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HIPCARE: A cluster randomised controlled trial with embedded process evaluation to investigate the clinical and cost effectiveness of multidisciplinary care in the management of patients with a fracture of the hip

Short title: HIPCARE

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The investigators declare no potential conflicts of interest

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1. LAY SUMMARY

The aim of this project is to improve quality of life for patients following hip fracture and to reduce healthcare costs related to hip fracture in Low- and Middle-Income Countries (LMIC) in Asia.

Background to the research

Older people are more likely to break (fracture) a bone such as a hip or wrist because of a fall, as their bones are weakened by osteoporosis. These 'fragility' fractures have serious consequences; in the UK, one in four patients who break their hip die within a year, and survivors have a reduction in their quality-of-life similar to having a stroke. Outcomes may be even worse in LMIC without the same level of healthcare resource.

Asia is particularly affected by rapidly ageing populations. The number of people experiencing hip fractures is expected to increase from 1.1 million now to 2.6 million in 2050. The healthcare costs will increase from US$9.5 billion to US$15 billion. Improving the care for patients with a hip fracture is therefore a priority in this region.

Looking after older, often frail, patients following a hip fracture requires healthcare workers from many different backgrounds to work together. These include surgeons, doctors specialising in looking after older patients, nurses and therapists. In the UK, this approach has reduced the number of people dying after hip fracture and improved their quality of life. This study is about testing the benefits of such 'multi-disciplinary' care in LMIC in Asia.

Design and methods

The main aim of this study is to see if the quality of life for patients in LMIC after hip fracture can be improved with the introduction of multi-disciplinary care and whether it reduces healthcare costs, compared with usual care.

The HIPCARE intervention is designed to address three key elements of multidisciplinary care to speed recovery: early surgery to fix the hip fracture, early assessment of patients by a doctor specialising in care of older people and early walking with the help of a healthcare worker.

After refining training materials to make the HIPCARE intervention specific to each country, we will do a large study to compare HIPCARE with usual care in approximately 40 hospitals across 5 LMIC. Half the hospitals will have the HIPCARE intervention and half continue with their usual care. Patients from 'usual care' and 'HIPCARE' hospitals will be asked to report their health-related quality of life before their injury and again 4 months after. Information about cost of the treatment and any care they receive in the 4 months after their injury will also be collected.

Community engagement

This proposal has been co-produced with members of the Global Health Fragility Fractures Community Engagement and Involvement Group. The views of patients and their carers, from Asia and the UK, informed all aspects of the study but in particular the choice of eligibility criteria and follow-up plan.

Dissemination

We will share the findings of this study in three ways:

1. Through plain language summaries specific to each country via social media and webpages as well as via printed hard-copies.

2. Through our partnership with the Global Fragility Fracture Network, with its many events worldwide.
3. Through scientific publications and presentations.

2. SYNOPSIS

Study Title	HIPCARE: a cluster randomised controlled trial with embedded process evaluation		
Short title	HIPCARE		
Study registration	ISRCTN23534273		
Sponsor	University of Oxford		
Funder	National Institute for Health and Care Research, Research and Innovation for Global Health Transformation (RIGHT).		
Study Design	Cluster randomised trial with embedded process evaluation		
Study Participants	Patients aged 60 years or over having surgery for a hip fracture		
Sample Size	4320 patients		
Planned Study Period	Study period: Nov 2022 – Mar 2027		
Planned Recruitment period	Nov 2024 – July 2026 Participants will be involved up to 120 days post-surgery.		
Overall Project Aim	To deliver a cluster randomised trial of the HIPCARE training package with embedded process and economic evaluations. *Analysis of the objectives below will be performed for the entire study population as well as for each LMIC individually.*		
	Objectives	**Outcome Measures**	**Timepoint(s)**
Primary aim cluster RCT	To compare Health-Related Quality of Life between treatment groups at 120 days post-surgery	Health-related Quality of Life Score (EuroQol): EQ-5D–5L	Baseline*, 120 days post-surgery
Secondary aims cluster RCT	To compare mortality between the treatment groups in the first 120 days post-surgery	Mortality	120 days post-surgery
	To compare mobility between the treatment groups at 120 days post-surgery	Modified New Mobility Score	Baseline*, 120 days post-surgery
	To compare the proportion of participants who have returned to their pre-fracture residential status by 120 days post-surgery	Bespoke Residential Status questionnaire	Baseline*, 120 days post-surgery
	To compare complication rate within the first 120 days post-surgery	Medical records and bespoke participant questionnaire	120 days post-surgery

	To compare healthcare and broader resource implications within the first 120 days post-surgery	Medical records and bespoke participant questionnaire	Baseline*, 120 days post-surgery
	To estimate the cost-effectiveness of the trial treatments	Medical records and bespoke participant questionnaire, plus the EQ-5D-5L	120 days post-surgery
Intervention(s)	HIPCARE intervention		
Comparator	Usual care		

** Pre-injury baseline data will be collected retrospectively*

3. ABBREVIATIONS

CRF	Case Report Form
CEI	Community Engagement and Involvement
RGEA	Research Governance, Ethics & Assurance Team, University of Oxford
GCP	Good Clinical Practice
LMIC	Low- and Middle-Income Countries
NHFD	National Hip Fracture Database
NGT	Nominal Group Technique
RES	Research Ethics Service
PI	Principal Investigator
PIS	Participant/ Patient Information Leaflet
PPI	Patient and Public Involvement
R&D	Research &Development Department
REC	Research Ethics Committee
REDCap	Research Electronic Data Capture
SARA	Service Availability and Readiness Assessment
SOP	Standard Operating Procedure

4. BACKGROUND AND RATIONALE

4.1. What is the problem being addressed?

Older people frequently sustain fractures after falls from a standing height, as their bones are weakened by osteoporosis. These 'fragility' fractures have serious consequences; 25% of hip fracture patients in the UK die within a year and survivors have a reduction in their health-related quality of life similar to having a stroke.[1]

The outlook is likely to be even worse for people in low- and middle-income countries (LMIC) with fewer resources to support recovery and long-term care. The number of patients with fragility fractures is increasing dramatically in LMIC, as more and more people live into older age (*Figure 1*).

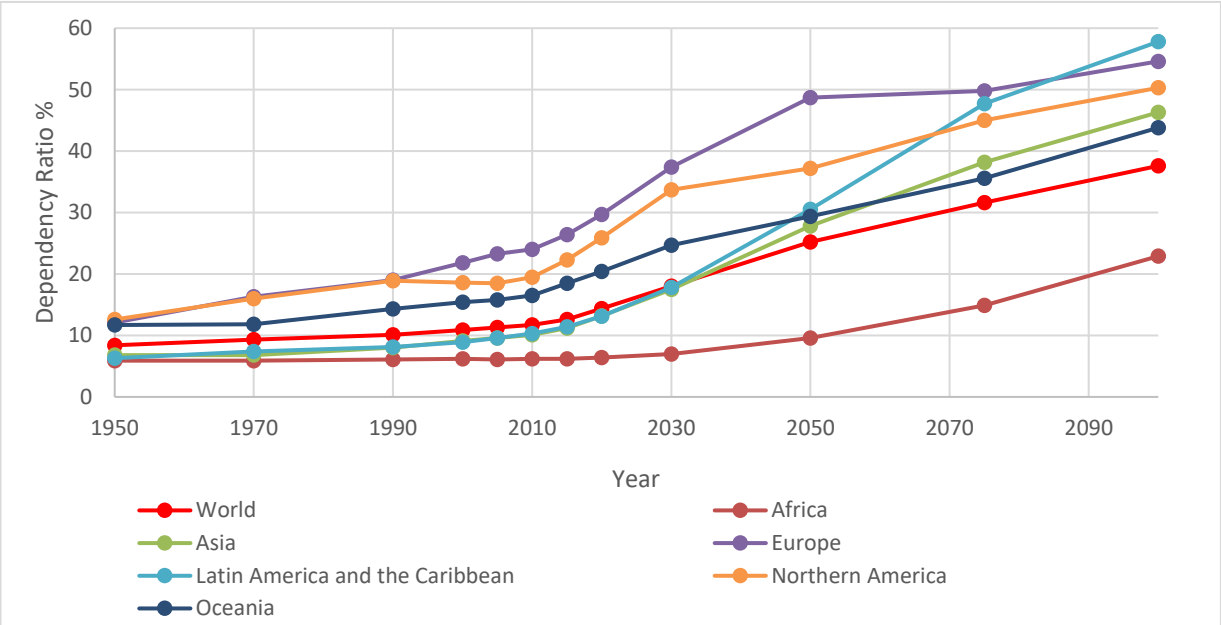

Figure 1: Old-age dependency ratios for the World and World regions for 1950-2100 (From World Population Prospects: Volume II: Demographic Profiles 2017 Revision. ST/ESA/SER.A/400, by Department of Economic and Social Affairs, Population Division, ©2017 United Nations)

Hip fracture is the most common fragility fracture requiring treatment in hospital. Many higher-income countries have introduced multidisciplinary care pathways for patients with hip fracture. Multidisciplinary care involves nurses, therapists, surgeons and medical specialists working together as a team with joint responsibilities and defined accountabilities. Each group of healthcare workers targets specific aspects of care to support the work of their colleagues; for example, surgeons and anaesthetists working towards early surgery, and physiotherapists and nursing staff to facilitate early mobilisation.

