NIHR Global Health Research Unit on Global Surgery

UNIVERSITY OF BIRMINGHAM | BCTU Birmingham Clinical Trials Unit

FEATHER Protocol

Follow-up within global surgEry triAls: a qualiTative investigation to improvE trial Retention (FEATHER)

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Aims

Loss to follow-up is a major challenge to international trials, and has been recognised as a global research priority through a James Lind Alliance Priority Setting Partnership (PRIORITY-II) (1). Trial retention may be particularly challenging in low resource setting where patients may have to travel long distances to return to hospital or take further time out of work where they are already financially vulnerable following their index operation. Minimising burden on trial participants during trial follow-up and identify culturally-attuned methods for encouraging ongoing participation may reduce risk of attrition bias in randomised studies (2). However, there is insufficient evidence to make recommendations for global surgery studies (3). FEATHER is a qualitative investigation embedded within several international multi-centre randomised trials (a study within a trial or SWAT). The protocol for FEATHER has previously been approved within FALCON (NCT03700749), a pragmatic multicentre factorial randomised controlled trial testing measures to reduce surgical site infection in low- and middle-income countries (LMICs).

This protocol describes the addition of the FEATHER study to two trial platforms:

(1) Sterile Glove and Clean Instrument Change at the Time of Wound Closure to Reduce Surgical Site Infection (ChEETAh) trial (NCT03980652)
(2) Perioperative respiratory care and outcomes for patients undergoing high risk abdominal surgery (PENGUIN) trial (NCT04256798)

The overall aim is to explore the reasons why patients are lost to follow-up in trial across LMICs, and to explore the potential impact of interventions to improve retention of patients in future research.

Objectives

(1) To explore the barriers and facilitators to retaining patients within in-person and telephone-based trial follow-up pathways in LMICs
(2) To explore how retention interventions could be applied to patients recruited to trials in LMICs in an ethical, culturally and contextually sensitive manner

Study design

The FEATHER study will use qualitative methods to explore patients experience of trial follow-up pathways, explore reasons for loss to follow-up and identify potential interventions to improve trial retention for future research.

Study registration

This sub-study has been registered on the MRC Hubs for Trial Methodology Research Study Within a Trial database (4) (IDXXX).

Interviews

Semi-structured interviews will be undertaken by a trained researcher to explore stakeholder perceptions of barriers and facilitators to retention within trial follow-up, including the role of the recruitment interview. Interview topic guides for patients will be designed to explore patient experiences of research involvement, their understanding of follow-up requirements from the recruitment consultation, and perceived and realized challenges to adhering to these. Interviews will also gather data on participant's proposed solutions to these challenges, and explore the reasons for these in depth.

Interviews with site investigators and site administration staff will review their experience of trial follow-up; for example, the logistics and acceptability of telephone follow-up or in-person follow-up where this is routinely performed, and the reasons patients have given for trial withdrawal, or inability of contact patients. Interviews will be conducted using practicable methods including in-person, telephone, or videoconference interviews, flexible to local customs and preferences. Where language barriers exist, a translator will be used to facilitate the interview conduct. Where possible, this translator will have had specific training in language relating to medical research. PPIR will be engaged to support the design of the interview schedule and questions, whilst ensuring culturally attuned conduct (5).

Sampling

Purposive sampling will be performed across selected countries within the host trial delivery networks. Three groups will be represented: (i) trial participants; (ii) site investigators; (iii) site administrative staff. Recruitment will continue until the point at which the research team judge that both the data and sample have sufficient depth and breadth (6). It is anticipated that approximately 40 interviews will be required in total. Purposive sampling will attempt to include a mix of interviewees in urban and rural hospitals, and of mixed levels of education (high school level and above / below high school level). For patient interviewees, where possible, trial participants that were and were not (or not easily) contactable for 30-day follow-up (either in-person or by telephone) will be sampled.

Recruitment and consent

Host trial participants will be identified in-hospital near the time of hospital discharge outcome assessment by a member of the research team. Verbal consent will be taken for further contact by an independent qualitative researcher, and the patient's details will be recorded on the FEATHER patient identification log. The qualitative researcher will contact patients for a further in-person, telephone or videoconference interview after the time of their 30-day outcome assessment, in whichever way is practicable. Recognising changing recommendation around travel and the safety hospital attendance during COVID-19, the decision on the optimal modality will be made in collaboration with local clinical team and patient partners. For patients who are able to undertake an in-person interview, written informed consent will be taken by the qualitative researcher and a FEATHER Patient Information Sheet will be provided. For patients who wish to undertake a telephone or videoconference interview, the qualitative researcher will take verbal consent and provide

specific details about the purpose and design of FEATHER as part of fully informed consent. No changes should be made to planned follow-up within the host trial.

