How does prior health status (age, comorbidities and frailty) determine critical illness and outcome?

Barbara Haas[a] *and Hannah Wunsch*[b,c]

Purpose of review
Critical illness has a significant impact on an individual's physical and mental health. However, it is less clear to what degree outcomes after critical illness are due to patients' preexisting characteristics, rather than the critical illness itself. In this review, we summarize recent findings regarding the role of age, comorbidity and frailty on long-term outcomes after critical illness.

Recent findings
Age, comorbidity and frailty are all associated with an increased risk of critical illness. Although severity of illness drives the risk of acute mortality, recent data suggest that longer term outcomes are much more closely aligned with prior health status. There are growing data regarding the important role of noncardiovascular comorbidity, including psychiatric illness and obesity, in determining long-term outcomes. Finally, preadmission frailty is associated with poor long-term outcomes after critical illness; further data are needed to evaluate the attributable impact of critical illness on the health trajectories of frail individuals.

Summary
Age, comorbidity and frailty play a critical role in determining the long-term outcomes of patients requiring intensive care.

Keywords
comorbidities, elderly, frailty, long-term outcomes

INTRODUCTION

The fact that critical illness can have a significant impact on an individual's physical and mental health is broadly recognized [1,2]. However, there are significant knowledge gaps in our understanding of whether poor post-ICU outcomes are due to the nature of the critical illness itself, or whether (after resolution of the acute illness) poor outcomes are due to patients' preexisting characteristics. In this review, we focus on the specifics of age, comorbidity and frailty and their impact on long-term outcomes after critical illness.

The Gordian knot of age, comorbidities and frailty

It is important to recognize that age, comorbidities and frailty may be considered to contribute 'independently' to both the risk of critical illness and to outcomes after critical illness but are also highly correlated. As people age, they generally accrue more comorbidities. Similarly, frailty is usually associated with elderly patients [3▪▪,4▪▪]. However, it is also important to recognize that some ICU patients may have comorbidities and/or frailty at a younger age [5]; hence, the need to distinguish between these three states as separate entities.

Factors influencing likelihood of admission to an ICU

There is no doubt that age, frailty and comorbidity all contribute to an individual's likelihood of admission to an ICU. The average age of patients admitted to ICU has increased over the past 25 years [6]. In

[a]Department of Surgery and Interdepartmental Division of Critical Care, University of Toronto, [b]Department of Critical Care Medicine, Sunnybrook Health Sciences Centre and [c]Department of Anesthesia and Interdepartmental Division of Critical Care, University of Toronto, Toronto, Ontario, Canada

Correspondence to Barbara Haas, MD, PhD, Sunnybrook Health Sciences Centre, 2075 Bayview Ave., Room H186, Toronto, ON, Canada M4N 3M5. Tel: +1 416 480 5850; e-mail: barbara.haas@sunnybrook.ca

Curr Opin Crit Care 2016, 22:500–505
DOI:10.1097/MCC.0000000000000342

KEY POINTS

- Prior health status is the main contributor to longer term outcomes for critically ill patients.
- Among many critically ill patients, particularly those who are frail with comorbidities, critical illness may represent only an incremental increase in intensity of care compared with previous healthcare encounters.
- An important minority of elderly patients return to their baseline function after critical illness.
- Due to variations in patient populations, outcome variables and specifically the comparison populations, conclusions regarding long-term outcomes among critically ill patients are highly heterogeneous.

population studies of mechanical ventilation, the 'risk' of mechanical ventilation increases exponentially with age [7]. Similarly, Bagshaw *et al.* [3▪▪] demonstrated that a high proportion (approximately 30%) of patients in a Canadian ICU cohort met criteria for frailty. Finally, 'comorbidity' may be a direct reason for ICU admission [such as an admission for heart failure or chronic obstructive pulmonary disease (COPD)] [8,9] or may indirectly contribute to ICU admission. For example, patients with any cognitive decline are at higher risk of admission to ICU for pneumonia than patients with normal cognition [10]. Given the large array of different comorbidities, and the complex interplay between mental and physical health, the combinations of comorbidities that are the strongest risk factors for ICU admission have not been clearly elucidated, and this question remains an important area of future research.

