Describing and measuring recovery and rehabilitation after critical illness

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Purpose of review
Rehabilitation is the cornerstone of management of postcritical illness morbidity. Selection of appropriate tools to measure response to rehabilitation therapy is vital to accurately document trajectory of change across the recovery continuum. In the context of physical-based strategies to redress critical illness associated muscle wasting and dysfunction, this review will discuss a framework to guide assessment of physical recovery in the critical illness population, clinimetric measurement properties for instruments and evidence for their implementation, and recent interventional trial data.

Recent findings
The International Classification of Functioning, Disability and Health (ICF) model is a useful framework to guide selection of outcome measures representing physical function at the level of impairment, activity limitation and participation restriction. Clinimetric data are emerging to support a number of physical function outcome measures in the ICU, albeit further research is required to corroborate tools used beyond ICU discharge. Factors associated with outcome measure selection have contributed to interpreting findings from recent interventional trials of physical rehabilitation.

Summary
Determining the future design, conduct and impact of physical therapy interventions for critically ill patients will rely on further development of clinimetrically robust metrics to capture individual patient response spanning the recovery pathway. This approach should be similarly applied to rehabilitation interventions addressing other postintensive care syndrome domains.

Keywords
critical illness, outcome measures, physical function, recovery, rehabilitation

INTRODUCTION

With advances in critical care medicine and reductions in levels of mortality, increasing attention has been paid in recent years to the issue of critical illness survivorship [1,2]; how to address the quality of survival of post-ICU patients and manage the complexity of lasting and often life-changing sequelae that are evident in this population. The burden of postcritical illness impairment and disability is profound and well documented in the literature, with morbidity encompassing domains of physical function, cognitive, psychological and health-related quality of life, with associated economic impact and increased demand on healthcare utilization and significant onus on families and caregivers. The clinical term 'postintensive care syndrome' (PICS) was recently developed by an international multidisciplinary consensus group to encapsulate and profile this multifaceted presentation [3].

In particular, the protracted nature of physical functional impairment is of clinical significance. Peripheral skeletal muscle wasting and dysfunction that occur early and rapidly during critical illness [4] contribute to the development of ICU-acquired weakness and underlie much of the persistent deficit. Residual limitations in walking capacity and associated physical health related quality of life have

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KEY POINTS

- Recovery postcritical illness is complex and rehabilitation interventions are required to address all domains of morbidity, including physical, cognitive and psychological.
- Disability can be considered at the level of impairment, activity limitation and participation restriction.
- Tools for assessing outcomes must demonstrate robust clinimetric properties, including reliability, validity and responsiveness for use across the continuum of recovery.
- For the domain of physical function morbidity, a small number of tools have been developed and evaluated for use in the ICU, but further research is required for instruments used beyond ICU discharge.
- Outcome measure selection can influence interpretation of interventional trial findings; future trials evaluating rehabilitation effectiveness must employ robust measures to accurately capture response to therapy.

been demonstrated in young, previously healthy survivors of acute respiratory distress syndrome 5 years following resolution of the index illness [5]. That these findings would likely be more pronounced in general, chronically comorbid and aged postcritical illness cohorts is without doubt.

Recovery from critical illness is a complex multifactorial process that should commence on admission to the ICU and where rehabilitation is an integral component [1,6,7]. Physical rehabilitation interventions designed to improve physical function in critically ill patients have been examined across the recovery continuum, commencing within the ICU [8–11], following transfer to the ward [12,13▪▪] and beyond hospital discharge [14▪]. In order to accurately determine the true magnitude of the effect of such interventions, selection of appropriate and robust outcome measures is essential [15,16].

In this article, we will review research describing and measuring recovery and rehabilitation after critical illness, in the context of the physical function domain of PICS. First, we will consider a framework to direct patient assessment and classify outcomes for measurement. Second, considerations for outcome measure selection will be discussed and evidence presented demonstrating the nascent focus of attention on development of robust tools for use in the critically ill. Finally, we will review data from recent interventional trials of physical rehabilitation spanning the trajectory of recovery, in particular examining aspects related to outcome measure selection and the interpretation of findings.

