DELPHI STUDY PROTOCOL

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Core Outcome Measures for Clinical Effectiveness Trials of Nutritional and Metabolic Interventions in Critical Illness: An International Modified Delphi Consensus Study

'Nutritional and metabolic treatments outcomes in critical care: development of a core outcome set'

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Introduction

Background/Rationale

An increasing number of patients who survive treatment in intensive care (ICU) are suffering from severe, prolonged functional disabilities [1, 2]. The post intensive care syndrome (PICS) describes new or worsening problems in physical, cognitive, or mental health arising after a critical illness and persisting beyond hospitalisation [3]. Optimal provision of nutritional therapy may help improve functional and quality of life outcomes, although currently, we have little information on metabolic and nutritional demands of ICU survivors, resulting in an unclear clinical response to nutritional and metabolic interventions in critical illness [4]. Significant heterogeneity therefore exists in the type of outcome measures used in research evaluating clinical nutrition and metabolic interventions in critically ill patients [5]. This complicates interpretation and comparison of results across studies, limiting the ability to conduct meta-analyses and contributing to selective reporting of trial outcomes. As a result, there is a need to establish a consensus about a minimum core outcome set (COS) for research in this field. We propose to use a modified Delphi consensus technique to select a core set of patient function outcome measures that should be reported in clinical effectiveness trials of nutritional and metabolic interventions in the critically ill population.

Objectives

To undertake a modified Delphi consensus process, selecting a core set of patient function outcome measures that should be reported in clinical effectiveness trials of nutritional and metabolic interventions in the critically ill population.

Research Question

What is the core set of patient function outcome measures that should be reported in clinical effectiveness trials of nutritional and metabolic interventions?

Scope of the Core Outcome Set and context for use

Health condition: Critical illness

Population: Adults over 18 years of age who are critically ill

Intervention: Any nutritional or metabolic intervention delivered during critical illness including enteral and parenteral nutrition

Context for use: Primarily for adoption in all research trials and clinical studies evaluating nutritional and metabolic interventions in in critical illness

Methods

Stakeholders

- The participants will comprise representatives from three key stakeholder categories: clinical academics, patients and caregivers, and healthcare professionals.

- A large panel will be convened, using national and international professional society organisations. They will be identified using existing national and international critical care networks.

    1) *Clinical academics*: representatives will be sought through the relevant chapters of the European Society of Intensive Care Medicine (ESICM), the American Society of Parenteral and Enteral Nutrition, (ASPEN) the Australia and New Zealand Intensive Care Society (ANZICS) and the UK Critical Care Research Group (UKCCRG) amongst others.

    2) *Patients and caregivers:* members of patient and public involvement groups, patient support groups and personal contacts amongst others will be approached to participate based on their experience of post-ICU recovery.

    3) *Healthcare professionals:* representatives will be sought through the UK Clinical Care Research Group (UKCCRG), the Intensive Care Society (ICS) and the National Rehabilitation Collaborative (NRC), the British Dietetic Association (BDA), the American Society for Parenteral and Enteral Nutrition (ASPEN), and the European Society for Parenteral and Enteral Nutrition (ESPEN) amongst others.

Recruitment

Representatives from each stakeholder group will be invited to participate in the Delphi process. The introductory email and participant information sheet will:

- Provide specific information about the project, and ask for their consent to participate. Participants will be able to withdraw from the project at any time. The study will be conducted entirely online. Consent will be implied by completion of the survey, consistent with standard practice for survey research. The

information sent out to potential participants will state that consent for the data being used for specified purposes is implied from participating in the survey, with a clause stating that an individual's responses would not be used in any way that would allow his/her identification.

- Illustrate a timeline and estimated completion time for each round of the Delphi.
- Request anonymity of the participants and further request the participant to avoid discussing their opinions with other members.
- Request that the participant will provide any conflict of interest.
- Advise that the participants name, and name of their organisations (if applicable), will be listed as part of the Delphi panel after the Delphi is completed, unless they request otherwise.
- Inform the participant that voting should be based on his/her own opinions, or the opinions of the organisation they are representing.

Contact with participants will be via email and strategies to ensure retention of participants will be used, including personalised invitation to the survey and regular reminders regarding completion. A unique identifier will be assigned to each participant to enable monitoring of completion.

