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Core Domains for Clinical Research in Acute Respiratory Failure Survivors: An International Modified Delphi Consensus Study

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Abstract

Objectives—To identify the core "domains" (i.e., patient outcomes, health-related conditions, or aspects of health) that relevant stakeholders agree are essential to assess in all clinical research studies evaluating the outcomes of acute respiratory failure survivors after hospital discharge.

Design—A two-round consensus process, using a modified Delphi methodology, with participants from 16 countries, including patient and caregiver representatives. Prior to voting, participants were asked to review: 1) results from surveys of clinical researchers, acute respiratory failure survivors, and caregivers, that rated the importance of 19 preliminary outcome domains, and 2) results from a qualitative study of acute respiratory failure survivors' outcomes after hospital discharge, as related to the 19 preliminary outcome domains. Participants also were asked to suggest any additional potential domains for evaluation in the first Delphi survey.

Setting—Web-based surveys of participants representing 4 stakeholder groups relevant to clinical research evaluating post-discharge outcomes of acute respiratory failure survivors: clinical researchers, clinicians, patients and caregivers, and US federal research funding organizations.

Interventions—None.

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Measurements and Main Results—Survey response rates were 97% and 99% in Round 1 and Round 2 respectively. There were 7 domains that met the *a priori* consensus criteria to be designated as core domains: physical function, cognition, mental health, survival, pulmonary function, pain, and muscle and/or nerve function.

Conclusion—This study generated a consensus-based list of core domains that should be assessed in all clinical research studies evaluating acute respiratory failure survivors after hospital discharge. Identifying appropriate measurement instruments to assess these core domains is an important next step toward developing a set of core outcome measures for this field of research.

Keywords

Patient Outcome Assessment; Follow-up studies; Intensive care; Disability Evaluation; Quality of Life; Clinical Trials

Introduction

Increasing intensive care unit (ICU) survival rates (1) and growing recognition that some ICU survivors experience new and long-lasting problems with their physical, cognitive, and mental health outcomes (2–5) highlight the diversity and magnitude of the challenges of ICU survivorship. In response, many groups, including the National Heart, Lung, and Blood Institute (NHLBI); Society of Critical Medicine; American Thoracic Society; and the Multi-society Task Force for Critical Care Research, have recommended prioritizing research on the outcomes of ICU survivors after hospital discharge (6–12). Although there have been >300 original research publications on ICU survivors' outcomes after hospital discharge since 2000 (13), comparing, synthesizing, and interpreting this work has been difficult. (14) A recent scoping review found that 250 unique measurement instruments were used between 1970 and 2013 to assess ICU survivors' outcomes after hospital discharge (13) making comparisons between studies difficult. Additionally, the psychometric properties of many of the instruments used in these studies have not been well-evaluated among ICU survivors. (15)

A core outcome set (COS) is a minimum collection of outcome measures reported in all studies within a specific field (16, 17). Importantly, a COS does not prevent investigators from collecting data on additional outcomes. Instead, a COS sets a minimum standard to ensure that the most basic and crucial outcomes in a given field are consistently assessed in the same way to facilitate comparisons, meta-analyses, and prevent bias from selective outcome reporting (18, 19). In developing a COS, relevant stakeholders participate in a deliberate and systematic process to identify measurement instruments that: 1) evaluate vitally important outcome domains, 2) have sound measurement properties, and 3) are accessible and feasible for the proposed purpose (20). As of September 2016, there are 7 projects registered with the Core Outcome Measures in Effectiveness Trials (COMET) Initiative (http://www.comet-initiative.org/) to develop COS related to critical care (21).

Before selecting measurement instruments for a COS there must be consensus on "Core Domains," defined as patient outcomes, health-related conditions, or aspects of health, that are essential to evaluate within a clinical field (20, 22). The process of identifying Core

Domains focuses on “what” types of outcomes to measure (e.g., muscle strength), before a subsequent step of determining “how” to measure these outcomes (e.g., hand grip dynamometry). Despite the hundreds of measurement instruments used to evaluate ICU survivors, it is likely that valid, reliable, and accessible instruments for measuring some core domains do not yet exist. However, focusing on those outcomes that are truly essential to evaluate in all clinical research studies of ICU survivors, regardless of current availability and feasibility, helps set long-term goals and identify methodologic research priorities within a field. Hence, our objective was to identify the Core Domains for clinical research evaluating the outcomes of survivors of acute respiratory failure (ARF), including acute respiratory distress syndrome, after hospital discharge using a rigorous consensus methodology and an international panel of relevant stakeholders.

Methods

We conducted a two-round, international consensus development process using a rigorous modified Delphi methodology with web-based communication and anonymous voting. The Delphi consensus methodology uses expert opinion to address questions for which empirical data are unavailable or inadequate (23). Recently, the Delphi method has been used to develop COS for research on conditions as diverse as multiple sclerosis (24), stroke (25), and preterm birth (26). More information about Delphi methodology, identifying outcome domains, and survey development is available in Table E1. We have reported this research study in accordance with current recommendations for establishing COS via the Delphi process (17, 27). A copy of the complete study protocol can be accessed at http://www.improvelto.com/. This project was registered with COMET Initiative (http://www.comet-initiative.org/studies/details/360) and funded by NHLBI (Grant R24HL111895, Improving Long-Term Outcomes Research for Acute Respiratory Failure – see www.ImproveLTO.com).

