# **Supplemental Data**

A Core Outcome Set for critical care ventilation trials

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**eAppendix 1 COVenT Methods**

COVenT I Delphi methods

To recruit the Delphi panel, we conducted a systematic web search of international organizations representing a broad range of stakeholders from many countries including: critical care clinical trials groups; nursing and allied health professional critical care societies; critical care medicine societies; ICU survivor and carer support groups; and industries involved with ventilation equipment. The organizational lead assisted in identifying and recruiting participants with clinical or research expertise, or personal experience with mechanical ventilation. In cases where participants belonged to a professional society and a trials group, we recorded their affiliation according to the group from which they were recruited.

COVenT stage 1 addressed ‘what’ outcomes to include in the COS. To generate a list of outcomes to be considered, we undertook a systematic review of critical care ventilation trials and extracted the most commonly reported outcomes (reported in five or more trials) [1]. Items included in Round 1 of the Delphi were generated from the review of 66 trials that described the most commonly reported outcomes. The outcomes reported were representative of the domains which should be measured. For example, the domain ‘ventilation duration’ was described in the trials in various ways as total duration of mechanical ventilation, weaning duration, and ventilator free days. To ensure we did not force a particular outcome, we included all these so the panel could decide which one was more critical for describing the domain. The only adaptation at this stage was that we removed the time measurement (e.g. if 30-day mortality was reported as most common, we only included ‘mortality’ because the time measurement point would become part of the COS consensus). For each outcome, the research team (authors) agreed a lay description. Each lay description was checked by a member of the local ICU survivor voluntary support group (ICU Steps Belfast). In this way we were assured that the outcome would be understood by medical, allied health professions and lay respondents. Delphi participants could add additional outcomes for rating in subsequent rounds. While this was an appropriate validation method and used by other core outcome set developers, a limitation is that we did not strengthen the questionnaire by testing other types of validity.

The three-round Delphi study was conducted online and supported by an e-management system (DelphiManager software, University of Liverpool, UK). Participants registered online and were allocated unique identifiers. The website presented the questionnaire, enabling participants to score outcomes (all rounds) and suggest additional outcomes (round 1 only). The questionnaire was displayed after successful registration or login, and after the introduction page was viewed. The bespoke software managed participant registrations, status (live), scores, and rounds completed and this was over seen by the IS manager or technical lead. Comma Separated Values (CSV) files were sent to the chief investigator after each round for statistical analysis. Further details of the Delphi participant recruitment and process are reported in the study protocol [2].

Delphi participants were asked to score perceived importance of each outcome using the 1 – 9 Grading, Recommendations Assessment, Development and Evaluation scale (1 = least important; 9 = most important) [3]. The distribution of scores for each outcome was calculated as a percentage of the total responses. Scores for each outcome after the first round were provided to participants in subsequent rounds. All outcomes were carried forward to the final round of the Delphi. COS inclusion criteria were >70% of responses rating the outcome at >7 and not more than 15% of responses rating the outcome <3, as used in previous COS development studies [4] In the final round, outcomes meeting consensus criteria were retained for discussion at consensus webinar meetings.

COVenT I Consensus Meetings

Consensus meeting participants were recruited from Delphi respondents completing all three rounds. Delphi participants were listed in order of subject identification number and stratified according to stakeholder group and country. The first 10 in each stratum were invited to join the consensus meetings and if unavailable, subsequent participants were invited. Additionally, we purposively invited a statistician, health economist, two critical care journal and social media editors, and others contributing methodological or clinical expertise.

The research team (the authors) conducted two webinars using Adobe Connect web conferencing software and an anonymized voting process. Each webinar lasted two hours and was conducted using Adobe Connect web conferencing software designed to maximize participation and interaction. Participants were informed that the webinars were being recorded. On the screen, participants could see a PowerPoint presentation, webcam video of the research team, and an attendee list. They provided ongoing commentary via a text box visible by everyone or dialogue using their microphone.

The research team provided a brief overview of the Delphi study and the specific aims of the webinar. Outcomes agreed as ‘critical’ by the Delphi panel were presented to participants one at a time and participants discussed and voted on each outcome. Members of the research team did not vote.

