Getting the bloods to the laboratory: developing interventions to improve the blood culture pathway for patient safety and antimicrobial stewardship

Combined protocol Version 3.0
22/07/24

Protocol cover sheet

Separate protocols
There are three separate protocols, due to different approvals being required for different parts of the project:
Part 1a – University ethics committee approval (requiring a data study protocol), HRA approval
Part 1b – University ethics committee approval
Part 1c & 2 – NHS ethics committee approval, CAG approval, HRA approval

Version 3.0 of the combined protocol includes the ethically approved protocols for all parts of the study.

Version control

Version	*Date*	*Description*
1.0	*06/06/24*	*Protocols for part 1a, and part 1c&2, post ethical approvals.*
2.0	*02/07/24*	*Protocols for part 1a, and part 1c&2, post ethical approvals; protocol for part 1b, pre ethical approval.*
3.0	*22/07/24*	*Protocols for all parts of the study (1a, 1b, 1c&2), post ethical approvals.*

FULL TITLE OF THE PROJECT

Getting the bloods to the laboratory: developing interventions to improve the blood culture pathway for patient safety and antimicrobial stewardship (Part 1a)

SHORT PROJECT TITLE / ACRONYM

i-SAMPLE: Improving blood sampling for AMS (Part 1a)

Ethics Number:

IRAS 338495

PROTOCOL VERSION NUMBER AND DATE:

V1.0 22/01/24

CHIEF INVESTIGATOR:

Carolyn Tarrant

SPONSOR:

University of Leicester

FUNDER:

National Institute for Health and Care Research (NIHR156452)

Ethical Approvals:

This protocol (part 1a) has received ethical approval from University of Leicester Medical and Biological Sciences Research Ethics Committee (Ref 0971). The protocol has received HRA and Health and Care Research Wales (HCRW) Approval (Ref 24/HRA/0561).

This protocol has regard to the Office for Data Release guidance on protocol content

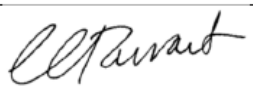
This protocol has regard for the HRA guidance on protocol content

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the project in compliance with the approved protocol and will adhere to the principles outlined in GCP guidelines, the Sponsor's (and any other relevant) SOPs, and other regulatory requirements as amended.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the clinical investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the project publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the project will be given; and that any discrepancies and serious breaches of GCP from the project as planned in this protocol will be explained.

Sponsor:	
Name (please print):	Dr Cat Taylor
Signature:	
Position:	Head of Research Governance
Date:	Mar 26, 2024
Chief Investigator:	
Name: (please print):	Prof Carolyn Tarrant
Signature:	
Date:	22/01/2024
Principal Investigator:	
Site:	
Name: (please print):	
Signature:	
Date:	

KEY PROJECT CONTACTS

Chief Investigator	Professor Carolyn Tarrant Population Health Sciences University of Leicester George Davies Centre

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Sponsor	University of Leicester Research Governance Office Leicester General Hospital Gwendolen Road Leicester LE5 4PW rgosponsor@le.ac.uk
Funder(s)	National Institute for Health and Care Research (NIHR156452)
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Statistician	Dr Clare Gillies
Name(s) and address(es) of all medical and/or technical department(s) and/or institutions involved in the project, including any data processors and/or collaborators that will process the data	

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LIST OF ABBREVIATIONS

CI	Chief Investigator
GCP	Good Clinical Practice
NHS R&D	National Health Service Research & Development
PI	Principal Investigator
PIC	Participant Identification Centre
PIS	Participant Information Sheet
REC	Research Ethics Committee
SOP	Standard Operating Procedure

PROJECT SUMMARY

Project Title	Getting the bloods to the laboratory: developing interventions to improve the blood culture pathway for patient safety and antimicrobial stewardship.	
Project Design	Cross-sectional study involving analysis of routine NHS data	
Planned Sample Size	No sample size was calculated as data will be extracted for all eligible participants	
Follow up duration	At time of extraction data will be extracted for the previous 12 months	
Planned Project Period	Jan 2023- June 2025	
	Objectives	Outcome Measures
Primary	To identify rate of occurrence and situational factors that affect whether blood culture sampling occurs, when broad-spectrum antibiotics for intravenous administration are prescribed within 24 hours of patient admission from emergency departments (ED).	% of participants where a blood culture sample was ordered
Secondary	To identify factors impacting on quality indicators e.g., number of sets, contamination, time to microbiology lab analyser; whether blood culture sampling occurs prior to administration of antibiotic. To conduct a secondary analysis to assess extent to which availability of blood samples was associated with changes to antibiotic choice at antibiotic review.	Adjusted odds ratios from logistic regression models

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this project)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
National Institute for Health Research (NIHR156452)	**Financial support (**£752,059.85)

ROLE OF PROJECT SPONSOR

The sponsor of this research is the University of Leicester. The University of Leicester is registered as a research sponsor with the Department of Health and routinely takes responsibility as sponsor for research activities within the NHS.

DATA FLOW DIAGRAM

1 BACKGROUND

Inappropriate antibiotic use contributes to the growing problem of antimicrobial resistance. In England in 2020, 55,000 patients were affected by antibiotic-resistant infections putting them at risk of poor outcomes and death (1). Evidence shows that resistance results from the overuse of broad-spectrum antibiotics, and prolonged courses of antibiotics, but the use of antibiotics, particularly broad-spectrum antibiotics, continues to increase in hospitals in England (2). As well as the harm posed to patients by the rise of antimicrobial resistance, increasing resistance poses a threat to the system in terms of increased costs and care burden.

Currently, in England, the rapid administration of broad-spectrum antibiotics is recommended for acutely unwell patients with sepsis (3). Additionally. broad-spectrum antibiotics are often initiated 'just in case', for suspected infection, to manage risk (4). In these circumstances, collecting and analysing timely and good quality blood cultures are important to inform the review and potential revision of the initial prescribing decision to an antibiotic that specifically targets the patients infection (5 6,7). The rapid identification of pathogens from blood cultures is known to play a role in reducing individual an population mortality from severe infection and sepsis (8, 9,10).

Performing blood cultures reliably has been identified as a key quality indicator for appropriate antibiotic use in hospitalised adults with suspected severe infection (11), and the presence of microbiology results for all patients identified as one of three priority factors with the greatest influence on optimising antibiotic use in hospitals (12).

Despite the known importance of the knowledge that blood analysis can realise, we also know that the process of blood collection and transportation to the microbiology laboratory can reduce the quality and utility of microbiology results (13). For example, an insufficient volume of blood taken for testing, the contamination of blood samples, and delays in transport are all factors that can substantially and adversely affect the diagnostic value of samples. (14).

Furthermore, an additional issue of concern is that, despite the importance of blood cultures for patient management and antimicrobial stewardship, around half of hospital patients do not have blood samples taken at all when antibiotics are started (15-19).

2 RATIONALE

Whilst we have ample evidence to indicate that blood sampling procedures and processes do not always meet the standards of best practice, we have little knowledge of why that occurs. We need to better understand the behavioural, social, and organisational factors that contribute to poor quality blood sampling in acute care.

There is a pressing need for novel theory-based research and intervention development to optimise the pre-analytic blood culture pathway to bolster both patient safety and effective antimicrobial stewardship. Although interventions have been developed to address problems in acute pathways, these have tended to focus on clinical and technical issues, as opposed to social, behavioural and other factors (14, 20, 21). The blood culture pathway is complex and involves many actors and the timely co-ordination of effort to get the blood to the lab. Blood

sampling practices are potentially underpinned by a complex range of behavioural, cultural and systems factors (22). Recommendations have been made for the need for multi-model approaches to improve blood culture collection practices, based on research using mixed-methods, to generate a holistic knowledge of pathways and thus mitigate barriers to quality improvement and stewardship. (23).

Following on from our previous theory-driven research into overuse of broad-spectrum antibiotics in acute medical patients (4, 24), we draw on theories of individual and collective behaviour to identify the behavioural, social and organisational influences on the reliability and quality of blood culture sampling in acute care, and to develop interventions that will be implementable across diverse health care settings.

As a whole the study used mixed methods. This protocol refers to Part 1 a which involves analysis of routine hospital data.

3 OBJECTIVES AND OUTCOME MEASURES/ENDPOINTS

3.1 Primary objective

To identify rate of occurrence and situational factors that affect whether blood culture sampling occurs, when broad-spectrum antibiotics for intravenous administration are prescribed within 24 hours of patient admission from emergency departments (ED).

3.2 Secondary objectives

To identify factors impacting on quality indicators e.g., number of sets, contamination, time to microbiology lab analyser; whether blood culture sampling occurs prior to administration of antibiotic.

To conduct a secondary analysis to assess extent to which availability of blood samples was associated with changes to antibiotic choice at antibiotic review.

3.3 Outcome measures/endpoints

3.4 Primary endpoint/outcome

Primary outcome measure is occurrence of blood culture sampling. In line with Shallcross (2016) (18) we define blood culture sampling as a request for a blood culture recorded in hospital records within 48 hours of patient arrival at ED (Y/N)

3.5 Secondary endpoints/outcomes

Quality indicators (e.g., number of sets, contamination, time to microbiology lab analyser; whether blood culture sampling occurs prior to administration of antibiotic.)

Changes to antibiotic choice at antibiotic review.

4 STUDY DESIGN

Study design: Cross-sectional study involving analysis of routine NHS data

Sample: All patients >18 years admitted to each trust, receiving broad-spectrum antibiotics for intravenous administration within 24 hours of admission, over a retrospective 12 month period (e.g. March 2023-February 2024).

Data sources: One hospital, with the main ED, will be selected from each trust. Data will be extracted from hospital electronic health records and electronic microbiology records. We will develop a standard schedule detailing the data points required and providing definitions. This will be discussed with the informatics team in each site to ensure comparable data can be provided. A data-sharing agreement will be established with each site.

Data will be fully anonymised within the trusts prior to transfer, by the nominated member of staff in the trust responsible for extracting and compiling the data. Identifying information e.g. date of birth and postcode will be substituted with higher level information e.g. age and Super Output Area. Primary data will be provided, trusts will Zip and encrypt data using 7-Zip software, and transfer using the University's secure Filedrop facility - https://filedrop.le.ac.uk/

We will incorporate internal checks of data-completeness (e.g. instances of patients with a blood culture result but no data on the time sample was ordered). Blood culture order time may not correlate with collection time. We will conduct a prospective data quality check, involving the use of stickers or audit forms to capture a manual record of actual blood culture sampling time. This will be checked against blood sample order time, and time of first dose of antibiotic, to assess the alignment between order time and collection time, and whether collection time precedes antibiotic administration, as a validation check of our use of blood culture sample order time as the primary outcome measure of blood culture sampling. Anonymised audit data will be transferred to the University of Leicester for and compiled for cross-site analysis.

5 INCLUSION/EXCLUSION CRITERIA

5.1 Inclusion criteria

- adults (>18 years)
- admitted to hospital through emergency routes between 01/03/2023 and 29/02/2024
- prescribed broad-spectrum antibiotics for intravenous administration within 24 hours of admission

5.2 Exclusion criteria

- individuals under the age of 18
- individuals admitted to hospital via through elective routes or not admitted to hospital between 01/03/2023 and 31/02/2024
- individuals not prescribed broad-spectrum antibiotics for intravenous administration within 24 hours of admission

6 STUDY PROCEDURES

6.1 Informed consent

We will be obtaining anonymised data sets from trusts in line with their Privacy Notice, therefore there is no need for consent as there will be no breach of the common law duty of confidence.

6.2 Definition of End of Study

When all analyses have been completed in line with the Statistical Analysis Plan, no later than the End Date approved by the Ethics Committee.

