

BMJ Open Community-based Interventions to prevent serious Complications (CIVIC) following spinal cord injury in Bangladesh: protocol of a randomised controlled trial

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ABSTRACT

Introduction: In low-income and middle-income countries, people with spinal cord injury (SCI) are vulnerable to life-threatening complications after they are discharged from hospital. The aim of this trial is to determine the effectiveness and cost-effectiveness of an inexpensive and sustainable model of community-based care designed to prevent and manage complications in people with SCI in Bangladesh.

Methods and analysis: A pragmatic randomised controlled trial will be undertaken. 410 wheelchair-dependent people with recent SCI will be randomised to Intervention and Control groups shortly after discharge from hospital. Participants in the Intervention group will receive regular telephone-based care and three home visits from a health professional over the 2 years after discharge. Participants in the Control group will receive standard care, which does not involve regular contact with health professionals. The primary outcome is all-cause mortality at 2 years. Recruitment started on 12 July 2015 and the trial is expected to take 5 years to complete.

Ethics and dissemination: Ethical approval was obtained from the Institutional Ethics Committee at the site in Bangladesh and from the University of Sydney, Australia. The study will be conducted in compliance with all stipulations of its protocol, the conditions of ethics committee approval, the NHMRC National Statement on Ethical Conduct in Human Research (2007), the Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95) and the Bangladesh Guidance on Clinical Trial Inspection (2011). The results of the trial will be disseminated through publications in peer-reviewed scientific journals and presentations at scientific conferences.

Trial registration numbers:

ACTRN12615000630516, U1111-1171-1876.

Strengths and limitations of this study

- This will be the first large, high-quality trial to determine the effect of post-hospital community-based care on mortality in people with spinal cord injury. It is also among the first randomised trials of community-based care for people with physical disabilities in low- or middle-income countries.
- The results of this trial will have implications for the development of inexpensive models of care for people with spinal cord injury and possibly also other causes of physical disability in low- and middle-income countries.
- The trial is being conducted from one specialised spinal cord injury unit in Bangladesh, which may not be representative of all people with spinal cord injury or hospitals in low-income and middle-income countries.

INTRODUCTION

The incidence of spinal cord injury (SCI) in low-income countries is four times that in high-income countries.^{1–4} In most low-income countries, people who sustain a SCI are discharged home with little access to support services. Not surprisingly, they often then develop life-threatening complications. Many die within a few years of discharge.^{5–11} We have recently shown that 19% of wheelchair-dependent patients discharged from a large SCI unit in Bangladesh die within 2 years of discharge.¹¹ The median (interquartile) age in this sample was 32 years (25–44) and the most common cause of death was sepsis due to pressure ulcers.^{11–14} There are no directly comparable data from high-income countries but death

in the first 2 years following discharge in those <40 years of age is unusual.^{15 16}

Pressure ulcers and most other complications of SCI can be prevented and treated through education and with simple, inexpensive home-based treatments, as outlined in numerous international clinical practice guidelines.^{17–22} These include strategies such as the provision of foam overlays on beds, regular change in position, appropriate bladder drainage, high-fibre diet and good fluid intake. The key to successful prevention and treatment of complications is not costly or complex medical interventions, but rather, patient and family monitoring, education and support.^{3 23} High-income countries have well-developed systems to provide community-based health services, especially in the period immediately after discharge, when patients are most vulnerable to complications. But it is not economically feasible to provide the same services in low-income countries. An inexpensive and sustainable model of community-based care is required.

The high incidence of serious but preventable complications following SCI in Bangladesh suggests that a suitable intervention could yield large health and social benefits at relatively little cost.³ We have developed a low-cost, sustainable community-based model of care for people who have returned home after SCI. The model of care involves regular telephone-based monitoring and provision of ongoing education, support and advice, along with a limited home-based service. The service can be provided in the first 2 years following discharge, when patients are most vulnerable to complications. It is thought that if high-risk patients can be supported over the first 2 years, most will go on to learn self-help skills and will become competent at managing their disabilities.

Inexpensive, community-based models of care for people with physical disabilities in low-income and middle-income countries are widely advocated.^{24 25} So it is surprising that there is very little robust data that demonstrate the effectiveness or cost-effectiveness of such interventions. Existing community-based models of care in low-income and middle-income countries are generally not based on rigorous evidence. A systematic and evidence-based approach to the provision of healthcare for the disabled is required.^{26–29} In particular, a high-quality clinical trial is essential to provide unbiased and precise estimates of the effectiveness and cost-effectiveness of a sustainable model of community-based care for people with SCI.