Anonymized voting was conducted in two parts.

1. Participants were asked to consider each outcome independently. Participants voted ‘In’, ‘Out’ or ‘On the fence’ and were blinded to results until voting finished whereupon the result was broadcast. Those in the minority were given an opportunity to express their views orally or in the commentary box, and these were discussed. In cases where the number of votes was similar for ‘In’ or ‘Out’, or if participants requested, we progressed to a revote. The revote result was final.
2. Participants were presented with the list of outcomes they had voted ‘In’. Where outcomes had an overlapping element (i.e. mortality and survival; changes in activities of daily living and health related quality of life; and duration of weaning and duration of invasive mechanical ventilation), participants were asked to consider the overlapping outcomes together and re-examine their importance for inclusion in the COS. Discussion followed on advantages and disadvantages of each before a final, deciding vote.

At the end of the webinar, participants were thanked and asked to maintain confidentiality around the final list of outcomes. No participant was present at both webinars and the results of the first webinar were not revealed to participants in the second webinar.

To ensure included outcomes were understood and agreed by participating ICU survivors and carers, a teleconference was scheduled after the webinars to provide clarification and confirm their agreement. The teleconference meeting was a *post hoc* meeting resulting from feedback from ICU survivors and carers who described not fully understanding some of the research focused discussions on outcome selection. The two-hour teleconference meeting was chaired by two members of the research team (BB and SR). Participants were asked if they agreed or not with those voted ‘In’ from the webinars. Subsequently, outcomes that had been voted ‘Out’ were discussed to determine whether or not any of these should also be included. A final list of agreed outcomes was drawn up and participants were thanked for their support and engagement.

Agreed outcomes from individual meetings were reviewed at an executive meeting of the research team. We established a priori that only outcomes universally agreed by all three consensus meeting groups were deemed ‘core’ for inclusion in the COS.

COVenT II Consensus Meetings

In COVenT stage 2, three further consensus meetings were held to determine ‘how’ the core outcomes should be defined and measured: two by webinar and one face-to-face at an InFACT meeting. To inform outcome definitions, we accessed published and unpublished information sources. Published sources included a systematic review of ventilation trials [1] and the Improve Long Term Outcome COS (www.improvelto.com). Unpublished sources included two, as of yet, unpublished reviews (Friedrich, Marshall, personal communication; Ringrow review registration [5]). We used the four outcome definition components recommended in the SPIRIT Statement 2013 (specific measurement variable; analysis metric; aggregation method; time-points) as a framework to develop preliminary definitions and measures for discussion [6]. We used the same voting system as in COVenT stage 1 to achieve consensus.

# **eAppendix 2 Delphi Questionnaire**

Round 1 list of 24 outcomes

1. **Accidental Extubation**

*When the breathing tube is dislodged or removed accidentally by the patient.*

1. **Acute Respiratory Distress Syndrome (ARDS)**

*Event of developing ARDS: a condition where the lungs become severely inflamed as a result of an infection or injury. The inflammation causes fluid from nearby blood vessels to leak into the tiny air sacs in the lungs, making breathing increasingly difficult.*

1. **Change in Activities of Daily Living**

Change in a patient’s ability to perform everyday tasks following their period of illness which required critical care support or mechanical ventilation.

1. **Clinical Workload**

A measure of the workload experienced by ICU staff delivering the intervention to the patient.

1. **Days of Intravenous (IV) Sedation**

The number of days during which a patient receives IV sedation *(medication to reduce consciousness through a drip)*

1. **Delirium**

Event of having delirium or *acute confusion* (confirmed with an assessment tool)

1. **Duration of Ventilation**

The start of ventilation until the first period of mechanical ventilation is complete.

1. **Duration of Weaning**

A measurement of the time from reducing ventilator support *(amount of support the breathing machine supplies)* until no support is required.

1. **Global Organ Dysfunction/ Multi-Organ Failure**

A score which measures dysfunction in all organ/ organ systems together to give an overall measure of organ failure but does not distinguish between organs/ organ systems

1. **Health Related Quality of Life**

A measure of the quality of life of the patient at particular time points in the context of the illness experience of the patient.

