PRACTICE: Development of a Core Outcome Set for Trials of Physical Rehabilitation in Critical Illness

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**Supplementary information**

This article has an online data supplement, which is accessible at the Supplements tab.

**ABSTRACT**

**Rationale**

Findings from individual trials of physical rehabilitation interventions in critically ill adults have limited potential for meta-analysis and informing clinical decision-making due to heterogeneity in selection and reporting of outcomes used for evaluation.

**Objective**

The objective of this study was to determine a core outcome set (COS) for use in all future trials evaluating physical rehabilitation interventions delivered across the critical illness continuum of recovery.

**Methods**

An international, two-round, online, modified Delphi consensus process, following recommended standards, was conducted. Participants (N=329) comprised three stakeholder groups (Researchers, n=58 (18%); Clinicians, n=247 (75%); Patients and Caregivers, n=24 (7%)), and represented 26 countries and 9 healthcare professions. Participants rated the importance of a range of relevant outcomes. Outcomes included in the COS were those prioritised of "critical importance" by all three stakeholder groups.

**Results**

Survey response rates were 88% (Round 1) and 91% (Round 2). From a total of 32 initial outcomes, the following outcomes reached consensus for inclusion in the COS: Physical Function, Activities of Daily Living, Survival, Health-related Quality of Life, Exercise Capacity, Cognitive Function, Emotional and Mental Wellbeing, and Frailty.

**Conclusion**

This study developed a consensus-generated COS for future clinical research evaluating physical rehabilitation interventions in critically ill adults across the continuum of recovery. Ascertaining recommended measurement instruments for these core outcomes is now required to facilitate implementation of the COS.

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**Registration**

PRACTICE was registered *a priori* on the COMET database (Record ID 288; http://www.comet-initiative.org/Studies/Details/288).

**INTRODUCTION**

Physical rehabilitation is an essential component in the management of critically ill patients to address post intensive care syndrome (PICS)-related impairments in physical function, exercise capacity, and health-related quality of life (1). Interventions are recommended across the recovery continuum of critical illness (2), and have been evaluated within the intensive care unit (ICU), after transfer to the ward, after hospital discharge, and across multiple stages of the recovery continuum (3-6). However, heterogeneity in selection and reporting of outcomes in trials evaluating physical rehabilitation interventions in critical illness limits the interpretation of individual study findings and precludes synthesis of multiple datasets (7). For example, four of the most recently published international trials of physical rehabilitation in the ICU each reported a different primary outcome and had total number of outcomes (primary and secondary) ranging between 7-18(3, 8-10). Only the outcome of physical function was consistent across the four trials, albeit with variability in outcome measure and timing of data collection; generic function measured using the World Health Organization Disability Assessment Schedule at Day 180 (3), functional independence measured using ambulation and Functional Independence Measure at hospital discharge and 1 year (8), peak modified ICU Mobility Scale measured within 48 hours of ICU discharge (9), and Physical Function Test for ICU-scored measured at 3 days after ICU discharge (with other measures of physical function also reported) (10). This heterogeneity fosters outcome reporting bias and research waste (11, 12), and reduces the usefulness of trials for informing evidence-based clinical decision-making in this area (13). Lack of consensus exists on the most appropriate outcomes for use in these trials (14).

Core outcome sets (COS) represent an approach for helping address the aforementioned issues. A COS is an agreed upon collection of outcomes to be measured and reported, as a minimum, in all clinical trials for a defined field of interest (11, 12). The value of a COS lies in harnessing consistency in all trials measuring a minimum set of identical outcomes; applying a COS to future trials would generate this consistency for facilitating data synthesis. Examples of existing COS in critical illness

include long-term outcomes after hospital discharge in survivors of acute respiratory failure (15), mechanical ventilation (16), cardiac arrest (17), and delirium (18). However, no COS exists for physical rehabilitation in critically ill adults.