Information Sources

An initial list of outcomes will be identified based on a systematic review related to outcomes used in randomised controlled trials (RCTs) of nutrition in the critically ill (6). This systematic review included RCTs published and/or registered between January 2000 and August 2018. We will conduct an additional systematic review based on the same protocol to capture any further research literature from August 2018 to present day. This will be

registered on PROSPERO. In addition, we will refine our outcome list based on a review which will include, but not limited to:

- International Classification of Functioning, Disability, and Health (ICF) [7]
- Post Intensive Care Syndrome (PICS) [8]
- Chelsea Critical Care Physical Assessment Tool (CPAx) [9]
- Post-ICU Presentation Screen (PICUPs) [10]
- Previous COS projects identifying the core outcome measures and measurement instruments that are essential to include in all clinical research studies evaluating acute respiratory failure survivors after discharge [11-13].
- Qualitative research including patient reported outcomes after critical illness [14-16].

Outcomes will be identified from the above, extracted and mapped to a standard taxonomy for COS development [17]. This outcome list will be peer reviewed by our international collaborators, including healthcare professionals, researchers and patients prior to being finalised for use in the Delphi.

Delphi Consensus Process

Stage 1: Determining the Core Outcome Set

Core outcomes identified will be incorporated in the initial questionnaire and participants will score each outcome according to the Grading of Recommendations Assessment, Development and Evaluation (GRADE) scale ranging from 1-9 in terms of importance for inclusion (1-3, not important for inclusion; 4-6, important but not critical; 7-9, critical to include) [18]. Criteria for inclusion will be a ’critical-to-include’ rating in >70% of responses. All Delphi survey rounds will be delivered electronically using DelphiManager software (COMET Initiative, University of Liverpool, UK).

Round 1: Demographic information will be collected for healthcare professionals, including profession, country of practice and number of years of critical care practice. The order of outcomes will be randomised. Participants will be able to provide additional comments or suggest additional outcomes for consideration.

Round 2: Participants will receive feedback on the distribution of scores and the average score of each outcome from each of the three stakeholder groups, along with their own score will and re-evaluate outcomes. Outcomes which met consensus (>70% of responses) in round 1 for 'not important for inclusion' will be removed.

Round 3: This will allow rating of any new suggested outcomes which didn't reach consensus in round 2.

Consensus meeting: This will be held via web conference comprising of at least 30% of the participants to ratify findings and deal with any uncertainty which may require additional voting.

Stage 2: Determining the Core Outcome Measurement Instruments

Once the COS has been established, we will determine which instruments to use to enable measurement of outcomes. A review of previous literature, including COS projects in critical illness, will be undertaken to see if the outcome measure has previously reached consensus and an appropriate measurement instrument suggested. If the outcome measure has not previously reached consensus then we will compile a list of suggested instruments. A repeat Delphi process will be conducted using the aforementioned methodology over 2 or 3 rounds to determine a consensus on a measurement instrument for each core outcome.

