COLLABORATION AND SUBGRANT AGREEMENT

for a Collaborative Project

Project full title: “Effects of Advanced Trauma Life Support® Training Compared to Standard Care on Adult Trauma Patient Outcomes (ADVANCE TRAUMA): A Cluster Randomised Trial”

Project Leader: Karolinska Institutet
(Martin Gerdin Wärnberg)

THIS COLLABORATION AND SUBGRANT AGREEMENT IS EFFECTIVE FROM ON 01-01-2024, HEREINAFTER REFERRED TO AS THE "EFFECTIVE DATE BETWEEN:

1. **Karolinska Institutet**, Department of Global Public Health, Nobels väg 6, 171 77, Stockholm, Sweden, org.nr 202100-2373 ("KI" or "Project Leader"), and

2. **George Institute for Global Health**, with its office at 308 Elegance Tower, Plot No. 8, Jasola District Centre, New Delhi 110025, India and company identification number U74900TG2007NPL055085 ("TGI" or "Study Coordinator")

hereinafter, jointly or individually, referred to as "Parties" or "Party".

WHEREAS:

A. The Parties have a mutual interest in achieving research results regarding the project entitled "Effects of Advanced Trauma Life Support® Training Compared to Standard Care on Adult Trauma Patient Outcomes (ADVANCE TRAUMA): A Cluster Randomised Trial", (the "Project").

B. KI has obtained grants from the Swedish Research Council (Vetenskapsrådet), and from the Laerdal Foundation, hereinafter referred to as the "Funding Entities" to conduct the Project, (hereinafter the "Research Grant").

C. The Parties wish to collaborate with KI to implement the Project and have therefore entered into this collaboration and subgrant agreement (hereinafter the "Agreement") for the purpose of setting out the terms and conditions of the collaboration.

NOW, THEREFORE, IT IS HEREBY AGREED AS FOLLOWS:

1 DEFINITIONS

Words beginning with a capital letter shall have the meaning defined herein.

"Access Rights" means user rights to Background or Results.

"Background" means any data, know-how or information which is held by the Parties prior to their accession to this Agreement, as well as copyrights or other intellectual property rights pertaining to such information, the application for which has been filed before their accession to this Agreement and which is needed for carrying out the Project or for Use of the Results.

"**Data**" means the data collected in India under the scope of the Trial.

"Exploitation" means the direct or indirect utilisation of Results, in particular through transfer or licensing by using them in further research activities other than those covered by the Project, or for developing, creating and marketing a product or process, or for creating and providing a service.

"**Funding Entity/ies**" means the organisation providing funding of the Project, in this case the Swedish Research Council (*Vetenskapsrådet*) and the Laerdal Foundation.

"Individual Result" means a Result which a Party can demonstrate has been generated solely by such Party or independently of any collaboration with the other Party.

"Needed" means:

(a) for the implementation of the Project: Access Rights are Needed if, without the grant of such Access Rights, carrying out the Project related tasks by the recipient Party would be impossible, significantly delayed, or require significant additional financial or human resources.

(b) for Use of own Results: Access Rights are Needed if, without the grant of such Access Rights, the Use of own Results would be technically or legally impossible.

"Personal Data" means any information relating to an identified or identifiable natural person ('data subject'); as this term is defined under Regulation (EU) 2016/679 of the European Parliament and of the Council of 27 April 2016 on the protection of natural persons with regard to the processing of personal data and on the free movement of such data, and repealing Directive 95/46/EC (General Data Protection Regulation, hereinafter "GDPR").

"Project Leader" means KI, the recipient of the Research Grant that is responsible for the administration of the Research Grant, the planning and implementation of activities according to the application approved by the Funding Entities.

"Project Plan" means the Protocol as first defined in Schedule 1.

"**Protocol**" means the description of the Trial developed jointly by KI and TGI, and all amendments thereto as the Parties may from time to time agree. Such amendments will form an integral part of this Agreement.

"Results" means any tangible or intangible output of the Project such as data, knowledge or information, whatever its form or nature, whether it can be protected or not, that is generated under the Project, as well as any rights attached to it, including intellectual property rights.

"Study Coordinator" means TGI as the organization responsible for the initiation, coordination and management of the Trial in India in accordance with applicable national laws, GCP and the Protocol.

"**Study Site**" means any hospital or clinic in India involved by TGI in the conduct of the Trial under TGI's responsibility.

"**Subject**" means a person recruited to participate in the Trial.

"Trial" means the academic driven, multicentre, prospective cluster randomized clinical trial of Advanced Trauma Life Support compared to standard care (clinicaltrials.gov NCT05417243) conducted by TGI in India pursuant to this Agreement.

Any reference to a statutory provision, code or guidance shall be deemed to include reference to any statutory modification or re-enactment of it.

2 PURPOSE

The purpose of this Agreement is to specify with respect to the Project the relationship among the Parties, in particular concerning the organisation of the work between the Parties, the management of the Project and the rights and obligations of the Parties concerning inter alia liability, intellectual property rights and dispute resolution.

3 DURATION AND TERMINATION

3.1 This Agreement shall have effect from the Effective Date identified at the beginning of this Agreement and shall continue in full force and effect until 31 December 2029 or until complete fulfilment of all obligations undertaken by the Parties under this Agreement. However, this Agreement may be terminated earlier in accordance with the terms of this Agreement and the General Terms and Conditions of the Research Grant as included in Schedule 2 of this Agreement. If a Party does not obtain all necessary approvals for the Project from relevant authorities, this Agreement shall be terminated as soon as practicable with due consideration to patient safety and research matters.

3.2 The provisions relating to Results and Intellectual Property, Confidentiality for the time period mentioned therein, as well as for Liability, Applicable law and Settlement of Disputes shall survive the expiration or termination of this Agreement.

4 RESPONSIBILITIES OF THE PARTIES

4.1 General principles

4.1.1 Each Party undertakes to take part in the efficient implementation of the Project, and to cooperate, perform and fulfil, promptly and on time, all of its obligations under this Agreement in accordance with the terms of the Research Grant as included in Schedule 2 of this Agreement and in a manner of good faith.

4.1.2 Each Party undertakes to notify promptly to the Project Leader any significant information, fact, problem or delay likely to affect the Project. Each Party shall carry out its responsibilities in accordance with the Project Plan and shall bear sole responsibility for ensuring that its acts within the Project do not knowingly infringe third party property rights.

4.1.3 Each Party shall promptly provide all information reasonably required by any of the other Party to carry out its tasks and shall take reasonable measures to ensure the accuracy of any information or materials it supplies to the other Party.

4.1.4 Each Party shall ensure that its work on the Project complies fully with all applicable local, government and international laws, regulations and guidelines which are effective during the period of the Research Grant, including those governing health and safety, data protection, and where relevant, the use of human or animal subjects and good clinical practice. In this regard, each Party shall maintain the confidentiality, in accordance with the applicable laws, regulations and guidelines, of all samples and data relating to the use of human subjects, which is created or used in the course of the Project.

4.1.5 Each Party shall secure all necessary approvals from the relevant research ethics committees before undertaking any part of the Project requiring ethics committee approval and shall, if required, obtain properly signed informed consent and acknowledgement forms from any human subjects, or their legal guardians, who they will involve in the Project.

4.1.6 Each Party shall handle the Project documentation in a manner acceptable for the collection of data for submission to or review by, a regulatory authority and in full compliance with the Protocol and all applicable laws and regulations (which includes Good Clinical Practice).

4.2 Breach

In the event that a Party is in breach of its obligations under this Agreement (e.g. improper implementation of the Project), the Project Leader will give formal notice to such Party requiring that such breach be remedied within a reasonable time frame after the notice. The Project Leader shall report the breach to the Funding Entities who may decide on the consequences thereof which may include suspension or termination of the Project.

4.3 Involvement of third parties

A Party that enters into a subcontract or otherwise involves third parties in the Project remains solely responsible for carrying out its relevant part of the Project and for such third party's compliance with the provisions of this Agreement, including the Protocol. Such Party has to ensure that the involvement of third parties does not affect the rights and obligations of the other Party under this Agreement.

4.4 Specific responsibilities of the Parties

4.4.1 Karolinska Institutet (KI)

KI will be responsible for distributing the Research Grant, in line with the approved budget, as further stated in Section 7 and schedule 3.

KI as the Project Leader of the Project will be responsible for:

a) the design of the Trial in collaboration with TGI;

b) the conduct of statistical analysis of Data and the interpretation of findings in collaboration with University of Birmingham (Karla Hemming);
c) coordination and drafting of publications;
d) preparation of dissemination messages in collaboration with the other Party;
e) compliance with Swedish laws and regulations related to storage of data;
f) registration of the Trial and reporting of results in www.clinicaltrials.org; and
g) signing up a separate collaboration agreement with the University of Birmingham to enable their participation in the Project in the form of expertise and know-how regarding the design of Data analysis and their contribution to publications and dissemination messages in collaboration with KI and TGI.

4.4.2 George Institute for Global Health (TGI)

TGI shall be the Study Coordinator responsible for the execution, coordination and management of the Trial in India. TGI shall assume all legal responsibilities for the implementation of the Trial in India in accordance with Good Clinical practice.

As Study Coordinator, TGI will be solely responsible for:

a) the design of the Trial in collaboration with KI and the direction and management of the Trial in India;
b) translating the Protocol and additional documentation, including Subject documents and informed consent forms into local language, as appropriate;
c) engaging Study Sites and any subcontractors and liaising with them and providing them all necessary information to ensure that the Trial is conducted in accordance with the Protocol, GCP and applicable laws;
d) entering into appropriate written agreements with the Study Sites for the conduct of the Trial, in accordance with applicable laws, to ensure recruitment of Subjects and collection of Data,;
e) monitoring the Trial;
f) conducting training,
g) collecting, documenting and reporting patient data and reporting serious adverse events;
h) ensuring Data quality;
i) Data storage;
j) reporting serious breaches;
k) any coordinating activities in accordance with the Protocol;
l) being a contact point for receiving all questions from Subjects, Principal Investigators and national regulatory authorities regarding the Trial and providing answers to them;
m) contributing to analyses, interpretation of findings; and
n) contributing to drafting publications and shaping dissemination messages in collaboration with KI and with University of Birmingham.

TGI shall secure all necessary approvals from the relevant research ethics committees in India and for registering the Trial, including any amendments thereof, with the relevant authorities in India before undertaking any part of the Trial. TGI shall obtain properly signed informed consent and acknowledgement forms from any Subjects who they involve in the Project. TGI shall ensure that all necessary approvals, indemnities and agreements from Study Sites involved are obtained.

TGI shall remain fully and directly liable for its own activities and for its compliance with applicable laws. TGI shall obtain and maintain complete and relevant insurances, including patient insurance, as required by applicable laws and shall if required provide KI with a certificate to such effect.

4.5 Personal data

4.5.1 Each Party shall maintain the confidentiality, in accordance with the applicable laws, regulations and guidelines, of all samples and personal data (including digital and paper data) relating to the use of human subjects, which is created or used in the course of the Project and shall ensure that all local communities, hospitals and primary health facilities involved in the Project comply with said obligations and any further instructions and security measures to ensure personal data is processed as required by applicable laws.

4.5.2 TGI shall ensure that documentation and collection of Data in the Trial is made in full compliance with the Protocol and all applicable laws and regulations, including GCP and that the collection of Data is conducted in a manner which provides for the correct submission to, or review by, relevant regulatory authorities.

4.5.3 The Parties acknowledge and agree that in relation to the Data (Personal Data) collected by TGI under and in connection with the Study, the Parties KI and TGI are joint controllers pursuant to Article 26 GDPR and their respective responsibilities will be agreed upon in the separate Joint Controller Agreement to be signed by KI and TGI.

4.5.4 In respect of Personal Data collected by TGI under and in connection with the Trial, TGI shall (i) comply with any applicable data protection laws; (ii) use reasonable endeavours to ensure that all Personal Data is processed lawfully, fairly and in a transparent manner and in compliance with the data protection laws to which it is subject; (iii) enter into such other written agreements with third parties, including Study Sites as may be required from time to time to enable the processing of Personal Data by the Parties.

5 LIABILITY

5.1 No warranties

In respect of any information or materials (including Results and Background) supplied by one Party to another under the Project, no warranty or representation of any kind is made, given or implied as to the sufficiency or fitness for purpose nor as to the absence of any infringement of any proprietary rights of third parties.

Therefore, the recipient Party shall in all cases be entirely and solely liable for the use to which it puts such information and materials, and no Party shall be liable in case of infringement of proprietary rights of a third party resulting from any other Party (or its affiliated entities) exercising its Access Rights.

5.2 Limitations of contractual liability

No Party shall be liable to the other Party for any indirect or consequential loss or similar damage such as, but not limited to, loss of profit, loss of revenue, loss of contracts or any other indirect loss.

Notwithstanding anything contained in this Agreement, a Party's aggregate liability towards the other Party shall be limited to 50 000 Euro, provided such damage was not caused by a wilful act or gross negligence.

TGI shall solely be liable for any claims and proceedings made or brought by or on behalf of Subjects or Study Sites against the Parties for personal injury to Subjects to the extent arising out of or relating to the conduct of the Study in accordance with this Agreement and the applicable Protocol (and any amendments thereto).TGI shall maintain clinical trial liability insurance in respect of its obligations to third parties and sufficient limits to cover the indemnification obligations in this Agreement, and the cost of such insurance will be included in the budget for the Project as specified in the financial plan, Schedule 3 of this Agreement.

The terms of this Agreement shall not be construed to amend or limit any Party's statutory liability.

5.3 Damage caused to third parties

Each Party shall be solely liable for any loss, damage or injury to third parties resulting from its performance under this Agreement or from its use of Results or Background.

5.4 Force Majeure

No Party shall be considered to be in breach of this Agreement if it is prevented from fulfilling its obligations under the Agreement by Force Majeure, i.e. any unforeseeable, exceptional situation or event which is beyond the reasonable control of a Party. Each Party will notify KI of any Force Majeure without undue delay.

6 IMPLEMENTATION

6.1 Each Party shall designate a responsible principal investigator (PI) who shall be responsible for all activities undertaken by the respective Party pursuant to this Agreement and shall supervise and lead the work as well coordinate the specific activities agreed upon. The PI shall serve as the primary contact for each Party. PIs at the time of signature of this Agreement are:

- Martin Gerdin Wärnberg at KI
- Vivekanand Jha at TGI

The Parties may invite Karla Hemming of the University of Birmingham to the meetings when considered relevant.

6.2 The Parties shall have regular contact to discuss the progress of the Project. The Project Leader shall convene ordinary follow-up meetings at least once a year and extraordinary meetings at any time upon written request by another Party.

The Project Leader shall be the intermediary between the Parties and the Funding Entities and shall perform all tasks assigned to it as described in this Agreement. In particular, the Project Leader shall be responsible for:

(a) monitoring compliance by the Parties with their obligations in accordance with the Research Grant;
(b) monitoring scientific implementation of the Project in accordance with the Project Plan;
(c) transmitting documents and information connected with the Project;
(d) administering the financial contribution of the Funding Entities and fulfilling the financial tasks described in Article 7.3; and
(e) preparing and submitting scientific and financial reports in accordance with the Funding Entities' instructions.

6.3 The Project Leader shall not be entitled to act or to make legally binding declarations on behalf of TGI, unless explicitly stated otherwise in the Research Grant or this Agreement.

7 FINANCIAL PROVISIONS

7.1 General Principles

7.1.1 Distribution of the Financial Contribution

7.1.1.1 TGI shall be funded only for its activities/tasks carried out in accordance with the Project Plan during the period specified in the Research Grant, (hereinafter referred to as "Grant Period"), in compliance with the Project Plan and in accordance with the General Terms and Conditions of the Research Grant as included in Schedule 2 of this Agreement up to the maximum amount specified in Schedule 3.

7.1.1.2 Payments shall be made in accordance with the payment plan specified in Schedule 4. KI assumes no obligation to provide funds in excess of the maximum total amount indicated

in Schedule 3. Any increase in the authorized total must be mutually agreed upon in writing by the Parties. Any significant changes concerning the agreed budget are subject to approval by KI following an amendment as agreed in Section 10.4.

7.1.1.3 The Research Grant shall be used in the manner specified in the Project Plan. Any significant changes concerning the Research Grant's use are subject to approval by the Funding Entities following a review.

7.1.1.4 TGI shall notify KI if a grant is offered or received from another funding body for the same or similar research during the Project. This notification must specifically indicate the extent to which another funding body could influence the implementation, analysis, interpretation and reporting of the Results.

7.1.2 Record Keeping

In accordance with its own usual accounting and management principles and practices, each Party shall be solely responsible for justifying its costs with respect to the Project towards the Funding Entities.

The Parties agree to collaborate and enable the audit of financial records and accounts associated with the Project by an auditor or equivalent appointed by the Funding Entities.

7.1.3 Financial Consequences for premature termination of the Project

In the event of premature termination of the Project, for which both parties shall provide 90 days written notice to the other party, each party shall refund the payments received under the Research Grant as required by the Funding Entities, after adjusting for all actual costs until the termination date.

7.2 Payments

7.2.1 Payments shall be made in SEK according to the payment plan in Schedule 4. The Project Leader shall incur no liability to TGI in the event that, for any reason not attributable the Project Leader's fault, any payment to KI, which would otherwise have been payable shall be withheld, delayed or adjusted by the Funding Entities. KI's sole financial obligation under this Agreement shall be to forward the payments allocated to TGI under the budget in Schedule 3.

7.2.2 Grant Payment requests (hereinafter called Invoices for convenience) shall be submitted to KI and will be payable within 30 days of receipt. The invoices shall contain a specification of the activities to be carried out and a specification of the costs to be covered. KI will not accept invoices relating to activities not described or specified in the invoice.

