



Understanding and Reducing Disability in Older Adults Following Critical Illness*

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Objective: To review how disability can develop in older adults with critical illness and to explore ways to reduce long-term disability following critical illness.

Data Sources: We searched PubMed, CINAHL, Web of Science and Google Scholar for studies reporting disability outcomes (i.e., activities of daily living, instrumental activities of daily living, and mobility activities) and/or cognitive outcomes among patients treated in an ICU who were 65 years or older. We also reviewed the bibliographies of relevant citations to identify additional citations.

Study Selection: We identified 19 studies evaluating disability outcomes in critically ill patients who were 65 years and older.

Data Extraction: Descriptive epidemiologic data on disability after critical illness.

Data Synthesis: Newly acquired disability in activities of daily living, instrumental activities of daily living, and mobility activities was commonplace among older adults who survived a critical illness. Incident dementia and less severe cognitive impairment were also highly prevalent. Factors related to the acute critical illness, ICU practices, such as heavy sedation, physical restraints, and immobility, as well as aging physiology, and coexisting geriatric conditions can combine to result in these poor outcomes.

Conclusions: Older adults who survive critical illness have physical and cognitive declines resulting in disability at greater rates than hospitalized, noncritically ill and community dwelling older adults. Interventions derived from widely available geriatric care models in use outside of the ICU, which address modifiable risk factors including immobility and delirium, are associated with improved functional and cognitive outcomes and can be used to complement ICU-focused models such as the ABCDEs. (*Crit Care Med* 2015; 43:1265–1275)

Key Words: aging; critical illness; dementia; disability; elderly; older adults; outcomes; survivorship

For millions each year, surviving a critical illness represents a life-altering event punctuated by physical and cognitive impairments resulting in new-onset disability (1–8). Patients of all ages are affected (8–10). Older adults (i.e., those 65 years or older), however, bear the lion's share of this burden as the demographic most likely to become critically

ill (11–14). Moreover, because the majority of patients with critical illness are older adults, the aging of the population in coming years is expected to drive a significant increase in the number of critical illness survivors with physical impairments, cognitive impairments, and disabilities (5, 7, 14, 15).

Regardless of age, critical illness survival implies resolution of the underlying illness, yet age may play an important role. In the case of respiratory failure, for example, older adults achieve physiologic recovery from their illness at least as fast as their younger counterparts (16, 17). After adjusting for potential confounders such as severity of illness, however, older adults are more likely to remain intubated and in the ICU (17). These data imply that ongoing and destructive processes—apart from those that resulted in the development of critical illness—may be responsible for poor physical and cognitive outcomes experienced by many older adults.

Critical illness survival also exists on a spectrum ranging from those who are free of disability to those who are severely disabled, a number of whom are “chronically critically ill” or “hospital dependent” (18–21). Why some patients “successfully” recover from critical illness, whereas others do not is unknown. Thus, a better understanding of the contributions to poor long-term physical and cognitive functioning that results in disability is needed to improve the lives of the growing number of older adults who survive a critical illness each year.

The disabling process results from the complex interrelationship between a patient’s preillness vulnerability and the acute stress of a critical illness and treatment in an ICU (22). In older adults, the normal aging process, also known as senescence, in combination with systemic pathology from comorbid medical conditions, injuries, environmental, and epigenetic factors can reduce physiologic reserves and the ability to “bounce back” from an acute stressor (23–25). Thus, a highly vulnerable patient (e.g., one who is frail or physically or cognitively impaired before their illness) may develop disability following a less severe illness (e.g., urinary tract infection).

Alternatively, a more robust patient who is less vulnerable will require a greater insult (e.g., septic shock with multiple organ failures) before developing disability.

This article, written by an interdisciplinary team of experts in critical care, geriatrics and gerontology, presents an integrative literature review of the epidemiology of disability in survivors of a critical illness; reviews how critical illness, in the setting of the physiology of aging, can result in disability following a critical illness; and, finally, presents expert opinion on steps that can be taken to make the ICU a more “friendly” place for older adults, with the ultimate goal of reducing the component of post-ICU suffering that is long-term disability.

THE DEVELOPMENT OF POSTCRITICAL ILLNESS DISABILITY

Optimizing long-term outcomes for survivors of critical illness must begin with a discussion of the disabling process in the setting of critical illness. This understanding will allow researchers and clinicians to communicate using the same terminology, to gain insights into how diseases and treatments may affect outcomes, to define better outcomes of importance to patients, and, eventually, to enhance clinical care.

Although different conceptual models exist to describe the disabling process, the framework originally proposed by Nagi (26), modified by Verbrugge and Jette (27), provides a robust, informative way to understand how critical illness may lead to disability. According to this model, diseases or injuries (*pathology*) result in dysfunction of body systems (*impairments*) leading to the inability to perform basic physical and cognitive functions (*functional limitations*) that alter the individual’s capability to meet the demands of his or her environment (*disability*) (Fig. 1). Hence, disability, simply defined, represents the difference between a person’s capabilities and the demands of a particular physical or social environment (27, 28).

To illustrate this process, let us explore a hypothetical case of Mrs. D, a 67-year-old widow who, prior to her illness, lived inde-

pendently and was employed as an executive secretary (Fig. 1). She developed pneumococcal pneumonia and severe sepsis (*pathology*) and was mechanically ventilated in the ICU for 7 days. She was sedated and confined to bed for the first 5 days of her illness and suffered 6 days of delirium while in the ICU (*pathology*). Following extubation, the ICU physical therapist notes that Mrs. D has significant muscle atrophy and weakness that is attributed to ICU-acquired weakness (*impairment*). With her delirium now resolved, Mrs. D’s daughter expresses concerns that her mother is having

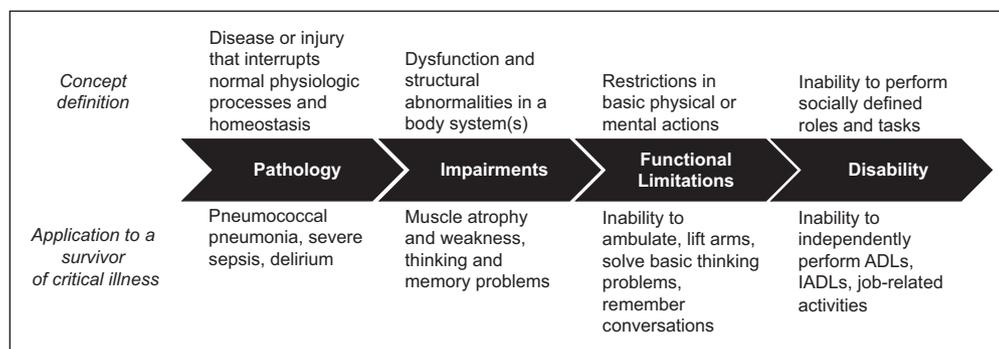


Figure 1. A conceptual model of the disablement process and its application to a survivor of a critical illness. This framework illustrates how diseases (pathology) result in body system dysfunction (impairments) that limits an individual’s ability to perform basic actions (functional limitations) and prevent that individual from performing socially expected activities (disability). When applied to a hypothetical survivor of critical illness, the effects of critical illness alter the functioning of skeletal muscle and the brain to result in the inability to move one’s arms and legs, as well as to remember and think clearly, preventing the patient from carrying out activities necessary to live independently such as basic activities of daily living (ADLs; dressing, bathing, walking across a room), instrumental ADLs (IADLs; managing money, cooking a meal), or to remain used. Adapted with permission from Verbrugge and Jette (1). Adaptations are themselves works protected by copyright. So in order to publish this adaptation, authorization must be obtained both from the owner of the copyright in the original work and from the owner of copyright in the translation or adaptation.

trouble thinking and remembering things (*impairment*). She notes that Mrs. D was “sharp as a tack” prior to her illness. After being transferred out of the ICU, Mrs. D continues to require assistance to ambulate and to lift her arms (*functional limitation*). She complains that she cannot complete crossword puzzles that she did easily before her illness and that she cannot recall the details of conversations with her family (*functional limitation*). As discharge planning progresses, Mrs. D’s daughter is nervous that her mother will be unable to manage her medications and her finances (*disability in instrumental activities of daily living* [IADLs]). She continues to require assistance to bathe, dress, and transfer from the bed to a chair (*disability in basic activities of daily living* [ADLs]). As a result of these newly acquired disabilities, Mrs. D is discharged to a skilled nursing facility, where she still resides 1 year later. She is unable to return to work (*disability in employment*).