CLASSIFYING OUTCOME SELECTION

The domain of physical function can be affected by critical illness at multiple levels for patients. The WHO International Classification of Functioning, Disability and Health (ICF) is a widely recognized framework classifying health and health-related domains, such as physical function [17,18] (Fig. 1). In this model, patient assessment can be examined at the level of impairment, activity limitation and participation restriction [18]. Disability describes dysfunctioning at one or more of these levels, and can be defined as follows:

(1) Impairments: problems in body function or structure resulting in significant abnormality or loss.
(2) Activity limitations: difficulties encountered at an individual level in executing functional activities.
(3) Participation restrictions: limitations experienced at an individual level in involvement in daily societal situations.

As Fig. 1 demonstrates, disability and functioning are also the product of interactions between health conditions and contextual factors, including extrinsic environmental factors (social attitudes and infrastructure, physical geography and environment) and intrinsic personal factors (sex, age, coping styles, behaviour, perceptions of disability).

Figure 2 depicts how the framework has been embedded in a conceptual model for guiding choice of assessment in studies of long-term outcomes after critical illness reported by Iwashyna and Netzer [19]; here, the authors provide examples of assessment and potential outcome measures for use according to each level. For recovery of physical function following critical illness, attention may be focused on assessment at an impairment level wherein the outcomes may be related to skeletal muscle strength or atrophy, an activity level through measures of walking capacity or physical function, or on participation, wherein measures could include activities of daily living, return to work status and social engagement [20]. Additional stages in the model identified by Iwashyna and Netzer [19] included determining the patient's premorbid baseline status and consideration of the cumulative effect of impairment, activity limitation and disability on health-related quality of life.

CONSIDERATIONS FOR SELECTING OUTCOME MEASURES AND EVIDENCE IN THE CRITICAL ILLNESS POPULATION

Identifying an appropriate outcome measure for evaluating recovery of physical function and

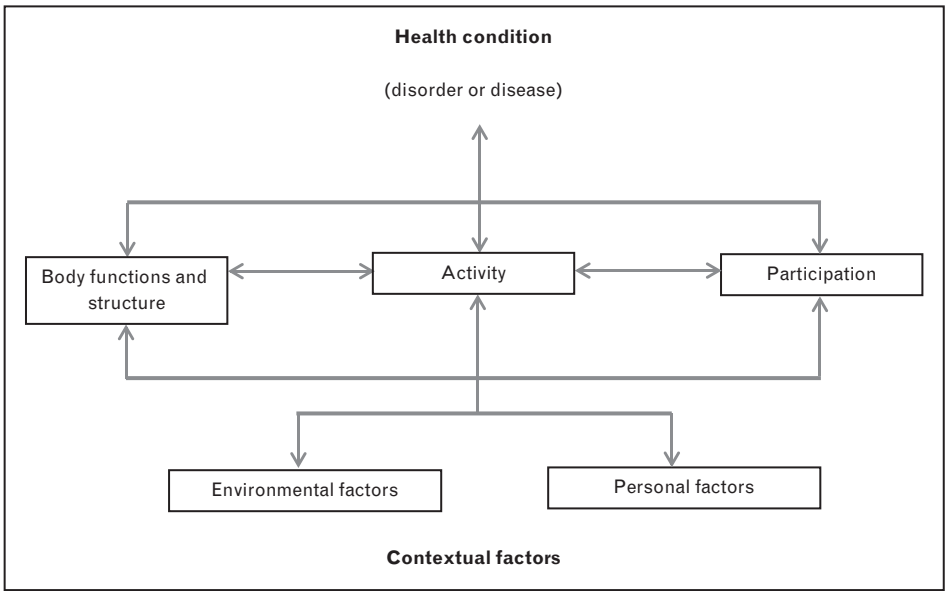

FIGURE 1. The WHO International Classification of Functioning, Disability and Health [18].

effect of rehabilitation interventions requires that the instrument demonstrates robust clinimetric properties [20,21▪▪]. These ensure that the outcome measure selected is 'fit for purpose', that it is reliable, responsive to change, valid and clinically applicable. A summary of these clinimetric properties is reported in Table 1 [22–24]. In addition, when selecting an outcome measure for use, factors such as whether the tool has previously been tested in the critical illness population, influence of the environment in which the tool will be used (e.g. in the ICU, on the hospital ward, in the outpatient or community setting) and other aspects such as equipment required, specialist training for implementation, number of clinicians required for assessment are all further considerations. Importantly, the degree of patient participation required for completion of the assessment is significant [25]. Even when standard operating protocols are used for implementation, patient-related factors may still influence the ability to perform the assessment and subsequent results of testing. This is particularly important when using volitional measures during critical illness that require patients to be fully alert with adequate cognitive ability for testing.