Therefore, the aim of the current study (PRACTICE; Physical Rehabilitation Core Outcomes in Critical Illness) was to develop a COS for trials of physical rehabilitation interventions delivered across the continuum of recovery for critically ill adults. Specifically, the scope of the COS primarily relates to quantitative clinical research studies evaluating physical rehabilitation interventions (e.g. mobilisation, exercise, or adjuncts such as cycling or electrical muscle stimulation), delivered to adult critically ill patients, at one or more stages of the recovery continuum (i.e. in-ICU, on hospital ward, or after hospital discharge).

**METHODS**

We conducted an international, two-round, online, modified Delphi consensus process to determine the core outcomes ('what' to measure) for the PRACTICE COS. Our methods align with recommended COS development and reporting (19-21); the study protocol has been published (22), with detail reported in the Online Data Supplement (ODS). In brief, we recruited a large, diverse, international participant panel representing three stakeholder groups of 'Researchers', 'Clinicians', and 'Patients and Caregivers' (full detail of recruitment processes reported in ODS E1). Participants rated the importance of a range of outcomes (ODS E2), sourced through prior systematic reviews of quantitative (23) and qualitative (24) literature, revised and refined by the study team, and supported by findings from patient and care partner interviews (*unpublished*). Participants were reminded that the goal of the PRACTICE COS was to determine the minimum set of outcomes for evaluation in all future trials of physical rehabilitation in critically ill adults across the recovery continuum. The two-round Delphi process commenced on 21st June 2018 and completed on 14th September 2018.

Each outcome was rated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) scale (25), ranging a score of 1-9 in terms of importance for inclusion in the final COS (1-3, "not important" for inclusion; 4-6, "important" but not critical; 7-9, "critical" for inclusion). Participants were also provided with an 'Unable to score' response if they considered themselves unable to rate an outcome. Consensus for determining importance of an outcome by a particular stakeholder group was defined as ≥70% of responses rating the outcome as 'critical', and ≤15% of responses rating the outcome not important. Core outcomes were those agreed on by all three stakeholder groups using these consensus criteria (26). Only participants fully completing Round 1 were invited to complete Round 2, where additional outcomes suggested by participants (from Round 1) were added to the consensus survey, and the wording of a number of outcomes was revised for clarity (ODS E3). In Round 2, participants were provided with feedback on Round 1 scoring in the form of histograms for the whole participant panel and for each stakeholder group and shown their previous individual score for each Round 1 outcome. Re-scoring was requested based on this feedback, with rationale requested in the event any change of score altered the overall category of importance rating (ODS E4). In both rounds, the order of outcomes was randomised to one of 4 different orders.

DelphiManager software (COMET Initiative, University of Liverpool, UK) was used to administer the consensus survey rounds. Response rates were defined as the proportion of recruited participants who completed each survey round out of the total number of participants for that stakeholder group. Rates were reported for each stakeholder group. Descriptive statistics were used to analyse and summarise survey round responses, using GraphPad Prism version 7.0d (GraphPad Software, La Jolla, CA, US, www.graphpad.com). Histograms and other data management were conducted using Microsoft Excel (Microsoft Office, WA, US). PRACTICE was registered *a priori* on the COMET database (Record ID 288; http://www.comet-initiative.org/Studies/Details/288), and follows

recommendations for COS development (20) and reporting (21). Confidentiality was ensured by allocation of a unique identifier to each participant, and data storage on secure, encrypted, password-protected, institutional devices. Participant information sheets were circulated during promotion of the project, and the landing page of the survey also included information regarding participation. Completion and submission of the electronic surveys indicated consent to participate. The study was approved by King's College London BDM (Biomedical Sciences, Medicine, Dentistry and Natural & Mathematical Sciences) Research Ethics Panel (LRS-17/18-4603), and the UK Health Research Authority National Research Ethics Service North-East Committee (18/NE/0018).

