

Study of Whole blood in Frontline Trauma (SWiFT)

Implementation Study Protocol

Abbreviation and Glossary

- **CTU:** Clinical Trials Unit.
- **SWiFT:** Study of Whole blood in Frontline Trauma.
- **Standard of care pathway:** whole process from donor to patients with pre-hospital blood component transfusion in patients with life-threatening haemorrhage.
- **WB pathway:** whole process from donors to patients with pre-hospital leukocyte-depleted whole blood (WB) transfusion in patients with life-threatening haemorrhage.

1. INTRODUCTION

1.1 Background

(see main study protocol)

1.2 Study Rationale

(see main study protocol)

Randomized controlled trials (RCTs) are widely used for establishing evidence of the effectiveness of interventions, yet health and care interventions are often complex, posing specific challenges for RCTs which implementation research can help address.(1)

RCTs are essential to demonstrate the efficacy of interventions, but often are insufficient for understanding implementation of interventions in authentic practice settings. Although RCTs are currently perceived as the “gold standard” in evaluation of health and care interventions, the research community is increasingly raising concerns about their limitations.(2,3) These include problems with internal validity of trials which failed to consider the broader contexts in which these trials are carried out, (4–7) as well as the need for tight control over the research environment to assess the outcome of the intervention and the very concept of complex healthcare systems.(8)

As a result, research examining the adoption of evidence into clinical practice found that after 17 years, only 14% of health care research was adopted into day-to-day clinical practice following the traditional clinical research pipeline.(9)

Implementation Science (IS) was born as a response to the lack of adoption of evidence-based interventions.(10) IS is the study of the adoption of evidence-based interventions into practice (10) that aim to address the processes used to integrate evidence-based interventions into the clinical settings by providers or organizational systems. In implementation research, the effects of the intervention are not the primary focus. Rather, the focus is on evaluating policies, procedures and contextual factors that are thought to affect the implementation process itself. The implementation

process could include the behaviour of providers or the overall system, which may facilitate or hinder implementation.(11)

Moreover, traditionally, researchers think of knowledge development and application as a unidirectional, stepwise progression in which different questions are addressed in isolation. First, an RCT is employed to determine if an intervention implemented under controlled conditions has efficacy in specific populations. Next, “effectiveness research” methods determine if the effect remains when implemented in less controlled conditions with broader populations. Finally, “implementation research” methods are used to understand the best methods to introduce the intervention into practice. While systematic, this unidirectional approach can take a great deal of time from the original efficacy study design to the final conclusions about implementation, and conditions may change so that original clinical and policy questions become less relevant.(12) Additionally, the unidirectional approach does not help us understand interaction effects between the intervention and the implementation strategy.(13)

Hybrid designs(14) involve the combination of two distinct research designs: effectiveness trials and implementation trials. These study designs observe intervention effects, while also considering how they are implemented. In this way, hybrid designs address the problem of substantial delays in the adoption of evidence-based interventions into routine clinical practice that is all too common when following the traditional research pipeline(9) while optimizing the understanding of identification of potential interactions between the intervention effectiveness and its implementation approach. Therefore, the hybrid design speeds up and adds consistency to the traditional research pipeline by assessing effects and implementation simultaneously, rather than adding a step to the research process.(1)

The SWiFT trial will adopt a hybrid study design and this study will focus on the implementation part of the trial.

Aim

Assess the acceptability and implementation of the intervention (pre-hospital leukocyte-depleted whole blood [WB] transfusion) in patients with life-threatening traumatic haemorrhage in the context of the SWiFT trial.

Objectives

- Gain a deeper understanding of the contexts within which the intervention will be delivered and its impact on local (hospitals) and central (central blood service) processes and systems.
- Identify implementation mechanisms and factors that might promote and inhibit the routine incorporation of the intervention in everyday life.
- Identify factors that influence the acceptability of the intervention from the perspective of healthcare professionals involved in the whole WB pathway (from donor to recipients).
- Inform future adoption and implementation of the WB pathway in other settings by identifying potential strategies for sustainable implementation.