1. **Incidence of Ventilator Associated Pneumonia**

The event of getting pneumonia *(chest infection)* that occurs as a result of being on a ventilator

1. **Intensive Care Unit Acquired Weakness**

Development of a profound muscle weakness that occurs as a result of critical illness.

1. **Length of Hospital Stay**

Number of days spent in hospital

1. **Length of ICU Stay**

Number of days spent in the Intensive care unit

1. **Mortality**

The event of death

1. **Pneumothorax**

Event of developing air in the pleural space *(in lay terms this means a punctured lung).*

1. **Reintubation**

Event where a replacement of the ET *(breathing)* tube is required.

1. **Single Organ Dysfunction/ Single Organ Failure**

A score which measures the dysfunction in individual organs/ organ systems that is not combined to give an overall measure of organ failure

1. **Successful Extubation**

An event recorded when the patient is free from an endo-tracheal (ET) tube *(the tube inserted into the patient’s airway to allow them to be connected to a ventilator)* at a specified time point

1. **Survival**

The event of surviving within a particular time frame

1. **Total Costs**

A measure of the value for money of an intervention

1. **Tracheostomy**

Event of requiring a tracheostomy *(an operation to create an opening in the neck at the front of the windpipe that can be used to insert a breathing tube)*

1. **Use of Non Invasive Ventilation (NIV)**

Following removal of the ET *(breathing)* tube the patient requires further ventilatory *(breathing)* support with non-invasive ventilation *(delivered by a specially fitted facemask*).

1. **Ventilator Free Days**

The number of days alive and free from mechanical ventilation within the clinical trial period that the researchers define.

*This is a combined measure of death and duration of ventilation.*

*[Here is an example if the clinical trial period is 28 days. If a patient survives and comes off the ventilator on day 5 during the trial, 23 days free are counted because s/he is 23 days free from the ventilator. If a patient comes off the ventilator on day 10, s/he will have 18 days free from the ventilator. If a patient is ventilated for longer than 28 days, then 0 days free are counted; and if a patient dies any time within the 28 day period 0 days free are counted. This means that in this outcome, death and ventilation for 28 days are counted the same.]*

If you would like to suggest other outcomes which have been (or might be) measured in clinical trials of mechanical ventilation and should be considered for a core outcome set, please list them here.

Additional 23 outcomes proposed by Delphi participants following Round 1. These were added to the original 24 outcomes for Rounds 2 and 3.

1. **Comfort**

*A measure of physical or psychological ease, often characterized as a lack of hardship. It may include senses such as hunger, thirst, anxiety, and fear*

1. **Destination following hospital discharge**

*The destination of the patient after discharge from hospital (e.g. home, nursing home, rehabilitative hospital, long care unit, weaning centre)*

1. **Duration of oxygen requirement post-extubation**

*The length of time that additional oxygen therapy is required after the breathing tube has been removed*

1. **Hospital free days**

*The number of days alive and free from hospital within a clinical trial period*

1. **Incidence of hospital readmission following hospital discharge**
2. **Incidence of ICU readmission following ICU discharge**
3. **Incidence of Bronchopulmonary Dysplasia**

*The event of developing this chronic lung disease which affects new-borns and infants. It results from damage to the lungs caused by mechanical ventilation and long-term use of oxygen.*

1. **Incidence of other health care associated infections**

*The event of picking up another infection while in ICU or caused by having devices in the body such as a urinary catheter or an intravenous line*

1. **Lung function**

*A measure of how the lungs are functioning, which shows how strong the muscles are for breathing and how well the lungs are able to work*

1. **Number of failed weaning attempts**

*Number of attempts at withdrawing ventilator support that failed*

1. **Nutritional status**

*Condition of the body in those respects influenced by the diet*

1. **Oral health status**

*Condition of the mouth and teeth*

1. **Persistent cognitive dysfunction**

*The event of developing a mental health disorder that mainly affects learning, memory, awareness, and problem solving, and includes amnesia, dementia, and delirium that persists after intensive care*

1. **Physical function**

*A measure of mobility, for example sitting at the side of the bed, standing, and walking*

1. **Pressure sore**

*The event of developing a sore on the skin because of pressure caused by lying in bed in one position*