**RESULTS**

A total of 329 participants completed Round 1, representing 88% of 376 eligible expressions of interest who received the survey link. The panel comprised 58 Researchers (18%), 247 Clinicians (75%), and 24 Patients and Caregivers (7%). Participant details are provided in Table 1 and ODS (E5). The mean (SD) age of participants was 44 (10) years, and the majority were female (n=193, 59%). Participants represented 26 countries (most (n=193, 59%) from the United Kingdom), and nine professions. Within the Researcher stakeholder group, the largest professional group was physicians (n=30, 52%), whereas in the Clinician stakeholder group, it was physical therapists (n=119, 48%). Mean (SD) years of professional experience were 22 (10) and 18 (8) for the Researcher and Clinician stakeholder groups respectively. Almost all researchers and clinicians managed patients in the ICU, with lesser involvement with post critical illness patients on the ward and after hospital discharge. Most Patient and Caregiver participants (n=17, 71%) were discharged from the ICU less than three years prior.

*Round 1*

A total of 30 outcomes were included in Round 1 (ODS, E2). Four outcomes reached consensus for inclusion as outcomes in the core set: activities of daily living, physical function, health-related

quality of life, and survival (Table 2). A full breakdown of scoring for each outcome according to stakeholder group is reported in the ODS (E6). Panel members suggested 51 additional outcomes for consideration in Round 2 (ODS E3); after removal of duplicate and non-relevant outcomes this resulted in the addition of two new unique outcomes to Round 2 (resilience and bone health). All other outcomes from Round 1 were carried forward into Round 2.

*Round 2*

A total of 300 participants (/329, 91%) completed Round 2. The panel comprised 55 Researchers (18% [/58, 95% of Round 1]), 226 Clinicians (75% [/247, 91% of Round 1]), and 19 Patients and Caregivers (6% [/24, 79% of Round 1]). Results are summarised in Table 3 and in detail in the ODS (E7). All four outcomes reaching consensus for the COS from Round 1 (activities of daily living, physical function, health-related quality of life, and survival) retained agreement for inclusion with increased support. One outcome (physical function) scored 100% for critical importance by all participants. Neither of the two additional outcomes suggested by participants in Round 1 met the consensus criteria (resilience, 40%; bone health, 16%). Four additional outcomes (exercise capacity, cognitive function, emotional and mental wellbeing, and frailty) were scored as critically important by all three stakeholder groups. The final COS is presented in Figure 1.

**DISCUSSION**

This study has determined a COS for future trials of physical rehabilitation in critically ill adults across the recovery continuum, via a rigorous international online modified Delphi consensus process. All three stakeholder groups - Researchers, Clinicians, and Patients and Caregivers – prioritised eight core outcomes that reflect a broad range of the impairments experienced by adult survivors of critical illness; physical function, activities of daily living, survival, health-related quality of life, exercise capacity, cognitive function, emotional and mental wellbeing, and frailty.

*Clinical interpretation*

Given the scope of this COS focused on outcomes for physical rehabilitation interventions in critically ill adults, it was relevant that results included multiple outcomes related to physical performance or ability; three were ultimately identified - physical function, activities of daily living, and exercise capacity. Indeed, the inclusion of physical function was unanimous. In addition, whilst health-related quality of life is an outcome that encapsulates multiple elements, it typically includes some reflection of the impact of an individual's physical status, and physical impairment is a contributor to poor health-related quality of life in survivors of critical illness up to 10 years thereafter (27). The importance of the interaction between physical and cognitive health after critical illness is recognised; a recent randomised trial reported a significant reduction in cognitive impairment at 1 year after hospital discharge in patients receiving an early rehabilitation co-treatment by physiotherapist and occupational therapist (24%, 24/99 participants) compared to usual care (43%, 43/99 participants, absolute difference –19%, 95% CI -32 to –6%, p=0.0043) (8).

Early mobilisation interventions in the ICU have been systematically reviewed, concluding no association with mortality compared to usual care (RR 0.98 [95% CI 0.87–1.12], p=0.81) (28). However, inclusion of survival as an outcome in PRACTICE mirrors other COS in critically ill populations (15, 16, 18), and capturing these data is important for trial process-reporting of patient flow. Reporting attribution of mortality to a physical rehabilitation intervention is essential; a previous trial of functional electrical stimulation in conjunction with in-bed cycle ergometry showed 85% of decedents allocated to the intervention group had never received the intervention prior to death (29). Physical health and emotional and mental wellbeing are closely inter-related when outcomes of critical care survivors are examined; poor physical functioning and independence are associated with worse mental health (30) and co-existence of physical impairment and mental health symptoms is common (31). Frailty is a complex syndrome that can be characterised through distinct models e.g. a physical phenotype, an accumulated deficits model across multiple domains,

