Core Outcomes for Clinical Research in Acute Respiratory Failure Survivors

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Create and nationally disseminate resources to assist Acute Respiratory Distress Syndrome (ARDS)/Acute Respiratory Failure (ARF) researchers in designing trials that appropriately evaluate long-term patient outcomes

Improving Long-Term Outcomes Research for Acute Respiratory Failure
R24 Grant Aims

**Aim 1:** Web-based electronic database of validated and recommended survey instruments and clinical testing methods for long-term outcomes

**Aim 2:** Practical resources for maximizing retention in long-term, longitudinal research

**Aim 3:** Statistical methods & programs for evaluating functional outcomes in the presence of high patient mortality (“competing risk of mortality”)

Outcome measurement in ICU survivorship research from 1970-2013: a scoping review of 425 publications


Peer-reviewed published studies 1970 - 2013

- ≥ 20 adult ICU survivors assessed after hospital discharge

**Excluded**

- Qualitative studies
- Studies only assessing survival
- Psychometric evaluations of measurement instruments or tests
- >50% of patients had neurologic injury
- >50% of patients had cardiac surgery
425 peer-reviewed papers

- Outcomes assessed using 250 different measurement instruments

**Why is this a problem?**

- Difficult to compare results
- Barrier to meta-analyses
- Selective outcome reporting bias

**Our goal**

Develop a core set of outcomes and related measures for survivors of acute respiratory failure (including ARDS) after hospital discharge using a rigorous methodology and an international panel of relevant stakeholders.
Definitions

- **Core outcome** - a concept, health-related condition, or aspect of health that must always be measured within a specific field of research
  
  *(What outcomes should we all measure?)*

- **Core measure** – a measurement instrument selected to assess a core outcome
  
  *(How should we measure them?)*

CORE MEASURE SET (CMS)

**Core measure set**: A minimum collection of agreed-upon measures (for core outcomes) reported in all studies within a specific field.

A CMS does NOT prevent investigators from collecting data on additional outcomes.
Work informing CMS development

- Scoping review
- Systematic reviews
- Psychometric evaluations of existing instruments
- Qualitative interviews with ARDS survivors

Modified Delphi Consensus Process

Uses expert opinion to address questions for which empirical data are unavailable or inadequate
Delphi – Expert Panel

Stakeholder groups
1. Clinical researchers (n=35)
   i. All International Forum for Acute Care Trialists (InFACT) members
   ii. Random sample of 6 corresponding authors from scoping review
   iii. 9 authors of internationally recognized ARF research
   iv. >16 countries represented
2. Clinicians/professional associations (n=19)
   i. ICU physicians, ICU nurses, rehabilitation clinicians
   ii. Australia, Canada, UK, & US
3. Patients/caregivers (n=17)
   i. Australia, Canada, UK, & US
4. Funding bodies (n=4)

Delphi Methodology

• Each outcome rated using GRADE scale
  (1 – 3) = Not Important
  (4 – 6) = Important but not Critical
  (7 – 9) = Critical
  Unable to score
Delphi Methodology

*a priori* consensus definition

≥70% rated outcome as Critical (≥7)

And

≤15% rated outcome as Not important (≤3)

1. All voting conducted online

2. Anonymity maintained

3. No consideration of the availability, ease of use, feasibility, or properties of available instruments
Phase I: Round 1

Before voting, review:

- Survey of corresponding authors of publications regarding potential core outcomes
- Phone-based survey of ARF survivors and caregivers about potential core outcomes
- Summary of qualitative study of ARF survivors regarding key outcomes

Then:

- Rate each of 19 preliminary outcomes from
  - Patient Reported Outcome Measurement Information System (PROMIS)
  - WHO’s International Classification of Functioning, Disability, & Health (ICF)
  - SCCM’s Post-Intensive Care Syndrome (PICS) framework
  - Clinician, researcher and patient input

- Option of proposing additional outcomes
Phase I: Round 1 - Results

- 96% participation rate
- 7 outcomes met consensus criteria
- 8 new outcomes suggested
- No outcomes dropped from consideration