Aim

The aim of the Community-based InterVentions to prevent serious Complications (CIVIC) trial is to provide unbiased and precise estimates of the effectiveness and cost-effectiveness of a model of community-based care for wheelchair-dependent people with SCI who have been discharged from hospital in Bangladesh. The primary hypothesis is that the community-based model

of care will be more effective than standard care in reducing all-cause mortality at 2 years. The secondary hypotheses are that the community-based model of care will be more effective than standard care in decreasing the burden of complications, decreasing the prevalence and severity of pressure ulcers, decreasing depression, improving quality of life, improving independence and increasing participation. In addition, it is hypothesised that the community-based model of care will be cost-effective from a health provider perspective.

METHODS AND ANALYSIS

Design

A pragmatic randomised controlled trial will be undertaken. The trial is investigator initiated. The protocol has been registered prospectively with the Australia New Zealand Clinical Trials Registry (ACTRN12615000630516).

Participants

The trial will have broad inclusion criteria in keeping with its pragmatic orientation. A person will be eligible to participate if he or she has sustained a traumatic or non-traumatic SCI within the last 2 years, is aged 15 years or over at the time of consent, is an inpatient at the Centre for the Rehabilitation of the Paralysed in Bangladesh, requires a wheelchair for mobility on a daily basis and is about to be discharged home. People will be excluded if they are planning to move to another country following discharge or if they are to be transferred to another hospital for medical care. Participants will be provided with trial information sheets. Trial staff will obtain written informed consent from all participants prior to inclusion in the trial.

Recruitment strategy and time frame

Four hundred and ten patients will be recruited prior to their discharge from the Centre for the Rehabilitation of the Paralysed. The Centre is a 100-bed spinal injury unit that admits 360 patients a year, making it one of the largest spinal injury units in the world.³⁰ We estimate that it will take 2 years to recruit the required sample based on data collected from admissions and discharges in 2011.¹¹

Recruitment started on 12 July 2015. Fifty-three participants were randomised between that date and 22 October 2015.

Assignment of intervention

Randomisation is stratified by severity of injury (paraplegia or tetraplegia). The allocation schedule was computer generated by an Australian-based investigator (RH). The schedule is concealed from potential participants, trial staff and investigators, except one investigator (RH) and two India-based trial staff members not involved in recruitment. Randomisation will occur shortly after discharge from hospital. The site coordinator will contact the central randomisation unit by email, whereupon the

central randomisation unit will notify the site coordinator of treatment assignment. Eligible participants will be randomised to one of two groups: an Intervention group that will receive community-based care or a Control group that will receive standard care.

Interventions

Intervention group

Participants allocated to the Intervention group will receive telephone-based support and a limited number of home visits in the first 2 years following discharge. Community-based healthcare workers or healthcare professionals will contact participants by telephone fortnightly in the first year and monthly in the second year. During the call, participants will be screened for complications using purpose-designed forms. Specifically, the healthcare workers will screen participants for pressure ulcers, urinary tract infection, bowel impaction, bladder infection, depression, autonomic dysreflexia and respiratory complications. At the first indication of any of these complications, the healthcare workers will provide advice to participants and their families about management, and then closely monitor them by telephone until the complication is resolved. The healthcare workers will refer participants to local service providers where necessary and when possible. The advice will follow international clinical practice guidelines^{17 18 20–22 31–34} appropriately modified for the Bangladesh context. Where available and appropriate, the camera and video facilities of smartphones will be used to help monitor a participant's condition. The healthcare workers will also provide ongoing education, support and advice over the telephone. They will reinforce self-help strategies important for preventing complications, minimising psychological stress and enhancing social engagement. They will also speak to and support participants' families.

On three occasions, the healthcare workers will also visit participants and their families in their homes. There will be two home visits in the first year and one home visit in the second year. At each home visit, the healthcare worker will assess the participant's home situation and provide advice as needed. For example, they will review cushions and mattresses used to prevent pressure ulcers, and provide advice on wound treatment, bladder and bowel management, and other aspects of ongoing care. Healthcare workers will seek solutions to mobility and self-care limitations. On the first home visit, the healthcare workers will also provide participants with a pictorial educational booklet specifically created for the trial. Participants will be provided with items of care such as wound dressings and urinary catheters if they cannot otherwise afford these items. The number of phone calls and home visits provided to the Intervention participants will be monitored.

Control group

Participants allocated to the Control group will receive the level of postdischarge care currently provided by the

Centre for the Rehabilitation of the Paralysed. That is, a social worker may telephone participants once after discharge. In addition, participants with tetraplegia deemed at high risk of complications by the social worker may receive one home visit. The format of these telephone contacts and home visits will not be structured but will typically include a discussion around any problems since discharge.

