., 2006), the cognitive screening tests did not discriminate between patients with and without cognitive sequelae or impairments in any cognitive domain in our patients. Our findings generally agree with Burker and colleagues' (1995) study in which the MMSE cutoff score of 23 at hospital discharge did not predict overall cognitive impairment in patients 6-week post-cardiopulmonary surgery. By contrast, Burker and colleagues found the education-corrected MMSE cutoff scores (19, 23, 27, and 29) predicted cognitive impairments at 6-week post-cardiopulmonary surgery, despite they accounted for only a small variance. Although we did not use the education-corrected MMSE cutoff scores for each patient, it should be noted that we used the MMSE cutoff scores of < 24 and < 27, as well as continuous scores, which did not predict cognitive sequelae in critically ill patients. Further, we controlled for education level, which did not reach significance

in our regression models. Thus, using education-corrected MMSE scores is unlikely to change our null findings.

Reasons why the MMSE and Mini-Cog did not predict cognitive sequelae are unclear, but may be due to several factors. First, cognitive impairments are highly prevalent in our patients as almost 65% of critically ill survivors' had cognitive impairments on the MMSE or Mini-Cog at hospital discharge and 57% had cognitive sequelae at 6 months, resulting in limited variability of the data. Further, we did not have a normal control group in our study, which likely would increase the range of scores. Second, only 8% of critically ill survivors' cognitive functioning improved to their pre-ICU baseline levels (i.e., normal range of cognitive functioning) by 6 month follow-up (Hopkins, Jackson et al., 2005). The rate of improvement in cognitive functioning over time in our patients is lower than the rate observed in previous studies (57% impaired in the current study and 45% in the Hopkins and colleagues' study (2005), which may be due to the earlier time post-hospital discharge during which cognitive function was assessed (6 months vs. 1 and 2 years). Since cognitive sequelae may continue to improve up to 12 or more months post-ICU discharge, the lower rate of cognitive sequelae in the Hopkins and colleagues' (2005) study may be due to additional recovery in cognitive function from 6 to 12 months.

A third possible reason that the MMSE and Mini-Cog did not predict long-term cognitive sequelae is that the MMSE and Mini-Cog were not designed for use in critically ill population, but rather to identify dementia in elderly populations. The diagnostic accuracy in identifying cases of cognitive sequelae in our patients was poor with a 35% specificity for the MMSE, which is substantially below the generally accepted cutoff of 80% or higher in other populations (Elena & Rebecca, 1994). Although the Mini-Cog has greater sensitivity and specificity compared with

the MMSE in studies of dementia (Borson et al., 2000; Borson et al., 2005), this finding was not observed in our critically ill patients. Further, the combined use of both screening tests did not improve overall diagnostic accuracy (sensitivity 55%; specificity 50%). This finding is somewhat surprising because studies in elderly or dementia populations (Bottino et al., 2009; Bustamante et al., 2003; Xu, Meyer, Thornby, Chowdhury, & Quach, 2002) have found the use of multiple screening tests improves overall diagnostic accuracy. The lack of sensitivity and specificity of the MMSE and Mini-Cog in our critically ill patients is likely due to the fact that these tests have poor psychometric properties (M. Folstein, 1998; Ihl, Frolich, Dierks, Martin, & Maurer, 1992; Nieuwenhuis-Mark, in press; Ravaglia et al., 2005) , were developed to detect dementia in elderly populations (Borson et al., 2000; M. F. Folstein et al., 1975), and not for use in younger medical populations. Therefore, the MMSE and Mini-Cog may not be suitable for predicting long-term cognitive impairments following critical illness and ICU treatments; however our findings need to be replicated.

Everyday Functioning

The patients' mean Lawton IADL score was 13.7 with 60% of patients reporting significant difficulty in everyday functioning at 6-months, including deficits in mobility and managing home, medication, and finances. In comparison, the patients' mean FAQ score was 5.8 with 19% patients scores indicate problems in everyday functioning, including shopping and managing transportation and finances. The prevalence of poor everyday functioning in our critically ill patients is similar to trauma ICU survivors in which 22% had difficulty managing financial or business affairs, as well as traveling or making travel arrangements (mean FAQ score of 4.9) (Jackson et al., 2007). The FAQ identified fewer patients with deficits in everyday functioning compared to the Lawton IADL (19% *vs*. 60%). This is likely due to the fact that the

FAQ is more reliable and valid than the Lawton IADL (Pfeffer et al., 1982; Senanarong et al., 2004). Further, the FAQ assessed IADLs primarily in terms of social function, whereas the Lawton IADL assesses IADLs primarily in terms of physical capacities (McDowell, 2006) suggesting that the deficits in everyday functioning reported by our patients reflect difficulty in tasks that impact social functioning.

On the ILS, a performance-based measure of everyday functioning, 10 (20%) had moderate to severe functional deficits in Memory/Orientation, 20 (40%) Managing Money, 9 (18%) Managing Home and Transportation, 15 (29%) Health and Safety, 27 (52%) Social Adjustment, 17 (34%) Problem Solving, and 18 (36%) had deficits on Performance/Information (Figure 5). The impairments in everyday functioning in our critically ill patients are similar to those reported in studies of older adults with memory complaints (Baird, 2006; Brooks, 2006), schizophrenia (Revheim & Medalia, 2004; Revheim et al., 2006), older adult general medicine patients (Henderson-Laribee, 2000), and patients following bone marrow transplantation (Hoffman, 2004). Further, impairments in everyday functioning following critical illness are consistent with previous studies of critically ill survivors (Herridge et al., 2003; Hopkins, Jackson et al., 2005; Jackson et al., 2003; Quality of Life After Mechanical Ventilation in the Elderly Study Investigators, 2002; Rothenhausler et al., 2001). For example, one year after critical illness 54 % of patients had mild to severe restrictions in everyday function including walking, participating in social activities (van der Schaaf, Beelen, Dongelmans, Vroom, & Nollet, 2009), managing finances, traveling, and making travel arrangements (Jackson et al., 2007).

Neither the MMSE nor Mini-Cog predicted everyday functioning at 6 months in our critically ill survivors. The reasons cognitive screening tests did not predict everyday functioning

are unclear, but may be due to two factors. First, impairments in everyday functioning among the critically ill survivors are common (up to 60% of patients) at 6 months in interpersonal relationships, money management, medication management, shopping, everyday memory, and home/transportation management. Second, our patients had a high rate of cognitive impairments (up to 65%) on cognitive screening tests at hospital discharge and similarly high rate of poor everyday functioning (60%), resulting in limited scores variability. As noted previously, we did not have a normal control group which likely would increase the variability. Thus, administration of cognitive screening tests at hospital discharge may not be the optimal time point. Cognitive screening tests administered later in the recovery process may improve predictability of long-term everyday functioning. Further, previous data suggests that cognitive functioning continues to improve one year or more after ICU discharge; therefore, assessment of long-term outcomes more distal from hospital discharge may improve predictive abilities (Hopkins, Weaver et al., 2005).

We did not find a relationship between long-term cognitive sequelae and everyday functioning. Our findings differ from that of Jackson, Obremskey, and colleagues (2007) who found a significant relationship ($p = .05$) between cognitive sequelae and the FAQ scores in trauma ICU survivors. The differences in findings may be due to differences in neuropsychological tests, statistical analysis used, and study populations. Specifically, we used more comprehensive measures of memory (e.g., the WMS-III Logical Memory and CVLT-II), rather than a single verbal memory test (Rey Auditory Verbal Learning Test). Additionally, we used a regression model adjusting for medical and demographic variables to examine the relationships between cognitive sequelae and everyday functioning rather than a simple analysis of correlations.

Alternatively when using cognitive domain test scores and not overall cognitive sequelae, impaired attention was associated with the ILS Memory/Orientation subscale score, Health and Safety subscale score, and Social Adjustment subscale score. Further, we found that impaired attention, mental processing speed, and memory were associated with the ILS Managing Home/Transportation subscale score, Impaired attention, mental processing speed, and memory resulted in significant problems in the patients' everyday memory (incorrect recall of current date, a list of items, and a hypothetical doctor's appointment), ability to manage their home and transportation needs (e.g., use of telephone and public transportation), awareness of safety and health problems (e.g., managing medical emergencies and hazards around the home), and interpersonal relationships ("I'm often angry at others"), accounting for 30% and 53% of the variances respectively. These findings are not surprising as attention is a frequent impairment following brain injury (Mateer & Sira, 2006) and is a complex cognitive process that includes focused, sustained, selective, alternating, and divided attention (Sohlberg & Mateer, 1989) that is needed for higher order cognitive processes such as memory and executive function. Deficits in attention may impede recovery of other cognitive and everyday functioning in that intact attention is required so that an effective utilization of higher functions may take place (Ben-Yishay, Piasetsky, & Rattock, 1987). Managing home and transportation, for example, requires a high-level cognitive functioning due to the complex nature of the tasks that requires temporary storage and manipulation of information (e.g., looking up a person's telephone number on the telephone book, picking up the telephone, and dialing the number; searching information on bus fare or routes). Thus, managing health, safety, home, and transportation is a complex process that places demands on attention and/or working memory. Our findings are in agreement with those

of Rothenhausler and colleagues (2001) who found significant relationships between attention and memory deficits and the ability to return to work, an important functional task.

Psychiatric Functioning

Psychiatric morbidity such as depression, anxiety, and PTSD are common morbidities of critical illness (Angus et al., 2001; Kapfhammer et al., 2004; McCartney & Boland, 1994; Weinert, 2001). Our critically ill patients had significant symptoms of depression and anxiety at 6-month follow-up. The rate of depression in our patients was 13% with mild, 11% moderate, and 8% severe symptoms of depression. The rate of anxiety in our patients was 25% with mild, 21% moderate and 6% severe symptoms of anxiety. The prevalence of depression and anxiety in our study falls between the rates of 10% and 58% observed in other ICU populations (Adhikari et al., 2009; Angus et al., 2001; Herridge et al., 2003; Hopkins, Weaver et al., 2005; Hopkins et al., 1999; Kapfhammer et al., 2004; McCartney & Boland, 1994; Mikkelsen et al., 2009; Milisen et al., 2001; Orme et al., 2003; Skodol, 1999; Szokol & Vender, 2001; Weinert et al., 1997). The median point prevalence of clinically significant depression among general ICU survivors is approximately 28% based on a recent review of 14 studies (Davydow et al., 2009). Similarly, the rate of depression is 22% to 33% in medical inpatients (Katon & Sullivan, 1990) and 25% to 28% in patients with cardiac and pulmonary disorders (Silverstone, 1996; Silverstone, Lemay, Elliott, Hsu, & Starko, 1996)

Nearly 20% of our patients met DSM-IV PTSD criteria, all of whom endorsed critical illness as the sole or primary traumatic event, compared to only 3 (6%) patients endorsing critical illness as their secondary traumatic event they had experienced at the time of the assessment. These findings not only highlight the high prevalence of PTSD symptoms following critical illness and ICU treatments, but also that critical illness was identified as the unique traumatic

experience in our patients, which has not been assessed in previous studies in ICU populations. The rate of PTSD in our study is similar to a review that found the PTSD point prevalence of 22% (n = 1104) and median point prevalence (based on clinician-administered measures) of 19% (n = 93) in general ICUs over the first 6 to 12 months post-ICU discharge (Davydow, Gifford et al., 2008). Psychiatric disorders following critical illness may be due to sequelae of brain injury sustained due to critical illness and its treatments, a psychological reaction to the emotional and physiological stress of critical illness, or both. Medications, physiological changes, pain, altered sensory inputs, and an unfamiliar environment are all potential contributors to the development of psychiatric sequelae (McCartney & Boland, 1994; Skodol, 1999; Szokol & Vender, 2001).