1. **Psychological problems**

*The event of developing a psychological problem (such as depression, anxiety, or post-traumatic stress disorder) during or following intensive care*

1. **Pulmonary complications**

*The event of developing a lung complication (such as physical damage to the lungs caused by air pressure within the lungs)*

1. **Return to work**

*The event of returning to work after discharge from hospital*

1. **Number of systemic antibiotic days**

*Number of days on which antibiotics are given*

1. **Time between initiation of ventilation and the first weaning attempt**

*Length of time from being put on the ventilator until the first attempt at withdrawing ventilator support*

1. **Total dose of analgesia/patient/day**

*The total dose of pain killer drugs received per patient per day in the trial*

1. **Total dose of sedatives/patient/day**

*The total dose of sedative drugs received per patient per day in the trial*

1. **Need for rescue therapies**

*The event of requiring additional therapy over and above the mechanical ventilator. It may include events such as being ventilated and nursed lying on the front or receiving support from a heart-lung bypass machine.*

**eAppendix 3** **Names and Affiliations of Delphi and Consensus Meeting Participants**

Delphi Study Participants

**Representative Affiliations**

**Patient Representatives (n=15)**

|  |  |
| --- | --- |
| Anon | Intensive Care Unit (ICU) Steps Ireland |
| Anon | ICU Steps Ireland |
| Anon | ICU Steps Ireland |
| Susan Truesdale | ICU Steps UK |
| Mrs Patricia Fereday | ICU Steps UK |
| Mr Andrew Davis | ICU Steps UK |
| Mr Ian Prothero | ICU Steps UK |
| Mrs Jane Gilneur | ICU Steps UK |
| Mr Mike Ross | ICU Steps UK |
| Ms Nikki Mathers | ICU Steps UK |
| Anon | ICU Steps UK |
| Anon | ICU Steps UK |
| Anon | ICU Steps UK |
| Lydia Emerson | Independent |
| Sylvie Debigaré, M.A. Psychologist | Independent |

**Industry Representatives (n=10)**

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| --- | --- |
| Mr Thomas Krueger | Dräger |
| Dr Aleh Satsishur | Hamilton Medical |
| Ms Francesca Walther | Hamilton Medical |
| Ms Alexandra Gerlach | Hamilton Medical |
| Anon | Hamilton Medical |
| Anon | Hamilton Medical |
| Anon | Hamilton Medical |
| Mr Mattias Himmelstoss | Hamilton Medical AG |
| Mr Christian Remus | IMT Medical |
| Ms Sharona Ghazy | Philips Healthcare |

**Researchers (n=56)**

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| Dr David Cooper | ANZICS Clinical Trials Group and Research Centre |
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| Dr Elizabeth H Skinner | ANZICS Clinical Trials Group and Research Centre |
| Dr Jason Phua | Asian Critical Care Clinical Trials Group |
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| Dr Alicia San | Critical Care Doctoral European Nurses Group (CC-DEN) |
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| Paul E Marik, MD | Eastern Virginia Medical School, USA |
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| Dr Despoina Koulenti | Head of the Working Group on Pneumonia of ESICM |
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| Dr Metaxia Papanikolaou | Hippokrateion Hospital of Athens, Greece |
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| Prof Stephen J Brett | Imperial College London, UK |
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| Prof Kathy Rowan | Intensive Care National Audit and Research Centre, UK |
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| Ms Ruth Canter | Intensive Care National Audit and Research Centre, UK |
| Prof David Harrison | Intensive Care National Audit and Research Centre, UK |
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| Dr Kevin Morris | Paediatric Intensive Care Society - Study Group |
| Dr Lee Ferguson | Paediatric Intensive Care Society – Study Group |
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| Anon | via PubMed Search |
| Anon | via PubMed Search |