EPIDEMIOLOGY OF DISABILITY FOLLOWING CRITICAL ILLNESS

The declines in Mrs. D’s physical and cognitive functioning represent a common scenario for the estimated 1.4 million older adults in the United States (and many more worldwide) who survive a critical illness each year (6). We searched PubMed, CINAHL, Web of Science, and Google Scholar for studies reporting disability outcomes (i.e., ADLs, instrumental ADL [IADLs], and mobility activities) and/or cognitive outcomes among patients treated in an ICU who were 65 years or older. We also reviewed the bibliographies of relevant citations to identify additional citations. Overall, 19 studies met these criteria (2, 3, 29–45): 17 studies reported disability outcomes (2, 29–38, 40–42, 44), two studies reported cognitive outcomes (3, 45), and two studies reported both (39, 43).

Of the studies that reported disability outcomes (Table S1, Supplemental Digital Content 1, <http://links.lww.com/CCM/B223>), 13 were single-center cohorts and 12 enrolled fewer than 300 patients. Patients were enrolled from mixed (medical and surgical) ICUs in 11 studies, from medical ICUs in four studies, and from surgical ICUs in two studies. The mean age of patients enrolled in the studies ranged from 69 to 89 years. Most (10 of 14) of the studies that assessed ADL function used the Katz ADL (46), two studies used the Barthel Index (47), and two other studies used other measures. All four studies that assessed IADLs used the Lawton Index (48). Of the three studies that assessed mobility status (2, 35, 44), each used different scoring measures (35, 49, 50). Most studies assessed outcomes less than 12 months following critical illness.

Disability in ADLs was highly prevalent after a critical illness and was present in 33% to 58% of patients when follow-up occurred less than 3 months after the index illness and 12% to 97% for follow-up time points occurring more than 6 months after the index illness. Among the nine studies that reported baseline (preillness) ADL function, new-onset or worsened ADL disability was present in 10% to 63% of patients assessed less than 1 year after their critical illness and in 22% to 37% of patients assessed at 1 year or later (29, 31, 34–37, 40–43). New or worsened IADL disability was also common and reported in 22% to 45% of patients evaluated 3 months to 2 years following

the index illness (34, 38, 43). A single study where a number of patients were disabled in ADLs and IADLs at baseline (43% and 60%, respectively) reported no change in disability at 3-month follow-up (42). Finally, disability in mobility activities (i.e., moving around one’s home, walking half a mile, walking up and down stairs) was present in 14% to 87% of patients assessed during the first year following their index illness.

Of the four studies that assessed cognitive outcomes, two were single-center cohorts. Each study used a different outcome measure and assessed cognition at time points ranging from 3 months to 8 years following the index illness (Table S2, Supplemental Digital Content 1, <http://links.lww.com/CCM/B223>) (3, 39, 43, 45). Three of four studies assessed preillness cognitive functioning and reported newly developed (i.e., incident) dementia in 12% to 18% of patients who were assessed between 1 and 8 years after their illness (3, 39, 45). Prevalent dementia (i.e., preillness dementia status was unknown) was reported in 15% of patients at hospital discharge and in 10% at 1-year follow-up (43). In addition to the prevalence of dementia, one study also reported newly acquired mild to moderate cognitive impairment was present in 56% of patients, yielding an overall proportion of cognitive impairment plus dementia of 73% of patients 4 years after critical illness (39).

The findings of this review indicate that disability in ADLs, IADLs, and mobility is common among older adults who survive a critical illness. They also highlight the substantial burden of newly acquired cognitive impairment and dementia following critical illness. Nevertheless, several limitations of these studies are worthy of mention. First, few studies have reported data on these important patient-centered outcomes after critical illness. Second, the majority of these studies are small, single-center cohorts that used heterogeneous assessment methods with follow-up time points that varied widely. Third, although some studies reported data on patients’ preillness disability, physical, and/or cognitive functioning, the majority did not. Thus, the lack of information on the trajectories of preillness disability and cognitive functioning may bias the results and the true effect of critical illness on these outcomes remains unclear (51). Nevertheless, the rates of postcritical illness disability reported in these studies are substantially higher than community dwelling persons (52–54) and older adults who are hospitalized without critical illness (55, 56). Finally, because disability and dementia are associated with mortality in older adults, the results of these studies likely underestimate the true burdens of these conditions following critical illness due to the large number of patients who were not included in follow-up assessments due to the competing risk of death.

INTERSECTIONS OF AGING PHYSIOLOGY AND CRITICAL ILLNESS

Some older adults who carry a low-burden of aging-related disease and disability remain highly functional, and can be thought of as aging “successfully” (57, 58). For the vast majority, however, “normal” aging is characterized by a progressive accumulation of molecular and cellular damage due to illness, injury, environmental, and epigenetic factors that lead to physiologic impairments of organ systems and an increased risk of disease,

disability, and death (23, 24). The rate of this decline of organ systems is controlled by homeostatic maintenance and repair mechanisms (23). Over time, maintenance and repair functions lose complexity, and maladaptive stress responses alter the body's ability to maintain homeostasis. The degree to which these functions are altered varies from person to person and from organ system to organ system and may explain, in part, variations in the speed of aging (23). Accelerated decline of homeostatic mechanisms, which often characterizes the geriatric condition known as frailty, is present in up to one third of all older adults and leads to a state of increased vulnerability and disproportionate changes in functional and cognitive status following an acute stressor, such as critical illness (59–64).

Although aging-related alterations to homeostatic mechanisms occur in nearly all organ systems, in the context of critical illness, changes to the structure and function of skeletal muscle and/or the brain place older patients at increased risk of developing newly acquired and/or worsened disability. The effects of critical illness on other organ systems, such as the aging cardiovascular, pulmonary, and renal systems, have been described elsewhere (65–67).

Aging Skeletal Muscles in Critical Illness

Roughly half of persons who are 65 years or older have clinically significant diminished skeletal muscle mass and strength due to age-related changes known as sarcopenia (68). The causes of sarcopenia are multifactorial and include disuse atrophy, changes in endocrine function, inflammation, and nutritional deficiencies (68, 69). Sarcopenia is characterized by a decrease in the size, number, and composition of muscle fibers, remodeling of motor units, increased intramuscular lipid concentration, inflammation, oxidative stress, and loss of anabolic stimuli (70, 71). The end result of sarcopenia is reduced muscle power and strength, progressive weakness, fatigue, slow gait speeds, and difficulty ambulating long distances (68, 70, 72). Sarcopenia is associated with a variety of poor clinical outcomes including increased length of hospital stay, hospital readmission, and death (73–76).

During critical illness, inflammation alters the atrophy-hypertrophy-signaling pathways within skeletal muscle, resulting in acute muscle wasting in the first few days of illness, particularly among those with multiple organ failures (77–79). This imbalance between muscle breakdown and recovery represents an additional degenerative insult that cannot be appropriately countered in aging muscle and may, in part, explain the higher prevalence of ICU-acquired weakness among older patients (78, 80).

Immobility, even among patients who were ambulatory prior to their illness, is common during hospitalization (81–83). For patients of all ages, bed rest results in losses in muscle mass, strength, and aerobic capacity (84); yet, these losses are accelerated by roughly a factor of three among older adults (85). In noncritically ill older patients, even short periods (e.g., 1–2 d) of reduced activity or bed rest can result in disability and nursing home admission (86, 87).