Recruitment of the Delphi Panel

We sought to recruit a diverse panel with emphasis on end-users of the COS (i.e., clinical researchers evaluating patient outcomes after ARF). Based on methodological guidance from the Patient-Centered Outcomes Research Institute (PCORI) (28), Agency for Healthcare Research and Quality (AHRQ) (29), and Outcome Measures in Rheumatology (OMERACT) (20), four stakeholder groups relevant to clinical research evaluating post-discharge outcomes of acute respiratory failure survivors were identified for this consensus project: 1) critical care clinical researchers, 2) clinicians caring for ARF patients/survivors, 3) ICU survivors or caregivers of ICU survivors, and 4) representatives of federal organizations that fund ARF clinical research. Given that the target end users were clinical researchers, we focused on an international recruitment strategy, as described in Table E1 and E2 of the electronic supplementary materials. For recruiting clinicians, and patients and caregivers to the consensus process, we focused on representatives from the U.S., U.K., Australia, and Canada as these were the top 4 English-speaking countries represented in a scoping review of outcome measurement in ICU survivorship research (13) and participants will be asked to review individual English-language measurement instruments in a future study. Recruitment methods and response rates by stakeholder group, as well as the list of

panel members are provided in Table E1 and Table E2. Invitation e-mails to all invited stakeholder representatives explained that survey completion would serve as informed consent and specified the need for commitment to, and timely participation in, the entire Delphi process. The Qualtrics online survey platform was used to collect demographic information about expert panel members, and DelphiManager software (COMET Initiative, Liverpool, UK) was used to administer the Round 1 and Round 2 surveys. The institutional review board of Johns Hopkins University approved this study.

Modified Delphi Methodology

At the start of both Delphi rounds, participants were reminded of the goal of the consensus project and the definition of a core domain. Each domain was rated using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) scale (30), which is a 9-point scale that is commonly divided into 3 categories for COS projects: Not Important (1 – 3), Important but Not Critical (4 – 6), and Critical (7 – 9). Additionally, panel members were provided an "Unable to Score" response and instructed to use it if they did not feel comfortable rating any specific domain. Consensus for designation as a "Core Domain" was defined *a priori* as: ≥70% of responses rating the domain as "Critical" (i.e., a score ≥7) and ≤15% of responses rating the domain as "Not Important" (i.e., score ≤3). This consensus definition has been used in other Delphi studies (31–34) and ensured that a domain would not achieve consensus if a minority stakeholder group (i.e. patients/caregivers or clinicians) commonly rated it as "Not Important". All steps in the Delphi process took place on-line, and the anonymity of panel members was maintained throughout.

Round 1

Round 1 started January 8, 2016. Prior to voting, participants were asked to review: 1) results from surveys of clinical researchers, ARF survivors, and caregivers, that rated the importance of 19 preliminary outcome domains, and 2) results from a qualitative study of ARF survivors' outcomes after hospital discharge, as related to the 19 preliminary outcome domains. The Round 1 survey asked Delphi panel members to rate the importance of each of the 19 preliminary domains without consideration of the availability, ease of use, feasibility, or measurement properties of any available instruments to assess the domain. Participants who scored the cognitive function domain as Critical (score ≥7) were then asked to rate the 9 cognitive function sub-domains, as described above. The survey asked an open-ended question about other potential core domain(s) missing from the preliminary list. Panel members were given the option to provide text-based comments or feedback after scoring each domain and at the end of the survey. To help prevent any potential bias from response order effects (i.e., primacy and recency effects(35)), the 19 preliminary domains were presented in one of four unique orders randomly generated using R statistical software (version 3.0.1; R Development Core Team, Vienna, Austria). Panel members were asked to complete the Round 1 survey within 7 days of receipt and encouraged to contact the research team if any of the following were needed: clarification regarding the instructions, additional information about the Delphi process, technical support, or additional time to complete the survey. Panel members who had not responded after 7 days received up to three reminder e-mails, and after two weeks, non-respondents were contacted by phone or text message to encourage completion of the survey.

Round 2

All panel members were invited to complete the Round 2 survey regardless of Round 1 participation. The documents from Round 1 (as described above) were provided with Round 2. Within Round 2, histograms of ratings for each domain aggregated from all Round 1 participants, as well as stratified by each stakeholder group, were displayed. Participants who completed Round 1 also were shown their personal Round 1 rating alongside group ratings. The Round 2 survey asked participants to re-rate the 19 preliminary domains as well as 8 new domains proposed during Round 1, and the 9 cognitive subdomains. As in Round 1, panel members were instructed to rate the importance of each domain in Round 2 without consideration of the availability, ease of use, feasibility, or measurement properties of any available instruments to assess the domain. Panel members were asked to complete the Round 2 survey within 72 hours. Those who had not responded after 7 days received up to four reminder e-mails, and after two weeks non-respondents were contacted by phone or text message.