AGE AND LONG-TERM OUTCOMES AFTER CRITICAL ILLNESS

There is an increasing understanding that chronological age alone is a poor predictor of physiologic reserve and functional status (physiologic age). Within any given age group, there exists considerable heterogeneity in terms of outcomes that are not accounted for by age alone. Nevertheless, age persists as a variable of interest in the majority of studies evaluating critical care outcomes. The reasons for this are likely two-fold. First, older age, on average, is associated with poorer outcomes for critically ill patients and is (in most models and risk scores) a strong predictor of mortality [11,12]. Second, it is a variable that is readily available in the medical record and in administrative data and is therefore easier to evaluate than measures of physiologic age. Data regarding the independent impact of advanced age on long-term outcomes following critical illness are conflicting. Some authors have concluded that age alone is not independently predictive of adverse long-term outcomes [13,14▪], but the majority have found age to be highly predictive [15–17,18▪,19,20].

For patients, the other important question is how they may do relative to noncritically ill individuals of their same age (as opposed to critically ill patients of different ages). A recent retrospective cohort study from Scotland compared 5-year mortality among ICU survivors with a matched cohort of hospitalized patients. The 5-year mortality among ICU survivors was 32%, with an adjusted hazard of death 33% higher at 5 years compared with hospital controls [21]. However, when patients aged 70 and over were compared, the difference in long-term mortality between ICU patients and other hospitalized patients was no longer observed. Other authors have similarly found that the long-term mortality gap between patients experiencing a hospitalization with or without intensive care narrows with age [21]. Moreover, as patients age, the relative impact of ICU admission on functional status becomes more comparable with the impact of a hospitalization not involving ICU [22].

These data highlight the important question of comparator groups when evaluating the relationship between critical illness and patient age. For many elderly individuals in particular, critical illness may represent only an incremental change in a trajectory of overall declining health, and only a slight increase in 'intensity' compared with other healthcare encounters. Given that hospitalization is, in general, a precipitant for loss of mobility and decrease in functional status among those with preexisting risk factors, it is not clear to what degree an admission containing an ICU episode differs from an admission without an ICU episode in terms of modifying these patients' health trajectories.

As the face of the elderly population changes, so has the age-related focus in the critical care literature. Increasing attention is being turned to the 'very elderly', with multiple articles focusing on octogenarians published in the past 5 years [23,24,25▪▪,26–28]. A recent multicenter study evaluated 1-year outcomes of individuals aged 80 and older admitted to the ICU [25▪▪]. Mortality in this patient cohort was high: 25% of patients died in hospital, and a further 25% died within 12 months. However, 25% of patients in the cohort had recovered to baseline physical function by 12 months. Paradoxically, although higher baseline physical function was associated with higher physical function and survival at 1 year, it was associated with lower probability of recovery to baseline.

Data from other studies support the interplay between baseline functional status and age in long-term survival among the very elderly critically ill. For example, in a single center study of 106 octogenarians admitted to ICU, only a third were alive at 1 year [28]. Among these survivors, however, 83% had been completely independent before ICU admission; it is also notable that 78% of survivors in this study said they would agree to another ICU admission. In another single-center study of octogenarians who survived their critical illness to hospital discharge, the median survival time was 1.5 years [29]. However, those with good premorbid functional status and no severe underlying illness had a median survival of 28 months, compared with only 3 months if either was present. Together, these data suggest that, among the very elderly, mortality following ICU discharge is very high, but that a select group of patients have reasonably good outcomes despite very advanced age; good outcomes in this population are clearly modulated by other factors.

COMORBIDITY AND LONG-TERM OUTCOMES AFTER CRITICAL ILLNESS

After a short period of recovery, comorbidity becomes one of the main predictors of outcome [1,14▪,30▪,31]. As we gain more information on the 'pre-ICU' status of patients, we are beginning to elucidate the role of individual key comorbidities. Some, such as obesity, psychiatric illness and sensory deficits, are forms of comorbidity that have recently gained increased attention in the critical care literature and will be highlighted here.