In high-income countries, we have shown that implementing a programme of multidisciplinary teamwork reduces mortality following hip fracture, improves patients' health-related quality of life and reduces economic costs. However, a multidisciplinary team approach to hip fracture is rare in LMIC settings.

This proposal aims to test a multidisciplinary team support package for improving the care provided to patients with hip fracture in LMIC in Asia, with the objective to reduce the global burden of unintentional injuries and urgent and emergency care.

4.2. Why is this research important in terms of improving the health and/or wellbeing of the public and/or to patients and health and care services?

The number of people with fragility fracture is increasing rapidly in many LMIC. Asia is particularly affected by rapidly ageing populations; a study in nine countries predicts a two-fold increase in the number of hip fractures alone, from 1,124,060 in 2018 to 2,563,488 in 2050.[2] Associated healthcare costs will increase from US$9.5 to $15 billion.[3] If healthcare systems in LMIC in Asia do not improve outcomes and, thereby, reduce the economic costs of caring for patients with hip fracture, their healthcare systems will be overwhelmed.

4.3. Review of existing evidence - How does the existing literature support this study?

Research from the UK, from our group and others, shows that introducing multidisciplinary teamwork for patients with hip fracture reduces mortality and improves health-related quality of life for patients whilst also reducing hospital bed days and associated healthcare costs.[4–8]

Research from LMIC in Asia shows that multidisciplinary shared care is rare. Our previous mixed methods study in India identified key gaps in management of hip fracture, with only 30% of patients receiving surgery within 48 hours of hospitalisation, and healthcare providers reporting inadequate access to resources, e.g. early physiotherapy, preventing timely treatment.[9] Similarly, our recent study from China highlighted long delays to surgery and lack of availability of geriatrician assessment.[10] However, the same hospital subsequently showed that a multidisciplinary care intervention could not only significantly reduce time to surgery but also improve other outcomes, and was cost-effective.[11,12]

In preparation for the HIPCARE project we used the framework of the World Health Organization's Service Availability and Readiness Assessment (SARA) to assess the service availability and readiness for managing patients with hip fracture in each partner LMIC. Over a period of 18 months, a bespoke data collection platform was used to collect resource availability and service readiness data from a subset of hospitals treating patients with hip fracture in each partner LMIC (~20 hospitals in each country).

SARA methodology uses systematic data collection to generate tracer indicators of service availability and readiness:

- *Service availability*: Mapping the number of facilities and beds per head of population, the healthcare workforce and those facilities specifically available for inpatient and community/social care, in each LMIC.
- *Service readiness*: Mapping the basic amenities, equipment, diagnostic services and medicines/implants available at a facility level in each LMIC.
- *Service-specific readiness:* Mapping the service readiness in each LMIC for the care of patients with fragility fracture of the hip specifically, including the current provisions for surgery, senior medical review and early mobilisation.

Results of this preliminary work showed that in 2020-21 the median time to surgery in Thailand was 3-4 days compared with 5 days or more in the Philippines and Nepal. Similarly, while specialist orthogeriatricians were available in many centres in Vietnam and India, rehabilitation medicine specialists provide much of the medical care for hip fracture patients in the Philippines and Thailand. And while nursing and physiotherapy staff were available in nearly all centres, they were not usually empowered to mobilise hip fracture patients with full weight-bearing on the first day following surgery.

This exploratory work gave us a detailed understanding of the current resources and service readiness in each country, leading to the development of the HIPCARE proposal.

Community engagement and involvement. In parallel to the quantitative study described above, we worked with the World Musculoskeletal Trauma Patient and Public Involvement (PPI) Group to learn about the patient experience and priorities of patients suffering fragility fractures in LMIC in Asia. The World Musculoskeletal Trauma PPI Group is represented on the Project Management Group (PMG) by the UK CEI representative.

5. OBJECTIVES

The primary objective is to improve health-related quality of life for patients following hip fracture and to reduce healthcare costs in LMIC.

The aim is to deliver a cluster randomised trial of the HIPCARE intervention with embedded process and economic evaluations.

Within the cluster RCT, the following objectives will be assessed for the entire study population and each LMIC individually:

i. To compare Health-Related Quality of Life between the treatment groups at 120 days post-surgery.
ii. To compare mortality between the treatment groups within the first 120 days post-surgery.
iii. To compare mobility between the treatment groups at 120 days post-surgery.
iv. To compare the proportion of participants returning to their pre-fracture residential status by 120 days post-surgery between the treatment groups.
v. To compare the complication rate between the treatment groups within the first 120 days post-surgery.
vi. To compare the healthcare and broader resource implications for both treatment groups up to 120 days post-surgery.
vii. To estimate the comparative cost effectiveness of the treatments up to 120 days post-surgery.

In addition, this study will consolidate a research collaboration and sustainable infrastructure that can be used to facilitate future service improvement in each LMIC.

6. STUDY DESIGN: Cluster RCT

The proposed randomised trial will be conducted using a cluster design, with allocation of the two trial groups done at the level of the recruiting hospital. For those participants treated in hospitals randomly allocated to the standard of care group of the trial, there will be no change to the treatment pathway they follow. The hospitals allocated to the HIPCARE intervention group will receive support on how to optimise the care pathway for hip fractures. This will be introduced as a policy change so the optimised approach will be adopted for all patients presenting to the hospital during the trial period. In both usual care and HIPCARE intervention hospitals, only one treatment pathway will be available and as such participants will not need to consent for the randomised element of the trial. The information they receive during the informed consent discussion will highlight the need to assess quality of life and levels of care required after a hip fracture, to improve care for all hip fracture patients. Consent will be sought for the collection of data already collected by the hospital as well as collection of patient-reported outcomes. Members of the CEI

group advocated for this approach. CEI representatives have often indicated that the randomisation component of any research trial is the most difficult part to understand. It is therefore expected that this simplified approach will benefit this group of often frail people during an already stressful period. The exact details of the consent procedure will be developed with each LMIC, with input from the local/national ethical boards where appropriate and described in the country-specific protocol.

7. PARTICIPANT IDENTIFICATION

7.1. Study Participants

Patients aged 60 years or over having surgery for a hip fracture.

7.2. Inclusion Criteria

Patients aged 60 years or over, having surgery for a hip fracture. The participant may not enter the study if they or a carer are unlikely to be available for follow-up at 120 days, e.g. foreign national returning to another country.

The eligibility criteria have been kept as broad as possible to ensure that the cohort of patients can be generalised as widely as possible to the background population with hip fractures. Throughout the study, screening logs will be kept to determine the number of patients assessed for eligibility and reasons for any exclusion.

8. PROTOCOL PROCEDURES

8.1. Setting

An academic/academic-related institution in each LMIC will act as the Trial Coordinating Centre – the LMIC co-applicants (Country Lead Investigators) will take a leading role for all activities at their Trial Coordinating Centre.

A Trial Coordinator will be appointed in each Trial Coordinating Centre to facilitate financial and contractual aspects associated with the grant, obtaining relevant approvals, training of research staff in the recruiting hospitals within their LMIC and to oversee the data collection process.

All recruiting hospitals will identify a Principal Investigator (PI), as well as a clinical trainee/associate PI, and will be provided with funds to appoint a research nurse to assist with the screening, recruiting and consenting of patients. The Country Lead Investigator will provide support to the PIs and their teams at the recruiting hospitals. Recruitment will be conducted at 8 hospitals in Nepal, India, the Philippines, Thailand and Vietnam, that each treat 200+ patients with hip fractures annually.