Statistical Reporting

Response rates were defined as the proportion of recruited panel members who completed each survey. Survey responses were summarized with descriptive statistics using SAS® version 9.4 (2013, Cary, NC).

Results

The expert panel had 77 participants, comprised of 35 (45%) clinical researchers, 19 (25%) clinicians and representatives of professional associations, 19 (25%) patients/caregivers, and 4 (5%) representatives of U.S. federal research funding organizations.(Table 1) There were 42 (55%) panel members from outside of the US, and 36 (47%) were female. The median years of professional experience (excluding patient and caregiver stakeholder group) was 14.5 (Interquartile range (IQR) 9 – 21).

In Round 1, 74 of 76 panel members (97%) responded, with non-response from 2 clinical researchers. Among the 19 outcome domains provided, 7 (37%) met consensus criteria as Core Domains: physical function, cognition, mental health, survival, pulmonary function, pain, and muscle and/or nerve function.(Table 2) Support for individual domains was similar across stakeholder groups except 2 domains that had substantially higher support from patients/caregivers vs. other stakeholder groups: financial impact on the patient (78% vs. 38%), and healthcare resource utilization (67% vs. 41%). Conversely, the domain of survival was rated as “Critical” by 94% of clinical researchers and only 50% of patients/caregivers. Among the 9 cognitive sub-domains, 7 (78%) met the consensus criteria. (Table 4) Panel members suggested 8 additional domains for consideration in Round 2: fatigability/endurance, susceptibility to repeated infections, renal function, self-efficacy/management, management of complex medication regimens, resilience, hearing, and loss of taste.(Figure 1)

The results of Round 2 are summarized in Tables 3 and 4. The overall response rate was 99% (75 of 76), with 1 patient/caregiver not responding. Each of the 7 domains meeting

consensus criteria in Round 1 were rated as Critical (score ≥7) by even larger proportions of the panel in Round 2. None of the 8 additional domains suggested by panel members in Round 1 met the consensus criteria. Among the 9 cognitive sub-domains, 8 (89%) met the consensus criteria, with all cognitive subdomains receiving similar levels of support and 13 (18%) of panel members selecting "Unable to score" for at least one domain. (Table 4) Patients/caregivers (vs. other stakeholder groups) continued to more strongly rate two domains as "Critical" for inclusion: financial impact on the patient (88% vs. 48%), and healthcare resource utilization (71% vs. 50%). However, with only 57% and 55%, respectively, of all panel members rating these domains as "Critical," they did not meet the consensus criteria as Core Domains. As in Round 1, support for the survival domain remained much greater among clinical researchers (100%) than patients/caregivers (59%). The distributions of responses for each domain in Round 2 are displayed in Table E3.

Discussion

This study used a two-round, modified Delphi consensus methodology with an international panel of 77 stakeholders to identify core domains for clinical research evaluating post-discharge outcomes of ARF survivors. The panel considered a preliminary list of 19 outcome domains, suggested 8 additional domains for consideration, and ultimately reached the *a priori* consensus criteria for 7 domains. Participation and retention of all stakeholder groups was excellent across both Delphi rounds.

Core domains are defined as patient outcomes, health-related conditions, or aspects of health, that are essential to evaluate within a specific field of research (20, 22). Notably, the "essential" nature of core domains may vary by stakeholder group. Hence, assembling a consensus panel requires careful consideration. Clinical trials seek to assess the efficacy of interventions so that evidence-based treatment decisions can be made for individual patients. Current guidelines recommend that these treatment decisions be shared by patients, their families, and their clinicians (36), making them the ultimate end-users of research. However, the potential benefits of many COS have not been realized because the COS was not widely adopted by clinical researchers who perform trials (37, 38). Unless research funders and journal editors require the use of COS, clinical researchers may not fully embrace them. Thus, to be successful, a COS must address outcomes that clinical researchers and their funders believe are important **and** that assist patients, their families, and clinicians in clinical decision-making (39). We chose to include representatives from each of these stakeholder groups in our expert panel.

A recent systematic review of studies to achieve consensus on domains for COS found that only 16% of studies involved patients or caregivers in the consensus process (40). An even smaller subset of these studies permitted patients or caregivers to participate in the prioritization of outcomes. The public is commonly excluded from Delphi panels because it can be challenging to identify appropriate patient and caregiver representatives, provide them with information tailored to their health literacy level, and incorporate them into the consensus process in a way that effectively utilizes and respects their area of expertise(41–43). We purposefully recruited a sufficient number of patient/caregiver representatives to ensure that if the most patient/caregivers rated a domain as "Not Important" (score ≤3) the

domain would not meet our *a priori* consensus criteria, effectively giving patients and caregivers veto power. Clinicians and professional association representatives also had similar veto power given the size of their membership on the panel.