TGI shall submit invoices according to the payment schedule as mentioned in Schedule 4. TGI shall upon request be able to show documentation in support of a certain invoice phase having been attained. Such documentation shall include necessary receipts and documentation concerning the costs. Invoicing charges are not acceptable.

The invoices shall include a clear reference to this Agreement including its contract nr and clearly state the period for which payment is made, information about whether partial or full payment.

Invoices shall be sent as a PDF-file (one file per invoice) to the following e-mail address: KI-fakturor@ki.se.

7.2.4 The Project Leader is entitled to withhold any payments due to a Party in breach of its obligations under this Agreement or when this is agreed with the Funding Entities. The Project Leader is entitled to recover any payments already paid to a defaulting Party.

7.3 Reporting

TGI shall collaborate with KI to enable the timely submission of any scientific and financial reports concerning the Project which may be requested by the Funding Entities and shall provide any necessary information in conjunction with the following up and evaluation of the research, either during or after termination of the Project.

The Parties shall also collaborate in order for KI to submit a final financial statement report every year, no later than one months after the Grant Period has expired.

In particular, each Party shall provide the Project Leader with all the information and documentation which needs to be included in the final financial report not later than one month after the Grant Period has expired or not later than one month after the date of premature termination of the Project.

TGI shall collaborate to enable the audit by KI of and financial records, accounts and documentation regarding the conduct of the Project and fulfilment of obligations by TGI.

8 RESULTS

8.1 Background

Background is, and shall remain, the property of the contributing Party, and may, during the term of the Agreement and without compensation, be used solely for the purpose of performing the Project. Other than expressly stated herein, this Agreement does not constitute any grant, option or license under the Background held by either Party.

8.2 Ownership of Results

Results are owned by the Party and/or by the researcher of the Party (if applicable) that generate them pursuant to each Party's national laws and policies on intellectual property. Title to any Results owned by KI which consist of intellectual property rights shall vest in the KI researchers where applicable in accordance with the Swedish professor's privilege.

Where Results are jointly generated by more than one Party and/or their researcher(s), such Results will be jointly owned in proportion to their intellectual contribution. In case of joint ownership each of the joint owners shall be entitled to use their jointly owned Results for non-commercial research activities on a royalty-free basis, and without requiring the prior consent of the other joint owner(s).

8.3 Access Rights

8.3.1 Parties are committed to public benefit and shall make Data and Results widely and freely available to maximise the benefits arising from research for non-commercial research, education and training purposes. The Parties commit to making the Data available in open access databases, such as Zenodo and GitHub, in accordance with open data rules and the FAIR (Findable, Accessible, Interoperable, and Reusable) principles. Parties shall be allowed to use Data and Results for the purpose of performing the Project.

8.3.2 Access Rights to Results and Background if Needed for Exploitation of a Party's own Results shall be granted on Fair and Reasonable conditions.

8.3.3 For the avoidance of doubt any grant of Access Rights not covered by the Research Grant or this Agreement shall be at the absolute discretion of the owning Party and subject to such terms and conditions as may be agreed between the owning and receiving Parties. The Research Grant funds are provided under this Agreement to carry out the Project and do not include financial consideration for any Access Rights.

8.4 Publications

8.4.1 Publication of own Results

8.4.1.1 The Parties agree that Results will be published in scientific journals with international scope in collaboration with University of Birmingham. The Parties shall not enter into agreements with any commercial actor or other stakeholder that could limit publication of the Results of research conducted with funding from the Swedish Research Council.

8.4.1.2 The Parties agree that the Results from the Project hereunder will be jointly published, in consistency with academic standards and with due consideration to the protection of intellectual property rights and applicable guidelines. The first publication will be prepared after Data analysis is available. TGI shall ensure that no publications by any individual Principal Investigator at Study Sites will be made, unless approved in advance by the Parties. The Parties agree to abide by the policies of journals in which publications will appear as to such matters as the public release or availability of data relating to the publication.

8.4.1.3 Authorship on publications will be based on academic standards and custom.
In accordance with normal academic practice, all investigators and contributors to a publication will be acknowledged, always in compliance with recognized standards concerning publication and authorship, including the most recent "Recommendations for the Conduct, Reporting, Editing and Publications of Scholarly Work in Medical Journals" developed by the International Committee of Medical Journal Editors (ICMJE). For clarity, researchers from the University of Birmingham will be included in the publications based on their contributions.

8.4.1.4 The Parties agree that research findings from the Project shall be made openly accessible (open access) within six (6) months of publications.

8.4.2 Dissemination of another Party's unpublished Results or Background

A Party shall not include in any dissemination activity another Party's Results or Background without obtaining the owning Party's prior written approval, unless they are already published.

8.4.3 Cooperation obligation

The Parties undertake to cooperate to allow the timely submission, examination, publication and defence of any dissertation or thesis for a degree which includes their Results or Background subject to the confidentiality and publication provisions agreed in this Agreement.

8.4.4 Use of names, logos or trademarks

Nothing in this Agreement shall be construed as conferring rights to use in advertising, publicity or otherwise the name of the Parties or any of their logos or trademarks without their prior written approval.

Publications and dissemination of the Project's Results shall include acknowledgement to the Swedish Research Council and the Laerdal Foundation as further specified in the Research Grant as included in Schedule 2 of this Agreement.

9 NON-DISCLOSURE OF INFORMATION

9.1 All information in whatever form or mode of communication, which is disclosed by a Party (the "Disclosing Party") to any other Party (the "Recipient") in connection with the Project during its implementation and which has been explicitly marked as "confidential" at the time of disclosure, or when disclosed orally has been identified as confidential at the time of disclosure and has been confirmed and designated in writing within 15 calendar days from oral disclosure at the latest as confidential information by the Disclosing Party, is "Confidential Information".

9.2 The Recipients hereby undertake in addition and without prejudice to any commitment of non-

disclosure under the Research Grant, for a period of 4 years after the end of the Project:

(a) to ensure that internal distribution of Confidential Information by a Recipient shall take place on a strict need-to-know basis; and
(b) not to use Confidential Information otherwise than for the purpose for which it was disclosed
(c) not to disclose Confidential Information to any third party without the prior written consent by the Disclosing Party; and
(d) to return to the Disclosing Party on demand all Confidential Information which has been supplied to or acquired by the Recipients including all copies thereof and to delete all information stored in a machine readable form. The Recipients may keep a copy to the extent it is required to keep, archive or store such Confidential Information because of compliance with applicable laws and regulations or for the proof of on-going obligations.

9.3 The Recipients shall be responsible for the fulfilment of the above obligations on the part of their employees or third parties involved in the Project (including the University of Birmingham) and shall ensure that they remain so obliged, as far as legally possible, during and after the end of the Project and/or after the termination of the contractual relationship with the employee or third party.

9.4 The above shall not apply for disclosure or use of Confidential Information, if and in so far as the Recipient can show that:

a) the Confidential Information becomes publicly available by means other than a breach of the Recipient's confidentiality obligations;
b) the Disclosing Party subsequently informs the Recipient that the Confidential Information is no longer confidential;
c) the Confidential Information is communicated to the Recipient without any obligation of confidence by a third party who is to the best knowledge of the Recipient in lawful possession thereof and under no obligation of confidence to the Disclosing Party;
d) the disclosure or communication of the Confidential Information is foreseen by provisions of the Research Grant;
e) the Confidential Information, at any time, was developed by the Recipient completely independently of any such disclosure by the Disclosing Party; or
f) the Confidential Information was already known to the Recipient prior to disclosure or
g) the Recipient is required to disclose the Confidential Information in order to comply with applicable laws or regulations or with a court or administrative order.

9.5 The Recipient shall apply the same degree of care with regard to the Confidential Information disclosed within the scope of the Project as with its own confidential and/or proprietary information, but in no case less than reasonable care.

9.6 Each Party shall promptly advise the other Party in writing of any unauthorised disclosure, misappropriation or misuse of Confidential Information after it becomes aware of such unauthorised disclosure, misappropriation or misuse.

9.7 For the avoidance of doubt, Personal Data shall always be treated as confidential and shall be protected with an adequate level of safety and confidentiality, subject to any applicable legal, regulatory or contractual requirements.

10 MISCELLANEOUS

10.1 Attachments, inconsistencies and severability

10.1.1 This Agreement consists of this core text and
Schedule 1 (Project Plan, Financial Plan and Payment Plan)

Schedule 2 (General Terms and Conditions for Research Grants)
Schedule 3 (Financial plan)
Schedule 4 (Payment plan)

10.1.2 In case the terms of this Agreement are in conflict with the terms of the Research Grant as included in Schedule 2, the terms of the latter shall prevail.

10.1.3 Should any provision of this Agreement become invalid, illegal or unenforceable, it shall not affect the validity of the remaining provisions of this Agreement. In such a case, the Parties concerned shall be entitled to request that a valid and practicable provision be negotiated which fulfils the purpose of the original provision.

10.2 No representation, partnership or agency

No Party shall be entitled to act or to make legally binding declarations on behalf of any other Party. Nothing in this Agreement shall be deemed to constitute a joint venture, agency, partnership, interest grouping or any other kind of formal business grouping or entity between the Parties.

10.3 Notices and other communication

11.3.1 Formal notices to be given under this Agreement shall be in writing and be delivered to the person stated below, unless the receiving Party has specifically notified the sending Party of another address for this purpose. The notice may either be served personally or sent by mail with recorded delivery or telefax with receipt acknowledgement.

To KI: Therese Lind (therese.lind@ki.se)

To TGI: Vivekanand Jha (vjha@georgeinstitute.org.in) with cc to Amit Khanna (akhanna@georgeinstitute.org.in)

11.3.2 Other communication between the Parties may also be effected by other means such as e-mail with acknowledgement of receipt, which fulfils the conditions of written form.

10.4 Assignment and amendments

11.4.1 No rights or obligations of the Parties arising from this Agreement may be assigned or transferred, in whole or in part, to any third party without the other Party' prior formal approval.

11.4.2 Amendments and modifications to the text of this Agreement require a separate written agreement to be signed between all Parties.

10.5 Mandatory statutory law

Nothing in this Agreement shall be deemed to require a Party to breach any mandatory statutory law under which the Party is operating.

10.6 Language

This Agreement is drawn up in English, which language shall govern all documents, notices, meetings, arbitral proceedings and processes relative thereto.

10.7 Applicable law and Settlement of Disputes

10.7.1 This Agreement shall be construed in accordance with and governed by the laws of Sweden excluding its conflict of law provisions.

10.7.2 The parties shall endeavour to settle their disputes amicably. However, where a conflict cannot be resolved within ten working days by persons at an operative level, a Party may request that negotiations be initiated between persons on executive management level.

11 SIGNATURES

AS WITNESS:
The Parties have caused this Agreement to be duly signed, using electronic signatures or otherwise, by the undersigned authorised representatives in separate signature pages the day and year first above written.

KAROLINSKA INSTITUTET

Date:

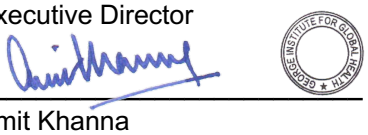
Signature _____
Name Marie Hasselberg
Title Head of Department
Department of Global Public Health

I acknowledge that I have read and agree to be bound by the above terms and conditions and I undertake to ensure that all personnel working in the Project will be aware of and accept all terms and conditions of this agreement.

Signature _____
Name Martin Gerdin Wärnberg
Title Principal Investigator
Department of Global Public Health

GEORGE INSTITUTE FOR GLOBAL HEALTH (TGI)
Date:

Signature _____
Name Vivekanand Jha
Title Executive Director



Signature _____
Name Amit Khanna
Title Director - Finance & Operations

SCHEDULE 1: PROJECT PLAN

CLINICAL TRIAL PROTOCOL

ADVANCE TRAUMA

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

Version 1.3.0, 2024-11-15

Table of contents

1 Administrative information

1.1 Changelog

Version	Date	Details
1.3.0	2024-11-15	• Updated names of events in the table of procedures • Added new references • Added nested staircase design for measuring adherence, quality of life, disability and return to work • Updated small sample correction to be based on best available evidence closer to the time of analysis • Added contributors • Removed reassessment of the sample size calculation from the interim analysis • Revised details on measuring ATLS adherence
1.2.0	2024-08-26	• Added details on measuring ATLS adherence • Clarified the section describing the consent process • Fixed minor issues with how the variables were listed • Indicated non-routinely recorded data in the list of variables • Added Administrative information section with contributors • Added CTRI registration number
1.1.0	2024-05-09	Updated the primary outcome to in-hospital mortality and spelling corrections. The primary outcome was updated following a voting procedure in the Trial Management Group.

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:

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

2 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 November 2024, to October 2029

3 Background and rationale

Each year, 4.3 million people die from trauma[1]. Among people aged 10-24 and 25-49 years trauma is the largest cause of disability adjusted life years[2]. Most deaths from trauma occur within the first 24-48 hours[3]. Traumatic brain injury and exsanguination are the most common causes of trauma deaths[4,5]. Most preventable trauma deaths are caused by clinical judgement errors during initial resuscitation or early care including airway management and haemorrhage control, even though the deaths occur later during the hospital stay[4,6].

Several trauma life support training programmes have been developed to improve the early management of patients in the hospital by providing a structured framework for assessment and treatment[7–11]. The proprietary Advanced Trauma Life Support® (ATLS®) is the most established trauma life support training programme and more than one million physicians in over 80 countries have been trained in the programme since the first course in 1978[12]. In the US and many other countries training in ATLS® is virtually mandatory for trauma care physicians[13]. Uptake in low- and middle income countries (LMIC) has been slow, potentially due to high costs[9].

There are three randomised studies showing that ATLS® improves knowledge and clinical skills[14–16], but there are no randomised controlled trials or high-quality quasi-experimental trials indicating that ATLS® improves patient outcomes[7,8,10,11,17]. We conducted an updated systematic review (unpublished), and estimated a pooled risk ratio of 0.82 (95% CI 0.60; 1.11) from ten heterogeneous (I^2 0.91) observational studies on the effect of ATLS on mortality (see Figure 1)[18–27].

We conducted a pilot cluster randomised controlled trial (ClinicalTrials.gov NCT05417243) between April 2022 and February 2023 as part of our network grant to assess the feasibility of a full scale trial. We published the protocol for this pilot study[28]. Our pilot study enrolled 376 patients from seven hospitals across India (unpublished data) and shows that it is feasible to conduct the proposed trial with a high percentage of patients consenting to out of hospital follow up (78%), low loss to follow-up rate (1%), and low missingness in key variables (mean 0.8%).

To involve patients and the public in the planning of this trial we conducted 19 semi-structured interviews with trauma patients, caregivers, and community representatives (unpublished data). The aim of these interviews was to understand their views on the trial and important outcomes and the interviews showed high acceptability of our research and emphasised the importance of better recovery before discharge and functional outcomes at and after discharge, including pain, mobility and self-care activities. The interviews also highlighted return to work as an important outcome.

3.1 Updated systematic review

We performed a systematic literature search in the Medline, Embase, Cochrane, Web of Science, CINAHL and Google Scholar databases (PROSPERO ID CRD42022373977). The last search was conducted on November 11, 2022. We developed the search strategy in Medline (Ovid) in collaboration with librarians at the Karolinska Institutet University Library. We limited the search to English language articles, searched all databases from inception, and screened a total of 7896 records. We used a random effects model to pool estimates across studies.

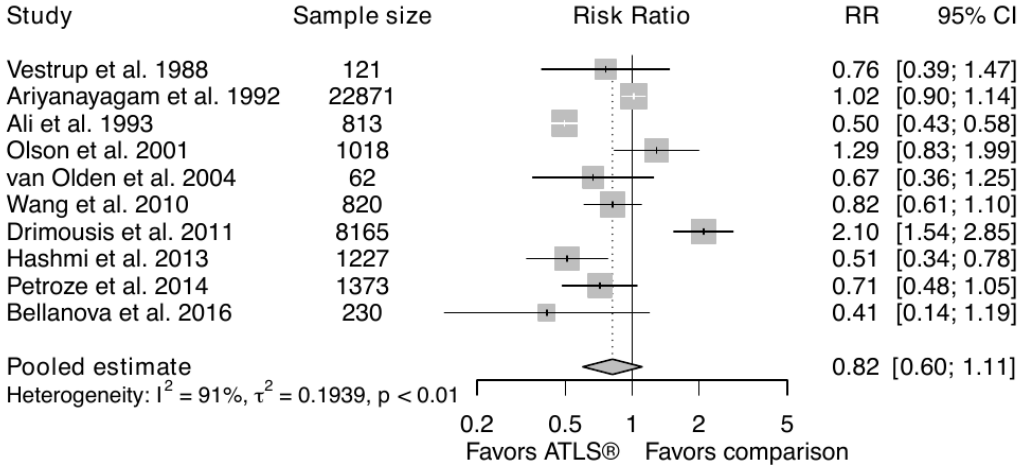

Figure 1: Summary of the updated system review. The forest plot shows the effect of ATLS on mortality. Abbreviations: RR, risk ratio; CI, confidence interval; ATLS, Advanced Trauma Life Support; I^2, heterogeneity.

4 Benefit-risk evaluation

The direct risks includes integrity violations and data leakage. We will mitigate these risks by employing rigorous data collection and storage mechanisms. The procedures that we will use to collect data will be direct observation of care, routine physical examinations, questionnaires, and extraction of already collected data from patient records, which are often seen as involving only minimal risk.

The long-term risks of the research and the risk that the research will be used in detrimental ways are minimal. Our trial will assess the effect of Advanced Trauma Life Support® (ATLS®) on patient outcomes. Training in ATLS® is standard in many health

care systems and it is unlikely that training physicians in this programme induces any harm to participants.