6.3 Source Data

Analysis will identify situational/contextual predictors of reliable blood culture sampling. We have specified a minimum set of measures, identified in agreement with the three participating hospitals based on routine data that is collected and could be made available from all three hospitals. This will be developed into a fully-specified data extraction schedule with input from our expert advisory group (e.g. listing the broad spectrum antibiotic that are of interest), tailored for each hospital to reflect variations in the way their data are coded. This will include the following measures:

- Date & time of arrival in ED/admissions unit
- Antibiotics patient is already taking prior to admission where applicable
- Location antibiotic prescribed (ED, AMU etc)
- Type of antibiotic prescribed
- Date and time antibiotic prescribed
- Dates and times of antibiotic administration
- Documented microbiology results
- Changes to antibiotic schedule
- Patient demographics (IMD based on postcode, year of birth, ethnicity, gender)
- Patient severity (NEWS score)
- Recorded diagnosis at admission and at discharge

Where available we will also collect data on quality indicators as secondary outcomes:

e.g., number of sets of blood culture bottles filled (guidelines recommend 2 sets of two bottles), contamination of sample, time to microbiology lab analyser

7 STATISTICS AND DATA ANALYSIS

Data analysis:

Descriptive statistics will be used to summarise the frequency and distribution of timing of blood culture ordering. We will also produce histograms or box plots to visualise the distribution of these measures. Logistic regression will be used to assess covariates associated with the probability of blood culture being ordered within 48 hours of admission (binary yes/no outcome). Relevant covariates to be assessed include situational/contextual factors, patients demographics, and patient outcomes.

To identify factors impacting on quality indicators e.g., number of sets, contamination, time to microbiology lab analyser; whether blood culture sampling occurs prior to administration of antibiotic, appropriate methods will be used depending on the data type of the quality indicator. Continuous variables will be assessed via linear regression, and binary quality indicators by logistic regression.

A final analysis to investigate the extent to which availability of blood samples was associated with changes to antibiotic choice at antibiotic review will be assessed again using logistic regression (with yes/no antibiotic changed as the dependent variable, and yes/no blood sample available as the independent.

All models will be fully adjusted for covariates such as patient age, and will be mixed effects to account for the clustering effect of hospital, as data is being drawn from three sites. We will conduct sensitivity analyses to test the robustness of our results to different assumptions and model specifications. This will help to assess the reliability of our findings and identify potential sources of bias. We will carefully consider the strengths and limitations of each method and choose the most appropriate approach for each research question.

8 DATA HANDLING AND RECORD KEEPING

We provide information on best practice in data handling and record keeping on our website

8. 1 Data Handling

8.1.1 DATASET CREATION

The study statistician will develop a standard schedule detailing the data points required and providing definitions. This will be discussed with the informatics team in each site to ensure comparable data can be provided. A data-sharing agreement will be established with each site. Data will be fully anonymised within the trusts prior to transfer, by the nominated member of staff in the trust responsible for extracting and compiling the data. Identifying information e.g. date of birth and postcode will be substituted with higher level information e.g. age and Super Output Area. Data will include local patient identifier numbers (a unique identifier for a patient within a health care provider); patients cannot be identified by these numbers once data are transferred

8.1.2 DATA TRANSFER

Trusts will Zip and encrypt data using 7-Zip software, and transfer using the University's secure Filedrop facility - https://filedrop.le.ac.uk/

8.1.3 Data Storage

All data will be stored on the University of Leicester r:drive and not transferred to personal devices. Access to the database will be restricted to study staff using a username and password. All data handling and record keeping will be kept in adherence to University of Leicester's and relevant NHS Organisation(s) policies.

8.1.3 DATA PROCESSING

Data will be processed at each of the three hospital sites, bringing together all required data into excel files. Once received by the University of Leicester the three excel files (one from each site) will be combined and analysed by the trial statistician.

8.1.4 DATA DESTRUCTION

Data will be destroyed 6 years after the end of study has been declared as per University of Leicester Policy. This will be undertaking by the study statistician, and observed by the University of Leicester *Deputy SIRO & Information Governance Lead (Research)*

8. 2 ACCESS TO DATA

Direct access will be granted to authorised representatives from the Sponsor, host institution and the regulatory authorities to permit project-related monitoring, audits and inspections.

8.3 ARCHIVING

Research data and archived files will be stored for a minimum of 6 years after the study has ended. Storage will comply with the University of Leicester archiving Standard Operating Procedure. Details can be found at: http://www2.le.ac.uk/offices/ias. Destruction of essential documents will require authorisation from the Sponsor.

9 MONITORING, AUDIT & INSPECTION

The study will be conducted in accordance with the current approved protocol, ICH GCP, relevant regulations and standard operating procedures.

The University of Leicester operate a risk-based audit programme to which this study will be subject to.

10 ETHICAL AND REGULATORY CONSIDERATIONS

10.1 RESEARCH ETHICS COMMITTEE (REC) REVIEW & REPORTS (ANNUAL AND FINAL)

The Lead Investigator and study statistician will ensure that participants' anonymity is maintained. No personal identifiable data will be available within the dataset. The Leicester team will make no attempts to identify participants within the dataset. If the statistician at Leicester notices that there is information in the database that can be used to identify any individual, general practitioner or general practice, they will inform the site immediately in writing, and the University of Leicester Information Assurance Team.

All delegated staff on the project with access to the data set will read and sign to say they will abide by the conditions of the data sharing agreement.

10.2 PEER REVIEW

This research has undergone extensive peer review during the course of the NIHR Health and Social Care Delivery Research funding process.

10.3 PUBLIC AND PATIENT INVOLVEMENT

Acceptability and Design

We convened a PPI group (Oct 2022) comprising six patients with experience of severe infection and hospital care to advise on study design (2F, 4M; 5 White British, 1 Asian). Group members were recruited from existing local PPI groups, and through informal contacts by the local Research Design Service PPI lead. The PPI engagement event took place online to enable participation from PPIE members who were unable to travel. The meeting consisted of a project presentation, where we presented our research questions and ideas for study design and methods.

Following the presentation, we invited an open discussion, allowing PPI group members to comment on all aspects of the presentation. PPI members were provided with a series of questions about study

value and study design, and how we could involve patients in research, co-design, and dissemination. These were discussed during the meeting, and also sent to participants by email following the meeting inviting further feedback. In addition a further focused discussion was held online between Tarrant (PI) and Locke (PPI co-applicant). PPI feedback included the importance of considering patients from whom it is difficult to take blood, and for studying inequalities in blood sampling across patient groups, suggestions for patient involvement and the potential for patient-facing interventions, and dissemination suggestions. All feedback was taken into account in preparing this application. This includes:

- ensuring PPI representatives are involved in study team meetings
- providing training to all PPI members on research methods and on specific topics e.g. sepsis, antimicrobial resistance
- involving PPI members in analysis of qualitative data and in giving presentations of the findings
- producing Plain English summaries and a video about findings aimed at the public
- ensuring that patients are fully involved in the co-design process and consider the potential for a patient held/led intervention
- paying costs for PPI member conference attendance.

Undertaking, analysing and disseminating the research

- Research methods training and training on the clinical context will be provided to the PPI participants. Training will take place in year 1, and include online research methods training, and additional bespoke training in specific topics e.g. sepsis and antimicrobial resistance.
- PPI members will be involved in the analysis of findings, and in supporting dissemination. Members will also be asked to review and feedback on materials by email, with appropriate remuneration. Supporting dissemination will involve preparing Plain English summaries and social media materials, identifying dissemination routes, filming a video about the findings, participating in feedback presentations at participating hospitals, and attending national conferences (e.g., Health Services Research UK Conference).
- At the end of the project, we will run a half-day face-to-face PPI event. This will include a debrief, where PPI members are invited to reflect on their experience of participating in the project. We will further explore their interest in future study involvement (e.g. in follow-up research or separate projects). Finally, PPI members will be invited to attend the wider end-of-project workshop alongside clinical and academic collaborators and other relevant stakeholders.
- In addition to the core PPI, we have a commitment from The Sepsis Trust and Antibiotic Research UK for support with some of our PPI activities, including helping us to engage with a wider group of patients with experience of infection to feed into latter stages of the co-design process, and to support public and patient dissemination of the outputs from our project.

10.4 PROTOCOL COMPLIANCE AND SERIOUS BREACHES

A study related deviation is a departure from the ethically approved study protocol or other study document or process or from Good Clinical Practice (GCP) or any applicable regulatory requirements. Planned deviations or waivers are not allowed however it is acknowledged that accidental protocol deviations may occur. Any deviations from the protocol will be

documented in a protocol deviation form and filed in the Trial Master File/Investigator Site File as applicable.

If a protocol deviation occurs, then the CI (or delegate) will document this in accordance with the University's Standard Operational Procedure (SOP) Identifying and Reporting Deviations and Serious Breaches of GCP and/or the Protocol.

Deviations from the protocol which are found to frequently recur will be explored and where necessary an amendment to the protocol will be made.

10.5 DATA PROTECTION AND DATA SUBJECT CONFIDENTIALITY

Data stored at the University of Leicester and analysed by the study statistician will be anonymised. All investigators will comply with the requirements of the Data Protection Act 2018 with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles.

10.6 INDEMNITY

University of Leicester's insurance applies.

10.7 ACCESS TO THE FINAL PROJECT DATASET

Only, the Chief Investigator, researcher and co- investigators will have access to the full dataset. Direct access will be granted to authorised representatives from the Sponsor and host institutions for monitoring and/or audit of the study to ensure compliance with regulations

11 DISSEMINATION POLICY

Our approach to dissemination will aim for significant reach across diverse stakeholders. We will share knowledge about our findings, generate learning to drive improvements in practices along the pre-analytic blood sampling pathway, provide initial evidence of feasibility and effectiveness of interventions to support applications for future research, inform ongoing NHSE work on optimising the blood culture pathway, and promote wider engagement and understanding of the research by patients and the public.

Dissemination will target: 1) Policy makers, national bodies including health professional organisations, and national interest groups; 2) Clinicians and healthcare professionals including microbiology staff and antimicrobials stewardship leads; 3) Academic audiences; 4) Patients and the public.

We will work closely with our patient and public contributors to develop and implement our dissemination plan, create appropriate outputs, and involve them in dissemination. The PPI co-applicant will lead on this. This will include the development of outputs, including creative outputs (infographics, short videos for hospital staff and the public) tailored to the needs and interests of patients and the public, and frontline healthcare staff. We will produce posters, videos that could be played in participating hospitals, and our PPI group members will attend presentations and external dissemination events to ensure that patient voice is heard.

We have strong links with the NHS England leads for improving the blood culture pathway across England, and will work with the NHSE Blood Cultures team to ensure we develop outputs that meet the needs of policy-makers. These connections will ensure the outputs have a direct pathway to impact for the national agenda. We will generate policy recommendations and disseminate through presentations at national AMR diagnostics policy board meetings and NHSE blood culture steering group. Through these connections we will reach influential national organisations including the UK Sepsis Trust and Antibiotic Research UK. We will also work through Coats, the ED project lead, to engage with the

Emergency Medicine (the NIHR Emergency Medicine Incubator, the Royal College of Emergency Medicine and HEE Deanery leads for Emergency Medicine).

We have access to the international platform provided by The British Society for Antimicrobial Chemotherapy [BSAC] via Jenkins to support dissemination of, and engagement with our research findings, and we will disseminate our findings through the network of regional antimicrobial stewardship leads.

We will reach academic audiences by presenting findings at key national and international academic conferences, and we will contribute to the current evidence on optimising the blood sampling pathway through papers in high impact journals. This will include publications in both clinical and social science journals, allowing us to make an important contribution to the body of social science research in antimicrobial resistance. We will publicise key academic outputs through press releases, media interviews and through our research group Twitter feed. We will hold an end of project round table workshop for academics, and healthcare and policy stakeholders.

The study as a whole, including part 1a, will produce the following outputs:

- A bundle of interventions to optimise blood sampling practices for patients with suspected severe infection in acute care, which will be implemented across diverse health care settings; implementation guidance, and supporting materials including service blueprints.
- Presentations at participating hospital sites, 3 national conferences (e.g., BSAC annual conference, Health Services Research conferences (HSRUK), and the UK society for Behavioural Medicine Annual Scientific Meeting), and 1 international conference (e.g., European Congress of Clinical Microbiology & Infectious Diseases, European Health Psychology Symposium (EHPS)).
- Policy recommendations and presentations to regional and national leads, policy-makers and national healthcare and infection organisations at the National AMR Diagnostics board and the NHSE blood culture task and finish group.
- Four open access publications in high impact peer-reviewed journals
- Plain English summaries of research findings.
- Creative outputs to disseminate findings to patients and the public, and frontline hospital staff. This will include videos, mixed-media outputs and infographics, similar to outputs previously developed by members of the team: https://antimicrobialsinsociety.org/commentary/re-envisaging-infection-practice-ecologies-in-nursing-ripen/; https://vimeo.com/368059130?login=true)
- A dedicated project website
- Blogs and social media, including a publication in The Conversation, to publicise findings more widely.
- A final report to the HSDR programme board, which will synthesise the findings across the stages of the study, and will set out recommendations for future evaluation of the intervention bundle.