Stakeholder groups rated the vast majority of domains similarly. The 3 notable exceptions were the domains of financial impact on patients, healthcare resource utilization, and survival. These differences likely reflect distinct stakeholders' perspectives. After hospital discharge, ARF survivors experience high rates of hospital readmission and unemployment(2, 44) creating a direct financial burden for patients and caregivers. Similarly, clinical researchers were likely aware of mortality as a competing risk in evaluating functional outcomes (45, 46) and thus, universally viewed survival as essential whereas all caregivers on the panel had family members who were still alive years after ARF. Additional research is needed to determine whether the outcomes prioritized by caregivers of living ARF survivors differ from those of caregivers to ARF "survivors" who subsequently died shortly hospital discharge.

The 7 core domains identified in this study encompass aspects of physical, mental, and cognitive health. Notably, there were no core domains within social health (20, 47). This might reflect an assumption that social health is largely determined by physical, cognitive, and mental health. However, the domain "Satisfaction with life, or personal enjoyment", which was rated as "Critical" by 69% of all panel members, including 82% of patients and caregivers, may reflect some aspects of social health. Notably, in previous pilot testing conducted before starting this project, the domain "health related quality of life" received strong support (48) as a core domain, but many clinical researchers struggled to conceptualize this domain separate from its most well-known measurement instruments. Thus, we re-named the domain, which may have resulted in lower ratings among clinical researchers (vs. patients/caregivers). Consistent with prior expert groups (6, 9, 48), we believe it is important to include a measure addressing survivors' subjective quality of life in a COS. We also encourage clinical researchers to consider assessing outcome domains that failed to meet the criteria for inclusion in a COS, but were rated as critical by the vast majority of patient and caregiver representatives, such as financial impact on patients (88%) and impact on family and/or caregivers (76%).

Limiting invitations to representatives of U.S. federal research funding organizations combined with the 50% recruitment rate of these organizations represents a limitation of this study. After consultation with their internal ethics advisors, three-quarters of the non-participating federal organizations believed that participating in this NIH-funded research represented a conflict of interest. However, COS may be less likely to be adopted if research funders do not endorse and enforce them, making funder input into COS development desirable. We also cannot determine how our results would have differed if the Delphi panel had included patient and caregiver representatives from countries other than the four major English-speaking countries included in this project.

In conclusion, research evaluating post-discharge outcomes of ARF survivors has flourished without any deliberate effort to standardize the outcome domains assessed or the measurement instruments used. Via a rigorous modified Delphi process, an international

panel of clinical researchers, clinicians, patients and caregivers, and US federal research funding organizations reached consensus on the following 7 core domains for clinical research evaluating post-discharge outcomes of ARF survivors: physical function, cognition, mental health, survival, pulmonary function, pain, and muscle and/or nerve function. These 7 domains should always be measured in this field of research. The next step is achieving consensus on what measurement instruments should be used to assess these core domains.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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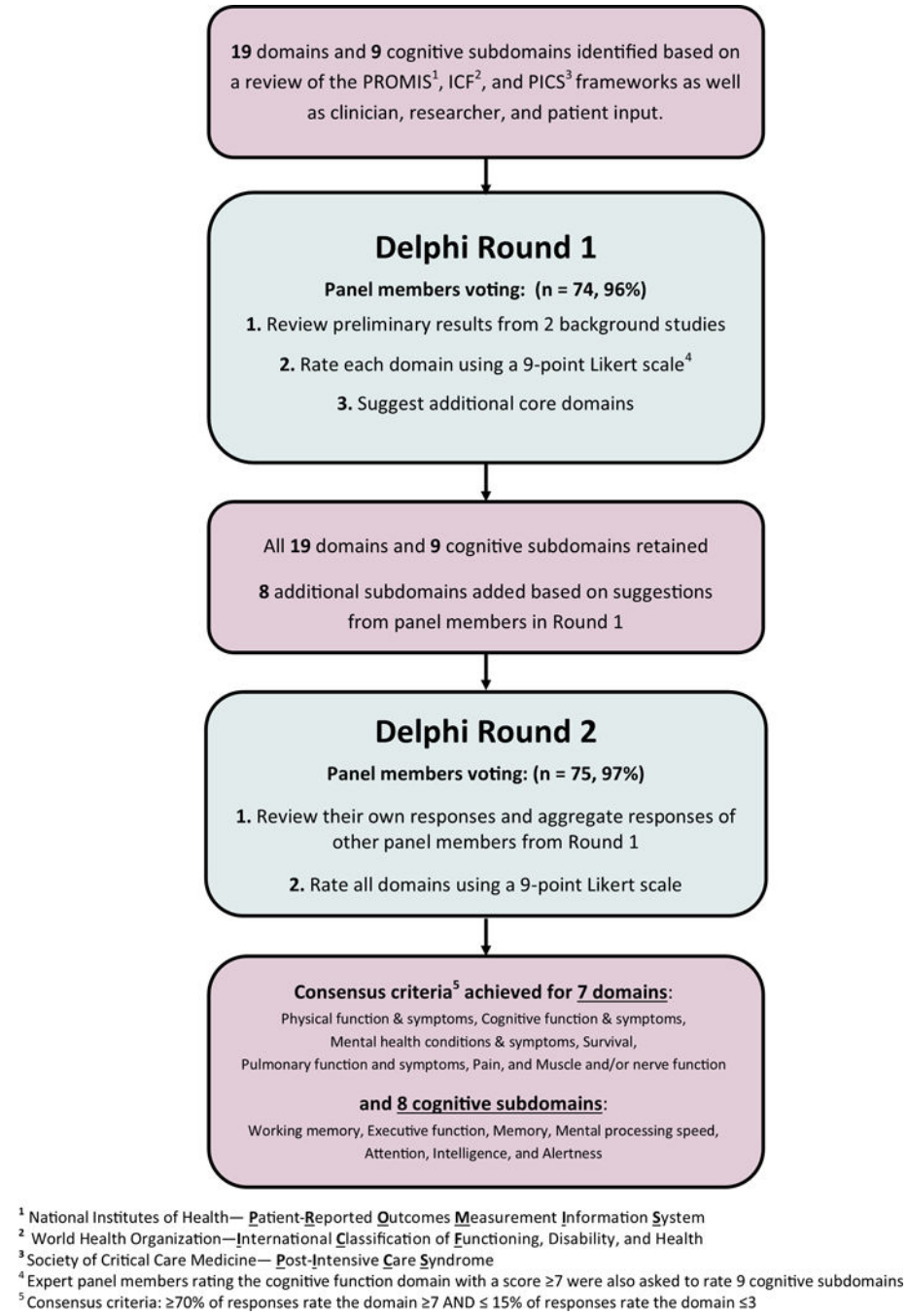