We consider these risks weighed up by the potential direct benefit for the participants in the intervention phase, if ATLS® is found to improve patient outcomes, and by the potential for improved care for the trauma patient population.

5 Trial aim

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

6 Regulatory approvals and trial registration

We will submit this trial to the Health Ministry Screening Committee at the Indian Council for Medical Research for their approval. We will apply for ethical approvals from each participating hospital, The George Institute for Global Health in India and the Swedish Ethical Review Authority. We will register this trial with Clinical Trials Registry-India and ClinicalTrials.gov.

7 Trial design and procedures

7.1 Overall trial design

We will conduct a batched stepped-wedge cluster randomised controlled trial (see Figure 2). The stepped-wedge trial is a uni-directional cross-over trial but the time point when clusters cross-over from standard care to the intervention is randomised[29]. Each cluster will be at least one unit of physicians performing initial resuscitation of trauma patients in the emergency department of tertiary hospitals in India. The number of units that we will train in each hospital will depend on the sizes of these units and the volumes of patients that they see. If more than one unit is trained in the same hospital these units will be considered one unit for the purpose of randomisation. We choose this approach for two reasons: 1) it will not be logistically or financially feasible to train all physician in a given hospital; and 2) we need to balance cluster size with the number of clusters. We will conduct this trial in India because physicians providing initial trauma care in India are so far not routinely trained in ATLS® or similar programmes.

We will roll out the interventions to 30 clusters over six batches, so there will be five clusters in each batch. The clusters in each batch will be randomised to one of five implementation sequences, with one hospital randomised to each implementation sequence.

All clusters will transition through three phases, first a standard care phase, then a one month transition phase during which the training is delivered, and finally an intervention phase, for a total of 13 months. The implementation sequence determines how long the phases of standard care and intervention are. Patient participants will be followed up for a total of three months.

7.2 Design justification

We use the cluster randomised design because the intervention cannot be randomised at the individual patient level. We use the stepped-wedge design for two reasons. First, this design is statistically more efficient than the parallel cluster design when the number of clusters is limited[30]. In this trial, the number of clusters is limited because of the costs associated with ATLS® training and the available slots for ATLS® training in India. Second, the stepped-wedge design is likely to enhance participation and engagement because all clusters receive the intervention. The batched stepped-wedge design further improves feasibility as it does not require all clusters to start at the same time, and it is robust to potential delays in cluster recruitment[31].

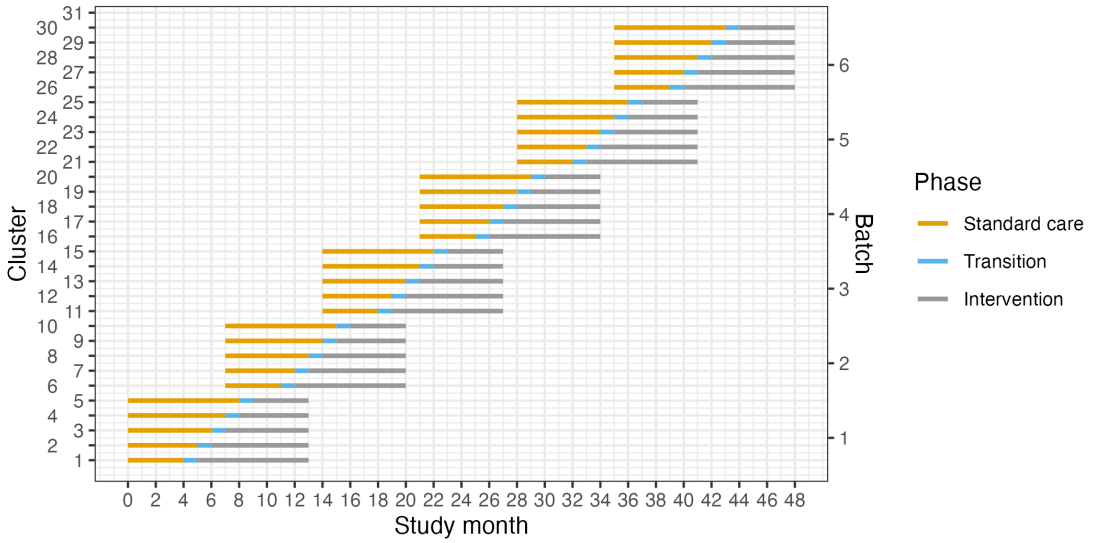

Figure 2: Trial design. Lines represent the duration of patient enrolment across clusters and phases. Clusters will be sequentially allocated to a batch based on when they enter the study. Within each batch clusters will then be randomised to an intervention implementation sequence.

7.3 Eligibility criteria

Our trial include eligibility criteria on three levels: hospitals, clusters and patient participants. We include eligibility on both the hospital and cluster level to facilitate the screening process.

7.4 Hospital selection

Hospitals will be secondary or tertiary hospitals providing trauma care in India. Hospital will be the unit of randomisation.

7.4.1 Inclusions criteria

Hospitals must meet the following criteria:

- admit or refer/transfer for admission at least 400 patients with trauma per year or 35 patients with trauma per month for at least the last six months;
- provide surgical and orthopaedic emergency services around the clock; and
- have at most 25% of physicians providing initial trauma care trained in a formalised trauma life support training programme, like ATLS® or Primary Trauma Care (PTC).

7.4.2 Exclusion criteria

Hospitals are excluded if they meet any of the following criteria:

- the hospital of the cluster implements a formalised trauma life support training programme [1] during the trial period; or
- the hospital of the cluster plan to implement or implements other major interventions[2] that affects trauma care during the trial period.

[1] These include but are not limited to the National Emergency Life Support (NELS) programme, the Basic Trauma Life Support (BTLS) programme, the Pre-Hospital Trauma Life Support (PHTLS) programme, the Trauma Nursing Core Course (TNCC) and the Advanced Trauma Care for Nurses (ATCN) programme.

[2] These include but are not limited to implementing of a trauma team approach, opening a trauma centre and implementing a trauma quality improvement programme.

7.4.3 Screening

The trial management group will compile a list of hospitals with potentially eligible clusters and reach out to them to assess their interest in participating in the trial. We will then screen hospitals for eligibility based on the criteria above, using a two-step procedure. First, we will approach hospitals to complete an initial hospital screening instrument (see Appendix Section 19.1). We will then discuss each eligible hospital individually in the Trial Management Group before deciding whether to include it in the trial. We have this discussion because we strive to include hospitals that to a large extent conducts primary resuscitation of trauma patients, rather than hospitals that primarily receives transferred patients from other hospitals, but this is difficult to formalise in the eligibility criteria. We will then perform a more in-depth interview with selected hospitals (See Appendix Section 19.2). To avoid excluding centres we will also discuss plans to implement other potentially competing interventions during the trial period, and take these plans into account when assigning clusters to batches. For example, we are aware of the ongoing implementation of the National Emergency Life Support (NELS) programme in India, and will therefore not include hospitals that plan to implement this programme during the trial period. All screening steps and decisions will be logged using REDCap[32,33].

7.5 Cluster selection

Clusters are one or more units of physicians providing initial trauma care in the emergency department of secondary or tertiary hospitals in India. These units already exist in the hospitals and rotate through the emergency department on specific days of the week.

7.5.1 Inclusion criteria

Clusters must meet the following criteria:

- admits or refers/transfers for admission at least 12 patients with trauma per month for at least the last six months; and
- no more than 25% of physicians providing initial trauma care trained in a formalised trauma life support training programme.

7.5.2 Screening

The screening of clusters is part of the hospital screening process.

7.6 Patient participants selection

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

7.6.1 Inclusion criteria

Patients participants must meet the following criteria:

- age of at least 15 years;
- trauma occurred less than 48 hours before arrival at the hospital;
- present to the emergency department of participating hospitals, with a history of trauma defined as having any of the reasons listed in the International Classification of Diseases chapter XX as the reason for presenting;
- admitted, or died between arrival at the hospital and admission, or referred/transferred from the emergency department of a participating hospital to another hospital for admission; and
- managed by a participating cluster in the emergency department.

7.6.2 Exclusion criteria

Patients participants are excluded if they meet the following criteria:

- present with isolated limb injuries; or
- are directly admitted to a ward without being seen by a physician in the emergency department.

7.6.3 Screening

Clinical research coordinators will screen patient participants either as they arrive to the emergency department or using emergency department registers. The patients or their representatives will receive written information about the study before they are discharged, including about their right to opt out at any time before final analysis. Phone numbers for out of hospital follow up will be extracted from the emergency department registers, and will be securely held only by the clinical research coordinators at each sites.

7.6.4 Withdrawal criteria

Patient participants can choose to withdraw their consent for collection of non-routinely recorded data at any time before the final analysis. If they withdraw their consent for this data collection the clinical research coordinator will not collect any more of this data, which also means that no further follow-ups will be conducted. They can also choose to have the data already collected about them removed from the trial at any time before final analysis of the data. Withdrawal of consent or removal of data from the trial will not affect their care in any way. If the patient participant withdraws consent, follow-up of this participant will be performed according to the participating hospitals routine.

7.7 Procedures

Table 3 shows an overview of trial procedures before and during patient admission, and Table 4 shows an overview of trial follow-up procedures. Clinical research coordinators will follow up patients daily until discharge to capture injury information. They will also follow up patients at 24 hours, 30 days and 90 days after arrival to the emergency department to capture mortality outcomes, and at 30 days and 90 days after arrival to the emergency department to capture functional outcomes and return to work. If patient participants are discharged before any of these follow-up time points, clinical research coordinators will follow up patients by phone.

Table 3: Overview of trial procedures before and during patient admission

Procedure	Screening	Consenting	Initial assessment	In-hospital care
Eligibility criteria	√			
Study information[1]		√		
Informed consent[1]		√		
Baseline data collection			√	
Prehospital data collection			√	
ATLS adherence[2]			√	
ED data collection[3]			√	
Hospital data collection				√
Surgery data collection				√
Imaging data collection				√
Transfusion data collection				√
Injury data collection				√
Mortality data collection				√
Assessment of safety events				√

[1]Clinical research coordinators will inform patient participants about the study, including that they are free to withdraw their data from the study at any time, and approach them for informed consent for collection of non-routinely recorded data in person or telephonically.
[2]ATLS adherence will be assessed by observing the care provided to a random sample of patient participants.
[3]Emergency Department

Table 4: Overview of trial follow-up procedures

Procedure	Within 7 days of discharge	30 days	90 days
Mortality data collection[1]	√	√	√
EQ-5D/WHODAS	√	√	√
Return to work		√	√
End of study			√

[1]Will be ascertained daily from when the patient participant arrive to hospital until they leave the hospital, are discharged or die.

7.8 Biological sampling procedures

This trial does not include biological sampling.

7.9 End of trial

The trial ends when the last patient participant has completed the last follow-up. The trial may be prematurely terminated if it this is necessary for safety reasons affecting the risk-benefit balance or if the recruitment of subjects cannot be met within reasonable time limits. If the trial is prematurely terminated or suspended, the investigator should immediately inform the subjects about this and ensure appropriate treatment and follow-up. Decisions on premature termination are taken by the joint Trial Steering and Data Monitoring Committee and Trial Management Group.

7.10 Intervention and control treatment

The intervention will be ATLS® training. The control will be standard care, meaning no formal trauma life support training. We will train the physicians that initially resuscitate and provide trauma care during the first hour after patient arrival at the emergency department. These physicians can be casualty medical officers, surgical residents, or emergency medicine residents, depending on the setup at each participating centre. The training will occur during the transition phase in each cluster. Our experience from our pilot study is that study sites adhere to the training slot alloted to them through the trial, so we judge the risk of clusters implementing ATLS® before their randomised implementation sequence as very low.

We will train the number units of physicians needed to reach the required patient sample size, but estimate that this will require training an average of ten physicians per hospital, which on average should be mean that we can train one to two units per hospital. This is possible because many hospitals in India organise physicians staffing their emergency departments in units, and the physicians in the same unit work together in the emergency

department on the same days of the week. We will therefore collect data only on the days when these units work. The units selected to constitute a cluster from each hospital will be a convenience sample out of all eligible units in those hospitals.

Advanced Trauma Life Support® (ATLS®)[12] is a proprietary 2.5 day course teaching a standardised approach to trauma patient care using the concepts of a primary and secondary survey. The programme was developed by the Committee of Trauma of the American College of Surgeons. The course includes intial treatment and resuscitation, triage and interfacility transfers. Leaning is based on practical scenario-driven skill stations, lectures and includes a final performance proficiency evaluation. Physicians will be trained in an accredited ATLS® training facility in India. We will assess adherence to ATLS principles before and after implementing ATLS training.

Standard care varies across hospitals in India, but trauma patients are initially managed by casualty medical officers, surgical residents, or emergency medicine residents. They are mainly first- or second-year residents who resuscitate patients, perform interventions and refer patients for imaging or other investigations. Compared with other settings where a trauma team approach is adopted, nurses and other healthcare professionals are only involved to a limited extent during the initial management.

7.10.1 Description of investigational medicinal products

This trial does not include any investigational medicinal products.

7.10.2 Auxiliary medicinal products

This trial does not include any auxiliary medicinal products.

7.10.3 Concomitant use of other medications or treatments

Other than implementing another formalised trauma life support training programme or other major interventions to change the care of trauma patients as specified in the exclusion criteria, concomitant use of other medications and treatments may be provided at the discretion of the investigators and will not be considered an exclusion criterion.

7.11 Randomisation

We will assign clusters to batches as they are found to be eligible and receive ethical approval. Batches will include clusters from hospitals in different regions to optimize trial

logistics. We will randomise the clusters alloted to each batch to the different intervention implementation sequences within that batch[3]. We will balance the randomisation within each batch on cluster size, defined as monthly volume of eligible patient participants, using covariate constrained randomisation. The cluster sizes are expected to vary between 12 and 20 patients per month, based on our previous experiences. We will conceal the randomisation order for as long as it is logistically possible, considering that arrangements for sending physicians to ATLS® training need to be made in advance.

7.12 Blinding

It is not possible to blind a stepped-wedge trial, because all clusters receive the intervention.

7.13 Treatment after trial end

When the trial ends, the intervention will have been implemented in all clusters.

7.14 Outcomes

7.14.1 Primary outcome

The primary outcome will be in-hospital mortality within 30 days of arrival at the emergency department. Clinical research coordinators will extract information on death from patient hospital records. If the patient has been transferred to another hospital, the clinical research coordinators will collect data on this outcome by calling the patient or a patient representative, or by contacting the hospital to which the patient was transferred. Data on this outcome will be collected continuously during the trial.

7.14.2 Secondary outcomes

- All cause mortality within 24 hours, 30 days and three months of arrival at the emergency department. Data on this outcome will be collected in the same way as for the primary outcome.
- Length of emergency department stay. Data on this outcome will be collected from patient hospital records.
- Length of hospital stay. Data on this outcome will be collected from patient hospital records.
- Intensive care unit admission. Data on this outcome will be collected from patient hospital records.

[3]Randomisation will be done using bespoke code from previous trials.

- Length of intensive care unit stay. Data on this outcome will be collected from patient hospital records.
- Adherence to ATLS® principles during initial patient resuscitation, up to one hour after the physician has first seen the patient. This assessment will be done using a 14 item checklist covering the key steps of the ATLS® primary survey, which was modelled based on previous work on ATLS® adherence[34]. We will consider completion of all 14 steps as 100% adherence. The clinical research coordinators collecting the data will be trained by the trial team to do this, prior to the start of the trial. We will collect this data by observing the care of a random sample of patients. The sampling will be designed as a nested staircase design.
- Quality of life within seven days of discharge, and at 30 days and three months of arrival at the emergency department, measured by the official and validated translations of the EQ5D3L. Data on this outcome will be collected in person if the patient is still in hospital, or by phone if the patient has been discharged. We will collect this data using a nested staircase design.
- Disability within seven days of discharge, and at 30 days and three months of arrival at the emergency department, assessed using the WHO Disability Assessment Schedule 2.0 (WHODAS 2.0). Data on this outcome will be collected in person if the patient is still in hospital, or by phone if the patient has been discharged. This data will also be collected using a nested staircase design.
- Return to work at 30 days and three months after arrival at the emergency department. Data on this outcome will be collected in person if the patient is still in hospital, or by phone if the patient has been discharged. This data will also be collected using a nested staircase design.

7.15 Handling of adverse and safety events

7.15.1 Definitions

7.15.1.1 Adverse event

Any untoward medical occurrence in a clinical trial subject and, which does not necessarily have a causal relationship with the treatment, can be an unfavorable and unintended sign (including an abnormal laboratory discovery), symptom or disease temporally associated with the inclusion in the trial, whether or not related to the trial.

7.15.1.2 Serious adverse event

Any untoward medical occurrence in a trial participant that:

- leads to death
- is life-threatening
- requires inpatient hospitalization or prolongation of existing hospitalization

- results in persistent or significant disability or incapacity
- results in a congenital anomaly/malformation

7.15.1.3 Safety event

Any unexpected serious complication that might occur as a consequence of the trial and that are not part of the natural history of trauma.

7.15.2 Reporting and assessment of adverse and safety events

In alignment with other current trials including critically ill patients[35], we will not collect adverse events or serious adverse events, because many of these events are expected in this patient population and we already collect many of these events, for example mortality, as part of our outcomes.

We will only report safety events, if they are life-threatening, prolong hospitalisation or result in meaningful harm to the participant. We cannot pre-define a comprehensive list of events that can be considered safety events, but will actively assess the presence of the following safety events:

- 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.

We will also report any other safety events that we identify during the trial, and the reporting of such will have to be based on the intuition of the clinical research coordinators and local investigators. Examples of such safety events could include missed injuries or missed investigations, which could be suspected if certain injuries or investigations were identified or conducted more often during the standard care phase than during the intervention phase.

