

Towards defining persistent critical illness and other varieties of chronic critical illness

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We contend that the concept of “persistent critical illness” has not been consistently described in the literature. It is our hypothesis that there exists a substantial and growing group of “persistently critically ill” patients who are intensive care unit-dependent because of a cascade of critical illnesses rather than because of their original ICU admitting diagnosis. These patients are likely to account for a substantial portion of our bed-days, and we believe their care can be improved by changes in management and communication practices in the ICU.

Persistent critical illness is not just relabelled chronic critical illness

The concept of persistent critical illness falls within the large family of syndromes encompassed by the term “chronic critical illness” (CCI), yet the term has been used for such a range of purposes that it lacks sufficient specificity to guide concrete interventions and mechanistic research. Within writings of various scholars on “chronic critical illness”, one can distinguish at least five concepts:

- persistent critical illness (as defined here)
- CCI or medically complex patients (see below)
- diseases with long intrinsic recovery times
- prolonged weaning
- prolonged ICU length of stay (LOS).

Van den Berghe and colleagues revived attention to the notion of CCI in the 1990s. They documented a series of profound endocrine derangements, which they hypothesised distinguish acute from chronic critical illness.^{1,2} More recently, Nelson and colleagues articulated a somewhat different definition in a seminal 2010 review.³ They argued that CCI occurs when patients with limited physiological reserve (due, often, to older age and chronic comorbidities) develop an acute critical illness that then tips them over into a syndrome of ongoing “ventilator dependence, brain dysfunction, neuromuscular weakness, endocrinopathy, malnutrition, anasarca [profound oedema], skin breakdown and symptom distress.”³

In the United States, the operational definition of this syndrome has been led by the ProVent group of investigators, who focused on one subset of patients of particular policy relevance in the US—patients on prolonged mechanical ventilation.^{4,5} Carson and Bach noted in an early

ABSTRACT

We hypothesise that there exists a substantial and growing group of “persistently critically ill” patients who appear to be intensive care unit-dependent because of a cascade of critical illnesses rather than their original ICU admitting diagnosis. These persistently critically ill patients are those who remain in the ICU because of ongoing complications of care that continue after their reason for admission has been treated and is no longer active. We believe such patients can be distinguished from patients currently labelled as “chronic critical illness” or “prolonged mechanical ventilation”. We further believe that their primary problem is not simply failure to wean from mechanical ventilation due to muscle weakness and impaired gas exchange. We outline a program of clinician consultation, epidemiological research, consensus conference and validation to develop a useful definition of persistent critical illness, with the aim of supporting investigations in preventing persistence, and improving the care of patients so affected.

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review that “somewhat arbitrary cutoffs for ‘prolonged ventilation’ have been suggested, including ventilation for more than 4, 7, 10, 14, 21, or 29 days.”⁶ ProVent and others⁷ have documented the poor (but not completely hopeless) outcomes of patients on prolonged mechanical ventilation, their high levels of health care needs, and the substantial mismatch between prognostic expectations of families, ICU physicians and the reality of patients’ lives.^{5,8}

At the same time that the ProVent group launched its investigations of prolonged mechanical ventilation, the US witnessed the rapid rise of a form of hospital unusual in other countries: the long-term acute care (LTAC) hospital. In principle, LTAC hospitals represented an alternative to weaning patients off mechanical ventilation in the typical ICU, as ICU providers were believed to be distracted by acute emergencies and inattentive to sustained incremental processes of rehabilitation. LTAC hospitals primarily cared and care for patients who are haemodynamically stable and require weaning from mechanical ventilation, typically with an F_{iO_2} of less than 50% and a positive end-expiratory

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pressure of less than 10 cmH₂O. In practice, the LTAC industry was dominated by for-profit providers, and nearly tripled its government-derived revenue to over US\$1.2 billion by 2006.^{9,10}

Facing evidence of little difference in outcomes, despite increased public cost,¹¹ the US reformed LTAC payments. The Research Triangle Institute (RTI) developed a definition of CCI that would then be useful for the specific task of prospectively paying hospitals for potential LTAC patients.¹² This definition was explicitly not built on purely clinical grounds. The RTI defined CCI as one of five

... eligible clinical conditions plus at least 8 days in an ICU during an acute care hospitalization. The five eligibility conditions were prolonged acute mechanical ventilation (i.e., mechanical ventilation for at least 96 hr in a single episode); tracheotomy; sepsis and other severe infections; severe wounds; and multiple organ failure, ischemic stroke, intercerebral hemorrhage, or traumatic brain injury.¹³

This RTI definition formed the basis of the ProVent group's recent estimation that, in the US each year, there are 380 001 cases of patients having prolonged mechanical ventilation which result in "107,880 in-hospital deaths and [US] \$26 billion in hospital-related costs."¹³

It is our fear that this intellectual evolution has limited the clinical usefulness of the concept of CCI.¹⁴ A specific research agenda has led to identification of a group of patients with CCI with prolonged mechanical ventilation, and then, increasingly, the specific causes of prolonged mechanical ventilation for which LTAC hospitals may be useful. This evolution has also recently led to a definition of CCI that is fundamentally shaped by the reimbursement requirements of fee-for-service US critical care in the context of a growing split between acute ICUs and LTAC hospitals. The usefulness of the RTI definition is unclear in other health care systems or at the bedside of patients. Its value and meaning in Australia, New Zealand and most of the rest of the world remain unexplored.

