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Core outcomes sets for studies evaluating critical illness and patient recovery

Victor D. Dinglas, MPH^{1,2}, Sai Phani Sree Cherukuri, MBBS^{1,2}, Dale M. Needham, FCPA, MD, PhD^{1,2,3,4}

¹Outcomes After Critical Illness and Surgery (OACIS) Group, Johns Hopkins University, Baltimore, MD

²Division of Pulmonary and Critical Care Medicine, School of Medicine, Johns Hopkins University, Baltimore, MD

³Department of Physical Medicine and Rehabilitation, School of Medicine, Johns Hopkins University, Baltimore, MD

⁴School of Nursing, Johns Hopkins University, Baltimore, MD

Abstract

Purpose of Review—Given the growing body of critical care clinical research publications, core outcome sets (COS) are important to help mitigate heterogeneity in outcomes assessed and measurement instruments used, and have potential to reduce research waste. This paper provides an update on COS projects in critical care medicine, and related resources and tools for COS developers.

Recent Findings—We identified 28 unique COS projects, of which 15 have published results as of May 2020. COS topics relevant to critical care medicine include mechanical ventilation, cardiology, stroke, rehabilitation, and long-term outcomes (LTO) after critical illness. There are 4 COS projects for COVID-19, with a “meta-COS” summarizing common outcomes across these projects. To help facilitate COS development, there are existing resources, standards, guidelines, and tools available from the Core Outcome Measures in Effectiveness Trials (COMET) Initiative (www.comet-initiative.org/) and the National Institutes of Health-funded Improve LTO project (www.improvelto.com/).

Summary—Many COS projects have been completed in critical care, with more on-going COS projects, including foci from across the spectrum of acute critical care, COVID-19, critical care rehabilitation, and patient recovery and long-term outcomes. Extensive resources are accessible to help facilitate rigorous COS development.

Address for Correspondence: Victor D. Dinglas, MPH, Pulmonary & Critical Care Medicine, Johns Hopkins University, 1830 E. Monument Street, 5th floor, Baltimore, MD 21287, victor.dinglas@jhmi.edu, Phone: 410-502-7040.

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Introduction

As the population ages, the number of critically ill patients is increasing.[1] This epidemiological trend, combined with a decreasing mortality rate, results in a growing number of survivors of critical illness.[2,3] Concomitantly, there has been an increasing number of research studies in critical care medicine, including trials that evaluate interventions to improve patient outcomes along with epidemiological studies of critical illness and recovery.[4,5] An important challenge associated with the steadily growing number of publications is significant heterogeneity in outcomes evaluated and reported, as well as the risk of selective outcomes reporting in trials.[4,6] These issues can lead to unnecessary research waste.[6] As is occurring in other healthcare areas, there is a growing interest in creating and implementing core sets of outcomes and related measurement instruments to mitigate this heterogeneity in critical care.[7] Hence, our objective is to provide an update on: (1) completed and “in process” core outcome set projects for critical care, and (2) tools and resources to assist with developing a core outcome set.

Core Outcome Sets (COS) and Core Outcome Measurement Sets (COMS)

A core outcome set (COS) is a minimum collection of outcomes recommended to be measured within a specific field of research or clinical practice. A core outcome measurement set (COMS) is the set of measurement instruments for a COS. Such core sets facilitate synthesis and comparison across different studies within a specific field.[8–11] Importantly, a COS/COMS does not preclude studies from including other outcomes/measures beyond the core set as primary or secondary outcomes. Since COS/COMS are intended to serve as the minimum set of outcomes/measures to be used by all studies within a specific field, they should be concise and feasible to facilitate widespread uptake.

Inclusion of Patients in COS/COMS

In creating COS/COMS, developers should focus on outcomes that are important to patients (i.e. “patient-important outcomes”).[12,13*] The patient perspective is vital throughout the COS/COMS development process, to reflect patient-important outcomes in the resulting COS.[14,15] For example, preparation for a COS/COMS project may include surveys and/or qualitative research with patients, such as done in the Improve Long-Term Outcome (LTO) COS/COMS project.[16,17] Results from these patient-related studies may be presented to consensus panel members as part of the COS/COMS consensus process.