All safety events will be recorded in the Case Record Form (CRF) and reported to the trial management team within 24 hours of its occurrence. The trial management team 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 joint Trial Steering and Data Monitoring Committee.

7.15.3 Follow up of safety events

All safety events should be followed up by the local investigator until they are fully evaluated.

7.16 Statistics

7.16.1 General principles

We will conduct all analysis by modified intention to treat. Clusters and observations within clusters will be considered exposed to the intervention after the date at which the cluster was scheduled to transition. All data will be included with the exception of the transition phases. We will not adjust for multiplicity of analyses because none of the secondary outcomes will be singularly more important. However, all secondary outcomes will be interpreted with due consideration for how all are affected by the intervention without putting any undue emphasis on a single outcome that might be statistically significant but where all others appear to have remained unchanged.

We will use a two-sided significance level of 5% and estimate 95% confidence intervals. The primary subgroup analyses will be based on geographical region because demonstrating the consistency of any effect across multiple regions will enhance the generalisibility of the results[4]. Additional subgroup analyses will include age across the groups older adolescents (15-19 years), young adults (20-24 years), adults (25-59 years), and older adults (60 years and older)[36]; sex; and the clinical cohorts blunt multisytem trauma, penetrating trauma, and severe isolated traumatic brain injury.

7.16.2 Analysis models

There are a number of requirements for the analysis model. Firstly, all analysis will consider the clustered nature of the design. Secondly, as the trial has only 30 clusters, it will be essential that the model allows for a correction due to the small number of clusters. Thirdly, as the design is a stepped-wedge study, we will adjust for temporal confounding using categorical effects for period of the study (month). Full details on how each of these will be undertaken, with justification is provided below[37].

For binary outcomes, a mixed effects binomial regression with a logit link will be used to estimate the odds ratio; and a binomial model with identity link used to estimate the risk difference. These models will be fitted using residual pseudo-likelihood estimation based on linearization with subject-specific expansion (RSPL). If the binomial model with the identity link does not converge then only a odds ratio will be reported.

[4]**Note:** Batches will not be based on regions because it will be logistically more feasible to include clusters from different regions in each batch.

We will include fixed effects for period and a fixed effect for intervention exposure. The primary analysis will allow for clustering by as a random cluster and random cluster by period effect. To correct the potential inflation of the type I error rate due to small number of clusters, a correction for a small number of clusters will be applied, but the correction that will be selected will be based on the best available evidence available closer to the time, and it may differ for the outcomes collected via the complete and incomplete designs. In a sensitivity analysis we will explore if models with more complicated correlation structures are a better fit to the data. These models are not being used as our primary analysis models as there is limited understanding as to when such models will converge and how to choose between the various different correlation structures which might be plausible.

To this end we will additionally fit generalised linear mixed models (with same link functions and fixed effects as described above) to include a discrete time decay correlation structure including a random cluster effect with auto-regressive structure (AR(1)). To allow for the randomisation by batches, a different secular trend will be included for each batch (interaction between batch and period). For continuous, count and prevalence outcomes similar model-based approaches will be used but with appropriate links and distribution functions, using transformations where appropriate.

7.16.3 Additional sensitivity analyses

To additionally explore if the fixed period effect is both parsimonious and adequate to represent the extent of any underlying secular trend, we will model the time effect using a spline function. Models will also be extended to include random cluster by intervention effects (with a non-zero covariance term) to examine if results are sensitive to the assumption of no intervention by cluster interaction. Models will also be extended to include an interaction between treatment and number of periods since first treated, to examine if there is any indication of a relationship between duration of exposure to the intervention and outcomes.

This will allow us to different lag effects (whereby it takes time for the intervention to become embedded within the culture before its impact can properly start to be realised); as well as weaning effects (whereby the effect of the intervention starts to decrease – or fade). This type of analysis attempts to disentangle how some clusters end up having a long exposure to the intervention and others have a much shorter exposure time. A fully adjusted covariate analysis will additionally adjust for a set of pre-specified individual-level covariates of known prognostic importance.

7.16.4 Estimation and reporting of within cluster correlations

We will report time adjusted within-cluster correlations for all outcomes with 95% confidence intervals. We will report correlations from the different assumed correlation

structures (so we will report intra-cluster correlations (ICC); within and between-period correlations; and within-period correlations and exponential decay). As well as reporting correlations we will additionally report all variance components. For all outcomes we will report correlations on the latent scale (i.e. proportions scale for binary outcomes) as is appropriate to inform future sample size calculations.

7.16.5 Sample size calculations

With 30 clusters across 6 batches and a total sample size of 4320 our study has ~90% power across different combinations of cluster autocorrelations (CAC) and intra-cluster correlations (ICC) to detect a reduction in the primary outcome of in-hospital mortality within 30 days from 20% under standard care to 15% after ATLS® training (see Figure 3). This effect is a conservative estimate and the reduction equals a risk ratio of 0.75, which would be clinically important while also being consistent with our pilot study and updated systematic review. We allowed for the clustered design and assumed an ICC of 0.02, but considered sensitivity across the range 0.01-0.05[38,39], and a CAC of 0.9 but considered sensitivity across the range 0.8-1.0, based on our pilot study and current guidance[40–42]. We included the CAC to allow for variation in clustering over time. We assume that each cluster will contribute approximately 12 observations per month to the analysis, based on our previous work.

7.16.6 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;
- compare characteristics across intervention conditions to monitor for differential recruitment/ascertainment between intervention and control.

7.17 Quality control and quality assurance

The George Institute for Global Health - India will ensure proper conduct of the trial through quality control measures including on-site training of personnel, standard operating procedures, ongoing quality metrics assessment, review of missing data and outliers, and round-the-clock availability of coordinating center personnel and Principal Investigators. The trial will strictly follow ICH GCP principles, Indian regulations, and George Institute procedures. The trial operations staff from the George Institute India will train local investigators, and trial site staff, before the trial, with continuous documentation

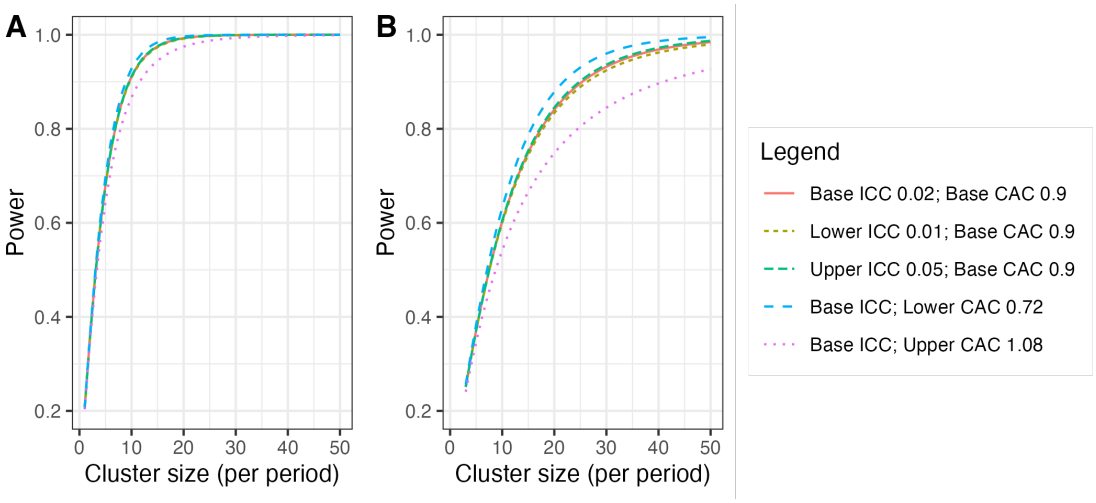

Figure 3: Power curves for different combinations of cluster autocorrelations (CAC) and intra-cluster correlations (ICC). **A)** Shows power curves assuming a reduction in the primary outcome of in-hospital mortality within 30 days from 20% under standard care to 15% after ATLS® training. **B)** Shows power curves assuming a reduction in the primary outcome from 10% under standard care to 7.5% after ATLS® training. Under this scenario, we would need to increase the sample size per month to around 30 observations to achieve 90% powere under most combinations of CAC and ICC.

in the site master file. All documentation will be stored securely and retained according to regulatory requirements.

7.18 Quality assurance and oversight

The Trial Management Group and Trial Team, comprising key project leaders and managers, will play a pivotal role in ensuring the highest standards of quality assurance and effective sponsor oversight throughout the trial. These groups will be responsible for facilitating consistent communication, maintaining fidelity in study implementation, and overseeing the quality of data collection.

To achieve these objectives, the groups will implement a comprehensive communication plan and provide extensive training to site personnel. The training will cover not only the study protocol but also practical aspects of various systems, supplemented by both written and electronic materials designed to educate study and clinical emergency staff.

The trial's quality assurance systems will be meticulously designed based on a thorough risk analysis. A key component of our quality assurance strategy will include the development and implementation of detailed operational manuals and regular meetings. These tools and interactions will ensure that all trial personnel will be used to uphold the trial's quality standards.

Central to our oversight approach will be a comprehensive monitoring and auditing plan. This plan will be tailored based on the identified risks associated with the trial. Through these comprehensive measures, the trial management group, in conjunction with the hospital staff, will ensure that the trial is conducted with the utmost rigor, adhering to the highest standards of quality assurance and effective sponsor oversight.

7.19 Monitoring

We will implement a multi-tiered monitoring strategy, including centralized data consistency checks, statistical monitoring, and selective on-site evaluations. Key integrity measures include source data verification, data entry validation, and regular audits. Any protocol deviations will be thoroughly documented, with serious breaches promptly addressed to ensure data integrity. Monitors from coordinating centres will assist investigators in maintaining high ethical, scientific, technical, and regulatory quality. Monitoring visits will review protocol adherence, participant recruitment, adverse event reporting, compliance with study procedures, and regulatory adherence. Regular remote monitoring of the web-based database will be conducted to ensure data integrity, using validation and consistency rules and regular data cleaning. The Trial Team and Trial Management Group will monitor baseline characteristics, opt-in consent rates and differential opt-in consent rates across trial arms, follow-up rates, CRF return and completeness rates, and safety data.

8 Deviations, serious breaches and other reporting obligations

The responsible investigator shall, without delay, report to the sponsor any serious breaches and deviations from the trial protocol, ICH-GCP and other regulations that significantly and directly affect, or with high likelihood could affect, the subjects' safety and integrity or the reliability and robustness of the data generated in the trial. The sponsor should assess the suspected serious breach and the consequences of deviations that have occurred. Minor deviations that do not affect subjects' integrity or safety, nor significantly affect the trial's scientific value, are documented in the trial documentation of the principal investigator and the sponsor and appropriate measures shall be taken. The deviations must be recorded in the clinical trial report.

9 Audits and inspections

Authorized representatives for the sponsor and Competent Authorities (CA) may carry out audits or inspections at the trial site, including source data verification. The investigator must ensure that all source documents are available for audits and inspections. The purpose of an audit or inspection is to systematically and independently review all trial-related activities and documents, to determine whether these activities were performed, registered, analyzed and reported correctly according to protocol, ICH- GCP and applicable regulations.

10 Ethics

10.1 Compliance to the protocol, ICH-GCP and regulations

The trial will be performed in compliance with this clinical trial protocol, the Declaration of Helsinki, ICH-GCP (Good Clinical Practice), and current national regulations governing this clinical trial. This is to ensure the safety and integrity of the trial subjects as well as the quality of the data collected.

10.2 Ethical review of the trial

The final protocol will be submitted for ethical review at all participating hospitals, where possible, as well as the The George Institute for Global Health in India and Swedish Ethical Review Atuhortiy.

10.3 Procedure for obtaining consent

In this trial, consent refers to data collection, as patients cannot opt out of the intervention. This is because the intervention is implemented at the cluster level, involving training physicians in ATLS®. It is unreasonable to expect these physicians to temporarily disregard their training. Patient participants will be included in this trial under the following modes of consent:

- Opt out consent for **routinely recorded data and measurement of adherence to ATLS® principles**. Consent for the collection of routinely recorded data, either through interviews or by extracting information from medical records, as well as for the measurement of adherence to ATLS® principles, will be presumed unless explicitly declined. This approach is justified because the trial is considered to pose minimal risk and because data collection will be non-invasive. Additionally, obtaining consent specifically for the measurement of adherence to ATLS® principles could interfere with the provision of care and cause undue stress for the patient and their representatives. Patients, or their legally authorized representatives, will be provided with written information about the study upon their arrival at the hospital. The variables assumed to be routinely recorded are listed in Section 13.2.
- Opt in consent and assent for **non-routinely recorded data**. Informed consent for non-routinely recorded data will be actively sought from patient participants or their legally authorized representative. For participants who are between 15 and 18 years of age we will obtain both the assent of the participant as well as the consent of their guardian or legally authorized representative. The clinical research coordinators will approach patient participants and their representatives after admission. The consent and assent will be written for patient participants who are admitted to the hospital and verbal for participants who are transferred or discharged before the clinical research coordinators have had an opportunity to approach them. The verbal consent will be audio recorded.
- Waiver of informed consent for patients who are unconscious or otherwise unable to provide consent and do not have a legally authorized representative. This group represents the most severly injured patients and they have to be included to make the trial representative of the entire population of trauma patients. Patients participants who regain consciousness will be informed about the study and asked for consent for collection of non-routinely recorded data.

10.4 Data protection

All data will be handled according to the Indian Council of Medical Research's guidelines and standard operating procedures of the George Institute for Global Health India on data security and protection. Trial data will be shared via the trial electronic CRF (eCRF) throughout the trial. The eCRF will be accessible via VPN with a two-factor

authentication and the data will be held on a secure server. All investigators and trial site staff involved in this trial must comply with the requirements of the ICMR Guidelines on data security and protection. The participant information sheet provided to participants, will inform them how:

- the trial data will be collected, used and disclosed;
- how trial data are stored to maintain confidentiality in accordance with national data legislation; and
- for verification of the data, representatives delegated by the sponsor, as well as relevant authorities, may require access to parts of medical records or trial records that are relevant to the trial, including the patient participant's medical history.

11 Insurances

The George Institute for Global Health, India is responsible for ensuring that any insurance cover required to cover the set-up, management and conduct of the study in India has been obtained. The George Institute for Global Health, India is also responsible for ensuring that India Sites have been obtained and/or will obtain insurance prior to the opening of the study in India and shall be maintained for the duration of the study and for an appropriate period thereafter. This includes being responsible for ensuring that there is appropriate insurance for the duration of the study to cover against claims for compensation by participants arising out of their participation in the trial in India. Compensation in case of injury or death will be provided by the George Institute for Global Health, India according to the regulations outlined in rules 39, 40 and 42 of the New Drugs and Clinical Rules (2019). x

12 Substantial changes to the trial

Substantial changes to the signed clinical trial protocol are only possible through approved protocol amendments and by agreement between the sponsor and the principal investigator.

13 Collection, handling, and archiving of data

Clinical research coordinators will collect data using a paper based CRF (see Appendix Section 19.3), which is then transferred to an eCRF. All trial data in the CRF must be extracted from and be consistent with the relevant source documents. The eCRF will be accessible to trial coordinators, data managers, the Investigators, Clinical Trial Monitors, Auditors, and Inspectors as required. All data will be registered, managed, and stored in a manner that enables correct reporting, interpretation, and verification. The complete

Trial Master File, as well as source documents, will be archived for at least 10 years after the trial is completed. Source data in the medical records system are stored and archived in accordance with national regulations. Metadata will be publicly accessible via a persistent DOI, and anonymised data will be released upon project completion. A detailed data management plan is available here https://doi.org/10.5281/zenodo.7748764.

13.1 Source data

The source data for each variable is given in Section 13.2. Whenever medical records are the source data, this includes imaging and lab reports. Whenever an interview is given as the source, the CRF will constitute the source data, as this is where the responses to questions will be recorded. The local investigator must keep source documents for each patient participant in the trial. A document describing what has been classified as source data in the trial (source data reference document) will be included in the Investigator Site File (ISF). The investigator must ensure that all source documents are accessible for monitoring and other quality control activities. Source data is further defined before trial start at each individual site and can, in cases where source data is not registered in another document, consist of the CRF. This should be decided in consultation with the monitor and clearly stated in the source data reference document. Access to trial-related documentation, such as patient participants' medical records, CRFs, other source data and other trial documentation will be provided for monitoring and auditing purposes. Access will also be granted in the context of regulatory inspections.