### Round 1 Survey Results by Stakeholder Group (96% response rate)

<table>
<thead>
<tr>
<th>Outcomes</th>
<th>Score</th>
<th>Proportion of stakeholders rating the outcome ≥7 on a 9-point Likert scale</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean (SD)</td>
<td>All Panel Members (n=74)</td>
<td>Clinical Researchers (n=33)</td>
</tr>
<tr>
<td>Fatigue</td>
<td>6.9 (1.6)</td>
<td>45 (61%)</td>
</tr>
<tr>
<td>Cognitive function and symptoms</td>
<td>8.3 (1.1)</td>
<td>68 (91%)</td>
</tr>
<tr>
<td>Physical function and symptoms</td>
<td>8.1 (1.0)</td>
<td>66 (90%)</td>
</tr>
<tr>
<td>Psychological function and symptoms</td>
<td>7.9 (1.0)</td>
<td>64 (86%)</td>
</tr>
<tr>
<td>Pulmonary function and symptoms</td>
<td>7.9 (1.0)</td>
<td>56 (76%)</td>
</tr>
<tr>
<td>Survivor</td>
<td>7.2 (1.5)</td>
<td>34 (74%)</td>
</tr>
<tr>
<td>Musculoskeletal function and symptoms</td>
<td>7.3 (1.5)</td>
<td>52 (70%)</td>
</tr>
<tr>
<td>Pulmonary function and symptoms</td>
<td>7.3 (1.5)</td>
<td>52 (70%)</td>
</tr>
<tr>
<td>Psychological function and symptoms</td>
<td>7.3 (1.5)</td>
<td>52 (70%)</td>
</tr>
<tr>
<td>Sleep quality</td>
<td>6.6 (1.6)</td>
<td>37 (50%)</td>
</tr>
<tr>
<td>Social roles, activities or relationships</td>
<td>6.5 (1.8)</td>
<td>35 (46%)</td>
</tr>
<tr>
<td>Type of residency</td>
<td>6.2 (1.8)</td>
<td>13 (41%)</td>
</tr>
<tr>
<td>Gastrointestinal function and symptoms</td>
<td>5.5 (1.6)</td>
<td>21 (28%)</td>
</tr>
<tr>
<td>Sexual function and symptoms</td>
<td>4.6 (1.8)</td>
<td>21 (28%)</td>
</tr>
</tbody>
</table>

*The consensus criteria for inclusion as a core outcome was defined as ≥70% of all panel members rating an outcome ≥7 and no more than 15% rating the outcome ≤6 on a 9-point scale.
*\( \geq 7 \) and no more than 15% rating the outcome ≤6 on a 9-point scale.
*The number of panel members selecting "Unable to Score" by outcome (\( n = 74 \)), Physical function and symptoms (15), Cognitive function and symptoms (10), Psychological function and symptoms (9), Pulmonary function and symptoms (15), Gastrointestinal function and symptoms (6), Sleep function and symptoms (6), Social roles, activities or relationships (12), Type of residency (6), and sexual function and symptoms (6).

**Additional Information:**
- The consensus criteria for inclusion as a core outcome was defined as ≥70% of all panel members rating an outcome ≥7 and no more than 15% rating the outcome ≤6 on a 9-point scale.
- The number of panel members selecting "Unable to Score" by outcome (\( n = 74 \)), Physical function and symptoms (15), Cognitive function and symptoms (10), Psychological function and symptoms (9), Pulmonary function and symptoms (15), Gastrointestinal function and symptoms (6), Sleep function and symptoms (6), Social roles, activities or relationships (12), Type of residency (6), and sexual function and symptoms (6).