The COS/COMS consensus process is another stage during which the patients’ perspective is paramount. Patients can be panel members during the formal consensus process, with *a priori* consensus thresholds allowing for patient influence even if they are a minority group in the consensus process. For instance, a modified Delphi consensus process can use a 2-part consensus threshold, e.g., requiring at least 70% of panel members vote an outcome/measure

“Critical” for inclusion in the COS/COMS, and no more than 15% vote “Not important” for inclusion. Such a threshold would allow consensus panels with 15% patient representation to potentially exclude an outcome/measure from consensus.[18,19] Additionally, presenting prior voting round’s results for both the overall consensus panel and by panel subgroup (e.g. clinicians, researchers, patients) will allow more explicit consideration of other groups’ voting results before each participant votes in a new round of a modified Delphi process.[20]

Critical Care COS/COMS

We searched the Core Outcome Measures in Effectiveness Trials (COMET) Initiative’s registry of COS projects (www.comet-initiative.org)[21] in February 2020. The COMET Initiative was created in 2010 to promote COS/COMS development. We also searched PUBMED and Embase in March 2020 (search strategy in Supplementary Material), for COS/COMS projects relevant to critical care medicine. We identified 28 unique COS/COMS projects (Figure 1). We briefly summarize current COS/COMS projects (additional details in Supplementary Table 1), with greater detail provided for COS/COMS related to COVID-19 (Table 1) and to patient recovery after critical illness (Table 2).

Current Completed COS/COMS—At least 15 critical care COS/COMS projects have been completed (Supplementary Table 1). For example, there is a COS for studies of extracorporeal membrane oxygenation, with a related COMS under development.[22*] For mechanical ventilation trials, there is both a COS and COMS.[23*] We found 3 relevant core set projects in cardiology, focused on in-hospital cardiac arrest with a COS and COMS,[24*] cardiac arrest effectiveness trials with a COS and COMS, [25*] and cardiac surgery effectiveness trials with COS, but no published COMS.[26] There are COS/COMS for patient-centered stroke care (ischemic stroke or intracerebral hemorrhage),[27] and for stroke recovery trials.[28]

Coronavirus Disease (COVID-19) and Other Severe Acute Respiratory Infection—Coronavirus disease 19 (COVID-19) was declared a global pandemic on March 11, 2020.[29] By the end of March 2020, there were 4 COS projects focused on COVID-19 patients registered with the COMET Initiative.[30**] Three of the projects have been completed (Table 1);[31–33*] and three are for clinical trials and one is for any type of research study. Despite each project having somewhat different methodology or scope, there is overlap in the findings of these COS projects. The COMET Initiative convened teleconferences with leaders from all projects that resulted in a “meta-COS” consisting of 2 outcomes (mortality and respiratory support).[30**] Interim results from the ongoing COVID-19 COS project,[34*] also agreed with the COVID-19 meta-COS.[30**]

Prior to the COVID-19 pandemic, there was an earlier COS project (uncompleted, with 1 round of a modified Delphi consensus project in 2014, Supplementary Table 1) for studies of severe acute respiratory infection epidemic/pandemic (e.g., H5N1, H1N1 and syndrome-associated coronavirus (SARS)).[35] As of the time of our literature search, no COVID-19 COS project had been published on post-hospital patient recovery, but there is work underway (Table 3).[34*] In previous research, patients who survived Ebola,[36–38] SARS, [39–42] and acute respiratory distress syndrome (ARDS),[43–46] frequently have prolonged

impairments in physical, cognitive and mental health, suggesting that COVID-19 survivors will face similar challenges. Hence, it is imperative that COVID-19 researchers planning to evaluate post-hospital outcomes of critically ill patients use the existing COS/COMS for this patient population (see next section for detail and Table 2) to facilitate comparison and synthesis of results across different follow-up studies related to COVID-19 and to allow comparison with the larger body of literature on critical illness survivorship.[18,47]

Post-hospital COS/COMS for Critical Illness—Three COS/COMS projects have been completed regarding ICU survivors and post-hospital outcomes. The first was for a physical therapy (PT) framework for ICU survivors after hospital discharge.[48] This project, focused on clinical practice (rather than research), recommended data collection items during hospitalization and at hospital discharge, along with PT goals, PT interventions, and patient outcomes after discharge. This PT framework COMS contains at least 14 outcome measures, covering 9 outcomes (Table 2). This project recognized the importance of post-intensive care syndrome (PICS),[49] and recommending additional screening measures for fatigue, sleep, nutrition, mental health, and cognition.