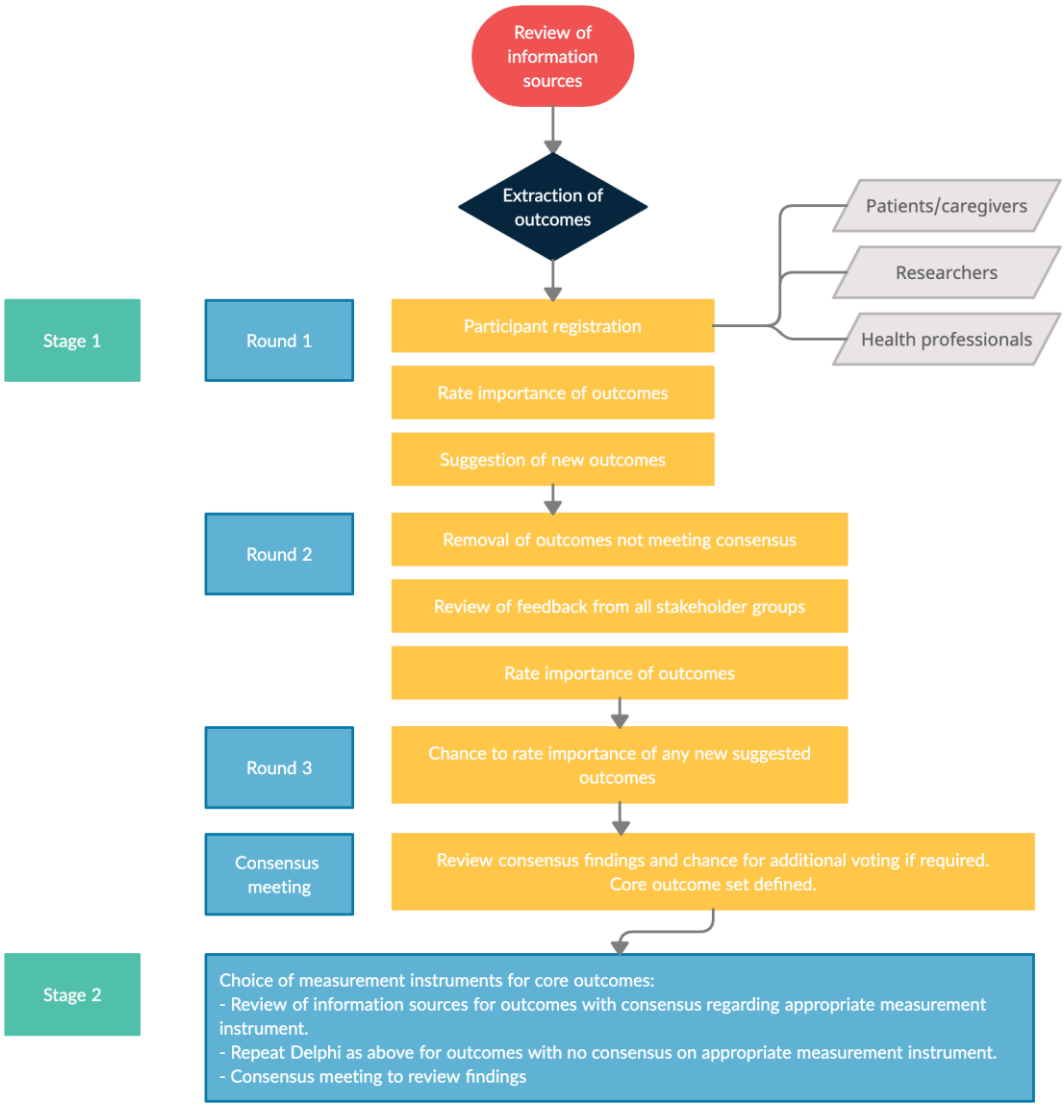
Round 1: Instrument cards will be provided to each participant in which will contain a description of the instrument including, but not limited to: feasibility

of use, instructions of completion, time to complete, administration mode, requirement of training, licencing information, cost and psychometric properties for target population. The highest COnsenus based Standards for selection of health Measurement INstruments (COSMIN) rating from a recent systematic review [19], on measurement properties of instruments used in ICU survivors will also be provided. To aid determination of psychometric properties of measurement instruments we will also search for any new relevant studies and assess the methodological quality in keeping with COSMIN guidelines for selecting outcome measurement instruments in COS projects [20, 21]. Participants will again be able to provide additional comments or suggest additional instruments for consideration.

Rounds 2 and 3: They will run the same way as described previously for Stage 1 to produce a consensus.

Consensus meeting: This will be conducted as described in stage 1 to ratify findings and address any uncertainty.

Workflow



Data Analysis

- Characteristics and demographics of participants will be presented.
- A breakdown of the number of participants involved in each round will be presented including the proportion of each stakeholder group participating in each round.
- Each core outcome measure and measurement instrument will be analysed based on total number of participants.

- Criteria for inclusion will be a 'critical-to-include' rating in >70% of responses.
- Descriptive statistics will be used to summarise and analyse the data.

Ethical Approval

Consent will be implied by completion of the survey, consistent with standard practice for survey research. Application for ethical approval will be made with the Queen Mary Ethics of Research Committee.

Dissemination of results

Results will be disseminated by peer reviewed publication in scientific journals, presentation at national or international conferences and circulation through patient and professional organisations relevant to nutrition and critical care. The final COS will also be circulated to all participants.

Administrative Information

Funding

No funding

Conflicts of interest

None

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