Follow-up of participants for research purposes after discharge will be organised centrally by the Trial Coordinating Centre in each LMIC.

8.2. Recruitment

A member of the clinical team, with routine access to the patient's personal data, will review each hip fracture patient to determine their age and whether they will be scheduled for surgery. Potentially eligible patients will then be screened and assessed for eligibility for entry into the study.

8.3. Screening and Eligibility Assessment

Participation will be offered regardless of the patients' gender, sexual orientation, marital status, ethnicity, religion, disability or socio-economic status. Screening logs will be kept at each recruitment centre to determine the number of eligible patients. Information will be gathered on the number of patients willing to participate, how many declined to provide consent and total number that were not approached for participation. Reasons for declining consent and for not approaching eligible patients will be recorded. Screening and recruitment data will be reviewed by the Trial Management Team to assess whether representative samples of patients are being approached and mitigate any selection bias occurring in any of the recruitment centres with regard to approach and inclusion/exclusion of specific groups of patients. Continued training of site staff on accurate and inclusive screening and recruitment will be through newsletters, regular Q&As/top tips, and refresher sessions.

8.4. Informed Consent

A member of the local research team in the recruiting hospitals will provide each eligible patient and/or their carer/next of kin with verbal and/or written study information as appropriate. As only one arm of the trial will be available in each hospital (usual care or HIPCARE intervention), patients will be asked if they are willing to provide informed consent for the collection of routine hospital data and the provision of baseline and follow-up questionnaire data. We will not ask for patient consent for the randomisation process as this will be applied at a hospital level before their participation. The patient will be given the opportunity to ask questions and discuss the study with their family and carers before deciding on participation.

It is anticipated that approximately 30-40% of hip fracture patients will lack capacity (permanently or temporarily) at the time when consent is being sought. As directed by the World Musculoskeletal Trauma Community Engagement and Involvement Panel, best efforts will be made to involve patients who, temporarily or permanently, lack capacity in the decision to be involved in the study. The CEI members felt that this was an important group of patients to include as they may benefit as much, or even more, than other patients from improvements in care pathways. The clinical team will make a judgement about the amount and complexity of the research information that the participant is able to understand and retain on an individual basis.

In accordance with national/local legislation, where a patient does not have capacity to consent for themself, we will seek agreement from an appropriate consultee or equivalent. Participants may decline to consent or withdraw from the study at any time without prejudice. If the participant withdraws from the study, data collected up until the point of withdrawal will be included in the final analysis.

8.5. Randomisation

Hospitals will be randomised to HIPCARE or usual care, via a centralised computer-based process stratified by country and will be carried out in advance of the start of recruitment using random permuted blocks within country. The HIPCARE intervention will be introduced in the hospitals allocated to the intervention as a policy change, which means that during the trial period all eligible patients, regardless of study participation, will follow the care pathway as outlined in the country specific HIPCARE instructions. Therefore, patients will not individually consent to the randomisation but will be asked for their consent for follow-up within the study.

8.6. Treatment groups

8.6.1. INTERVENTION

The hospitals allocated to the HIPCARE intervention group will receive support on how to optimise the care pathway for hip fractures. It is expected this optimised approach will be adopted for all patients presenting to the hospital during the trial period. HIPCARE intervention hospitals will be given additional funds to allocate time of a senior clinician to act as a Champion for the new pathway, as outlined in the Intervention package. The local PI and the Intervention 'Champion' will establish a HIPCARE Working Group to oversee the implementation of the HIPCARE intervention; this Working Group will include healthcare staff from all the relevant disciplines and hospital managers.

HIPCARE intervention hospitals will be provided with a multi-disciplinary intervention training package with online support, which will describe:

- The current service availability and readiness for hip fracture care in that LMIC
- An evidence-based package of current evidence for each element of the HIPCARE intervention, refined for use in their healthcare system, and for the associated metric of 'success':
    1. Reduced time to surgery from admission to hospital – target: surgery <36 hours.
    2. Rapid mobilisation post-surgery – target: patient helped out of bed and to stand/walk with unrestricted weight-bearing <24h after surgery.
    3. Prompt review by a senior physician with an interest in older patients, to include a review of co-morbidity, medication, delirium screening, bone health assessment and falls assessment – target: review <72h of admission.

The HIPCARE Working Group in each centre will then be trained in the use of the local online dashboard modelled on the National Hip Fracture Database 'dashboard' used in the UK and other countries with established multidisciplinary models of care. Regular Working Group meetings will be established to review data collected to date and provide local real-time feedback regarding that hospital's performance against these metrics of success. Each month, data will be presented showing the trend in metrics of success over time, providing rapid audit of current care and feedback to the working group leaders during the delivery of the trial.

Additional onsite training will be provided as required, supplemented by further online and telephone training and support from the Trial Coordinating Centre in each country.

8.6.2. USUAL CARE

Patients will be treated as per the pre-trial pathways for hip fracture patients.

All hospitals randomised to the usual care group will be offered access to the HIPCARE training and support package at the conclusion of the trial.

8.7. Outcomes measures

In addition to hospital derived information on the care that each individual participant receives, data will be collected directly from participants and from routinely collected hospital data on health-related quality of life, mortality, mobility, residential status, resource use and complications. A schedule of data collection can be found in Table 1. For those participants who are unable to self-report, the outcome questionnaire may be proxy-reported by an appropriate individual.

Table 1: Schedule of data collection

Outcome Measure	Baseline*	120 days post-surgery**
Socio-demographic questionnaire	X	
EQ-5D-5L	X (pre-injury)	X
Mortality		X
Mobility	X (pre-injury)	X
Residential Status	X (pre-injury)	X
Resource use questionnaire	X	X
Complications		X

* Baseline data will be collected in hospital after the participant has provided informed consent.

** 120 day post-surgery data will be collected through electronic questionnaires or telephone interview.

Funds have been set aside for the translation and validation of the outcome elements of the questionnaires and demographics data, in official languages, for implementation into Research Electronic Data Capture (REDCap). The creation of the questionnaires in these additional languages will facilitate future research in many areas of healthcare and be part of the project's ongoing legacy.

Health-related quality of life

The primary outcome measure for the cluster RCT is the EuroQol EQ-5D-5L[13] index at 120 days post-surgery. The EQ-5D-5L index is a validated measure of health-related quality of life, consisting of a five dimension health status classification system and a separate visual analogue scale.[13,14] Parsons et al. demonstrated that the EQ-5D correlated strongly with a hip specific patient reported outcome measure (Oxford Hip Score), it has an independently determined minimally clinically important difference for hip fracture surgery and can be completed by patient proxies, such as relatives where the patients are unable to self-report.[15] Health status plateaus 120 days after hip fracture surgery and this is the time point where this measure is collected for the UK national hip fracture database. Assessing EQ-5D outcomes provides consistency with other clinical studies in this patient population.[15,16] EQ-5D is the recommended instrument in the core outcome set for hip fracture.[15,17]

EQ-5D-5L summary index values will be derived in accordance with jurisdiction-specific methodological guidance. India, Thailand, Philippines and Vietnam have their own national valuation sets for the EQ-5D-5L.[18,19,20,21] A national EQ-5D-5L valuation set for Nepal is not currently available or planned, but in these circumstances, the EuroQol Foundation recommends two possible solutions. First, the application of values from a neighbouring country and, second, the application of a cross-walk algorithm from an available EQ-5D-3L valuation set.[22] Currently the cross-walk algorithm is not available for all the countries in our study (it is available only for Thailand) and therefore we will use only the first solution. in the event that a national EQ-5D-5L valuation set for Nepal is not available upon completion of the HIPCARE study.

Using an anchor point for death, EQ-5D can be imputed for participants who do not survive to the primary time-point of 120 days post-surgery which is particularly relevant in this population. Parsons et al. modelled patient EQ-5D recovery trajectories after hip fracture surgery to assess the extent of any bias in 120-days outcomes by comparing complete case analysis, model-based projections and data imputation.[23] They showed that imputing a utility value of zero for death resulted in a very close

approximation to the much more complex projection methods, which were highly dependent on early EQ-5D score data that would not be available in the setting of a trial.[23] The EQ-VAS will also be collected as part of the EQ-5D-5L questionnaire.

Mortality data

Death is a major risk in this population where there is a 20%[24] one-year mortality in high income healthcare economies. Death of patients in the hospital will be recorded from the medical records in each recruitment centre, or at any point during follow-up.