The OQ-45.2 is a brief, robust screening and outcome assessment tool that can be useful in assessing patient global and specific areas of psychological functioning post-hospital discharge. On the OQ-45.2, our critically ill patients endorsed fewer interpersonal difficulties (e.g., "I feel loved and wanted," I feel my love relationships are full and complete") compared to normal community dwelling adults. One possible reason for the comparatively better interpersonal functioning of our patients may be due to the observations that many patients who had impairments in everyday functioning depended on their loved ones (spouse or family members) for caregiver support. Previous studies show a high rate (between 57% and 78%) of critically ill patients requires caregiver support (Chelluri et al., 2004; Quality of Life After Mechanical Ventilation in the Elderly Study Investigators, 2002).

Our critically ill patients psychological dysfunction was high with 21% of patients reporting global psychological distress, 34% symptom distress, 11% interpersonal relations difficulties, and 21% social role difficulties (e.g., "I feel that I'm not doing well at work."). However, our patients did not display global psychological distress, symptom distress, and social

role performance difficulties compared to data from normal community dwelling adults. Depression and anxiety are frequently assessed in studies of critical illness (Adhikari et al., 2009; Angus et al., 2001; Davydow et al., 2009; Herridge et al., 2003; Hopkins, Weaver et al., 2005; Hopkins et al., 1999; Kapfhammer et al., 2004; McCartney & Boland, 1994; Mikkelsen et al., 2009; Milisen et al., 2001; Orme et al., 2003; Skodol, 1999; Szokol & Vender, 2001; Weinert et al., 1997), but global psychological functioning, as well as symptom distress, interpersonal relations, and social role, has not been assessed in this population. Psychological dysfunction remains a concern in survivors of critical illness years after hospital discharge. General psychological dysfunction negatively impacts quality of life and delays return to work in other patient populations, such as traumatic brain injury (Zatzick et al., 2008). Health care professionals should be aware of potential global and specific psychological dysfunction, in addition to symptoms of depression, anxiety, and PTSD in critically ill patients. A referral for psychiatric consultation and outpatient psychotherapy might be warranted to treat consequences of psychiatric morbidity following critical illness.

Quality of Life

Our critically ill patients had reduced quality of life for physical functioning, role-physical, bodily pain, general health, vitality, social functioning, and role-emotional domains compared to normal population data (Figure 6). The findings of decreased quality of life in our patients are similar to previous studies of critically ill patients (Angus et al., 2001; Christie et al., 2006; Davidson, Caldwell, Curtis, Hudson, & Steinberg, 1999; Dowdy et al., 2005; Herridge et al., 2003; Hopkins et al., 2004; Hopkins et al., 1999; McHugh et al., 1994; Mikkelsen et al., 2009; Rothenhausler et al., 2001; Schelling et al., 1998; van der Schaaf et al., 2008; Weinert et al., 1997). Dowdy and colleagues (2005) in a recent meta-analysis of quality-of-life studies

consistently found lower quality of life scores than matched, normative controls at all time points (from hospital discharge to 66 months later) after ICU discharge in survivors of critical illness. Further, they found larger decrements in the 4 physical domains (physical functioning, role-physical, bodily pain, and general health perceptions) compared to the mental domains (vitality, social functioning, role-emotional, and mental health). Improvements in quality of life are uneven and time- and domain-specific (Hopkins, Weaver et al., 2005). The greatest gains occur in physical functioning, social functioning, and role-physical in the first 6 months, with only modest additional improvements thereafter (Dowdy et al., 2005).

Cognitive sequelae at 6 months predicted poor quality of life for Role-Physical, accounting for 20% variability in role limitations due to physical causes (e.g., cut down the amount of time spent on work or other activities). Our findings suggest that there may be a relationship between cognitive function and poor physical function. Data in non-ICU populations suggest that better physical health is associated with better learning and memory (Erickson et al., 2009), prevents age-related cognitive decline (Heyn, Abreu, & Ottenbacher, 2004), and improves recovery from brain injury and disease. Moderate to strong associations between physical health and cognition, mood, and brain function are reported (Kramer, Colcombe, McAuley, Scalf, & Erickson, 2005). Other studies show that decreased quality of life is associated with psychiatric sequelae, including depression and PTSD (Davydow, Desai et al., 2008; Davydow et al., 2009; Davydow, Gifford et al., 2008; Schelling et al., 1998; Weinert et al., 1997). Thus, factors besides including cognitive functioning may contribute to decreased quality of life following critical illness.

Our finding is consistent with that of Rothenhausler and colleagues in that ARDS survivors with cognitive sequelae had worse quality of life than individuals without cognitive

sequelae (Rothenhausler et al., 2001). Conversely, cognitive sequelae was not associated with reduced quality of life or the physical role domain (Christie et al., 2006; Mikkelsen et al., 2009) or any quality-of-life domains (Hopkins, Weaver et al., 2005; Sukantarat et al., 2005); however, there was significant overlap between the critically ill survivors with and without cognitive impairments on nearly all quality-of-life domains and both subgroups reported lower quality of life than normal individuals (Christie et al., 2006; Hopkins, Weaver et al., 2005; Mikkelsen et al., 2009; Rothenhausler et al., 2001; Sukantarat et al., 2005). Compared to the studies by Hopkins, Sukantarat, Mikkelsen, and Christie and colleagues, the differences in findings may be due to study differences in neuropsychological tests administered, length of follow-up testing, definition of cognitive sequelae; specifically, Sukantarat and colleagues used only executive tests, Hopkins and colleagues did a follow-up testing at 2 years, and Christie and colleagues and Mikkelsen and colleagues defined cognitive sequelae defined as any 2 test scores 1 *SD* or more below the population norm or a single test score 1.5 *SD*s below the population norm.

Mortality

Ten of our critically ill patients died during the 6-month follow-up period, reflecting a 6-month mortality rate of 15% (10 patients). The mortality rate is substantially higher than the 5% (3 patients) in ARDS patients (Hopkins et al., 2004; Hopkins et al., 1999) at 1-year follow-up, and 8% (9 patients) reported by Herridge and colleagues (2003) at 6-month follow-up. While the reason for the high death rate in the current study is unclear, the patients who died (mean age 65 years) were significantly older than patients who survived (mean age 52 years). In fact, our overall sample was substantially older by a mean of almost 10 years than previous studies by Hopkins, Weaver, and colleagues (2004; 1999) and Herridge and colleagues (2003) (mean age 45 years in all 3 studies). Older age in critically ill patients is associated with higher ICU

mortality (Eachempati, Hydo, Shou, & Barie, 2007) and post-ICU mortality (Weycker, Akhras, Edelsberg, Angus, & Oster, 2003) due to physiologic limitations in response to critical illness (Gee et al., 1990; Sevransky & Haponik, 2003). The post-hospital mortality rate in healthy elderly patients age ≥ 65 years admitted to an ICU was 24% and occurred a mean of 522 days post-hospital discharge (Sacanella et al., 2009). Post-hospital mortality in critically ill patients is associated with a greater number of baseline chronic (e.g., cardiovascular and liver diseases) and acute (e.g., hypotension and renal disease) comorbid diseases increase (Kasal et al., 2004), increased number of organ system dysfunction during ICU treatments (Weycker et al., 2003), use of vasopressors during ICU treatments (Perl, Dvorak, Hwang, & Wenzel, 1995), and poor pre-ICU everyday functioning and quality of life (Sacanella et al., 2009).

Study Strengths and Limitations

The strengths of this study include the longitudinal prospective cohort study design, consistent follow-up times, high follow-up rates, and comprehensive measures of cognitive, psychiatric, and every functioning. One limitation of this study is the small sample size. A larger study might find a relationship between cognitive screening tests and cognitive sequelae, as well as everyday functioning. A second limitation of this study and most prior ICU outcome studies was a lack of measures for premorbid cognitive, psychiatric, and everyday functioning, as well as quality of life. Third, this study did not include a normal control group; however, it should be noted that we used demographically (i.e., age, sex, and education) corrected neuropsychological test scores for statistical analyses, which correct for variables known to effect test performance.

Conclusions

Our findings support emerging evidence that critically ill patients exhibit significant cognitive impairments, psychiatric dysfunction, poor everyday functioning, and reduced quality

of life. We found that the MMSE and Mini-Cog, despite their brevity and efficiency, did not predict long-term cognitive sequelae, impairments in specific cognitive domains, or everyday functioning. While the MMSE and Mini-Cog identified cognitive impairments at hospital discharge in our patients, they were not effective in predicting long-term cognitive outcome and everyday functioning. Cognitive sequelae were not associated with poor everyday functioning; however, impaired attention, memory, and mental processing speed predicted problems with managing home/transportation, and impaired attention predicted problems in health and safety, social adjustment, and memory/orientation. Cognitive sequelae were associated with reduced quality of life in the role physical domain. Altogether, these findings lend additional knowledge to the literature regarding cognitive and psychiatric sequelae, everyday functioning, and reduced quality of life in critically ill patients, and may have clinical implications for the critical care providers, patients, and caregivers.

Given the large population of survivors of critical illness each year, strategies aimed at recognizing, preventing and treating these morbidities are important research and public health concerns. Investigations into the clinical and economic burden of these morbidities and methods to mitigate them, including patient screening and referral to appropriate mental health and rehabilitation services, are warranted. Future examinations within larger samples should be conducted to determine the nature, risk factors, and nuances of the brain-related morbidity in critical illness. A better understanding of the pathophysiology of cognitive dysfunction, psychiatric morbidity, and poor everyday functioning is central to development of interventions to improve outcomes. While findings have suggested early physical rehabilitation could improve physical outcome (Bailey et al., 2007; Hopkins & Spuhler, 2009), it remains to be seen whether cognitive rehabilitation, which is widely employed in patients with traumatic brain injury and

stroke, is effective for the critically ill patients. In the meantime, psycho-education and support interventions to meet the changing needs of patients and their families during recovery are needed (Lee, Herridge, Matte, & Cameron, 2009).

References

Adhikari, N. K., McAndrews, M. P., Tansey, C. M., Matte, A., Pinto, R., Cheung, A. M., et al. (2009). Self-reported symptoms of depression and memory dysfunction in survivors of ARDS. *Chest, 135*(3), 678-687. doi:10.1378/chest.08-0974

Angus, D. C., Musthafa, A. A., Clermont, G., Griffin, M. F., Linde-Zwirble, W. T., Dremsizov, T. T., et al. (2001). Quality-adjusted survival in the first year after the acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine, 163*(6), 1389-1394.