Thus, the skeletal muscles of older adults in the ICU face the concurrent insults of inflammation and bed rest, which are intensified by both the severity and the duration of the underlying critical

illness. The end result is muscle atrophy, weakness, and diminished aerobic capacity, contributing to the inability to perform basic self-care activities (i.e., disability) following critical illness.

The Aging Brain in Critical Illness

Aging results in a variable trajectory of declines in cognitive abilities, particularly in working memory, short-term memory, and processing speed (88–90). In the aging brain, oxidative stress, epigenetic factors, diminished autophagy, decreased insulin/insulin-like growth factor-1 signaling, impaired stress responses and clearance of toxic proteins in combination alter hormonal and immunologic feedback mechanisms (89, 91–95). Loss of these feedback mechanisms can result in exuberant inflammatory responses to acute stress, resulting in neurodegeneration, which then drives additional inflammation. Thus, the aging brain can be caught in a vicious cycle that, over time, results in neuronal loss and clinically significant cognitive decline.

The acute stress of critical illness and age-related changes to the brain makes critically ill older adults particularly susceptible to developing delirium (96). Delirium results from the complex interaction of a patient's underlying vulnerability, neurotransmitter imbalances, inflammatory responses, oxidative stress, physiologic stressors, and metabolic derangements that result in the large-scale disruption of neural networks, resulting in fluctuating acute confusion, altered consciousness, inattention, and disorganized thinking (96–100).

In some cases, delirium may resolve without long-term consequences. Nevertheless, evidence now supports an association between delirium and long-term cognitive sequelae, including dementia and accelerated cognitive decline (8, 101–103). In critically ill patients, delirium duration is one of the strongest independent predictors of significant cognitive deficits after critical illness (8, 104). Although the precise mechanisms are unclear, it is hypothesized that delirium, triggered by an acute insult, initiates or exacerbates the pathologic age-related structural, immune, neurochemical, and neurohormonal brain changes, resulting in a cycle of neuroinflammation and neurodegeneration leading to cognitive impairment (95, 105, 106).

REDUCING POSTCRITICAL ILLNESS DISABILITY

Postcritical illness disability results from the interaction of a patient's baseline health status and vulnerability to the acute stress of critical illness with the effects of the acute illness itself and treatment practices during and after the ICU admission (55, 107, 108). Thus, because it is not (yet) possible to prevent aging, to reverse vulnerability in the setting of critical illness which is most often an unplanned event, or to completely avoid critical illness-related organ system impairments, the focus of preventing disabilities should lie with the identification of critically ill patients who are at risk for developing/exacerbating disabilities and in addressing specific iatrogenic contributors to postcritical illness disability.

Identifying High-Risk Older Patients

Outside the ICU, several tools exist to identify patients at risk for posthospital disability (109–112). Although the content of these tools differs slightly, each incorporates the patient's preillness functional and cognitive status, highlighting the important contribution of baseline status to posthospital outcomes. Despite an association with improved survival and ability to reside in their own home following a hospitalization (113), few hospitalized older adults undergo functional and cognitive status assessments during hospitalization (114). This practice is even less common in the ICU, where few clinicians have training in assessment

techniques. Additional barriers to functional and cognitive status assessment in critically ill patients include the inability of many patients to communicate directly due to endotracheal tubes, sedation, and/or delirium, as well as time constraints of the busy ICU workflow. These barriers, however, may be overcome using a pragmatic functional and cognitive assessment adapted for the unique needs of critically ill patients (Table 1).

Addressing Modifiable Risk Factors for Disability

Two of the most common and modifiable risk factors for subsequent functional and cognitive decline are immobility and

TABLE 1. Pragmatic Functional and Cognitive Assessment for Older Adults With Critical Illness

	Domain Assessed		
	Activities of Daily Living	Mobility	Cognition
As soon as possible after ICU admission (use surrogate to obtain information, as needed)	Katz ADL Index (46) ^a : Is assistance required to 1) Bathe or shower 2) Get dressed 3) Get to the restroom 4) Transfer from bed to chair 5) Control bladder or bowels 6) Eat a meal Consider high risk for postcritical illness disability if requires assistance to complete any ADL	Sit → stand → walk Assess patient's ability to 1) Sit up in bed 2) Stand at edge of bed 3) Walk a few feet (using assistive devices if needed) Consider high risk for postcritical illness disability if unable to get out of bed and stand	If patient alert and nondelirious: mini-Cog or if patient comatose or delirious: IQCODE (perform with surrogate) Mini-Cog (158): 1) Three-item recall (e.g., banana, sunrise, and chair) 2) ask patient to draw a clock face showing the time as 11:10 (patient should draw circle, numbers, and hands at appropriate time) 3) ask patient to recall three words (one point for each correct word, two points for correct clock) Consider high risk for postcritical illness disability if scores < 2 points IQCODE (159) ^a : 16-question tool comparing current cognitive functioning to 10 years ago (supplementary materials, Supplemental Digital Content 1, http://links.lww.com/CCM/B223) for IQCODE questionnaire. (Scores range from 1 to 5, where 1 indicates much improved functioning, 5 indicates much worse functioning, and 3 indicates no change) Consider high risk for postcritical illness disability if scores 3.44 or greater
Daily while in ICU	Have patient perform ADLs. Directly observe or obtain information from patient's family, bedside nurses, physical, or occupational therapists. Consider high risk for postcritical illness disability if requires assistance to complete any ADL	Sit → stand → walk Directly observe or obtain information from patient's family, bedside nurses, physical, or occupational therapists. Consider high risk for postcritical illness disability if requires assistance to get out of bed and stand	Delirium screening Use Confusion Assessment Method for the ICU or Intensive Care Delirium Screening Checklist Each day of delirium increases risk for postcritical illness disability

ADL = activities of daily living, IQCODE = Informant Questionnaire on Cognitive Decline in the Elderly

^aThe complete Katz Index of Activities of Daily Living instrument and the Informant Questionnaire on Cognitive Decline in the Elderly instrument are available in the supplementary materials (Supplemental Digital Content 1, <http://links.lww.com/CCM/B223>).

delirium. Immobility is an “under-recognized epidemic” among hospitalized older adults with deleterious effects on subsequent physical and cognitive function (62, 87, 115, 116). Delirium, present in up to 80% of all mechanically ventilated patients, is among the strongest predictors of subsequent cognitive impairment and also contributes to long-term disability in ADLs (8, 104, 117, 118). Both immobility and delirium exacerbate underlying age-related physiologic changes; thus, efforts to shorten their duration (or prevent their occurrence all together) can have substantial impacts on postcritical illness outcomes (116, 119, 120).

For over half a century, the untoward effects of immobility and delirium have been the focus of clinicians caring for hospitalized older adults outside of the ICU, yet only recently has become the focus of those caring for the critically ill (108, 121–128). Thus, geriatricians have had a significant head start in preventing and managing immobility and delirium through interdisciplinary “geriatric care models” (119, 129–132). Within the past decade, however, ICU-focused interdisciplinary strategies, such as the “ABCDE bundle,” have been described and implemented (133–138). Using a synthesis of the literature and expert opinion, we now will discuss how components of geriatric care models can be used to complement the ABCDE bundle and other “best practices” of ICU care.

Recommended Interventions to Improve Functional and Cognitive Outcomes

Members of the ICU team should assess a patient’s functional and cognitive status as soon as possible after admission either through direct patient evaluation or from the patient’s surrogate, to identify patients at high risk for postcritical illness disability. In addition, because functional and cognitive status can fluctuate during a hospitalization, daily monitoring should be performed to alert clinicians to potential changes.