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Phase I: Round 2

Before voting, review:
Your Round 1 response compared to:
• aggregate responses for the entire panel
• aggregate responses of each stakeholder group

Phase I: Round 2

Then:
Rate each of 19 preliminary outcomes and the 8 newly suggested outcomes
Phase I: Round 2 - Results

- 97% participation rate
- 7 outcomes met consensus inclusion criteria
- No newly suggested outcomes met inclusion criteria

### Table 3: Round 2 Survey Results by Stakeholder Group

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Mean (SD)</th>
<th>All Panel Members (n=75)</th>
<th>Clinical Researchers (n=30)</th>
<th>Professional Associations (n=30)</th>
<th>Patients and Caregivers (n=17)</th>
<th>Research Funding Organizations (n=4)</th>
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<tr>
<td>Fatigue</td>
<td>7.5 (0.5)</td>
<td>7.5 (0.5)</td>
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<td>6.5 (0.3)</td>
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<td>Fatigue</td>
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### Abbreviations:
- SD: Standard Deviation
- Mean: Average
- SD: Standard Deviation
- All Panel Members (n=75)
- Clinical Researchers (n=30)
- Professional Associations (n=30)
- Patients and Caregivers (n=17)
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- Fatigue, Fatigue, Fatigue, Fatigue, Fatigue, Fatigue
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<td>Somatic</td>
<td>7.0 (0.4)</td>
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<tbody>
<tr>
<td>Fatigue / Endurance</td>
<td>6.1 (1.6)</td>
<td>61 (82%)</td>
<td>19 (54%)</td>
<td>27 (49%)</td>
<td>16 (73%)</td>
<td>3 (75%)</td>
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<tr>
<td>Mental health-and-symptoms</td>
<td>7.7 (1.4)</td>
<td>71 (95%)</td>
<td>32 (94%)</td>
<td>18 (95%)</td>
<td>15 (100%)</td>
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<tr>
<td>Pulmonary function and symptoms</td>
<td>7.5 (1.4)</td>
<td>64 (85%)</td>
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<td>Cognitive susceptibility</td>
<td>6.4 (1.5)</td>
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<td>Social relationships</td>
<td>6.1 (1.4)</td>
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<td>Survival</td>
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<td>Satisfaction with, or potential displacement</td>
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Outcomes suggested by stakeholders during Round 1 (face meeting consensus criteria):

- Fatigue / Endurance
- Mental health-and-symptoms
- Pulmonary function and symptoms
- Fat
- Gastrointestinal symptoms
- Cognitive susceptibility
- Social relationships
- Work function
- Impact on family and/or caregivers
- Survival
- Hearing
- Medication adherence

Note: *Face meeting consensus criteria.*

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- Gastrointestinal symptoms
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Note: *Face meeting consensus criteria.*

*Abbreviations: SD, Standard Deviation*
Differing stakeholder perspectives

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<th>Outcome</th>
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</tr>
</thead>
<tbody>
<tr>
<td>Financial impact on patient</td>
<td>19 (54%)</td>
<td>8 (42%)</td>
<td>15 (88%)</td>
<td>1 (25%)</td>
</tr>
<tr>
<td>Healthcare resource utilization</td>
<td>20 (57%)</td>
<td>7 (37%)</td>
<td>12 (71%)</td>
<td>2 (50%)</td>
</tr>
</tbody>
</table>

CORE OUTCOMES

1. Survival
2. Satisfaction with life, or personal enjoyment
3. Physical function and symptoms
4. Cognitive function and symptoms
5. Mental health conditions and symptoms
6. Pulmonary function and symptoms
7. Pain
8. Muscle and/or nerve function
PHASE I results


If you’re planning a study of ARF survivors:

**Contact us!**

improveLTO@jhmi.edu
R24 Project Team Members

PI: Dale M. Needham, FCPA, MD, PhD

Co-investigators and faculty:
- Clifton Bingham, MD - OMERACT
- Kitty Chan, PhD – Psychometrician
- Elizabeth Colantuoni, PhD – Biostatistician
- Victor Dinglas, MPH – Research Associate/Manager
- Michelle Eakin, PhD – Qualitative researcher/psychologist
- Karen Robinson, PhD – Systematic review expert
- Alison Turnbull, DVM, MPH, PhD – Epidemiologist/Methodologist

Research fellows and staff:
- Caroline Chessare, MS
- Lisa Friedman, ScM
- Andrew Leroux, MS
- Elizabeth Pfoh, PhD
- Kristin Sepulveda, BA
- Amy Wozniak, MS

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