Bailey, P., Thomsen, G. E., Spuhler, V. J., Blair, R., Jewkes, J., Bezdjian, L., et al. (2007). Early activity is feasible and safe in respiratory failure patients. *Critical Care Medicine, 35*(1), 139-145. doi:10.1097/01.CCM.0000251130.69568.87

Baird, A. (2006). Fine tuning recommendations for older adults with memory complaints: using the Independent Living Scales with the Dementia Rating Scale. *The Clinical Neuropsychologist, 20*(4), 649-661. doi:10.1080/13854040590967072

Barberger-Gateau, P., Commenges, D., Gagnon, M., Letenneur, L., Sauvel, C., & Dartigues, J. F. (1992). Instrumental activities of daily living as a screening tool for cognitive impairment and dementia in elderly community dwellers. *Journal of the American Geriatrics Society, 40*(11), 1129-1134.

Beck, A. T., & Steer, R. A. (1993). *Beck Anxiety Inventory*. San Antonio, TX: The Psychological Corporation.

Beck, A. T., Steer, R. A., & Brown, G. (1996). *Beck Depression Inventory* (2nd ed.). San Antonio, TX: The Psychological Corporation.

Ben-Yishay, Y., Piasetsky, E. B., & Rattock, J. A. (1987). A systematic method for ameliorating disorders in basic attention. In M. J. Meier, A. L. Benton & L. Diller (Eds.), *Neuropsychological Rehabilitation* (pp. 165-181). New York: Churchill Livingstone.

Bernard, G. R., Artigas, A., Brigham, K. L., Carlet, J., Falke, K., Hudson, L., et al. (1994). The American-European Consensus Conference on ARDS: Definitions, mechanisms, relevant outcomes, and clinical trial coordination. *American Journal of Respiratory and Critical Care Medicine, 149*(3 Pt 1), 818-824.

Bigler, E. D., & Tucker, D. M. (1981). Comparison of verbal IQ, Tactual Performance, Seashore Rhythm and Finger Oscillation Tests in the blind and brain-damaged. *Journal of Clinical Psychology, 37*(4), 849-851.

Blessed, G., Tomlinson, B. E., & Roth, M. (1968). The association between quantitative measures of dementia and of senile change in the cerebral grey matter of elderly subjects. *British Journal of Psychiatry, 114*(512), 797-811.

Boise, L., Camicioli, R., Morgan, D. L., Rose, J. H., & Congleton, L. (1999). Diagnosing dementia: Perspectives of primary care physicians. *Gerontologist, 39*(4), 457-464.

Bornstein, R. A., Baker, G. B., & Douglass, A. B. (1987). Short-term retest reliability of the Halstead-Reitan Battery in a normal sample. *Journal of Nervous and Mental Disease, 175*(4), 229-232.

Borson, S., Scanlan, J., Brush, M., Vitaliano, P., & Dokmak, A. (2000). The Mini-Cog: A cognitive "vital signs" measure for dementia screening in multi-lingual elderly. *International Journal of Geriatric Psychiatry, 15*(11), 1021-1027.

Borson, S., Scanlan, J. M., Watanabe, J., Tu, S. P., & Lessig, M. (2005). Simplifying detection of cognitive impairment: Comparison of the Mini-Cog and Mini-Mental State Examination in a multiethnic sample. *Journal of the American Geriatrics Society, 53*(5), 871-874.

Bottino, C. M., Zevallos-Bustamante, S. E., Lopes, M. A., Azevedo, D., Hototian, S. R., Jacob-Filho, W., et al. (2009). Combined instruments for the screening of dementia in older people with low education. *Arquivos de Neuro-Psiquiatria, 67*(2A), 185-190. doi:S0004-282X2009000200003 [pii]

Boustani, M., Perkins, A. J., Fox, C., Unverzagt, F., Austrom, M. G., Fultz, B., et al. (2006). Who refuses the diagnostic assessment for dementia in primary care? *International Journal of Geriatric Psychiatry, 21*(6), 556-563.

Boustani, M., Peterson, B., Hanson, L., Harris, R., & Lohr, K. N. (2003). Screening for dementia in primary care: A summary of the evidence for the U.S. Preventive Services Task Force. *Annals of Internal Medicine, 138*(11), 927-937.

Brazier, J. E., Harper, R., Jones, N. M., O'Cathain, A., Thomas, K. J., Usherwood, T., et al. (1992). Validating the SF-36 health survey questionnaire: new outcome measure for primary care. *BMJ, 305*(6846), 160-164.

Brewer, M. (2000). Research design and issues of validity. In H. Reis & C. Judd (Eds.), *Handbook of research methods in social and personality psychology* (pp. 81-99). Cambridge: Cambridge University Press.

Brodaty, H., Howarth, G. C., Mant, A., & Kurrle, S. E. (1994). General practice and dementia: A national survey of Australian GPs. *Medical Journal of Australia, 160*(1), 10-14.

Brodaty, H., Low, L. F., Gibson, L., & Burns, K. (2006). What is the best dementia screening instrument for general practitioners to use? *American Journal of Geriatric Psychiatry, 14*(5), 391-400.

Brooks, B. L. (2006). The relationship between executive functioning and independent living skills in mild cognitive impairment and mild dementia. *Dissertation Abstracts International: Section B: The Sciences and Engineering, 66(8-B)*, 4473.

Brummel-Smith, K. (2000). Assessment in rehabilitation. In D. Osterweil, K. Brummel-Smith & J. C. Beck (Eds.), *Comprehensive geriatric assessment* (pp. 139-172). New York: McGraw-Hill.

Burgess, P. W., & Shallice, T. (1997). *The Hayling and Brixton Tests*. Bury St. Edmunds, UK: Thames Valley Test.

Bustamante, S. E., Bottino, C. M., Lopes, M. A., Azevedo, D., Hototian, S. R., Litvoc, J., et al. (2003). [Combined instruments on the evaluation of dementia in the elderly: preliminary results]. *Arquivos de Neuro-Psiquiatria, 61*(3A), 601-606. doi:S0004-282X2003000400014 [pii]

Chelluri, L., Im, K. A., Belle, S. H., Schulz, R., Rotondi, A. J., Donahoe, M. P., et al. (2004). Long-term mortality and quality of life after prolonged mechanical ventilation. *Critical Care Medicine, 32*(1), 61-69.

Cherpitel, C. J. (1995). Screening for alcohol problems in the emergency room: A rapid alcohol problems screen. *Drug and Alcohol Dependence, 40*(2), 133-137.

Christie, J. D., Biester, R. C., Taichman, D. B., Shull, W. H., Jr., Hansen-Flaschen, J., Shea, J. A., et al. (2006). Formation and validation of a telephone battery to assess cognitive function in acute respiratory distress syndrome survivors. *Journal of Critical Care, 21*(2), 125-132.

Christie, J. D., DeMissie, E., Gaughan, C., Taichman, D., Plotkin, R., & Hopkins, R. O. (2004). Validity of a brief telephone-administered battery to assess cognitive function in survivors of the Adult Respiratory Distress Syndrome (ARDS). [Abstract]. *American Journal of Respiratory and Critical Care Medicine, 169*, A781.

Dasta, J. F., McLaughlin, T. P., Mody, S. H., & Piech, C. T. (2005). Daily cost of an intensive care unit day: The contribution of mechanical ventilation. *Critical Care Medicine, 33*(6), 1266-1271.

Davidson, T. A., Caldwell, E. S., Curtis, J. R., Hudson, L. D., & Steinberg, K. P. (1999). Reduced quality of life in survivors of acute respiratory distress syndrome compared with critically ill control patients. *JAMA, 281*(4), 354-360. doi:jce80026 [pii]

Davis, B. A., Martin-Cook, K., Hynan, L. S., & Weiner, M. F. (2006). Caregivers' perceptions of dementia patients' functional ability. *American Journal of Alzheimer's Disease and Other Dementias, 21*(2), 85-91.

Davydow, D. S., Desai, S. V., Needham, D. M., & Bienvenu, O. J. (2008). Psychiatric morbidity in survivors of the acute respiratory distress syndrome: a systematic review. *Psychosomatic Medicine, 70*(4), 512-519. doi:10.1097/PSY.0b013e31816aa0dd

Davydow, D. S., Gifford, J. M., Desai, S. V., Bienvenu, O. J., & Needham, D. M. (2009). Depression in general intensive care unit survivors: a systematic review. *Intensive Care Medicine, 35*(5), 796-809. doi:10.1007/s00134-009-1396-5

Davydow, D. S., Gifford, J. M., Desai, S. V., Needham, D. M., & Bienvenu, O. J. (2008). Posttraumatic stress disorder in general intensive care unit survivors: a systematic review. *General Hospital Psychiatry, 30*(5), 421-434. doi:10.1016/j.genhosppsych.2008.05.006

Delis, D. C., Kramer, J. H., Kaplan, E., & Ober, B. A. (2000). *California Verbal Learning Test – Adult Version* (2nd ed.). San Antonio, TX: The Psychological Corporation.

Denny, S. D., Kuchibhatla, M. N., & Cohen, H. J. (2006). Impact of anemia on mortality, cognition, and function in community-dwelling elderly. *American Journal of Medicine, 119*(4), 327-334.

Dikmen, S. S., Heaton, R. K., Grant, I., & Temkin, N. R. (1999). Test-retest reliability and practice effects of expanded Halstead-Reitan Neuropsychological Test Battery. *Journal of the International Neuropsychological Society, 5*(4), 346-356.

Dodrill, C. B., & Troupin, A. S. (1975). Effects of repeated administrations of a comprehensive neuropsychological battery among chronic epileptics. *Journal of Nervous and Mental Disease, 161*(3), 185-190.

Doraiswamy, P. M. (1996). Current cholinergic therapy for symptoms of Alzheimer's disease. *Primary Psychiatry, 3*(11), 56-68.

Dowdy, D. W., Eid, M. P., Sedrakyan, A., Mendez-Tellez, P. A., Pronovost, P. J., Herridge, M. S., et al. (2005). Quality of life in adult survivors of critical illness: a systematic review of the literature. *Intensive Care Medicine, 31*(5), 611-620. doi:10.1007/s00134-005-2592-6

Drake, A. I., McDonald, E. C., Magnus, N. E., Gray, N., & Gottshall, K. (2006). Utility of Glasgow Coma Scale-Extended in symptom prediction following mild traumatic brain injury. *Brain Injury, 20*(5), 469-475.

Duning, T., van den Heuvel, I., Dickmann, A., Volkert, T., Wempe, C., Reinholz, J., et al. (2010). Hypoglycemia aggravates critical illness-induced neurocognitive dysfunction. *Diabetes Care, 33*(3), 639-644. doi:10.2337/dc09-1740

Eachempati, S. R., Hydo, L. J., Shou, J., & Barie, P. S. (2007). Outcomes of acute respiratory distress syndrome (ARDS) in elderly patients. *Journal of Trauma, 63*(2), 344-350. doi:10.1097/TA.0b013e3180eea5a1

Earnst, K. S., Wadley, V. G., Aldridge, T. M., Steenwyk, A. B., Hammond, A. E., Harrell, L. E., et al. (2001). Loss of financial capacity in Alzheimer's disease: The role of working memory. *Aging, Neuropsychology, and Cognition, 8*(2), 109-119.

