
JOINT TRIAL STEERING AND DATA MONITORING
COMMITTEE CHARTER

ADVANCE TRAUMA

Effects of Advanced Trauma Life Support® Training Compared to Standard Care on Adult Trauma Patient Outcomes: A Cluster Randomised Trial

Version 1.0.0, 2024-10-07

THIS DOCUMENT IS BASED ON THE MRC CTU TEMPLATE TRIAL STEERING
COMMITTEE CHARTER (VERSION 1.02) AND THE MRC CTU TEMPLATE
INDEPENDENT DATA MONITORING COMMITTEE CHARTER (VERSION 2.01).

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1 Administrative information

1.1 Changelog

This changelog will record all changes made to this document following version 1.0.0







| Version | Date | Details |
|---------|------|---------|
| | | |











1.2 Study identifiers

- ClinicalTrials.gov identifier: [NCT06321419](#)
- Clinical Trials Registry - India identifier: CTRI/2024/07/071336

1.3 Contributors

The following have contributed to the design and implementation of the trial:

| Name and ORCID | Affiliation | Role |
|--|--|---|
| Martin Gerdin Wärnberg  | Karolinska Institutet, Stockholm, Sweden | Principal Investigator, TMG chair and TT member |
| Girish D Bakhshi  | Grant Govt. Medical College & Sir J. J. Group of Hospitals, Mumbai, India | TMG member |
| Debojit Basak  | Institute of Post Graduate Medical Education & Research and Seth Sukhlal Karnani Memorial Hospital, Kolkata, India | TMG member |
| Abhinav Bassi  | The George Institute for Global Health, New Delhi, India | TMG and TT member |
| Johanna Berg  | Karolinska Institutet, Stockholm, Sweden | TMG member |
| Shamita Chatterjee  | Institute of Post Graduate Medical Education & Research and Seth Sukhlal Karnani Memorial Hospital, Kolkata, India | TMG member |

| Name and ORCID | Affiliation | Role |
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| Lovisa Strömmer  | Karolinska Institutet, Stockholm, Sweden | TMG member |
| Li Felländer-Tsai  | Karolinska Institutet, Stockholm, Sweden | TMG member |

Abbreviations: TMG, Trial Management Group; TT, Trial Team.

1.4 Trial organisation

Trial management and oversight is governed by three trial committees and groups: the Trial Team (TT), the Trial Management Group (TMG), the joint Trial Steering and Data Monitoring Committee (SDMC). These groups and their relationships are briefly described in Figure 1. Details about each committee and group are available in their respective charter.

2 Introduction

The purpose of this document is to describe the membership, terms of reference, roles, responsibilities, authority, decision-making and relationships of the joint Trial Steering and Data Monitoring Committee (SDMC) for this trial, including the timing of meetings,

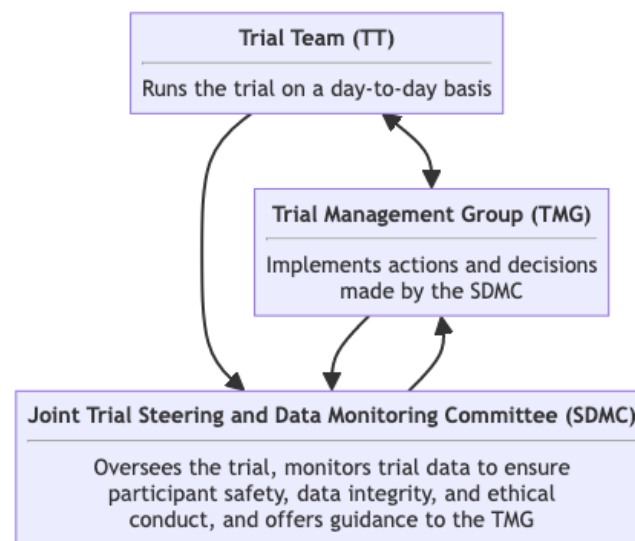


Figure 1: Trial organisation overview.

methods of providing information to and from the SDMC, frequency and format of meetings, statistical issues and relationships with other committees.

2.1 Trial synopsis

Title Effects of Advanced Trauma Life Support® Training Compared to Standard Care on Adult Trauma Patient Outcomes: A Cluster Randomised Trial

Rationale Trauma is a massive global health issue. Many training programmes have been developed to help physicians in the initial management of trauma patients. Among these programmes, Advanced Trauma Life Support® (ATLS®) is the most popular, having trained over one million physicians worldwide. Despite its widespread use, there are no controlled trials showing that ATLS® improves patient outcomes. Multiple systematic reviews emphasise the need for such trials.

Aim To compare the effects of ATLS® training with standard care on outcomes in adult trauma patients.

