Author’s response to reviews

Title: Sepsis Survivors Monitoring and Coordination in Outpatient Health Care (SMOOTH) - Study Protocol for a randomized controlled trial

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Author’s response to reviews: see over
Dear Editors, dear Prof. Lacroix,

Many thanks for encouraging us to refine the manuscript. Your comments were very useful and we feel they have improved our research. We are able to address all reviewer comments. You will find the changes we have made in a detailed “point-to-point-reply”. If you have any further questions, please do not hesitate to contact us.

Yours sincerely,

Konrad Schmidt
MAJOR COMPULSARY REVISIONS METHODOLOGY

• Patients. – In the section entitled “Recruitment of patients and randomization”, the authors must provide more details on how patients are screened. Are they screened on a daily basis? Is the screening done by research assistants?

  1. The screening process is done on a daily basis by ICU consultants - added in the manuscript, see p. 4

  • It is written in the manuscript that all critically ill adults are considered for recruitment if their cognitive capacity is “sufficient”; please, define what is meant by “sufficient”.

  1. A sufficient cognitive status is defined by a Telephone Interview of Cognitive Status (TICS-M) evaluation ≤ 27 points - see p. 5

  • Most of the text presently imbedded in the section entitled “Recruitment of patients and randomization” must be moved to a section on “Data collection and data management” or to a section on “Outcomes monitoring”.

  1. Done

• Randomization. – A section devoted to the randomization process must be added. In this section, the authors must describe how randomization concealment is done.

  1. Done

• Intervention and co-interventions. – The standardized procedures are well described. However, compliance and how will be checked compliance are not described.

  1. Compliance check of patients will be covered by monthly monitoring calls - see p. 6

  GP compliance will be reviewed by treatment data, collected at 6, 12 and 24 month after ICU stay - see p. 7

  • Cross-overs are not defined.

  1. Cross-over trials are common in studies with multiple interventions, differing in their order. Within the Smooth study, each patient in the intervention group receives the same intervention in the same order: 1) discharge management, 2) training, 3) monitoring. So there is no cross-over design.

• Statistical analysis. – What will be time zero?

  1. T=0 is defined as time of diagnosis on ICU. T=1 is defined as baseline assessment of patient outcome data at discharge from ICU.

  • How will be handled lost to follow-up in the statistical analysis?

  1. For the estimation of average treatment effects we use the intent-to-treat sample. Missing follow-up data will be imputed and on that way included in effect analysis.

DISCUSSION

• What this study can add to the available literature can be better discussed.

  1. Discussion has been elaborated, see. p. 9 “In contrast to former studies, to our knowledge SMOOTH is the first study evaluating the effects of a primary care based intervention for patients after a critical illness i.e. sepsis. Using established primary care structures, SMOOTH may provide a cost-effective addition of care to sepsis aftercare. In addition, considering the long-term impact of sepsis sequelae, 24 month follow-up data will be provided, which are rarely published and will allow analysis of intervention sustainability. As a further innovative element, an external medical consultant in primary care (the liaison physician) might help to support quality of care in primary care settings – strengthening the GP as a reliable clinical partner for patients after critical illness.”
• The greatest risk of the trial is contamination: patients and/or practitioners could talk to each other about the maneuver in the two arms of the study and might start to change their standard care in ICU survivors. This can hurt very much the study. A cluster randomized clinical trial would have prevented such problem. Please, comment this point in the discussion.

**Central Place of the intervention will be the GP Practice: Each GP will be allocated only to patients of one group - either control or intervention. We will have only one patient for each GP, which most work single handed. So there is very little risk of contamination by information flow between intervention and control group, see p.4/9**

• It is said in the manuscript that the control group will receive standard care. This is not exactly the case: phone calls to participants will be done in the control arm, which is not usually done. The trial cannot be done without such phone calls since it is indeed the only way to get data on the primary outcome measure (quality of life). Please, comment in the discussion.

**All patients will be contacted for follow up data at 6, 12 and 24 month. Since for data collection only, we expect marginal effect only (Hawthorne effect), which would underestimate the intervention effect. This would be acceptable, because we would not overuse any effect of the trial.**

MINOR ESSENTIAL REVISIONS (not for publication). General suggestions.
• The authors use two times for the verb in their manuscript: present and future. Since the trial is on going, I suggest using the present all over the manuscript.

**Done, except the statistical analysis, which will take place in future, after data collection**

**Background.**
• Last paragraph: I suggest deleting “to our knowledge for the first time”.

**Done**

**Methods.**
• Section “Aim of the study”. 3rd line: “… survivors will be improved by…” rather than “… survivors will improve by…”.

**Done**

• Section “Control treatment”: I do not understand the 2nd paragraph (According to…”).

**Paragraph has been deleted**

• Section “Data analysis”, 2nd paragraph, 1st line: “we will analyze” rather than “we analyze).

**Done**

• Section “Description of risks”, last line: “Thus, there is no stopping rules” rather than “Thus, there is no definition of stop criteria”.

**Done**

List of abbreviations.
• A list of abbreviations and acronyms must be added after the discussion.

**Has been added**
A section on authors’ contributions is missing.

- Has been added

References.
Please, embed the references in the main document of the manuscript. The references must be formatted according to the editorial standards of the journal TRIALS.

- Done

Reference 16. – Please, update this reference.

- Done

Tables and captions.
- Legends of all tables must be typewritten below the table.
- The legend of each table must include the definitions of all acronyms used (ICD, SF, NSS, KFM, DeMOL, etc).

- Done

Editorial requests:

1. Please include a statement in your Methods section explaining that you obtained informed consent from each participant.

- Done

2. Please include an Authors’ Contributions section at the end of your manuscript, after your Competing Interests section. Each author needs to be listed individually (please use initials to refer to each author's contribution). This section must demonstrate that each author meets all three points of the following criteria in order to qualify for authorship:

- Substantial contributions to: the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; AND
- Drafting the work or revising it critically for important intellectual content; AND
- Final approval of the version to be published

We suggest the following kind of format:

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