Publications and outputs will be available on open access via the University's Library database

Authorship eligibility guidelines and any intended use of professional writers

All members of the research team in its current form will be given authorship on the final study report and other outputs as appropriate.

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FULL/LONG TITLE OF THE STUDY

Getting the bloods to the laboratory: developing interventions to improve the blood culture pathway for patient safety and antimicrobial stewardship (Part 1b).

SHORT STUDY TITLE / ACRONYM

Attitudes and Beliefs around blood culture sampling for treating acute infection

PROTOCOL VERSION NUMBER AND DATE: Protocol Version 1.0 – 25-06-2024

FUNDER: National Institute for Health and Care Research (NIHR156452)

Ethical Approvals: This protocol (part 1b) has received ethical approval from the University of Leicester Medical and Biological Sciences Research Ethics Committee (Ref 0457)

Short lay summary

Blood culture sampling is a diagnostic tool that is used to detect severe infection, like sepsis. Blood culture samples provide important clinical information that enables healthcare professionals to make decisions about patient treatment. This means that patients are more likely to get the right antibiotics for their infection, increasing their chances of survival and reducing antibiotic overuse and antimicrobial resistance. Previous research has shown that blood culture sampling does not always happen and if it does happen, samples are sometimes taken too late or not adhering to the required quality standards.

The purpose of this study is to find out why blood culture sampling is not always successfully undertaken. Specifically, we plan to conduct an online survey of UK healthcare professionals to measure their attitudes and beliefs towards blood culture sampling for acute hospital patients with suspected severe infection. We also want to find out what healthcare professionals identify as key barriers to successful blood culture sampling. To obtain representative results that generalise across hospital settings in England, we plan to recruit a national sample of healthcare professionals across different job roles and varying levels of seniority, who are involved in either requesting blood culture samples, taking blood culture samples or using the results from blood culture samples to inform their treatment. This will mean recruiting healthcare assistants, nurses and doctors, amongst other healthcare staff. We will recruit via two established cohorts of healthcare professionals, who previously gave consent to participate in research and provided their contact details for this particular purpose. Up to 400 participants will be recruited from the NHS CHECK and UK REACH cohorts and via social media and professional contacts and networks. Participants will complete an online questionnaire of approximately 20 minutes length. We will analyse the data to identify common attitudes around blood culture sampling and perceived barriers. We will also test whether attitudes differ across different professional roles or clinical settings. Finally, we will test what attitudes and beliefs may predict whether or not healthcare staff engage in blood culture sampling as part of their clinical activities.

This study is part of a wider project that aims to create a bundle of interventions to optimise blood culture sampling practices (IRAS 338495 and 332310).

Study Summary

Study Title	Attitudes and Beliefs around blood culture sampling for treating acute infection
Study Design	Quantitative: online survey
Study Participants	Healthcare professionals responsible for requesting blood culture samples, taking blood culture samples and/or using blood culture test results to inform clinical practice
Planned Size of Sample (if applicable)	400
Follow up duration (if applicable)	N/A
Planned Study Period	14 July 2024 – 30 May 2025
Research Question/Aim(s)	The primary research questions are: What are NHS healthcare professionals' attitudes towards blood culture sampling for adult patients with suspected severe infection? Do these attitudes differ by professional role and clinical setting? The secondary questions are: • Does our newly developed attitude questionnaire capture key components of the Theory of Planned Behaviour within the context of blood culture sampling? • What are predictors of self-reported engagement in clinical activities that form part of the blood culture pathway? • What are perceived barriers to healthcare staff engaging in clinical activities related to blood culture sampling for managing suspected severe infection? Do these perceived barriers differ by professional role or clinical setting?

1. Background

Blood culture sampling is a diagnostic tool that is used to detect severe infection in hospital patients. Blood sampled from patients is analysed in microbiology laboratories to detect the presence of bacteraemia (clinically significant bacteria in the bloodstream), to identify the type of bacteria causing the infection, and to measure the susceptibility of the bacteria to various antibiotics. This provides vital information to inform clinical decision-making about patient treatment (1), thereby increasing chances of patient survival (2, 3) and reducing antibiotic overuse and antimicrobial resistance.

In England in 2020, 55,000 patients were affected by antibiotic-resistance infections putting them at risk of poor outcomes and death, as well as contributing to increased healthcare costs (4). However, the use of antibiotics, particularly broad-spectrum antibiotics, continues to increase in hospitals in England (5). Despite the clinical importance of blood culture sampling, around half of hospital patients do not have blood samples taken at all when antibiotics are started, and when they are taken, they often fall shall of national quality standards (6-10). Optimising the blood culture pathway is a current priority for NHS England.

Blood culture sampling practices are underpinned by a range of behavioural, cultural and systems factors that may be difficult to address (11). Attitudinal barriers include the importance attached to blood culture diagnostics and views on the utility of blood culture sampling (12, 13). An unpublished systematic review of barriers and enablers to blood culture sampling identified a range of key barriers within the Theoretical Domains Framework domains of: knowledge, behavioural regulation, environmental connect and resources, memory, attention and decision processes, beliefs, and social influence (14). In our recent study involving interviews with acute care clinicians (15), we identified a range of barriers including lack of time and skills, problems of coordination and diffused responsibility, and lack of feedback on the consequences of blood cultures for subsequent patient management.

The purpose of this study is to find out why blood culture sampling is not always successfully undertaken and to increase generalisability of findings through taking a national sample of UK healthcare professionals. Specifically, we set out to assess the behaviours, beliefs and attitudes held by staff who prescribe antibiotics, take blood samples and/or use blood culture test results to inform clinical practice, about blood culture sampling and microbiological testing in acute care. We will also identify predictors of self-reported engagement in timely and appropriate blood culture sampling. This study is part of a wider project that aims to create a bundle of interventions to optimise blood culture sampling practices for acute care patients with suspected severe infection (IRAS 338495 and 332310).

2. Research Questions/Aim

The primary research questions for this study are:

- What are NHS healthcare professionals' attitudes towards blood culture sampling for adult patients with suspected severe infection?
- Do these attitudes differ by professional role and clinical setting?

The secondary research questions are:

  - Does our newly developed attitude questionnaire capture key components of the Theory of Planned Behaviour within the context of blood culture sampling?
  - What are predictors of self-reported engagement in clinical activities that form part of the blood culture pathway?
  - What are perceived barriers to healthcare staff engaging in clinical activities related to blood culture sampling for managing suspected severe infection? Do these perceived barriers differ by professional role or clinical setting?

3. Study Design

This study will use a quantitative approach, using an online survey as a low cost and quick way of nationally sampling UK healthcare professionals across various clinical roles and grades increasing the generalisability of findings.

3.1. Study Participants

3.1.1. Sample size

The target sample size is 400 healthcare professionals. We considered sample size requirements across a number of different statistical analyses, which we are planning. For our plans to validate a new questionnaire measure, we followed White (2021)'s recommendation to sample 250-350 participants. For our ANOVAs, we ran a G*power calculation for ANOVA (repeated measures, between factors) with 4 groups and 4 measurements, assuming a correlation of up to 0.5. We estimated a power of .80 and an α error probability of .01 to detect a medium effect size f = .25, which returned 236 participants. For our linear multiple regression analysis (fixed model, R2 increase) with 10 predictors, we ran a G*power calculation, estimating a power of .80 and an α error probability of .01 to detect a medium effect size f = .15, which returned 160 participants. To satisfy sampling requirements for all types of analyses and to account for potential data loss from incomplete submissions and exclusions, we will recruit up to 400 participants.

3.1.2. Recruitment

Participants will be recruited via NHS CHECK and UK REACH cohorts, and via social media and professional contacts and networks. Administrators for the two study cohorts (UK REACH and NHS CHECK) will distribute the online survey to their participants who consented to involvement in future research. The survey will be shared via an email invitation, which contains a link to the REDCap online platform, where the survey will be hosted.

3.1.3. Eligibility criteria

Inclusion criteria:

- UK healthcare professionals whose role involves requesting blood culture samples, taking blood culture samples and/or using the results from blood cultures for adult patients with suspected severe infection.

Exclusion criteria:

- UK healthcare professionals working in neonatal or paediatric acute care or children's emergency department.
- UK healthcare professionals working outside of adult acute care.
- Healthcare professionals working outside of the UK.

3.1.4. Consent and withdrawal

A participant information sheet (PIS), privacy notice and e-consent form will be integrated within the landing page of the online survey. Only if participants agree to the items on the consent form and indicate their agreement via a tick box can they proceed to the next stages of the survey. The PIS will provide an email address, which they can contact in case of questions. Participants can take as long as they like to decide whether they want to take part, although the survey will be closed once the maximum number of participants has been recruited. Participants will have the option to provide their name and email address and can indicate whether they would like to receive an electronic summary of the study results and/or be entered into a prize draw.

Participants will be informed in the PIS that they can withdraw during the participation by closing the online questionnaire. Their data will not be included in the analysis if they complete less than half of the questionnaire. It will not be possible to withdraw participant data after the questionnaire is completed. This is because individual questionnaire responses will not be identifiable, because no names/email addresses/identification numbers will be stored alongside the research data.

4. Methods of data collection

We will use a newly developed and piloted questionnaire (Appendix A) informed by the Theory of Planned Behaviour (16, 17). The questionnaire contains 3 questions to measure self-reported levels of (1) requesting blood culture samples, (2) taking blood culture samples and (3) using the results from blood culture samples. This is followed by 20 questions pertaining to attitudes and beliefs around blood culture sampling and 30 items listing potential barriers to blood culture sample, which were informed by a literature research and hospital stakeholder visits. All items will require rating, using likert-scales. The questionnaire will conclude with a final open-ended question asking for suggestions about potential interventions to improve blood culture sampling.

4.1. Data analysis

Data analysis will involve quantitative methods, including: (1) descriptive statistics of beliefs and perceived barriers to blood culture sampling, rated on likert scales; (2) confirmatory factor analysis to test the hypothesized factor structure of our newly developed questionnaire; (3) Analysis of variance (ANOVA) to test for interactions and effects of professional roles and clinical setting on attitude ratings regarding blood culture sampling; (4) multiple regression analyses to identify predictors or self-reported engagement in the blood culture pathway, and (5) qualitative content analysis of an open-ended question around potential interventions to improve blood culture sampling. The full analysis plan can be found as Appendix B.

4.2. Access to data

Before the study starts, only the administrators of the two study cohorts will have access to names and email addresses of individuals, who have previously agreed to participate in

research. During the study, the immediate research team will have access to the names and email addresses of participants, who provided contact details to receive result summaries or be entered into the prize draw. This data will not be transferred to external collaborators. The study research team will also have access to the de-identified research data (including demographic details and attitude ratings). These de-identified data will be shared with project collaborators at RAND Europe for analysis and may be deposited on Open Science Framework data repository. Consent will be sought from participants to do so.

5. Ethics

Individuals invited to participate in the survey will be provided with full study information and informed that participation is voluntary. Consent to participate will be obtained via the landing page of the survey to which participants will affirm their consent before entering the survey. Participants are not required to give their name or any personal information for completion of the online survey, unless they wish to receive a study summary or enter a prize draw to win a £50 shopping voucher, in which case they can leave their name and contact details at the end of the survey. This personal information will be stored separately from their main research data in a password protected file on the University of Leicester's secure drive. After sharing the study summary, this data will be destroyed.

In addition to these optional identifiable data, we will collect some personal data, which is required to obtain statistics about sample diversity and which will be used for some of the analyses. These personal data include age, gender and ethnicity. For all of these items, participants will have the option to select "prefer not to specify". Fully anonymised survey data will be shared with project collaborators from RAND Europe for analysis, stored on the University of Leicester servers for at least six years, and shared via the Open Science Framework research repository, in line with open science good practice.

The survey involves the completion of a short online survey about beliefs and attitudes about blood culture sampling. Blood culture sampling will be a usual or routine part of the participants' clinical role. We do not envisage there to be any adverse effects, discomfort or distress. Completion of the survey is entirely voluntary. Participants can withdraw during the survey.

