

# FEATHER Protocol

**Follow-up within global surgery trials: a qualitative investigation to improve trial Retention (FEATHER)**

<b>Version Number:</b>	v2.0
<b>Version Date:</b>	6 May 2021

### Aims

Retention is a major challenge in international trials, and has been recognised as a global research priority through a James Lind Alliance Priority Setting Partnership (PRIORITY-II) (1). The Standard Protocol Items: Recommendations for Interventional Trials' (SPIRIT) guidelines define non-retention as 'instances where participants are prematurely "off-study" (i.e., consent withdrawn or lost to follow-up) so outcome data cannot be obtained from them (2). 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 identifying culturally-attuned methods for encouraging ongoing participation may reduce risk of both risk of attrition bias and the cost randomised studies (3-5). However, there is insufficient evidence to make recommendations for global surgery studies (6, 7). FEATHER is an investigation using qualitative methods embedded within several international multi-centre randomised trials (a study within a trial or SWAT). The protocol for FEATHER has previously been approved by an International Ethics Committee at the University of Birmingham.

This protocol describes the addition of the FEATHER study to three host trials:

- (1) A pragmatic multicentre factorial randomised controlled trial testing measures to reduce surgical site infection in low- and middle-income countries (LMICs) (FALCON, NCT03700749)
- (2) Sterile Glove and Clean Instrument Change at the Time of Wound Closure to Reduce Surgical Site Infection (ChEETAh) trial (NCT03980652)
- (3) Perioperative respiratory care and outcomes for patients undergoing high risk abdominal surgery (PENGUIN) trial (NCT04256798)

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

### Objectives

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

### Study design

The FEATHER study will use qualitative methods, informed by a behavioural science approach, to explore participants experience of trial follow-up pathways, explore reasons for

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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 repository (8) (SWAT154).

### **Stage 1: Semi-structured interview ('Diagnosis phase')**

The overall aim of semi-structured interviews in Stage 1 is to explore challenges to trial retention across a diverse range of settings, investigating participant and investigator perspectives informed by behavioural change theory.

Two specific behaviours to be examined will be: (1) participant not attending a trial follow-up clinic; (2) participant not completing trial telephone follow-up. Using the Action, Actor, Context, Target, Time (ACCTT) framework these behaviours are defined as (9):

<b>Behaviour 1. Participant not attending a trial follow-up clinic</b>
<ul style="list-style-type: none"><li>• <b>Action:</b> Attendance to an outpatient clinic with the research team for an in-person wound assessment</li><li>• <b>Actor:</b> Trial site investigator (doctor or research nurse) attempting to perform trial follow-up.</li><li>• <b>Context:</b> Outpatient clinic or ambulatory ward at a hospital site in a LMIC.</li><li>• <b>Target:</b> Patients undergoing planned or unplanned abdominal surgery that provide informed consent for participation in a host global surgery randomised trial.</li><li>• <b>Time:</b> 30 to 37-days postoperatively, with the day of surgery as Day 0.</li></ul>

<b>Behaviour 2. Participant not completing trial telephone follow-up</b>
<ul style="list-style-type: none"><li>• <b>Action:</b> Receiving or making a telephone call from the research team and responding to questions about wound healing</li><li>• <b>Actor:</b> Trial site investigator (doctor or research nurse) attempting to perform trial follow-up.</li><li>• <b>Context:</b> At home in the community after discharge from a hospital in a LMIC.</li><li>• <b>Target:</b> Patients undergoing planned or unplanned abdominal surgery that provide informed consent for participation in a host global surgery randomised trial.</li><li>• <b>Time:</b> 30 to 37-days postoperatively, with the day of surgery as Day 0.</li></ul>

Semi-structured interviews will be undertaken by a trained researcher to explore stakeholder (participant, trial investigator and trial administrative staff) perceptions of barriers and facilitators to retention, from point of consent/recruitment through to trial follow-up. Interview

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topic guides for participants will be designed to explore patient experiences of research participation, their understanding of follow-up requirements from the recruitment consultation, and both perceived and realized challenges to maintenance of follow-up. Topic guides will be informed by behavioural science to explore capability, opportunity, motivation and behaviours in maintenance of trial follow-up (10, 11). They will learn from behavioural interviews in other disease areas, and be piloted with selected collaborators from the trial network (12-17).