The second project focused on clinical (rather than research) screening for PICS in the healthcare setting, after hospital discharge.[50*] Twenty healthcare providers from a single country participated in 3 semi-structured consensus meetings to select the outcomes and measures to evaluate PICS. After each meeting, feasibility was assessed with 5, 5, and 7 patients, respectively. For clinical practice, this project recommended a screening COMS, estimated to take 20 minutes, and an extended assessment COMS, estimated to take approximately 2 hours (Table 2).

The third project is a rigorous, international COS/COMS project focused on research on acute respiratory failure (ARF)/ARDS survivors after hospital discharge.[18,47] Notably, this COS/COMS does not mandate that all ICU studies conduct post-hospital follow-up; instead, it provides a COS/COMS for studies planning to do post-discharge follow-up, as either primary or secondary study outcomes. This project's consensus panel, representing 6 continents, included clinical researchers (n=35), clinicians/professional associations representatives (n=19), patients/caregivers (n=19), and US federal research funding organizations (n=4). It reached consensus on 8 outcomes and on measures for 4 of these outcomes. The project also provided suggested measures (i.e., measures that had the greatest support, but did not reach the threshold for consensus) for 3 of the 4 outcomes that were without consensus on measures (Table 2). Although this COS/COMS was focused on ARF/ARDS survivorship research, the resulting COS/COMS encompasses physical, cognitive, and mental health impairments (i.e., PICS) that may be experienced by all ICU survivors, including critically ill COVID-19 survivors.[49] Lastly, a National Heart, Lung, and Blood Institute (NHLBI) working group recently recommended use of this COS/COMS in all ARF/ARDS studies evaluating post-hospital outcomes.[51**] By using this COMS, researchers will help mitigate heterogeneity, and research waste, in ICU survivorship research.[4]

Ongoing/Planned Critical Care COS/COMS Projects—As of May 2020, we identified 13 projects that are either ongoing or not yet published (Table 2). For instance,

there is a COVID-19 project focused on suspected or confirmed cases in both in-patient and out-patient settings.³³ A COS/COMS for trials to treat or prevent delirium has been completed and awaits publication of results.[52] There is also a project focused on research with critically ill pregnant women,[53] a project for dysphagia intervention trials,[54] and on physical therapy in ICU.[55] There is one project on trials of traditional Chinese medicine in myocardial infarction,[56] and 7 projects relating to brain injury and stroke.[57–63]

Next Steps for Existing COS/COMS—For several projects, the most immediate next step is creating a COMS. Other “next steps” include evaluating uptake of the COS/COMS, as well as seeking feedback from users (i.e., researchers and participants) of the core sets. Moreover, to facilitate widespread uptake, it is important for COMS to be consistent and parsimonious. For example, a new COMS project should avoid selecting new instruments if a prior COMS (with the same outcome – e.g., health-related quality of life) has already conducted a rigorous project to select an instrument.

Resources for Future Critical Care COS/COMS and COS/COMS Dissemination

For future COS/COMS projects in critical care, there are existing guidelines and resources to facilitate a carefully planned, executed, and disseminated project as highlighted herein.

Guidelines and Resources for COS/COMS Projects—In addition to its COS registry, the COMET Initiative (www.comet-initiative.org) is a central resource for COS developers. For example, it has resources to help orient COS/COMS project participants, including written and audiovisual materials in understandable language, consistent with their goal of including patients and the public in COS/COMS projects. They also provide resources related to COS/COMS uptake, including a list of ongoing and published research evaluating uptake. Lastly, the COMET Initiative provides leadership in COS/COMS development, recently evident in facilitating a “meta-COS” to unify different COS/COMS projects for COVID-19 disease.[30**]

For those endeavoring to develop a COS/COMS, the following resources and guidelines are important (Figure 2; for more information: www.comet-initiative.org/Resources):

1. The COMET Handbook version 1.0 [20]

The handbook outlines a 5-stage process of developing a COS/COMS. Additionally, the COMET Handbook outlines a “sixth” stage of the COS/COMS development process that includes: implementing and assessing uptake, and reviewing the COS/COMS for needed changes and updates. This final stage facilitates successful dissemination and uptake of the COS/COMS, and ensures continued relevance by allowing the COS/COMS to evolve as the field requires.