3. STUDY DESIGN

This study is part of a type 1 effectiveness-implementation hybrid design.(14) Hybrid type 1 design is primarily an effectiveness trial of an intervention that secondarily observes and collects data on the implementation of that intervention. This study design aims to measure patient functioning or symptoms in response to a clinical intervention, while simultaneously evaluating acceptability and implementation of intervention through qualitative, process-oriented and mixed-methods.(13)

In this study qualitative methods will be used, involving in-depth interviews and focus groups with operational staff involved in the implementation of the WB pathway during the SWiFT trial as well as patient and blood donor representatives. Qualitative research methods have been chosen as they can offer important insights into the contextual circumstances of complex health care interventions.(1,15,16) Pope and Mays(17) claim that qualitative research “is a prerequisite of good quantitative research, particularly in areas that have received little previous investigation”. For these reasons qualitative methods increasingly are being used as part of RCTs to guide the implementation and evaluation of interventions.(1,15)

The study design includes the following steps (*Figure 1*):

- Review of literature, document analysis (e.g. local protocols) and informal discussions with the research team members to have a preliminary “As-is” (Standard of care pathway) and “To-be” (WB pathway) Process map. (Sep 2021 -Sep 2022)
- Focus group 1 (operational staff involved in the WB pathway across the SWiFT sites) aimed at consolidating the “As-is” and “To-be” Process maps and to check whether they need adaptations across sites. The “To-be” Process map will be used to support implementation across all trial sites and the health economic evaluation of the implementation. (Sep - Nov 2022)
- Qualitative interviews with operational staff involved in the WB pathway with different roles across the SWiFT sites to explore perspectives on acceptability and the impact of the implementation of the intervention in the current system and processes. (Jan-Sep 2023)
- Focus groups (n=4), 3 with different groups (focus group 2, 3, 4; Sep-Dec 2023) of operational staff involved in the WB pathway and 1 with patient and donor representatives (focus group 5; Jan-Feb 2024) to review and consolidate findings emerging from the interviews and discuss strategies to improve implementation and spread in other contexts.
- Focus group with operational staff involved in the WB pathway, patient and donor representatives (focus group 6) to consolidate and validate findings.(Mar-Apr 2024).

This design was selected because it enables detailed examination of perceptions about implementation and offers opportunity to explore and construct meaning relevant to implementation