Until recently, many available outcome measures for assessing physical function in critically ill patients lacked robust measurement properties, rendering data acquired through their use subject to greater methodological scrutiny and influencing the integrity of study findings. Of late, increasing work has been undertaken to examine existing tools and develop ICU population-specific measures to address this problem.

In a recent comprehensive systematic review, Parry *et al.* [21▪▪] identified all available outcome measures used to evaluate muscle mass, strength and physical function in the critically ill population across the recovery trajectory (within the ICU, within the hospital and posthospital discharge), predominantly representing the impairment and activity limitation categories within the ICF framework. The measurement properties of each tool were subsequently analysed using the COSMIN criteria (COnsensus-based Standards for the selection of health status Measurement INstrument) [26]. Other systematic reviews have focused on single areas of investigation or aspects of measurement property, for example ultrasound for the assessment of peripheral skeletal muscle architecture during critical illness [27▪] or the reliability of tools specifically assessing peripheral skeletal muscle strength [28▪].

In the most detailed piece of work of its kind, Parry *et al.* [21▪▪] identified three measures pertaining to assessment of muscle mass (bioimpedance spectroscopy, ultrasound and anthropometry), four measures to evaluate muscle strength (handheld dynamometry, handgrip dynamometry, manual muscle testing and chair-stand testing) and 26 potential tools for measuring physical function of which six had been specifically designed for the ICU environment (Chelsea Critical Care Physical Assessment Tool, CPAx [29▪,30], Physical Function in ICU Test-scored, PFIT-s [31,32], Perme mobility scale [33▪,34▪], ICU Mobility scale [35▪], Surgical ICU Optimal Mobility Score [36] and Functional Status Score-ICU [37]) (Table 2). Overall, ultrasonography, dynamometry, PFIT-s and CPAx functioned most robustly for