and a multidimensional approach capturing holistic impairment (32). Interestingly, this was the outcome which, whilst meeting criteria for inclusion in the COS, showed greatest variation in ratings between Researcher and Clinician, and Patients and Caregiver, stakeholders. Frailty is associated with increased post-ICU disability (33). That this was rated so highly by patients and caregivers (95% rated as critically important) may reflect the personal perspective of these participants and the cumulative impact of multiple sequelae following their critical illness, and which is important for Researchers and Clinicians to be cognisant of.

Beyond the core outcomes agreed upon, the outcomes that individual stakeholder groups considered important are valuable for appreciating their different perspectives with regards physical rehabilitation interventions. For example, patients and caregivers highly rated the experience of participating in rehabilitation; a finding that should focus researchers and clinicians on how interventions are designed and delivered to maximise engagement, adherence, and fidelity. Furthermore, clinicians highly rated delirium, perhaps influenced by knowledge and experience of how this condition can impact on patients' ability to participate in rehabilitation activities in the ICU. In addition, clinicians' role in discharge planning and rehabilitation requirements at later recovery stages may have contributed to their views on the importance of place of residence and return to work or prior role as outcomes.

Outcomes prioritized in the PRACTICE COS reflect three of the areas highlighted by the COMET taxonomy; Death, Life Impact, and Physiological/Clinical (34), with Resource Use and Adverse Events not represented in the final COS. Resource Use typically captures economic data, which may be assessed separately in physical rehabilitation trials through parallel health economic analyses (e.g. (35, 36)), or outcomes related to hospital admission (e.g. ICU and hospital length of stay, or mechanical ventilation duration) and/or the need for concomitant interventions such as other organ support or medications (34). The latter data are frequently captured as baseline characteristic

features of populations enrolled into physical rehabilitation trials. The final domain within Resource Use is that of societal/carer burden, which captures outcomes relating to the financial or time implications on individual carers or society (34). The impact on families and caregivers following a patient's critical illness is increasingly appreciated (37-40); the inclusion of outcomes related to caregiver burden as a result of physical rehabilitation interventions delivered to patients may be important to consider in future trials to ensure a holistic approach. With regard to the area of Adverse Events, these data are typically defined during protocol development, specific to an individual trial, and reported as part of clinical trial conduct (41), thereby removing the need for inclusion as a core outcome.

Finally, the scope of the PRACTICE COS was defined as physical rehabilitation interventions in critically ill adults across the recovery continuum, agnostic to any specific clinical condition or patient population. However, we observed considerable overlap in core outcomes with COS focused on other aspects of managing critically ill patients such as long-term outcomes, nutrition and metabolic interventions, and delirium, that reflects the homogeneity of key features of survivorship e.g. survival (15, 18, 42), physical function (15, 42), cognition, health-related quality of life, and emotional wellbeing (15, 18), and activities of daily living (42). Nonetheless, this still does not preclude researchers from referring to other bespoke COS to select outcomes where a particular context is warranted e.g. patients with COVID-19 (43), cardiac arrest (17), or receiving extracorporeal membrane oxygenation (44).

*Critique of the method*

This study benefited from rigorous methods that followed published recommendations for COS development and reporting (20, 21), were published *a priori* (22), and were consistent with those adopted by similar studies in critical care (15-18). Our participant panel was large, international, and multi-professional. That said, despite wide attempts to engage participation in as many countries as

possible, some regions are relatively under-represented where contact details were difficult to obtain. In addition, organisational policy precluded circulation of study information to local memberships of some professional societies which limited dissemination of the project via these channels. Our survey was limited to the English language, and the predominance of participants from high income countries may reflect responses from those with differential experience of greater access to rehabilitation services. Our Patient and Caregiver stakeholder group was modest in size in comparison to the Researcher and Clinician groups, albeit this is similarly observed in other critical care COS (16, 44). Despite recognition of the importance of patient and public involvement in COS development (45), this remains a challenging stakeholder group to recruit to for various reasons (46). However, we ensured their voice was equally balanced with the other two stakeholder groups, thereby avoiding potential bias from results based on size of stakeholder group, and ensuring our results reflect outcomes that are meaningful to patients and caregivers (47, 48). Our study also benefited from the input of two former ICU patients within the study team (CD, GS) (19, 46). Notably, we had minimal participant attrition with more than 90% of researchers and clinicians, and nearly 80% of patients and caregivers, participating in both survey rounds.