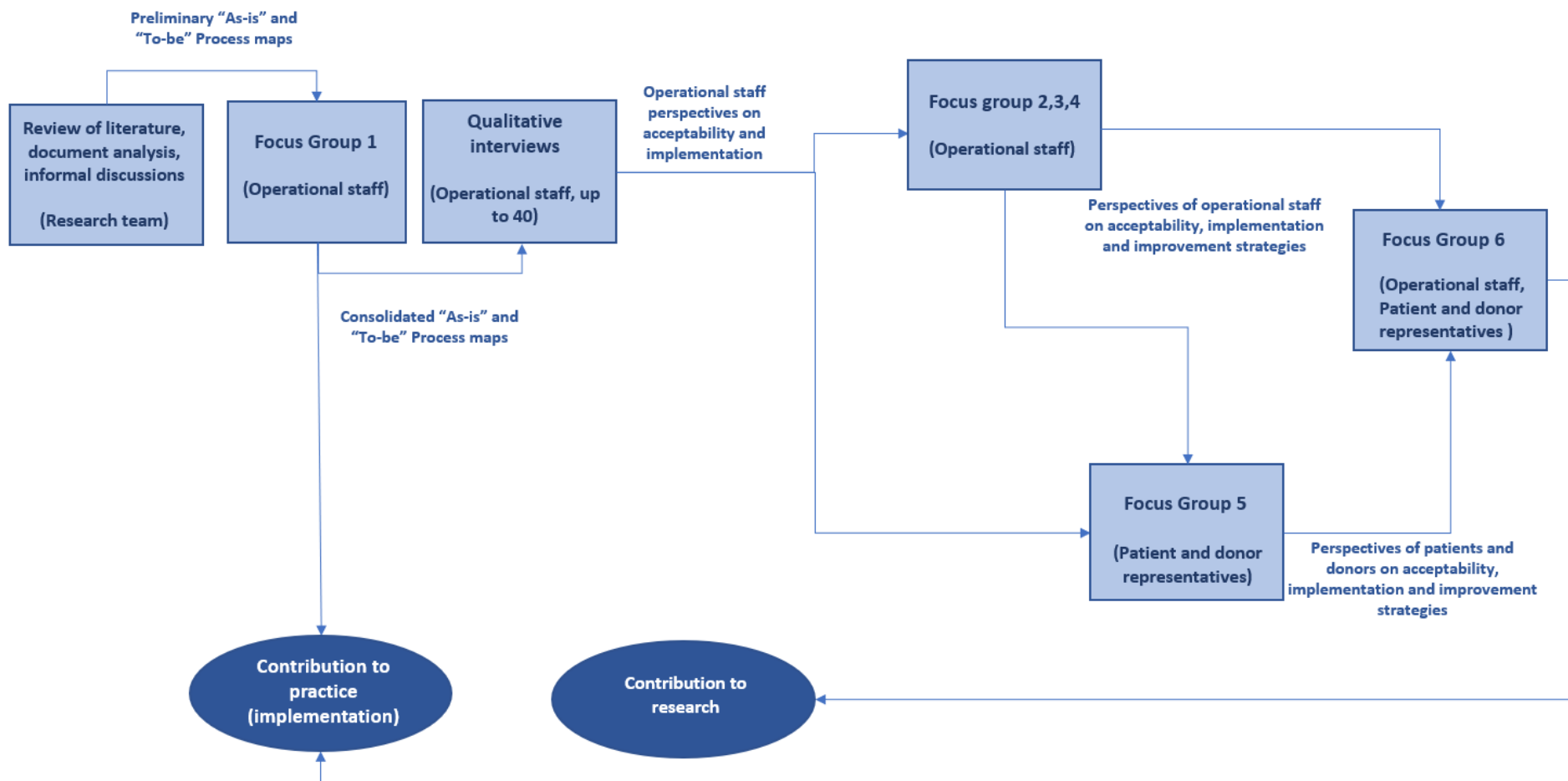


Figure 1: Study Design

3.1 Setting

(see main study protocol)

3.2 Recruitment methods

Operational staff

Individuals will be approached in person, via phone or email by the coordinating CTU (who have contacts with the transfusion laboratories, staff working across NHSBT, and healthcare professionals working at each of the participating sites). Other participants may be identified through snowballing. In these cases, the interviewee will be asked to contact the recommended individual to gauge interest in taking part in an interview. Interested participants will be asked to contact the research team for further information. Interview participants will be asked if they consent to be contacted to participate in the focus groups 2 or 3 or 4. Participants in the focus groups 2 or 3 or 4 will be asked if they consent to be contacted to participate in focus group 6.

Patient representatives

Patient representatives will be recruited through existing patient networks (e.g. Centre for Trauma Sciences- www.c4ts.qmul.ac.uk/get-involved/get-involved, People in Research - [Home - People in Research](#), Oxford Trauma and Emergency Care Patient and Public Involvement group - [Patient and Public Involvement — Nuffield Department of Orthopaedics, Rheumatology and Musculoskeletal Sciences \(ox.ac.uk\)](#)).

Patient representatives will be contacted by the research team via email or phone.

Participants in the focus group 5 will be asked if they consent to be contacted to participate in focus group 6.

Donor representatives

The NHS Blood and Transplant (NHSBT) Patient and Public Advisory Group (PPAG) will be used to seek blood donors who are happy to participate in one or both focus groups as part of this study. These contact details will be shared with the SWiFT research team. Donor representatives will be contacted by the research team via email.

Participants in the focus groups 5 will be asked if they consent to be contacted to participate in focus group 6.

All study participants will be sent a copy of the study information sheet via email prior to the interview date. The email/letter will explain that participation in the interviews and focus groups is voluntary.

Prior to the interview each interviewee will sign an informed consent form and be reminded that participation is voluntary, and respondents may withdraw at any time.

Operational staff participating in the interviews will receive a £10 honorarium (Amazon voucher) to compensate them for their time.