Participants might find it interesting and valuable to participate in this research project and share their views on blood culture sampling. They will be contributing to the wider project's co-design process to create a bundle of interventions to optimise blood culture sampling practices in acute care for patients with suspected severe infection. They might enjoy receiving a summary of the results, which will provide insights into fellow healthcare workers' attitudes and the overall project. Additionally, a potential benefit is the chance to win a £50 shopping voucher to thank them for their time.

The study will be submitted for approval by the University of Leicester Research Ethics Committee.

6. Patient and public involvement

We convened a PPI group for the wider study comprising 7 individuals with experiences of severe infection and hospital care to advise on the study design. This PPI group reviewed and provided feedback on a survey draft via email. They commented on the general acceptability, length, and wording of questions asked. The PPI group will also be involved in

the interpretation and dissemination of results. Methods training will be provided for this purpose.

7. Dissemination

Survey results will be disseminated via conference presentation, our research group's X (Twitter) feed, as an open access peer reviewed journal article, and as part of the formal report to funder. Publications and outputs will be available on open access via the University of Leicester's library database/repository.

Participants can opt in to receive a summary of the study results. Should they wish to obtain results, they may enter their email address for this particular purpose. We will store this information separately from their data and use it for the sole purpose of sending the results summary. After sharing the summary, this data will be destroyed.

APPENDIX A – Survey about healthcare professionals' beliefs and attitudes towards blood culture sampling

1 QUESTIONS ABOUT THE PARTICIPANTS

1.1 Do you request blood culture samples to be taken for adult patients as part of your regular day-to-day work? Yes/No

1.2 Do you take blood culture samples for adult patients as part of your regular day-to-day work? Yes/No

1.3 Do you receive results from blood culture samples for adult patients in your regular day-to-day work? Yes/No

1.4 Which best describes the clinical setting you currently work in for the majority of your clinical time?
Acute Ward (medical) / Acute Ward (surgical) / Critical Care Unit (HDU or ICU) / Emergency Department / Other acute care setting (please specify) / I do not work in hospital acute care

[Anybody answering "no" to all of the first three questions or "I do not work in hospital acute care" to 1.4 will receive a statement that they aren't eligible for the study and will be directed to an exit page.]

1.5 What is your gender?
Female/Male/Other/Prefer not to say

1.6 What is your age (in years)?
_____ years/prefer not to say

1.7 How do you describe your ethnicity?
White/Mixed or Multiple ethnic groups/Asian or Asian British/Black, African, Caribbean or Black British/Other (please specify)/Prefer not to say

1.8 Which best describes your job role?
Advanced Clinical Practitioner / Doctor/ Healthcare assistant/ Nurse/ Paramedic/ Phlebotomist/ Physician's Associate / Other (please specify) /Prefer not to say

1.9 ***A: For doctors only****:* What is your career stage?
FY1/FY2/CT1/CT2/CT3/ST4+/Consultant/Other (please specify)/Prefer not to say
B: For nurses/HCAs only*:* What is your current grade?
Band 3/Band 4/Band 5/Band 6/Band 7/Band 8/Band 9/Other (please specify)/Prefer not to say
C: APCs only*:* What is your current stage of training?
Trainee / Qualified / Credentialled/Other (please specify)/Prefer not to say

2 QUESTIONS ABOUT PROFESSIONAL ENGAGEMENT IN BLOOD CULTURE SAMPLING

Please answer the following questions about your engagement in blood culture sampling for acute medical adult patients with suspected severe infection. Severe infections broadly refer to infections severe enough to require IV antibiotic treatment. There are no right or wrong answers and your responses will be completely anonymous.

2.1 In the last month, how often have you **requested** blood culture samples to be taken for acute adult medical patients with suspected severe infection?
1= Never, 2 = Hardly any shift, 3 = Some shifts, 4 = Most shifts, 5 = Almost every shift, N/A = this isn't part of my job role.

2.2 How often do you **collect** blood culture samples for acute adult medical patients with suspected severe infection?
1= Never, 2 = Hardly any shift, 3 = Some shifts, 4 = Most shifts, 5 = Almost every shift, N/A = this isn't part of my job role.

2.3 How often do you **use** blood culture results to inform your treatment for acute adult medical patients with suspected severe infection?
1= Never, 2 = Hardly any shift, 3 = Some shifts, 4 = Most shifts, 5 = Almost every shift, N/A = this isn't part of my job role.

3 QUESTIONS ABOUT BELIEFS AND ATTITUDES

Please answer the following questions about your personal opinions in the context of blood culture sampling for acute adult medical patients with suspected severe infection. There are no right or wrong answers and we are simply interested in your personal attitudes. Please rate your agreement with the questions using the following rating scale:

1 = Strongly disagree
2 = Disagree
3 = Somewhat disagree
4 = Neither agree or disagree
5 = Somewhat agree
6 = Agree
7 = Strongly agree

[Questions 3.1-3.20 will be presented in fully randomised order to each participant. Questions for reverse-coding are italicised.]

Attitudes pertaining to the general importance of blood culture sampling

3.1 In my role, blood culture sampling benefits patients with suspected severe infections.
3.2 Obtaining blood culture samples is a valuable activity that influences treatment choices in patients with suspected severe infection.
3.3 *The difficulties of obtaining meaningful blood culture samples outweigh the benefits.*
3.4 *I sometimes feel that obtaining blood culture samples is not worthwhile.*
3.5 *Compared to other clinical tasks, I find the activities involved in obtaining blood culture samples to be unpleasant.*

Perceptions of subjective norms

3.6 Colleagues I respect make time to request or collect blood cultures.
3.7 Obtaining blood cultures for every patient with suspected severe infection is part of our normal working culture within my unit of work.
3.8 Colleagues I respect value timely blood culture sampling in patients with suspected severe infection.
3.9 *I feel under pressure from colleagues to prioritise other activities over obtaining blood culture samples for patients with suspected severe infection.*

3.10 *Where I work, blood culture sampling is not considered valuable for patients with suspected severe infections.*

Perceived behavioural control (self-efficacy)

3.11 In my experience, there are many practical difficulties in obtaining timely blood culture samples.
3.12 I do not feel confident requesting or collecting blood cultures or using blood culture results.
3.13 Blood culture sampling is a routine procedure of little technical difficulty.
3.14 I often struggle to obtain blood culture samples from patients.
3.15 I have not received adequate training or guidance for activities related to blood culture sampling.

Perceived behavioural control (controllability)

3.16 Whether or not blood culture samples are obtained is out of my personal control.
3.17 There are a lot of factors outside of my control that influence whether or not blood culture samples are obtained.
3.18 It is up to me whether blood culture samples are taken from patients with suspected severe infection.
3.19 Whether blood cultures are used to inform the treatment of patients with suspected severe infection is beyond my control.
3.20 I feel like my personal choices and behaviours matter for the overall success of blood culture sampling for severe infection management.

4 QUESTIONS ABOUT FACTORS THAT AFFECT BLOOD CULTURE SAMPLING

Below is a list of factors that have been suggested as barriers to blood culture sampling for adult patients with suspected severe infection. Please rate to what extent you agree that these factors influence current blood culture sampling practices in acute hospital care in England. There is also an option to include additional factors that you have identified based on your professional experience. Please add as many factors as you consider relevant.

1 = Strongly disagree [that this factor influences blood culture sampling]
2 = Disagree [that this factor influences blood culture sampling]
3 = Somewhat disagree [that this factor influences blood culture sampling]
4 = Neither agree or disagree [that this factor influences blood culture sampling]
5 = Somewhat agree [that this factor influences blood culture sampling]
6 = Agree [that this factor influences blood culture sampling]
7 = Strongly agree [that this factor influences blood culture sampling]

[The list of factors will be presented in randomised order to each participant.]

Barriers to requesting blood culture samples

4.1 Staff forget to request blood culture samples.
4.2 The request to collect a blood culture sample is not always communicated to staff who need to take the sample.

Barriers to collecting blood culture samples

4.3 Staff forget to take blood culture samples that have been requested.
4.4 Staff find it unpleasant to take blood culture samples.
4.5 It is technically difficult to obtain blood culture samples (e.g., due to difficulties with canulation).
4.6 Staff are insufficiently skilled or experienced in taking blood culture samples.

4.7 Blood culture kits (bottles, needles, syringes) are not easily available.

Barriers to packaging, storing and transporting samples

4.8 There is insufficient knowledge about storage requirements for blood culture samples.

4.9 There is insufficient knowledge about the prevention of contamination throughout all stages of blood culture sampling.

4.10 Blood samples get delayed during transfer to the laboratories.

4.11 Blood samples get lost during transfer to the laboratories.

4.12 The location of the nearest microbiology laboratory is inconvenient (e.g., too far away).

Barriers to laboratory testing of blood culture samples

4.13 There are concerns about the financial costs of doing too many laboratory tests.

4.14 There are concerns about the quality and reliability of laboratory tests.

4.15 There is limited laboratory capacity (e.g., due to limited staff, facilities and consumables).

Barriers to using blood culture results

4.16 Staff think blood cultures are not useful, because results take too long to come back.

4.17 There is a lack of *immediate* clinical value of taking blood culture samples.

4.18 Staff think that blood culture results make little difference to patient treatment.

Barriers concerning general attitudes, knowledge and individual staff priorities

4.19 Staff members feel too busy to engage in blood culture sampling.

4.20 Obtaining blood culture samples is seen as less of a priority than other clinical activities.

4.21 There is a perceived lack of evidence that blood culture sampling improves patient care.

4.22 Staff do not know enough about how blood cultures affect antibiotic prescribing.

4.23 Not enough staff know about national or hospital guidelines around blood culture sampling.

4.24 National and hospital blood culture collection guidance is difficult or impractical to follow.

4.25 Clinical colleagues don't value blood culture sampling.

4.26 Senior colleagues or managers don't value blood culture sampling.

Barriers pertaining to team management and communication

4.27 There is a lack of clarity about roles and responsibilities (e.g., it is unclear who is responsible for taking blood culture samples).

4.28 The person requesting the blood culture samples is not the one who will receive the results.

4.29 The person requesting blood culture samples doesn't find out how these blood culture results inform care later on.

Other barriers

4.30 Other, please specify: _____

5 OPEN-ENDED QUESTIONS

5.1 In your opinion, what actions or interventions might be useful to improve blood culture sampling practice to inform the treatment of patients with acute infection?

5.2 Many thanks for sharing your opinions about blood culture sampling with us. Are there any other thoughts, opinions or suggestions you would like to share about blood culture sampling for patients with suspected severe infection?

APPENDIX 2 – Analysis plan

1) Have any data been collected for this study already?
No, no data have been collected for this study yet.

2) What's the main question being asked or hypothesis being tested in this study?
Q1. Does our newly developed attitude questionnaire capture key components of the Theory of Planned Behaviour within the context of blood culture sampling?
Q2. What are NHS healthcare professionals' attitudes towards blood culture sampling for adult patients with suspected severe infection? Do these attitudes differ by professional role and clinical setting?
Q3. What are predictors of self-reported engagement in clinical activities that form part of the blood culture pathway?
Q3. What are perceived barriers to healthcare staff engaging in clinical activities related to blood culture sampling for managing suspected severe infection? Do these perceived barriers differ by professional role or clinical setting?
H1. Healthcare staff's attitudes around blood culture sampling will map on to a four-factor structure proposed by the Theory of Planned Behaviour: (1) perceived importance, (2) social norms, (3) self-efficacy and (4) controllability.
H2a. There will be significant differences between the mean ratings of the four attitude dimensions.
H2b. Individuals' professional roles and the clinical setting they work in will have a significant effect on their ratings of the four attitude dimensions.
H3. The four attitude dimensions will be significant predictors for self-reported engagement in the requesting of blood cultures, collection of blood culture samples and use of blood culture results.
H4. Perceptions of the most influential barriers to blood culture sampling will differ across professional roles and clinical settings.

3) Describe the key dependent variable(s) specifying how they will be measured.
1. **Attitude variables:** We will assess beliefs and attitudes pertaining to blood culture sampling via 20 author-designed questions, created to capture different attitude dimensions that are modelled on the Theory of Planned Behaviour. Each attitude question will be measured on a 7-point likert scale ranging from 1 (strongly disagree) to 7 (strongly agree).
2. **Engagement variables:** We will assess three single-item, self-reported variables measuring how frequently healthcare staff engage in different aspects of blood culture sampling: (1) requesting samples, (2) collecting samples, and (3) using the results from samples. Variables will be measured on a 5-point likert scale (1= Never, 2 = Hardly any shift, 3 = Some shifts, 4 = Most shifts, 5 = Almost every shift, N/A = this isn't part of my job role).
3. **Barrier variables:** We will assess the perceived influences of 29 barriers to blood culture sampling, measured via a 7-point likert scale ranging from 1 (strongly disagree that this factor influences blood culture sampling) to 7 (strongly agree that this factor influences blood culture sampling).