Outcome measures

Outcomes will be measured at 2 years in participants' homes. Most outcomes will also be measured at baseline (ie, prior to randomisation while participants are still in hospital). Outcome data will be collected by blinded assessors. The success of blinding (patterns of belief about allocations of participants) will be monitored and reported. Extensive contact details for all participants will be collected at baseline to minimise loss to follow-up.

The primary outcome is all-cause mortality. Bangladesh does not have a death registry so the date of death will be confirmed by interviewing next of kin or carers at 2 years. Wherever possible, independent corroboration of the date of death will be obtained, for example, from local community leaders.³⁵

The secondary outcome measures will be burden of complications, prevalence and severity of pressure ulcers, depression, quality of life, independence and participation. Questionnaires used to elicit self-reported outcomes will be administered in the Bangla language, under the guidance of the assessor. The details of each secondary outcome are as follows:

1. *The burden of complications* will be measured using the SCI Secondary Conditions Scale (SCI-SCS).^{36 37} This is a 16-item scale. Each item is scored from 0 (did not experience the complication in the last 3 months) to 3 (significant or chronic problem over the past 3 months). The score for each item will be determined by the assessor after asking the participant any question deemed relevant and after physically examining the participant, if necessary. The scores will be summed to provide an overall score with a total possible score of 48, where 0 represents no complications and 48 represents severe complications over the past 3 months. Incidence of complications over the 2-year period after discharge will not be measured because doing so would require ongoing monitoring of participants in the Control group, which is not feasible and could contaminate the intervention.
2. The presence of pressure ulcers will be evaluated by the assessor. He or she will inspect the participant's skin for pressure ulcers. Skin damage due to injuries not related to pressure (eg, cuts or burns) will not be included. Prevalence of pressure ulcers at 2 years, rather than incidence of pressure ulcers over 2 years, will be measured to avoid the need for ongoing monitoring of participants in the Control group.

- This would not be feasible and could contaminate the intervention.
- Severity of pressure ulcers will be assessed using the Pressure Ulcer Scale for Healing V.3 (PUSH). The assessor will examine the participant and rate any pressure ulcers on a scale of 0–17. The rating takes into account the area of the pressure ulcer, amount and type of exudate, and extent of tissue damage.³⁸ Area of the pressure ulcer will be measured using commercially available grid paper designed for this purpose. If a participant has more than one pressure ulcer, the worst pressure ulcer will be assessed. The PUSH is the most widely used tool for assessment of pressure ulcers and has demonstrated validity and sensitivity.^{39 40}
 - Depression will be assessed using the Center for Epidemiologic Studies Depression Scale revised version (CESD-R). The CESD-R is a widely used instrument to screen for depression and depressive disorders. It measures symptoms defined by the American Psychiatric Association Diagnostic and Statistical Manual (DSM-IV) for a major depressive episode. The questionnaire contains 20 items, each scored on a four-point scale. Each item refers to feelings in the past week. Scores are tallied to a total score of 60, where higher scores are indicative of more depressive symptoms. The CESD-R has been translated into the Bangla language.^{41 42} The questionnaire will be administered as a self-reported questionnaire under the guidance of the assessor.
 - Health-Related Quality of Life will be self-assessed using the Short Form Health Survey-12 (SF12) questionnaire. The SF12 consists of 12 questions designed to measure functional health and well-being from the individual's perspective, and is derived from the physical and mental domains of the SF36. The questionnaire has been translated into the Bangla language⁴³ and will be administered as a self-reported questionnaire under the guidance of the assessor.
 - Independence will be assessed using the Spinal Cord Independence Measure Self Report (SCIM-SR).⁴⁴ This is a 16-item test covering key aspects of independence. It rates self-care (4 items), respiration and sphincter management (4 items), and mobility (8 items).⁴⁵ Each item is scored and weighted differently but summed to an overall score of 100 points, where a higher score reflects more independence than a lower score. The SCIM is a valid and sensitive measure of independence for this population.^{46–48} The self-report version⁴⁴ intended for telephone interview will be administered by the assessor during the face-to-face assessments.
 - Participation will be assessed using the eight participation items of the World Health Organisation Disability Assessment Schedule V.2 36 Item self-report questionnaire (WHODAS 2.0).⁴⁹ WHODAS 2.0 is a generic assessment tool for measuring health and disability. It was developed to be administered for all health conditions, across all cultures, and is valid in both, clinical and general populations. The participant is asked how much of a problem they have had with each item over the past 30 days. Each item is scored on a five-point scale ranging from none (1 point) to extreme/cannot do (5 points). The scores will be tallied to provide an overall score with a total possible score of 40, where 0 represents no problems with community participation and 40 represents extreme problems with participation. The officially translated Bangla version of the WHODAS will be administered as a self-reported questionnaire under the guidance of the assessor.
 - Out-of-bed, out-of-house and employment activities will be assessed only at the 2-year assessment. These three additional questions ask participants if they (i) got out of bed, (ii) got out of the house and (iii) engaged in paid work in the preceding week; and if so, on how many days in the preceding week this occurred. The questions have been devised specifically for this trial and translated into the Bangla language. The three questions will be self-administered under the guidance of the blinded assessor.
- In addition, cost data will be collected. Participants will be asked to estimate the costs incurred over the 2 years since discharge that relate to their SCI. This may include, for example, costs of hospitalisation, visit to doctors or healthcare workers, transport for medical or rehabilitation care, catheters, wheelchairs, cushions, mattresses, vocational training, set-up for new employment, wound dressings, medications, standing or rehabilitation equipment, home modifications and vocational training. The costs of care and goods or services provided as part of the trial, including staff and training costs, will also be assessed. If participants do not know the costs of an item or service, they will be asked to provide a detailed description so an estimate of the cost can be obtained.