Primary Outcome In-hospital mortality within 30 days of arrival at the emergency department.

Trial Design Batched stepped-wedge cluster randomised trial in India.

Trial Population Adult trauma patients presenting to the emergency department of a participating hospital.

Sample Size 30 clusters and 4320 patients.

Eligibility Criteria

Hospitals are secondary or tertiary hospitals in India that admit or refer/transfer for admission at least 400 patients with trauma per year.

Clusters are one or more units of physicians providing initial trauma care in the emergency department of tertiary hospitals in India.

Patients participants are adult trauma patients who presents to the emergency department of participating hospitals and are admitted or transferred for admission.

Intervention The intervention will be ATLS® training, a proprietary 2.5 day course teaching a standardised approach to trauma patient care using the concepts of a primary and secondary survey. Physicians will be trained in an accredited ATLS® training facility in India.

Ethical Considerations We will use an opt-out consent approach for collection of routinely recorded data. We will obtain informed consent for collection of non-routinely recorded data, such as quality of life and disability outcomes. Patients who are unconscious or lack a legally authorized representative will be included under a waiver of informed consent. Note that consent here refers to consent to data collection.

Trial Period October 1, 2024, to September 30, 2029

2.2 Special considerations

2.3 Funding

This trial is not yet fully funded. The Trial Management Group has decided to proceed with the trial with the expectation that additional funding will be secured. The Trial Steering Committee will be informed of the funding status at each meeting. If funding is not secured, the trial will be stopped. This will likely result in an underpowered trial. The justification for this decision is that the intervention is considered standard of care in many countries and the data collection is considered minimal risk. There is therefore a very small risk of harm to patient participants, but a potential direct benefit to those patient participants who receive the intervention. The benefit-risk ratio is therefore considered to be favourable, even in the case of an underpowered trial.

2.4 Potential amendments

There are ongoing discussions about re-framing the trial as a hybrid effectiveness-implementation trial and include a cost-effectiveness analysis. This would involve adding additional data collection to assess the implementation and costs of the intervention. This would involve additional funding and amended ethical approvals.

3 Roles and responsibilities

The SDMC's responsibility is to oversee and safeguard the trial and the trial participants, monitor the main outcome measures including safety and efficacy, and monitor the overall conduct of the trial. The SDMC also should receive and review information on the progress and accruing data of this trial and provide advice on the conduct of the trial to the Trial Management Group (TMG). The specific roles of the SDMC are detailed below.

3.1 Expert supervision and monitoring

- Providing expert supervision of the trial.
- Monitoring recruitment figures, follow-up rates, and losses to follow-up.
- Monitoring compliance with the protocol by investigators.
- Assessing data quality, including completeness, and encouraging the collection of high-quality data.
- Overseeing the completion of CRFs and advising on TMG's future strategies for satisfactory completion.
- Reviewing interim analyses including main outcomes and safety data.
- Assessing the impact and relevance of external evidence.
- Monitoring planned sample size assumptions, preferably with regards to:
 - a priori assumptions about the control arm outcome; and/or
 - emerging differences in clinically relevant subgroups.

3.2 Advising and approving changes

- Sanctioning any changes to the protocol proposed by the TMG (e.g., to design, inclusion criteria, trial endpoints, or sample size).
- Approving TMG's proposals for new substudies.
- Suggesting additional data analyses if necessary.

3.3 Decision making on trial continuation

- Deciding whether to recommend that the trial continues to recruit participants or whether recruitment should be terminated either for everyone or for some treatment groups and/or some participant subgroups.
- Deciding whether trial follow-up should be stopped earlier.

3.4 Oversight of trial completion and findings

- Supervising the prompt disclosure of trial findings.
- Providing input on the policy for publication.
- Approving and giving feedback on the main trial manuscript.

3.5 Confidentiality and appropriateness

- Maintaining confidentiality of all trial information that is not in the public domain.
- Monitoring the continuing appropriateness of patient information.

4 Early in the trial

All potential SDMC members should have sight of the protocol before agreeing to join the committee. Before recruitment begins the trial will have undergone review by the TMG and research ethics committees.

Therefore, if a potential SDMC member has major reservations about the trial (e.g. the protocol or the logistics) they may decide not to accept the invitation to join.

SDMC members should be independent and constructively critical of the ongoing trial, but also supportive of aims and methods of the trial.

The SDMC will first meet within one year of enrolment commencing, to discuss the protocol, the trial, the analysis plan, future meetings, and to have the opportunity to clarify any aspects with the Principal Investigator (PI) and TMG.

SDMC members will not formally sign a contract but will formally register their assent to join the group by confirming (1) that they agree to be on the SDMC and (2) that they agree with the contents of this Charter. Any competing interests should be declared at the same time.