2. Core Outcome Set-STAndards for Development (COS-STAD)[64]

The COS-STAD is a set of minimum requirements for a COS/COMS project. The COS-STAD includes 11 recommendations covering 3 domains: specifying scope, stakeholders, and the consensus process. Those who are in the planning stages can use COS-STAD as a starting point, while COS users can consider these criteria in evaluating a COS/COMS project.

3. Core Outcome Set-STANDARDISED Protocol Items (COS-STAP)[65**]

The COS-STAP Statement outlines 13 checklist items for inclusion in published protocols of COS/COMS projects. Key users of COS-STAP are journal editors and peer reviewers, who can use this resource to help assess a protocol. COS/COMS developers can use this statement to ensure they design COS-STAP compliant project protocols.

4. Core Outcome Set-STANDARDS for Reporting (COS-STAR)[66]

The COS-STAR Statement describes 18 required elements in reporting COS/COMS project results, to ensure completeness and transparency. At the time of this statement, most projects (>60%) have only reported the COS and no accompanying COMS;[67] hence, the statement focuses on reporting of COS results.

Additional resources are available through the U.S. National Institutes of Health (NIH)/NHLBI funded the Improving Long-Term Outcomes Research for Acute Respiratory Failure project (grant R24HL111895, www.improvelto.com) that include a rigorous international COS/COMS project. This critical care project has customizable COS/COMS templates to assist others who are designing and conducting COS/COMS (www.improvelto.com/cos-resources/), including email templates (e.g., invitation to participate, notice of Delphi round commencement, reminders) and a template for standardized presentation of information for each outcome measure being considered for the COMS. The latter has been successfully adopted by the NIH/National Institute on Aging-funded NIDUS project that has created infrastructure for delirium research (<https://deliriumnetwork.org/measurement/>)).

Another resource from the Improve LTO project includes a feedback survey for panel members after completion of a modified Delphi consensus process.[68] This COS/COMS project achieved >90% response through 5 Delphi rounds (2 rounds for COS, and 3 for COMS).[18,47] This high response was due, in part, to the rigorous participant retention efforts employed, akin to those used in longitudinal follow-up studies of critical illness survivors. These techniques to maximize panel member response included collecting extensive contact information at the time of panel member recruitment, and sending several email reminders plus outreach via phone and text messages. Results of this feedback survey provide assurance that these retention efforts were not bothersome and that the time commitment required to participate in the consensus process was appropriate.[68] Lastly, this feedback survey also reinforced that frequent reminders of the project objectives (i.e. why COS/COMS is needed), as well providing accessible language and definitions (e.g. definition of a measurement property, such as reliability) are important for panel members. [68*]

Dissemination of COS/COMS Results—In addition to seeking feedback from panel members in the Improve LTO COS/COMS project, they were asked to suggest ideas for disseminating the COS/COMS.[69*] Their feedback fit into 7 dissemination categories, with many of these dissemination ideas consistent with subsequent COS/COMS guidelines: 1) dissemination to professional and research groups; 2) advocacy by funding bodies; and 3) providing proof of uptake (i.e. such as this webpage www.improvelto.com/publications-

[coms-minimum/](#) that lists published work and study protocols that utilize the COS/COMS). [20,70] Only one dissemination idea from these published guidelines was not elicited during the survey: advocacy by systematic review organizations.[70]

Additional suggestions from this survey included: 1) use of social media to promote COS/COMS; 2) providing educational materials and programs (e.g. webinars); 3) creating publications; and 4) sharing web-based resources (e.g. www.improvelto.com/coms/). The Improve LTO COS/COMS project completed activities encompassing all 7 dissemination categories, demonstrating their feasibility. In this project, social media efforts and emails to stakeholders (e.g. research groups) resulted in registration surges for the COS/COMS website, a metric of successful dissemination outreach. In addition, regular electronic newsletters are sent to Improve LTO website registrants. Aside from being more cost-effective than in-person presentations, electronic modes of dissemination allow greater world-wide outreach. For example, the electronic newsletter to website registrants is sent to recipients in over 62 countries.[69]