Trial site investigators and administrative staff will be identified from the trial delegation log in collaboration with the Hub lead investigators. For these interviewees, written informed consent will be taken by the qualitative researcher and a FEATHER Patient Information Sheet will be provided.

Table 1. Example host trial schedule of assessments, including the FEATHER study within a trial

Process	CRF	Trial entry	Intra operative	Discharge	Postop day 30	Postop day 37+
Valid informed trial consent	Consent form	X				
Eligibility check, Baseline data collection, Randomisation	Randomisation notepad	X				
Adherence to allocated interventions	Intra-operative from		X			
Clinical examination for SSI, Return to normal activities, Death	Follow-up form			X	X	
FEATHER eligible patient identified and verbal consent for further contact	FEATHER patient identification log			X		
Qualitative researcher contacts patient to arrange FEATHER interview	FEATHER interview topic guide					X

Focus groups

Existing retention interventions identified from PRIORITY-II (1, 7) and the MRC Hubs for Trial Methodology Research Study Within a Trial database (4) (Queen's University Belfast), will be compared to the 'retention themes' identified from the semi-structured interviews. Topic guides will be informed by previous exploration of trial retention with the Theoretical Domains Framework (8), a checklist for design of retention strategies (9), and a Cochrane Review of retention interventions (10, 11). Focus groups will be held in selected countries (two focus groups per country) including: (A) trial participants, carers and family members; (B) site investigators and administrative staff. It is anticipated that the focus group will include between 5 and 8 participants per group. The focus groups will explore the optimal characteristics of a retention intervention relevant to their interests and reflect on the distribution of existing interventions across the identified 'retention themes'. Highlighted retention interventions will be explored in detail, including ethical and culturally appropriate methods of implementation and the cultural, contextual and societal implications of each.

Analysis

Interviews and focus groups will be audio-recorded with the consent of participants and transcribed clean verbatim for analysis. Analysis will be undertaken with reference to

recordings, transcriptions and field notes taken at the time of data collection. Data management will be facilitated with NVivo V12 (QSR International, Victoria, Australia). Thematic analysis of content will be undertaken informed by the Framework analytical approach (12). Following initial familiarisation with the data, development of thematic frameworks and data coding will proceed in an iterative manner. Data collection and analysis will run concurrently so that emergent analytical themes can inform further data collection. Interpretation will be aided by shared within-team analysis, including PPIR representation. Understanding of motivators and behaviours around retention intervention will be explored using the COM-B model of behavioural change (13). Data from this qualitative research will be triangulated with retention rates and attendance to in-person follow-up to assess patient and clinician experience of trial follow-up, and prioritise retention interventions for implementation in future trials.

Ethics and approvals

The protocol for FEATHER has been constructed in accordance with guidelines from the Global Health Network for qualitative research in LMICs (14). The additional risks and ethical implications within FEATHER have been considered very low by a BCTU internal review board, and an equivalent protocol has already been approved by a University of Birmingham International Ethics Committee and several international ethics committees within the FALCON, ChEETAh and PENGUIN trial. Submissions will be made to national, regional or hospital-level ethics committees for selected centres, in accordance with local protocols. Acknowledging global variations in SARS-CoV-2 infection and vaccination rates, in areas where patients and clinical staff are not routinely attending hospital outpatient appointments due to concerns about patient safety, alternative methods such as telephone and video-conference interviews will be adopted. In order to compensate patients for time taken for interviews, small monetary or non-monetary incentives may be offered for study completion. Ethical and responsible implementation of these incentives will be ensured in collaboration with local site lead investigators and each country's NIHR Global Surgery research hub. All participant data for FEATHER will be fully anonymised and unlinked and stored securely within a password-protected NVivo V12 data management system. All patient identifiable data (including telephone numbers) will be held at host trial sites on an encrypted, password-protected spreadsheet, and only used for the purpose of telephone follow-up within the trial and FEATHER.

Dissemination

The results of the FEATHER will be submitted for publication in peer reviewed journals and will be presented to selected international host trial co-investigators to share learning, and feedback into the design of future trials. In line with publications arising from the host trials, all publications arising from this work will be attributed to the "Global Surgery FEATHER Collaborative Group", with the writing committee and order approved by the NIHR Unit on Global Surgery Executive Committee.

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