13.2 Variables

13.2.1 Screening

- **Screening ID**
- **1. Date of screening**
- **2. Date of data entry**
- **1. Is the patient at least 15 years old?** Source: Medical record or interview
    1. Yes
    2. No
- **2. Did the patient present with a history of trauma defined as having any of the reasons listed in the International Classification of Diseases chapter XX as the reason for presenting? Please see https://icd.who.int/browse10/2019/en#/XX for a complete list of ICD-10 codes** Source: Medical record or interview

1. Yes
2. No

- **3. Did the trauma occur less than 48 hours before arrival to the hospital?** Source: Medical record or interview

  1. Yes
  2. No

- **4. Was the patient admitted?** Source: Medical record

  1. Yes
  2. No

- **5. Did the patient die after arrival but before admission?** Source: Medical record

  1. Yes
  2. No

- **6. Was the patient transferred to another hospital for admission?** Source: Medical record

  1. Yes
  2. No

- **1. Did the patient present with isolated limb injury?** Source: Medical record

  1. Yes
  2. No

- **2. Was the patient directly admitted to a ward without being seen by a physician in the emergency department?** Source: Medical record

  1. Yes
  2. No

13.2.2 Consent

- **1. Is this patient included under the waiver of informed consent because the patient is unconscious or otherwise unable to provide consent and do not have a legally acceptable representative?**

  1. Yes
  2. No

- **1. Did the participant/ or legally acceptable representative (LAR) provided consent for collection of non-routinely recorded data**

    1. Yes
    2. No

- **2. Who gave consent for collection of non-routinely recorded data?**

    1. Patient participant
    2. Legally acceptable representative

- **3. Relation of LAR with the Participant**
- **4. Why was Legally acceptable representative (LAR) approached for consent for collection of non-routinely recorded data?**

    1. The participant is incapacitated because of the trauma
    2. The participant is younger than 18 years

- **5. Date when participant or legally acceptable representative (LAR) gave consent for collection of non-routinely recorded data?**
- **6. How did the participant or legally acceptable representative (LAR) consent for collection of non-routinely recorded data?**

    1. In writing
    2. Verbally

- **7. Date when the participant was reconsented?**
- **1. Did the minor give assent for collection of non-routinely recorded data?**

    1. Yes
    2. No

- **2. Date when the minor gave assent for collection of non-routinely recorded data.**
- **3. In case the minor refused to participate, date when minor refused**
- **1. Is the participant or LAR wants to opt out from study?**

    1. Yes
    2. No

- **2. Who opted-out of the routinely recorded data (in-hospital)?**

    1. Patient participant

2. Legally acceptable representative (LAR)

- **3. Date when participant or legally acceptable representative (LAR) opted-out.**
- **4. Did the participant or legally acceptable representative (LAR) suggested to delete all the previously recorded data?**

1. Yes
2. No

13.2.3 Consent withdrawn

- **1. Does the participant or legally acceptable representative (LAR) want to withdraw the consent?**

1. Yes
2. No

- **2. Date of consent withdrawal for follow-up data collection.**
- **3. Procedure(s) for which consent has been withdrawn**

1. Data collection prior to withdrawal
2. All data collection after withdrawal
3. Both

13.2.4 Baseline

- **1. Age in years** Source: Medical record of interview
- **2. Sex** Source: Medical record of interview

1. Female
2. Male
3. Other
4. Not known

- **3. Current marital status** Requires opt-in consent, not routinely recorded. Source: Interview

1. Never married
2. Currently married
3. Separated
4. Divorced
5. Widowed

6. Cohabiting
7. Not known

- **4. Education level** Requires opt-in consent, not routinely recorded. Source: Interview

1. Not attended school
2. Primary school
3. Secondary school
4. Higher secondary school
5. Graduate
6. Post graduate and above
7. Other
8. Not known

- **5. If other, please specify** Requires opt-in consent, not routinely recorded. Source: Interview
- **6. Main work status** Requires opt-in consent, not routinely recorded. Source: Interview

1. Paid work, such as daily wage earner, teacher, factory worker and government employee
2. Self-employed, such as own your business or farming
3. Non-paid work, such as volunteer or charity
4. Student
5. Keeping house/homemaker
6. Retired
7. Unemployed (health reasons)
8. Unemployed (other reasons)
9. Other
10. No income
11. Not known

- **7. If other, please specify** Requires opt-in consent, not routinely recorded. Source: Interview
- **8. Income level in INR per month** Requires opt-in consent, not routinely recorded. Source: Interview

1. Below 10,000
2. 10,001-20,000
3. 20,001-30,000
4. 30,001-50,000
5. 50,001-80,000
6. 80,001-1,00,000

7. Above 1,00,000
8. Not known

- **9. Mechanism of injury** Coded using ICD 10. Source: Medical record
- **10. Clinical Frailty Scale** Source: Medical record or treating physician

1. 1. Very fit
2. 2. Fit
3. 3. Managing well
4. 4. Living with very mild frailty
5. 5. Living with mild frailty
6. 6. Living with moderate frailty
7. 7. Living with severe frailty
8. 8. Living with very severe frailty
9. 9. Terminally ill
10. Not known

- **11. Comorbidities (Charlson Comorbidity Index)** Source: Medical record, treating physician or interview

1. Myocardial infarction
2. Congestive heart failure
3. Peripheral vascular disease
4. Cerebrovascular disease
5. Dementia
6. Chronic pulmonary disease
7. Rheumatologic disease
8. Peptic ulcer disease
9. Liver disease
10. Diabetes
11. Hemiplegia or paraplegia
12. Renal disease
13. Malignancy
14. Leukemia
15. Lymphoma
16. AIDS
17. Not known
18. None

- **12. Severity of liver disease** Source: Medical record, treating physician or interview

    1. Mild
    2. Moderate or severe
    3. Not known

- **13. Severity of diabetes** Source: Medical record, treating physician or interview

    1. Controlled
    2. Uncontrolled
    3. Not known

- **14. Severity of malignancy** Source: Medical record, treating physician or interview

    1. Localized
    2. Metastatic tumor
    3. Not known

13.2.5 Prehospital

- **1. Date and time of injury** Source: Medical record of interview
- **2. Mode of transport to the participating hospital** Source: Medical record of interview

    1. Ambulance
    2. Police
    3. Private vehicle
    4. Walking
    5. Others
    6. Not known

- **3. If other, please specify** Source: Medical record of interview
- **4. Referred or transferred to the participating hospital from another hospital** Source: Medical record of interview

    1. Yes
    2. No
    3. Not known

13.2.6 ATLS adherence

- **1. Airway patency checked** Source: Observation
    1. Yes
    2. No
- **1. Chest wall palpated** Source: Observation
    1. Yes
    2. No
- **2. Breath sounds checked** Source: Observation
    1. Yes
    2. No
- **3. Respiratory rate measured** Source: Observation
    1. Yes
    2. No
- **4. Saturation (SpO2) measured** Source: Observation
    1. Yes
    2. No
- **1. Heart rate measured** Source: Observation
    1. Yes
    2. No
- **2. Blood pressure measured** Source: Observation
    1. Yes
    2. No
- **3. Abdomen palpated** Source: Observation
    1. Yes
    2. No
- **4. Thighs palpated** Source: Observation
    1. Yes
    2. No
- **5. IV access obtained** Source: Observation

1. Yes
2. No

- **1. GCS checked** Source: Observation

1. Yes
2. No

- **2. Pupils checked** Source: Observation

1. Yes
2. No

- **1. Patients exposed for assessment**

1. Yes
2. No

- **2. Temperature measured** Source: Observation

1. Yes
2. No

- **1. Which airway interventions were performed?** Source: Observation

1. None
2. Manual airway procedure such as chin lift or jaw thrust
3. Nasopharyngeal or Oropharyngeal airway inserted
4. Supraglottic airway device
5. Tracheal intubation
6. Surgical airway
7. Other
8. Not known

- **2. If other airway Interventions given, specify**
- **3. Were airway interventions performed while minimising c-spine movement?** Source: Observation

1. Yes
2. No
3. Not known

- **1. Which breathing interventions were performed?** Source: Observation

1. None
2. Oxygen applied
3. Intracostal drain placement

4. Other
5. Not done
6. Not known

- **2. If other breathing Interventions done, specify**
- **1. Which circulation interventions and adjuncts were performed?** Source: Observation

1. None
2. Control of external bleeding
3. Fluid bolus
4. Blood transfusion
5. eFast
6. Pelvic binder applied
7. Reduction of highly displaced fracture
8. Other
9. Not known

- **2. If other circulation Interventions done, specify**
- **1. Which disability intervention was performed?** Source: Observation

1. None
2. Placement of definitive airway if the patient had a GCS of 8 or less
3. Log Rolling
4. Spine board during transportation
5. Other
6. Not known

- **2. If other disability interventions done, specify**
- **1. Which exposure intervention was performed?** Source: Observation

1. None
2. Covered with warmer or blanket
3. Warm fluids administered
4. Other
5. Not known

- **2. If other exposure interventions done, specify**

13.2.7 Emergency department

- **1. Date and time of arrival to the emergency department at the participating hospital** Source: Medical record of interview
- **2. First recorded systolic blood pressure (mmHg)** Source: Medical record
- **3. First recorded diastolic blood pressure (mmHg)** Source: Medical record
- **4. First recorded heart rate (beats per minute)** Source: Medical record
- **5. First recorded respiratory rate (breaths per minute)** Source: Medical record
- **6. First recorded Glasgow Coma Scale** Source: Medical record
- **7. First recorded body temperature (°C)** Source: Medical record
- **8. First recorded oxygen saturation (%)** Source: Medical record
- **9. Emergency department disposition** Source: Medical record

    1. Admitted
    2. Referred or transferred for admission
    3. Dead
    4. Others
    5. Not known

- **10. If other, please specify** Source: Medical record
- **11. Date and time of referral or transfer for admission** Source: Medical record

13.2.8 Hospital

- **1. Date of admission to the participating hospital** Source: Medical record
- **1.1 Time of admission to the participating hospital** Source: Medical record
- **2. Type of admitting ward** Source: Medical record

    1. General surgery
    2. Orthopaedics
    3. Neurosurgery
    4. Intensive care unit
    5. High dependency unit
    6. Medicine
    7. Trauma ward
    8. Not known

- **3. Ward name or number** Source: Medical record
- **4. Admitted to intensive care unit during admission** Source: Medical record

    1. Yes
    2. No
    3. Not known

- **5. Date of first intensive care unit admission** Source: Medical record
- **5.1 Time of first intensive care unit admission** Source: Medical record
- **6. Date of first intensive care unit discharge** Source: Medical record
- **6.1 Time of first intensive care unit discharge** Source: Medical record
- **7. Hospital disposition** Source: Medical record

    1. Alive
    2. Dead
    3. Transferred for admission
    4. Not known

- **8. Was the patient transferred to another hospital for admission?** Source: Medical record

    1. Yes
    2. No
    3. Not known

- **9. Date of discharge or transfer from participating hospital** Source: Medical record
- **9.1 Time of discharge or transfer from participating hospital** Source: Medical record

13.2.9 Surgery

- **1. Date of surgical procedure** A surgical procedure is defined as any procedure performed in the operating room, interventional dropdownlogy suite, or at the bedside, requiring general or regional anesthesia. Source: Medical record
- **1. Time of surgical procedure** A surgical procedure is defined as any procedure performed in the operating room, interventional dropdownlogy suite, or at the bedside, requiring general or regional anesthesia. Source: Medical record
- **2. Preoperative ASA score** Source: Medical record or treating physician

    1. 1. A normal healthy patient

2. 2. A patient with mild systemic disease
3. 3. A patient with severe systemic disease
4. 4. A patient with severe systemic disease that is a constant threat to life
5. 5. A moribund patient who is not expected to survive without the operation
6. 6. A declared brain-dead patient whose organs are being removed for donor purposes
7. 999. Not known

- **3. Description of procedure** Source: Medical record
- **4. Procedure coded according to SNOMED CT** Source: Medical record

13.2.10 Imaging

- **1. Date and time of imaging** Source: Medical record
- **1.1 Time of imaging** Source: Medical record
- **2. Type of imaging** Source: Medical record

1. Ultrasound
2. X-ray
3. Computed Tomography (CT)
4. Magnetic Resonance Imaging (MRI)

13.2.11 Transfusion

- **1. Date of transfusion** Source: Medical record
- **1.1 Time of transfusion** Source: Medical record
- **2. Type of blood product** Source: Medical record

1. Packed red blood cells
2. Platelets
3. Fresh frozen plasma
4. Whole blood
5. Other

- **2.1 Other specify**
- **3. Number of units transfused** Source: Medical record

13.2.12 Injury

- **1. Injury description** Source: Medical record
- **2. ICD 10 code** Coded using ICD 10. Source: Medical record
- **3. Injury source data** Source: Medical record

    1. Medical record
    2. X-ray report
    3. CT-report
    4. Surgical notes

- **4. Injury time**

13.2.13 Individual mortality status

- **1. Is the patient dead?** Source: Medical record or interview

    1. Yes
    2. No

- **2. Date and time of death** Source: Medical record or interview

13.2.14 Quality of life (EQ5D5L)

- **Date of filling this form**
- **First, I would like to ask you about MOBILITY. Would you say that:** Requires opt-in consent, not routinely recorded. Source: Interview

    1. You have no problems in walking about?
    2. You have slight problems in walking about?
    3. You have moderate problems in walking about?
    4. You have severe problems in walking about?
    5. You are unable to walk about?

- **Next, I would like to ask you about SELF-CARE. Would you say that:** Requires opt-in consent, not routinely recorded. Source: Interview

    1. You have no problems washing or dressing yourself?
    2. You have slight problems washing or dressing yourself?
    3. You have moderate problems washing or dressing yourself?
    4. You have severe problems washing or dressing yourself?
    5. You are unable to wash or dress yourself?

- **Next, I would like to ask you about USUAL ACTIVITIES, for example, work, study, housework, family or leisure activities. Would you say that:** Requires opt-in consent, not routinely recorded. Source: Interview

    1. You have no problems doing your usual activities?
    2. You have slight problems doing your usual activities?
    3. You have moderate problems doing your usual activities?
    4. You have severe problems doing your usual activities?
    5. You are unable to do your usual activities?

- **Next, I would like to ask you about PAIN OR DISCOMFORT. Would you say that:** Requires opt-in consent, not routinely recorded. Source: Interview

    1. You have no pain or discomfort?
    2. You have slight pain or discomfort?
    3. You have moderate pain or discomfort?
    4. You have severe pain or discomfort?
    5. You have extreme pain or discomfort?

- **Finally, I would like to ask you about ANXIETY OR DEPRESSION. Would you say that:** Requires opt-in consent, not routinely recorded. Source: Interview

    1. You are not anxious or depressed?
    2. You are slightly anxious or depressed?
    3. You are moderately anxious or depressed?
    4. You are severely anxious or depressed?
    5. You are extremely anxious or depressed?

- **I would now like you to tell me the point on this line where you would put your health TODAY.(Note to interviewer: mark the line at the point indicating the respondent's health today.)** Requires opt-in consent, not routinely recorded. Source: Interview

13.2.15 Disability (WHODAS 2.0)

- **Date of form filling**
- **1. Who are you interviewing?** Requires opt-in consent, not routinely recorded. Source: Interview

    1. Patient participant
    2. Patient representative

- **2. What is the relationship between the representative and the participant?** Requires opt-in consent, not routinely recorded. Source: Interview

1. Husband or wife
2. Parent
3. Son or daughter
4. Brother or sister
5. Other relative
6. Friend
7. Professional carer
8. Other (specify)

- **3. If other, please specify**
- **1. Standing for long periods such as 30 minutes?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do
6. None
7. Mild
8. Moderate
9. Severe
10. Extreme or cannot do

- **2. Taking care of your household responsibilities?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do

- **3. Learning a new task, for example, learning how to get to a new place?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do
6. None
7. Mild
8. Moderate

9. Severe
10. Extreme or cannot do

- **4. How much of a problem did you have joining in community activities (for example, festivities, religious or other activities) in the same way as anyone else can?** Requires opt-in consent, not routinely recorded. Source: Interview

    1. None
    2. Mild
    3. Moderate
    4. Severe
    5. Extreme or cannot do

- **5. How much have you been emotionally affected by your health problems?** Requires opt-in consent, not routinely recorded. Source: Interview

    1. None
    2. Mild
    3. Moderate
    4. Severe
    5. Extreme or cannot do

- **1. Concentrating on doing something for ten minutes?** Requires opt-in consent, not routinely recorded. Source: Interview

    1. None
    2. Mild
    3. Moderate
    4. Severe
    5. Extreme or cannot do
    6. None
    7. Mild
    8. Moderate
    9. Severe
    10. Extreme or cannot do

- **2. Walking a long distance such as a kilometre [or equivalent]?** Requires opt-in consent, not routinely recorded. Source: Interview

    1. None
    2. Mild
    3. Moderate
    4. Severe
    5. Extreme or cannot do
    6. None

7. Mild
8. Moderate
9. Severe
10. Extreme or cannot do

- **3. Washing your whole body?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do

- **4. Getting dressed?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do
6. None
7. Mild
8. Moderate
9. Severe
10. Extreme or cannot do

- **5. Dealing with people you do not know?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do

- **6. Maintaining a friendship?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do
6. None

7. Mild
8. Moderate
9. Severe
10. Extreme or cannot do

- **7. Your day-to-day work/school?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do

- **2. Taking care of his or her household responsibilities?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do

- **4. How much of a problem did he or she have joining in community activities (for example, festivities, religious or other activities) in the same way as anyone else can?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do

- **5. How much has your relative been emotionally affected by his or her health condition?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do

- **3. Washing his or her whole body?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do

- **5. Dealing with people he or she does not know?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do

- **7. His or her day-to-day work/school?** Requires opt-in consent, not routinely recorded. Source: Interview

1. None
2. Mild
3. Moderate
4. Severe
5. Extreme or cannot do

- **1. Overall, in the past 30 days, how many days were these difficulties present?** Requires opt-in consent, not routinely recorded. Source: Interview
- **2. In the past 30 days, for how many days were you totally unable to carry out your usual activities or work because of any health condition?** Requires opt-in consent, not routinely recorded. Source: Interview
- **3. In the past 30 days, not counting the days that you were totally unable, for how many days did you cut back or reduce your usual activities or work because of any health condition?** Requires opt-in consent, not routinely recorded. Source: Interview

13.2.16 Return to work

- **Date of form filling**
- **1. Did participant returned to work?**

1. Yes
2. No

- **2. Date and time of return to work** Requires opt-in consent, not routinely recorded. Source: Interview
- **3. Work status** Requires opt-in consent, not routinely recorded. Source: Interview

    1. Paid work
    2. Self-employed, such as own your business or farming
    3. Non-paid work, such as volunteer or charity
    4. Student
    5. Keeping house/homemaker
    6. Not known

13.2.17 Safety events

- **1. Date reported to trial management team of safety event**
- **2. Type of safety event** Source: Medical record or treating physician

    1. Prolonged mechanical ventilation (> 7 days)
    2. Initiation of renal replacement therapy
    3. Prolonged (> 2 days) use of vasopressors such as norepinephrine or vasopressin
    4. Renewed (restart after at least 2 days without) use of vasopressors such as norepinephrine or vasopressin
    5. Other

- **3. Elaborate on other safety event** Source: Medical record or treating physician
- **4. Investigator assessment of safety event** Source: Investigator

13.2.18 End of study

- **1. What is the reason for the end of study?**

    1. Completed follow up
    2. Lost to follow up
    3. Death
    4. Discharge and no consent for follow up
    5. Opt-out from routinely recorded (in-hospital) data collection and no consent for follow-up
    6. Opt-out from routinely recorded (in-hospital) data collection and withdrawn consent for follow-up

- **2. Date and time of end of study**

14 Trial organisation

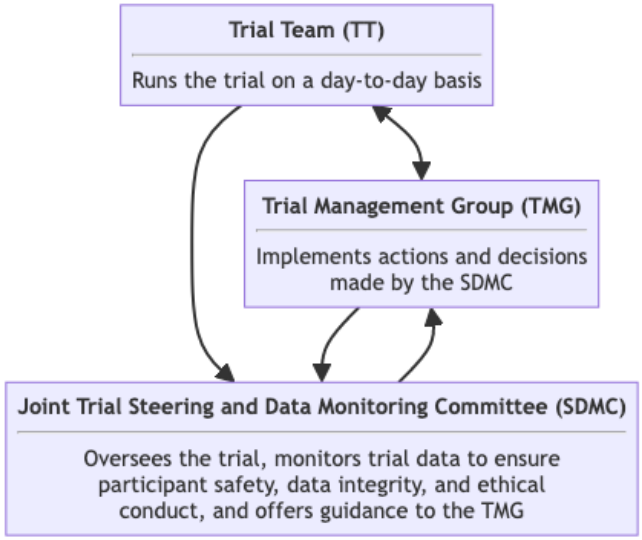

Figure 4: Trial organisation overview.