As the trial interventions are all provided in-theatre at the time of surgery, adherence to trial interventions will not be considered. 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 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 performed, and the reasons participants have given for non-maintenance and/or withdrawal from trial follow-up. 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 (18).

### *Sampling*

Purposive sampling will be performed across selected countries and sites within the host trial delivery networks. FEATHER will be trial agnostic (no minimum recruitment from any single host trial) as all three trials have the same primary outcome and follow-up procedures. Two groups will be represented: (i) trial participants; (ii) site investigators. Recruitment will continue until the point at which the research team judge that both the data and sample have sufficient depth and breadth (19). It is anticipated that approximately 40 interviews will be required in total.

Purposive sampling of trial participants will attempt to include a mix of interviewees that were planned for in-person and telephone follow-up, urban and rural hospitals, of older and younger age ( $\leq 50$  years, 50-70 years,  $\geq 70$  years), mixed levels of education (high school level and above / below high school level) and trial participants that: (1) were contactable for 30-day follow-up (either in-person or by telephone); (2) were not contactable; (3) were contactable outside the trial follow-up window (for example  $\geq 37$  days data after surgery). Site investigators directly involved in the trial follow-up procedures will be sampled from several trial sites in each country. This follows sampling matrices and procedures established in other studies of participants lost to follow-up in randomised trials and aims, and aims to represent the diverse perspectives involved in the behaviour of maintaining trial involvement to completion (5).

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**Table 2. 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 form		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

### *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 by the discharge assessor 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.

### *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). Inductive thematic analysis of content will be undertaken informed by the Framework

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analytical approach (20). 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. A random sample of 5% of the data will be double-coded. Inter-rater reliability will be assessed using Cohen's kappa with  $\geq 0.75$  or more accepted as high agreement. Interpretation will be aided by shared within-team analysis, including patient and public partners from LMICs. Understanding of motivators and behaviours around trial non-retention will be interpreted using the AACTT framework to define behaviour (9) and the COM-B model for behaviour change (11). 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.

### **Stage 2: Focus groups ('Treatment phase')**

The overall aim of the focus groups in Stage 2 are to identify and prioritise retention interventions for evaluation and/or adoption into future global surgery trials.

Existing retention interventions identified from PRIORITY-II (1, 21), the MRC Hubs for Trial Methodology Research Study Within a Trial database (8) (Queen's University Belfast) and Cochrane review of retention interventions (22, 23), will be mapped to the behavioural retention themes identified from the semi-structured interviews with reference to a taxonomy for behaviour change techniques (24, 25). Topic guides will be informed by the theoretical framework of acceptability (26, 27) and a checklist for design of retention strategies (28).

#### *Recruitment and consent*

Focus groups will be held in selected countries (two focus groups per country) including: (A) trial participants, carers or family members; (B) site investigators and administrative staff. It is anticipated that the focus group will include between 5 and 8 participants per group. Again, sampling will seek to represent a diverse range of age groups, geographical locations of residence, education levels, and those that were and were not retained in trial follow-up. Informed consent will be required for participation following provision of written or structured verbal patient information.

#### *Conduct and analysis*

The focus groups will explore the optimal characteristics of a retention intervention relevant to their settings and reflect on the distribution of existing interventions across the identified 'retention themes'. Prompts will be informed using the APEASE (affordability, practicability, effectiveness, acceptability, safety and equity) criteria (29). 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. Flexibility will be allowed to include emergent interventions proposed by focus group members. Finally, group members will be asked to prioritise retention interventions based on the discussion, attitudes and experiences, and informed by the six-item COM-B questionnaire measure (10). We will summarise this data to co-produce 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 (30). 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 implemented in the design of ongoing and 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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