The list of outcomes presented in Round 1 was comprehensive and widely sourced. We initially planned to present outcomes in the consensus survey rounds according to which stage of the recovery continuum after critical illness they had reportedly been evaluated (22). However, we found that this was not necessary as outcomes typically featured across multiple stages; we therefore elected instead to present outcomes as one whole list, and randomised into four different orders with the benefit of avoiding potential response order bias (49). We had also anticipated for a third consensus survey round to enable two rounds of importance rating for any additional outcomes introduced through Round 1. However, as there were only two of these outcomes, both scoring low for importance rating, a third consensus round was unnecessary. We ensured clear participant information through the consensus survey rounds that reinforced the purpose and scope

of the PRACTICE COS. However, some participants' responses may still have been informed by prior preferences on items they felt were important or related to (physical) recovery overall after critical illness, rather than as an outcome to evaluate effectiveness of a physical rehabilitation intervention per se.

Our data collection pre-dates the COVID-19 pandemic, therefore considering the stability of our findings during the interim and their contemporary representativeness with current reporting, is important. COS are not typically updated on a frequent basis; updated COS from many other clinical conditions (there are no known updates to critical care-related COS) have, on average, occurred approximately 15 years after first development, with the majority nearer to 20 years (50-57). The predominant reason for updating is to reflect advancements in COS methodology e.g. enhanced inclusion of patient and public partners. Relatively earlier updates have been in response to significant treatment advancements in the field that impact potential clinical and patient-reported outcomes e.g. novel immuno- and targeted-therapy in lung cancer (51). The robust approach to the development of the PRACTICE COS supports its methodological longevity and rigour. Furthermore, its external validity can be evidenced in the three trials of physical rehabilitation interventions described earlier. These were published subsequent to PRACTICE data collection and continue to demonstrate outcome heterogeneity. However importantly, all individual primary and secondary outcomes were reflected in outcomes included for rating in the PRACTICE Delphi consensus process (3, 8, 9). The mixed findings from these, and other physical rehabilitation studies to date, highlight challenges in interpretation of different rehabilitation *interventions*, but their choice of *outcomes* used for evaluation indicate stability in the representativeness and reliability of the PRACTICE COS.

The PRACTICE COS may not immediately impact the ability to synthesise data across existing trials of physical rehabilitation interventions in critically ill adults, unless they report any of the core outcomes and have commonality in outcome measures and timing of data collection. The true value

of the COS lies in encouraging future trials to refer to and adopt it when designing their trial protocols, and the exponential application of the COS in this way would result in greater consistency and synthesis across studies. Determining consensus on measurement variables for the core outcomes is vital if the COS is to be successfully implementable and is the focus of the next stage of the PRACTICE study. As part of this, existing measures, tools, or instruments will be identified as potential candidates, and a further Delphi process conducted. Importantly, given the similarity across many existing COS in critical illness, regardless of intervention, overlapping outcomes where agreement has already been achieved for measurement will be reviewed and considered for PRACTICE e.g. health-related quality of life and emotional and mental wellbeing. In this way, unnecessary duplication of efforts will be avoided, and participant effort focused on those core outcomes in PRACTICE without agreed outcome measures. In the future, development of COS for other aspects of critical care management may only need to focus on outcomes that are bespoke to that particular scope i.e. there may be potential for a central COS for critical illness, with additional outcomes relevant to certain interventions or aspects of care.