Obesity and outcomes after critical illness

Although traditionally associated with an increased degree of comorbidity, particularly with regard to diabetes, dyslipidemia and coronary artery disease, the impact of obesity on outcomes among ICU survivors remains unclear. Data regarding short-term mortality associated with increased weight are mixed; some authors have shown no clear relationship between obesity and in-hospital mortality during an episode of critical illness [32,33▪,34], whereas others have found a protective effect for short-term mortality [35,36]. A recent large, multicenter retrospective cohort study performed in Holland demonstrated a U-shaped relationship between BMI and in-hospital mortality among critically ill patients [37]. For patients who were underweight, mortality was increased, but a higher BMI appeared to confer a survival advantage up to a BMI of 42.6 (BMI 25 was used as reference). The finding that being underweight on admission to ICU increases the risk of hospital mortality is almost universal [33▪,35,38].

There is a growing literature suggesting that obesity may also confer a paradoxically protective effect for long-term mortality among patients with critical illness [32,35,36,39▪]. Work by Prescott *et al.* [40▪] found that older Americans (>65 years) who were obese and survived a hospitalization with severe sepsis were less likely to die within a year after hospital discharge compared with nonobese patients. Moreover, the protective effect was present in a dose response, with the most severely obese patients having the lowest mortality at 1 year. Reasons for this potential protective effect on either short-term or long-term mortality remain speculative [41].

Psychiatric illness and outcomes after critical illness

The high burden of mental illness experienced by survivors of critical illness has led to a call for greater research into preventing and treating post-ICU depression, anxiety, posttraumatic stress disorder (PTSD) and other psychiatric diagnoses [42]. However, it is important to recognize that we often have limited information regarding the pre-ICU burden of psychiatric comorbidities among critically ill patients, as well as the relationship between preexisting mental illness, need for ICU admission and ICU-related outcomes (both psychiatric and nonpsychatric).

A population-based, retrospective cohort study conducted in Denmark provides data that suggest mental illness may confer an increased risk of critical illness [43▪▪]. Among patients admitted to ICU and requiring mechanical ventilation, 6.2% had a psychiatric diagnosis, compared with only 2.4% of the general population. Strong data exist for outcomes such as acute myocardial infarction to suggest that depression and other psychiatric illnesses may contribute to an increased risk [44]. It is possible a similar relationship exists between psychiatric illness and critical illness.

Premorbid psychiatric illness appears to predispose patients to increased psychiatric illness after ICU admission. For example, a recent cohort study assessing PTSD also found a strong relationship between PTSD before critical illness and new PTSD related to the critical illness itself [45]. However, the ways in which psychiatric illness modulate other long-term outcomes, such as mortality, after critical illness are not well described. Both old and new onset psychiatric illness may well contribute to the excess mortality and morbidity of many survivors of critical illness, but this remains speculative.

Sensory deficit

A recent article assessed individuals from the Precipitating Events Project, a longitudinal study of 754 community-dwelling persons aged 70 years or older [39▪]. For the individuals who survived a critical illness ($n = 186$), functional recovery (defined as returning to a disability count less than or equal to the pre-ICU disability count) was substantially decreased in individuals with preexisting hearing or visual impairments [hazard ratio 0.38, 95% confidence interval (CI) 0.22–0.66 and 0.59, 95% CI 0.37–0.95, respectively]. These data highlight the need to look beyond common 'comorbidities' such as hypertension to elucidate factors that may be associated with poor outcomes for critically ill individuals.

FRAILTY AND LONG-TERM OUTCOMES AFTER CRITICAL ILLNESS

Although many definitions exist, frailty can broadly be defined as a multidimensional loss of physiologic reserve that accumulates gradually, and that places a patient at higher risk of adverse outcomes in a number of clinical situations [46]. It is, therefore, not surprising that frailty has been linked to poor long-term outcomes after critical illness. However, the magnitude of decline caused by ICU admission in frail patients remains somewhat unclear. Part of the difficulty associated with defining the precise relationship between frailty, critical illness and long-term outcomes is the difficulty of measuring frailty itself. First, there are many tools and instruments to measure frailty, rendering comparisons across studies challenging [47]. In addition, due to the nature of critical illness, the elements required to evaluate frailty (e.g. information about ability to perform activities of daily living or direct observation of gait) often cannot be acquired directly through a history and physical of the patient. As a result, data regarding the elements of frailty are often collected retrospectively or from patients' families – an approach that can lead to an incorrect estimate of premorbid functional status and frailty [23,25▪▪,48,49].