Conclusion

We identified 28 critical care-related COS/COMS projects at various stages of completion, included detailed discussion of projects related to patient recovery after critical illness and to COVID-19. We shared extensive existing resources for developing a COS/COMS, including project registry and manuals, and guidelines to help with planning, protocol development, and dissemination of results.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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KEY POINTS

- As of May 2020, at least 15 core outcome set (COS) projects have published results, including in mechanical ventilation, cardiology, stroke, rehabilitation, and long-term outcomes, with at least 13 other ongoing COS.
- At least 3 COVID-19 COS have been completed, and the COMET Initiative has led efforts to synthesize a “meta-COS” with common elements from all COVID-19 projects.
- There is existing COS for research on acute respiratory failure/acute respiratory distress syndrome survivors after hospital discharge that can be applied to COVID-19 and other critical illness survivorship studies.
- There are extensive resources and guidelines for developing and disseminating COS for those who plan to develop COS for their field as outlined in this article.

Figure 1.

Filling-in Pieces of the Critical Care Core Outcome Set Puzzle

The inter-linked puzzle pieces in shades of white and light gray represent completed COS projects, while puzzle pieces in dark gray represent COS projects that are planned, ongoing or pending publication of results as of May 2020.

Abbreviation: COS, Core Outcome Set

COMET Handbook Version 1.0	COS-STAD Core Outcome Set-STAndards for Development	COS-STAP Core Outcome Set-STANDARDISED Protocol Items	COS-STAR Core Outcome Set-STAndards for Reporting
<p>This document outlines 5 stages in developing a core set project:</p> <ol style="list-style-type: none"> Define scope Ensure need and register in COMET database Develop project protocol Identify what to measure (COS) Define how to measure (COMS) <p>Subsequent steps:</p> <ul style="list-style-type: none"> - implement COS/COMS, - assess uptake of COS/COMS, - review COS/COMS for changes and updates 	<p>Scope</p> <ol style="list-style-type: none"> Setting/practice for COS Health condition for COS Patient/Population for COS Intervention for COS <p>Stakeholders</p> <ol style="list-style-type: none"> Users of COS Clinicians experienced with health condition Patients/proxies experienced with health condition <p>Consensus process</p> <ol style="list-style-type: none"> Initial catalog of outcomes Defining consensus process/method and definition of consensus <i>A priori</i> criteria for including, dropping, or adding outcomes for consideration Clear language to describe outcomes to all stakeholders 	<ol style="list-style-type: none"> Title/Abstract Introduction Background and objectives Setting and scope of COS: Health condition, population & intervention Methods Stakeholders involved How outcomes are identified Consensus process Consensus definition Analysis Outcome scoring/feedback Missing data Ethics & Dissemination Ethics approval Results dissemination Administrative Info Funding Conflicts of interest 	<ol style="list-style-type: none"> Title mentions COS/Abstract Introduction Background and objectives Setting and scope of COS: Health condition, population & intervention Methods Protocol/Registry Stakeholders involved How outcomes are identified Consensus process Outcome scoring Consensus definition Ethics and informed consent Results Protocol deviation Participant characteristics Enlist probable outcomes Final COS Discussion Limitations Conclusions Other information Funding Conflicts of interest

COS: core outcome set, a minimum set of outcomes recommended to be measured in all studies within a specific field
COMS: core outcome measurement set, the set of measurement instruments for the COS

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Figure 2.
 Key Resources for Core Outcome Set Developers