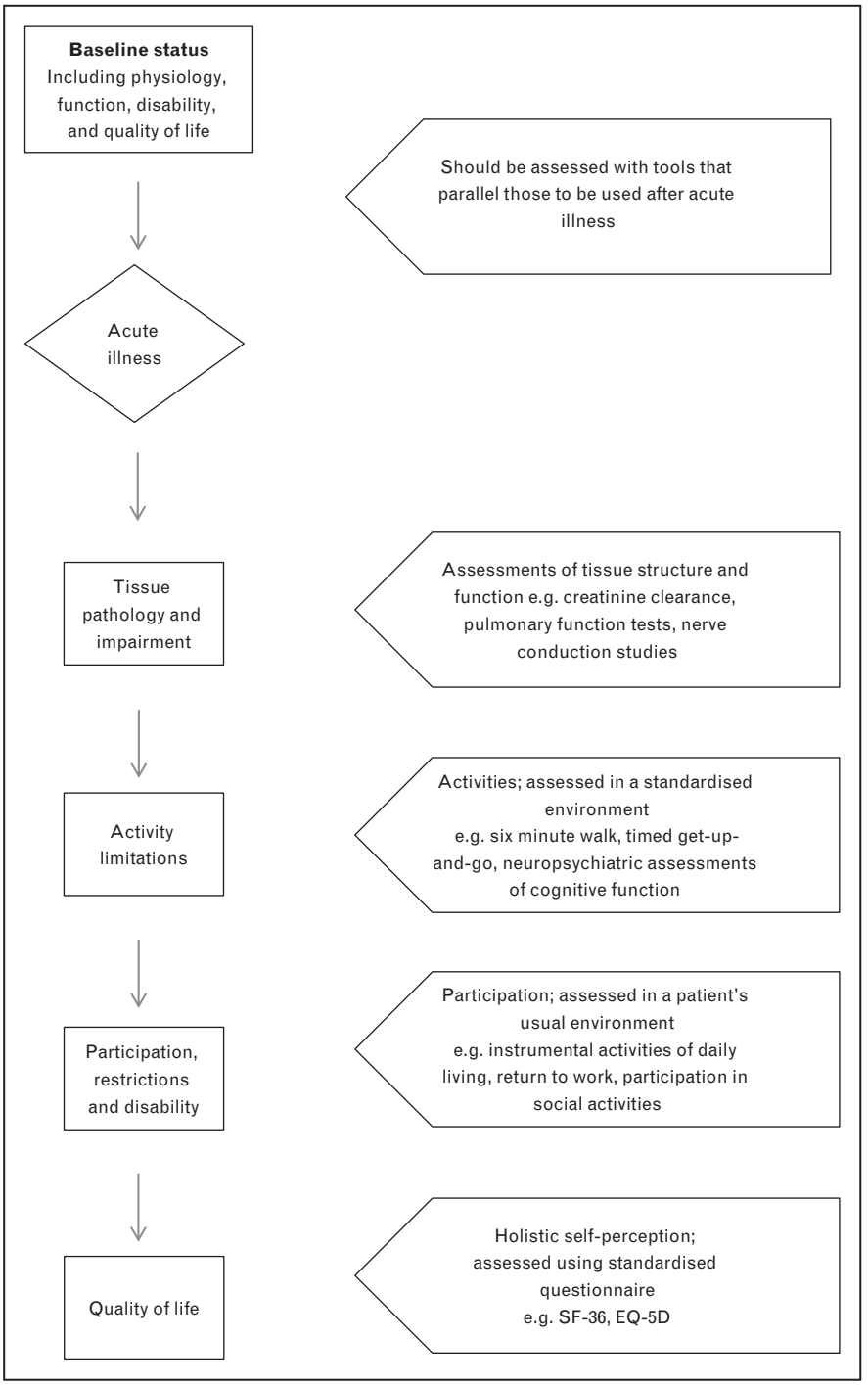

FIGURE 2. Conceptual model for studying long-term outcomes after critical illness [19].

clinimetric properties as instruments for muscle mass, strength and function, respectively.

In an associated prospective observational study, Parry *et al.* [38▪▪] further examined a number of these ICU-specific physical function tools in ICU patients assessed at awakening and discharge. Importantly, the study included a sample size adequate for assessment of clinimetric properties to enable generalizability of findings ($n = 66$). The PFIT-s was found to significantly positively correlate with the FSS-ICU, ICU Mobility Scale and the Short Physical Performance Battery (SPPB), with the three former instruments all performing well for construct validity with muscle strength. Furthermore, both PFIT and FSS-ICU had small floor and ceiling effects at both time-points. Interestingly, this study included examination of the SPPB, albeit in a smaller opportunistic sample ($n = 23$), a tool derived

Table 1. Clinimetric properties required for outcome measures

Clinimetric property	Definition
Reliability	Ability of the measure to obtain accurate results
Inter-rater reliability	Reliability demonstrated when measure performed by multiple assessors
Intra-rater reliability	Reliability demonstrated when measure repeated longitudinally
Validity	Ability of the tool to measure what it is intended to measure
Construct or convergent validity	Validity when compared with a tool measuring a similar construct
Criterion-concurrent validity	Validity when compared with the gold standard measurement tool
Criterion-predictive validity	Validity in predicting future scores or outcomes
Responsiveness	Ability to detect clinically or statistically meaningful change over time
Floor/ceiling effect	Ability to detect performance at lower/higher level of functional performance
Minimum important difference	Smallest clinically relevant change in the measure

Adapted with permission from [24–26].

from the geriatric literature and involving components of balance, sit-to-stand and short-distance mobility. Preliminary data demonstrate that this measure may be useful for discriminating functional ability and consequent rehabilitation requirements in survivors of critical illness following ICU and hospital discharge [39]. Certainly, further examination of the role of this instrument as a measure for potential use at this intermediate recovery stage seems warranted. Parry *et al.* [38▪▪] demonstrated a floor effect of 78 and 56% at ICU awakening and discharge, respectively, highlighting its limited use in the acute stage.

Responsiveness, minimum important difference and floor and ceiling effects of the CPAx have recently been demonstrated in a cohort of severe burns ICU patients with promising results for its functionality in detecting improvements in physical performance in the acute setting [40▪]. Fifty-two patients had scores tracked from preadmission (reported direct or via proxy), ICU admission, ICU discharge and hospital discharge. In the future, as the evidence base for outcome measure robustness in critically ill patients increases, so too will the need for additional work to validate their use in specialist ICU populations. In a much larger cohort ($n = 499$), the CPAx has also demonstrated ability to distinguish between functional levels and ongoing rehabilitation requirements in postcritical illness survivors at hospital discharge [29▪].