Ehlenbach, W. J., Hough, C. L., Crane, P. K., Haneuse, S. J., Carson, S. S., Curtis, J. R., et al. (2010). Association between acute care and critical illness hospitalization and cognitive function in older adults. *JAMA, 303*(8), 763-770. doi:10.1001/jama.2010.167

Elena, P., & Rebecca, V. (1994). Selection of preschool language tests: A data-based approach. *Language, Speech, and Hearing Services in Schools, 25*, 15-24.

Erickson, K. I., Prakash, R. S., Voss, M. W., Chaddock, L., Hu, L., Morris, K. S., et al. (2009). Aerobic fitness is associated with hippocampal volume in elderly humans. *Hippocampus, 19*(10), 1030-1039. doi:10.1002/hipo.20547

Ernest, C. S., Worcester, M. U., Tatoulis, J., Elliott, P. C., Murphy, B. M., Higgins, R. O., et al. (2006). Neurocognitive outcomes in off-pump versus on-pump bypass surgery: A randomized controlled trial. *The Annals of Thoracic Surgery 81*(6), 2105-2114.

Esteban, A., Anzueto, A., Frutos, F., Alia, I., Brochard, L., Stewart, T. E., et al. (2002). Characteristics and outcomes in adult patients receiving mechanical ventilation: A 28-day international study. *Journal of the American Medical Association, 287*(3), 345-355.

Farias, S. T., Harrell, E., Neumann, C., & Houtz, A. (2003). The relationship between neuropsychological performance and daily functioning in individuals with Alzheimer's disease: Ecological validity of neuropsychological tests. *Archives of Clinical Neuropsychology, 18*(6), 655-672.

Fillenbaum, G. G. (1985). Screening the elderly: A brief instrumental activities of daily living measure. *Journal of the American Geriatrics Society, 33*(10), 698-706.

Fischer, J. S., Hannay, H. J., Loring, D. W., & Lezak, M. D. (2004). Observational methods, rating scales, and inventories. In M. D. Lezak, D. B. Howieson, D. W. Loring, H. J. Hannay & J. S. Fischer (Eds.), *Neuropsychological assessment* (2nd ed., pp. 698-739). New York: Oxford University Press.

Foa, E. B. (1995). *The Posttraumatic Diagnostic Scale (PDS) manual*. Minneapolis, MN: National Computer Systems.

Folstein, M. (1998). Mini-mental and son. *International Journal of Geriatric Psychiatry, 13*(5), 290-294.

Folstein, M. F., Folstein, S. E., & McHugh, P. R. (1975). Mini-mental state: A practical method for grading the cognitive state of patients for the clinician. *Journal of Psychiatric Research, 12*(3), 189-198.

Franzen, J. E., & Wilhelm, K. L. (1996). Conceptual foundations of ecological validity in neuropsychology. In R. J. Sbordone & C. J. Long (Eds.), *Ecological validity of neuropsychological testing*. Boca Raton, FL: CRC Press LLC.

Franzen, M. D., Tishelman, A. C., Sharp, B. H., & Friedman, A. G. (1987). An investigation of the test-retest reliability of the Stroop Color-Word Test across two intervals. *Archives of Clinical Neuropsychology, 2*(3), 265-272.

Gallo, J. J., & Paveza, G. J. (2005). Activities of daily living and instrumental activities of daily living assessment. In J. J. Gallo, H. R. Bogner, T. Fulmer & G. J. Paveza (Eds.), *Handbook of geriatric assessment* (4th ed., pp. 193-240). Sudbury, MA: Jones & Bartlett

Gambert, S. R. (1997). Is it Alzheimer's disease? *Postgraduate Medicine, 101*(6), 42-43, 48-49, 52-44 passim.

Gavin, D. R., Ross, H. E., & Skinner, H. A. (1989). Diagnostic validity of the drug abuse screening test in the assessment of DSM-III drug disorders. *British Journal of Addiction, 84*(3), 301-307.

Gee, M. H., Gottlieb, J. E., Albertine, K. H., Kubis, J. M., Peters, S. P., & Fish, J. E. (1990). Physiology of aging related to outcome in the adult respiratory distress syndrome. *Journal of Applied Physiology, 69*(3), 822-829.

Girard, T. D., Shintani, A. K., Jackson, J. C., Gordon, S. M., Pun, B. T., Henderson, M. S., et al. (2007). Risk factors for post-traumatic stress disorder symptoms following critical illness requiring mechanical ventilation: a prospective cohort study. *Critical Care, 11*(1), R28. doi:10.1186/cc5708

Golden, C. J. (1978). *Stroop Color and Word Test: A manual for clinical and experimental uses*. Chicago: Stoelting.

Griffin, S. L., Mindt, M. R., Rankin, E. J., Ritchie, A. J., & Scott, J. G. (2002). Estimating premorbid intelligence: Comparison of traditional and contemporary methods across the intelligence continuum. *Archives of Clinical Neuropsychology, 17*(5), 497-507.

Griffiths, R. D., & Jones, C. (2007). Delirium, cognitive dysfunction and posttraumatic stress disorder. *Curr Opin Anaesthesiol, 20*(2), 124-129. doi:10.1097/ACO.0b013e3280803d4b

Halstead, W. C. (1947). *Brain and intelligence: A quantitative study of the frontal lobes*. Chicago: University of Chicago Press.

Heaton, R. K., Miller, S. W., Taylor, M. J., & Grant, I. (2004). *Revised comprehensive norms for an expanded Halstead-Reitan Battery: Demographically adjusted neuropsychological norms for African American and Caucasian adults*. Lutz, FL: Psychological Assessment Resources.

Henderson-Laribee, D. L. (2000). Independent living scales: Relationship to cognitive functioning, depression, medical burden, and level of after-care in geriatric medical patients. *Dissertation Abstracts International: Section B: The Sciences and Engineering, 61(6-B)*, 3278.

Herridge, M. S., Cheung, A. M., Tansey, C. M., Matte-Martyn, A., Diaz-Granados, N., Al-Saidi, F., et al. (2003). One-year outcomes in survivors of the acute respiratory distress syndrome. *New England Journal of Medicine, 348*(8), 683-693.

Herridge, M. S., Tansey, C. M., L., M. A., Al-Saidi, F., Cheung, A. M., & McAndrews, M. P. (2006). Five-year neuropsychological outcomes in acute respiratory distress syndrome (ARDS) survivors. [Abstract]. *Proceedings of the American Thoracic Society, 3*, A571.

Heun, R., Papassotiropoulos, A., & Jennssen, F. (1998). The validity of psychometric instruments for detection of dementia in the elderly general population. *International Journal of Geriatric Psychiatry, 13*(6), 368-380.

Heyn, P., Abreu, B., & Ottenbacher, K. (2004). The effects of exercise training on elderly persons with cognitive impairment and dementia: a meta-analysis. *Archives of Physical Medicine and Rehabilitation, 85*(10), 1694-1704.

Ho, M. R., & Bennett, T. L. (1997). Efficacy of neuropsychological rehabilitation for mild-moderate traumatic brain injury. *Archives of Clinical Neuropsychology, 12*(1), 1-11.

Hoffman, B. (2004). Everyday cognitive capacity before and after blood or marrow transplantation. *Dissertation Abstracts International: Section B: The Sciences and Engineering, 64(11-B)*, 5810.

Hom, J., & Reitan, R. M. (1990). Generalized cognitive function after stroke. *Journal of Clinical and Experimental Neuropsychology, 12*(5), 644-654.

Hopkins, R. O., & Brett, S. (2005). Chronic neurocognitive effects of critical illness. *Current Opinion in Critical Care, 11*(4), 369-375. doi:00075198-200508000-00015 [pii]

Hopkins, R. O., Gale, S. D., & Weaver, L. K. (2006). Brain atrophy and cognitive impairment in survivors of acute respiratory distress syndrome. *Brain Injury, 20*(3), 263-271.

Hopkins, R. O., & Jackson, J. C. (2006). Long-term neurocognitive function after critical illness. *Chest, 130*(3), 869-878. doi:10.1378/chest.130.3.869

Hopkins, R. O., & Jackson, J. C. (2009). Short- and long-term cognitive outcomes in intensive care unit survivors. *Clinics in Chest Medicine, 30*(1), 143-153. doi:10.1016/j.ccm.2008.11.001

Hopkins, R. O., Jackson, J. C., & Wallace, C. J. (2005). *Neurocognitive impairments in ICU patients with prolonged mechanical ventilation.* Paper presented at the International Neuropsychological Society 33rd Annual Meeting Program and Abstracts, St. Louis, MO.

Hopkins, R. O., Key, C. W., Suchyta, M. R., Weaver, L. K., & Orme Jr., J. F. (2010). Risk factors for depression and anxiety in survivors of acute respiratory distress syndrome. *General Hospital Psychiatry, 32*(2), 147-155.

Hopkins, R. O., & Spuhler, V. J. (2009). Strategies for promoting early activity in critically ill mechanically ventilated patients. *AACN Advanced Critical Care, 20*(3), 277-289. doi:10.1097/NCI.0b013e3181acaef0

Hopkins, R. O., Weaver, L. K., Chan, K. J., & Orme, J. F., Jr. (2004). Quality of life, emotional, and cognitive function following acute respiratory distress syndrome. *Journal of the International Neuropsychological Society, 10*(7), 1005-1017.

Hopkins, R. O., Weaver, L. K., Collingridge, D., Parkinson, R. B., Chan, K. J., & Orme, J. F., Jr. (2005). Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine, 171*(4), 340-347.

Hopkins, R. O., Weaver, L. K., Pope, D., Orme, J. F., Bigler, E. D., & Larson-Lohr, V. (1999). Neuropsychological sequelae and impaired health status in survivors of severe acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine, 160*(1), 50-56.

Hopkins, R. O., & Woon, F. L. (2006). Neuroimaging, cognitive, and neurobehavioral outcomes following carbon monoxide poisoning. *Behavioral and Cognitive Neuroscience Reviews, 5*(3), 141-155.

Hoskin, K. M., Jackson, M., & Crowe, S. F. (2005). Can neuropsychological assessment predict capacity to manage personal finances? A comparison between brain impaired individuals with and without administrators. *Psychiatry, Psychology and Law, 12*, 56-67.

Hunsley, J., & Mash, E. J. (2008). *A guide to assessments that work*. New York: Oxford University Press.

Ihl, R., Frolich, L., Dierks, T., Martin, E. M., & Maurer, K. (1992). Differential validity of psychometric tests in dementia of the Alzheimer type. *Psychiatry Research, 44*(2), 93-106.

Inouye, S. K., Viscoli, C. M., Horwitz, R. I., Hurst, L. D., & Tinetti, M. E. (1993). A predictive model for delirium in hospitalized elderly medical patients based on admission characteristics. *Annals of Internal Medicine, 119*(6), 474-481.