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|  |  |
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| Prof Mark Griffiths | Barts Health National Health Service (NHS) Trust, UK |
| Dr Seby Sebastian | Birmingham Children's Hospital, UK |
| Dr Adrienne Randolph MD | Boston Children's Hospital, Harvard Medical School, Boston, USA |
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| Mr Sebastien Tessier BRT, RRT | Canadian Society of Respiratory Therapists |
| Troy Denton | Canadian Society of Respiratory Therapists |
| Sarah Enriquez, RRT | Canadian Society of Respiratory Therapists |
| Asst Prof Katy Spurr | Canadian Society of Respiratory Therapists |
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| Anon | Polish Critical Care Nurses Association |
| Anon | Polish Critical Care Nurses Association |
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| Anon | World Federation of Physical Therapy; South Africa |
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COVenT I Webinar Participants

**Representative Affiliation**

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| Mr Ian Prothero | ICU Steps UK |
| Mrs Jane Gilneur | ICU Steps UK |
| Susan Truesdale | ICU Steps UK |
| Lydia Emerson | Independent |
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**Industry Representatives (n=1)**

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| Prof Paolo Navalesi | Anesthesia and Intensive Care, Department of Medical and Surgical Sciences, Magna Graecia University,Catanzaro, Italy |
| Prof Dr Ary Serpa Neto | The PROtective VEntilation (PROVE) Network |
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**Clinicians (n=10)**

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| Dr Adrienne Randolph MD | Boston Children's Hospital, Harvard Medical School |
| Dr David Inwald | Paediatric Intensive Care Unit, Imperial College Healthcare NHS Trust |
| Dr Philippe Jouvet MD PhD | Sainte-Justine Hospital, University of Montreal, Canada |
| Dr Lyvonne Tume | Paediatric Intensive Care Society Nursing |
| Anita Duyndam MSc | Afdeling IC-kinderen, Erasmus MC, Sophia Kinderziekenhuis |
| Dr Martin Spångfors | Dept Clinical Sciences, Anaesthesiology and Intensive Care Medicine, Lund University with Kristinstad Hospital, Sweden |
| Ms Carley King | Chartered Society of Physiotherapy, London, UK |
| Prof Bernie Carter | Edge Hill University, UK |
| Anon | Swedish CCN Association |

**Invited participants (n=4)**

Anon Royal Victoria Hospital, Belfast, UK

Mrs Jane Cracknell Cochrane: Anaesthesia, Critical and Emergency Care Group

Dr Ashley Agus, Health Economist Northern Ireland, Clinical Trials Unit, UK

Prof Derek C Angus, MD, MPH, FRCP Dept Critical Care Medicine, University of Pittburgh, USA

COVenT II Webinar Participants

**Representatives (n=22) Affiliations**

|  |  |
| --- | --- |
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| Dr Despoina Koulenti | Head of the Working Group on Pneumonia of ESICM |
| Prof Alain Mercat | Réseau européen de Recherche en ventilation Artificielle (REVA Network) |
| Prof Kevin Morris | Paediatric Intensive Care Society - Study Group |
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InFACT Meeting Participants

**Representative s (n=13) Affiliations**

|  |  |
| --- | --- |
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| Prof Steve Webb | Monash University, Melbourne, Australia, Vice-chair, INFACT |

# **eTable 1. Participant characteristics of the Delphi study**

|  |  |  |
| --- | --- | --- |
| Panel Composition by Stakeholder Group.  No. (%) of 161 participants completing all three Delphi rounds | | |
| Clinical trial group members | 35 (22%) |  |
| Physicians | 33 (21%) |  |
| Nurses | 26 (16%) |  |
| AHPs | 21 (13%) |  |
| PubMed trial investigators1 | 21 (13%) |  |
| Patient/caregivers | 15 (9%) |  |
| Industry | 10 (6%) |  |
| Panel Composition by Geography No. (%) | | |
| Europe | 108 (57%) |  |
| North America | 35 (22%) |  |
| Australia | 11 (7%) |  |
| Asia | 3 (2%) |  |
| Africa | 3 (2%) |  |
| South America | 1 (1%) |  |

1 PubMed trial investigators were primary and senior authors of reports of clinical trials evaluating interventions aiming to reduce duration of mechanical ventilation and were identified from a systematic search of publications in PubMed from 2005 to 2015.