The ABCDE bundle is advocated by a number of professional societies including the Society for Critical Care Medicine and combines evidence-based strategies to reduce the harms associated with sedation, mechanical ventilation, delirium, and immobility in critically ill patients of all ages. Although a complete description of each of the components of the ABCDE bundle is beyond the scope of this review, excellent resources that detail the specific components of the ABCDE bundle and the evidence behind them are available at both <http://www.iculiberation.org> and <http://www.icudelirium.org>. Briefly, the ABCDE bundle includes daily spontaneous Awakening and spontaneous Breathing trial Coordination (“ABC”), Choosing to sedate patients only when necessary and to “lighter” levels (“C”), screening for Delirium (“D”), and the Early mobilization/physical and occupational therapy (“E”). Implementation of the ABCDE bundle is independently associated with a doubling of the odds of a patient being mobilized out of bed and a 45% decrease in the odds of developing delirium (139). In addition, individual components of the ABCDEs are associated with improved functional status at hospital discharge and decreased mortality following critical illness (116, 140).

Older adults, however, face additional risk factors for poor functional and cognitive outcomes not addressed by the ABCDE

bundle, including social isolation, enforced dependence in ADLs, restraints, poor nutrition, polypharmacy, and unnecessary medical tests and procedures (119, 129, 132). To address these risk factors, three widely implemented “geriatric care models”—The Acute Care for Elders model, the Hospital Elder Life Program, and the Nurses Improving Care for Healthsystem Elders—were developed (119, 129, 132). The specific interventions contained in these programs differ; yet, each addresses the risk factors faced more commonly by older adults. In general, each care model reduces falls, prevents functional decline, decreases the proportion of patients who develop delirium, shortens hospital length of stay, and increases the likelihood of being discharged to home (130, 141). Whether these same outcomes can be achieved in older adults who are critically ill is an area in need of further research.

Nevertheless, given their association with improved outcomes in less-severely ill older adults, we propose a group of evidence-based interventions that can be used to complement existing ICU best-practices and care bundles to reduce functional and cognitive decline among older adults with critical illness (Fig. 2). Because ICUs differ with regard to the specifics by which patient care is delivered, there is no one-size-fits-all approach to implementing these suggested interventions. Yet, because one common thread running through modern ICU practice is close, collaborative interdisciplinary patient care, the ICU serves as an ideal environment to adapt and implement components of these geriatric care models. For example, preventing inappropriate medication use requires cooperation between physicians, pharmacists, and bedside nurses each of whom contribute to the process of ordering, dispensing and administering medications, and communicating these changes to the next level of care. Technologies ranging from simple checklists, to electronic medical records, computerized dashboards, and telemedicine have been used to augment therapeutic intervention delivery in severe sepsis and prevent iatrogenic harms such as central line infections and thus could serve as a model for implementing the proposed interventions (142–145).

The aforementioned assessment tools and interventions are intended to be a pragmatic approach to caring for critically ill older adults; thus, they are far from comprehensive. To address the specific age-related issues that affect over half of all ICU patients better (1), critical care clinicians are encouraged to further their knowledge of clinical geriatrics and to seek help from experts trained in the care of older adults. Several educational resources are available both in print (e.g., American Geriatrics Society’s *Geriatrics at your Fingertips*) (146) and online (e.g., the Portal of Geriatrics Online Education [www.pogoe.org] and the Hartford Institute for Geriatric Nursing’s “Try This” series [www.hartfording.org/practice/try_this]). ICU clinicians and educators seeking to develop even greater expertise in the care of older adults may be eligible for “mini-fellowships” in geriatrics sponsored by the Donald W. Reynolds Foundation, which provide intensive courses in geriatrics and geriatrics education as well as follow-up support to enhance these endeavors (147). In the future, the development of collaborative training programs between critical care medicine and geriatrics, two specialties that already share a number of overlapping “Entrustable Professional

Suggested enhancements to make the ICU more 'friendly' for older adults with critical illness	
<p style="text-align: center;">Environment</p> <p><u>Risk Factor</u> <i>Sensory Deprivation</i></p> <ul style="list-style-type: none"> • Vision aids (eye glasses & magnifying glasses) • Hearing aids (portable amplifying devices & hearing aids) <p><i>Disorientation</i></p> <ul style="list-style-type: none"> • Clocks with large numbers • Single date calendar or day/date visible on white board • Names of care team visible on white board • Frequent orientation to surroundings <p><i>Sleep disruption</i></p> <ul style="list-style-type: none"> • Reduce nighttime noise and light (pagers on vibrate, quiet hallways, dim lights, turn off TVs) • Adjust care schedules to allow sleep (reschedule medications & procedures) 	<p style="text-align: center;">Medical Care</p> <p><u>Risk Factor</u> <i>Polypharmacy/ psychoactive medications</i></p> <ul style="list-style-type: none"> • Avoid potentially inappropriate medications, particularly sedative-hypnotics • See http://www.americangeriatrics.org/files/documents/beers/2012BeersCriteria_JAGS.pdf <p><i>Unnecessary tests and procedures</i></p> <ul style="list-style-type: none"> • Consider need for routine labs/blood draws, central lines, bladder catheters, iv fluids, iv medications, supplemental oxygen • Avoid procedures and tests that will not alter management <p><i>Unclear patient wishes/ goals of care</i></p> <ul style="list-style-type: none"> • Have frequent and ongoing discussions regarding patient wishes/ goals of care • Establish thresholds for continuation/ discontinuation of medical therapies
<p style="text-align: center;">Patient-centered care</p> <p><u>Risk Factor</u> <i>Social Isolation</i></p> <ul style="list-style-type: none"> • Encourage family/partner/friend visitation, including overnight visitation • Cognitive stimulating activities (discuss current events, structured reminiscence, word games) <p><i>Reduced mobility/ encouraged dependence</i></p> <ul style="list-style-type: none"> • Avoid 'bed rest' orders • Have patients perform ADLs, as able • Ensure prosthetics/assistive devices available • Early PT/OT within 72 hours of admission <p><i>Undernutrition/ dehydration</i></p> <ul style="list-style-type: none"> • Meet daily caloric and fluid needs • Ensure dentures/dental appliances available • Avoid NPO, • Start enteral feeding within 48 of admission <p><i>Sleep deprivation</i></p> <ul style="list-style-type: none"> • Warm milk/herbal tea, relaxation music, massage • Avoid pharmacologic sleep agents 	<p style="text-align: center;">Post-hospital care planning</p> <p><u>Risk Factor</u> <i>No planning for return to home</i></p> <ul style="list-style-type: none"> • Focus on 'planning for home' • Assess what is needed to return home throughout ICU stay • Include social workers and home health nurses in assessment, if indicated • Transfer to specialized geriatric unit such as ACE or GEM unit, if available <p><i>Chronic critical illness</i></p> <ul style="list-style-type: none"> • Utilize prognostic scores such as ProVent (<i>Crit Care Med</i> 2012;40;1171-1176) to guide goals of care discussions with patients and proxy decision makers for patients with chronic critical illness (mechanically ventilated for ≥21 days or new tracheostomy) <p><i>Unclear patient wishes/goals of care</i></p> <ul style="list-style-type: none"> • Substantial mortality in the first year after a critical illness warrants ongoing goals of care discussions.

Figure 2. Interventions adapted for the ICU from geriatric care models may be used to improve care for older adults with critical illness. PT/OT = physical and occupational therapy, ACE = acute care for elders, GEM = geriatric evaluation and management.

Activities" (148–150), will enable trainees to face the important challenges of caring for older adults with critical illness better.

Finally, co-management strategies, such as the hip fracture "Orthogeriatric" model (i.e., co-management by both the orthopedic surgeon and a geriatrician) have been used to improve outcomes, including reductions in delirium and length of stay, improve functional status and mortality among older adults could serve as a potential care model for older adults in the ICU (151–154).