A recent evaluation of frailty and long-term survival after critical illness was conducted in a cohort of Medicare beneficiaries using purely administrative data to define frailty [30▪]. Frailty had an additive effect when combined with other risk factors for long-term mortality and was associated with an overall 3-year mortality of approximately 50%. Another study using a more rigorous definition of frailty (Frailty Index) collected on individuals on admission to ICU also found that frailty is significantly associated with long-term mortality after discharge among survivors of critical illness [25▪▪].

In addition to predicting long-term mortality, frailty appears to be associated with worse functional outcomes after ICU discharge, as well as lower likelihood of recovery to baseline function [3▪▪,25▪▪,49]. For example, one study demonstrated that patients with frailty had lower quality of life at 6 months and at 12 months compared with nonfrail ICU patients using multiple measures of quality of life and functional status, even after adjusting for age, comorbidity and severity of illness [4▪▪]. These authors also demonstrated that difficulties with mobility and other aspects of functional status were magnified by age and magnitude of pre-ICU frailty. On the contrary, the authors had no measures of quality of life in their cohort before ICU admission; as such, it is unclear whether the discrepancies observed between frail and nonfrail patients had any relationship to the ICU admission.

Controversy continues to exist regarding the proportion of post-ICU disability observed among frail patients that is attributable directly to critical illness, compared with the proportion that represents ongoing deterioration in functional status that predates critical illness. For example, Iwashyna *et al.* [50] demonstrated that, although the prevalence of functional disability is high among survivors of severe sepsis, accumulation of these disabilities predated ICU admission.

To better evaluate the relationship between gradually deteriorating health and post-ICU outcomes, Ferrante *et al.* [51▪▪] recently evaluated the pre-ICU and post-ICU health trajectories of critically ill patients from the Precipitating Events Project (described previously). Rather than focus on functional status at a single point in time, they modeled patient trajectories in the year before, and the year following, ICU admission. Compared with those with a pre-ICU trajectory of minimal disability, patients with a pre-ICU trajectory of mild-to-moderate or severe disability had a doubling or tripling (respectively) in the risk of death within a year of ICU discharge. Pre-ICU trajectory with severe disability was the single greatest predictor of death at 1 year. Moreover, using trajectory modeling, the authors demonstrated that pre-ICU functional trajectory was very closely linked to post-ICU functional trajectory.

Are the outcomes of ICU survivors modifiable?

Understanding the relationship between age, comorbidities, frailty and critical care outcomes is, for many, closely associated with the hope that

identifying patients at risk for poor outcomes will help guide the development of interventions that will ultimately improve the outcomes of these patients [51▪▪].

Although interventions aimed at improving mobility and reducing duration of mechanical ventilation may improve outcomes of critically ill patients [52,53], the degree to which such interventions benefit very elderly patients, patients with specific comorbidities (such as COPD) or frailty remains very unclear. For high-risk surgical patients having procedures that can be scheduled, 'prehab' may provide an approach to intervening for frail individuals; studies to assess this approach are ongoing [54]. Specific care pathways that ensure appropriate follow-up (such as for patients with a COPD exacerbation) may be associated with a reduction in likelihood of a repeat hospitalization [55,56]. Finally, approaches to end-of-life care planning that emphasize discussions regarding the appropriateness of ICU admission may ultimately shift the population of elderly patients admitted to ICU to ensure those who will not benefit are provided with alternative options.

CONCLUSION

The role of critical illness within an individual's healthcare experience is far from uniform. Among younger patients, an ICU admission may represent a sudden, catastrophic, isolated event (e.g. severe injury in a motor vehicle crash or respiratory failure from influenza) in a previously healthy individual. Such a paradigm may not hold true for older individuals, and particular those with poor preexisting health [57]. Patient characteristics, including specific comorbidities and frailty, are clearly large determinants of longer term outcomes for the majority of patients. The magnitude of the impact of the critical illness and our ability to modify this impact are uncertain; better characterization of patients before illness will help to contribute to our understanding of the relative contributions of each to long-term morbidity and mortality.