Other varieties of CCI

We hypothesise that persistent critical illness is distinct from the RTI definition, but is not the only variety of CCI.

Patients with persistent critical illness should, by definition, be distinguished from patients with diseases with long intrinsic recovery times, or who simply cannot recover regardless. For a patient with persistent critical illness, the disease for which the patient was admitted (eg, septic shock or dissecting ascending aortic aneurysm) has been treated and is no longer active. In contrast, a patient with a disease with a long intrinsic recovery time remains in the ICU because of that disease and the inability of current

medical care to speed recovery (eg, Guillain-Barré syndrome). There also exists a subset of patients whose underlying physiology can no longer support homeostasis, regardless of whether new complications have occurred. This could apply to patients with cirrhosis or end-stage pulmonary disease who remain in the ICU because their basic disease is simply too advanced, but whose course is still well explained by that admitting diagnosis.

Patients in the ICU for prolonged weaning off mechanical ventilation have traditionally been defined as patients who were eligible for a spontaneous breathing trial (SBT), but for whom the SBT failed at least three times over the course of 7 or more days.¹⁵⁻¹⁷ Such patients remain mechanically ventilated after resolution of their other critical illnesses. While they may have other problems, the "failure to wean" or "prolonged weaning" label has traditionally oriented care towards persistent deficits in respiratory muscle strength, respiratory mechanics and gas exchange.

Contrasting with these physiologically based types of CCI, some authors have also argued for a simple definition of "prolonged ICU LOS".¹⁸ Such a definition is purely quantitative, and identifies a group of patients who are "off-trajectory" for recovery, and so require additional attention. The concept of prolonged ICU LOS is particularly useful in high-turn-over ICUs where beds are needed to support ongoing operating room activities.

Each concept has its own strengths and weaknesses, and brings to mind different prototypical patients with different needs, implying different therapeutic strategies. We hypothesise that there exists a large group of persistently critically ill patients who are not well characterised by the existing labels of diseases with long intrinsic recovery times, prolonged weaning from mechanical ventilation, prolonged ICU LOS, or the RTI definition. The extent of overlap in these definitions and their evolution are important empirical areas to explore.

Process for a path forward

We plan to develop a clinically useful definition of persistent critical illness, building on the conceptual definition of the persistently critically ill as patients whose reason for being in the ICU is now more related to their ongoing critical illness than their original reason for admission to the ICU. We believe that such a definition, including validated strategies for identifying persistently critically ill patients, is essential for developing new interventions to improve their care. We aim to begin a conversation leading to a valid definition, study and then improved treatment of this condition. As part of our research plan, we conducted a survey of Australian and New Zealand ICU clinicians and report the results in this issue of the Journal;¹⁹ we are

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carrying out several data analyses; and we have presented this work to the Australian and New Zealand Intensive Care Society's Clinical Trials Group for refinement. This process will then be followed by a multistep consensus conference process to develop clear definitions and operationalisations of persistent critical illness, with a focus on global relevance with local adaptability.

We envisage that the first stage of the consensus conference will generate working case definitions with face, content and construct validity. The content and face validity will come from a clear focus on the underlying clinical reality we seek to capture, informed by the broad input of clinicians through the survey. Construct validity is defined as the extent to which patients with persistent critical illness differ from other patients in clearly hypothesised ways. As part of this process, analyses of existing data will inform the selection of appropriate cutoff points in what are, admittedly, continuous phenomena. However, the articulation of boundaries is useful to provide tangibility to the definitions. The benefits of categorisation are clear in many other syndromic definitions. We recognise the dangers of confusing a convenient categorisation from a pathophysiologically defined fundamental difference, and will strive to remember the provisional nature of any early definition of persistent critical illness as this work advances.

We propose testing these case definitions against standards of criterion and predictive validity. To assess criterion validity, we will conduct prospective surveillance of several ICUs to identify patients meeting the initial proposed definitions. We will take a random sample of charts (as well as charts of negative control patients not meeting the initial definition) and clinicians will perform blinded reviews to assess the extent to which the charts reflect the concepts. Thus, clinical judgement serves as our gold standard for criterion validity. We will also assess predictive validity by examining the long-term outcomes of patients who do or do not meet the persistent critical illness definition. A valid definition should identify patients with very high subsequent rehospitalisation rates and mortality after ICU discharge, and those rates should be higher than the rates observed in similarly comorbid, disabled and frail patients who did not recently experience an ICU stay. These validity checks will then be communicated back to a second round of consensus conferences to produce a final case definition.