**CONCLUSION**

Evidence regarding physical rehabilitation for critically ill patients along the recovery continuum continues to grow, albeit limited by the diverse range of outcomes used for evaluating effectiveness. This study has rigorously developed a consensus-generated COS (PRACTICE) for use in future trials to address this particular methodological challenge, containing eight critically important outcomes agreed by Researcher, Clinician, and Patient and Caregiver stakeholder groups. Ascertaining measurement instruments for the PRACTICE core outcomes is now required to facilitate implementation of the COS.

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**FIGURE LEGENDS**

**Figure 1.** The PRACTICE core outcome set; Physical Rehabilitation Core Outcomes in Critical Illness

These are the eight outcomes agreed as critically important for inclusion in the core outcome set by all three stakeholder groups (Researchers, Clinicians, Patients and Caregivers) and forming the core outcome set. This core outcome set can be used for future clinical research trials in physical rehabilitation for critically ill patients across the recovery continuum

**TABLES**

**Table 1.** Participant characteristics

| Characteristic | Researchers (n=58) | Clinicians (n=247) | Patient and caregivers (n=24) |
|---|---|---|---|
| Female#[a] | 24 (41) | 151 (61) | 18 (75) |
| Age (years)*[b] | 47 (10) | 42 (8) | 54 (13) |
| Region of residence#[c] | | | |
| - UK | 15 (26) | 167 (67) | 11 (46) |
| - N America | 12 (21) | 27 (11) | 12 (50) |
| - Europe | 15 (26) | 27 (11) | 0 |
| - Australasia | 10 (17) | 13 (5) | 1 (4) |
| - S America | 4 (7) | 4 (2) | 0 |
| - Africa | 0 | 6 (2) | 0 |
| - Asia | 2 (3) | 3 (1) | 0 |
| Occupation#[d] | | | |
| - PT | 17 (29) | 119 (48) | N/A |
| - Physician | 30 (52) | 80 (32) | N/A |
| - Nurse | 6 (10) | 23 (9) | N/A |
| - SLT/P | 0 | 10 (4) | N/A |
| - Dietitian | 0 | 8 (3) | N/A |
| - OT | 0 | 5 (2) | N/A |
| - Other | 5 (9) | 2 (<1) | N/A |
| Professional experience (years)*[e] | 22 (10) | 18 (8) | N/A |
| Professional involvement with patients#[f] | | | |
| - In the ICU | 55 (95) | 243 (98) | N/A |
| - Ward-based | 18 (31) | 112 (45) | N/A |
| - Post hospital | 21 (36) | 49 (20) | N/A |
| Years since ICU discharge# | | | |
| - 0 - ≤3 | N/A | N/A | 17 (71) |
| - >3 - ≤6 | N/A | N/A | 1 (4) |
| - >6 - ≤9 | N/A | N/A | 2 (8) |
| - 9+ | N/A | N/A | 4 (17) |

Data presented as n (%)# or mean (SD)*. Note % are rounded to nearest whole and therefore may not total 100. [a]n=327; 2 participants (n=2 Clinician stakeholder group) did not report sex. [b]n=324; 5 participants (n=1 Researcher stakeholder group, n=4 Clinician stakeholder group) did not report age. [c]n=26 individual countries represented (for further details see ODS, Table E5). [d]n=7 'Other' professions included CTU Researchers (n=3), Nurse Practitioner (n=1), Respiratory Therapist (n=1). [e]7 participants (n=4 Researcher stakeholder group, n=3 Clinician stakeholder group) did not report duration of professional experience. [f]Respondents could select more than on option related to working across more than one setting.

*Abbreviations:* UK = United Kingdom. PT = Physical/Physio-Therapist. SLT/P = Speech and Language Therapist/Pathologist. OT = Occupational Therapist. ICU = intensive care unit. CTU = Clinical Trials Unit.