DIRECTIONS FOR FUTURE RESEARCH

Today, older adults who survive a critical illness are having the burdens of disability, physical, and/or cognitive impairments that previous generations did not face due to death and effective interventions are needed to aid this growing segment of the population. The central role that hospitalization for a critical illness plays in the development of disability afterward is becoming clear. Nevertheless, additional research is needed to understand how the trajectory of a patient's preillness functional status, as well as factors relating to the patient's critical illness, and ICU treatment result in postcritical illness disabilities better. In addition, deeper knowledge of the unique

contributions of post-ICU physical and cognitive dysfunction and mental health impairments to the disabling process should be sought. Interventions that can be implemented throughout the continuum of critical illness from the earliest days in the ICU to a variety of post-ICU settings (e.g., hospital ward, rehabilitation facilities, nursing facilities, and home) to prevent, treat, and rehabilitate disabilities in this vulnerable and growing segment of the population should be studied and implemented. Although in need of testing in survivors of critical illness, physical exercise, resistance training, and nutritional supplementation, which are effective in improving physical functioning among those with aging-related muscle loss (e.g., sarcopenia) (155) as well as cognitive rehabilitation that is associated with improve cognitive functioning in patients with acquired brain injuries (e.g., traumatic brain injury and stroke) (156, 157), may serve as readily available platforms by which to reduce disability after critical illness.

CONCLUSIONS

For the 1.4 million older adults in the United States (and many more worldwide) who survive a critical illness each year, the subsequent months and years are fraught with significant

declines in functional and cognitive status, resulting in long-term disability for as many as two of every three patients. We argue that aging physiology, complications of critical illness, and common ICU practices contribute significantly to the development of postcritical illness disability.

Interventions derived from widely available geriatric care models in use outside of the ICU, which address modifiable risk factors including immobility and delirium, are associated with improved functional and cognitive outcomes and can be used to complement ICU-focused models such as the ABCDEs.

REFERENCES

- Angus DC, Shorr AF, White A, et al; Committee on Manpower for Pulmonary and Critical Care Societies (COMPACCS): Critical care delivery in the United States: Distribution of services and compliance with Leapfrog recommendations. *Crit Care Med* 2006; 34:1016–1024
- Barnato AE, Albert SM, Angus DC, et al: Disability among elderly survivors of mechanical ventilation. *Am J Respir Crit Care Med* 2011; 183:1037–1042
- Ehlenbach WJ, Hough CL, Crane PK, et al: Association between acute care and critical illness hospitalization and cognitive function in older adults. *JAMA* 2010; 303:763–770
- Iwashyna TJ, Ely EW, Smith DM, et al: Long-term cognitive impairment and functional disability among survivors of severe sepsis. *JAMA* 2010; 304:1787–1794
- Angus DC, Kelley MA, Schmitz RJ, et al; Committee on Manpower for Pulmonary and Critical Care Societies (COMPACCS): Caring for the critically ill patient. Current and projected workforce requirements for care of the critically ill and patients with pulmonary disease: Can we meet the requirements of an aging population? *JAMA* 2000; 284:2762–2770
- Wunsch H, Guerra C, Barnato AE, et al: Three-year outcomes for Medicare beneficiaries who survive intensive care. *JAMA* 2010; 303:849–856
- Iwashyna TJ, Cooke CR, Wunsch H, et al: Population burden of long-term survivorship after severe sepsis in older Americans. *J Am Geriatr Soc* 2012; 60:1070–1077
- Pandharipande PP, Girard TD, Jackson JC, et al; BRAIN-ICU Study Investigators: Long-term cognitive impairment after critical illness. *N Engl J Med* 2013; 369:1306–1316
- Herridge MS, Tansey CM, Matté A, et al; Canadian Critical Care Trials Group: Functional disability 5 years after acute respiratory distress syndrome. *N Engl J Med* 2011; 364:1293–1304
- Hopkins RO, Weaver LK, Collingridge D, et al: Two-year cognitive, emotional, and quality-of-life outcomes in acute respiratory distress syndrome. *Am J Respir Crit Care Med* 2005; 171:340–347
- Rubinfeld GD, Caldwell E, Peabody E, et al: Incidence and outcomes of acute lung injury. *N Engl J Med* 2005; 353:1685–1693
- Angus DC, Wax RS: Epidemiology of sepsis: An update. *Crit Care Med* 2001; 29:S109–S116
- Kumar G, Kumar N, Taneja A, et al; Milwaukee Initiative in Critical Care Outcomes Research Group of Investigators: Nationwide trends of severe sepsis in the 21st century (2000–2007). *Chest* 2011; 140:1223–1231
- Carson SS, Cox CE, Holmes GM, et al: The changing epidemiology of mechanical ventilation: A population-based study. *J Intensive Care Med* 2006; 21:173–182
- U.S. Census Bureau: Population Projections [online]. 2010. Available at: <http://www.census.gov/population/projections/>
- Ely EW, Evans GW, Haponik EF: Mechanical ventilation in a cohort of elderly patients admitted to an intensive care unit. *Ann Intern Med* 1999; 131:96–104
- Ely EW, Wheeler AP, Thompson BT, et al: Recovery rate and prognosis in older persons who develop acute lung injury and the acute respiratory distress syndrome. *Ann Intern Med* 2002; 136:25–36
- Nelson JE, Cox CE, Hope AA, et al: Chronic critical illness. *Am J Respir Crit Care Med* 2010; 182:446–454
- Nelson JE, Tandon N, Mercado AF, et al: Brain dysfunction: Another burden for the chronically critically ill. *Arch Intern Med* 2006; 166:1993–1999
- Kahn JM, Benson NM, Appleby D, et al: Long-term acute care hospital utilization after critical illness. *JAMA* 2010; 303:2253–2259
- Reuben DB, Tinetti ME: The hospital-dependent patient. *N Engl J Med* 2014; 370:694–697
- Gill TM: Disentangling the disabling process: Insights from the precipitating events project. *Gerontologist* 2014; 54:533–549
- Kirkwood TB: Understanding the odd science of aging. *Cell* 2005; 120:437–447
- López-Otín C, Blasco MA, Partridge L, et al: The hallmarks of aging. *Cell* 2013; 153:1194–1217
- Quinlan N, Marcantonio ER, Inouye SK, et al: Vulnerability: The crossroads of frailty and delirium. *J Am Geriatr Soc* 2011; 59(Suppl 2):S262–S268
- Committee on a National Agenda for the Prevention of Disabilities IoM. Disability in America: Toward a National Agenda for Prevention. Washington, DC: National Academy Press, 1991
- Verbrugge LM, Jette AM: The disablement process. *Soc Sci Med* 1994; 38:1–14
- Jette AM: Toward a common language for function, disability, and health. *Phys Ther* 2006; 86:726–734
- Parno JR, Teres D, Lemeshow S, et al: Two-year outcome of adult intensive care patients. *Med Care* 1984; 22:167–176
- Mahul P, Perrot D, Tempelhoff G, et al: Short- and long-term prognosis, functional outcome following ICU for elderly. *Intensive Care Med* 1991; 17:7–10
- Kass JE, Castriotta RJ, Malakoff F: Intensive care unit outcome in the very elderly. *Crit Care Med* 1992; 20:1666–1671
- Chelluri L, Pinsky MR, Donahoe MP, et al: Long-term outcome of critically ill elderly patients requiring intensive care. *JAMA* 1993; 269:3119–3123
- Rockwood K, Noseworthy TW, Gibney RT, et al: One-year outcome of elderly and young patients admitted to intensive care units. *Crit Care Med* 1993; 21:687–691
- Broszowski GE, Elkins M, Albus M: Functional abilities of elderly survivors of intensive care. *J Am Osteopath Assoc* 1995; 95:712–717
- Ip SP, Leung YF, Ip CY, et al: Outcomes of critically ill elderly patients: Is high-dependency care for geriatric patients worthwhile? *Crit Care Med* 1999; 27:2351–2357
- Montuclard L, Garrouste-Orgeas M, Timsit JF, et al: Outcome, functional autonomy, and quality of life of elderly patients with a long-term intensive care unit stay. *Crit Care Med* 2000; 28:3389–3395
- Udekwi P, Gurkin B, Oller D, et al: Quality of life and functional level in elderly patients surviving surgical intensive care. *J Am Coll Surg* 2001; 193:245–249
- Boumendil A, Maury E, Reinhard I, et al: Prognosis of patients aged 80 years and over admitted in medical intensive care unit. *Intensive Care Med* 2004; 30:647–654
- de Rooij SE, Govers AC, Korevaar JC, et al: Cognitive, functional, and quality-of-life outcomes of patients aged 80 and older who survived at least 1 year after planned or unplanned surgery or medical intensive care treatment. *J Am Geriatr Soc* 2008; 56:816–822
- Balas MC, Happ MB, Yang W, et al: Outcomes Associated With Delirium in Older Patients in Surgical ICUs. *Chest* 2009; 135:18–25
- Somme D, Andrieux N, Guérot E, et al: Loss of autonomy among elderly patients after a stay in a medical intensive care unit (ICU): A randomized study of the benefit of transfer to a geriatric ward. *Arch Gerontol Geriatr* 2010; 50:e36–e40
- Daubin C, Chevalier S, Séguin A, et al: Predictors of mortality and short-term physical and cognitive dependence in critically ill persons