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 4. Details about each committee and group are available in their respective charter.

14.1 Trial team

Responsibility

To run the trial on a day-to-day basis, maintain trial databases, randomise clusters, ensuring complete and correct data, preparing reports for meetings (including those of the TMG and SDMC) and dealing with research governance and, if appropriate, regulatory matters.

Composition

Includes the project manager, clinical research associates, principal investigator and co-investigators as needed.

Relationships

Reports to the TMG and SDMC. Operationalises decisions made by the TMG.

Meeting frequencies

As often as needed, often weekly or bi-weekly.

14.2 Trial Management Group (TMG)

Responsibility

To manage the trial, including its clinical and practical aspects.

Composition

Includes members with broad expertise appropriate to the trial. The TMG will be chaired by the Principal Investigator.

Relationships

Receives reports from TT. Provides input to the SDMC. Implements decisions made by the SDMC.

Meeting frequencies

Monthly to every six months.

14.3 Joint Trial Steering and Data Monitoring Committee (SDMC)

Responsibility

The SDMC's responsibility is to oversee the trial, review results of interim analyses and safety events reported by the TMG, and review trial data for each batch, assessing data quality, completeness, cluster performance in recruitment and loss to follow-up rates, and external factors affecting trial validity, safety, or ethics. This committee also offer guidance to the TMG.

Composition

A majority of independent members, including a chair and three additional external experts specializing in the clinical area, biostatistics, and a community or patient representative, as well as and a minority of members with a direct interest in the trial, including the principal investigator. The chair should be independent of the trial, and the coordinating institutions Karolinska Institutet and The George Institute for Global Health.

Relationships

Receives reports from the trial team and TMG.

Meeting frequencies

After the completion of each batch, but may be more frequent if needed.

15 Funding

- Swedish Research Council (reg. no. 2023-03128)
- Laerdal Foundation (reg. no. 2023-0297)

16 Special considerations

16.1 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.

16.2 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.

17 Notification of trial completion, reporting, and publication

The trial will be reported to the Funders within a year of completion. The results of the trial will also be prepared as manuscripts for publication. Authorship on trial manuscripts will be based on the International Committee of Medical Journal Editors (ICMJE) criteria[43]:

- 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 reviewing it critically for important intellectual content; AND
- Final approval of the version to be published; AND

- Agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved.

In addition to being accountable for the parts of the work done, an author should be able to identify which co-authors are responsible for specific other parts of the work. In addition, authors should have confidence in the integrity of the contributions of their co-authors.

The most recent version of the ICMJE criteria will be adhered to. We will also use the ICMJE criteria for non-author contributorship.

Before work on a trial manuscript is initiated, a writing group will be formed and first and last authors will be designated. This writing group will be formed by discussion in the Trial Management Group.

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43. ICMJE | Recommendations | Defining the Role of Authors and Contributors.

19 Appendices

19.1 Initial hospital screening instrument

Screening call

This form is for screening potentially eligible clusters for the ATLS vs standard care trial. Please fill it in while talking to the hospital representative. Thank you so much for helping with this task!

Please complete the questions below.

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. Advanced Trauma Life Support® (ATLS®) is the most popular of these programmes and have been used to train 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

Cluster will be hospitals with a baseline admission rate of at least 400 patients with trauma per year or 35 patients with trauma per month for at least the last six months, that provide emergency surgical and orthopaedic services around the clock, and where no more than 25% of initial trauma care providers trained in a formalised trauma life support training programme.

Patients will be at least 15 years old, who present to the emergency department of participating hospitals with a history of trauma occuring less than 48 hours before arrival, and who are admitted or die between and admission, or who are transferred from the emergency department of a participating hospital to another hospital 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 In-hospital data collection will be conducted under a waiver of informed consent. Patients will be informed about the trial and their right to opt out of data collection. Patients will be informed that they can withdraw their data from the trial at any time.

Trial Period 2024-10-01 to 2029-10-01

Hospital details

Hospital name and address

Eligibility assessment

Does the hospital admit trauma patients?	◯ Yes ◯ No
Is the hospital representative interested in potentially participating?	◯ Yes ◯ No (Comment: _____)
If the hospital representative is not interested in participating then you can go ahead and submit the form.	
How many trauma patients aged 15 years or older, excluding patients with isolated limb injuries, are admitted each month?	◯ < 30 ◯ 30-60 ◯ > 60 ◯ Not sure (Comment: _____)
Does the hospital provide emergency surgery and orthopaedic services around the clock?	◯ Yes ◯ No (Comment: _____)
Out of the physicians involved in the initial resuscitation of trauma patients, are less than 25% trained in a formalised trauma life support training programme like ATLS or Primary Trauma Care?	◯ Yes ◯ No (Comment (like name of other training programme): _____)
Unfortunately, the hospital does not fulfil the eligibility criteria and you may go ahead and submit the form.	
The hospital fulfills the cluster eligibility criteria. Please enter the hospital representative's contact details: Name E-mail Phone number _____ _____ _____	
Before you can proceed to fill in descriptive information about the potential cluster, please confirm that the contact details are complete: _____	

Cluster descriptive information

Out of the patients with trauma who present to the emergency department, what percentage are referrals or transfers from other hospitals?	◯ < 20% ◯ 20-50% ◯ 51-80% ◯ > 80% ◯ Not sure (Comment: _____)
Out of the patients with trauma who are admitted, what percentage are transferred to other hospitals?	◯ < 10% ◯ 10-20% ◯ 21-30% ◯ >30% ◯ Not sure (Comment: _____)

Who performs the initial resuscitation of trauma patients as they arrive to the hospital?	☐ Casualty medical officers ☐ Emergency medicine residents ☐ Surgical residents ☐ Not sure (Comment: _____)
How many CMOs work in the emergency department? This question is here to help us estimate the number of people we will need to train.	◯ < 10 ◯ 10-20 ◯ 21-30 ◯ > 30 ◯ Not sure (Comment: _____)
How many emergency medicine/general surgery residents are admitted each year? This question is here to help us estimate the number of people we will need to train.	◯ < 10 ◯ 10-20 ◯ 21-30 ◯ > 30 ◯ Not sure (Comment: _____)
What specialities are available around the clock to care for trauma patients?	☐ General surgery ☐ Orthopaedics ☐ Neurosurgery ☐ Vascular surgery ☐ Interventional radiology ☐ Emergency medicine ☐ Not sure (Comment: _____)
What facilities are available around the clock?	☐ X-ray ☐ Ultrasound/FAST ☐ CT ☐ MRI ☐ Blood bank ☐ Not sure (Comment: _____)
How many beds does the hospital have?	◯ < 250 ◯ 250-500 ◯ 501-750 ◯ 751-1000 ◯ >1000 ◯ Not sure (Comment: _____)
How many ICU beds does the hospital have?	◯ No ICU beds ◯ 1-10 ◯ 11-20 ◯ 21-30 ◯ > 30 ◯ Not sure (Comment: _____)
How many dedicated trauma beds does the hospital have?	◯ No dedicated trauma beds ◯ 1-10 ◯ 11-20 ◯ 21-30 ◯ > 30 ◯ Not sure (Comment: _____)

Please submit the form once you have completed all questions above.

19.2 In-depth hospital screening interview instrument

Hospital screening interview for the ATLS vs standard care trial

This is the screening interview form for the Advanced Trauma Life Support® vs Standard Care trial planned by Karolinska Institutet along with The George Institute. You have expressed preliminary interest inparticipating in this trial. We are undertaking this hospital screening interview inorder to assess whether the study could be conducted at your hospital. We appreciate your efforts to answer as many of these questions as possible and we will follow up on your responses and any questions you may have in a separate call. Thank you!

Synopsis 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 All-cause 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, in which consent is presumed unless actively declined. Note that consent here refers to consent to data collection, as it will not be possible for patients to opt out from being subjected to the intervention. This approach is justified because the trial can be considered to involve only minimal risk and the data

collection is non-invasive and mostly involve extracting routinely collected data from medical records. Patient participants will be informed about the study and their right to opt out once they are admitted or telephonically if they are transferred. Patients will be informed that they can withdraw their data from the trial at any time before final analysis of the data.

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

Hospital details

[hospital_address]

Contact person details

Name [contact_name]
E-mail [contact_email]
Phone number [contact_phone_number]

Will you [contact_name] also be the site investigator?	◯ Yes ◯ No

Investigator details

Please enter the name and contact details of the site investigator

Name _____
E-mail _____
Phone number _____

Please enter these additional investigator details

Designation _____
Specialization _____
State Medical Council registration number _____

Is the investigator trained in International Council for Harmonisation, Guideline for Good Clinical Practice (ICH GCP)?	◯ Yes ◯ No
Will there be a co-investigator at your site?	◯ Yes ◯ No
Will you [contact_name] be the co-investigator?	◯ Yes ◯ No

Please enter the name and contact details of the site investigator

Name _____
E-mail _____
Phone number _____

Please enter these additional co-investigator details Designation _____ Specialization _____ State Medical Council registration number _____	
Is the co-investigator trained in International Council for Harmonisation, Guideline for Good Clinical Practice (ICH GCP)?	◯ Yes ◯ No

Ethical review details

Does your hospital have an ethics committee registered with CDSCO?	◯ Yes ◯ No
Please enter the ethics committee registration number	_____
In the next three months when is your IEC meeting up?	_____
What is the expected timeline for ethics review at your site?	_____
In which languages do you think the consent form should be translated, considering the languages spoken by the potential participants treated at your hospital?	_____

Departmental logistics

Does your hospital require any additional departmental review besides the ethics? Can you please elaborate on that review?	_____
Are there any potential logistical issues which may interfere with set up or running ofthis project at your site?	_____ (E.g. contract review, adequate space, lack of resources etc.)
What is the expected timeline for contract review, negotiations and execution (in days)?	_____
What is the maximum expected timeline?	_____

Initial trauma care	
How do patients typically arrive to your hospital?	
Who are involved in the management of trauma patients in the emergency department?	
What happens when additional expertise is needed?	
What is the role of the casualty medical officers?	
Are physicians organised in units?	
How big are those units?	
How are those units composed in terms of residents and faculty?	
How often do the units rotate?	
How many units are there working in the emergency department?	
How many trauma patients aged 15 years or older are admitted per day, excluding patients with isolated limb injuries and those who are admitted directly to the ward?	

Intervention and patient inclusion	
How many patients do you think you could include in to the proposed trial per month? (We need to include at least 12 patients per month)	
What is the basis of your patient enrollment estimate?	(For example database review, emergency department record, review of patient records, other)
Do you see any problems with including 12 patients per month at your site? Can you please elaborate on those problems?	

All hospitals in this trial will receive the intervention. The intervention is that we will train approximately 10 physicians providing initial trauma care in ATLS in your hospital. Who do you think we should train to maximise the effect?	_____ (Surgical residents? Emergency medicine residents? Casualty medical officers? Someone else??)
The time point when the training will be implemented will be randomised, but there will be a minimum of three months between the start of the data collection and the training. The training will happen during a one month long "transition period". How long notice do you need to plan the participation of the physicians from your hospital?	_____
Are you aware of any plans to train providers in any formalised trauma life support training programme during the next few years?	_____
Are you aware of any plans to implement other interventions or changes that may radically change how you treat trauma patients at your site?	_____ (For example building a trauma centre, building a new emergency department, shifting the CT)
If we would like to visit your hospital to observe trauma care delivery in the emergency department and talk to providers, how can that be arranged?	_____

General

How are the patient medical records organised at your site?	☐ Hard-copy ☐ Electronic ☐ Not sure
Do you currently have any competing studies or are you committed to new competing studies?	_____
Do you have access to a computer with high-speed internet access?	◯ Yes ◯ No
Do you currently have the necessary study team including research coordinator and co-investigators to conduct this study? Can you please elaborate on the composition and experience of that team?	_____
What are your expectations of this trial?	_____
Do you have any questions or comments regarding this trial?	_____
Are you interested in participating in this trial?	◯ Yes ◯ No

If you have any questions, feel free to contact Martin Gerdin Wärnberg (martin.gerdin@ki.se), Monty Khajanchi (monta32@gmail.com) or Samriddhi Ranjan (sranjan@georgeinstitute.org.in)

19.3 Case Record Form

Screening V1.0.01.10.24

Screening ID	_____
1. Date of screening	_____
2. Date of data entry	_____

Inclusion criteria

1. Is the patient at least 15 years old?	◯ Yes ◯ No (Source: Medical record or interview)
2. Did the patient present with a history of trauma defined as having any of the reasons listed in the International Classification of Diseases chapter XX as the reason for presenting? Please see https://icd.who.int/browse10/2019/en#/XX for a complete list of ICD-10 codes	◯ Yes ◯ No (Source: Medical record or interview)
3. Did the trauma occur less than 48 hours before arrival to the hospital?	◯ Yes ◯ No (Source: Medical record or interview)
4. Was the patient admitted?	◯ Yes ◯ No (Source: Medical record)
5. Did the patient die after arrival but before admission?	◯ Yes ◯ No (Source: Medical record)
6. Was the patient transferred to another hospital for admission?	◯ Yes ◯ No (Source: Medical record)

Exclusion criteria

1. Did the patient present with isolated limb injury?	◯ Yes ◯ No (Source: Medical record)
2. Was the patient directly admitted to a ward without being seen by a physician in the emergency department?	◯ Yes ◯ No (Source: Medical record)

Eligibility

The patient is not eligible for inclusion.

Consent V1.0.01.10.24

Study Consent

In this trial, consent refers to consent for data collection. It is not possible for patients to opt out from being subjected to the intervention, as the intervention is delivered at the cluster level. Patient participants will be included in this trial under the following modes of consent:
• Opt-out consent for collection of routinely recorded data
• Opt-in consent and assent for non-routinely recorded data, including but not restricted to Quality of Life (EQ5D5L), Disability (WHODAS 2.0) and Return to Work.
• Waiver of informed consent for patients who are unconscious or otherwise unable to provide consent and do not have a legally acceptable representative.
When possible, all patient participants must be approached and provided with information about the study, the option to opt out, and consent for collection of non-routinely recorded data.

Section I: Consent Wavier

Please note that the consent for the collection of the routinely recorded data (in-hospital) will be presumed unless actively declined by the participant/ legally acceptable representative (LAR), using the opt-out form. Information for all forms except for baseline characteristics (marital and work status, education and income), follow-up (Quality of Life (EQ5D5L), Disability (WHODAS 2.0) and Return to Work) will be presumed, unless opted-out.