Jackson, J. C., Girard, T. D., Gordon, S. M., Thompson, J. L., Shintani, A. K., Thomason, J. W., et al. (in press). Long-Term Cognitive and Psychological Outcomes in the Awakening and Breathing Controlled Trial. *American Journal of Respiratory and Critical Care Medicine*. doi:10.1164/rccm.200903-0442OC

Jackson, J. C., Gordon, S. M., Hart, R. P., Hopkins, R. O., & Ely, E. W. (2004). The association between delirium and cognitive decline: A review of the empirical literature. *Neuropsychological Review, 14*(2), 87-98.

Jackson, J. C., Hart, R. P., Gordon, S. M., Shintani, A., Truman, B., May, L., et al. (2003). Six-month neuropsychological outcome of medical intensive care unit patients. *Critical Care Medicine, 31*(4), 1226-1234.

Jackson, J. C., Hopkins, R. O., Miller, R. R., Gordon, S. M., Wheeler, A. P., & Ely, E. W. (2009). Acute respiratory distress syndrome, sepsis, and cognitive decline: a review and case study. *Southern Medical Journal, 102*(11), 1150-1157. doi:10.1097/SMJ.0b013e3181b6a592

Jackson, J. C., Obremskey, W., Bauer, R., Greevy, R., Cotton, B. A., Anderson, V., et al. (2007). Long-term cognitive, emotional, and functional outcomes in trauma intensive care unit survivors without intracranial hemorrhage. *Journal of Trauma, 62*(1), 80-88. doi:10.1097/TA.0b013e31802ce9bd

James, K. M., Snyder, J. L., Lambert, M. J., Neeley, E. S., Carpenter, B. N., & Bigler, E. D. (2010). Use of the OQ-45.2 for evaluating of psychological status during inpatient physical rehabilitation (manuscript submitted for publication).

Jones, C., Griffiths, R. D., Slater, T., Benjamin, K. S., & Wilson, S. (2006). Significant cognitive dysfunction in non-delirious patients identified during and persisting following critical illness. *Intensive Care Medicine, 32*(6), 923-926. doi:10.1007/s00134-006-0112-y

Jones, R. C., Harding, S. A., Chung, M. C., & Campbell, J. (2009). The prevalence of posttraumatic stress disorder in patients undergoing pulmonary rehabilitation and changes in PTSD symptoms following rehabilitation. *Journal of Cardiopulmonary Rehabilitation and Prevention, 29*(1), 49-56. doi:10.1097/HCR.0b013e318192787e

Kane, R. A., & Kane, R. L. (1981). *Assessing the elderly: A practical guide to measurement*. Lexington, MA: Lexington Books.

Kapfhammer, H. P., Rothenhausler, H. B., Krauseneck, T., Stoll, C., & Schelling, G. (2004). Posttraumatic stress disorder and health-related quality of life in long-term survivors of acute respiratory distress syndrome. *American Journal of Psychiatry, 161*(1), 45-52.

Karagiozis, H., Gray, S., Sacco, J., Shapiro, M., & Kawas, C. (1998). The Direct Assessment of Functional Abilities (DAFA): A comparison to an indirect measure of instrumental activities of daily living. *Gerontologist, 38*(1), 113-121.

Karlawish, J. H., & Clark, C. M. (2003). Diagnostic evaluation of elderly patients with mild memory problems. *Annals of Internal Medicine, 138*(5), 411-419.

Kasal, J., Jovanovic, Z., Clermont, G., Weissfeld, L. A., Kaplan, V., Watson, R. S., et al. (2004). Comparison of Cox and Gray's survival models in severe sepsis. *Critical Care Medicine, 32*(3), 700-707. doi:00003246-200403000-00013 [pii]

Katon, W., & Sullivan, M. D. (1990). Depression and chronic medical illness. *Journal of Clinical Psychiatry, 51 Suppl*, 3-11; discussion 12-14.

Kauppi, M., Hartikainen, S., Kautiainen, H., Laiho, K., & Sulkava, R. (2005). Capability for daily activities in old people with rheumatoid arthritis: A population based study. *Annals of the Rheumatic Diseases, 64*(1), 56-58.

King, J. T., Jr., DiLuna, M. L., Cicchetti, D. V., Tsevat, J., & Roberts, M. S. (2006). Cognitive functioning in patients with cerebral aneurysms measured with the Mini Mental State Examination and the telephone interview for cognitive status. *Neurosurgery, 59*(4), 803-810.

Knaus, W. A., Draper, E. A., Wagner, D. P., & Zimmerman, J. E. (1985). APACHE II: a severity of disease classification system. *Critical Care Medicine, 13*(10), 818-829.

Knopman, D. S. (1998). The initial recognition and diagnosis of dementia. *American Journal of Medicine, 104*(4A), 2S-12S.

Koch, H. J., Gurtler, K., & Szecsey, A. (2005). Correlation of Mini-Mental-State-Examination (MMSE), Syndrom-Kurztest (SKT) and Clock test (CT) scores in patients with cognitive impairment assessed by means of multiple regression and response surface analysis. *Archives of Gerontology and Geriatrics, 40*(1), 7-14.

Kramer, A. F., Colcombe, S. J., McAuley, E., Scalf, P. E., & Erickson, K. I. (2005). Fitness, aging and neurocognitive function. *Neurobiology of Aging, 26 Suppl 1*, 124-127. doi:10.1016/j.neurobiolaging.2005.09.009

Kukull, W. A., Larson, E. B., Teri, L., Bowen, J., McCormick, W., & Pfanschmidt, M. L. (1994). The Mini-Mental State Examination score and the clinical diagnosis of dementia. *Journal of Clinical Epidemiology, 47*(9), 1061-1067.

Lambert, M. J., Morton, J. J., Hatfield, D., Harmon, C., Hamilton, S., Reid, R. C., et al. (2004). *Administration and scoring manual for the OQ-45.2*. Orem, UT: American Professional Credentialing Services L.L.C.

Lawton, M. P. (1988). Scales to measure competence in everyday activities. *Psychopharmacology Bulletin, 24*(4), 609-614.

Lawton, M. P., & Brody, E. M. (1969). Assessment of older people: Self-maintaining and instrumental activities of daily living. *Gerontologist, 9*(3), 179-186.

Lawton, M. P., Moss, M., Fulcomer, M., & Kleban, M. H. (1982). A research and service oriented multilevel assessment instrument. *Journal of Gerontology, 37*(1), 91-99.

Lee, C. M., Herridge, M. S., Matte, A., & Cameron, J. I. (2009). Education and support needs during recovery in acute respiratory distress syndrome survivors. *Critical Care, 13*(5), R153. doi:10.1186/cc8053

Levine, A. J., Miller, E. N., Becker, J. T., Selnes, O. A., & Cohen, B. A. (2004). Normative data for determining significance of test-retest differences on eight common neuropsychological instruments. *Clinical Neuropsychologist, 18*(3), 373-384.

Loeb, P. A. (1996). *Independent Living Scales manual*. San Antonio, TX: The Psychological Corporation.

Loewenstein, D. A., Amigo, E., Duara, R., Guterman, A., Hurwitz, D., Berkowitz, N., et al. (1989). A new scale for the assessment of functional status in Alzheimer's disease and related disorders. *Journal of Gerontology, 44*(4), P114-121.

Lorentz, W. J., Scanlan, J. M., & Borson, S. (2002). Brief screening tests for dementia. *Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie, 47*(8), 723-733.

Malloy, P. F., Cummings, J. L., Coffey, C. E., Duffy, J., Fink, M., Lauterbach, E. C., et al. (1997). Cognitive screening instruments in neuropsychiatry: A report of the Committee on Research of the American Neuropsychiatric Association. *Journal of Neuropsychiatry and Clinical Neurosciences, 9*(2), 189-197.

Marquis, K., Curtis, J., Caldwell, E., Davidson, T., Davis, J., Sanchez, P., et al. (2000). Neuropsychological sequelae in survivors of ARDS compared with critically ill control patients. [Abstract]. *American Journal of Respiratory and Critical Care Medicine, 161*, A383.

Martin-Cook, K., Davis, B. A., Hynan, L. S., & Weiner, M. F. (2005). A randomized, controlled study of an Alzheimer's caregiver skills training program. *American Journal of Alzheimer's Disease and Other Dementias, 20*(4), 204-210.

Matarazzo, J. D., & Herman, D. O. (1984). Base rate data for the WAIS-R: Test-retest stability and VIQ-PIQ differences. *Journal of Clinical Neuropsychology, 6*(4), 351-366.

Mateer, C. A., & Sira, C. S. (2006). Cognitive and emotional consequences of TBI: intervention strategies for vocational rehabilitation. *NeuroRehabilitation, 21*(4), 315-326.

Matthew, C. G., & Klove, K. (1964). *Instruction manual for the Adult Neuropsychology Test Battery*. Madison, WI: University of Wisconsin Medical School.

McCartney, J. R., & Boland, R. J. (1994). Anxiety and delirium in the intensive care unit. *Critical Care Clinics, 10*(4), 673-680.

McColl, M. A., Davies, D., Carlson, P., Johnston, J., Harrick, L., Minnes, P., et al. (1999). Transitions to independent living after ABI. *Brain Injury, 13*(5), 311-330.

McDowell, I. (2006). *Measuring health: A guide to rating scales and questionnaires*. New York: Oxford University Press.

McDowell, I., Kristjansson, B., Hill, G. B., & Hebert, R. (1997). Community screening for dementia: The Mini-Mental State Exam (MMSE) and Modified Mini-Mental State Exam (3MS) compared. *Journal of Clinical Epidemiology, 50*(4), 377-383.

McHugh, L. G., Milberg, J. A., Whitcomb, M. E., Schoene, R. B., Maunder, R. J., & Hudson, L. D. (1994). Recovery of function in survivors of the acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine, 150*(1), 90-94.

McKhann, G., Drachman, D., Folstein, M., Katzman, R., Price, D., & Stadlan, E. M. (1984). Clinical diagnosis of Alzheimer's disease: Report of the NINCDS-ADRDA Work Group under the auspices of Department of Health and Human Services Task Force on Alzheimer's Disease. *Neurology, 34*(7), 939-944.

Meyers, J. E., & Meyers, K. R. (1995). *Rey Complex Figure and Recognition trial*. Lutz, Fl: Psychological Assessment Resources.

Michel, J. A., & Mateer, C. A. (2006). Attention rehabilitation following stroke and traumatic brain injury: A review. *Europa Medicophysica, 42*(1), 59-67.

Mikkelsen, M. E., Shull, W. H., Biester, R. C., Taichman, D. B., Lynch, S., Demissie, E., et al. (2009). Cognitive, mood and quality of life impairments in a select population of ARDS survivors. *Respirology, 14*(1), 76-82. doi:10.1111/j.1440-1843.2008.01419.x

Milisen, K., Foreman, M. D., Abraham, I. L., De Geest, S., Godderis, J., Vandermeulen, E., et al. (2001). A nurse-led interdisciplinary intervention program for delirium in elderly hip-fracture patients. *Journal of the American Geriatrics Society, 49*(5), 523-532.