4) How many and which conditions will participants be assigned to?
We will employ a quasi-experimental design, where professional role (doctors vs. advanced clinical practitioners, nurses, paramedics & physician associates vs. healthcare assistants & phlebotomists) and clinical setting (acute medical ward vs. acute surgical ward vs. emergency department vs. critical care unit) will be treated as between-subject IVs.

5) Specify exactly which analyses you will conduct to examine the main question/hypothesis.
H1: We will run a confirmatory factor analysis to test our hypothesized factor structure and validate our attitude questionnaire in the context of blood culture sampling. We will use Maximum Likelihood for our estimation method and assess the goodness of fit of the resulting models using six key statistics: chi-square ($\chi 2$); relative chi-square (CMIN/DF); comparative fit index (CFI); non-normed fit index (NNFI); root mean square error of approximation (RMSEA); and standardized root mean square residual (SRMR). Following identification

of the best model fit, four latent attitude variables will be confirmed, which will be based on the theoretical dimensions of (1) perceived importance, (2) social norms, (3) self-efficacy and (4) controllability in the context of blood culture sampling. For each of these latent variables, factor scores will be calculated by deriving the mean of all constituent variables. We will use these latent variables for our subsequent analyses.
H2a,b: We will run a 3×4 between-within subjects ANOVA to test for interactions and simple main effects of professional role and latent attitude dimension on mean attitude ratings.
We will run a 4×4 between-within subjects ANOVA to test for interactions and simple main effects of clinical setting and latent attitude dimension on mean attitude ratings.
If significant main effects are detected for either ANOVA, we will conduct Bonferroni-corrected pairwise comparisons as follow-up analyses.
H2: We will run three multiple regression analyses, one for each of our engagement variables. For each regression analysis, predictors will be entered hierarchically in blocks.
Block 1: Demographic variables. This will include *age*, *gender* → female/other (1), male (0); and *ethnicity* → people of colour (1), white (0). **Block 2: Professional variables.** This will include *professional role* → healthcare assistants & phlebotomists (2), advanced clinical practitioners, nurses, paramedics & physician associates (1), doctors (0); *clinical setting* → acute surgical ward (3); emergency department (2); critical care unit (1); acute medical ward (0); and *seniority* → junior (1), senior (0). **Block 3: Attitudes and beliefs**. This will include the latent attitude variables identified in our factor analysis.
H3: We will produce descriptive statistics for the influence ratings pertaining to each of the 29 barriers to blood culture sampling. We will produce an overall ranking of the 3 most influential barriers and separate rankings of barriers for different professional roles and clinical settings.

6) Describe exactly how outliers will be defined and handled, and your precise rule(s) for excluding observations.
We will exclude participants, who took less than five [revise after piloting] minutes to complete the survey.
We will exclude participants, who did not complete all 20 attitude questions.
We will exclude participants suspected of "straight-lining". We will test for this separately across the 20 questions measuring attitudes and 29 questions assessing the influence of key barriers by calculating the standard deviation. Participants will be excluded from analyses if their likert ratings from either section have a standard deviation of ≤ 0.45.

7) How many observations will be collected or what will determine sample size?
No need to justify decision, but be precise about <u>exactly</u> how the number will be determined.
We considered sample size requirements across our different analyses. Sample size recommendations for scale validation vary depending on the sample type used. For more specific samples (as opposed to samples drawn from the general population), 250-350 participants have been recommended (White, 2021). For our ANOVAs, we ran a G*power calculation for ANOVA (repeated measures, between factors) with 4 groups and 4 measurements, assuming a correlation of up to 0.5. We estimated a power of .80 and an α error probability of .01 to detect a medium effect size f = .25, which returned 236 participants. For our linear multiple regression analysis (fixed model, R^2 increase) with 10 predictors, we ran a G*power calculation, estimating a power of .80 and an α error probability of .01 to detect a medium effect size f = .15, which returned 160 participants. To satisfy sampling requirements for all types of analyses and to account for potential data loss from incomplete submissions and exclusions, we will recruit up to 400 participants.

8) Anything else you would like to pre-register?
(e.g., secondary analyses, variables collected for exploratory purposes, unusual analyses planned?)
N/A

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FULL/LONG TITLE OF THE STUDY

Getting the bloods to the laboratory: developing interventions to improve the blood culture pathway for patient safety and antimicrobial stewardship.

SHORT STUDY TITLE / ACRONYM

iSAMPLE-Improving blood sampling for AMS (Parts 1c & 2)

PROTOCOL VERSION NUMBER AND DATE: Protocol Version 1.0 – 22-01-2024

IRAS Number:332310

SPONSOR Number: 0946

FUNDER:

National Institute for Health and Care Research (NIHR156452)

Ethical approvals:

This protocol (parts 1c&2) has received ethical approval from South West – Frenchay NHS Research Ethics Committee (Ref 24/SW/0030). The protocol has received HRA and Health and Care Research Wales (HCRW) Approval (Ref 24/SW/0030), and full Confidentiality Advisory Group (CAG) support (Ref 24/CAG/0044).

This protocol has regard for the HRA guidance and order of content

SIGNATURE PAGE

The undersigned confirm that the following protocol has been agreed and accepted and that the Chief Investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the principles outlined in the Declaration of Helsinki, the Sponsor's SOPs, and other regulatory requirement.

I agree to ensure that the confidential information contained in this document will not be used for any other purpose other than the evaluation or conduct of the investigation without the prior written consent of the Sponsor

I also confirm that I will make the findings of the study publicly available through publication or other dissemination tools without any unnecessary delay and that an honest accurate and transparent account of the study will be given; and that any discrepancies from the study as planned in this protocol will be explained.

Sponsor:	
Name (please print):	Dr Cat Taylor
Signature:	
Position:	Head of Research Governance
Date:	06th June 2024
Chief Investigator:	
Name: (please print):	Prof Carolyn Tarrant
Signature:	
Date:	06/06/24
Principal Investigator:	
Site:	
Name: (please print):	
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CONTENTS

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Funder(s)	The study has been funded by NIHR Health and Social Care Delivery Research (HSDR) / (NIHR156452)
Key Protocol Contributors	Professor Carolyn Tarrant Dr Eva Krockow Professor Alison Prendiville Tony Locke Professor Laura Shallcross Dr David Jenkins Professor Tim Coats Dr Nicky Fahy

STUDY SUMMARY

Study Title	Getting the bloods to the laboratory: developing interventions to improve the blood culture pathway for patient safety and antimicrobial stewardship.
Study Design	Qualitative: observations and interviews [Part 1c] Iterative: solution-focused, intervention co-design, piloting and evaluation [Part 2]
Study Participants	Staff members responsible for requesting and taking blood samples in emergency departments, admission units, other hospital wards, and microbiology laboratories [Part1c] Patient participants from PPI groups and hospital staff Part 2]
Planned Size of Sample (if applicable)	**Part 1c** • 150 hours of ethnographic observations across the three sites in emergency departments, admissions units, other hospital wards, and microbiology laboratories. • **Interviews:** a maximum of 15 staff from each site (36-45 in total). **Part 2a** • **Co-design Workshops:** a maximum of 16 participants (mixture of staff and/or patients) from each site (48 in total). **Part 2b** • **Pilot Intervention:** Detail to be added via an amendment. Interventions will be co-designed during the stage 2 workshops and may take different forms e.g. a new staff role to take bloods, a new approach to feeding back audit data, a redesign of blood sampling equipment packs. The approach to piloting and evaluating these will be designed to reflect the nature of and users of the interventions. **Part 2c** • **Evaluation Focus groups:** a maximum of 8 staff from each site (24 in total). • **Evaluation Interviews:** a maximum of 6 staff from each site (18 in total)
Follow up duration (if applicable)	N/A
Planned Study Period	May 24-September 25 [Part 1c]

	Feb 24- Feb 26 [Part 2]
Research Question/Aim(s)	As a whole, **i-SAMPLE** is designed to *understand* [Part 1] and *improve* [Part 2], through embedded co-design and evaluation, the blood culture pathway in acute settings. The aims of the study are: •to ensure patients receive the best infection specific antibiotic at the earliest stage of their treatment •to decrease the overuse of antibiotics which causes antimicrobial resistance To understand the pathway, we will undertake 1a. A quantitative analysis of routine hospital data to see when samples are taken and cultures are done, and how that affects antibiotic prescribing. 1b. A Survey of healthcare professionals' attitudes and beliefs about blood culture 1c. Observations of, and interviews with staff who are engaged with the blood culture pathway In parallel, to improve the pathway, the knowledge gained from Part 1 will be fed into, and support a co-design process, Part 2. Part 2 is intended to discover the factors that affect the blood culture pathway for good or ill, to define/represent a detailed archetypical blood culture pathway with the aim of using that to develop and evaluate interventions to improve the pathway. The evaluation work will utilise focus groups and interviews. This protocol has reference to Part 1c and Part 2 ***only*** of the **i-SAMPLE** study. The other components of the study (part 1a and b) comprise separate applications/protocols.

FUNDING AND SUPPORT IN KIND

FUNDER(S) (Names and contact details of ALL organisations providing funding and/or support in kind for this project)	**FINANCIAL AND NON FINANCIALSUPPORT GIVEN**
National Institute for Health Research (NIHR156452)	**Financial support (**£752,059.85)

ROLE OF STUDY SPONSOR

The sponsor of this research is the University of Leicester. The University of Leicester is registered as a research sponsor with the Department of Health and routinely takes responsibility as sponsor for research activities within the NHS.

ROLES AND RESPONSIBILITIES OF STUDY MANAGEMENT COMMITTEES/GROUPS & INDIVIDUALS

Study management group

The PI (Tarrant) will take overall responsibility for delivering the project, for overall oversight and coordination of all activities, for ensuring effective integration of study components, and for monitoring progress and quality of outputs.

Each part of the study will have a named lead: 1c (Tarrant) and 2 (Prendiville). Tarrant and Krockow will manage the full-time RA at University of Leicester, Prendiville will manage the part-time RA at the University of the Arts London, while Krockow will be the PPI lead and will work closely with Locke (the PPI co-applicant).

The study management group is made up of the co-applicants, research staff and the PPI representative. The group will share responsibility for the quality and delivery of the project, creation of outputs and dissemination of findings. Meetings with all co-applicants will be convened at least twice per year.

Those involved in delivering each part of the project and the PPI representative will meet monthly to share and monitor progress and to coordinate activities

The patient advisory group meetings will be held three times per year.

Expert steering committee

There will also be an expert steering committee of around 6-8 members, including academics, stakeholders from government organisations, national charities, professional bodies, and clinical leaders. The steering group includes an expert in behavioural science, representatives from NHS England Blood Culture Team, the Royal College of Emergency Medicine, national charities and societies (The Sepsis Trust, British Society for Antimicrobial Chemotherapy) - all of whom have expressed their commitment to supporting the study), and a diagnostics representative (Chief Executive Officer, Cytecom Limited).

The steering committee will meet with the study team up to three times a year to review progress and reflect on findings. The study team will discuss implications for practice and policy with the steering committee and seek advice and input into dissemination and generating impact.

Patient and public involvement

Prior to developing this project, we convened a PPI group (Oct 2022) comprising six patients, with experience of severe infection and hospital care, to advise on study design. We invited an open discussion, about the design of the project and about how best to involve patients in research, co-design, and dissemination.

All feedback was taken into account and designed into this project. For example, we have ensured that PPI representatives are involved in study team meetings; offered to provide training to all PPI members on research, methods and on specific research topics; have set aside funding for PPI members to attend/present at conferences.

The project will include two dedicated roles designed to facilitate PPI support and engagement: PPI co-applicant (Locke), will represent the PPI group at project management

meetings and act as a liaison, and PPI lead (Krockow) will be responsible for collaborating with PPI members to develop PPI plans and identify training and support needs. The PPI lead (Krockow) will be accessible to PPI members throughout the project.