Patient and donor representatives will be paid according to NIHR guidance for patient and public contributors.

3.3 Data collection and analysis

Number of participants

- Focus group 1: 18 operational staff
- Interviews: up to 40 operational staff
- Focus group 2: 18-20 operational staff
- Focus group 3: 18-20 operational staff
- Focus group 4: 18-20 operational staff
- Focus group 5: 10 patient and donor representatives
- Focus group 6: 7 patient and donor representatives and 18 operational staff

Operational staff can decide whether to participate only in the focus group, only in the interviews or both.

Sampling

A purposive sampling strategy will be used to recruit interviewees.

Operational staff

We will purposefully sample operational staff from a range of professional backgrounds to ensure that we will capture broad variations in settings and experience across the sample. Different professionals will have different roles in the WB pathway and their perceptions and experiences of implementing it will vary according to their roles. Similarly, we will recruit participants from across the different sites participating in the trial, because the organisational processes, and therefore implementation strategies and experiences of implementation are likely to vary, providing us with rich data from across the study settings.

Operational staff will be selected based on:

- the hospital they work in (any of SWiFT recruiting sites)
- the part of the WB pathway which they work in: transfusion laboratory, pre-hospital clinical team – receiving hospital trauma team, national blood service (NHSBT)
- their professional group: doctors, nurses, paramedics, etc.

This approach aims to maximize the diversity of perspectives gained from the interviews.

Patient and donor representatives

Opportunity sampling will be used to select patient representatives who have suffered trauma in the past and are interested to help with research.

Consenting donor representatives will be opportunistically sampled from interested members of the NHSBT PPAG.

Below are the details of the sampling frame for the different research activities:

- **Focus group 1:** 18 operational staff – we will aim to ask for representative from each of the recruiting sites, representing the 3 different steps in the WB pathway.
- **Interviews:** up to 40 healthcare staff – 6-7 people from each area of expertise (i.e. 10 transfusion laboratory, 20 pre-hospital setting including doctors and other healthcare professionals, 10 national blood service).
- **Focus group 2:** 18-20 healthcare staff - 6-7 people for each of the recruiting hospitals working in pre-hospital setting (trauma team) with different professional roles.
- **Focus group 3:** 18-20 healthcare staff- 6-7 people for each of the recruiting hospitals working in the transfusion laboratory with different professional roles (biomedical scientists, transfusion practitioners and haematologists).
- **Focus group 4:** 18-20 healthcare staff working in the national blood service with different professional roles (from donor teams to manufacturing and logistics team).
- **Focus group 5:** 10 patient and donor representatives .
- **Focus group 6:** 7 patient and donor representatives (volunteers from focus group 5-7 and additional participants if required) and 18 healthcare staff – ideally representing all recruiting sites, across the 3 different main steps of the WB pathway with different professional roles (volunteers from focus group 2, 3 ,4 and additional participants if required).

Data collection

We will decide on whether to conduct focus groups and interviews face-to-face or using online communication technologies/ telephone based on the evolution of the Covid-19 pandemic, HM Government guidance at the time and preferences of participants. Face-to-face focus groups will take place in one of the study sites.

- **Interviews**
Up to 40 1:1 interviews with operational staff across the WB production, delivery and pre-hospital pathway (expected duration: 45 minutes, no more than 1 hour) will be conducted by one researcher. Interviews will be digitally audio recorded and transcribed by a professional transcription service.
Open ended questions will be used to explore perceptions of participants. Sampling will continue until theoretical saturation will be reached. Interview guides will be informed by literature on acceptability and implementation.(18,19)
The interview guide will be reviewed by the SWiFT research team and piloted with 1 researcher and 2 healthcare professionals working across the WB pathway.
Open-ended questions will enquire about: (i) acceptability of the intervention to operational staff (ii) implementation contexts, systems and processes, (iii) barriers and facilitators to implementation.