Morris, A. H., Wallace, C. J., Menlove, R. L., Clemmer, T. P., Orme, J. F., Jr, Weaver, L. K., et al. (1994). Randomized clinical trial of pressure-controlled inverse ratio ventilation and extracorporeal CO2 removal for adult respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine, 149*(2), 295-305.

Nieuwenhuis-Mark, R. E. (in press). The Death Knoll for the MMSE: Has It Outlived Its Purpose? *Journal of Geriatric Psychiatry and Neurology*. doi:10.1177/0891988710363714

Numa, A. H. (2001). Acute lung injury: Outcomes and new therapies. *Paediatric Respiratory Reviews, 2*(1), 22-31.

O' Connor, D. P., Pollitt, P. A., Hyde, J. B., Brook, C. P., Reiss, B. B., & Roth, M. (1988). Do general practitioners miss dementia in elderly patients? *British Medical Journal, 297*(6656), 1107-1110.

O'Bryant, S. E., Humphreys, J. D., Smith, G. E., Ivnik, R. J., Graff-Radford, N. R., Petersen, R. C., et al. (2008). Detecting dementia with the mini-mental state examination in highly educated individuals. *Archives of Neurology, 65*(7), 963-967. doi:10.1001/archneur.65.7.963

Oh, H. S., Seo, W. S., Lee, S., & Song, H. (2006). Comparisons of the prognostic predictors of traumatic brain Injury according to admission Glasgow Coma Scale scores based on 1- and 6-month assessments. *Taehan Kanho Hakhoe Chi, 36*(4), 621-629.

Orme, J., Jr., Romney, J. S., Hopkins, R. O., Pope, D., Chan, K. J., Thomsen, G., et al. (2003). Pulmonary function and health-related quality of life in survivors of acute respiratory distress syndrome. *American Journal of Respiratory and Critical Care Medicine, 167*(5), 690-694.

Osterrieth. (1944). Le teste de copie d'une figure complexe: Contribution a l'etude de la perception et la memoire. *Archives de Psychologie, 30*, 286-356.

Perl, T. M., Dvorak, L., Hwang, T., & Wenzel, R. P. (1995). Long-term survival and function after suspected gram-negative sepsis. *JAMA, 274*(4), 338-345.

Perneczky, R., Wagenpfeil, S., Komossa, K., Grimmer, T., Diehl, J., & Kurz, A. (2006). Mapping scores onto stages: Mini-Mental State Examination and Clinical Dementia Rating. *American Journal of Geriatric Psychiatry 14*(2), 139-144.

Petersen, R. C., Stevens, J. C., Ganguli, M., Tangalos, E. G., Cummings, J. L., & DeKosky, S. T. (2001). Practice parameter: Early detection of dementia: Mild cognitive impairment (an evidence-based review). Report of the Quality Standards Subcommittee of the American Academy of Neurology. *Neurology, 56*(9), 1133-1142.

Pfeffer, R. I., Kurosaki, T. T., Harrah, C. H., Jr., Chance, J. M., & Filos, S. (1982). Measurement of functional activities in older adults in the community. *Journal of Gerontology, 37*(3), 323-329.

Porter, V. R., Buxton, W. G., Fairbanks, L. A., Strickland, T., O'Connor, S. M., Rosenberg-Thompson, S., et al. (2003). Frequency and characteristics of anxiety among patients with Alzheimer's disease and related dementias. *Journal of Neuropsychiatry and Clinical Neurosciences, 15*(2), 180-186.

Quality of Life After Mechanical Ventilation in the Elderly Study Investigators. (2002). 2-month mortality and functional status of critically ill adult patients receiving prolonged mechanical ventilation. *Chest, 121*(2), 549-558.

Ravaglia, G., Forti, P., Maioli, F., Servadei, L., Martelli, M., Brunetti, N., et al. (2005). Screening for mild cognitive impairment in elderly ambulatory patients with cognitive complaints. *Aging Clin Exp Res, 17*(5), 374-379. doi:2865 [pii]

Reitan, R. M., & Davison, L. A. (1974). *Clinical neuropsychology: Current status and applications*. New York: Hemisphere.

Reitan, R. M., & Wolfson, D. (1993). *The Halstead-Reitan Neuropsychological Test Battery: Theory and clinical interpretation* (2nd ed.). Tucson, AZ: Neuropsychological Press.

Revheim, N., & Medalia, A. (2004). The Independent Living Scales as a measure of functional outcome for schizophrenia. *Psychiatric Services, 55*(9), 1052-1054.

Revheim, N., Schechter, I., Kim, D., Silipo, G., Allingham, B., Butler, P., et al. (2006). Neurocognitive and symptom correlates of daily problem-solving skills in schizophrenia. *Schizophrenia Research, 83*(2-3), 237-245.

Rey, A. (1941). L'examen psychologieque dans les cas d'ecnephalopathie traumatique. *Archives de Psychologie, 28*, 286-340.

Rothenhausler, H. B., Ehrentraut, S., Stoll, C., Schelling, G., & Kapfhammer, H. P. (2001). The relationship between cognitive performance and employment and health status in long-term survivors of the acute respiratory distress syndrome: Results of an exploratory study. *General Hospital Psychiatry, 23*(2), 90-96.

Rubenfeld, G. D., Caldwell, E., Peabody, E., Weaver, J., Martin, D. P., Neff, M., et al. (2005). Incidence and outcomes of acute lung injury. *New England Journal of Medicine, 353*(16), 1685-1693.

Ruff, R. M., & Parker, S. B. (1993). Gender- and age-specific changes in motor speed and eye-hand coordination in adults: Normative values for the Finger Tapping and Grooved Pegboard tests. *Perceptual and Motor Skills, 76*(3 Pt 2), 1219-1230.

Sacanella, E., Perez-Castejon, J. M., Nicolas, J. M., Masanes, F., Navarro, M., Castro, P., et al. (2009). Mortality in healthy elderly patients after ICU admission. *Intensive Care Medicine, 35*(3), 550-555. doi:10.1007/s00134-008-1345-8

Scanlan, J., & Borson, S. (2001). The Mini-Cog: Receiver operating characteristics with expert and naive raters. *International Journal of Geriatric Psychiatry, 16*(2), 216-222.

Schelling, G., Stoll, C., Haller, M., Briegel, J., Manert, W., Hummel, T., et al. (1998). Health-related quality of life and posttraumatic stress disorder in survivors of the acute respiratory distress syndrome. *Critical Care Medicine, 26*(4), 651-659.

Schmitz, R., Lantin, M., & White, A. (1998). *Future needs in pulmonary and critical care medicine*. Cambridge, MA: ABT Associates.

Selnes, O. A., Royall, R. M., Grega, M. A., Borowicz, L. M., Jr., Quaskey, S., & McKhann, G. M. (2001). Cognitive changes 5 years after coronary artery bypass grafting: Is there evidence of late decline? *Archives of Neurology, 58*(4), 598-604.

Senanarong, V., Cummings, J. L., Fairbanks, L., Mega, M., Masterman, D. M., O'Connor, S. M., et al. (2004). Agitation in Alzheimer's disease is a manifestation of frontal lobe dysfunction. *Dementia and Geriatric Cognitive Disorders, 17*(1-2), 14-20. doi:10.1159/000074080

Sevransky, J. E., & Haponik, E. F. (2003). Respiratory failure in elderly patients. *Clinics in Geriatric Medicine, 19*(1), 205-224.

Silverstone, P. H. (1996). Prevalence of psychiatric disorders in medical inpatients. *Journal of Nervous and Mental Disease, 184*(1), 43-51.

Silverstone, P. H., Lemay, T., Elliott, J., Hsu, V., & Starko, R. (1996). The prevalence of major depressive disorder and low self-esteem in medical inpatients. *Canadian Journal of Psychiatry. Revue Canadienne de Psychiatrie, 41*(2), 67-74.

Sjogren, P., Thomsen, A. B., & Olsen, A. K. (2000). Impaired neuropsychological performance in chronic nonmalignant pain patients receiving long-term oral opioid therapy. *Journal of Pain and Symptom Management, 19*(2), 100-108.

Skodol, A. E. (1999). Anxiety in the medically ill: Nosology and principles of differential diagnosis. *Seminars in Clinical Neuropsychiatry, 4*(2), 64-71.

Sohlberg, M. M., Ehlhardt, L., & Kennedy, M. (2005). Instructional techniques in cognitive rehabilitation: A preliminary report. *Seminars in Speech and Language, 26*(4), 268-279.

Sohlberg, M. M., & Mateer, C. A. (1989). *Introduction to cognitive rehabilitation: Theory and practice*. New York: Guilford Press.

Staley, D., & el-Guebaly, N. (1990). Psychometric properties of the Drug Abuse Screening Test in a psychiatric patient population. *Addictive Behaviors, 15*(3), 257-264. doi:0306-4603(90)90068-9 [pii]

Starr, J. M., & Whalley, L. J. (1994). Drug-induced dementia: Incidence, management and prevention. *Drug Safety: An International Journal of Medical Toxicology and Drug Experience, 11*(5), 310-317.

Stewart, A. L., Hays, R. D., & Ware, J. E., Jr. (1988). The MOS short-form general health survey. Reliability and validity in a patient population. *Med Care, 26*(7), 724-735.

Stroop, J. R. (1935). Studies of interference in serial verbal reactions. *Journal of Experimental Psychology, 18*(6), 643-662.

Suchyta, M. R., Hopkins, R. O., White, J., Jephson, A., & Morris, A. H. (2004). The incidence of cognitive dysfunction after ARDS. [Abstract]. *American Journal of Respiratory and Critical Care Medicine, 169*(7), A18.

Sukantarat, K. T., Burgess, P. W., Williamson, R. C., & Brett, S. J. (2005). Prolonged cognitive dysfunction in survivors of critical illness. *Anaesthesia, 60*(9), 847-853.

Szokol, J. W., & Vender, J. S. (2001). Anxiety, delirium, and pain in the intensive care unit. *Critical Care Clinics, 17*(4), 821-842.

Thompson, G. E., Pope, D., East, T. D., Morris, A. H., Kinder, A. T., Carlson, D. A., et al. (1994). Clinical performance of a rule-based decision support system for mechanical ventilation of ARDS patients. In C. Safran (Ed.), *Patient-centered computing: Symposium on computer applications in medical care.* (pp. 339-343). New York: McGraw-Hill.

Tuokko, H., & Hadjistavropoulos, T. (1998). *An assessment guide to geriatric neuropsychology*. Mahwah, NJ: Lawrence Erlbaum Associates.

van der Schaaf, M., Beelen, A., Dongelmans, D. A., Vroom, M. B., & Nollet, F. (2009). Functional status after intensive care: a challenge for rehabilitation professionals to improve outcome. *J Rehabil Med, 41*(5), 360-366. doi:10.2340/16501977-0333

van der Schaaf, M., Dettling, D. S., Beelen, A., Lucas, C., Dongelmans, D. A., & Nollet, F. (2008). Poor functional status immediately after discharge from an intensive care unit. *Disability and Rehabilitation, 30*(23), 1812-1818. doi:10.1080/09638280701673559

Waber, D. A., & Holmes, J. M. (1986). Assessing children's memory productions of the Rey-Osterrieth Complex Figure. *Journal of Clinical and Experimental Neuropsychology, 8*(5), 563-580.