# **eTable 2. The 19 Delphi prioritized outcomes arranged by COMET taxonomy**

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **Category** | | | | | |
| **Death** | Mortality | Survival | VFD |  |  |
| **Physiological/Clinical** | Global organ dysfunction | Reintubation | Duration of weaning | Duration of IMV | Successful extubation |
| **Life Impact** | Changes in ADL | HRQOL |  |  |  |
| **Resource Use** | ICU LOS | Hospital LOS | ICU readmission | Need for rescue therapies |  |
| **Adverse Events** | ARDS | VAP | ICU acquired weakness | Pulmonary complications | Delirium |

Abbreviations: ADL, activities of daily living; ARDS, acute respiratory distress syndrome; HRQOL, health related quality of life; ICU, intensive care unit; LOS, length of stay; IMV, invasive mechanical ventilation; VAP, ventilator associated pneumonia; VFD, ventilator free days.

# **eTable 3. Webinar 1, voting results on outcomes to be included in the core outcome set**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Ist Vote No. (%) | | | | Revote No. (%) | | | | 2nd Vote on overlapping outcomes | | | |
| Outcome | In | Out | Unsure | Consensus | In | Out | Unsure | Consensus | In | Out | Unsure | Consensus |
| Mortality | 16 (94) | 1 (6) | 0 | Revote | 16 (94) | 0 | 1 (6) | IN | 12 (100) | 0 | 0 | IN |
| Survival | 14 (82) | 1 (6) | 2 (12) | Revote | 16 (89) | 1 (6) | 1 (6) | IN | 2 (17) | 9 (75) | 1 (8) | OUT |
| VFD | 12 (67) | 3 (17) | 3 (17) | Revote | 8 (50) | 6 (38) | 2 (13) | IN | 2 (15) | 9 (69) | 2 (15) | OUT |
| ADL | 6 (38) | 7 (44) | 3 (19) | Revote | 5 (29) | 11 (65) | 1 (6) | OUT | - | - | - | OUT |
| HRQOL | 14 (88) | 0 | 1 (13) | IN | - | - | - | IN | - | - | - | IN |
| ICULOS | 8 (47) | 7 (41) | 2 (12) | Revote | 5 (29) | 11 (65) | 1 (6) | OUT | - | - | - | OUT |
| Readmission | 5 (31) | 6 (38) | 5 (31) | Revote | 2 (13) | 11 (69) | 3 (19) | OUT | - | - | - | OUT |
| Duration IMV | 14 (88) | 2 (13) | 0 | IN | - | - | - | IN | - | - | - | IN |
| Duration weaning | 6 (35) | 7 (41) | 4 (24) | Revote | 2 (13) | 13 (81) | 1 (6) | OUT | - | - | - | OUT |
| Successful extubation | 10 (63) | 2 (13) | 4 (25) | Revote | 11 (69) | 4 (25) | 1 (6) | IN | 9 (75) | 1 (8) | 2 (17) | IN |
| ARDS | 5 (31) | 7 (44) | 4 (25) | Revote | 1 (7) | 13 (87) | 1 (7) | OUT | - | - | - | OUT |
| ICU acquired weakness | 2 (13) | 9 (56) | 5 (31) | Revote | 1 (6) | 15 (94) | 0 | OUT | - | - | - | OUT |
| VAP | 6 (38) | 9 (56) | 1 (6) | Revote | 7 (47) | 8 (53) | 0 | OUT | - | - | - | OUT |
| GOD | 2 (17) | 6 (50) | 4 (33) | Revote | 2 (13) | 10 (67) | 3 (20) | OUT | - | - | - | OUT |
| Hospital LOS | 7 (54) | 5 (38) | 1 (8) | Revote | 7 (54) | 6 (46) | 0 | OUT | - | - | - | OUT |
| Rescue therapies | 9 (7) | 10 (71) | 3 (21) | OUT | - | - | - | OUT | - | - | - | OUT |
| Delirium | 1 (8) | 8 (62) | 4 (31) | Revote | 1 (8) | 11 (85) | 1 (8) | OUT | - | - | - | OUT |
| Pulmonary complications | 9 (64) | 1 (7) | 4 (28) | IN | - | - | - | IN | - | - | - | IN |
| Reintubation | 8 (62) | 2 (15) | 3 (23) | IN | - | - | - | IN | 5 (42) | 5 (42) | 2 (17) | IN |

Shaded rows highlight outcomes voted in by participants.