Acknowledgements

None.

Financial support and sponsorship

None.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as

- ▪ of special interest
- ▪▪ of outstanding interest

1. Herridge MS, Tansey CM, Matté A, *et al.* Functional disability 5 years after acute respiratory distress syndrome. N Engl J Med 2011; 364:1293–1304.
2. 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.
3. ▪▪ 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; 186:95–102.

This study highlights the high prevalence of frailty among ICU patients aged over 50, and demonstrates a clear dose–response relationship between degree of premorbid frailty and long-term mortality after critical illness.

4. ▪▪ Bagshaw SM, Stelfox HT, Johnson JA, *et al.* Long-term association between frailty and health-related quality of life among survivors of critical illness: a prospective multicenter cohort study. Crit Care Med 2015; 43:973–982.

The present study demonstrates that frail survivors of critical illness had significantly worse quality of life at 6 months and one year compared with nonfrail survivors and matched controls in the general population. However, the same proportion of frail and nonfrail survivors experienced a clinically significant improvement in quality of life between 6 months and 1 year after hospital discharge, demonstrating that even frail patients may experience improvements after ICU discharge.

5. Rockwood K, Song X, Mitnitski A. Changes in relative fitness and frailty across the adult lifespan: evidence from the Canadian National Population Health Survey. CMAJ 2011; 183:E487–E494.
6. Zimmerman JE, Kramer AA, Knaus WA. Changes in hospital mortality for United States intensive care unit admissions from 1988 to 2012. Crit Care 2013; 17:R81.
7. Wunsch H, Linde-Zwirble WT, Angus DC, *et al.* The epidemiology of mechanical ventilation use in the United States. Crit Care Med 2010; 38:1947–1953.
8. Dres M, Tran T-C, Aegerter P, *et al.* Influence of ICU case-volume on the management and hospital outcomes of acute exacerbations of chronic obstructive pulmonary disease. Crit Care Med 2013; 41:1884–1892.
9. Safavi KC, Dharmarajan K, Kim N, *et al.* Variation exists in rates of admission to intensive care units for heart failure patients across hospitals in the United States. Circulation 2013; 127:923–929.
10. Shah FA, Pike F, Alvarez K, *et al.* Bidirectional relationship between cognitive function and pneumonia. Am J Respir Crit Care Med 2013; 188:586–592.
11. Knaus WA, Draper EA, Wagner DP, Zimmerman JE. APACHE II: a severity of disease classification system. Crit Care Med 1985; 13:818–829.
12. Le Gall JR, Lemeshow S, Saulnier F. A new simplified acute physiology score (SAPS II) based on a European/North American multicenter study. JAMA 1993; 270:2957–2963.
13. Bo M, Massaia M, Raspo S, *et al.* Predictive factors of in-hospital mortality in older patients admitted to a medical intensive care unit. J Am Geriatr Soc 2003; 51:529–533.
14. ▪ Garland A, Olafson K, Ramsey CD, *et al.* Distinct determinants of long-term and short-term survival in critical illness. Intensive Care Med 2014; 40:1097–1105.

This study divides survival after critical illness into two distinct phases, each with different risk factors for mortality.

15. Kaarlola A, Tallgren M, Pettilä V. Long-term survival, quality of life, and quality-adjusted life-years among critically ill elderly patients. Crit Care Med 2006; 34:2120–2126.
16. Somme D, Maillet J-M, Gisselbrecht M, *et al.* Critically ill old and the oldest-old patients in intensive care: short- and long-term outcomes. Intensive Care Med 2003; 29:2137–2143.
17. Chelluri L, Im KA, Belle SH, *et al.* Long-term mortality and quality of life after prolonged mechanical ventilation. Crit Care Med 2004; 32:61–69.
18. ▪ Nabozny MJ, Barnato AE, Rathouz PJ, *et al.* Trajectories and prognosis of older patients who have prolonged mechanical ventilation after high-risk surgery. Crit Care Med 2016; 44:1091–1097.

This article highlights the impact of prolonged mechanical ventilation on long-term outcomes after surgical intervention.