A positive reply including potential competing interests to the invitation email will be taken as formal agreement to join the SDMC.

5 Composition

The majority of members of the SDMC, including the Chair, are independent of the trial. Non-independent members will also be part of the SDMC.

The Chair should have previous experience of serving on trial committees and experience of Chairing meetings, and should be able to facilitate and summarise discussions.

There will be an additional Facilitator who will be responsible for arranging meetings of the SDMC, coordinating reports, producing and circulating minutes and action points.

The SDMC membership will include a statistician to provide independent statistical expertise, especially with regards to interpretation of accumulating data and guidance through the report. The statistician will not prepare the SDMC report.

The TT will have overall responsibility for the production of the report to the SDMC and the trial statistician will participate in SDMC meetings, guiding the SDMC through the report, participating in SDMC discussions and, on some occasions, taking notes.

The PI is a member of the SDMC but will, at the request of the Chair or other independent members, abstain from participating in certain parts of or entire meetings. Other members of the TMG are not expected to participate in the SDMC meetings, but may be invited by the SDMC Chair to observe, provide information or answer questions.

The members of the SDMC for this trial are, in alphabetical order by surname, with their roles and affiliations:

Ganesan Karthikeyan (Chair, Independent Member)

Clinical, interventional cardiologist and a Professor of Cardiology at All India Institute of Medical Sciences, New Delhi, India

Richard Hooper (Independent Member, Statistician)

Professor of Medical Statistics at Queen Mary University of London, UK

Kathryn Chu (Independent Member, Clinical expert)

Director and Professor of Global Surgery at Centre for Global Surgery, Stellenbosch University, South Africa

Elamurugan TP (Independent Member, Clinical expert)

Additional Professor of Surgery and Associate Dean at Jawaharlal Institute of Postgraduate Medical Education and Research, Puducherry, India

Sai Kulkarni (Independent Member, Lay person representative)

Martin Gerdin Wärnberg (Principal Investigator, Non-independent Member)

Associate professor of clinical epidemiology at Karolinska Institutet, Stockholm, Sweden

Samriddhi Ranjan (Facilitator, Non-independent Member)

Project Manager, The George Institute for Global Health, India

6 Relationships

The SDMC will receive reports from the TMG, and will provide advice to the TMG. The SDMC will not be involved in the day-to-day running of the trial. No payments will be made to SDMC members for their time.

Any competing interests, both real or potential, should be disclosed. These are not restricted to financial matters – involvement in other trials or intellectual investment could be relevant. Although members may well be able to act objectively despite such connections, complete disclosure enhances credibility.

7 Organisation of meetings

The SDMC meetings will coincide with the completion of data collection for each batch, so six meetings in total during the trial period of two years. The format is primarily virtual. The Facilitator will arrange the meetings and invite SDMC members. The SDMC chair may convene additional meetings to review safety and any other aspect of the study.

If an independent member does not attend a meeting or provide comments when requested between meetings, it should be ensured that the independent member is available for the next meeting. If an independent member does not attend the next meeting or provide comments when next requested, they should be asked if they wish to remain part of the SDMC. If an independent member does not attend a third meeting, strong consideration should be given to replacing this member.

8 Trial documentation and procedures

A report will be prepared by the TT and approved by the TMG after the completion of data collection for each batch, before being shared with the SDMC. The report will follow a standard template. The report will be circulated to the SDMC at least 2 weeks prior to the meeting. The SDMC will review the report and provide feedback to the TMG.

The report to the SDMC will include the following information:

- Number of clusters included in the batch
- Number of clusters dropping out in the batch
- Number of potentially eligible participants screened in the batch
- Number of participants who did not consent to out of hospital follow up in the batch
- Number of participants included in the batch

- Number of participants lost to follow-up in the batch
- Summary statistics of included clusters and patient participants, including outcomes and missing data
- Adherence to randomisation schedule and reasons for non-adherence
- Number of physicians trained in ATLS® in each hospital in the batch
- Protocol deviations
- Proposed protocol amendments
- Safety events
- Relevant external evidence

Relevant external evidence, proposed trial design and protocol changes, and any new substudies will be detailed. Proposed updates on sample size calculations and statistical assumptions, patient information and consent processes, and trial timelines and milestones will be provided.

Identification and circulation of external evidence (e.g. from other trials/ systematic reviews) is not the responsibility of the SDMC members. The PI and the TT will collate any such information for presentation during the meeting.