Mobility

The modified New Mobility Score (mNMS)[25], is a multi-component instrument that was developed originally to measure mobility in older adults with hip fracture in post-acute and community settings. The instrument assesses ambulation inside the home, outside the home and whilst shopping. A score of 0-3 points is given for each component, resulting in a total score of 0-9 points. The patients' mobility pre-injury and at 120 days post-surgery will be collected.

Residential status

Changes in residential status provide a marker for the patients' independence through their hip fracture recovery. Data will be collected on the participants residential status pre-fracture and 120 days post-surgery, allowing for a comparison of the proportion of participants returning to their pre-fracture residential status between treatment groups.

Complications

Serious Adverse Events (SAEs) which are related to and expected in the course of the hospital treatment for the hip fracture will be reported as 'complications'. These will be recorded by the research nurses in each recruiting centre from the participants' medical record. Participants will also be asked to report any complication after they are discharged from hospital in their 120-day post-surgery follow-up questionnaires.

Related and expected complications are:

- Chest Infection/Pneumonia
- Urinary Tract Infection
- Cerebrovascular Accident
- Myocardial Infarction/Acute Coronary Syndrome
- Blood transfusion
- Acute Kidney Injury
- Pulmonary Embolism
- Deep Vein Thrombosis
- Additional surgery related to the hip fracture (including intra-operative)
- Damage to a nerve, tendon or blood vessel
- Dislocation
- Surgical wound Infection
- Failure of fixation
- Fall requiring medical review
- Non-union
- Peri-implant fracture

Health and social care resource use

Clinical Reporting Forms will be designed to collect information on use of resources from medical records at the treating hospital during the initial inpatient stay, and post discharge up to 120 days following surgery. Further resource use data will be collected from the participants to complement the medical records. Data collected will include hospital contacts related to the index fracture with hospitals other than the index treating sites, rehabilitation units and other care settings. Questions will also be asked about use of equipment and changes to the home, such as bath rails. To estimate burden on families, questions will be asked about private expenses with rehabilitation services, informal care and loss of productivity.

Resources required to deliver the different types of treatment will be valued by liaising with local finance departments in each country. Further health and social care will be valued using national unit cost estimates for health and social care when available. We will also use unit estimates for equipment and home changes. Informal care, productivity losses and lost income will be valued using equivalent weekly average earnings estimates following a human capital approach. In a sensitivity analyses, assumptions will be varied to estimate robustness of results to different costing approaches.

8.8. Data collection

Participant information will be presented, and consent decisions recorded, in either electronic or paper format. Baseline information will be recorded after surgery on an electronic tablet in the hospital setting. Participants or their carers can indicate whether they prefer to be contacted for follow-up data at 120 days post-surgery via telephone interview or electronic questionnaire. A team of data entry clerks will be assigned in each Trial Coordinating Centre to allow for central follow-up of participants. Electronic follow-up assessment questionnaires can be accessed online through personal links which can be sent to participants via text message and/or email. A schedule of email/text reminders and follow-up phone calls for those participants failing to complete the questionnaires will be outlined in the Data Management Plan (DMP). Participants may be offered compensation for any mobile data they have used in completing the trial questionnaires. This could be in the form of money, mobile phone credit or vouchers as appropriate for the local setting and in line with local policy/regulations.

8.9. Blinding

The primary outcome data will be collected from participants and entered directly onto the trial central database. As participants will not be aware of their hospital's allocation they will be considered blinded to treatment. It will not be possible to blind those delivering the interventions. The local research team reviewing hospital records will also not be blind to the treatment allocation.

8.10. Process evaluation

A mixed-methods process evaluation of the implementation strategy will provide detailed information on the contextual factors influencing success or failure of the proposed model of care in each setting.

The approach to the process evaluation has been informed by two theoretical frameworks: i) the RE-AIM framework (Reach, Effectiveness, Adoption, Implementation and Maintenance), which emphasises the need to look into the proportion and representativeness of the participants involved in the intervention, the impact of the intervention, the implementation of the intervention and how the model of care may be institutionalised within the health system; and ii) the Realist framework (Context, Mechanism, Outcomes), which has been successfully used in process evaluations as a theoretical basis for identifying potential

causal mechanisms for how an intervention works for whom, under what contexts and therefore fosters uptake of research-based knowledge into practice. We will explore quantitative data from HIPCARE Intervention hospitals (e.g. number/mix of Working Group members, regularity of team meetings, buy-in from administration) to explore factors influencing successful implementation. We will also conduct qualitative research to understand context. From a representative sample of 10 HIPCARE Intervention hospitals across the five countries included we expect to conduct interviews or focus groups with senior clinicians, administrators, managers and members of the multidisciplinary team (5-8 people) to explore the contextual influencers (facilitators and barriers) of implementation, adoption of and adaptations to the model of care, and perceived impact. We also aim to conduct 2 focus groups per hospital with 6-8 patients and their carers to assess acceptability and perceived effectiveness.

All sample sizes are approximate and may be revised based on thematic saturation during concurrent analysis. The qualitative data will be collected in conjunction with local research staff, transcribed and translated, and analysed with input from the country Lead for HIPCARE to ensure in-depth knowledge of local context. We will provide real time data back to study hospitals to inform quality improvement during the study. For the analysis, we will use a mix of top-down (deductive) and bottom-up (inductive) coding. The first set of coding will be top-down, guided by the realist framework in which parts of the data are identified as context, mechanism or outcome. Within each category, further bottom-up coding will identify themes that expand these constructs.

8.11. Early Discontinuation/Withdrawal of Participants

During the course of the trial, participants may decline to consent or withdraw from the study at any time without prejudice.

Participants will **not** have the option to withdraw the data collected up until the point of withdrawal, as the data will be required for safety analysis.

8.12. Definition of End of Study

The end of study is the point at which all the study data has been entered and queries resolved.

9. SAFETY REPORTING

Safety reporting for each participant will begin from registration and will end when the participant has reached their final main follow-up time point, at 120 days post-surgery. HIPCARE is low risk as participants will be treated according to the standard of care hip fracture care pathways at intervention and control hospitals. Considering this, we do not anticipate serious adverse events associated with the study.

9.1. Definition of Serious Adverse Events

A serious adverse event is any untoward medical occurrence that:

- results in death
- is life-threatening
- requires inpatient hospitalisation or prolongation of existing hospitalisation
- results in persistent or significant disability/incapacity
- consists of a congenital anomaly or birth defect.

Other 'important medical events' may also be considered a serious adverse event when, based upon appropriate medical judgement, the event may jeopardise the participant and may require medical or surgical intervention to prevent one of the outcomes listed above.

NOTE: The term "life-threatening" in the definition of "serious" refers to an event in which the participant was at risk of death at the time of the event; it does not refer to an event which hypothetically might have caused death if it were more severe.

9.2. Reporting Procedures for Serious Adverse Events

For this study, the following events are considered expected (including the need for hospital admission and/or further surgery):

- All complications from surgery.
- All complications from rehabilitation.

Reportable adverse events

- SAEs unexpected (not listed above) and related to the HIPCARE intervention. These need to be reported within 24 hours of becoming aware of the event.
- AEs expected (listed above) and related to the hip fracture and its treatment. These details need to be recorded in the Complications CRF, nothing further is required.

Non-reportable adverse events

- AEs and SAEs unrelated to the injury, treatment or intervention.
- AEs related to the injury, treatment or intervention but not classed as serious.

Complications related to the hip fracture or its treatment will be recorded as outcomes, as per the objectives of the trial. For the purpose of safety recording for this trial, only unforeseeable SAEs potentially related to the intervention will be reported immediately to the central trial team. When the local research team becomes aware of an SAE in a study participant, the PI will review the SAE locally and make a decision about the causality (i.e. likelihood of the event to be related/attributed to the intervention). Further guidance will be provided in the Investigator Site File. Following the assessment of causality, the PI will assess any related events for expectedness. For any SAEs assessed as unforeseeable and potentially related, the details of the event will be entered on an SAE reporting form on the database, and the local research team will notify the Trial Coordinating Centre via email or telephone within 24 hours of the PI becoming aware of the event. Once received, causality and expectedness will be confirmed by the Country Lead Investigator or delegate (Nominated Person). In the event that consensus is not reached between the PI and Nominated Person about assessment of causality and expectedness, this will be escalated to the Lead Investigator for further discussion. However, if no consensus decision is reached about expectedness after further discussion within one working day, and the SAE is judged to be unexpected by any one of the PI, Nominated Person or CI, the event will be classified as such.

