The MARCH Trial

Mucoactives in Acute Respiratory failure: Carbocisteine and Hypertonic saline

Mucoactive drugs for acute respiratory failure: A 2x2 factorial, randomised, controlled, open-label, Phase 3, pragmatic, clinical and cost effectiveness trial with internal pilot

STUDY WITHIN A TRIAL (SWAT 51)

We plan to include the following Study Within A Trial (SWAT) embedded within the trial. This SWAT is registered on the Northern Ireland Methodology Hub's SWAT Repository (SWAT 51, Lead Contact: Agus, https://go.qub.ac.uk/SWAT-SWAR).

This SWAT will assess the effect on the 6-month follow-up questionnaire return rates of a Self-Categorisation Theory intervention to actively promote group identity in trial participants. According to Self-Categorisation Theory[2], if a person identifies as a member of a particular group they are more likely to cooperate and pursue the joint interests of the group. By applying this theoretical framework to clinical trials, it may be possible to influence participant retention. Retaining patients in clinical trials in order to obtain follow up after their treatment has finished is a significant challenge[2] and one that has been relatively under-examined in methodology research[3]. High levels of attrition can introduce bias and reduce the generalisability of a trial's results. Retention is particularly difficult in critical care trials[4,5] for many reasons. This may be due to patients' poor health status, or because they are recruited onto trials where the intervention may have occurred early during their illness course and ICU admission, and when they do not fully understand the importance of assessing their outcomes several months after discharge from ICU. We aim to actively promote group identity for randomly selected patients in the MARCH trial using theory-informed study materials consisting of an adapted trial logo, thank you cards, promotional items, and letters. We will also prospectively record the resource use associated with delivering the SWAT (e.g. additional study materials, promotional items, and trial team time input).

We have worked closely with our Patient and Family Advisory Group to discuss the nature and content of the SWAT study materials with particular emphasis on how to increase the salience of the MARCH trial as a "group" and how to encourage participants to feel part of this group.

Research Question
What is the effect on 6-month follow-up questionnaire return rates of a Self-Categorisation Theory-based intervention to actively promote group identity in trial participants?

Hypothesis
A Self-Categorisation Theory-based intervention to actively promote group identity in trial participants will improve rates of return of 6 month follow-up questionnaires

Participants
MARCH participants who have regained capacity, given consent to continue participation in the main trial, and who have been discharged from hospital.

Consent
Separate consent will not be required for SWAT participation.

Interventions and comparator

Participants will be randomised to one of three arms (Table 1) comprising two SWAT group identity intervention arms (S1 and S2) and one control arm (S3). S1 and S2 will receive the same correspondence but S2 will also receive a promotional item (e.g. reusable coffee cup or water bottle). Patients allocated to the SWAT control arm will receive the standard trial follow-up correspondence.

Table 1. SWAT arms and schedule of events

Time point	SWAT group identity intervention arm 1 (S1)	SWAT group identity intervention arm 2 (S2)	SWAT control arm (S3)
2 weeks post discharge	Thank you card incorporating theory-informed wording and adapted trial logo	Thank you card and promotional item incorporating theory-informed wording and adapted trial logo	Nothing
60 days post randomisation	Letter and questionnaire incorporating theory-informed wording and adapted trial logo	Letter and questionnaire incorporating theory-informed wording and adapted trial logo	Letter and questionnaire incorporating standard trial follow-up wording and standard trial logo
6 months post randomisation	Letter and questionnaires incorporating theory-informed wording and adapted trial logo	Letter and questionnaires incorporating theory-informed wording and adapted trial logo	Letter and questionnaires incorporating standard trial follow-up wording and standard trial logo

Outcomes

The primary outcome will be the return rates for the 6-month questionnaires. We will compare the combination of S1 and S2 versus S3 to assess the impact of increasing the salience of the MARCH trial as a "group" on the return rate. We will also compare S1 versus S2 to assess the additional impact of sending a promotional item on the return rate.

Secondary outcomes will include:

i) Group identification scores; measured using the single-item social identification instrument[6], and another study specific question asking about group membership. We will compare the combination of S1 and S2 versus S3 to assess the impact of increasing the salience of the MARCH trial as a "group" on group identification. We will also compare S1 versus S2 to assess the additional impact of sending a promotional item on group identification

ii) Cost per additional questionnaire returned

iii) Total costs associated with embedding the SWAT in the MARCH trial

Randomisation

Participants will be randomised (1:1:1) to S1, S2, or S3. The randomisation process will be separate from the main trial randomisation. The trial statistician will generate the randomisation sequence, which will be accessed by a member of the trial team at the CTU on confirmation of a participants' regained capacity, consent to continue participation in the main trial, and hospital discharge. This should be done within 2 weeks of hospital discharge.

We intend to include as many of the MARCH trial participants in the SWAT as possible, but if randomisation to the SWAT does not occur this will not be a protocol deviation from the MARCH trial, and these non-SWAT participants will receive the standard follow-up correspondence as per the SWAT control group in accordance with the MARCH trial protocol. Further details and full descriptions of analyses will be given in the SWAT Analysis Plan.

1. Turner J. Introducing the problem: individual and group. Rediscovering the Social Group: A Self-categorization Theory. Oxford: Blackwell 1987.
2. Brueton VC, Tierney J, Stenning S, et al. Strategies to improve retention in randomised trials. Cochrane Database of Systematic Reviews 2013;(12):MR000032. doi: 10.1002/14651858.MR000032.pub2
3. Daykin A, Clement C, Gamble C, et al. 'Recruitment, recruitment, recruitment' – the need for more focus on retention: a qualitative study of five trials. Trials 2018;19(1):76. doi: 10.1186/s13063-018-2467-0
4. Agus A, Hulme C, Verghis RM, et al. Simvastatin for patients with acute respiratory distress syndrome: long-term outcomes and cost-effectiveness from a randomised controlled trial. Critical Care 2017;21(1):108. doi: 10.1186/s13054-017-1695-0
5. Agus A, Phair G, Page VJ, et al. Simvastatin for the prevention and treatment of delirium in critically ill, mechanically ventilated patients (MoDUS): a cost-effectiveness analysis. The Lancet Respiratory Medicine 2018;6(3):e9-e10. doi: 10.1016/S2213-2600(18)30070-5
6. Postmes T, Haslam SA, Jans L. A single-item measure of social identification: reliability, validity, and utility. British Journal of Social Psychology 2013;52(4):597-617. doi: 10.1111/bjso.12006 [published Online First: 2012/11/06]