8.1 Interim Analysis

There will be one interim analyses after half of the batches have completed the trial. The interim analyses will be assessed by the joint Trial Steering and Data Monitoring Committee. The purposes of this interim analysis will be to:

- assess the trial's feasibility and recommend stopping the trial if the trial is not feasible, for example if hospitals fail to adhere to the randomisation schedule or if there are substantial missing data in outcomes;
- assess if sample size calculations should be revised, primarily by increasing the number of clusters to be included; and
- compare characteristics across intervention conditions to monitor for differential recruitment/ascertainment between intervention and control.

8.2 Safety monitoring

The SDMC will review safety events, as defined below, continuously as reported by the TMG.

In alignment with other current trials including critically ill patients, this trial will not collect adverse events or serious adverse events, because many of these events are expected in this patient population and for example mortality is collected as part of the outcomes.

Instead the presence of the following safety events, if they are life-threatening, prolong hospitalisation or result in meaningful harm to the participant, will

A comprehensive list of events that can be considered safety events cannot be pre-specified, but the presence of the following safety events will actively assessed:

- Prolonged mechanical ventilation (> 7 days)
- Initiation of renal replacement therapy
- Prolonged (> 2 days) or renewed (restart after at least 2 days without) use of vasopressors such as norepinephrine or vasopressin

These events are considered safety events because they suggest pulmonary, renal, septic or bleeding complications and an increase in their occurrence following ATLS® training could indicate that the intervention is harmful.

These events therefore need to be tracked during the standard care phase as well as the intervention phase, but will only be considered indicative of harm related to the intervention if they occur more often during the intervention phase than during the standard care phase.

Any other safety events that are identified by the clinical research coordinators or local investigators during the trial will also be reported, for example include missed injuries or missed investigations, which could be suspected if certain injuries or investigations are identified or conducted more often during the standard care phase than during the intervention phase.

All safety events will be recorded in the CRF and reported to the TMG within 24 hours of its occurrence. The TMG will then assess if the event can be considered related to the trial or the intervention within 24 hours of it being reported. Events that are considered probably related will be reported immediately to the SDMC.

9 Decision making

After reviewing the relevant reports, possible decision from the SDMC includes:

- No action needed, trial continues as planned;
- Early stopping due, for example, to the trial not being feasible (for example if clusters fail to adhere to the randomisation schedule or if there are substantial missing data in outcomes), or if there is a safety concern based on the reporting of safety events;
- Stopping recruitment within a subgroup (care should be taken if this is not a pre-specified subgroup);
- Extending recruitment (based on actual control arm response rates being different to predicted rather than on emerging differences);
- Extending follow-up;

- Proposing or commenting on proposed protocol changes; and
- Commenting on Statistical Analysis Plan.

The Chair is to summarise discussions and encourage consensus; it is usually best for the Chair to give their own opinion last. Every effort should be made to reach a consensus. If a consensus cannot be reached, a vote will be taken. The Chair will have the casting vote.

Efforts should be made to ensure that all members can attend. The SDMC is quorate if at least the independent chair and the statistician, as well as the PI and trial statistician, are present. The PI will not participate in the decision-making process if the Chair or other independent members request this, and will not vote on stopping the trial early.

If the SDMC is considering recommending major action after a meeting in which some of the independent SDMC members could not attend, the SDMC Chair should communicate with the absent members as soon after the meeting as possible to check they agree. If they do not, a further meeting should be arranged with the full SDMC.

SDMC members who will not be able to attend the meeting may pass comments to the SDMC Chair for consideration during the discussions.

If a member does not attend a meeting, it should be ensured that the member is available for the next meeting. If a member does not attend the following meeting, they should be asked if they wish to remain part of the SDMC. If a member does not attend a third meeting, they should be replaced.

10 Reporting

The SDMC will report their decisions via the Facilitator to the TMG who will be responsible for implementing any actions resulting. Notes of key points and actions will be made by the Facilitator and circulated to the SDMC within 1 week of the meeting. The SDMC Chair will sign off the final version of minutes or notes.

The SDMC is the oversight body for the trial. However, the SDMC should have good reason before deciding not to accept requests from the TMG. If there are serious problems or concerns with the SDMC decision following an DMC recommendation, a joint meeting of the SDMC and DMC should be held. The information to be shown would depend upon the action proposed and each committees' concerns.

Depending on the reason for the disagreement data may have to be revealed to all or some of those attending such a meeting: this would be minimised where possible. The meeting would be Chaired by an external expert who is not directly involved with the trial.

11 After the trial

The SDMC will oversee the timely analysis, writing up and publication of the main trial results. The independent members of the SDMC will have the opportunity to read and comment on the proposed main publications of trial data prior to submission and abstracts and presentations during the trial. This review may be concurrent to that of the trial investigators and SDMC.

12 Amendments

This SDMC charter can be amended as needed during the course of the study. All amendments will be documented with sequential version numbers and revision dates, and will be recorded in the SDMC notes.