1. Is this patient included under the waiver of informed consent because the patient is unconscious or otherwise unable to provide consent and do not have a legally acceptable representative?	◯ Yes ◯ No

Section II: Opt in consent for follow up data collection

1. Did the participant/ or legally acceptable representative (LAR) provided consent for collection of non-routinely recorded data	◯ Yes ◯ No
2. Who gave consent for collection of non-routinely recorded data?	◯ Patient participant ◯ Legally acceptable representative
3. Relation of LAR with the Participant	_____
4. Why was Legally acceptable representative (LAR) approached for consent for collection of non-routinely recorded data?	☐ The participant is incapacitated because of the trauma ☐ The participant is younger than 18 years
5. Date when participant or legally acceptable representative (LAR) gave consent for collection of non-routinely recorded data?	_____

6. How did the participant or legally acceptable representative (LAR) consent for collection of non-routinely recorded data?	◯ In writing ◯ Verbally
7. Date when the participant was reconsented?	_____

Section III: Assent form

1. Did the minor give assent for collection of non-routinely recorded data?	◯ Yes ◯ No
2. Date when the minor gave assent for collection of non-routinely recorded data.	_____
3. In case the minor refused to participate, date when minor refused	_____

Section IV: Opt out form

1. Is the participant or LAR wants to opt out from study?	◯ Yes ◯ No
2. Who opted-out of the routinely recorded data (in-hospital)?	◯ Patient participant ◯ Legally acceptable representative (LAR)
3. Date when participant or legally acceptable representative (LAR) opted-out.	_____
4. Did the participant or legally acceptable representative (LAR) suggested to delete all the previously recorded data?	◯ Yes ◯ No

Consent_Withdrawn V1.0.01.10.24

Consent withdrawal	
1. Does the participant or legally acceptable representative (LAR) want to withdraw the consent?	◯ Yes ◯ No
2. Date of consent withdrawal for follow-up data collection.	_____
3. Procedure(s) for which consent has been withdrawn	◯ Data collection prior to withdrawal ◯ All data collection after withdrawal ◯ Both

Baseline V1.0.01.10.24

1. Age in years	_____ (Source: Medical record of interview)
2. Sex	◯ Female ◯ Male ◯ Other ◯ Not known (Source: Medical record of interview)
3. Current marital status	◯ Never married ◯ Currently married ◯ Separated ◯ Divorced ◯ Widowed ◯ Cohabiting ◯ Not known (Requires opt-in consent, not routinely recorded. Source: Interview)
4. Education level	◯ Not attended school ◯ Primary school ◯ Secondary school ◯ Higher secondary school ◯ Graduate ◯ Post graduate and above ◯ Other ◯ Not known (Requires opt-in consent, not routinely recorded. Source: Interview)
5. If other, please specify	_____ (Requires opt-in consent, not routinely recorded. Source: Interview)
6. Main work status	◯ Paid work, such as daily wage earner, teacher, factory worker and government employee ◯ Self-employed, such as own your business or farming ◯ Non-paid work, such as volunteer or charity ◯ Student ◯ Keeping house/homemaker ◯ Retired ◯ Unemployed (health reasons) ◯ Unemployed (other reasons) ◯ Other ◯ No income ◯ Not known (Requires opt-in consent, not routinely recorded. Source: Interview)
7. If other, please specify	_____ (Requires opt-in consent, not routinely recorded. Source: Interview)

8. Income level in INR per month	◯ Below 10,000 ◯ 10,001-20,000 ◯ 20,001-30,000 ◯ 30,001-50,000 ◯ 50,001-80,000 ◯ 80,001-1,00,000 ◯ Above 1,00,000 ◯ Not known (Requires opt-in consent, not routinely recorded. Source: Interview)
9. Mechanism of injury	_____ (Coded using ICD 10. Source: Medical record)
10. Clinical Frailty Scale	◯ 1. Very fit ◯ 2. Fit ◯ 3. Managing well ◯ 4. Living with very mild frailty ◯ 5. Living with mild frailty ◯ 6. Living with moderate frailty ◯ 7. Living with severe frailty ◯ 8. Living with very severe frailty ◯ 9. Terminally ill ◯ Not known (Source: Medical record or treating physician)
11. Comorbidities (Charlson Comorbidity Index)	☐ Myocardial infarction ☐ Congestive heart failure ☐ Peripheral vascular disease ☐ Cerebrovascular disease ☐ Dementia ☐ Chronic pulmonary disease ☐ Rheumatologic disease ☐ Peptic ulcer disease ☐ Liver disease ☐ Diabetes ☐ Hemiplegia or paraplegia ☐ Renal disease ☐ Malignancy ☐ Leukemia ☐ Lymphoma ☐ AIDS ☐ Not known ☐ None (Source: Medical record, treating physician or interview)
12. Severity of liver disease	◯ Mild ◯ Moderate or severe ◯ Not known (Source: Medical record, treating physician or interview)
13. Severity of diabetes	◯ Controlled ◯ Uncontrolled ◯ Not known (Source: Medical record, treating physician or interview)

14. Severity of malignancy	◯ Localized ◯ Metastatic tumor ◯ Not known (Source: Medical record, treating physician or interview)

Prehospital V1.0.01.10.24

1. Date and time of injury	_____ (Source: Medical record of interview)
2. Mode of transport to the participating hospital	◯ Ambulance ◯ Police ◯ Private vehicle ◯ Walking ◯ Others ◯ Not known (Source: Medical record of interview)
3. If other, please specify	_____ (Source: Medical record of interview)
4. Referred or transferred to the participating hospital from another hospital	◯ Yes ◯ No ◯ Not known (Source: Medical record of interview)

ATLS adherence V1.1.22.10.24

ATLS adherence checklist

Airway	
1. Airway patency checked	◯ Yes ◯ No (Source: Observation)
Breathing	
1. Chest wall palpated	◯ Yes ◯ No (Source: Observation)
2. Breath sounds checked	◯ Yes ◯ No (Source: Observation)
3. Respiratory rate measured	◯ Yes ◯ No (Source: Observation)
4. Saturation (SpO2) measured	◯ Yes ◯ No (Source: Observation)
Circulation	
1. Heart rate measured	◯ Yes ◯ No (Source: Observation)
2. Blood pressure measured	◯ Yes ◯ No (Source: Observation)
3. Abdomen palpated	◯ Yes ◯ No (Source: Observation)
4. Thighs palpated	◯ Yes ◯ No (Source: Observation)
5. IV access obtained	◯ Yes ◯ No (Source: Observation)

Disability	
1. GCS checked	◯ Yes ◯ No (Source: Observation)
2. Pupils checked	◯ Yes ◯ No (Source: Observation)
Exposure	
1. Patients exposed for assessment	◯ Yes ◯ No
2. Temperature measured	◯ Yes ◯ No (Source: Observation)
3. Interventions and adjuncts performed according to ATLS	
Airway interventions	
1. Which airway interventions were performed?	☐ None ☐ Manual airway procedure such as chin lift or jaw thrust ☐ Nasopharyngeal or Oropharyngeal airway inserted ☐ Supraglottic airway device ☐ Tracheal intubation ☐ Surgical airway ☐ Other ☐ Not known (Source: Observation)
2. If other airway Interventions given, specify	_____
3. Were airway interventions performed while minimising c-spine movement?	◯ Yes ◯ No ◯ Not known (Source: Observation)
Breathing interventions	
1. Which breathing interventions were performed?	☐ None ☐ Oxygen applied ☐ Intracostal drain placement ☐ Other ☐ Not done ☐ Not known (Source: Observation)
2. If other breathing Interventions done, specify	_____

Circulation interventions

1. Which circulation interventions and adjuncts were performed?	☐ None ☐ Control of external bleeding ☐ Fluid bolus ☐ Blood transfusion ☐ eFast ☐ Pelvic binder applied ☐ Reduction of highly displaced fracture ☐ Other ☐ Not known (Source: Observation)
2. If other circulation Interventions done, specify	_____

Disability interventions

1. Which disability intervention was performed?	☐ None ☐ Placement of definitive airway if the patient had a GCS of 8 or less ☐ Log Rolling ☐ Spine board during transportation ☐ Other ☐ Not known (Source: Observation)
2. If other disability interventions done, specify	_____

Exposure interventions

1. Which exposure intervention was performed?	☐ None ☐ Covered with warmer or blanket ☐ Warm fluids administered ☐ Other ☐ Not known (Source: Observation)
2. If other exposure interventions done, specify	_____

Emergency Department V1.0.01.10.24

1. Date and time of arrival to the emergency department at the participating hospital	_____ (Source: Medical record of interview)
2. First recorded systolic blood pressure (mmHg)	_____ (Source: Medical record)
3. First recorded diastolic blood pressure (mmHg)	_____ (Source: Medical record)
4. First recorded heart rate (beats per minute)	_____ (Source: Medical record)
5. First recorded respiratory rate (breaths per minute)	_____ (Source: Medical record)
6. First recorded Glasgow Coma Scale	_____ (Source: Medical record)
7. First recorded body temperature (°C)	_____ (Source: Medical record)
8. First recorded oxygen saturation (%)	_____ (Source: Medical record)
9. Emergency department disposition	◯ Admitted ◯ Referred or transferred for admission ◯ Dead ◯ Others ◯ Not known (Source: Medical record)
10. If other, please specify	_____ (Source: Medical record)
11. Date and time of referral or transfer for admission	_____ (Source: Medical record)

Hospital V1.0.01.10.24

1. Date of admission to the participating hospital	_____ (Source: Medical record)
1.1 Time of admission to the participating hospital	_____ (Source: Medical record)
2. Type of admitting ward	◯ General surgery ◯ Orthopaedics ◯ Neurosurgery ◯ Intensive care unit ◯ High dependency unit ◯ Medicine ◯ Trauma ward ◯ Not known (Source: Medical record)
3. Ward name or number	_____ (Source: Medical record)
4. Admitted to intensive care unit during admission	◯ Yes ◯ No ◯ Not known (Source: Medical record)
5. Date of first intensive care unit admission	_____ (Source: Medical record)
5.1 Time of first intensive care unit admission	_____ (Source: Medical record)
6. Date of first intensive care unit discharge	_____ (Source: Medical record)
6.1 Time of first intensive care unit discharge	_____ (Source: Medical record)
7. Hospital disposition	◯ Alive ◯ Dead ◯ Transferred for admission ◯ Not known (Source: Medical record)
8. Was the patient transferred to another hospital for admission?	◯ Yes ◯ No ◯ Not known (Source: Medical record)

9. Date of discharge or transfer from participating hospital	_____ (Source: Medical record)
9.1 Time of discharge or transfer from participating hospital	_____ (Source: Medical record)

Surgery V1.0.01.10.24

1. Date of surgical procedure	_____ (A surgical procedure is defined as any procedure performed in the operating room, interventional dropdownlogy suite, or at the bedside, requiring general or regional anesthesia. Source: Medical record)
1. Time of surgical procedure	_____ (A surgical procedure is defined as any procedure performed in the operating room, interventional dropdownlogy suite, or at the bedside, requiring general or regional anesthesia. Source: Medical record)
2. Preoperative ASA score	◯ 1. A normal healthy patient ◯ 2. A patient with mild systemic disease ◯ 3. A patient with severe systemic disease ◯ 4. A patient with severe systemic disease that is a constant threat to life ◯ 5. A moribund patient who is not expected to survive without the operation ◯ 6. A declared brain-dead patient whose organs are being removed for donor purposes ◯ 999. Not known (Source: Medical record or treating physician)
3. Description of procedure	_____ (Source: Medical record)
4. Procedure coded according to SNOMED CT	_____ (Source: Medical record)

Imaging V1.0.01.10.24

1. Date and time of imaging	_____ (Source: Medical record)
1.1 Time of imaging	_____ (Source: Medical record)
2. Type of imaging	◯ Ultrasound ◯ X-ray ◯ Computed Tomography (CT) ◯ Magnetic Resonance Imaging (MRI) (Source: Medical record)

Transfusion V1.0.01.10.24

1. Date of transfusion	_____ (Source: Medical record)
1.1 Time of transfusion	_____ (Source: Medical record)
2. Type of blood product	◯ Packed red blood cells ◯ Platelets ◯ Fresh frozen plasma ◯ Whole blood ◯ Other (Source: Medical record)
2.1 Other specify	_____
3. Number of units transfused	_____ (Source: Medical record)

Injury V1.0.01.10.24

1. Injury description	_____ (Source: Medical record)
2. ICD 10 code	_____ (Coded using ICD 10. Source: Medical record)
3. Injury source data	◯ Medical record ◯ X-ray report ◯ CT-report ◯ Surgical notes (Source: Medical record)
4. Injury time	_____

Individual Mortality Status V1.0.01.10.24

1. Is the patient dead?	◯ Yes ◯ No (Source: Medical record or interview)
2. Date and time of death	_____ (Source: Medical record or interview)

Health Questionnaire

English version

VERSION FOR INTERVIEWER ADMINISTRATION

Note to interviewer: although allowance should be made for the interviewer's particular style of speaking, the wording of the questionnaire instructions should be followed as closely as possible. In the case of the EQ-5D-5L descriptive system of the questionnaire, the precise wording must be followed.

If the respondent has difficulty choosing a response or asks for clarification, the interviewer should repeat the question word for word and ask the respondent to answer in a way that most closely resembles his or her thoughts about his or her health today.

INTRODUCTION

(Note to interviewer: please read the following to the respondent.)

We are trying to find out what you think about your health. I will explain what to do as I go along, but please interrupt me if you do not understand something or if things are not clear to you. There are no right or wrong answers. We are interested only in your personal view.

First, I am going to read out some questions. Each question has a choice of five answers. Please tell me which answer best describes your health TODAY.

Do not choose more than one answer in each group of questions.

(Note to interviewer: first read all five options for each question. Then ask the respondent to choose which one applies to him/herself. Repeat the question and options if necessary. Mark the appropriate box under each heading. You may need to remind the respondent regularly that the timeframe is TODAY.)

EQ-5D DESCRIPTIVE SYSTEM

Date of filling this form

First, I would like to ask you about MOBILITY. Would you say that:
(Requires opt-in consent, not routinely recorded. Source: Interview)

◯ You have no problems in walking about?
◯ You have slight problems in walking about?
◯ You have moderate problems in walking about?
◯ You have severe problems in walking about?
◯ You are unable to walk about?

Next, I would like to ask you about SELF-CARE. Would you say that:
(Requires opt-in consent, not routinely recorded. Source: Interview)

◯ You have no problems washing or dressing yourself?
◯ You have slight problems washing or dressing yourself?
◯ You have moderate problems washing or dressing yourself?
◯ You have severe problems washing or dressing yourself?
◯ You are unable to wash or dress yourself?

Next, I would like to ask you about USUAL ACTIVITIES, for example, work, study, housework, family or leisure activities. Would you say that:
(Requires opt-in consent, not routinely recorded. Source: Interview)

◯ You have no problems doing your usual activities?
◯ You have slight problems doing your usual activities?
◯ You have moderate problems doing your usual activities?
◯ You have severe problems doing your usual activities?
◯ You are unable to do your usual activities?

Next, I would like to ask you about PAIN OR DISCOMFORT. Would you say that:
(Requires opt-in consent, not routinely recorded. Source: Interview)

◯ You have no pain or discomfort?
◯ You have slight pain or discomfort?
◯ You have moderate pain or discomfort?
◯ You have severe pain or discomfort?
◯ You have extreme pain or discomfort?

Finally, I would like to ask you about ANXIETY OR DEPRESSION. Would you say that:
(Requires opt-in consent, not routinely recorded. Source: Interview)

◯ You are not anxious or depressed?
◯ You are slightly anxious or depressed?
◯ You are moderately anxious or depressed?
◯ You are severely anxious or depressed?
◯ You are extremely anxious or depressed?

EQ-5D VAS

Now, I would like to ask you to say how good or bad your health is TODAY.

I would like you to picture in your mind a vertical line that is numbered from 0 to 100.
(Note to interviewer: if interviewing face-to-face, please show the respondent the VAS line.)

100 at the top of the line means the best health you can imagine.
0 at the bottom of the line means the worst health you can imagine.

I would now like you to tell me the point on this line where you would put your health TODAY.
(Note to interviewer: mark the line at the point indicating the respondent's health today.)

0 - The worst health you can imagine

50

100 - The best health you can imagine

(Place a mark on the scale above)

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Disability (WHODAS 2.0)

Date of form filling	_____
1. Who are you interviewing?	◯ Patient participant ◯ Patient representative (Requires opt-in consent, not routinely recorded. Source: Interview)
2. What is the relationship between the representative and the participant?	◯ Husband or wife ◯ Parent ◯ Son or daughter ◯ Brother or sister ◯ Other relative ◯ Friend ◯ Professional carer ◯ Other (specify) (Requires opt-in consent, not routinely recorded. Source: Interview)
3. If other, please specify	_____

Instructions to the interviewer are written in bold - do not read these aloud.

Text for the respondent to hear is written in italic print in blue. Read this text aloud.

Say to respondent:
The interview is about difficulties people have because of health conditions.

By health condition I mean diseases or illnesses, or other health problems that may be short or long lasting; injuries; mental or emotional problems; and problems with alcohol or drugs.

Remember to keep all of your health problems in mind as you answer the questions. When I ask you about difficulties in doing an activity think about...

Increased effort Discomfort or pain Slowness Changes in the way you do the activity When answering, I'd like you to think back over the past 30 days. I would also like you to answer these questions thinking about how much difficulty you have had, on average, over the past 30 days, while doing the activity as you usually do it.

Use this scale when responding: None, mild, moderate, severe, extreme or cannot do.

In the past 30 days, how much difficulty did you have in:

1. Standing for long periods such as 30 minutes?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
2. Taking care of your household responsibilities?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
3. Learning a new task, for example, learning how to get to a new place?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
4. How much of a problem did you have joining in community activities (for example, festivities, religious or other activities) in the same way as anyone else can?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
5. How much have you been emotionally affected by your health problems?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
In the past 30 days, how much difficulty did you have in:	
1. Concentrating on doing something for ten minutes?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
2. Walking a long distance such as a kilometre [or equivalent]?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)

3. Washing your whole body?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
4. Getting dressed?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
5. Dealing with people you do not know?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
6. Maintaining a friendship?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
7. Your day-to-day work/school?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)

Instructions to the interviewer are written in bold - do not read these aloud.

Text for the respondent to hear is written in italic print in blue. Read this text aloud.

Say to respondent:
The interview is about difficulties people have because of health conditions.

By health condition I mean diseases or illnesses, or other health problems that may be short or long lasting; injuries; mental or emotional problems; and problems with alcohol or drugs.

Remember to keep all of your health problems in mind as you answer the questions. When I ask you about difficulties in doing an activity think about...