If, in the opinion of the PI/country lead, the event was 'related' (resulted from administration of any of the research procedures) and 'unexpected' in relation to those procedures, the SAE will be reported as per the research ethics approval in each country. All such events will also be reported to the PMG at their next meeting.

Adverse events (AEs) that are unrelated to the injury, intervention or treatment will not be reported.

10. STATISTICS AND ANALYSIS

10.1. Statistical Analysis Plan (SAP)

A statistical analysis plan (SAP) and health economic analysis plan (HEAP) with full details of all analyses planned for the data of this study will be drafted early in the trial and finalised prior to any primary outcome analysis. A summary of the planned statistical analysis for the primary outcome is included in section 12.3. Full details will be included in a Statistical Analysis Plan which will be finalised prior to any comparative analysis.

10.2. Sample Size Determination

The original sample size calculation for HIPCARE was based upon conservative assumptions in the absence of any existing data sources in the five collaborating countries. The sample size calculation as outlined below is a re-estimation based on blinded real data predictions of total number of participants and cluster sizes after recruiting the first 2000 participants.

The trial is powered at 82% assuming 40 clusters (hospitals), 2-sided significance at 5% level to detect a minimum clinically important difference of 0.07 in the EQ-5D-5L utility index.[26] With conservative assumptions of standard deviation of 0.3,[15] and an ICC of 0.05, assuming a coefficient of variation of cluster sizes of 0.5 and an average cluster size of 76, a total sample size of 3040 patients contributing to the primary outcome analysis will be needed. Assuming an average drop-out of 29-30% per hospital we anticipate that on average 108- participants will need to be recruited per cluster leading to a total of approximately 4320 participants.

10.3. Statistical Analysis

Principal analyses will be on a “as randomised” (“intention to treat”) basis, that is by randomised allocation irrespective of non-compliance at the participant level. Demographic variables will be summarised by intervention group (overall and by country) using means and standard deviation or medians and interquartile ranges for continuous variables, and numbers and percentages for binary and categorical variable. The 5% (2-sided) significance level will be used with corresponding 95% confidence intervals produced as appropriate.

Participants providing EQ-5D-5L utility index at 120 days post-surgery, or who have died prior to this timepoint will be included in the main analysis of the primary outcome (those who have died will be imputed a score of zero). Analyses will be based on a mixed-effects modelling approach using individual patient data incorporating country as a fixed effect and adjusting for pre-injury EQ-5D-5L, and hospital as a random effect to take into account differences between clusters. Supporting analyses will explore the impact of selection bias, non-compliance with allocation, and the presence of missing data. Secondary outcomes will be analysed using logistic or ordinal regression as appropriate adjusting for country.

10.4. Procedure for Accounting for Missing, Unused, and Spurious Data.

Missing data will be summarised and patterns analysed. The main analyses will be performed on an available case basis. Sensitivity analyses will be conducted to explore the impact of missing data on the primary outcome results (e.g. using a pattern mixture model).

10.5. Procedures for Reporting any Deviation(s) from the Original Statistical Plan

Any proposed changes from the original SAP will be included in an updated protocol, updated SAP and/or reported in the final report as appropriate to the timing of the changes.

10.6. Health Economic Evaluation

The economic evaluation will provide a robust estimate of the incremental costs associated with the HIPCARE programme using information extracted from the trial case report forms, semi-structured interviews with clinical providers, and brief economic questionnaires completed by trial participants at baseline and at 120 days post-surgery. Resource impacts associated with the delivery of the interventions will encompass the cost of service delivery, monitoring, follow-up, and associated administrative activities. Individual-level data on broader resource consequences and associated economic costs will be informed by the resource use questionnaires completed by trial participants and will capture downstream costs to the health systems, as well as costs to individuals, including any charges or fees, transport costs or time away from work or usual activities. Resources will be valued using national estimates of unit costs or primary research methods where necessary. We will use the responses to the EuroQol EQ-5D-5L to generate quality-adjusted life-year (QALY) using the trapezoid rule.

The results of the economic evaluation will be presented using incremental cost-effectiveness ratios, expressed in terms of incremental cost per QALY gained, and cost-effectiveness acceptability curves generated via non-parametric bootstrapping. More extensive economic modelling using decision-analytic methods will extend the target population, time horizon and decision context, drawing on best available information from the literature together with stakeholder consultations to supplement the trial data. Longer-term costs and consequences will be discounted to present values using nationally recommended discount rates. The results of the economic evaluation will also be presented in a disaggregated way to provide a clear policy-relevant summary for the contexts in Nepal, India, Philippines, Thailand and Vietnam. Our analytical and reporting methods will follow good practice guidance for economic evaluations that cross national jurisdictions.[27]

11. DATA MANAGEMENT

The data management aspects of the study are summarised here with details fully described in the DMP.

11.1. Data Collection

Personal data collected during the study will be handled and stored in accordance with local/national Data Protection legislation. Identifiable patient information, including contact details and consent documentation, will only be accessible to research staff from participating centres. Direct access to source data/documentation will be made available as required for study-related monitoring or audit by regulatory authorities, relevant R&D staff or ethics committees.

Where possible, data will be processed on the country specific data collection system. Any data transferred to other institutions for analysis will be pseudonymised before transfer from the host country, using existing research information technology to ensure compliance with the host countries and UK Data Protection legislation. Data will be retained according to any country specific requirement that must be complied with.

At the end of the study, all other information collected about patient treatment and the questionnaires completed by study participants will be de-identified. The information will be securely transferred to the University of Oxford (United Kingdom) and the University of New South Wales (Australia) for analysis of the study results.

The study database/data stores will be hosted either in the cloud (AWS or Azure) or by a hosting provider in the host country and will be set up and managed by the Information Specialist Fellows and all specifications/ requirements determined by the PMG. The procedure for data entry will be documented in the data management plans.

Once the project is complete, the co-developed data collection system will be left in place as part of the "legacy" of this project, with minimal ongoing costs.

11.2. Data Security

Data from each country will be stored on instances of REDCap[28] hosted on country specific secure servers hosted in the "cloud", with appropriate edit checks implemented to assure data completeness and integrity. The Trial Coordinating Centre in each country will act as the "DataProcessor" within that country when processing data for the purpose of HIPCARE; where partner countries do not have a legal definition of such, we will ensure that our processes are the same as if one exists to ensure consistency.

Two of our partner LMICS have data protection legislation: Philippines has the Data Privacy Act 2012 and Thailand has "Personal Data Protection Act 2019".[29] Vietnam does not have a single comprehensive data protection law,[30] rather the legislation is split across many different laws. The general rights are currently provided in the Constitution (2013) and Civil Code (2015), whilst security is covered by the Cyber Security Law (Law No. 24/2018/QH14 - 2018). A draft personal data protection decree with the aim of consolidating existing legislation has been released for consultation.[31] India has a draft Personal Data Protection bill that is currently being considered[32] that is expected to become law in 2023. Until then then there are several acts/regulations that cover data protection and the rights of the individual, the most important being Article 21 of the Indian Constitution.[33] In Nepal there is no one act that deals with data protection, rather it is covered through Article 29[34] of the Constitution, the Individual Privacy Act 2075 (2018)[35], Individual Privacy regulations (2020), and the National Penal code (2017).[36]

To facilitate compliance with these acts the following living documents will be used: a Privacy Impact Assessment (like the UK Data Protection Impact Assessment), a privacy manual (similar to the data processing statements used in the UK) and an information asset register for the project will be maintained and will be reported on (in addition to the quality of data collected) at project management meetings. Only anonymised (not aggregated) data will be provided to the statistical teams for analysis (the principles of data minimisation and anonymisation will form the basic tenants of our design). The release of data to the statistical team outside of the host country will be approved by the Country Lead Investigator. As is best practice, during the data collection phases of this project edit checks (on data entry) and data quality checks (on data review) will be undertaken to ensure that high-quality data is recorded.

Anonymised, aggregated data will be made available to the project management team for purposes of monitoring.

Anonymised data will be archived from the end of the study for a minimum of 5 years according to local policy.

Clinical trial data (where possible due to applicable laws in the counties of collections) will be owned by the Sponsor. The Sponsor will grant the Trial Coordinating Centre(s) non-exclusive, non-transferable, non-sub-licensable, royalty-free licence to use their respective in-country clinical trial data for teaching and non-commercial research, subject to publication restrictions.