Figure 1. Modified Delphi Process Flow Diagram

1National Institutes of Health – Patient-Reported Outcomes Measurement Information System

2World Health Organization – International Classification of Functioning, Disability, and Health

3Society of Critical Care Medicine – Post-Intensive Care Syndrome

4Expert panel members rating the cognitive function domain with a score ≥7 were also asked to rate 9 cognitive subdomains

5Consensus criteria: ≥70% of responses rate the domain ≥7 and ≤15% of responses rate the domain ≤3

Table 1

Characteristics of Panel Members

Characteristic	All Panel Members (n=77)[a]	Clinical Researchers (n=35)	Clinicians / Professional Assoc. (n=19)	Patients and Caregivers (n=19)[b]	US Federal Research Funding Organizations (n=4)
Age, n (%)					
25 – 44	31 (40%)	14 (40%)	7 (37%)	9 (47%)	1 (25%)
45 – 64	43 (56%)	21 (60%)	12 (63%)	7 (37%)	3 (75%)
≥65	3 (4%)	0 (0%)	0 (0%)	3 (16%)	0 (0%)
Female, n (%)	36 (47%)	11 (31%)	12 (63%)	10 (53%)	3 (75%)
Years of education, median (IQR)	20 (18 – 22)	21 (19 – 22.5)	20 (19 – 21)	16 (15 – 18)	22 (21 – 22)
Country of residence, n (%)					
United States	35 (45%)	8 (23%)	10 (53%)	13 (68%)	4 (100%)
Canada, United Kingdom, and Australia	28 (37%)	13 (37%)	9 (47%)	6 (32%)	0 (0%)
Other[c]	14 (18%)	14 (40%)	0 (0%)	0 (0%)	0 (0%)
Professional interest in critical illness, n (%)[d]					
Research – Clinical	51 (66%)	35 (100%)	15 (79%)	0 (0%)	1 (25%)
Research – Basic or translational	16 (21%)	11 (31%)	4 (21%)	0 (0%)	1 (25%)
Clinical work	44 (57%)	23 (66%)	18 (95%)	2 (11%)	1 (25%)
None of the above	19 (25%)	0 (0%)	0 (0%)	17 (89%)	2 (50%)
Years of professional experience, median (IQR)[e]	14.5 (9 – 21)	13 (9.5 – 19.5)	17 (9.5 – 21)	NA	18.5[g]
Area of professional expertise, n (%)[d]					
Physical health and functioning	42 (55%)	27 (77%)	13 (68%)	NA	1 (25%)
Mental health	17 (22%)	12 (34%)	4 (21%)	NA	0 (0%)
Cognitive function	17 (22%)	11 (31%)	6 (32%)	NA	0 (0%)
Other	8 (10%)	4 (11%)	3 (16%)	NA	1 (25%)
None	8 (10%)	3 (9%)	3 (16%)	NA	1 (25%)
Clinical work: Type of training, n (%)[f]					
Physician – Critical Care	25 (57%)	20 (87%)	5 (28%)	0 (0%)	1 (100%)
Physical, Occupational, or Respiratory Therapist and/or Speech Language Pathologist	12 (27%)	6 (26%)	7 (39%)	0 (0%)	0 (0%)
Nurse or Nurse Practitioner	6 (14%)	0 (0%)	4 (22%)	2 (11%)	0 (0%)

Characteristic	All Panel Members (n=77)[a]	Clinical Researchers (n=35)	Clinicians / Professional Assoc. (n=19)	Patients and Caregivers (n=19)[b]	US Federal Research Funding Organizations (n=4)
Physician – Physical Medicine & Rehabilitation	2 (5%)	0 (0%)	2 (11%)	0 (0%)	0 (0%)
Other clinical training	4 (9%)	3 (13%)	1 (5%)	0 (0%)	0 (0%)

Abbreviations: IQR, Inter-quartile Range; Assoc, Association

[a] One panel member represented Clinical Researcher and Clinician/Professional association groups; total number of survey respondents n=76.