Increased effort Discomfort or pain Slowness Changes in the way you do the activity When answering, I'd like you to think back over the past 30 days and, to the best of your knowledge, answer these questions thinking about how much difficulty your friend, relative or carer had while doing the following activities. I will use the term "relative" to mean "friend", "relative"

or "carer". For each question, please give only one response. **In the past 30 days, how much difficulty did your relative have in:**	
1. Standing for long periods such as 30 minutes?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
2. Taking care of his or her household responsibilities?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
3. Learning a new task, for example, learning how to get to a new place?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
4. How much of a problem did he or she have joining in community activities (for example, festivities, religious or other activities) in the same way as anyone else can?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
5. How much has your relative been emotionally affected by his or her health condition?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
In the past 30 days, how much difficulty did your relative have in:	
1. Concentrating on doing something for ten minutes?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
2. Walking a long distance such as a kilometre [or equivalent]?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)

3. Washing his or her whole body?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
4. Getting dressed?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
5. Dealing with people he or she does not know?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
6. Maintaining a friendship?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
7. His or her day-to-day work/school?	◯ None ◯ Mild ◯ Moderate ◯ Severe ◯ Extreme or cannot do (Requires opt-in consent, not routinely recorded. Source: Interview)
Number of days	
1. Overall, in the past 30 days, how many days were these difficulties present?	_____ (Requires opt-in consent, not routinely recorded. Source: Interview)
2. In the past 30 days, for how many days were you totally unable to carry out your usual activities or work because of any health condition?	_____ (Requires opt-in consent, not routinely recorded. Source: Interview)
3. In the past 30 days, not counting the days that you were totally unable, for how many days did you cut back or reduce your usual activities or work because of any health condition?	_____ (Requires opt-in consent, not routinely recorded. Source: Interview)

Return To Work V1.0.01.10.24

Date of form filling	_____
1. Did participant returned to work?	◯ Yes ◯ No
2. Date and time of return to work	_____ (Requires opt-in consent, not routinely recorded. Source: Interview)
3. Work status	◯ Paid work ◯ Self-employed, such as own your business or farming ◯ Non-paid work, such as volunteer or charity ◯ Student ◯ Keeping house/homemaker ◯ Not known (Requires opt-in consent, not routinely recorded. Source: Interview)

Safety Events V1.0.01.10.24

1. Date reported to trial management team of safety event	_____
2. Type of safety event	◯ Prolonged mechanical ventilation (> 7 days) ◯ Initiation of renal replacement therapy ◯ Prolonged (> 2 days) use of vasopressors such as norepinephrine or vasopressin ◯ Renewed (restart after at least 2 days without) use of vasopressors such as norepinephrine or vasopressin ◯ Other (Source: Medical record or treating physician)
3. Elaborate on other safety event	_____ (Source: Medical record or treating physician)
4. Investigator assessment of safety event	_____ (Source: Investigator)

End Of Study V1.0.01.10.24

1. What is the reason for the end of study?	◯ Completed follow up ◯ Lost to follow up ◯ Death ◯ Discharge and no consent for follow up ◯ Opt-out from routinely recorded (in-hospital) data collection and no consent for follow-up ◯ Opt-out from routinely recorded (in-hospital) data collection and withdrawn consent for follow-up
2. Date and time of end of study	_____

End Of Study V10 Dated22mar24

What is the reason for the end of study?	◯ Completed follow up ◯ Lost to follow up ◯ Death ◯ Discharge and no consent for follow up ◯ Opt-out from routinely recorded (in-hospital) data collection and no consent for follow-up ◯ Opt-out from routinely recorded (in-hospital) data collection and withdrawn consent for follow-up
Date and time of end of study	_____

SCHEDULE 2: RESEARCH GRANT

Decision of the Swedish Research Council and the applicable General Terms and Conditions for Research Grants applicable to the Project.

Vetenskapsrådet (Swedish Research Council) General Terms and Conditions

The Swedish Research Council's general terms and conditions for funding awarded to research and research-supporting activities

The terms and conditions were adopted by the Swedish Research Council on 19 December 2022. The terms and conditions apply for decisions to award funding made as from 1 January 2023. The terms and conditions shall be applied unless otherwise follows from the decision to award funding or from specific terms and conditions. In the event of a conflict between the general terms and conditions and specific terms and conditions issued for a decision, the specific terms and conditions shall take precedence.

Definitions

In these terms and conditions, the following definitions are used with the meaning stated below.

Administrating organisation

A legal entity approved by the Swedish Research Council as a recipient of research funding awarded.

Applicant

A physical person (project leader) or legal entity who has applied for funding from the Swedish Research Council and is responsible for planning and implementing activities according to the approved application.

Activities

The research or research-supporting activities covered by the Swedish Research Council's decision to award funding

Terms and conditions

These general terms and conditions and the specific terms and conditions that follow from a decision or call text.

1. About the Swedish Research Council's decisions and terms and conditions

1.1 Approval of terms and conditions

The Swedish Research Council's decision to award funding applies on condition that the administrating organisation and applicant agree to the terms and conditions according to the Swedish Research Council's instructions.

1.2 Responsibility to comply with terms and conditions

The administrating organisation and applicant are responsible for complying with the terms and conditions. If the administrating organisation is also the applicant, the administrating organisation is responsible for complying with the terms and conditions in both these capacities.

1.3 Period of validity of terms and conditions

The terms and conditions are valid as from their approval up to and including the date when final reports have been received by the Swedish Research Council or, as applicable, unused funds have been repaid and the case has been closed.

1.4 Changed preconditions for the Swedish Research Council's funding allocation
The Swedish Research Council may change its decision to award funding if the Swedish Research Council's Government appropriation is not as large as the amount the decision was based on, or if the preconditions for the Swedish Research Council's allocation of funding is changed in some other way.

2. Implementation

2.1 Implementation according to the decision and the terms and conditions
The administrating organisation and applicant are responsible for ensuring activities are implemented according to the Swedish Research Council's decision and the terms and conditions.

2.2 Implementation according to legislation as applicable in Sweden
The administrating organisation and applicant are responsible for ensuring activities are implemented according to legislation as applicable in Sweden.

2.3 Implementation according to the application
The applicant is responsible for ensuring activities are implemented as described in the application to Swedish Research Council. The responsibility includes planning and conducting activities mainly according to the application and plan for implementation submitted. Necessary changes to the implementation are allowed, provided they do not significantly impact on the activities as stated in the application, and they comply with the applicable terms and conditions. Other changes to the implementation require approval from the Swedish Research Council.

2.4 Scientific responsibility
If the activities include research, the applicant has scientific responsibility for the implementation of the research in respect of object and method. As scientifically responsible, the applicant is responsible for ensuring the research is implemented according to the application and research plan as stated in Section 2.3.

As scientifically responsible, the applicant shall also
• ensure that the research is implemented according to good research practice
• ensure that the permits and approvals required have been obtained before the research is started. These may include permits from the Swedish Medical Products Agency or approval from the Swedish Ethical Review Authority or an ethical committee on animal experiments.
• submit scientific reports according to the Swedish Research Council's instructions and
• publish the results of the research according to the Swedish Research Council's instructions and terms and conditions (see Section 3.1).

2.5 Organisational responsibility
The administrating organisation is responsible for ensuring there is a fit-for-purpose organisation for implementing the activities.

The responsibility includes
• in its capacity as employer, ensuring that the personnel involved, including the project leader, are able to use their working hours to the extent required to implement the activities according to the approved application which also includes publishing the results

• ensuring the personnel involved have access to premises, equipment and other resources required to implement the activities, and
• ensuring that the permits and approvals required have been obtained before the activities are started.

If the activities include research, the administrating organisation is also responsible for ensuring that
• the research is implemented according to good research practice
• the research does not have commercial ties that affect its objectivity, independence or openness, and
• a data management plan is drawn up before the research starts, and that the plan is maintained and complied with.

2.6 Reporting on implementation
The applicant is responsible for submitting reporting on the implementation of activities according to the Swedish Research Council's instructions.

2.7 Employment relationship
If the applicant is a physical person, they shall be employed by the administrating organisation stated in the decision to award funding or by another approved administrating organisation that, following an application to change, has been approved by the Swedish Research Council. The employment relationship shall exist at the start of the grant payment period and last throughout the payment period and any further availability period.

An exception from the requirement to be employed by the administrating organisation may be allowed, after approval by the Swedish Research Council, for applicants employed by a Swedish region but where activities are implemented at an other administrating organisation, or otherwise where the Swedish Research Council on application allows an exception.

2.8 Equipment
The administrating organisation shall be the owner of the equipment and other fixtures and fittings procured for the activities. The equipment shall be used for the activities for as long as they are conducted.

2.9 Changed preconditions for implementation
The administrating organisation and applicant shall inform the Swedish Research Council without delay if circumstances arise that entail the activities cannot be implemented within the availability period according to what follows from the application, grant decision, or terms and conditions. The same applies if equipment, for which purchase funding has been awarded, cannot be procured. In this case, the administrating organisation shall also report how the activities are affected by the equipment being impossible to procure.

2.10 Changing administrating organisations
If the activities can no longer be implemented at the administrating organisation due to changed circumstances, the Swedish Research Council may, on application from the administrating organisation and applicant, assess the issue of changing administrating organisations. The corresponding applies if the applicant is changing employers to another approved administrating organisation. An application to change administrating organisations shall be made in consultation with the administrating organisations involved.

2.11 Changing project leaders

If the activities can no longer be implemented due to changed circumstances for the project leader, the Swedish Research Council may on application approve a change of project leaders. The Swedish Research Council's decisions shall, if possible, be preceded by consultation with the project leaders.

2.12 Other funding
A precondition for the Swedish Research Council's decision is that the administrating organisation or applicant have not already received or will receive other funding for the same costs and purpose.

If other funding is awarded for the same costs and purpose, the administrating organisation and applicant must without delay notify the Swedish Research Council of this. The notice shall state what the overall funding for the purpose is, how the preconditions for the application the Swedish Research Council's decision was based on have been affected, and also to what extent other funding may impact on the implementation of the activities. The notice shall also describe any impact on the analysis, interpretation or reporting of the results, and also who will dispose of these.

The Swedish Research Council may change a decision to award funding on the basis of information about other funding.

3. Publication and dissemination of results and information

3.1 Publication of results
The applicant is responsible for ensuring the results of activities are published according to the Swedish Research Council's instructions. The obligation to publish results only applies to the extent the publication may be done according to legislation as applicable in Sweden.

The results of research shall be published in scientific journals and books with national and international reach, or be made available in another corresponding way. An agreement with a commercial actor or other stakeholder must not limit the opportunities to publish the results of research carried out with funding from the Swedish Research Council. Nor may such an agreement delay publication by more than two months. However, the delay may amount to at most four months if the purpose is to enable a patent application based, wholly or partly, on the research results referred to above.

Research results shall be published in accordance with the Swedish Research Council's guidelines for publication with open access.

The applicant is also responsible for ensuring research results of general interest are disseminated to recipients outside the research community.

3.2 Information about the Swedish Research Council's funding
When publishing or otherwise disseminating results, the applicant is responsible for ensuring it is stated that the activities were conducted with funding awarded by the Swedish Research Council. When publishing original scientific articles, the name "Swedish Research Council" and the registration number of the application to the Swedish Research Council shall be stated under the heading "Acknowledgements" or corresponding.

3.3 The Swedish Research Council's right to disseminate data
The Swedish Research Council may reproduce and disseminate whole or parts of reports from activities submitted to the Swedish Research Council, and also otherwise make available information about the activities.

4. Payment and use of the funding

4.1 Payment and availability period

The funding is paid out to the administrating organisation. The administrating organisation is responsible for receiving and administering the funding.
The decision to award funding states the period during which the funds will be paid out (the 'payment period'). Unless the decision states otherwise, the funding may be used for one additional year after the end of the payment period.

If special reasons exist, and following application, an extension of the period during which funding paid out is available may be allowed.
Such an application shall be submitted by the applicant and, as applicable, be approved by the administrating organisation via the Swedish Research Council's application system after the end of the payment period, but no later than 60 calendar days before the end of the availability period.

4.2 Use of the funding

Funding awarded shall be used to cover costs for implementing the activities according to the terms and conditions and mainly in the way stated in the application, however with such adjustments as may be required if the funding awarded is less than the amount applied for, or the grant period is shorter. For more major changes to the use of the funding, approval by the Swedish Research Council is required. A 'major change' refers to a change in the cost type of more than 25 per cent of the amount awarded, and entails a change that amounts to no less than 500 000 SEK, in relation to the entire grant period. Such as request shall be made by the administrating organisation and the applicant in conjunction with the need for the change arising.

The funding covers direct costs and indirect costs as a percentage of the direct costs, according to the cost basis decided on by the administrating organisation.

Funding awarded may only be used for annual depreciation costs for equipment during the period when the funding is available.

The funding awarded may not be used
- for scholarships
- for costs that are not directly related to implementing the activities, as described in the application
- to co-fund projects funded by grants from other research funding bodies, or
- for economic activities within the administrating organisation.

5. Financial reporting

5.1 Annual financial report

The administrating organisation shall submit an annual financial report to the Swedish Research Council. The financial report shall be submitted according to the Swedish Research Council's instructions.
The Swedish Research Council does not accept costs that are not directly related to implementing the activities, as described in the application.

5.2 Final financial report

The administrating organisation shall submit a final financial report no later than three months after the end of the availability period. The financial report shall be submitted according to the Swedish

Research Council's instructions. The Swedish Research Council may decide that the financial report shall be submitted at another time.
The Swedish Research Council does not accept costs that are not directly related to implementing the activities, as described in the application.

5.3 Final financial report if funding is discontinued or the activities are terminated early
If the Swedish Research Council decides that the funding shall be discontinued or if the activities are terminated early, the administrating organisation shall submit a final financial report to the Swedish Research Council within 30 days. The time is calculated from the day the activities were terminated early or the day the Swedish Research Council decided to discontinue the payment of funding. The Swedish Research Council may decide that the financial report shall be submitted at another time.

5.4 Final financial report after changing administrating organisations
If the Swedish Research Council has decided on a change of administration organisations, the retiring administrating organisation shall submit a final financial report to the Swedish Research Council within 30 days after the Swedish Research Council's decision.

5.5 Repayment of unused funding
Unused funding accounted for in the final financial report shall be repaid to the Swedish Research Council within 30 days after the final financial report was submitted via the Swedish Research Council's application system.

Unused funding corresponding to less than one half of a price base amount for the year the final report is submitted may be retained on condition that it can be used for purposes similar to that of the grant. If the unused funding exceeds one half of a price base amount, it must be repaid in its entirety.

6. Follow-up and audit

6.1 Providing information for follow-up, etc.
The administrating organisation and the applicant shall provide the information requested by the Swedish Research Council in conjunction with follow-up and evaluation of the activities, both during and after the payment period.

Accounts and reports relating to the activities funded by the Swedish Research Council shall be submitted according in the order stated in the decision to award funding, or when the Swedish Research Council so requests.

6.2 Audit
An auditor or corresponding appointed by the Swedish Research Council is entitled to scrutinise the book-keeping and reporting relating to the activities awarded funding by the Swedish Research Council. For this purpose, the administrating organisation shall give the person conducting the audit full insight, for example by supplying copies of all verifications relating to expenses and income attributable to the activities.

7. Actions if terms and conditions are not complied with

7.1 Demand to comply with terms and conditions and action plan
If the administrating organisation or applicant disregards or otherwise fails to comply with terms and conditions, and the failure cannot easily be corrected, the Swedish Research Council may require correction within a certain time. The Swedish Research Council may also require that the

administrating organisation or applicant submits an action plan describing when and how the terms and conditions will be complied with. The Swedish Research Council will evaluate whether the action plan can be approved, or whether the funding shall no longer be paid out.

7.3 Decision to discontinue payment of funding
The Swedish Research Council may decide to discontinue the payment of funding wholly or partly if
• there are no preconditions for implementing the activities according to the application, decision, or terms and conditions
• the funding has not been used according to the terms and conditions
• the applicant or the administrating organisation caused the funding to be awarded incorrectly or in too high an amount, through providing incorrect information or in some other way
• the funding was awarded incorrectly or in too high an amount for some other reason, and the administrating organisation or applicant should have realised this
• the applicant, or another person participating in the implementation of the activities, has been found guilty of scientific misconduct according to Swedish legislation on good research practice (SFS 2019:504), or in some other way has not complied with good research practice
• the applicant, in or in conjunction with the research, through actions or otherwise has shown themselves to be an unsuitable recipient of funding from the Swedish Research Council, or
• the terms and conditions have not been complied with in some other way, and the failure cannot easily be corrected.

Laerdal Foundation

1.

The following will be sent to the administrator of the Foundation within 12 months from date:
a.
a report of the progress/results of the project (e.g. an abstract, or a published article), and

b.
a specification of expenditures from the grant money, as well as total funding of the project.

2.

It is realized and agreed that the Foundation shall bear no responsibility for the project, whether legal, ethical or of any other nature.

It is further agreed that any involvement of patients/persons in the project shall be in accordance with the regulations of the Institutional Research Review Committee, or equivalent which is acceptable to the nation(s) concerned.

3.

In any publication about the project, the Laerdal Foundation will be referenced/.acknowledged.

4.

A final report within 3 years after receiving support.

5.

Should it, for whatever reason, not be possible to start the project for which financial support has been granted from the Foundation according to our application within 12 months from receipt of the grant, the grant will be returned to the Foundation.

SCHEDULE 3: FINANCIAL PLAN

This financial plan covers the setup and conduct of the Trial in the first 10 Study Sites.

Cost	Amount (SEK)
Project management and data collection	2 250 000
Ethics and regulatory submissions	250 000
Site monitoring	160 000
Study intervention and insurance	1 050 000
Total	3 710 000

SCHEDULE 4: PAYMENT PLAN

Invoice	Time period covered	Amount (SEK)
1 upon signing of this agreement	Jan 1 – December 31 2024	1 310 000
2 in Jan 2025	Jan 1 – Jun 30 2025	1 200 000
3 in Jul 2025	Jul 1 – Dec 31 2025	1 200 000