Interviews will be digitally audio recorded and transcribed verbatim by a professional transcription service.
- **Focus groups**
The focus groups (expected duration: 2 hours except for focus group 6 - expected duration: 3 hours if online and half day if in person) will be audio recorded and transcribed by a professional transcription service. During the workshop field notes will be collected. In case of online focus groups, collaborative online tools (e.g. Miro) will be used to revise and

comment on process maps as well as to support discussion and share ideas. These tools allow to collect and record notes and comments from participants and facilitator throughout the focus group.

In focus group 1, participants will be asked to provide their input about the steps, activities and resources involved in performing the “As is” process and about how this process should change with the intervention (“To be” process).

Throughout the workshops Process Maps will be used as a tool to prompt discussion. While the discussion in focus group 1 will be mainly focused on processes and activities, focus group 2, 3, 4 will be mainly focused on acceptability and implementation. In these focus groups the research team will present interview findings and will prompt discussion about the implementation process, factors facilitating or hindering acceptability and implementation and potential strategies to overcome emerging challenges to implementation. In focus group 5 the research team will gather patient and donor perspectives about acceptability and implementation issues in order to understand what is important for services to be aware of if this treatment is implemented on a wider scale.

In focus group 6, the research team will present the main themes about implementation and acceptability of the intervention emerging from the interviews with operational staff, the four focus groups with operational staff and the focus group with patient and donor representatives. During the focus group participants will be invited to discuss key findings about acceptability and implementation in the context of the SWiFT trial and key strategies for adoption and sustainable implementation of the WB pathway in other settings.

Focus group and interview data will be complemented by observational, documentary, process and outcomes data that will be collected during the conduct of the SWiFT trial by the research team.

Analysis

Transcripts will be imported into NVivo for analysis. Thematic content analysis will be used to analyse and categorise qualitative data collected during the focus groups and in the interviews into recurrent and common themes.

- *Interviews*

Transcripts will be imported into NVivo for analysis. A qualitative database will be developed using Nvivo software where a coding framework will be developed throughout an inductive and deductive process to identify themes specific to the research questions to be derived.

Following an initial stage of data familiarisation, the data will be analysed through an iterative process of coding and using the constant comparative method.(20) Two researchers will read the transcripts in full to familiarise with the interviews. They will then individually open-code 5 transcripts before coming together to agree and define the coding structure, which will be then applied to subsequent interviews and codes refined and added. In a second stage, the 2 researchers will meet again to examine how the codes obtained through open coding fit with Acceptability Theoretical Framework (ATF) (acceptability)(19) and Normalisation Process Theory (NPT) core concepts (implementation).(18) This process will continue until theoretical saturation will be reached.

Acceptability is “a multi-faceted construct that reflects the extent to which people delivering or receiving a healthcare intervention consider it to be appropriate, based on anticipated or experienced cognitive and emotional responses to the intervention”.(19) ATF will be used to support the analysis of findings related to acceptability as it has been successfully used in a

number of studies in different healthcare settings to guide the assessment of acceptability from the perspectives of intervention deliverers and recipients, prospectively and retrospectively (including RCTs). This theoretical framework describes acceptability as a multi-faceted construct, represented by seven component constructs: (1) how an individual feels about taking part in an intervention ('Affective attitude'), (2) the perceived amount of effort that is required to participate in the intervention ('Burden'), (3) ('Perceived effectiveness'), (4) the extent to which the intervention has good fit with an individual's value system ('Ethicality'), (5) the extent to which the participant understands the intervention, and how the intervention works ('Intervention coherence'), (6) the extent to which benefits, profits, or values must be given up to engage in an intervention ('Opportunity costs'), and (7) the participant's confidence that they can perform the behaviour(s) required to participate in the intervention ('Self-efficacy').(19)

NPT will be used to examine, theorise and improve how pre-hospital WB should be embedded in routine delivery. We considered that Normalization Process Theory would be a useful analytical tool because NPT is a robust theory of implementation that helps provide awareness of the work involved in embedding and sustaining practices associated with an intervention, and thus aids understanding of what becomes normalized into everyday settings.(21) NPT is a sociological theory which explains the processes people adopt when implementing new interventions, to allow the intervention to become 'normalised' or embedded in routine practice. Four core constructs describe generative mechanisms that facilitate normalisation and help examine: (1) the ways that people make sense of the practice ('Coherence'); (2) how they engage and participate with it ('Cognitive participation'); (3) how stakeholders come to engage with or 'enact' the practice ('Collective action'); and (4) how they appraise its effects ('Reflexive monitoring').(22)

Interview findings will then be analysed alongside other notes, documents and trial data. Findings will be discussed, refined and validated with the SWiFT research team. Results will serve as input for discussion in the focus groups 2,3,4,5.