Beyond ICU and hospital discharge, two studies have investigated measurement properties of the six-minute walk test (6MWT), one of the most common field walking tests applied to postcritical illness rehabilitation studies to measure exercise capacity. In the first, Chan *et al.* [41▪▪] pooled data from four large international studies ($n = 641$) to examine the construct validity and responsiveness, and estimated minimal important difference (MID) in survivors of acute lung injury. Good convergent and discriminant validity were demonstrated with moderate to strong correlations with physical health measures. Differences in walking distance were observed according to muscle strength, and furthermore, responsiveness was evident with patients reporting improved function, walking greater

Table 2. Outcome measures for assessment of physical function in critically ill patients [23]

Identified outcome measures
Katz ADL; Lawton IADL; Barthel Index; Modified Rankin; CPAx; Fried's frailty index; RMI; SOMS; FIM; FSS-ICU; PFIT-s; TUG test; Perme mobility scale; University of Rochester Scale; Kansas Hospital University Acute Care Tool; Functional Ambulatory Category; Global motor performance (50 m); Elderly Mobility Scale; Functional disability scale; ICU mobility scale; 6MWT; ISWT; 4-m walk test; 2-min walk test; 10-m walk test; Berg Balance Scale
Reported clinimetric properties
6MWT; Katz ADL; Lawton IADL; Barthel Index; Perme mobility scale; ICU Mobility scale; CPAx; SOMS; PFIT-s; FSS-ICU; FIM; Fried's Frailty index; TUG test; Kansas Hospital University Acute Care Tool; Berg Balance scale
Developed specifically for the ICU setting
CPAx; PFIT-s; Perme mobility scale; ICU Mobility scale; SOMS; FSS-ICU

6MWT, six-min walk test; ADL, activities of daily living; CPAx, Chelsea critical care assessment tool; FIM, functional; independence measure; FSS-ICU, functional status score in the ICU; IADL, independence in activities of daily living; ISWT, Incremental Shuttle Walk Test; PFIT-s, physical function in the ICU test (scored); RMI, Rivermead Mobility Index; SOMS, surgical ICU optimal mobilization score; TUG, timed up and go.

distances. 6MWT was also predictive of outcomes, including future mortality, hospitalization and health-related quality of life, with an MID of 20–30 m.

Second, Denehy *et al.* [42▪▪] conducted the first investigation of the relationship between physical performance [6MWT, Timed Up and Go (TUG), Sit-to-Stand x5 (STS-5), Berg Balance Scale (BBS)] and self-reported physical function [SF-36 physical function domain and physical component score (PCS)] in ICU survivors at 3 months post-ICU discharge. 6MWT correlated well against all other objective measures and also the SF-36 physical function domain, and explained 54 and 33% of variance in SF-36 physical function and PCS scores, respectively. However, large floor and ceiling effects were evident in the STS-5 and BBS tests, respectively, indicating that the 6MWT and TUG were acceptable measures of physical function in the short-term post-ICU discharge. Importantly, these data also highlighted the different constructs measured using performance-based rather than self-reported measures. Choice of these outcomes should closely align with study aims to ensure selection of the most appropriate tool [42▪▪].

OUTCOME MEASURE SELECTION IN RECENT INTERVENTIONAL PHYSICAL REHABILITATION TRIALS

A number of recent trials have published findings of physical rehabilitation interventions delivered across the continuum of recovery. Although many factors are influential in the results of these studies, we will focus on the potential contribution of outcome measure selection to their interpretation with the caveat that this element should not be considered in isolation. In a study evaluating the effect of an early physical rehabilitation programme (targeted individualized therapy involving electrical muscle stimulation and functional mobilization techniques) in patients with sepsis syndromes, Kayambu *et al.* [43▪] adopted the Acute Care Index of Function (ACIF) as their primary outcome for physical function. At ICU discharge, there was no difference in physical function between trial arms. The ACIF tool was originally developed in the neurology population, and although it contains elements of functional mobility of potential clinical relevance (e.g. bed mobility, transfers and mobility), the tool has not previously been used in critically ill patients. Many of the secondary outcomes (including manual muscle strength testing and PFIT) that have been evaluated in ICU patients also showed no difference. Self-reported physical function using the SF-36 questionnaire significantly improved at 6-months follow-up (81.8 ± 22.2 vs. 60.0 ± 29.4, $P = 0.04$). The selection of these two different outcome measures reflected the need to consider timing of outcome assessment and opportunity for direct patient assessment in this study. The objective ACIF was feasible at ICU discharge, but at the 6-months stage, a remote form of assessment was required to accommodate the geographical location of patients, which the SF-36 allowed.