Abbreviations: ADL, activities of daily living; ARDS, acute respiratory distress syndrome; GOD, global organ dysfunction; HRQOL, health related quality of life; ICU, intensive care unit; LOS, length of stay; IMV, invasive mechanical ventilation; VAP, ventilator associated pneumonia; VFD, ventilator free days.

# **eTable 4. Webinar 2, voting results on outcomes to be included in the core outcome set**

|  |  |  |  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Ist Vote No. (%) | | | | Revote No. (%) | | | | 2nd Vote on overlapping outcomes | | | |
| Outcome | In | Out | Unsure | Consensus | In | Out | Unsure | Consensus | In | Out | Unsure | Consensus |
| Mortality | 15 (94) | - | 1 (6) | IN | - | - | - | - | 11 (79) | 3 (21) | - | IN |
| Survival | 13 (81) | 2 (13) | 1 (6) | IN | - | - | - | - | 11 (79) | 2 (14) | 1 (7) | IN |
| VFD | 10 (63) | 6 (38) | - | Revote | 6 (38) | 8 (50) | 2 (13) | OUT |  |  |  | OUT |
| ADL | 10 (63) | 4 (25) | 2 (13) | Revote | 9 (56) | 6 (38) | 1 (6) | IN | 7 (50) | 7 (50) | - | NONE |
| HRQOL | 13 (81) | - | 3 (19) | IN | - | - | - | - | 12 (86) | 2 (14) | - | IN |
| ICULOS | 12 (71) | 2 (12) | 3 (18) | Revote | 12 (71) | 3 (18) | 2 (12) | IN | - | - | - | IN |
| Readmission | 6 (35) | 8 (47) | 3 (18) | Revote | 3 (19) | 12 (75) | 1 (6) | OUT | - | - | - | OUT |
| Duration MV | 12 (80) | 1 (7) | 2 (13) | IN | - | - | - | - | - | - | - | IN |
| Duration weaning | 2 (13) | 11 (73) | 2 (13) | OUT | - | - | - | - | - | - | - | OUT |
| Successful extubation | 11 (65) | 3 (18) | 3 (18) | IN | - | - | - | - | 11 (79) | 2 (14) | - | IN |
| ARDS | 4 (24) | 10 (59) | 3 (18) | Revote | 1 (7) | 12 (87) | 1 (7) | OUT | - | - | - | OUT |
| ICU acquired weakness | 2 (13) | 14 (88) | - | OUT | - | - | - | - | - | - | - | OUT |
| VAP | 2 (13) | 13 (81) | 1 (6) | OUT | - | - | - | - | - | - | - | OUT |
| GOD | 6 (33) | 12 (67) | - | Revote | 1 (6) | 15 (83) | 2 (11) | OUT | - | - | - | OUT |
| Hospital LOS | 8 (44) | 7 (39) | 3 (17) | Revote | 2 (12) | 13 (76) | 2 (12) | OUT | - | - | - | OUT |
| Rescue therapies | 4 (24) | 10 (59) | 3 (18) | Revote | 5 (29) | 11 (65) | 1 (6) | OUT | - | - | - | OUT |
| Delirium | - | 18 (100) | - | OUT | - | - | - | - | - | - | - | OUT |
| Pulmonary complications | 2 (11) | 15 (83) | 1 (6) | OUT | - | - | - | - | - | - | - | OUT |
| Reintubation | 7 (41) | 8 (47) | 2 (12) | Revote | 12 (67) | 4 (22) | 2 (11) | IN | 10 (71) | 4 (29) | - | IN |

Shaded rows highlight outcomes voted in by participants.

Abbreviations: ADL, activities of daily living; ARDS, acute respiratory distress syndrome; GOD, global organ dysfunction; HRQOL, health related quality of life; ICU, intensive care unit; LOS, length of stay; IMV, invasive mechanical ventilation; VAP, ventilator associated pneumonia; VFD, ventilator free days.