Table 1.**COVID-19 Core Set Completed Projects ***

Scope	Core Outcome Set	Core Outcome Measurement Set
"Meta-COS" for research in hospitalized COVID-19 patients[30]	Mortality Respiratory support	All-cause mortality -hospital discharge. Respiratory support type/respiratory failure
World Health Organization for COVID-19[33]	Viral burden Mortality Disease progression	Quantitative polymerase chain reaction Death at hospital discharge or 60 days WHO-Clinical Progression Scale
Clinical trials on COVID-19[32]	Disease stage: Mild Ordinary Severe Critical Rehabilitation	Time to negative SARS-CoV-2 RT-PCR Hospital length of stay Composite events (number with severe, critical status, all-cause death) Clinical symptoms score (See Supplementary Table 1 for detail) Time to negative SARS-CoV-2 RT-PCR Composite events (number with critical status, all-cause death) Hospital length of stay PaO ₂ /FiO ₂ Mechanical ventilation duration Time to negative 2 SARS-CoV-2 RT-PCR Mortality, all-cause Pulmonary function
Trials of traditional Chinese and Western medicine in COVID-19[31]	Clinical outcome: Recovery Improvement Progression Death Etiology Inflammatory factor Vital signs: Temperature Respiration Blood and lymphatic: Lymphocyte Virus antibody Respiratory outcomes:	Recovery rate/prevalence Improvement rate (severe to ordinary) To severe state, rate/prevalence Mortality Proportion of negative SARS-CoV-2 Time to negative SARS-CoV-2 RNA Decline speed of SARS-CoV-2 CRP level and CRP recovery time Fever Prevalence/clearance time Dyspnea prevalence; respiratory rate improvement; time to normal respiration rate; dyspnea clearance prevalence Lymphocyte count Virus antibody level

Scope	Core Outcome Set	Core Outcome Measurement Set
	Pulmonary imaging	Inflammation resolution/recovery time
	Oxygen saturation	Blood oxygen saturation or improvement prevalence PaO ₂ /FiO ₂ Arterial blood-gas analysis
	Mechanical ventilation	Mechanical ventilation duration/frequency/prevalence Supplemental oxygen duration/frequency/prevalence
	Oxygen intake	Oxygen-intake mode
	Pneumonia severity	Pneumonia severity index
	Clinical efficacy	Prevalence of disease progression
	Symptoms	Clinical symptom score

Abbreviations: COS, core outcome set; WHO, World Health Organization; COVID-19, coronavirus disease 2019; RT PCR, real time polymerase chain reaction; SARS-CoV-2, severe acute respiratory syndrome coronavirus 2; RNA, ribonucleic acid; CRP, C-reactive protein; PaO₂, partial pressure of oxygen in the arterial blood; FiO₂, fraction of inspired oxygen

*
For more details about each project see Supplementary Table 1

Table 2.

Critical Care Survivorship Core Set Completed Projects *

Scope	Core Outcome Set	Core Outcome Measurement Set
Post-hospital research studies of acute respiratory failure survivors[18,47]	Survival Health-related quality of life Mental health Pain Cognition Physical function Muscle and/or nerve function Pulmonary function	Date and location of death EQ-5D; <i>optional</i> , SF-36 v2 Hospital Anxiety and Depression Scale, and Impact of Event Scale-Revised EQ-5D pain question None, suggested MoCA-Blind None, suggested 6-minute walk test None, suggested manual muscle strength and handgrip strength None, consensus reached to reject all measures
Screening for Post intensive care syndrome (PICS) in outpatient healthcare setting[50]	<u>Screening:</u> Mental health Cognition Physical function Health-related quality of life 2 items on new/worsened health problems <u>Extended testing **:</u> Mental health Cognition Physical function Health-related quality of life 2 items on new/worsened health problems	Patient Health Questionnaire-4 MiniCog; Animal naming Timed Up-and-Go and handgrip strength EQ-5D-5L Numeric rating scale (1 to 10) Patient Health Questionnaire-8, Generalized Anxiety Disorder Scale-7, and Impact of Event Scale-Revised RBANS, and Trail Making Test A and B 2-Minute Walk Test, Handgrip strength, and SPPB EQ-5D-5L 12-Item WHO Disability Assessment Schedule Numeric rating scale (1 to 10)
Physical rehabilitation framework after hospital discharge for clinical practice and all research studies[48]	<u>Core Outcome Set</u> Exercise capacity and intensity Overall muscle strength Respiratory muscle function Pulmonary function Body composition tests Physical function and mobility	6-minute walk, 4-meter timed walk, & cycle ergometry Handgrip strength or hand-held dynamometry Maximal inspiratory/expiratory pressure Spirometry/Medical Research Council dyspnea scale Ultrasound/anthropometry Katz's ADL or Barthel Index or Lawton's IADL

Scope	Core Outcome Set	Core Outcome Measurement Set
	Quality of life Pain <u>Screen for Other PICS Outcomes:</u> Fatigue Sleep Nutrition Mental/cognition	SF-36 Physical Function domain or Timed Up & Go or Functional Independence Measure or de Morton Mobility Index or SPPB SF-36 and EQ-5D Visual analog scale for pain Multidimensional Fatigue Inventory Richards-Campbell Sleep Questionnaire Malnutrition Universal Screening Tool/ Short Nutritional Assessment Questionnaire Hospital Anxiety and Depression Scale, Impact of Events Scale—Revised, and Mini-Mental State Examination