ABBREVIATIONS

AMR	anti- microbial resistance
AWaRe	Access, Watch and Reserve
BSAC	British Society for Antimicrobial Chemotherapy
EHPS	European Health Psychology Symposium
HSDR	Health and Social Care Delivery Research
HSRUK	Health Services Research UK conference
NASSS	non-adoption, abandonment, scale-up, spread, sustainability
NASSS-CAT	(Complexity Assessment Toolkit)
NHSE	NHS England
NIHR	National Institute for Health and Care Research
PPI	Patient and Public Involvement

KEY WORDS:

Anti-Microbial resistance

Antibiotic stewardship

Blood cultures

Blood sampling pathway

Co-design

STUDY FLOW CHARTS

Figure 1 **I-SAMPLE**: Study Design- emphasis on **Qualitative elements Part 1c and Part 2**

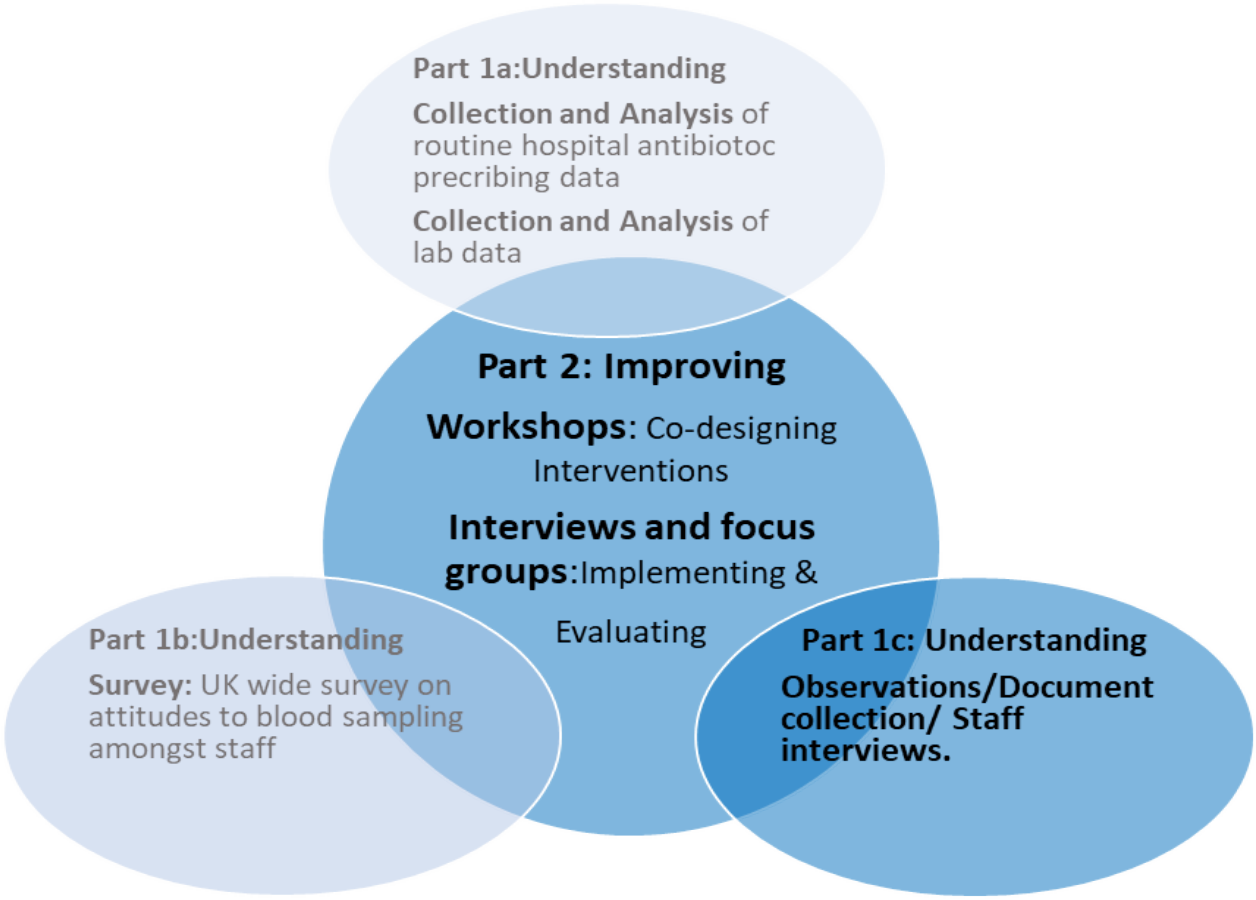
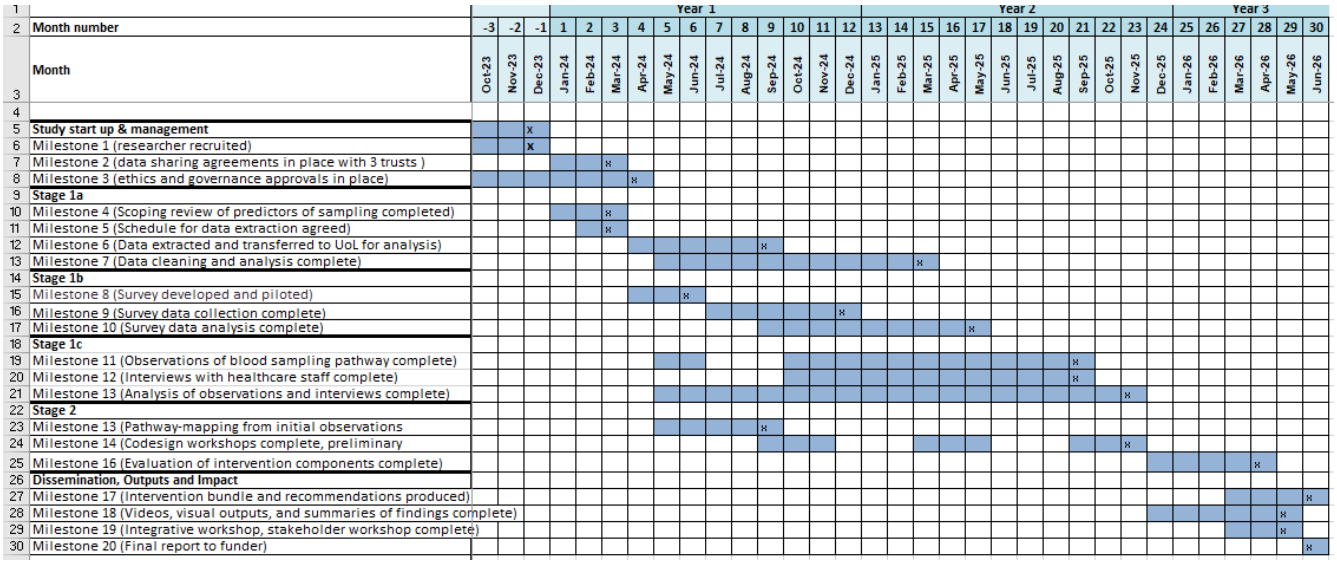


Figure 2- **I-SAMPLE**: Study **Gantt chart**



	Year 1														Year 2												Year 3					
Month number	-3	-2	-1	1	2	3	4	5	6	7	8	9	10	11	12	13	14	15	16	17	18	19	20	21	22	23	24	25	26	27	28	29	30
Month	Oct-23	Nov-23	Dec-23	Jan-24	Feb-24	Mar-24	Apr-24	May-24	Jun-24	Jul-24	Aug-24	Sep-24	Oct-24	Nov-24	Dec-24	Jan-25	Feb-25	Mar-25	Apr-25	May-25	Jun-25	Jul-25	Aug-25	Sep-25	Oct-25	Nov-25	Dec-25	Jan-26	Feb-26	Mar-26	Apr-26	May-26	Jun-26
Study start up & management			x																													
Milestone 1 (researcher recruited)			x																													
Milestone 2 (data sharing agreements in place with 3 trusts)						x																										
Milestone 3 (ethics and governance approvals in place)							x																									
Stage 1a																																
Milestone 4 (Scoping review of predictors of sampling completed)						x																										
Milestone 5 (Schedule for data extraction agreed)						x																										
Milestone 6 (Data extracted and transferred to UoL for analysis)												x																				
Milestone 7 (Data cleaning and analysis complete)																		x														
Stage 1b																																
Milestone 8 (Survey developed and piloted)									x																							
Milestone 9 (Survey data collection complete)															x																	
Milestone 10 (Survey data analysis complete)																				x												
Stage 1c																																
Milestone 11 (Observations of blood sampling pathway complete)																								x								
Milestone 12 (Interviews with healthcare staff complete)																								x								
Milestone 13 (Analysis of observations and interviews complete)																										x						
Stage 2																																
Milestone 13 (Pathway-mapping from initial observations												x																				
Milestone 14 (Codesign workshops complete, preliminary																										x						
Milestone 16 (Evaluation of intervention components complete)																															x	
Dissemination, Outputs and Impact																																
Milestone 17 (Intervention bundle and recommendations produced)																																x
Milestone 18 (Videos, visual outputs, and summaries of findings complete)																															x	
Milestone 19 (Integrative workshop, stakeholder workshop complete)																															x	
Milestone 20 (Final report to funder)																																x

1. BACKGROUND

Inappropriate antibiotic use contributes to the growing problem of antimicrobial resistance. In England in 2020, 55,000 patients were affected by antibiotic-resistant infections putting them at risk of poor outcomes and death (1). Evidence shows that resistance results from the overuse of broad-spectrum antibiotics, and prolonged courses of antibiotics, but the use of antibiotics, particularly broad-spectrum antibiotics, continues to increase in hospitals in England (2). As well as the harm posed to patients by the rise of antimicrobial resistance, increasing resistance poses a threat to the system in terms of increased costs and care burden.

Currently, in England, the rapid administration of broad-spectrum antibiotics is recommended for acutely unwell patients with sepsis (3). Additionally, broad-spectrum antibiotics are often initiated 'just in case', for suspected infection, to manage risk (4). In these circumstances, collecting and analysing timely and good quality blood cultures are important to inform the review and potential revision of the initial prescribing decision to an antibiotic that specifically targets the patient's infection (5 6,7). The rapid identification of pathogens from blood cultures is known to play a role in reducing individual and population mortality from severe infection and sepsis (8, 9,10).

Performing blood cultures reliably has been identified as a key quality indicator for appropriate antibiotic use in hospitalised adults with suspected severe infection (11), and the presence of microbiology results for all patients identified as one of three priority factors with the greatest influence on optimising antibiotic use in hospitals (12).

Despite the known importance of the knowledge that blood analysis can realise, we also know that the process of blood collection, and sample transportation to the microbiology laboratory can reduce the quality and utility of microbiology results (13). For example, an insufficient volume of blood taken for testing, the contamination of blood samples, and delays in transport are all factors that can substantially and adversely affect the diagnostic value of samples. (14).

Furthermore, an additional issue of concern is that, despite the importance of blood cultures for patient management and antimicrobial stewardship, around half of hospital patients do not have blood samples taken at all when antibiotics are started (15-19).

2. RATIONALE

Whilst we have ample evidence to indicate that blood sampling procedures and processes do not always meet the standards of best practice, we have little knowledge of why that occurs. We need to better understand the behavioural, social, and organisational factors that contribute to poor quality blood sampling in acute care. The blood culture pathway is complex and involves many factors and the timely co-ordination of effort to get the blood to the lab. Blood sampling practices are potentially underpinned by a complex range of behavioural, cultural and systems factors (23).

There is a pressing need for novel theory-based research and intervention development to optimise the pre-analytic blood culture pathway to improve patient safety, outcomes, and effective antimicrobial stewardship. Although interventions have been developed to address

problems in acute pathways, these have tended to focus on clinical and technical issues, as opposed to social, behavioural and other factors (14, 20, 21). Recommendations have been made for the need for multi-model approaches to improve blood culture collection practices, based on research using mixed-methods, to generate a holistic knowledge of pathways and thus mitigate barriers to quality improvement and stewardship. (22).

Following on from our previous theory-driven research into overuse of broad-spectrum antibiotics in acute medical patients (4, 27), we draw on theories of individual and collective behaviour to identify the behavioural, social and organisational influences on the reliability and quality of blood culture sampling in acute care, and to develop interventions that will be implementable across diverse health care settings.