If this process succeeds, it will yield an implementable definition of persistent critical illness relevant to the Australian and New Zealand context and elsewhere. This will support further epidemiological work around the time-course of transition from acute critical illness to persistence, and clinical investigation to better characterise their derangements. Such work will help us develop risk-stratification tools for new interventions to prevent persistent

critical illness and improve care of affected patients. Our research will also define the relationship of persistent critical illness to other forms of CCI and their respective natural histories. In this "manifesto" we contend that nihilism about the recovery possibilities of the persistently critically ill is unwarranted. Instead, we believe that there may be substantial opportunities to improve the care of these growing numbers of patients if they can be reliably categorised and studied. We hope the Australian and New Zealand critical care community will join this attempt to define, explain, study, and improve care of persistent critical illness.

Competing interests

None declared.

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References

- 1 Van den Berghe GH. Acute and prolonged critical illness are two distinct neuroendocrine paradigms. *Verh K Acad voor Geneesk Belg* 1998; 60: 487-518; discussion: 520.
- 2 Vanhorebeek I, Langouche L, Van den Berghe G. Endocrine aspects of acute and prolonged critical illness. *Nat Clin Prac Endocrinol Metab* 2006; 2: 20-31.

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- 3 Nelson JE, Cox CE, Hope AA, Carson SS. Chronic critical illness. *Am J Respir Crit Care Med* 2010; 182: 446-54.
- 4 Carson SS, Kahn JM, Hough CL, et al. A multicenter mortality prediction model for patients receiving prolonged mechanical ventilation. *Crit Care Med* 2012; 40: 1171-6.
- 5 Unroe M, Kahn JM, Carson SS, et al. One-year trajectories of care and resource utilization for recipients of prolonged mechanical ventilation: a cohort study. *Ann Intern Med* 2010; 153: 167-75.
- 6 Carson SS, Bach PB. The epidemiology and costs of chronic critical illness. *Crit Care Clin* 2002; 18: 461-76.
- 7 Damuth E, Mitchell JA, Bartock JL, et al. Long-term survival of critically ill patients treated with prolonged mechanical ventilation: a systematic review and meta-analysis. *Lancet Respir Med* 2015; May 20: pii: S2213-2600(15)00150-2.
- 8 Cox CE, Martinu T, Sathy SJ, et al. Expectations and outcomes of prolonged mechanical ventilation. *Crit Care Med* 2009; 37: 2888-94; quiz 904.
- 9 Kahn JM, Benson NM, Appleby D, et al. Long-term acute care hospital utilization after critical illness. *JAMA* 2010; 303: 2253-9.
- 10 Kahn JM, Werner RM, Carson SS, Iwashyna TJ. Variation in long-term acute care hospital use after intensive care. *Med Care Res Rev* 2012.
- 11 Kahn JM, Werner RM, David G, et al. Effectiveness of long-term acute care hospitalization in elderly patients with chronic critical illness. *Med Care* 2013; 51: 4-10.
- 12 Kandilov A, Ingber M, Morley M, et al. Chronically critically ill population payment recommendations (CCIP-PR): final report. Research Triangle Park, NC: RTI International, 2014. <http://innovation.cms.gov/Files/reports/ChronicallyCriticallyIllPopulation-Report.pdf> (accessed Mar 2015).
- 13 Kahn JM, Le T, Angus DC, et al. The epidemiology of chronic critical illness in the United States. *Crit Care Med* 2015; 43: 282-7.
- 14 Sjoding MW, Cooke CR. Chronic critical illness: a growing legacy of successful advances in critical care. *Crit Care Med* 2015; 43: 476-7.
- 15 Perren A, Brochard L. Managing the apparent and hidden difficulties of weaning from mechanical ventilation. *Intensive Care Med* 2013; 39: 1885-95.
- 16 Boles JM, Bion J, Connors A, et al. Weaning from mechanical ventilation. *Eur Respir J* 2007; 29: 1033-56.
- 17 Beduneau G, Pham T, Schortgen F, et al. A new classification for patients weaning from mechanical ventilation [webcast]. Brussels: European Society of Intensive Care Medicine, 2014. <http://www.esicm.org/webcasts/barcelona-2014/4871> (accessed 25 Mar 2015).
- 18 Kramer AA, Zimmerman JE. A predictive model for the early identification of patients at risk for a prolonged intensive care unit length of stay. *BMC Med Inform Decis Mak* 2010; 10: 27.
- 19 Iwashyna TJ, Hodgson CL, Pilcher D, et al. Persistent critical illness characterised by Australian and New Zealand ICU clinicians. *Crit Care Resusc* 2015; 17: 153-158. □