**eTable 5. Preliminary and agreed definitions at each consensus meeting**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| **Outcome Measures** | **Preliminary definition [1]** | **13th Nov Webinar [2]** | **17th Nov Webinar [3]** | **InFACT meeting [4]** |
| **Mortality** | | | | |
| Specific measurement variable | Medical confirmation of death | Confirmation of death | Confirmation of death | Not discussed |
| Analysis Metric | Event | Event | Event + Date |  |
| Aggregation Method | Rate | Rate | Rate |  |
| Time-point | 60 or 90 days | 60 days from randomization/ recruitment depending on trial design | 60 days from randomization/ recruitment depending on trial design |  |
| **Duration of Mechanical Ventilation** | | | | |
| Specific measurement variable | Liberation from mechanical support including NIV from randomization to unassisted breathing at 48 hours | From randomization/ recruitment depending on trial design until unassisted breathing (no inspiratory support) for 48 hours | From randomization/ recruitment depending on trial design until unassisted breathing (no inspiratory support or extracorporeal support) for 48 hours | Not discussed |
| Analysis Metric | Number of hours ventilated | Number of hours ventilated | Number of hours ventilated |  |
| Aggregation Method | Mean and median | Mean and median no of hours for survivors and non-survivors | Mean and median no of hours for survivors and non-survivors |  |
| Time-point | 60 days | 60 days | 60 days |  |
| **HRQOL** | | | | |
| Specific measurement variable | EQ-5D-5L | EQ-5D- 5L as a quality of life tool | EQ-5D- 5L as a quality of life tool | Not discussed |
| Analysis Metric | Distribution of responses for each item | Distribution of responses for each item | Distribution of responses for each item |  |
| Aggregation Method | % for each response for each category | % for each response for each category | % for each response for each category |  |
| Time-point | 6 months from randomization/ recruitment depending on trial design | 6 months from randomization/ recruitment depending on trial design | 6 months from randomization/ recruitment depending on trial design |  |
| **Length of Stay** | | | | |
| Specific measurement variable | Record both ICU and hospital length of stay | ‘Critical care length of stay’ and ‘hospital length of stay’ both must be a priori defined | ‘Critical care length of stay’ and ‘hospital length of stay’ both must be a priori defined; including censoring points | Not discussed |
| Analysis Metric | Number hours | Number of hours | Number of hours with date of start and stop |  |
| Aggregation Method | Mean and median | Mean and median | Mean and median |  |
| Time-point | Randomization to discharge | From randomization/ recruitment depending on trial design until patient physically leaves the relevant facility. Censor for inter-hospital transfer | From randomization/ recruitment depending on trial design until patient physically leaves the relevant facility. |  |
| **Reintubation** | | | | |
| Specific measurement variable | Reinsertion of the endotracheal tube and re-cannulation of a tracheostomy | Reintubation following deliberate extubation | Reintubation only of endotracheal tubes | Reintubation of either endotracheal tube or tracheostomy after a planned extubation |
| Analysis Metric | Number of reintubations | All reintubations with date and time | All reintubations with date and time | All reintubations (with date and time) |
| Aggregation Method | Rate of reintubation as the core outcome (proportion) | Reintubations vs no reintubations as proportion | No of events/patient | Reintubation rate (first) - numerator (all reintubations following planned), denominator (number of all planned extubations) |
| Time-point | 60 day | 60 day with censor at hospital discharge | 60 day | 60 day or hospital censoring |
| **Successful Extubation** | | | | |
| Specific measurement variable | Successful removal of any and all breathing tubes (i.e. endotracheal and tracheostomy) when the patient maintains 48 consecutive hours tube free | 48hr free of endotracheal tube (censor for tracheostomy) | Free from the endotracheal tube for 48hrs and free from tracheostomy cannula for 48hrs (separate endpoints) | 48hours free from all tubes |
| Analysis Metric | Event | No consensus | Time to first extubation, hours | Time to establishment of natural airway |
| Aggregation Method | Rate | No consensus | Mean and median for survivors and non-survivors | Mean and median |
| Time-point | 60 day | No consensus | 60 day | 60 day or hospital censoring |

Abbreviation: HRQOL, health related quality of life; ICU, intensive care unit; NIV, non-invasive ventilation

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