[b] A patient caregiver was replaced by another patient caregiver member after round 2. Data from both panel members presented (patients n= 10, Caregivers n = 9).

[c] Other countries: Singapore = 1, China = 1, Brazil = 1, Panama = 1, France = 2, Germany = 1, Belgium = 1, Greece = 1, Netherlands = 1, Norway = 1, Italy = 1, Ireland = 1

[d] Panel members could select >1 response

[e] All panel members from the Clinical Researcher, Clinicians /Professional Associations, and U.S. Federal Research Funding Organizations (n=58) provided data

[f] 44 (57%) panel members selected Clinical training, 5 of which selected 2 types of clinical work. Other clinical training includes Anesthesiology = 2, Internal medicine = 1, Pharmacy = 1.

[g] Two funding body representatives responded and reported 14 and 23 years of professional experience.

Table 2

Round 1 Survey Results by Stakeholder Group

Domain	Score	Proportion of stakeholders rating the domain ≥7 on a 9-point Likert scale				
	Mean (SD) (n=74)	All Panel Members (n=74)	Clinical Researchers (n=33)	Clinicians / Professional Associations (n=19)	Patients and Caregivers (n=18)	US Federal Research Funding Organizations (n=4)
Domains meeting consensus criteria[a]						
Cognitive function and symptoms	8.1 (1.1)	68 (92%)	32 (97%)	18 (95%)	14 (78%)	4 (100%)
Physical function and symptoms	8.1 (1.0)	66 (89%)	30 (91%)	17 (89%)	15 (83%)	4 (100%)
Mental health conditions and symptoms	7.9 (1.0)	64 (86%)	30 (91%)	16 (84%)	14 (78%)	4 (100%)
Survival	7.9 (1.6)	56 (76%)	31 (94%)	14 (74%)	9 (50%)	2 (50%)
Pain	7.2 (1.5)	54 (73%)	23 (70%)	15 (79%)	13 (72%)	3 (75%)
Muscle and/or nerve function	7.3 (1.5)	52 (70%)	23 (70%)	12 (63%)	13 (72%)	4 (100%)
Pulmonary function and symptoms	7 (1.6)	52 (70%)	20 (61%)	14 (74%)	15 (83%)	3 (75%)
Domains not meeting consensus criteria[a]						
Satisfaction with life, or personal enjoyment	7.1 (1.4)	51 (69%)	21 (64%)	14 (74%)	14 (78%)	2 (50%)
Return to work or prior activities	6.9 (1.6)	45 (61%)	24 (73%)	11 (58%)	8 (44%)	2 (50%)
Fatigue	6.8 (1.7)	44 (59%)	20 (61%)	11 (58%)	11 (61%)	2 (50%)
Impact on family and/or caregivers	6.7 (1.7)	40 (54%)	17 (52%)	11 (58%)	11 (61%)	1 (25%)
Swallowing function and symptoms	6.4 (1.8)	37 (50%)	15 (45%)	9 (47%)	11 (61%)	2 (50%)
Financial impact on patient	6.2 (1.9)	35 (47%)	13 (39%)	7 (37%)	14 (78%)	1 (25%)
Healthcare resource utilization	6.3 (1.7)	35 (47%)	16 (48%)	5 (26%)	12 (67%)	2 (50%)
Sleep function and symptoms	6.3 (1.6)	35 (47%)	16 (48%)	7 (37%)	10 (56%)	2 (50%)
Social roles, activities or relationships	6.3 (1.8)	34 (46%)	17 (52%)	7 (37%)	9 (50%)	1 (25%)
Type of residence	6.2 (1.8)	32 (43%)	13 (39%)	10 (53%)	8 (44%)	1 (25%)
Gastrointestinal function and symptoms	5.5 (1.8)	21 (28%)	7 (21%)	5 (26%)	7 (39%)	2 (50%)
Sexual function and symptoms	4.8 (1.8)	11 (15%)	3 (9%)	2 (11%)	5 (28%)	1 (25%)

Abbreviations: SD, Standard Deviation

[a]The consensus criteria for inclusion as a core domain was defined as ≥70% of all panel members rating a domain ≥7 and no more than 15% rating the domain ≤3 on a 9-point scale. Domains are ordered by the proportion of panel members rating the domain ≥7.