All pseudonymised data will be transferred to the University of Oxford, and respective HIPCARE collaborators for the purpose of analysis.

All pseudonymised data may be used in further research (subject to considerations set out in the consent form) carried out with academic and industrial collaborators.

11.3. Access to Data

Direct access will be granted to authorised representatives from the Sponsor and host institution for monitoring and/or audit of the study to ensure compliance with regulations. Hospital staff will have access to the centrally collected patient-reported outcome data for participants that they recruit at their site on REDCap, to ensure that they can download a complete dataset for their patients at the end of the trial.

12. QUALITY ASSURANCE PROCEDURES

A rigorous programme of quality control will be implemented to ensure compliance to the current approved protocol, Good Clinical Practice (GCP), relevant regulations and University of Oxford Standard Operating Procedures (SOPs). Quality assurance checks will be undertaken by Trial Coordinating Centre in country and via the Project Management Group to ensure integrity of study entry procedures and data collection. The processes of consent taking will be monitored centrally by each Trial Coordinating Centre.

Additionally, the study may be monitored or audited by sponsor or host sites in accordance with the current approved protocol, GCP, relevant regulations and SOPs.

12.1. Risk assessment

A risk assessment and monitoring plan will be prepared before the study opens and will be reviewed as necessary over the course of the study to reflect significant changes to the protocol or outcomes of monitoring activities.

12.2. Study monitoring

The monitoring activities will be based on the outcome of the risk assessment. Quality control procedures will be undertaken during the recruitment and data collection phases of the study to ensure research is conducted, generated, recorded and reported in compliance with the protocol and ethics committee recommendations. The Lead Investigator and the Project manager will develop data management and monitoring plans in collaboration with the research teams at the Trial Coordinating Centres.

12.3. Study Committees and key staff

12.3.1. Project Manager

The day-to-day management of the project will be the responsibility of an UK-based Project manager. The Project manager will be the main point of contact for the Trial Coordinating Centres, acting as a support with staff appointments and training, obtaining relevant regulatory approvals, assisting with financial and

data queries. They will also be responsible for the facilitating meetings between the central UK team and any of the collaborators. The Project manager will be supported by the Lead and co-lead for clinical and LMIC specific issues, Co-applicant Achten for resource, financial and risk management issues and Co-applicant Appelbe for any data/informatics issues.

12.3.2. Project Management Group

This project is co-led by Professor Matthew Costa, Professor of Orthopaedic Trauma, University of Oxford and Dr Irewin Tabu, Associate Professor at the University of Philippines Manila and President of the Fragility Fracture Network Philippines.

The Lead Investigator and Co-Lead Investigator, together with key members of the PMG will meet (virtually) with the coordinating trial teams at each individual LMIC to discuss progress and to provide support. Separate training sessions will be scheduled for the information specialists, the qualitative researchers, research nurses during those times that their contributions will be most prominent. Once every quarter, the whole PMG will meet virtually to provide trial wide updates and to allow cross-country learning.

12.3.3. Community Engagement and Involvement Panel

The CEI panel will meet at least once a year to review the trial progress and to ensure that all procedures remain acceptable from a patient perspective.

The panel is chaired by the UK CEI representative. Other CEI representatives will be identified across the five countries recruiting patients.

12.3.4. The International Scientific Advisory Committee

The HIPCARE trial will be guided by an **International Scientific Advisory Group** which has been assembled for its clinical expertise, practical experience of collecting quality data in LMICs and academic know-how in clinical research methods.

The Independent Scientific Advisory Committee will be available for support and advice throughout the project. An introductory meeting will be held during the first 3 months of the project starting and a meeting schedule will be agreed upon. It is expected that the committee will meet at least once a year, with meetings coinciding with important project milestones.

12.3.5. Communications between the committees.

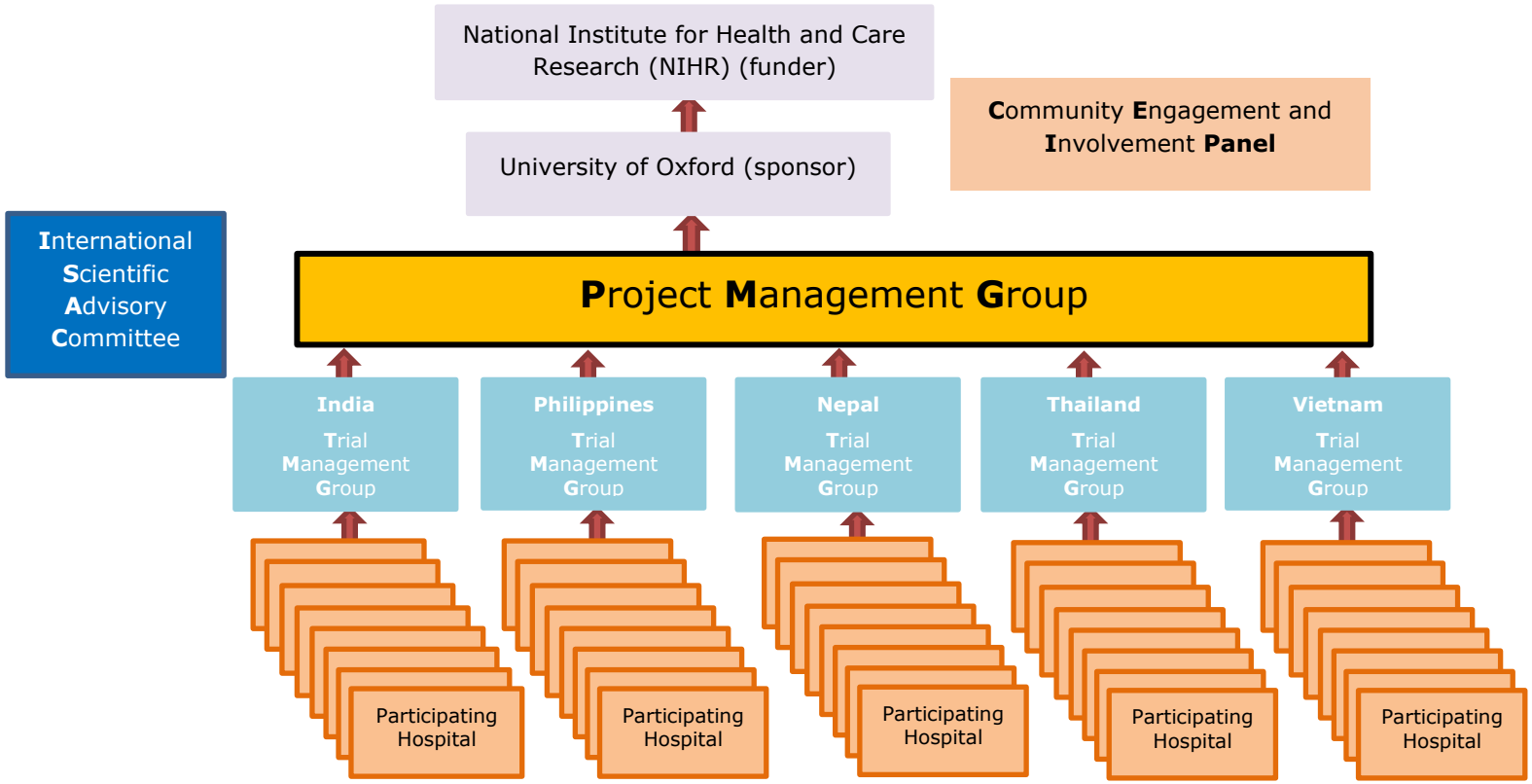

Figure 2 shows the lines of communications between the committees, Coordinating Trial Teams and participating hospitals in each country.

Each country will have its own budget allocation, with the country coordinating institution responsible for the control of those funds with an overarching overview being maintained by the Project Management Group. Each collaborating institution will receive specific funds to allow for appropriate financial management including invoice-based cost request and interim reconciliation.

13. PROTOCOL DEVIATIONS

A study related deviation is a departure from the ethically approved study protocol or other study document or process (e.g., consent process or administration of study intervention) or from GCP or any applicable regulatory requirements. Any deviations from the protocol will be documented in a protocol deviation form and filed in the study master file. The PMG will decide on a case-by-case basis if a protocol deviation is considered important. All protocol deviations will be evaluated in accordance with University of Oxford SOPs.