- 75 years and older: A prospective cohort study. *Health Qual Life Outcomes* 2011; 9:35
43. Sacanella E, Pérez-Castejón JM, Nicolás JM, et al: Functional status and quality of life 12 months after discharge from a medical ICU in healthy elderly patients: A prospective observational study. *Crit Care* 2011; 15:R105
 44. Pavoni V, Giancesello L, Paparella L, et al: Outcome and quality of life of elderly critically ill patients: An Italian prospective observational study. *Arch Gerontol Geriatr* 2012; 54:e193–e198
 45. Guerra C, Linde-Zwirble WT, Wunsch H: Risk factors for dementia after critical illness in elderly Medicare beneficiaries. *Crit Care* 2012; 16:R233
 46. Katz S, Ford AB, Moskowitz RW, et al: Studies of illness in the aged. The index of ADL: A standardized measure of biological and psychosocial function. *JAMA* 1963; 185:914–919
 47. Mahoney FI, Barthel DW: Functional evaluation: The Barthel Index. *Md State Med J* 1965; 14:61–65
 48. Lawton MP, Brody EM: Assessment of older people: Self-maintaining and instrumental activities of daily living. *Gerontologist* 1969; 9:179–186
 49. Rosow I, Breslau N: A Guttman health scale for the aged. *J Gerontol* 1966; 21:556–559
 50. The EuroQol G. EuroQol—a new facility for the measurement of health-related quality of life. *The EuroQol Group. Health Policy* 1990; 16:199–208
 51. Iwashyna TJ, Netzer G, Langa KM, et al: Spurious inferences about long-term outcomes: The case of severe sepsis and geriatric conditions. *Am J Respir Crit Care Med* 2012; 185:835–841
 52. Gill TM, Hardy SE, Williams CS: Underestimation of disability in community-living older persons. *J Am Geriatr Soc* 2002; 50:1492–1497
 53. Wiener JM, Hanley RJ, Clark R, et al: Measuring the activities of daily living: Comparisons across national surveys. *J Gerontol* 1990; 45:S229–S237
 54. Federman AD, Penrod JD, Livote E, et al: Development of and recovery from difficulty with activities of daily living: An analysis of national data. *J Aging Health* 2010; 22:1081–1098
 55. Boyd CM, Xue QL, Guralnik JM, et al: Hospitalization and development of dependence in activities of daily living in a cohort of disabled older women: The Women's Health and Aging Study I. *J Gerontol A Biol Sci Med Sci* 2005; 60:888–893
 56. Covinsky KE, Palmer RM, Fortinsky RH, et al: Loss of independence in activities of daily living in older adults hospitalized with medical illnesses: Increased vulnerability with age. *J Am Geriatr Soc* 2003; 51:451–458
 57. Rowe JW, Kahn RL: Successful aging. *Gerontologist* 1997; 37:433–440
 58. McLaughlin SJ, Connell CM, Heeringa SG, et al: Successful aging in the United States: Prevalence estimates from a national sample of older adults. *J Gerontol B Psychol Sci Soc Sci* 2010; 65B:216–226
 59. Clegg A, Young J, Iliffe S, et al: Frailty in elderly people. *Lancet* 2013; 381:752–762
 60. Lipsitz LA: Dynamics of stability: The physiologic basis of functional health and frailty. *J Gerontol A Biol Sci Med Sci* 2002; 57:B115–B125
 61. Fried LP, Ferrucci L, Darer J, et al: Untangling the concepts of disability, frailty, and comorbidity: Implications for improved targeting and care. *J Gerontol A Biol Sci Med Sci* 2004; 59:255–263
 62. Gill TM, Allore HG, Gahbauer EA, et al: Change in disability after hospitalization or restricted activity in older persons. *JAMA* 2010; 304:1919–1928
 63. Rockwood K, Song X, MacKnight C, et al: A global clinical measure of fitness and frailty in elderly people. *CMAJ* 2005; 173:489–495
 64. Bagshaw SM, Stelfox HT, McDermid RC, et al: Association between frailty and short- and long-term outcomes among critically ill patients: A multicentre prospective cohort study. *CMAJ* 2014; 186:E95–102
 65. Marik PE: Management of the critically ill geriatric patient. *Crit Care Med* 2006; 34:S176–S182
 66. Pisani MA: Considerations in caring for the critically ill older patient. *J Intensive Care Med* 2009; 24:83–95
 67. Balas M, Casey CM, Happ MB: Assessment and management of older adults with complex illness in the critical care unit. Available at: http://hartfordign.org/uploads/File/gnec_state_of_science_papers/gnec_critical_care.pdf: Hartford Institute for Geriatric Nursing, 2008.
 68. Fielding RA, Vellas B, Evans WJ, et al: Sarcopenia: An undiagnosed condition in older adults. Current consensus definition: Prevalence, etiology, and consequences. International working group on sarcopenia. *J Am Med Dir Assoc* 2011; 12:249–256
 69. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al: European Working Group on Sarcopenia in Older People: Sarcopenia: European consensus on definition and diagnosis: Report of the European Working Group on Sarcopenia in Older People. *Age Ageing* 2010; 39:412–423
 70. Frontera WR, Hughes VA, Fielding RA, et al: Aging of skeletal muscle: A 12-yr longitudinal study. *J Appl Physiol (1985)* 2000; 88:1321–1326
 71. Frontera WR, Zayas AR, Rodriguez N: Aging of human muscle: Understanding sarcopenia at the single muscle cell level. *Phys Med Rehabil Clin N Am* 2012; 23:201–207, xiii
 72. Lauretani F, Russo CR, Bandinelli S, et al: Age-associated changes in skeletal muscles and their effect on mobility: An operational diagnosis of sarcopenia. *J Appl Physiol (1985)* 2003; 95:1851–1860
 73. Bunout D, de la Maza MP, Barrera G, et al: Association between sarcopenia and mortality in healthy older people. *Australas J Ageing* 2011; 30:89–92
 74. Landi F, Liperoti R, Fusco D, et al: Sarcopenia and mortality among older nursing home residents. *J Am Med Dir Assoc* 2012; 13:121–126
 75. Arango-Lopera VE, Arroyo P, Gutiérrez-Robledo LM, et al: Mortality as an adverse outcome of sarcopenia. *J Nutr Health Aging* 2013; 17:259–262
 76. Gariballa S, Alessa A: Sarcopenia: Prevalence and prognostic significance in hospitalized patients. *Clin Nutr* 2013; 32:772–776
 77. Puthuchery ZA, Rawal J, McPhail M, et al: Acute skeletal muscle wasting in critical illness. *JAMA* 2013; 310:1591–1600
 78. Batt J, dos Santos CC, Cameron JJ, et al: Intensive care unit-acquired weakness: Clinical phenotypes and molecular mechanisms. *Am J Respir Crit Care Med* 2013; 187:238–246
 79. Puthuchery Z, Harridge S, Hart N: Skeletal muscle dysfunction in critical care: Wasting, weakness, and rehabilitation strategies. *Crit Care Med* 2010; 38:S676–S682
 80. Muscaritoli M, Lucia S, Molino A: Sarcopenia in critically ill patients: The new pandemic. *Minerva Anesthesiol* 2013; 79:771–777
 81. Brown CJ, Redden DT, Flood KL, et al: The underrecognized epidemic of low mobility during hospitalization of older adults. *J Am Geriatr Soc* 2009; 57:1660–1665
 82. Zisberg A, Shadmi E, Sinoff G, et al: Low mobility during hospitalization and functional decline in older adults. *J Am Geriatr Soc* 2011; 59:266–273
 83. Pedersen MM, Bodilsen AC, Petersen J, et al: Twenty-four-hour mobility during acute hospitalization in older medical patients. *J Gerontol A Biol Sci Med Sci* 2013; 68:331–337
 84. Puthuchery Z, Montgomery H, Moxham J, et al: Structure to function: Muscle failure in critically ill patients. *J Physiol* 2010; 588:4641–4648
 85. Kortebein P, Ferrando A, Lombeida J, et al: Effect of 10 days of bed rest on skeletal muscle in healthy older adults. *JAMA* 2007; 297:1772–1774
 86. Brown CJ, Friedkin RJ, Inouye SK: Prevalence and outcomes of low mobility in hospitalized older patients. *J Am Geriatr Soc* 2004; 52:1263–1270
 87. Gill TM, Allore HG, Holford TR, et al: Hospitalization, restricted activity, and the development of disability among older persons. *JAMA* 2004; 292:2115–2124
 88. Mattson MP: Cellular and neurochemical aspects of the aging human brain. In: Hazzard's Geriatric Medicine and Gerontology. Sixth Edition. Halter JB, Ouslander JG, Tinetti ME, Studenski S, High KP, Asthana S (Eds). New York: McGraw-Hill Medical, 2009. pp 739–750
 89. Yankner BA, Lu T, Loerch P: The aging brain. *Annu Rev Pathol* 2008; 3:41–66
 90. Hayden KM, Reed BR, Manly JJ, et al: Cognitive decline in the elderly: An analysis of population heterogeneity. *Age Ageing* 2011; 40:684–689