Why this research is needed now

Our work aligns with the NIHR priority area of Antibiotic Resistance, and supports delivery of the national anti- microbial resistance (AMR) action plan through increasing use of diagnostic tests to inform antibiotic use (29). Optimising the blood culture pathway is a current priority for NHS England (NHSE).

A national survey in 2018 by NHSE identified significant scope for improvement in adherence to national quality standards for blood cultures (29). NHSE set out requirements for the volume of blood to be collected, and for the timely transport of blood samples to the laboratory-ideally within a maximum of 4 hours. Further, the NHS standard contract for 2022-2023 includes a requirement of demonstrable improvement in compliance with these standards (30). This is being supported by a programme of work led by NHSE involving national audit, new training modules developed in collaboration with the British Society for Antimicrobial Chemotherapy (BSAC), and recommendations for leadership and multidisciplinary involvement (31). Further, many new rapid tests for antibiotic sensitivity are being developed and implemented (32), which are dependent on the reliable collection of bloods.

Our research will support and inform efforts and interventions to meet standards, by providing a deeper, holistic understanding of the barriers to optimising the blood culture pathway in acute settings.

3. THEORETICAL FRAMEWORK

Our project aims to develop a midrange theory of individual, collective and organisational influences on blood sampling in acute hospital care. We plan to do this by drawing on existing theory and previous empirical data. We will test and revise our framework through Part 1a, b, and c (part 1a and 1b are the subject of separate applications), and through the project's co-design process: Part 2, develop a proposal for theory-based interventions, which will be piloted and evaluated. These may include feedback on outcomes to staff taking the bloods or new staff roles dedicated to taking bloods. We will assess feasibility and acceptability through the co-design work, and small-scale testing of feasibility and uptake.

We will draw on both psychological and social science theory to develop our framework. Psychological insights will be taken from the Theory of Planned Behaviour (25), which posits that a combination of personal attitudes, subjective norms and perceived behavioural control may influence the actions of those involved in the sampling pathway. From this perspective, we hypothesise that perceived behavioural control is likely a key factor in blood sampling due to the often-unclear clinical responsibilities of different healthcare staff and the fact that blood sampling results often benefit other clinicians' decision-making at a later treatment stage.

Further, we will draw upon Collective Action Theory (26) which is concerned with how conflicts of interests between individuals and the wider community play out. Collective action theory (27) sensitises us to the possibility that individual healthcare staff may be subject to competing priorities. For example, the link between successful blood sampling to improve diagnosis and target antibiotic treatment and the longer-term consequences for antimicrobial resistance may be in tension with short-term priorities of ensuring patient survival. Capturing and understanding where and why tensions arise will enable us to see how priorities and expectations play out across and between organisational settings and hierarchies.

In Part 2, we will develop a range of visual co-design tools including: journey mapping of the blood culture pathway; key actors mapping; development of archetypes of key actors; story-boards of patient journeys; and potential barriers from the ethnographic work Part 1c and the survey Part 1b. These methodological tools will scaffold the co-design workshops to elicit creative ideas and design grounded interventions through ongoing dialogue with stake holders. For this part of our work, we will be applying the Design Council's (33) double diamond framework for service innovation which is an iterative process of; discover, define, develop and deliver.

We will draw on the NASSS (non-adoption, abandonment, scale-up, spread, sustainability) framework (34), and NASSS-CAT (Complexity Assessment Toolkit) tools (35), to assess usability and plan for implementation issues during the intervention development process, and to guide the initial evaluation of feasibility, acceptability and likely uptake of each intervention. Our evaluation work will include 5-6 staff interviews in each site to explore feasibility, uptake and usability. It will also include a focus group, with 6-8 staff in each site using vignettes and walkthroughs of the proposed bundle of interventions within the specific context of each site, to assess feasibility and considerations for implementation, using the NASSS-CAT interview guide.

4. RESEARCH QUESTION/AIM(S)

As a whole, i-SAMPLE is designed to understand [Part 1] and improve [Part 2], through embedded co-design and evaluation, the blood culture pathway in acute settings. The overall aims of the study are:

- to ensure patients receive the best infection specific antibiotic at the earliest stage of their treatment
- to decrease the overuse of antibiotics which causes antimicrobial resistance

To understand the pathway, we will undertake

- A quantitative analysis of routine hospital data to see when samples are taken and cultures are done, and how that affects antibiotic prescribing: Part 1a.
- A Survey of healthcare professionals' attitudes and beliefs about blood culture: Part 1b.
- Observations of, and interviews with staff who are engaged with the blood culture pathway: Part 1c

In parallel, to improve the pathway, the knowledge gained from Part 1 will be fed into, and support a co-design process, Part 2. Part 2 is intended to map out the factors that affect the blood culture pathway for good or ill, and to define/represent a detailed archetypical blood culture pathway with the aim of using that to develop, pilot and evaluate interventions to improve the pathway.

4.1 Primary Objectives

- To understand the organisational, social, and behavioural factors that impact on practices along the pre-analytic blood culture pathway in acute care: [Part 1c]
- To co-design interventions to target barriers for optimising practices in the pre-analytic blood culture pathway in acute care, to pilot the intervention and to conduct initial evaluation of feasibility and usability: [Part 2]

4.2 Outcomes

- To generate information on organisational, social, and behavioural influences on the pre-analytic blood culture pathway, to inform the co-design process, and to publish outputs describing the dynamics of collective action in the pre-analytic blood culture pathway [Part 1]
- To produce and evaluate a bundle of interventions to optimise practices along the pre-analytic blood culture pathway, which will be implementable across diverse health care settings [Part 2]
- To create a range of mixed media outputs which will include:
    - a set of visual tools for hospital staff to identify their current blood cultural pathways and processes with templates to support scaffold local enquiry into practices and opportunities.
    - video outputs will be created to reflect narratives which support the research findings, approaches and interventions from our study in a format that can be easily shared across different stakeholders - patient groups, and staff.
    - A set of service blueprints will be produced for prototyped interventions to show how the interventions will strengthen current systems of good practice around blood culture sampling.
    - A set of high-level policy recommendations will further support blood culture sampling practices and be hosted on a dedicated project website.

5. STUDY DESIGN

As a whole the study will use a mixed methods approach. **This protocol refers to Part 1c and Part 2 of the study design which both use qualitative methods**:

- Part 1c: Ethnographic observations and participant interviews
- Part 2: 2 is made up of 3 sections.
    - Part a = Co-design workshops
    - Part b = Piloting and evaluating the intervention
    - Part c = Evaluation interviews and focus groups
- Details relating to Part 2b will be added via an amendment as information pertaining to this part of the study will be developed during the part 2a workshops.

5.1 Schedule of Procedures

Part 1c – Interviews

	Visits		
	Observation Period 1 (lasting approx. 7 days)	**Observation Period 2** (lasting approx. 7 days)	**Visit 1**
Study timeline	Month 3-20		Month 10-20
Procedures			
Identification of potential participants	5 mins	5 mins	
Collect expressions of interest in participating in part 1c	5 mins	5 mins	
Collect expressions of interest in participating in part 2a	5 mins	5 mins	
Consent			30 mins
Interviews			60 mins

Part 2a - Workshops

		Visits			
Procedures	**Pre-Workshop**	**Workshop 1 (x3)**	**Workshop 2 (x3)**	**Workshop 3 (x3)**	**Workshop 4 (x3)**
Identification of potential participants	5 mins				
Consent for workshop		30 mins	30 mins – new	30 mins – new	30 mins – new

		(Prior to any research activity taking place)	participants only) (Prior to any research activity taking place)	participants only) (Prior to any research activity taking place)	participant sonly) (Prior to any research activity taking place)
Co-design Workshop (Participant can attend any one or all four)		60 mins	60 mins	60 mins	60 mins

Part 2c – Evaluation Focus Groups and Interviews

	Visits		
Procedures	**Pre-Interview/ Focus group**	**Visit 1**	**Visit 2 (optional)**
Identification and approach of potential participants (healthcare staff)	5 mins		
Consent		30 mins (Prior to any research activity taking place)	30 mins – new participants only) (Prior to any research activity taking place)
Interviews		60 mins	60 mins
Focus Groups		60 mins	60 mins

5.2 Sample and Recruitment

5.2.1 Eligibility Criteria

Part 1c – Interviews

Inclusion criteria

- Healthcare staff who occupy key roles in the blood sampling pathway in each site.

Exclusion criteria

- Healthcare staff who do not occupy key roles in the blood sampling pathway in each site.

Part 2a – Co-design Workshops

Inclusion criteria

- Health care staff who have experience of the acute care pathway and /or the blood culture pathway.
- Patients who:

- Have experience of the acute care pathway and /or the blood culture pathway.
- Are aged 18 years old or over
- Have the ability to understand verbal and written English.
- Have the ability to provide informed consent to take part.

Exclusion criteria

- Health care staff who do not have experience of the acute care pathway and /or the blood culture pathway.
- Patients who:
  - Do not have experience of the acute care pathway and /or the blood culture pathway.
  - Are aged under 18 years old
  - Do not have the ability to understand verbal and written English
  - Lack the ability to provide informed consent to take part.

Part 2c – Evaluation Interviews and Focus Groups

Inclusion criteria

- Staff who have been involved in the piloting of interventions

Exclusion criteria

- Staff who have not been involved in the piloting of interventions.

5.2.2 Sampling

Site Sampling

Part 1c and Part 2 will take place in three trusts which have been sampled for diversity, University Hospitals Leicester, University College London Hospitals, and Kettering General Hospital NHS Foundation Trust. These trusts serve populations with diverse health needs, ethnicity, and socio-economic status, and are located in different geographical regions.

The trusts vary in antibiotic use (total antibiotic prescribing, and prescribing from the 'Watch' and 'Reserve' WHO AWaRe categories, defined daily doses per 1000 admissions) compared to the England average (51). The trusts use different electronic patient record systems and have differing levels of digital maturity. They include trusts with in-hospital, and outsourced, microbiology laboratory services.

Within-site (Participant) sampling

Part 1c – Interviews: Purposive Sampling

- Hospital staff will be identified during the observation period. Purposive sampling will be undertaken whereby individuals who have been identified during the observations as being key decision-makers/staff with key roles along the pathway will be approached by the site lead, or directly by the researcher if they have already engaged with the researcher during observations, to see if they would be interested in taking part. This will include junior doctors and other staff responsible for requesting and taking blood samples, as well as other key staff along the pathway including microbiology staff.

Part 2a – Co-design Workshops: Purposive and snowball sampling

Patients

- Potential patient participants will be recruited from each of the hospitals' PPI groups to include patients with experience of the acute care pathway.

Healthcare staff

- Hospital staff will be recruited through purposive snowball sampling with support from the local clinical and junior doctor lead in each trust. Staff will be approached by the site lead and provided with a copy of the study information leaflet.

Part 2c – Evaluation Focus groups and interviews: Purposive sampling

Healthcare staff

- In each site, we will purposively sample interview and focus group participants from hospital staff who have been involved with the local blood culture pathway, those who took part in the workshops and/ or been involved in the piloting of interventions. Staff will be approached by the site lead and provided with a copy of the participant information sheet. Staff can choose to participate in the focus group, an individual interview, or both.

5.2.3 Size of sample

Part 1c

- **Interviews:** a maximum of 15 staff from each site (36-45 in total).

Part 2a

- **Co-design Workshops:** a maximum of 16 participants (mixture of staff and/or patients) from each site (48 in total).

Part 2c

- **Evaluation Focus groups:** a maximum of 8 staff from each site (24 in total).

- **Evaluation Interviews:** a maximum of 6 staff from each site (18 in total)

It is expected that some people will participate in more than one element of the study and so the actual number of participants in Part 1c and Part 2 will be less than 135.

5.3 Consent and withdrawal

For part 1c (interviews) and Part 2a and c- informed consent will be obtained prior to a participant taking part in any study activity using the latest approved version of the informed consent form.

Potential participants will be provided with written information about the study and informed that participation is completely voluntary. They will be given the opportunity to ask questions and will have these satisfactorily answered. Participants will be advised that they can decide to withdraw from the study at any point, without giving a reason but that any data collected up to the point of withdrawal will be retained. This will be stipulated in the Participant Information Sheet. The Participant Information sheets will describe the purpose of the research, what is expected of participants, how data will be collected, stored and used; and how research findings will be disseminated.