Sample size

The sample size of 410 gives a better than 80% probability of detecting an increase in survival from 83%¹¹ to 93% at 2 years with a two-sided log-rank test, uniform follow-up time of 2 years, loss to follow-up in both groups of 15% at 2 years and α of 0.05.

Data analysis

Statistical plan

All analyses will be conducted on an intention-to-treat basis, with the possible exception of secondary analyses, which will estimate complier average causal effects and survivor average causal effects. Complier average causal effects⁵⁰ on primary and secondary outcomes will be estimated if there is substantial non-compliance with the intervention, and survivor average causal effects⁵¹ of secondary outcomes will be estimated if there is a substantially different survival in the Intervention and Control groups. The analysis will follow a detailed statistical plan developed prior to inspection of the data.

Effectiveness analysis

The primary effectiveness analysis will compare the rates of all-cause mortality in the Intervention and Control groups using the log-rank test (two-tailed $\alpha=0.05$). Between-group comparisons of secondary outcomes will be conducted using linear models. In these models, the outcome will be a linear function of a dummy-coded variable representing group membership (Intervention or Control group) and a dummy-coded variable for stratum (paraplegia or tetraplegia). Baseline scores will be included in the model to increase statistical precision and statistical power.⁵² If more than 5% of data are missing for a particular analysis, multiple imputation will be used to account for the missing data provided the assumption of missing at random appears plausible.⁵³

Cost-effectiveness analysis

The cost-effectiveness analysis will initially involve a trial-based economic evaluation based on differences observed between groups in costs, overall survival and quality-adjusted survival at 2 years. This will enable an estimate of an incremental cost per Quality Adjusted Life Year of the intervention over standard care.

Given that the potential survival advantage will largely be that which occurs beyond 2 years, a model-based evaluation will be conducted through a state-transition model that extrapolates long-term costs and outcomes (survival and quality of life). A literature review and trial data will be used to establish the parameters in the model, including transition probabilities between health states, and costs and quality of life associated with such states. Locally relevant life tables will be used to estimate survival. These analyses will be based on the perspective of the healthcare provider. We recognise that this perspective is limited and that a broader perspective would capture costs borne by people with SCI (eg, for local healthcare services or equipment) and society. However, such costs are normally captured by diary-keeping or regular telephone follow-up. In the context of this trial, it is not feasible to ask participants to keep diaries, and regular follow-up of Control group participants would risk contamination of interventions. Instead, by taking the perspective of the healthcare provider, we will identify, measure and value costs incurred by provision of services to both, the Intervention and Control groups. Costs will be valued using standard economic evaluation guidelines. Costs will be expressed in real terms. Future costs and outcomes will be discounted at 5% per annum. The robustness of findings will be examined in sensitivity analyses.

As in all economic evaluations, the costs captured in this trial are likely to be skewed, so non-parametric bootstrap methods will be used for hypothesis tests and interval estimation. A threshold incremental cost-effectiveness ratio of three times gross domestic product per capita will be used to assess value for money.⁵⁴

Data integrity

Data will be collected in paper format, transferred to George Clinical India, and entered into an electronic database. The data files will have identifying information removed and will be kept confidential and secure, but the data will be re-identifiable. The original Case Report Forms will be stored at the Centre for the Rehabilitation of the Paralysed. Electronically transcribed data will be stored and managed by the Biostatistics and Data Management Division of George Clinical India. Data will be double-entered with automated checks for errors. Data queries will be emailed to the site coordinator and stored on the database. George Clinical India has rigorous procedures for data protection and backup in place.