91. Whalley LJ, Deary IJ, Appleton CL, et al: Cognitive reserve and the neurobiology of cognitive aging. *Ageing Res Rev* 2004; 3:369–382
92. Bishop NA, Lu T, Yankner BA: Neural mechanisms of ageing and cognitive decline. *Nature* 2010; 464:529–535
93. Miller DB, O'Callaghan JP: Aging, stress and the hippocampus. *Ageing Res Rev* 2005; 4:123–140
94. Luo XG, Ding JQ, Chen SD: Microglia in the aging brain: Relevance to neurodegeneration. *Mol Neurodegener* 2010; 5:12
95. Perry VH: The influence of systemic inflammation on inflammation in the brain: Implications for chronic neurodegenerative disease. *Brain Behav Immun* 2004; 18:407–413
96. Maldonado JR: Neuropathogenesis of delirium: Review of current etiologic theories and common pathways. *Am J Geriatr Psychiatry* 2013; 21:1190–1222
97. Inouye SK, Westendorp RG, Saczynski JS: Delirium in elderly people. *Lancet* 2014; 383:911–922
98. Inouye SK, Charpentier PA: Precipitating factors for delirium in hospitalized elderly persons. Predictive model and interrelationship with baseline vulnerability. *JAMA* 1996; 275:852–857
99. Sanders RD: Hypothesis for the pathophysiology of delirium: Role of baseline brain network connectivity and changes in inhibitory tone. *Med Hypotheses* 2011; 77:140–143
100. Maldonado JR: Pathoetiological model of delirium: A comprehensive understanding of the neurobiology of delirium and an evidence-based approach to prevention and treatment. *Crit Care Clin* 2008; 24:789–856, ix
101. Gross AL, Jones RN, Habtemariam DA, et al: Delirium and Long-term Cognitive Trajectory Among Persons With Dementia. *Arch Intern Med* 2012; 172:1324–1331
102. Davis DH, Muniz Terrera G, Keage H, et al: Delirium is a strong risk factor for dementia in the oldest-old: A population-based cohort study. *Brain* 2012; 135:2809–2816
103. Fong TG, Jones RN, Shi P, et al: Delirium accelerates cognitive decline in Alzheimer disease. *Neurology* 2009; 72:1570–1575
104. Girard TD, Jackson JC, Pandharipande PP, et al: Delirium as a predictor of long-term cognitive impairment in survivors of critical illness. *Crit Care Med* 2010; 38:1513–1520
105. van Gool WA, van de Beek D, Eikelenboom P: Systemic infection and delirium: When cytokines and acetylcholine collide. *Lancet* 2010; 375:773–775
106. Khan BA, Zawahir M, Campbell NL, et al: Biomarkers for delirium—a review. *J Am Geriatr Soc* 2011; 59 Suppl 2:S256–S261
107. Covinsky KE, Pierluissi E, Johnston CB: Hospitalization-associated disability: “She was probably able to ambulate, but I'm not sure”. *JAMA* 2011; 306:1782–1793
108. Creditor MC: Hazards of hospitalization of the elderly. *Ann Intern Med* 1993; 118:219–223
109. Braes T, Flamaing J, Sterckx W, et al: Predicting the risk of functional decline in older patients admitted to the hospital: A comparison of three screening instruments. *Age Ageing* 2009; 38:600–603
110. McCusker J, Kakuma R, Abrahamowicz M: Predictors of functional decline in hospitalized elderly patients: A systematic review. *J Gerontol A Biol Sci Med Sci* 2002; 57:M569–M577
111. Mehta KM, Pierluissi E, Boscardin WJ, et al: A clinical index to stratify hospitalized older adults according to risk for new-onset disability. *J Am Geriatr Soc* 2011; 59:1206–1216
112. Inouye SK, Wagner DR, Acampora D, et al: A predictive index for functional decline in hospitalized elderly medical patients. *J Gen Intern Med* 1993; 8:645–652
113. Ellis G, Whitehead MA, O'Neill D, et al: Comprehensive geriatric assessment for older adults admitted to hospital. *Cochrane Database Syst Rev* 2011(7):CD006211
114. Bogardus ST Jr, Towle V, Williams CS, et al: What does the medical record reveal about functional status? A comparison of medical record and interview data. *J Gen Intern Med* 2001; 16:728–736
115. Brown CJ, Roth DL, Allman RM, et al: Trajectories of life-space mobility after hospitalization. *Ann Intern Med* 2009; 150:372–378
116. Schweickert WD, Pohlman MC, Pohlman AS, et al: Early physical and occupational therapy in mechanically ventilated, critically ill patients: A randomised controlled trial. *Lancet* 2009; 373:1874–1882
117. Abelha FJ, Luis C, Veiga D, et al: Outcome and quality of life in patients with postoperative delirium during an ICU stay following major surgery. *Crit Care* 2013; 17:R257
118. Brummel NE, Jackson JC, Pandharipande PP, et al: Delirium in the ICU and subsequent long-term disability among survivors of mechanical ventilation. *Crit Care Med* 2014; 42:369–377
119. Inouye SK, Bogardus ST Jr, Charpentier PA, et al: A multicomponent intervention to prevent delirium in hospitalized older patients. *N Engl J Med* 1999; 340:669–676
120. Morris PE, Griffin L, Berry M, et al: Receiving early mobility during an intensive care unit admission is a predictor of improved outcomes in acute respiratory failure. *Am J Med Sci* 2011; 341:373–377
121. Asher RA. The dangers of going to bed. *Br Med J* 1947;2(4536):967.
122. Engel GL, Romano J: Delirium, a syndrome of cerebral insufficiency. *J Chronic Dis* 1959; 9:260–277
123. Francis J, Martin D, Kapoor WN: A prospective study of delirium in hospitalized elderly. *JAMA* 1990; 263:1097–1101
124. Ely EW, Inouye SK, Bernard GR, et al: Delirium in mechanically ventilated patients: Validity and reliability of the confusion assessment method for the intensive care unit (CAM-ICU). *JAMA* 2001; 286:2703–2710
125. Bergeron N, Dubois MJ, Dumont M, et al: Intensive Care Delirium Screening Checklist: Evaluation of a new screening tool. *Intensive Care Med* 2001; 27:859–864
126. Bailey P, Thomsen GE, Spuhler VJ, et al: Early activity is feasible and safe in respiratory failure patients. *Crit Care Med* 2007; 35:139–145
127. Morris PE, Goad A, Thompson C, et al: Early intensive care unit mobility therapy in the treatment of acute respiratory failure. *Crit Care Med* 2008; 36:2238–2243
128. Inouye SK, Wagner DR, Acampora D, et al: A controlled trial of a nursing-centered intervention in hospitalized elderly medical patients: The Yale Geriatric Care Program. *J Am Geriatr Soc* 1993; 41:1353–1360
129. Fulmer T, Mezey M, Bottrell M, et al: Nurses Improving Care for Healthsystem Elders (NICHE): Using outcomes and benchmarks for evidenced-based practice. *Geriatr Nurs* 2002; 23:121–127
130. Baztán JJ, Suárez-García FM, López-Arrieta J, et al: Effectiveness of acute geriatric units on functional decline, living at home, and case fatality among older patients admitted to hospital for acute medical disorders: Meta-analysis. *BMJ* 2009; 338:b50
131. Bachmann S, Finger C, Huss A, et al: Inpatient rehabilitation specifically designed for geriatric patients: Systematic review and meta-analysis of randomised controlled trials. *BMJ* 2010; 340:c1718
132. Landefeld CS, Palmer RM, Kresevic DM, et al: A randomized trial of care in a hospital medical unit especially designed to improve the functional outcomes of acutely ill older patients. *N Engl J Med* 1995; 332:1338–1344
133. Vasilevskis EE, Pandharipande PP, Girard TD, et al: A screening, prevention, and restoration model for saving the injured brain in intensive care unit survivors. *Crit Care Med* 2010; 38:S683–S691
134. Vasilevskis EE, Ely EW, Speroff T, et al: Reducing iatrogenic risks: ICU-acquired delirium and weakness—crossing the quality chasm. *Chest* 2010; 138:1224–1233
135. Balas MC, Vasilevskis EE, Burke WJ, et al: Critical care nurses' role in implementing the “ABCDE bundle” into practice. *Crit Care Nurse* 2012; 32:35–8, 40
136. Morandi A, Brummel NE, Ely EW: Sedation, delirium and mechanical ventilation: The ‘ABCDE’ approach. *Curr Opin Crit Care* 2011; 17:43–49
137. Balas M, Buckingham R, Braley T, et al: Extending the ABCDE bundle to the post-intensive care unit setting. *J Gerontol Nurs* 2013; 39:39–51
138. Balas MC, Burke WJ, Gannon D, et al: Implementing the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle into everyday care: Opportunities, challenges, and lessons learned for implementing the ICU Pain, Agitation, and Delirium Guidelines. *Crit Care Med* 2013; 41:S116–S127