14. SERIOUS BREACHES

A "serious breach" is a breach of the protocol or of the conditions or principles of GCP which is likely to affect to a significant degree –

(a) the safety or physical or mental integrity of the trial subjects; or (b) the scientific value of the research.

In the event that a serious breach is suspected the Sponsor must be contacted within 1 working day. In collaboration with the CI, the serious breach will be reviewed by the Sponsor and, if appropriate, the Sponsor will report it to the approving REC committee and the relevant NHS host organisation within seven calendar days.

15. ETHICAL AND REGULATORY CONSIDERATIONS

15.1. Declaration of Helsinki

The Lead Investigator will ensure that this study is conducted in accordance with the principles of the Declaration of Helsinki.

15.2. Guidelines for Good Clinical Practice

The Lead Investigator will ensure that this study is conducted in accordance with relevant regulations and with GCP.

15.3. Approvals

Following sponsor approval, the protocol, informed consent form, participant information sheet and all patient-facing documents will be submitted to an appropriate Research Ethics Committee (REC) in each country and host institutions for written approval.

The Lead Investigator in each country will submit and, where necessary, obtain approval from the above parties for all substantial amendments to the original approved documents.

15.4. Ethical issues

Our CEI representatives identified the importance of the key ethical issue of the inclusion of patients lacking capacity for informed consent. We have explored the arrangements for ethical committee review and appropriate approvals in the Philippines, Vietnam, Nepal, India and Thailand. Our national collaborators are all experienced in gaining national/local research ethics approvals for projects as those proposed and are committed to securing all necessary regulatory approvals.

The proposed randomised trial will be conducted using a cluster design (i.e. rather than randomising individual participants, allocation of the two trial groups will be done at the level of the recruiting hospital). For those participants treated in hospitals randomly allocated to the usual care group of the trial, there will be no change to the treatment pathway they follow. The hospitals allocated to the HIPCARE intervention group, will receive training on how to optimise the care pathway for hip fractures and it is expected the optimised approach will be adopted for all patients presenting to the hospital during the trial period. In both usual care and HIPCARE intervention hospitals, only one treatment pathway will be available and as such participants will not need to consent for the randomised element of the trial. The information they receive during the informed consent discussion will highlight the need to assess quality of life and levels of care required after a hip fracture, to improve care for all hip fracture patients. Consent will be sought for the harvest of data already collected by the hospital as well as collection of patient-reported outcomes. Members of the CEI group advocated for this approach. CEI representatives have often indicated that the randomisation component of any research trial is the most difficult part to understand. It is therefore expected that this simplified approach will benefit this group of often frail people during an already stressful period. The exact details of the consent procedure will be developed with each LMIC, with input from the local/national ethical boards where appropriate.

15.5. Risk management

We will take a conservative approach to risk management within the project, following best practice in clinical research and compliance to national guidelines (where these guidelines differ, we will adopt those from the most stringent partner nation across the whole project). Each country will have its own risk assessment, undertaken prior to any work being started. The Project Manager in collaboration with Lead Investigator and senior members of the PMG with the support of the project management team will ensure a consistent approach across the project.

Risk assessments, including safeguarding, and monitoring plans will be prepared before the study opens. Quality control procedures will ensure data is generated, recorded and reported as appropriate.

The University of Oxford will take responsibility for the acceptance of the award and the appropriate flow down of relevant funds. Collaboration agreements will be executed with all partner institutions, outlining responsibilities for each partner and the associated remuneration. The University of Oxford will have a dedicated grants and finance team assigned to this project, with support from the legal advisors in the Clinical Trials and Research Governance team. Previous experience with global research has created expertise and potential pitfalls will be mitigated. Official Development Assistance (ODA) compliance checks have been done and will continue to be re-evaluated. Specific expertise within the University has been sought to assist with this (https://globalresearch.admin.ox.ac.uk/gcrf-oda/oda-background).

15.6. Safeguarding

All participants rights and safety will be monitored using a common approach based on the country with the strictest requirements and with clinical trials regulations.

We will take all appropriate measures to prevent actual, attempted or threatened sexual exploitation, abuse or harassment of any person involved in this project, may that be employed staff, volunteers, patients or carers. We will work closely with the NIHR, University of Oxford as Sponsor and each of the participating institutions in the LMIC to develop and adopt robust procedures for the reporting of suspected misconduct, illegal acts or failures to investigate. Funds have been included to allow access to

Human Resource experts in each LMIC to guide us through this process to ensure guidelines and reporting structures fit within the context of each country.

15.7. Reporting

The Lead Investigator shall submit once a year throughout the study, or on request, an Annual Progress report to the Sponsor and funder (where required). In addition, an End of Study notification and final report will be submitted to the same parties. The Lead Investigator will submit progress reports to the funder according to their reporting requirements.

15.8. Transparency in Research

Prior to the recruitment of the first participant, the trial will have been registered on a publicly accessible database (ISRCTN registry). The trial information will be kept up to date during the trial, and the Lead Investigator or their delegate will upload results to any public registries within 12 months of the end of the trial declaration.

15.9. Participant Confidentiality

The participants will be identified only by a trial ID number on all study documents and any electronic database. The authorisation functionality within the data collection system will be utilised to ensure that identifiable data can only be accessed by appropriate members of the trial team. All documents will be stored securely and only be accessible to study staff and authorised personnel. The study staff will safeguard the privacy of participants' personal data. The study will comply with the General Data Protection Regulation and the Data Protection Act (2018), which requires data to be de-identified as soon as it is practical to do so.

15.10. Expenses and Benefits

Participants will not undergo any hospital visits in addition to normal care, therefore no travel expenses will be payable. However, patients will be reimbursed for any mobile phone data which is required by them to complete the patient-facing questionnaires.

16. FINANCE AND INSURANCE

16.1. Funding

Research and Innovation for Global Health Transformation (RIGHT) Programme: NIHR203194

16.2. Insurance

The Sponsor has a specialist insurance policy in place – Newline Underwriting Management Ltd, at Lloyd's of London – which would operate in the event of any participant suffering harm as a result of their involvement in the research.

16.3. Contractual arrangements

A contract will be drawn up between the Department of Health and the University of Oxford. The University of Oxford will execute a collaboration agreement with the employing institutions of the grant

collaborators, and coordinating centre agreements for institutions acting as such. A non-commercial agreement will be executed between the coordinating centres and each hospital site.

17. DISSEMINATION, OUTPUTS AND ANTICIPATED IMPACT

The impact plan for the HIPCARE trial uses Beckhard's model:

Change = (Dissatisfaction + Vision + First steps) > Resistance

where the *Change* we are seeking is improved quality of life for people suffering hip fracture in LMIC in South Asia.

Dissatisfaction The Global Fragility Fracture Network mission is to create national Networks, bringing together policy influencers from healthcare management, geriatric/internal medicine, orthopaedic surgery, perioperative care, fragility fracture nursing, physiotherapy, occupational and rehabilitation, nutrition, metabolic bone disease and fracture liaison specialists, to change policy and practice in their country to improve care for people with fragility fractures. Dissatisfaction with the current level of care provided for patients has already been demonstrated by the creation and governmental endorsement of a national Fragility Fracture Network in each of our partner LMIC.

The *Vision* is to use the HIPCARE training and support package to establish multi-disciplinary care for patients with hip fracture in each LMIC.

We have taken the *First Steps* by completing the SARA process and CEI Panel engagement described above, to map the existing service availability and readiness in each LMIC. By engaging in this process, each national Fragility Fracture Network has demonstrated its commitment to HIPCARE and to improving outcomes for patients with hip fracture.

The key barrier to change will be the inertia due to existing models of working in each LMIC. We will address the *Resistance* created by current, established healthcare pathways, by providing each LMIC with a bespoke HIPCARE intervention and, at the end of the trial, provide quantifiable improvements in health-related quality of life for patients with hip fracture AND data regarding the cost effectiveness of the HIPCARE intervention. These data will provide tangible benefits at both a patient and health service level, which we will use to drive change through our dissemination plan:

We have identified three key target audiences for dissemination:

1. *Policy makers.* Our partnership with the Global Fragility Fracture Network and its national leadership in Philippines, India, Nepal, Vietnam and Thailand, provides immediate access to the key opinion leaders and policy influencers in each country. These leaders have existing contact with their national policy makers; policy makers who have already endorsed the creation of the national Fragility Fracture Network in each country at governmental level. Therefore, we have clearly established lines of communication with the policy makers who can implement the HIPCARE evidence generated by this project.