Abbreviations: MoCA-Blind, Montreal Cognitive Assessment – Blind; RBANS, Repeatable Battery for the Assessment of Neuropsychological Status; SPPB, Short Physical Performance Battery; ADL, Activities of Daily Living; IADL, Instrumental Activities of Daily Living

* For more details about each project see Supplementary Table 1

** Extended testing suggested if below threshold in any screening measures

Table 3.

Core Outcome Set Projects that are Planned, Ongoing or Pending Publication

Scope	Method	Panel Members/ Stakeholders	Registry Link	Estimated Completion Date
COVID-19 research	Two rounds of modified Delphi, and three online consensus meetings	Clinical experts, ethicists, patient, caregivers, families, pharmaceutical representatives, researchers	http://www.comet-initiative.org/Studies/Details/1548	August 2020
Physical rehabilitation outcomes in critical illness for trials	Three rounds of modified Delphi process	Researcher, clinician, patient/caregivers, publication authors, clinical professional organizations, and patient support groups	http://www.comet-initiative.org/Studies/Details/288	Completed, pending publication
Prevention and/or treatment of delirium	Two rounds of modified Delphi process and consensus process	Clinicians, researchers, trialists, patients, and family	http://www.comet-initiative.org/Studies/Details/796	Completed, pending publication
Critically ill pregnant women	Two round of modified Delphi process	Clinical experts, caregivers, patients, families, researchers, service providers, journal editors	http://www.comet-initiative.org/Studies/Details/916	June 2018
Dysphagia intervention trials in ICU	Two rounds of modified Delphi, and consensus meeting	Clinical researchers, researchers and service users	http://www.comet-initiative.org/Studies/Details/1565	June 2021
Myocardial infarction outcomes in traditional Chinese medicine	Two rounds of modified Delphi, and consensus meeting	Traditional Chinese Medicine experts, Western medicine experts, methodologists in evidence-based medicine, journal editors and patients	http://www.comet-initiative.org/Studies/Details/1243	January 2020
Severe acquired acute brain injury trials	Modified Delphi process	Clinical experts, patients, caregivers, families, methodologists and researchers	http://www.comet-initiative.org/Studies/Details/1541	January 2025
Trials of traditional Chinese Medicine in hypertensive cerebral hemorrhage	Two or three rounds of modified Delphi process, and consensus meeting	Clinical experts, conference participants, caregivers, patients, journal editors, patient/support group representatives, researchers, statisticians	http://www.comet-initiative.org/Studies/Details/1475	December 2021
Trials of traditional Chinese medicine in cerebral infarction	Two or three rounds of modified Delphi process, and consensus meeting	Clinical experts, conference participants, caregivers, patients, journal editors, patient/support group representatives, researchers, statisticians	http://www.comet-initiative.org/Studies/Details/1472	December 2021
Trials of traditional Chinese medicine in ischemic stroke	Two rounds of modified Delphi process, and consensus meeting	Clinical experts, conference participants, caregivers, patients, journal editors, patient/support group representatives, researchers, statisticians, methodologists	http://www.comet-initiative.org/Studies/Details/1282	January 2020
Life after stroke effectiveness trials	Modified Delphi process, and consensus meeting	Charities, clinical experts, caregivers, patients, researchers, service commissioners	http://www.comet-initiative.org/Studies/Details/1114	November 2021
Chinese medicine in stroke rehabilitation	Two rounds of modified Delphi, and consensus meeting	Clinical experts, ethicists, patients, journal editors, methodologists, patient/support group representatives, policy makers, regulatory agency representatives, researchers, statisticians	http://www.comet-initiative.org/Studies/Details/1286	February 2020
Trials of upper limb rehabilitation after stroke	Modified Delphi process, focus groups, and interviews with stakeholders	Stroke survivors and their caregivers, relevant researchers, trialists, and clinicians	http://www.comet-initiative.org/Studies/Details/653	September 2017 Pending publication

Abbreviations: ICU, intensive care unit; COVID-19, coronavirus disease 2019