[b] A total of 7 of 74 (9%) unique panel members ever selected "Unable to Score." The number of panel members selecting "Unable to Score" by domain: Physical function and symptoms (1), Mental health conditions and symptoms (1), Survival (3), Muscle and/or nerve function (1), Pulmonary function and symptoms (1), Return to work or prior activities (3), Impact on family and/or caregivers (3), Swallowing function and symptoms (2), Healthcare resource utilization (1), Sleep function and symptoms (1), and Social roles, activities or relationships (1).

Table 3

Round 2 Survey Results by Stakeholder Group

Domain	Score	Proportion of stakeholders scoring the domain ≥7 on a 9-point Likert scale				
	Mean (SD) (n=75)	All Panel Members (n=75)	Clinical Researchers (n=35)	Clinicians / Professional Associations (n=19)	Patients and Caregivers (n=17)	US Federal Research Funding Organizations (n=4)
Domains meeting consensus criteria[a]						
Physical function and symptoms	8.4 (0.8)	73 (97%)	34 (97%)	18 (95%)	17 (100%)	4 (100%)
Cognitive function and symptoms	8.4 (0.9)	71 (95%)	34 (97%)	18 (95%)	15 (88%)	4 (100%)
Mental health conditions and symptoms	8.0 (0.8)	70 (93%)	33 (94%)	18 (95%)	15 (88%)	4 (100%)
Survival	8.2 (1.3)	64 (85%)	35 (100%)	16 (84%)	10 (59%)	3 (75%)
Pulmonary function and symptoms	7.3 (1.4)	64 (85%)	29 (83%)	14 (74%)	17 (100%)	4 (100%)
Pain	7.5 (1.1)	63 (84%)	29 (83%)	17 (89%)	14 (82%)	3 (75%)
Muscle and/or nerve function	7.3 (1.2)	62 (83%)	27 (77%)	16 (84%)	15 (88%)	4 (100%)
Domains not meeting consensus criteria[a]						
Satisfaction with life, or personal enjoyment	7.2 (1.2)	52 (69%)	22 (63%)	14 (74%)	14 (82%)	2 (50%)
Impact on family and/or caregivers	7.1 (1.4)	50 (67%)	23 (66%)	12 (63%)	13 (76%)	2 (50%)
Fatigue	6.9 (1.4)	49 (65%)	23 (66%)	12 (63%)	12 (71%)	2 (50%)
Return to work or prior activities	7.0 (1.3)	48 (64%)	23 (66%)	13 (68%)	10 (59%)	2 (50%)
Swallowing function and symptoms	6.7 (1.6)	47 (63%)	20 (57%)	11 (58%)	13 (76%)	3 (75%)
Financial impact on patient	6.7 (1.5)	43 (57%)	19 (54%)	8 (42%)	15 (88%)	1 (25%)
Healthcare resource utilization	6.6(1.2)	41 (55%)	20 (57%)	7 (37%)	12 (71%)	2 (50%)
Sleep function and symptoms	6.4 (1.4)	38 (51%)	17 (49%)	7 (37%)	12 (71%)	2 (50%)
Social roles, activities or relationships	6.6 (1.3)	37 (49%)	19 (54%)	6 (32%)	11 (65%)	1 (25%)
Type of residence	6.3 (1.6)	30 (40%)	12 (34%)	9 (47%)	8 (47%)	1 (25%)
Gastrointestinal function and symptoms	5.5 (1.5)	16 (21%)	4 (11%)	5 (26%)	6 (35%)	1 (25%)
Sexual function and symptoms	4.9 (1.2)	7 (9%)	3 (9%)	0 (0%)	4 (24%)	0 (0%)
Domains suggested by stakeholders during Round 1 (none meeting consensus criteria[a]**)**						

Domain	Score	Proportion of stakeholders scoring the domain ≥7 on a 9-point Likert scale				
	Mean (SD) (n=75)	All Panel Members (n=75)	Clinical Researchers (n=35)	Clinicians / Professional Associations (n=19)	Patients and Caregivers (n=17)	US Federal Research Funding Organizations (n=4)
Fatigability / endurance	6.9 (1.4)	47 (63%)	19 (54%)	12 (63%)	14 (82%)	2 (50%)
Susceptibility to repeated infections	6.7 (1.5)	46 (61%)	17 (49%)	12 (63%)	14 (82%)	3 (75%)
Renal Function	6.5 (1.5)	42 (56%)	17 (49%)	9 (47%)	14 (82%)	2 (50%)
Self-efficacy/management	6.4 (1.7)	36 (48%)	16 (46%)	7 (37%)	10 (59%)	3 (75%)
Management of Complex Medication Regimens	6.2 (1.7)	35 (47%)	13 (37%)	10 (53%)	11 (65%)	1 (25%)
Resilience	6.4 (1.7)	34 (45%)	14 (40%)	6 (32%)	12 (71%)	2 (50%)
Hearing	5.8 (1.6)	23 (31%)	14 (40%)	3 (16%)	3 (18%)	3 (75%)
Loss of Taste	5.6 (1.6)	18 (24%)	10 (29%)	3 (16%)	4 (24%)	1 (25%)

Abbreviations: SD, Standard Deviation

[a]The consensus criteria for inclusion as a core domain was defined as ≥70% of all panel members rating a domain ≥7 and no more than 15% rating the domain ≤3 on a 9-point scale. Domains are ordered by the proportion of panel members rating the domain ≥7.