Trial management

The trial will be managed by a Steering Committee, a Management Committee and an Advisory Committee.

Site monitoring

Trial monitoring will be performed by staff from George Clinical India in coordination with the Senior Project Manager and the Clinical Research Associate. George Clinical India is affiliated with the George Institute of Global Health, Australia, and has extensive experience managing and monitoring large-scale clinical trials in Asia. Best practice conduct of the trial will be ensured through frequent monitoring by phone and in person (where possible). Site visits and site contacts will enable the independent monitors to maintain current, personal knowledge of the trial through review of the records, comparison with source documents, and observation and discussion of the conduct of the trial with the investigators and Site Coordinator. The monitors will be responsible for monitoring adherence to the protocol and with local and international guidelines,⁵⁵⁻⁵⁷ as well as ensuring completion of the Case Report Forms and other documentation. In order to ensure the accuracy of data, the monitors, auditors, regulatory agencies, representatives of the Steering Committee, Management Committee and Ethics Committee will be given direct access to source documents, if requested. Anonymity of participants will be maintained at all times.

Trial monitoring

An independent Data Monitoring Committee (DMC) will meet periodically to monitor the safety of trial participants and the quality of trial data. The responsibilities and procedures of the DMC have been detailed in a DMC Charter.⁵⁸ The DMC will conduct an unblinded interim analysis of effectiveness and safety end points once 205 participants have completed the trial. The DMC may recommend continuing the trial, early termination of the trial, or modification of the trial. A recommendation to terminate the trial early will be made only if there is clear evidence of a clinically important beneficial or harmful effect. The trial will not be stopped early on the grounds of futility.

Provenance and ethical review

The study will be conducted in compliance with all stipulations of this protocol, the conditions of ethics committee approval, the National Health and Medical Research Council National Statement on Ethical Conduct in Human Research (2007),⁵⁹ the Note for Guidance on Good Clinical Practice (CPMP/ICH-135/95)⁵⁶ and the Bangladesh Guidance on Clinical Trial Inspection (2011).⁵⁵

Ethical approval will be sought for all protocol modifications. Any changes to the protocol will be updated on the registry.

Serious adverse events

A serious adverse event will be defined as any event that results in death, is life-threatening, requires inpatient hospitalisation or prolongation of existing hospitalisation, or results in a persistent or significant disability or incapacity. Serious adverse events will be recorded and reported to the lead Human Research Ethics Committee.

Dissemination plan

The results of this study will be published in peer reviewed journals. It is expected that the principal investigators will co-author primary reports of the trial. Associate Investigators and trial staff may also be invited to author publications where appropriate (eg, provided they comply with the International Committee of Medical Journal Editors' policy on authorship) at the discretion of the Steering Committee. Results will also be presented at national and international conferences. To maximise the benefits to research, the re-identifiable data may be provided to approved and appropriately qualified researchers for use in future as-yet unidentified research studies.

DISCUSSION

The CIVIC trial will provide unbiased and precise estimates of the effectiveness and cost-effectiveness of an inexpensive and sustainable model of community-based care for people with SCI in Bangladesh. Evidence of effectiveness and cost-effectiveness will have widespread implications for provision of health services for people with SCI and other conditions that cause serious disability in low-income and middle-income countries.

It is anticipated that the trial will take 5 years to complete. The first participant was randomised on 12 July 2015. It is expected outcome assessments will be completed in 2019.

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Contributors MSH, LAH, RDH, IC, RL, SJB, SM and VT were responsible for the design of the intervention and the trial. MSH, LAH, RDH, IC, RL, SJ, SM, VT, FB-S, IC, RL and HSC secured funding. RDH and QL are responsible for statistical design and analysis. JB is responsible for trial support, including contributions to data acquisition and analysis and drafting the work. SJ is responsible for the economic analyses. MSH, MSI, VT, SM and AR are responsible for the local site. MD is the trial coordinator. All the authors have read and approved the final manuscript.

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Competing interests None declared.

Ethics approval Ethics Review Committees of the Centre for the Rehabilitation of the Paralysed, Bangladesh (CRP-R&E-0401-126), and the University of Sydney, Australia (2015/041).

Provenance and peer review Not commissioned; peer reviewed for ethical and funding approval prior to submission.

Data sharing statement To maximise the benefits to research, the re-identifiable data may be provided to approved and appropriately qualified researchers for use in future as-yet unidentified research studies.

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