The Lead Investigator in each country will present a bespoke report including the clinical results of the trial and cost-effectiveness evaluation to these key opinion leaders at the annual national Fragility Fracture Network meeting in their country at the end of the trial. Since these leaders are already engaged in the HIPCARE project and have already established governmental support for their national Fragility Fracture Network, we anticipate rapid changes in healthcare policy for fragility fracture care in each LMIC as a direct result the HIPCARE study - within one year of the completion of the trial dissemination plan – leading to

the routine use of a multi-disciplinary shared care model for patients with hip fracture in every hospital in the country. We do not anticipate the need for additional resources to realise this change in policy.

2. *Healthcare workers.* We will work with the Global Fragility Fracture Network Communications Committee to maximise the reach of our website, press and publicity outputs from this project. The Chair of the Communications Committee of the Global Fragility Fracture Network is also the Communications Lead for our group. The Global Fragility Fracture Network has committed to use its website and membership newsletters and blogs to disseminate the outputs from this project to its members in over 50 countries around the world. We will also work with the WHO Department of Ageing and Life Course to augment the 'Decade of Healthy Ageing' dataset. All protocols, clinical reporting forms will be freely available via the study website. We also propose to provide unrestricted access to the digital data collection platforms in each LMIC; these will form the basis of bespoke data collection systems in each country, to facilitate future national audit programmes. We have costed the application to include free-to-access publications in the mainstream literature. The final results will also be submitted for presentations at the Annual Congress of the Global Fragility Fracture Network and the annual Asia-Pacific Fragility Fracture Network Regional Experts Meeting. Presentation slide decks showing the methodology, results and interpretation of the study outputs will be created and made available on open access. The LMIC Lead for HIPCARE will also ensure that specialty specific presentations are presented at the annual meetings of each national specialist society (Trauma and Orthopaedic, Acute Medicine, Therapy etc). In addition, we are developing complementary systems incorporating non-traditional media, including an enhanced web presence through blogging. These blogs engage both clinical and research communities. They have been very successful and have provided a means for rapid dissemination.
3. *Community Engagement and Involvement*. Our lead patient/public representative will liaise with their counterparts in each LMIC to disseminate the findings of this project to patients and carers directly through their national network of patient advocacy organisations (please see details of CEI Panel). They will help generate a country-specific plain language summary and infographic for patients and the public in each language. These documents will be available in paper copy, podcast, as a blog and formatted for social media. In the UK, an abstract will be submitted to the annual Musculoskeletal Trauma Patient and Public Involvement Meeting and presented. Posters will also be prepared with the CEI team for inclusion at any workshop, focus group or conference where relevant national CEI is involved or discussed. In addition, to disseminate directly to study participants, country specific plain language summaries will be made available to participants directly, via the study website and through posters in appropriate outpatient rooms and by liaising with identified local service user groups.

18. PUBLICATION POLICY

A detailed publication policy will be developed at the start of the project. The PMG will be involved in reviewing drafts of the manuscripts, abstracts, press releases and any other publications arising from the study. Authors will acknowledge that the study was funded by the NIHR. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged.

The internationally recognised experts of the project Advisory Group and members of the Community Engagement and Involvement Panel will be recognised on all study outputs.

The LMIC Fellows will be supported by the co-Leads and Communications Lead to disseminate study results at conferences, in journal articles and to patients and the public via targeted social media activities.

19. DEVELOPMENT OF A NEW PRODUCT/ PROCESS OR THE GENERATION OF INTELLECTUAL PROPERTY

Ownership of IP generated by employees of the University vests in the University of Oxford. The University of Oxford will ensure appropriate arrangements are in place as regards any new IP arising from the trial. The materials used for the intervention were developed at Oxford University and therefore background IP is held by the University.

20. ARCHIVING

Documents and electronic systems will be archived as per the appropriate University of Oxford and country specific SOPs.

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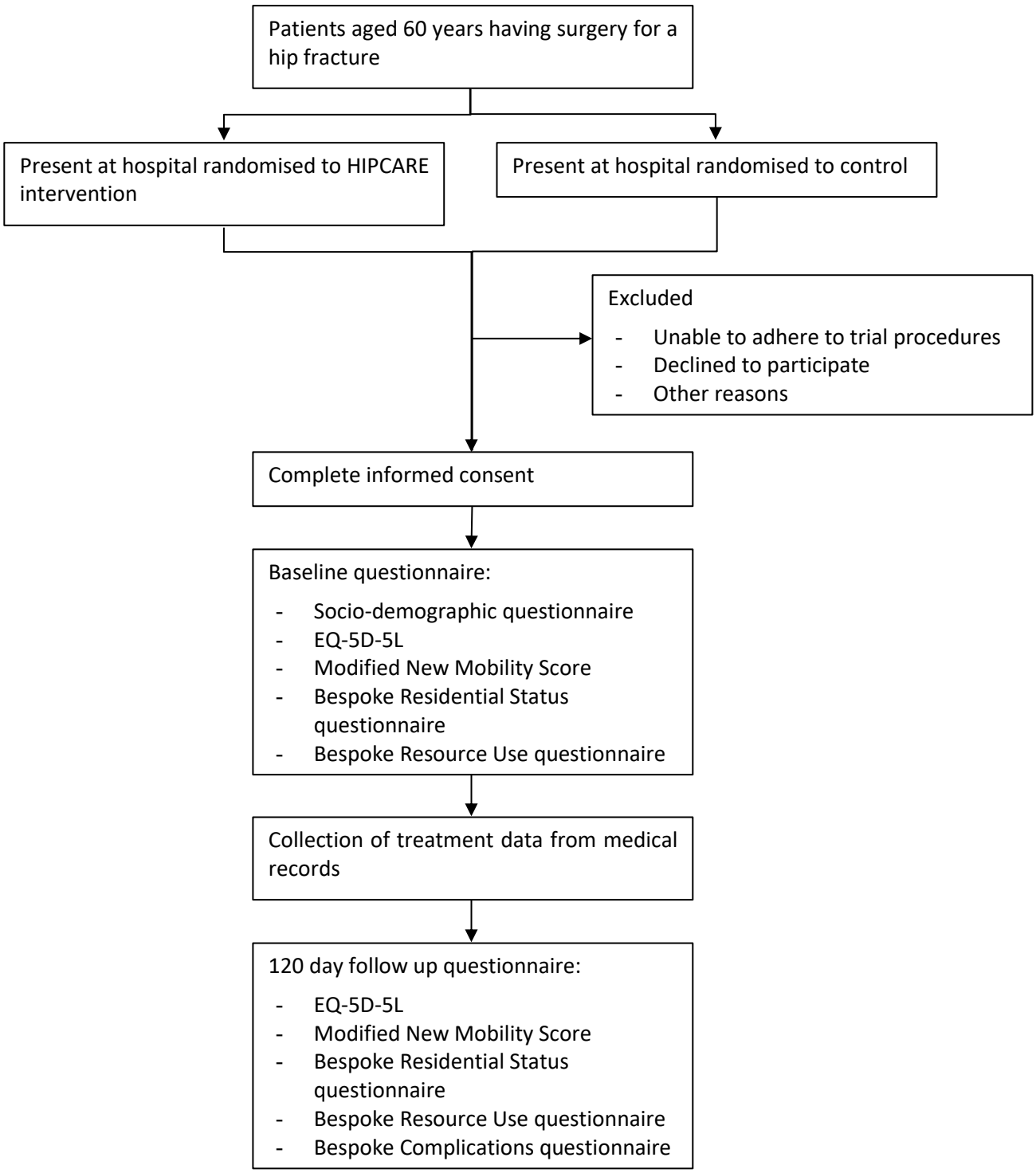
22. APPENDIX A: STUDY FLOW CHART



23. APPENDIX B: AMENDMENT HISTORY

Amendment No.	Protocol Version No.	Date issued	Author(s) of changes	Details of Changes made
1	2.0	24Mar2026	HIPCARE Lead Investigators and Trial Management team	- Sample size calculation updated - Recruitment period revised from May 2024–Oct 2025 to Nov 2024–July 2026 - Study end date extended from Oct 2026 to Mar 2027 - ISRCTN trial registration added. - Co-lead investigator changed - Project Management Group membership updated - ISAC membership updated - Safety reporting procedures updated to include more detail

List details of all protocol amendments here whenever a new version of the protocol is produced.

Protocol amendments must be submitted to the Sponsor for approval prior to submission to the OxTREC and country-specific ethic committees (where required).