Similarly, in a landmark trial evaluating a complex rehabilitation protocol of enhanced rehabilitation (including increased frequency of mobility and exercise therapy, increased dietetic assessment and treatment, individualized goal setting and provision of greater illness-specific information) delivered by a dedicated rehabilitation practitioner during the post-ICU hospital period, no differences were found between groups for the primary outcome of Rivermead Mobility Index (RMI) [13▪▪]. The RMI also originates from the neurological field, as a metric for evaluating function in stroke survivors that has yet to be psychometrically evaluated in the critical illness population, and appeared to demonstrate an early ceiling effect that may have precluded capturing the true effect of the intervention.

Kho *et al.* [44▪▪] conducted a pilot randomized, sham-controlled trial of neuromuscular electrical stimulation (NMES) commenced within the first week of ICU admission, with the specific aim of evaluating outcomes beyond ICU discharge, namely lower extremity muscle strength at hospital discharge assessed using manual muscle testing. No difference was evident between groups, although as a secondary analysis, the intervention arm showed a greater mean increase in strength from the point of ICU awakening to both ICU [5.3 (5.9) vs. 0.8 (3.8), $P = 0.47$] and hospital [5.7 (5.1) vs. 1.8 (2.7), $P = 0.19$] discharge. An important take-home reflection from this study is the acknowledgement from the authors that their primary outcome (muscle strength) represented a measure of impairment rather than function, which mapped to the original study aim of determining whether NMES improved muscle strength.

In addition to association with study aim, specificity of outcome assessment in relation to intervention type is also an important consideration. In a recent posthospital discharge rehabilitation intervention involving a programme of cycle ergometry, Batterham *et al.* [45] found significant, albeit short-term only, improvements in associated measures of cardiopulmonary fitness in patients receiving the intervention vs. control patients [anaerobic threshold at 9 weeks, mean (95% confidence interval, 95% CI) difference 1.8 (0.4–3.2) mlO_2/kg/min].

However this approach must be balanced by the limited generalizability of such findings.

In a trial investigating nutritional supplementation and enhanced physiotherapy with a structured exercise programme in combination with ICU recovery manuals [46▪], those patients receiving both additional modalities as the intervention demonstrated the steepest recovery slope in terms of distance covered in the 6MWT, increasing by 124% from 170 to 380 m. Similar increases in walking capacity using this measure were also reported by Connolly *et al.* [47] in a pilot feasibility trial of posthospital discharge exercise-based rehabilitation with median (interquartile range, IQR) changes of 185 (40–285) and 140 (36–210) m in usual care and intervention groups, respectively. That these improvements far exceed the estimated minimum important difference reported by Chan *et al.* [41▪▪] suggest that further work is required for evaluating the 6MWT as a tool for measuring response to physical rehabilitation interventions in the postcritical illness population.

Finally, choice of assessment tool to determine eligibility into trials of physical rehabilitation is also an important factor [47]. In the study by Connolly *et al.* [47], patients were included on the basis of diagnosis of ICU-acquired weakness measured using manual muscle strength testing (Medical Research Council Sum-score less than 48 out of 60). However, this technique demonstrated a clinically significant ceiling effect between ICU discharge (randomisation) and hospital discharge (intervention commencement) that would otherwise have influenced enrolment rates.

CONCLUSION

The rehabilitation literature describing physical interventions to promote recovery in critically ill patients is steadily increasing. However, there is a clear need for development of clinimetrically robust tools to measure response to therapeutic options in patients as they transition through the recovery pathway from ICU admission, post-ICU discharge within the hospital and following hospital discharge. Adopting the ICF framework can guide physical function assessment, albeit multiple tools will be required to accurately capture data pertaining to impairment, activity limitation and participation restriction. No single outcome measure will likely meet the necessary requirements; moreover, an armoury of tools that clinicians and researchers can select from, mapped to this framework and with proven measurement properties will have greatest utility [21▪▪]. In addition, this would allow flexibility to account for individual trajectories of recovery [48]. In the future, a core set of outcomes for trials in this area would facilitate standardization of measurement, future systematic review and meta-synthesis of findings and clinical translation of trial results [16,49]. These same principles apply across the spectrum of PICS morbidity. Long-term outcomes postcritical illness extend beyond traditional mortality-related indicators [50▪▪,51]. As a clinical and research community, our focus now needs to be directed to determining outcomes and their associated metrics of evaluation that best describe and measure domains of physical, cognitive and psychological dysfunction during recovery after critical illness. Significantly, these outcomes must include those considered meaningful by our patients.

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Conflicts of interest

There are no conflicts of interest.

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