Ware, J. E. (1993). *SF-36 health survey manual and interpretation guide*. Boston: The Health Institute, New England Medical Center.

Ware, J. E., Kosinski, M., & Keller, S. D. (1994). *SF-36 physical and mental health summary scales: A user 's manual.* Boston: The Health Institute, New England Medical Center.

Weaver, L. K., Hopkins, R. O., Chan, K. J., Churchill, S., Elliott, C. G., Clemmer, T. P., et al. (2002). Hyperbaric oxygen for acute carbon monoxide poisoning. *New England Journal of Medicine, 347*(14), 1057-1067. doi:10.1056/NEJMoa013121

Wechsler, D. (1981). *Wechsler Adult Intelligence Scale-Revised Edition manual*. New York: The Psychological Corporation.

Wechsler, D. (1997). *Wechsler Memory Scale* (3rd ed.). San Antonio, TX: The Psychological Corporation.

Wechsler, D. (1999). *Wechsler Abbreviated Scale of Intelligence manual*. San Antonio, TX: The Psychological Corporation.

Weinert, C. R. (2001). Epidemiology of psychiatric medication use in patients recovering from critical illness at a long-term acute-care facility. *Chest, 119*(2), 547-553.

Weinert, C. R., Gross, C. R., Kangas, J. R., Bury, C. L., & Marinelli, W. A. (1997). Health-related quality of life after acute lung injury. *American Journal of Respiratory and Critical Care Medicine, 156*(4 Pt 1), 1120-1128.

Weycker, D., Akhras, K. S., Edelsberg, J., Angus, D. C., & Oster, G. (2003). Long-term mortality and medical care charges in patients with severe sepsis. *Critical Care Medicine, 31*(9), 2316-2323. doi:10.1097/01.CCM.0000085178.80226.0B

Wilber, S. T., Lofgren, S. D., Mager, T. G., Blanda, M., & Gerson, L. W. (2005). An evaluation of two screening tools for cognitive impairment in older emergency department patients. *Academic Emergency Medicine, 12*(7), 612-616.

Wilkinson, G. S. (1993). *Wide Range Achievement Test-3*. Lutz, FL: PAR.

Xu, G., Meyer, J. S., Thornby, J., Chowdhury, M., & Quach, M. (2002). Screening for mild cognitive impairment (MCI) utilizing combined mini-mental-cognitive capacity examinations for identifying dementia prodromes. *International Journal of Geriatric Psychiatry, 17*(11), 1027-1033. doi:10.1002/gps.744

Young, B. (1995). Neurologic complications of systemic critical illness. *Neurologic Clinics, 13*, 645-658.

Zatzick, D., Jurkovich, G. J., Rivara, F. P., Wang, J., Fan, M. Y., Joesch, J., et al. (2008). A national US study of posttraumatic stress disorder, depression, and work and functional outcomes after hospitalization for traumatic injury. *Annals of Surgery, 248*(3), 429-437. doi:10.1097/SLA.0b013e318185a6b8

Appendix

Cognitive Screening Tests

Cognitive Screening Tests	Sensitivity and Specificity
1. Mini-Mental State Examination (M. F. Folstein et al., 1975)	Sensitivity = 88% and Specificity = 66%
2. Mini-Cog (Borson et al., 2000)	Sensitivity = 99% and Specificity = 93%

Mini-Mental State Examination (MMSE). The MMSE is a brief cognitive screening test that takes 5 to 10 minutes to administer. The MMSE consists of a series of questions and tasks in 11 cognitive categories, with a maximum score of 30 points. To increase test sensitivity, a cutoff score of < 27 was used to indicate cognitive impairments (Fischer et al., 2004; Kukull et al., 1994; O'Bryant et al., 2008). The MMSE with a cutoff score of < 27 has a test sensitivity of 88% and specificity of 66% in classifying patients with cognitive deficits (Kukull et al., 1994).

Mini-Cog. The Mini-Cog is a cognitive screening test that has been used to detect presence of dementia in older adults (Borson et al., 2000). The Mini-Cog combines uncued recall of three unrelated words with a clock drawing test. The Mini-Cog can be administered in three to five minutes, with minimal training (Scanlan & Borson, 2001). The Mini-Cog has excellent sensitivity (99%) and specificity (93%; Scanlan & Borson, 2001), and is relatively unaffected by education level and cultural background (Lorentz et al., 2002). In the current study, patients were classified as "impaired" if they recalled no word, or, recall 1 to 2 words with a clock drawing test score ≥ 1 (Scanlan & Borson, 2001).

Neuropsychological Test Battery

Domain Assessed	Test	Test-retest Reliability Coefficients
Intelligence	1. Wide Range Achievement Test-3 (Wilkinson, 1993)	.91 to .98
	2. Wechsler Abbreviated Scale of Intelligence (Wechsler, 1999)	.79 to .92
Executive function	1. Trail Making Test Part A (Reitan & Wolfson, 1993)	.79
	2. Trail Making Test Part B (Reitan & Wolfson, 1993)	.85
	3. Hayling Sentence Completion Test (Burgess & Shallice, 1997)	.52 to .78
Motor function	1. Hand Dynamometer Test (Reitan & Davison, 1974)	.52 to .96
	2. Grooved Pegboard Test (Matthew & Klove, 1964)	.67 to .86
	3. Finger Tapping Test (Halstead, 1947)	.58 to .93
Memory	1. Logical Memory subtest (Wechsler, 1997)	.70 to .79
	2. California Verbal Learning Test-II (long-delay free recall trial; Delis et al., 2000)	.80 to .89
	3. Rey-Osterrieth Complex Figure Test (30-minute delay trial; Osterrieth, 1944; Rey, 1941)	.79
Attention	Stroop Test (Interference trial; Golden, 1978)	.67
Mental processing speed	Digit Symbol subtest (Wechsler, 1981)	.82 to .88

Test of premorbid and current intelligence.

Wide Range Achievement Test-3 (WRAT-3). Premorbid intelligence was assessed with the reading subtest of the WRAT-3, a 42-word reading test that yields a standard score using the normative data in the manual (Wilkinson, 1993). The standards scores were converted into T-scores in this study. The WRAT-3 Reading subtest reliably estimates premorbid intelligence in the general population (Griffin, Mindt, Rankin, Ritchie, & Scott, 2002) and test-retest reliability coefficients range from .91 to .98 (Wilkinson, 1993).

Wechsler Abbreviated Scale of Intelligence (WASI). Patients' current intellectual functioning was assessed with the WASI, an abbreviated test of intelligence for examinees ages 6 through 89 (Wechsler, 1999). The WASI yields a Full Scale, Verbal, and Performance IQs. Data for test-retest reliability coefficients with a testing interval of 2 to 12 weeks for adults range from .87 to .92 for IQ scores (Wechsler, 1999). T-scores of the Full Scale, Verbal, and Performance IQs are calculated using the normative data in the manual (Wechsler, 1999) and describe the patient's current intelligence level.

Test of Executive Function.

Trail Making Test Part A. As part of the Halstead-Reitan Neuropsychological Battery, the Trail Marking Test Part A is a timed paper-and-pencil test that measures attention, visual scanning, and motor speed (Halstead, 1947; Reitan & Wolfson, 1993). The test requires the patient to draw a line in sequence between numbered circles scattered across the page. The score of interest is the time to completion. Normative data were provided separately for men and women and were stratified by age, education, and ethnicity (Heaton et al., 2004). A test-retest reliability coefficient of .79 was in 384 neurologically stable adults assessed over an 11-month period (Dikmen, Heaton, Grant, & Temkin, 1999).

Trail Making Test Part B. As part of the Halstead-Reitan Neuropsychological Battery, the Trail Making Test Part B measures executive function, visual scanning, motor speed, and attention (Halstead, 1947; Reitan & Wolfson, 1993). This timed test requires the patient to draw a line while alternating between numbers and letters in sequence. The score of interest is the time to completion. Normative data were provided separately for men and women and were stratified by age, education, and ethnicity (Heaton et al., 2004). A test-retest reliability coefficient of .85 was in 384 neurologically stable adults assessed over an 11-month period (Dikmen et al., 1999).

Hayling Sentence Completion Test (HSCT). The HSCT is a two-part test of executive function (Burgess & Shallice, 1997). In Part A, the patient was read a series of 15 sentences in which the last word is omitted, and must provide the word which completes the sentence. In each case, this last word is cued by the sentence content. In Part B, the patient was required to produce a word that does not fit in the sentence context, a measure of executive function (e.g., response suppression and time to respond). The score of interest is the total time of response in each Part A and Part B. Age-corrected standard score will be derived from normative data presented in the HSCT manual. Test-retest reliability values are .62 and .78 for Part A and Part B, respectively (Burgess & Shallice, 1997).

Test of Motor Function.

Hand Dynamometer Test. The Hand Dynamometer test or Grip Strength test, is used to assess the integrity of motor function (Reitan & Davison, 1974; Reitan & Wolfson, 1993). This test requires the patient to hold the dynamometer in the palm of the hand and squeeze the stirrup with the fingers as hard as possible. Two measurements within 5 kg of each other were recorded and the mean scores for each hand were calculated. Normative data are provided separately for men and women and stratified by age, education, and ethnicity (Heaton et al., 2004). Test-retest

reliability coefficients in normal individuals aged 15 years and older are .90 and .90 for dominant and nondominant hands, respectively (Dikmen et al., 1999).

Grooved Pegboard Test. The Grooved Pegboard test measures motor function and eye-hand coordination (Matthew & Klove, 1964). It consists of a metal board with a matrix of 25 holes with randomly positioned slots. Pegs have a ridge along one side and must be rotated to match the hole to be inserted. The score of interest is the time to completion for each hand. Normative data are provided separately for men and women and stratified by age, education, and ethnicity (Heaton et al., 2004). With retest intervals of about 4 to 24 months, reliability coefficients range from .67 to .86 in normal individuals aged 15 years and older (Dikmen et al., 1999; Levine, Miller, Becker, Selnes, & Cohen, 2004; Ruff & Parker, 1993).

Finger Tapping Test. The Finger Tapping Test, originally called the Finger Oscillation Test, measures motor function (Bigler & Tucker, 1981; Hom & Reitan, 1990). This test requires the patient to tap as rapidly as possible for 10 seconds using the index finger of each hand. Mean of five consecutive 10-second trials within a range of 5 taps were recorded for each hand in this study. Normative data are provided separately for men and women, and stratified by age, education, and ethnicity (Heaton et al., 2004). Reliability coefficients ranging from .58 to .93 are reported in normal samples (Bornstein, Baker, & Douglass, 1987), epileptics (Dodrill & Troupin, 1975), and chronic pain patients (Sjogren, Thomsen, & Olsen, 2000).

Test of Memory.