- *Focus groups*

Transcripts will be imported into NVivo and analysed using thematic analysis. Transcripts, field notes, comments and ideas shared by participants using physical or digital tools (including annotated process maps) will be analysed by researchers with the objective to refine and validate findings emerging from the interviews. Emerging ideas on strategies to address challenges to sustainable implementation and spread of the intervention to other contexts will be inductively coded using NVivo and organised in themes. One researcher will open-code the transcripts and then the coding system will be discussed with another researcher and applied to the dataset. Findings will then be compared with relevant literature and discussed with the wider SWiFT trial team.

3. PARTICIPANT RECRUITMENT

4.1 Inclusion criteria

Healthcare professionals

Operational staff involved in the WB pathway at NHS Blood and Transplant and the sites participating in the SWiFT trial.

Patient representatives

- Patient (of any age) who has suffered a traumatic injury.
- Consenting to be contacted to participate in the study focus groups.

Donor representatives

- Blood donor (of any age)
- Consenting to be contacted to participate in the study focus groups.

4.2 Exclusion criteria

Healthcare professionals

- Under 18-years old.
- Inability or refusal to provide consent for the study.
- Participants who are not capable of communicating in English both verbal and written.

Patient and donor representatives

- Not consenting to be contacted to participate in the study focus groups.
- Participants who are not capable of communicating in English both verbal and written.

4.3 Withdrawal Criteria

As indicated in the information sheet, participants can withdraw from the study at any time by sending an email to the PI. If a participant chooses to withdraw from the study, we will inform the participant that we will no longer contact them regarding the study and no further information will be collected from them. We will inform them that as indicated in the participant information sheet we will keep information about them that we already have and that we won't be able to let them see or change the data we hold. We will also remind them that all data kept will use the minimum personally-identifiable information possible (all personally identifiable information will be removed from the interview transcripts) and will be anonymised any dissemination purposes.

5. ASSESSMENT AND FOLLOW UP

Draft case reports/findings will be sent to participants to ask for any feedback or comments. Participants will be asked if the account is realistic and accurate and if the interpretation of the data resonated with their experiences.

6. CONSENT

(see main study protocol)

Consent to enter the implementation study will be sought from each participant after a full explanation will be given, an information sheet offered, and time allowed for consideration.

Prior to the agreed interview date, we will share the participant information sheet via email and reiterate that participation is voluntary. We will ensure that the study information sheet for potential participants has the complete description of the research study including detail on the participants' right to anonymity, confidentiality of the data, right to withdraw and the benefits of participation. At the time of the interview, we will ask the interviewee to sign the informed consent form and remind participants of their right to withdraw their consent at any time.

As the majority of participants will be NHS staff members, it is anticipated that all participants will have sufficient understanding of English to read and understand the participant information sheet and consent form. Patient and donor representatives will be asked if they are capable of communicating in English (both verbal and written) as part of their consent process and will be invited in the focus groups only if they meet this requirement.

7. CONFIDENTIALITY

The Principal Investigator will preserve the confidentiality of participants taking part in the study and fulfil transparency requirements under the General Data Protection Regulation for health and care research. Data and all appropriate documentation will be stored for a minimum of 15 years after the completion of the study, including the follow-up period.

Confidentiality will be maintained by removing all personally identifiable information from the interview transcripts. A unique study number will be assigned to participants to keep their personal identifiable data anonymous. Any verbatim quotes used in the reports and publications will be anonymised and referred to only by the date of the interview and/or the type of role of the interviewee. To maximise confidentiality of individual participants, the word "patient" or generic job titles (e.g. Orthopaedic nurse, Haemostasis and Transfusion consultant) will be used instead of names, specific grades or specialty titles.

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