**Table 2.** Consensus results for Round 1 outcome scoring

| | **Proportion of participants scoring outcome 7-9*** | | | |
|---|---|---|---|---|
| **Outcome** | **All participants (n=329)#** | **Researchers (n=58)** | **Clinicians (n=247)** | **Patients and caregivers (n=24)** |
| **CONSENSUS MET** | | | | |
| Physical function | 313 (95) | 56 (97) | 236 (96) | 21 (88) |
| Activities of daily living | 290 (88) | 50 (86) | 221 (90) | 19 (80) |
| Survival | 265 (81) | 49 (85) | 194 (79) | 22 (91) |
| Health-related quality of life | 264 (80) | 45 (78) | 202 (82) | 17 (71) |
| **CONSENSUS NOT MET** | | | | |
| Cognitive function | 246 (75) | 39 (67) | 188 (76) | 19 (79) |
| Return to work or prior role | 228 (69) | 36 (62) | 180 (73) | 12 (50) |
| Exercise capacity | 225 (68) | 38 (66) | 171 (69) | 16 (67) |
| Duration of mechanical ventilation | 220 (67) | 40 (69) | 164 (66) | 16 (67) |
| Frailty | 215 (65) | 38 (66) | 159 (64) | 18 (75) |
| Fatigue | 215 (65) | 37 (64) | 163 (66) | 15 (62) |
| Emotional and mental wellbeing | 214 (65) | 37 (64) | 160 (65) | 17 (71) |
| Delirium and related symptoms | 209 (64) | 36 (62) | 159 (64) | 14 (58) |
| Healthcare resource utilisation | 206 (63) | 35 (60) | 154 (62) | 17 (71) |
| Respiratory (pulmonary) function and symptoms | 202 (61) | 27 (47) | 155 (63) | 20 (83) |
| Place of residence | 199 (61) | 36 (62) | 150 (61) | 13 (54) |
| Muscle and/or motor nerve function | 189 (57) | 30 (52) | 143 (58) | 16 (67) |
| Communication difficulties | 185 (56) | 23 (40) | 141 (57) | 21 (88) |
| Swallowing function and symptoms | 182 (55) | 30 (52) | 134 (54) | 18 (75) |
| Pain | 166 (51) | 27 (47) | 126 (51) | 13 (54) |
| Patient experience of physical rehabilitation | 163 (50) | 18 (31) | 128 (52) | 17 (71) |
| Successful extubation | 156 (47) | 25 (43) | 114 (46) | 17 (71) |
| Reintubation | 143 (44) | 20 (35) | 112 (45) | 11 (46) |
| Social roles, activities, or relationships | 137 (42) | 21 (36) | 105 (43) | 11 (46) |
| Sleep and related symptoms | 129 (39) | 19 (33) | 95 (39) | 15 (62) |
| Nutrition-related parameters | 104 (32) | 16 (28) | 80 (32) | 8 (33) |
| Joint function | 91 (28) | 16 (28) | 63 (26) | 12 (50) |
| Financial impact on patient | 87 (26) | 18 (31) | 57 (23) | 12 (50) |
| Urinary function | 57 (17) | 7 (12) | 38 (15) | 12 (50) |

| | | | | |
|---|---|---|---|---|
| Gastrointestinal symptoms | 54 (16) | 8 (14) | 36 (15) | 10 (42) |
| Sexual function | 46 (14) | 7 (12) | 53 (22) | 5 (21) |

Data are reported as n (%). *Each outcome was scored according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) scale (25), ranging 1-9 in terms of importance for inclusion in the final core outcome set (1-3, not important for inclusion; 4-6, important but not critical; 7-9, critical for inclusion). Consensus for inclusion of an outcome by a particular stakeholder group was defined as ≥70% of responses rating the outcome as 'critical', and less than or equal to 15% of responses rating the outcome ≤3. Consensus for an outcome included in the core outcome set was defined as all three stakeholder groups scoring the outcome as critical for inclusion. Outcomes are ordered by the proportion of all participants scoring 7-9 according to meeting, and not meeting, consensus. The maximum number of participants who indicated 'Unable to score' for any outcome was 4. For full scoring breakdown, see ODS (Table E6).