19. Combes A, Costa M-A, Trouillet J-L, *et al.* Morbidity, mortality, and quality-of-life outcomes of patients requiring ≥14 days of mechanical ventilation. Crit Care Med 2003; 31:1373–1381.
20. Baldwin MR, Narain WR, Wunsch H, *et al.* A prognostic model for 6-month mortality in elderly survivors of critical illness. Chest 2013; 143:910–919.
21. Lone NI, Gillies MA, Haddow C, *et al.* Five year mortality and hospital costs associated with surviving intensive care. Am J Respir Crit Care Med 2016; 194:198–208.
22. Wunsch H, Guerra C, Barnato A. Three-year outcomes for Medicare beneficiaries who survive intensive care. JAMA 2010; 303:849–856.

23. Roch A, Wiramus S, Pauly V, *et al.* Long-term outcome in medical patients aged 80 or over following admission to an intensive care unit. Crit Care 2011; 15:R36.

24. Boumendil A, Angus DC, Guitonneau A-L, *et al.* Variability of intensive care admission decisions for the very elderly. PLoS One 2012; 7:e34387.

25. ■■ Heyland DK, Garland A, Bagshaw SM, *et al.* Recovery after critical illness in patients aged 80 years or older: a multicenter prospective observational cohort study. Intensive Care Med 2015; 41:1911–1920.

The authors demonstrate that one quarter of patients aged 80 and over admitted to ICU have returned to their baseline function at one year. This study emphasizes that, although ICU mortality among elderly patients is high, an important minority of elderly patients have good post-ICU outcomes.

26. Bagshaw SM, Webb SAR, Delaney A, *et al.* Very old patients admitted to intensive care in Australia and New Zealand: a multicentre cohort analysis. Crit Care 2009; 13:R45.

27. Garrouste-Orgeas M, Boumendil A, Pateron D, *et al.* Selection of intensive care unit admission criteria for patients aged 80 years and over and compliance of emergency and intensive care unit physicians with the selected criteria: an observational, multicenter, prospective study. Crit Care Med 2009; 37:2919–2928.

28. Tabah A, Philippart F, Timsit JF, *et al.* Quality of life in patients aged 80 or over after ICU discharge. Crit Care 2010; 14:R2.

29. 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.

30. ■ Hope AA, Gong MN, Guerra C, Wunsch H. Frailty before critical illness and mortality for elderly Medicare beneficiaries. J Am Geriatr Soc 2015; 63:1121–1128.

The authors use an administrative approach to defining frailty. The study demonstrates the additive impact of frailty on long-term survival among ICU patients with other comorbidities.

31. Ou S-M, Chu H, Chao P-W, *et al.* Long-term mortality and major adverse cardiovascular events in sepsis survivors: a nationwide population-based study. Am J Respir Crit Care Med 2016. doi:10.1164/rccm.201510-2023OC.

32. Wardell S, Wall A, Bryce R, *et al.* The association between obesity and outcomes in critically ill patients. Can Respir J 2015; 22:23–30.

33. ■ Sakr Y, Alhussami I, Nanchal R, *et al.* Being overweight is associated with greater survival in ICU patients: results from the Intensive Care over Nations Audit. Crit Care Med 2015; 43:2623–2632.

The present study evaluates the relationship between obesity and ICU outcomes in a large, international cohort.

34. Martino JL, Stapleton RD, Wang M, *et al.* Extreme obesity and outcomes in critically ill patients. Chest 2011; 140:1198–1206.

35. Abhyankar S, Leishear K, Callaghan FM, *et al.* Lower short- and long-term mortality associated with overweight and obesity in a large cohort study of adult intensive care unit patients. Crit Care 2012; 16:R235.

36. Peake SL, Moran JL, Ghelani DR, *et al.* The effect of obesity on 12-month survival following admission to intensive care: a prospective study. Crit Care Med 2006; 34:2929–2939.

37. Pickkers P, de Keizer N, Dusseljee J, *et al.* Body mass index is associated with hospital mortality in critically ill patients: an observational cohort study. Crit Care Med 2013; 41:1878–1883.

38. Finkielman JD, Gajic O, Afessa B. Underweight is independently associated with mortality in postoperative and nonoperative patients admitted to the intensive care unit: a retrospective study. BMC Emerg Med 2004; 4:3.