Logical Memory Subtest. The Logical Memory subtest from the Wechsler Memory Scale-III (WMS-III; Wechsler, 1997) is a measure of short-term and long-term verbal memory. The patient was read two stories and was asked to recall the details of each story immediately following presentation and following a 30-minute delay. The score of interest is the total number

of story details recalled both immediately and following a delay for both stories. Age-corrected standard score was derived from normative data presented in the WMS-III manual. Test-retest reliability coefficients for the Logical Memory subtest range from .70 to .79 (Wechsler, 1997).

California Verbal Learning Test-II (CVLT-II). The 20-minute delayed recall trial of the CVLT-II measures memory (Delis et al., 2000). The patients were presented 16 words from List A over 5 trials. A 16-word interference trail, List B was then presented immediately followed by a short-delay free-recall trial and cued-recall trial of List A. After a 20-minute delay, the patients were again asked to recall the words from List A (long-delay free-recall trial). The score of interest is the total number correct in long-delay free-recall trial. Age- and education-corrected standard scores are derived from normative data in the CVLT-II scoring system (Delis et al., 2000). Test-retest reliability coefficients for the long-delay free-recall trial varied from .80 to .89 (Delis et al., 2000).

Rey-Osterrieth Complex Figure Test (ROCFT). The 30-minute delayed recall trial was used to assess visual memory (Meyers & Meyers, 1995; Osterrieth, 1944; Rey, 1941; Waber & Holmes, 1986). Using a paper and pencil, the patient was required to reproduce from memory a complex figure that was previously presented during the copy trial. The score of interest is the total number of items correctly drawn using the standardized scoring procedures (Meyers & Meyers, 1995). Age-corrected standard score are derived from normative data presented in the ROCFT manual. Test-retest reliability coefficients for the 30-min delayed trials is .79 (Levine et al., 2004).

Test of Attention.

Stroop Test. The Stroop Test measures attention (Stroop, 1935). The Golden (1978) Version consists of three trials; the patient quickly read color words printed in black ink (Word-

Reading trial), named colors printed in letter "X" (Color-Naming trial), and named colors in which color words were printed (Color-Word trial). The score of interest is the Interference score as determined by contrasting the actual score on the Color-Word trial with a predicted score based on the patient's performance on the Word-Reading and Color-Naming trials (Golden, 1978). Age-corrected standard score is derived from normative data presented in the manual (Golden, 1978). Test-retest reliability coefficient is .67 for the Interference score (M. D. Franzen, Tishelman, Sharp, & Friedman, 1987).

Test of Mental Processing Speed.

Digit Symbol Subtest. The Digit Symbol subset from the Wechsler Adult Intelligence Scale-Revised (WAIS-R) was used to measure mental processing speed (Wechsler, 1981). It consists of rows containing small blank squares, each paired with a randomly assigned number from one to nine. The patient must quickly fill in the blank squares with the symbol that is paired to the number above the blank space. The score of interest is the number of items completed in 90 seconds. Normative data are provided separately for men and women, and stratified by age, education, and ethnicity (Heaton et al., 2004). Test-retest reliability are high, with correlation coefficients in the .82 to .88 range (Matarazzo & Herman, 1984; Wechsler, 1981).

Measures of Everyday Functioning

Domains Assessed	Measures	Inter-rater Reliability Coefficients
1. Shopping, transportation, climbing stairs, housework, telephone, laundry, recreation, employment, driving, meals preparation, and financial and medication management	Lawton and Brody's IADL (Lawton & Brody, 1969)	.85
2. Shopping, recreation, preparing meals, understanding current events, appointments, transportation, and managing finance and medications.	Functional Activities Questionnaires (Pfeffer et al., 1982)	.97
3. Memory, problem solving, information, social adjustment, health and safety, and financial, home, and transportation management	Independent Living Scale (Loeb, 1996)	.95 to .99

Lawton IADL. The Lawton IADL is one of the widely used self-report or informant-report IADL instrument (Brummel-Smith, 2000). It is used to assess everyday functioning including shopping, managing transportation, climbing stairs, managing finances, doing housework, using the telephone, doing the laundry, managing medications, walking outdoors, driving, holding down a paying job, and preparing meals (Lawton & Brody, 1969). Positive scores on four items – telephone use, transportation, medication management, and handling finances – correlate with diagnosis of dementia (Barberger-Gateau et al., 1992). The Lawton IADL items are scored as 0 (completely dependent), 1 (need some assistance), and 2 points (independent), and then summed for a total score ranging from 0 (cannot perform any of the functions independently) to 16 (able to perform all the functions independently). An individual score lower than 2 is considered impaired, as it indicates inability to perform the specific IADL

independently. Total scores below 16 are indicative of impairment (Lawton, 1988). Inter-rater reliability is .85 (Lawton & Brody, 1969).

Functional Activities Questionnaire (FAQ). The FAQ is a self-report or informant-report IADL instrument assessing the ability to perform 10 high-level skills used in everyday tasks, including shopping, preparing meals, handling finances, and understanding current events (Pfeffer et al., 1982). Each test item is scored on a 3-point Likert scale (0=independent; 3=dependent) of increasing caregiver dependence. The total score ranges from 0 to 30, with a higher score indicating poorer functional performance. A cutoff score of 9 or greater indicates impaired function or dependence in functional activities. Inter-rated reliability was .97 (Pfeffer et al., 1982).

Independent Living Scale (ILS). The ILS is used to assess competency in everyday functioning (Loeb, 1996). There are five subscales (Memory/Orientation, Managing Money, Managing Home and Transportation, Health and Safety, and Social Adjustment), as well as two summary scales (Problem Solving and Performance/Information). The Memory/Orientation subscale contains items including orientation to time and place, recall of a brief shopping list and doctor's appointment, and recognition of a missing object. The Managing Money subscale includes concrete tasks designed to assess monetary calculations and budgetary precautions. The Managing Home and Transportation subscale assesses abilities to use the telephone and public transportation as well as home management skills. The Health and Safety subscale assesses awareness of health problems, medical emergencies, and potential hazards around the home. The Social Adjustment subscale reflects the patient's concerns and attitudes about interpersonal relationships. The Performance/Information summary scale reflects actual knowledge or skills used to perform tasks – for example, using a telephone book or making change. The Problem

Solving summary scale evaluates abstract reasoning and judgment required for daily living (e.g., "What would you do if your lights and television went out simultaneously?" and "What would you do if you unintentionally lost ten pounds in a month?") Normative data are provided in the ILS manual. Standardized scores ranging from 20 to 39 suggest maximum (full-time) supervision for daily living (i.e., inpatient hospitalization or nursing home setting), scores from 40 to 49 suggest moderate supervision (i.e., structured community residence, adult home), and scores from 50 to 63 suggest minimum supervision or independent living on the following scales: Memory/Orientation, Managing Money, Managing Home and Transportation, Health and Safety, Social Adjustment, Problem Solving, and Performance/Information. Inter-rater reliability ranges from .95 to .99 for the subscales, factors, and full scale (Loeb, 1996).

Psychiatric Functioning

Domain Assessed	Questionnaires	Test-retest Reliability Coefficients
Depression	Beck Depression Inventory-2nd Edition (Beck et al., 1996)	.93
Anxiety	Beck Anxiety Inventory (Beck & Steer, 1993)	.62 to .75
Symptom Distress, Interpersonal Relations, and Social Role	Outcome Questionnaire-45.2 (Lambert et al., 2004)	.84 (Total Score)

Beck Depression Inventory-2nd Edition (BDI-II). The BDI-II was used to assess the presence of depression (Beck et al., 1996). Scores of 0-13 indicate *minimal*, 14-19 *mild*, 20-28 *moderate*, and 29-63 *severe* depression. Test-retest reliability correlation was .93 based on 26 outpatient clients one week apart (Beck et al., 1996).

Beck Anxiety Inventory (BAI). The BAI was used to assess presence the presence of anxiety (Beck & Steer, 1993). Scores of 0-9 indicate *minimal,* 10-16 *mild*, 17-29 *moderate*, and 30-63 *severe* anxiety. A 1-week test-retest correlation of .75 and a 7-week correlation of .62 for the BAI were reported (Beck & Steer, 1993).

Posttraumatic Diagnostic Scale (PDS). The PDS is a self-report 49-item scale that is used to assist with the diagnosis of PTSD and to provide a means of quantifying the severity of PTSD symptoms (Foa, 1995). The PDS has been validated on a clinical population aged 18 to 65 years, and has six subscales: exposure to a traumatic event, reexperiencing symptoms, avoidance symptoms, symptom duration, and the level of impairment of functioning. The PDS yields a total severity score (ranging from 0 to 51) that largely reflects the frequency of the 17 symptoms of PTSD. Scores of 0 indicate no symptom, 1-10 *mild*, 11-20 *moderate*, 21-35 *moderate to severe*, 36-51 *severe* symptoms of PTSD. A test-retest reliability coefficient of .73 was of .74 is reported, with 87.3% inter-rater reliability (Foa, 1995).

Outcome Questionnaire-45.2 (OQ-45.2). The OQ-45.2 was used to measure the patient's subjective experience, as well as the way he or she functioned in the real world (Lambert et al., 2004). The OQ-45.2 was designed for use in individuals from ages 17 through 80 years. There are three subscales (i.e., Symptom Distress, Interpersonal Relations, and Social Role), as well as a Total Score that is the sum of the subscale scores. The Symptom Distress subscale score > 36 indicates presence of significant emotional distress; Interpersonal Relations score of > 15 suggests presence of significant interpersonal problems and dissatisfaction with the quality of intimate relationships; and, Social Role subscale score > 12 indicates significant difficulties fulfilling workplace, student, or home duties. A Total Score of > 63 indicates patients are experiencing significant symptoms of distress, interpersonal difficulties, and difficulties in

social roles, and quality of life. Test-retest reliability coefficients are .78, .90, .82, and .84 for Symptom Distress, Interpersonal Relations, Social Role, and Total Score, respectively (Lambert et al., 2004). The questionnaire has three primary uses; it 1) measures current level of psychological distress; 2) measures outcome or ongoing treatment response; and 3) improves quality of patient care assessed using accompanying computer decision support tools (Lambert et al., 2004). This study assessed critically ill survivors current level of psychological distress at 6-month follow-up.

Quality of Life

The Medical Outcome Study 36-Item Short Form Health Survey (SF-36; Stewart et al., 1988; Ware, 1993; Ware et al., 1994) was administered at 6-month follow-up to assess health-related quality of life. The eight domains of the SF-36 (physical functioning, role-physical, bodily pain, general health, vitality, social functioning, role-emotional, and mental health) are clustered to form two higher order domains, the physical and mental health scores. Each domain is scored from 0 to 100, with higher scores indicating better quality of life (Ware, 1993). The SF-36 has been used in a variety of patient populations and norms for age and gender are available (Ware, 1993; Ware et al., 1994). The test-retest reliability coefficient for each domain was presented below (Brazier et al., 1992):

Domains Assessed	Test-retest Reliability Coefficients
Physical functioning	.93
Social Functioning	.74
Role Limitations (physical problems)	.88
Role Limitations (emotional problems)	.79
Pain	.84
Mental Health	.91
Vitality	.87
General Health Perception	.80