**Table 3.** Consensus results for Round 2 outcome scoring

| | **Proportion of participants scoring outcome 7-9*** | | | |
|---|---|---|---|---|
| **Outcome** | **All participants (n=300)#** | **Researchers (n=55)** | **Clinicians (n=226)** | **Patients and caregivers (n=19)** |
| **CONSENSUS MET** | | | | |
| Physical function | 294 (100) | 55 (100) | 225 (100) | 19 (100) |
| Activities of daily living | 295 (98) | 54 (98) | 224 (99) | 17 (90) |
| Survival | 276 (92) | 54 (98) | 204 (90) | 18 (95) |
| Health-related quality of life | 268 (90) | 47 (86) | 209 (93) | 15 (79) |
| Exercise capacity | 253 (84) | 45 (82) | 192 (85) | 16 (84) |
| Cognitive function | 251 (83) | 41 (75) | 194 (86) | 16 (84) |
| Emotional and mental wellbeing | 232 (78) | 41 (75) | 178 (79) | 15 (79) |
| Frailty | 227 (76) | 41 (75) | 168 (74) | 18 (95) |
| **CONSENSUS NOT MET** | | | | |
| Duration of mechanical ventilation | 230 (77) | 42 (76) | 176 (78) | 12 (63) |
| Return to work or prior role | 229 (76) | 38 (69) | 181 (80) | 10 (53) |
| Fatigue | 229 (76) | 46 (84) | 172 (76) | 11 (58) |
| Respiratory (pulmonary) function and symptoms | 221 (74) | 31 (56) | 172 (76) | 18 (95) |
| Healthcare resource utilisation | 214 (71) | 39 (71) | 162 (72) | 13 (68) |
| Delirium and related symptoms | 211 (70) | 38 (69) | 162 (72) | 11 (58) |
| Place of residence | 210 (70) | 38 (69) | 160 (71) | 12 (63) |
| Muscle and/or motor nerve function | 202 (67) | 37 (67) | 151 (67) | 14 (74) |
| Swallowing function and symptoms | 192 (64) | 34 (62) | 142 (63) | 16 (84) |
| Communication difficulties | 184 (61) | 27 (49) | 140 (62) | 17 (90) |
| Patient experience of physical rehabilitation | 163 (54) | 22 (40) | 127 (56) | 14 (74) |
| Pain | 155 (52) | 24 (44) | 120 (53) | 11 (58) |
| Successful extubation | 147 (49) | 25 (46) | 111 (50) | 11 (58) |
| Reintubation | 147 (49) | 25 (46) | 112 (50) | 10 (53) |
| Social roles, activities or relationships | 116 (39) | 15 (27) | 90 (40) | 11 (58) |
| Sleep and related symptoms | 111 (37) | 17 (31) | 85 (38) | 9 (48) |
| Joint function | 63 (21) | 12 (22) | 42 (19) | 9 (47) |
| Nutrition-related parameters | 60 (20) | 9 (16) | 44 (20) | 7 (37) |
| Financial impact on patient | 59 (20) | 15 (27) | 32 (14) | 12 (63) |
| Urinary function | 32 (11) | 3 (5.5) | 21 (10) | 8 (42) |

| | | | | |
|---|---|---|---|---|
| Gastrointestinal symptoms | 32 (11) | 5 (9) | 21 (9) | 6 (32) |
| Sexual function | 30 (10) | 6 (11) | 19 (9) | 5 (26) |
| **ADDITIONAL OUTCOMES FROM ROUND 1** | | | | |
| Resilience | 121 (40) | 19 (35) | 88 (39) | 14 (74) |
| Bone health | 49 (16) | 10 (18) | 32 (14) | 7 (37) |

Data are reported as n (%). *Each outcome was scored according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) scale (25), ranging 1-9 in terms of importance for inclusion in the final core outcome set (1-3, not important for inclusion; 4-6, important but not critical; 7-9, critical for inclusion). Consensus for inclusion of an outcome by a particular stakeholder group was defined as ≥70% of responses rating the outcome as 'critical', and less than or equal to 15% of responses rating the outcome ≤3. Consensus for an outcome included in the core outcome set was defined as all three stakeholder groups scoring the outcome as critical for inclusion. Outcomes are ordered by the proportion of all participants scoring 7-9 according to meeting, and not meeting, consensus. The maximum number of participants who indicated 'Unable to score' for any outcome was 5. For full scoring breakdown, see ODS (Table E7).

**FIGURES**

**Figure 1.**