39. ■ Ferrante LE, Pisani MA, Murphy TE, *et al.* Factors associated with functional recovery among older ICU survivors. Am J Respir Crit Care Med 2016. [Epub ahead of print]

The authors highlight the impact of sensory deficit on the probability of functional recovery after critical illness.

40. ■ Prescott HC, Chang VW, O'Brien JM, *et al.* Obesity and 1-year outcomes in older Americans with severe sepsis. Crit Care Med 2014; 42:1766–1774.

The authors evaluate the relationship between obesity and long-term ICU outcomes, including functional outcomes.

41. Wunsch H. Comorbidity or covert advantage? The obesity conundrum. Crit Care Med 2014; 42:1935–1936.

42. Needham DM, Davidson J, Cohen H, *et al.* Improving long-term outcomes after discharge from intensive care unit: report from a stakeholders' conference. Crit Care Med 2012; 40:502–509.

43. ■■ Wunsch H, Christiansen CF, Johansen MB, *et al.* Psychiatric diagnoses and psychoactive medication use among nonsurgical critically ill patients receiving mechanical ventilation. JAMA 2014; 311:1133–1142.

The authors demonstrate patients requiring ICU admission have a higher burden of psychiatric comorbidity than the general population and a much higher rate of new psychiatric diagnoses and medication use after critical illness; these findings highlight the complex relationship between psychiatric illness, the need for intensive care and long-term psychiatric outcomes after critical illness.

44. Daskalopoulou M, George J, Walters K, *et al.* Depression as a risk factor for the initial presentation of twelve cardiac, cerebrovascular, and peripheral arterial diseases: data linkage study of 1.9 million women and men. PLoS One 2016; 11:e0153838.

45. Patel MB, Jackson JC, Morandi A, *et al.* Incidence and risk factors for ICU-related posttraumatic stress disorder in veterans and civilians. Am J Respir Crit Care Med 2016; 193:1373–1381.

46. Rockwood K, Song X, MacKnight C, *et al.* A global clinical measure of fitness and frailty in elderly people. CMAJ 2005; 173:489–495.

47. Vries NM, De Staal JB, van Ravensberg CD, *et al.* Outcome instruments to measure frailty: a systematic review. Ageing Res Rev 2011; 10:104–114.

48. Khouli H, Astua A, Dombrowski W, *et al.* Changes in health-related quality of life and factors predicting long-term outcomes in older adults admitted to intensive care units. Crit Care Med 2011; 39:731–737.

49. Baldwin MR, Reid MC, Westlake AA, *et al.* The feasibility of measuring frailty to predict disability and mortality in older medical intensive care unit survivors. J Crit Care 2014; 29:401–408.

50. Iwashyna TJ, Netzer G, Langa KM, Cigolle C. Spurious inferences about long-term outcomes: the case of severe sepsis and geriatric conditions. Am J Respir Crit Care Med 2012; 185:835–841.

51. ■■ Ferrante LE, Pisani MA, Murphy TE, *et al.* Functional trajectories among older persons before and after critical illness. JAMA Intern Med 2015; 175:523–529.

Due to its prospective design, this study provides critical information about the relationship between pre-ICU functional trajectory and post-ICU functional trajectory. These data confirm that a significant minority of elderly patients survive ICU with good functional status.

52. 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.

53. 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.

54. Lemanu DP, Singh PP, MacCormick AD, *et al.* Effect of preoperative exercise on cardiorespiratory function and recovery after surgery: a systematic review. World J Surg 2013; 37:711–720.

55. Prieto-Centurion V, Markos MA, Ramey NI, *et al.* Interventions to reduce rehospitalizations after chronic obstructive pulmonary disease exacerbations. A systematic review. Ann Am Thorac Soc 2014; 11:417–424.

56. van Walraven C, Mamdani M, Fang J, Austin PC. Continuity of care and patient outcomes after hospital discharge. J Gen Intern Med 2004; 19:624–631.

57. Iwashyna TJ. Trajectories of recovery and dysfunction after acute illness, with implications for clinical trial design. Am J Respir Crit Care Med 2012; 186:302–304.