[b]A total of 4 of 75 (5%) unique panel members ever selected “Unable to Score.” Number of panel members selecting “Unable to Score” by domain: Survival (1), Impact on family and/or caregiver (1), Hearing (1), and Management of complex medication regimens (1)

Table 4

Results for Cognitive Subdomains by Stakeholder Group

	Score	Proportion of stakeholders scoring the domain ≥7 on a 9-point Likert scale[a]				
Subdomain	**Mean (SD)**	**All Panel Members[b]**	**Clinical Researchers**	**Clinicians / Professional Associations**	**Patients and Caregivers**	**US Federal Research Funding Organizations**
		ROUND 1				
Domains meeting consensus criteria[a]	**(n=74)**	**(n=74)**	**(n=33)**	**(n=19)**	**(n=18)**	**(n=4)**
Working memory	8.0 (1.0)	60 (81%)	28 (85%)	16 (84%)	12 (67%)	4 (100%)
Executive function	8.1 (1.0)	58 (78%)	26 (79%)	16 (84%)	12 (67%)	4 (100%)
Memory	8.0 (1.0)	58 (78%)	24 (73%)	18 (95%)	12 (67%)	4 (100%)
Mental processing speed	7.6 (1.2)	56 (76%)	27 (82%)	13 (68%)	12 (67%)	4 (100%)
Attention	7.8 (1.2)	54 (73%)	28 (85%)	12 (63%)	10 (56%)	4 (100%)
Intelligence	7.6 (1.3)	54 (73%)	27 (82%)	12 (63%)	12 (67%)	3 (75%)
Alertness	7.5 (1.3)	52 (70%)	22 (67%)	15 (79%)	12 (67%)	3 (75%)
Core domain consensus criteria: ≥70% of all stakeholders rating the domain ≥7						
Language / Verbal fluency / Naming	7.5 (1.4)	50 (68%)	25 (76%)	11 (58%)	11 (61%)	3 (75%)
Visuospatial ability or construction	7.0 (1.5)	42 (57%)	20 (61%)	10 (53%)	10 (56%)	2 (50%)
		ROUND 2				
Domains meeting consensus criteria[a]	**(n=75)**	**(n=75)**	**(n=35)**	**(n=19)**	**(n=17)**	**(n=4)**
Working memory	8.3 (0.8)	72 (96%)	34 (97%)	18 (95%)	16 (94%)	4 (100%)
Memory	8.3 (0.9)	70 (93%)	33 (94%)	18 (95%)	15 (88%)	4 (100%)
Mental processing speed	8.2 (0.9)	69 (92%)	34 (97%)	15 (79%)	16 (94%)	4 (100%)
Executive Function	7.8 (0.9)	69 (92%)	33 (94%)	18 (95%)	14 (82%)	4 (100%)
Attention	7.9 (1.1)	65 (87%)	33 (94%)	15 (79%)	13 (76%)	4 (100%)
Intelligence	7.8 (1.1)	63 (84%)	32 (91%)	15 (79%)	12 (71%)	4 (100%)
Alertness	7.4 (1.0)	62 (83%)	29 (83%)	15 (79%)	14 (82%)	4 (100%)
Language / Verbal Fluency / Naming	7.7 (1.2)	59 (79%)	31 (89%)	12 (63%)	13 (76%)	3 (75%)
Core domain consensus criteria: ≥70% of all stakeholders rating the domain ≥7						

	Score	Proportion of stakeholders scoring the domain ≥7 on a 9-point Likert scale[a]				
Subdomain	**Mean (SD)**	**All Panel Members[b]**	**Clinical Researchers**	**Clinicians / Professional Associations**	**Patients and Caregivers**	**US Federal Research Funding Organizations**
Visuospatial Ability or Construction	7.1 (1.2)	51 (68%)	25 (71%)	10 (53%)	13 (76%)	3 (75%)

Abbreviations: SD, Standard Deviation

[a]The consensus criteria for inclusion as a core domain was defined as ≥70% of all panel members rating a domain ≥7 and no more than 15% rating the domain ≤3 on a 9-point scale. Domains are ordered by the proportion of panel members rating the domain ≥7.

[b]In Round 1 a total of 13 of 74 (18%) unique panel members ever selected “Unable to Score”. Number of panel members selecting “Unable to Score” by domain: Working memory (8), Executive function (10), Memory (10), Mental processing speed (6), Attention (8), Intelligence (6), Alertness (8), Language/Verbal fluency/Naming (7), and Visuospatial ability or construction (7). In Round 2 a total of 3 of 75 (4%) unique panel members ever selected “Unable to Score”. Number of panel members selecting “Unable to Score” by domain: Working memory (1), Memory (1), Mental processing speed (1), Executive function (1), Attention (1), Intelligence (1), Alertness (1), Language/Verbal fluency/Naming (1), and Visuospatial ability or construction (1).