139. Balas MC, Vasilevskis EE, Olsen KM, et al. Effectiveness and safety of the awakening and breathing coordination, delirium monitoring/management, and early exercise/mobility bundle. *Crit Care Med* 2014; 42:e680–e681
140. Girard TD, Kress JP, Fuchs BD, et al: Efficacy and safety of a paired sedation and ventilator weaning protocol for mechanically ventilated patients in intensive care (Awakening and Breathing Controlled trial): A randomised controlled trial. *Lancet* 2008; 371:126–134
141. Fox MT, Persaud M, Maimets I, et al: Effectiveness of acute geriatric unit care using acute care for elders components: A systematic review and meta-analysis. *J Am Geriatr Soc* 2012; 60:2237–2245
142. Pronovost PJ: Enhancing physicians' use of clinical guidelines. *JAMA* 2013; 310:2501–2502
143. Kahn JM, Gunn SR, Lorenz HL, et al: Impact of nurse-led remote screening and prompting for evidence-based practices in the ICU*. *Crit Care Med* 2014; 42:896–904
144. Berenholtz SM, Pronovost PJ, Lipsett PA, et al: Eliminating catheter-related bloodstream infections in the intensive care unit. *Crit Care Med* 2004; 32:2014–2020
145. Waitman LR, Phillips IE, McCoy AB, et al: Adopting real-time surveillance dashboards as a component of an enterprisewide medication safety strategy. *Jt Comm J Qual Patient Saf* 2011; 37:326–332
146. American Geriatrics Society. *Geriatrics at Your Fingertips*. Belle Mead, NJ: Excerpta Medica, 2013.
147. Heflin MT, Bragg EJ, Fernandez H, et al: The Donald W. Reynolds Consortium for Faculty Development to Advance Geriatrics Education (FD~AGE): A model for dissemination of subspecialty educational expertise. *Acad Med* 2012; 87:618–626
148. Fessler HE, Addrizzo-Harris D, Beck JM, et al: Entrustable professional activities and curricular milestones for fellowship training in pulmonary and critical care medicine: Executive summary from the Multi-Society Working Group. *Crit Care Med* 2014; 42:2290–2291
149. Fessler HE, Addrizzo-Harris D, Beck JM, et al: Entrustable professional activities and curricular milestones for fellowship training in pulmonary and critical care medicine: Report of a multisociety working group. *Chest* 2014; 146:813–834
150. Leipzig RM, Sauvigné K, Granville LJ, et al: What is a geriatrician? American Geriatrics Society and Association of Directors of Geriatric Academic Programs end-of-training entrustable professional activities for geriatric medicine. *J Am Geriatr Soc* 2014; 62:924–929
151. Marcantonio ER, Flacker JM, Wright RJ, et al: Reducing delirium after hip fracture: A randomized trial. *J Am Geriatr Soc* 2001; 49:516–522
152. González-Montalvo JI, Alarcón T, Mauleón JL, et al: The orthogeriatric unit for acute patients: A new model of care that improves efficiency in the management of patients with hip fracture. *Hip Int* 2010; 20:229–235
153. Adunsky A, Lusky A, Arad M, et al: A comparative study of rehabilitation outcomes of elderly hip fracture patients: The advantage of a comprehensive orthogeriatric approach. *J Gerontol A Biol Sci Med Sci* 2003; 58:542–547
154. Boddart J, Cohen-Bittan J, Khiami F, et al: Postoperative admission to a dedicated geriatric unit decreases mortality in elderly patients with hip fracture. *PLoS One* 2014; 9:e83795
155. Cruz-Jentoft AJ, Landi F, Schneider SM, et al: Prevalence of and interventions for sarcopenia in ageing adults: A systematic review. Report of the International Sarcopenia Initiative (EWGSOP and IWGS). *Age Ageing* 2014; 43:748–759
156. Cicerone KD, Langenbahn DM, Braden C, et al: Evidence-based cognitive rehabilitation: Updated review of the literature from 2003 through 2008. *Arch Phys Med Rehabil* 2011; 92:519–530
157. Cicerone KD, Dahlberg C, Malec JF, et al: Evidence-based cognitive rehabilitation: Updated review of the literature from 1998 through 2002. *Arch Phys Med Rehabil* 2005; 86:1681–1692
158. Borson S, Scanlan J, Brush M, et al: The mini-cog: A cognitive 'vital signs' measure for dementia screening in multi-lingual elderly. *Int J Geriatr Psychiatry* 2000; 15:1021–1027
159. Jorm AF: A short form of the Informant Questionnaire on Cognitive Decline in the Elderly (IQCODE): Development and cross-validation. *Psychol Med* 1994; 24:145–153