For consent to be ethical and valid in law, participants must be capable of giving consent for themselves. A capable person will indicate on the consent form that they have read the information leaflet and that they:

- Understand the purpose and nature of the research
- Understand what the research involves, its benefits (or lack of benefits), risks and burdens
- Consent to the voice recording of the interview/focus group
- Consent to their anonymised and pseudonymised data being used in outputs
- Consent to their anonymised and pseudonymised data being stored on University of Leicester secure services in restricted access folders

Where consent takes place in person, written informed consent will be obtained by means of the participant personally initially each statement on the consent from before printing, dating and signing the consent form as a whole. The researcher who presented and obtained the informed consent will then countersign, date and print their name.

Where consent is obtained remotely, the participant will be sent a copy of the informed consent form via email. The participant will be asked to either manually or electronically initial each statement before dating and signing the consent form as a whole. This will be returned by email for the researcher to countersign, after which a fully signed copy will be returned to the participant via email.

In either case, the person who obtains the consent will be suitably qualified and experienced, and will have been authorised to do so by the Principal Investigator as detailed on the Delegation of Authority and Signature Log for the study. The original signed consent form will be retained at the study site within the Trial Master File (TMF) or Investigator Site File (ISF) and a copy of the fully signed Informed Consent Form will be returned to the participant.

Part 1c – Ethnographic Observations

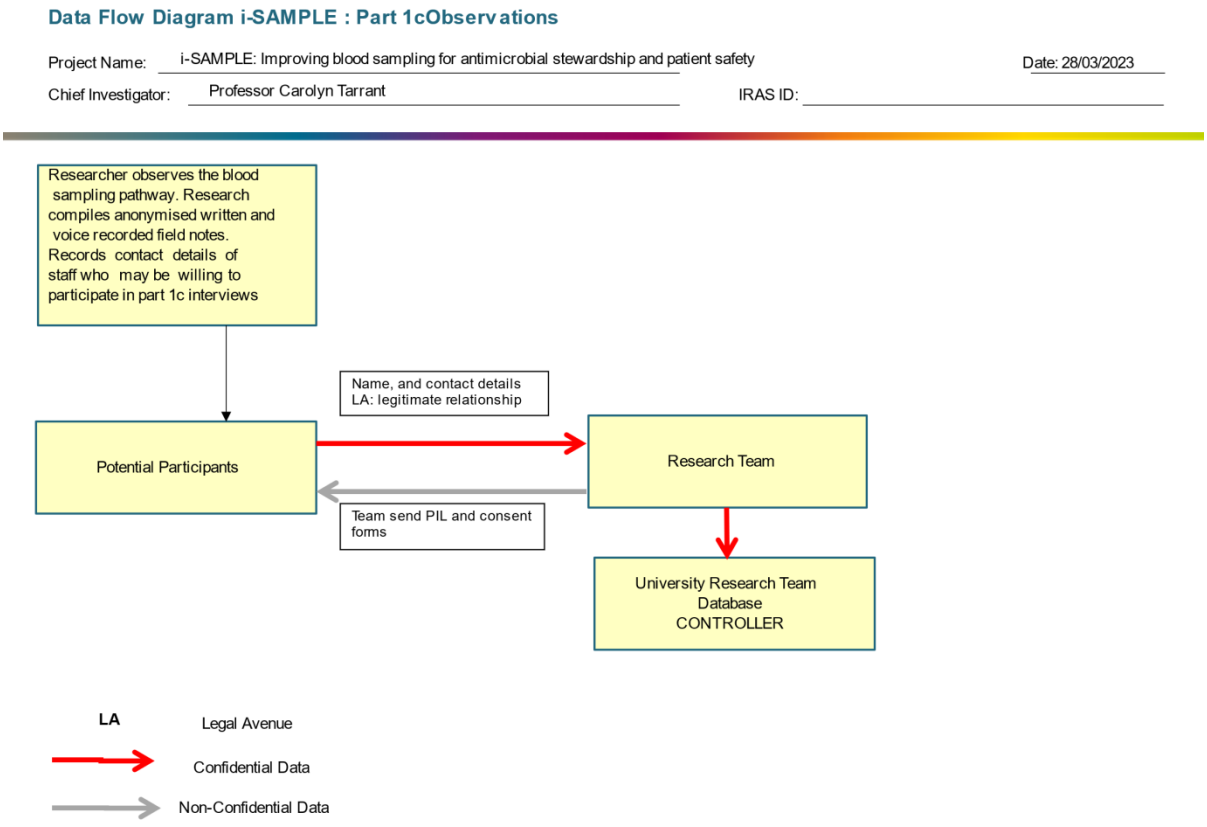
In the case of ethnographic observations [Part 1c], it will not be possible to obtain individual consent from patients, their families, and hospital staff, for the presence of a researcher conducting observations along the blood culture pathway. Information about the study will be displayed in relevant areas that the researcher will visit. During observations the researcher will explain who they are and will wear an identifying badge. They will obtain verbal permission to conduct observations. If the researcher is observing an interaction between a healthcare professional and a patient or their family, the healthcare professional will seek permission of the patient and/or family for the researcher to be present. The researcher will immediately withdraw from any situation if requested to do so. Given that the research will be conducted in emergency department and acute medical settings, some patients may not have capacity to consent e.g. when observing ward rounds. CAG approval will be sought.

5.4 Definition of End of Study

When all the data has been collected analysed.

6. METHODS of DATA COLLECTION, DATA ANALYSIS & DATA HANDLING

6.1 Data Flow Diagram (*Mandatory requirement*)



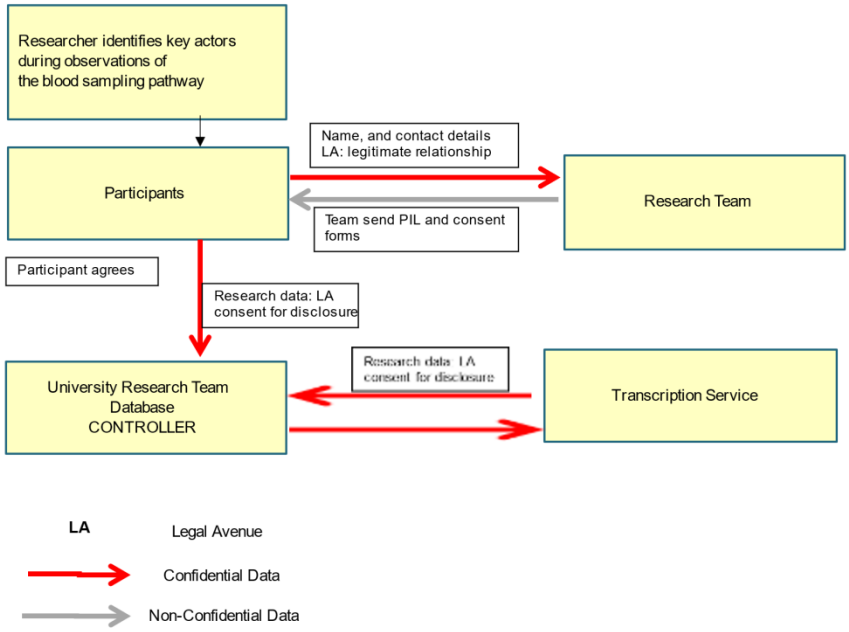
Data Flow Diagram i-SAMPLE : Part2- Staff interviews and focus groups

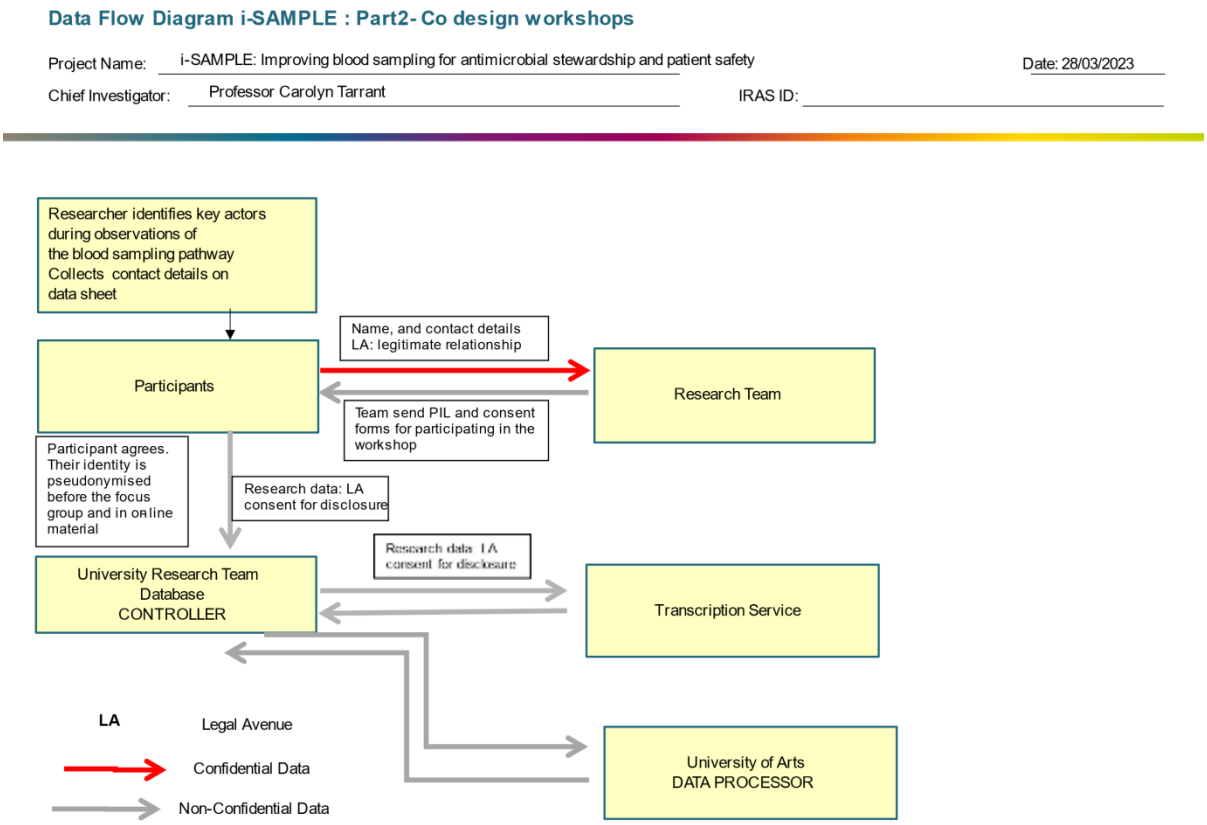
Project Name: i-SAMPLE: Improving blood sampling for antimicrobial stewardship and patient safety

Date: 28/03/2023

Chief Investigator: Professor Carolyn Tarrant

IRAS ID:





6.2. Methods

Part 1c: Ethnographic observations

We will conduct ethnographic observations in the three participating trusts to understand the factors that impact on practices along the pre-analytic blood culture pathway in acute care. Observations will be centred on but not limited to the main emergency department in each trust. We will conduct around 150 hours of observations in total across the three sites in emergency department and admissions units, other hospital wards, and microbiology laboratories. Two periods of observation will be conducted in each site, each over several days. In each case, posters will be displayed which will inform people of the researcher's presence, give an outline of the study, and contain the contact details of the researcher and the PI [Tarrant].

The initial observation period will focus on documenting which staff members are responsible for requesting and taking blood samples, and researcher familiarisation with how the blood sampling pathway operates within the site.

The next observation period will include in-depth observations of practice related to antibiotic prescribing and decision-making about blood sampling and blood sample collection. We will

explore the factors that impact on sample quality. For example, organisational factors; such as levels of demand on the emergency department / admissions unit, and shift patterns. Our observational research will also include exploring trust policy, practice and training. We will also observe antibiotic reviews, to capture the impact of blood results on antibiotic review decisions.

Observational data will be captured through fieldnotes and audio-recorded data summaries. Photographs will be taken of key activities and artefacts, e.g. of blood sampling equipment, blank sample order form forms; no individuals or identifying patient details will be included in photographs or any of the data collected as part of these observations. Copies of local template documents relevant to the blood sampling pathway will be collected and added to the data set.

Interviews

We will conduct 12-15 interviews with staff from each site to explore perceptions and behaviours, norms, and social influences that shape individual behaviour and collective action.

Interviews will be conducted face to face at the participating hospital sites during fieldwork, or via telephone/online if preferred for the participant's convenience. Interviews and fieldnotes will be audio-recorded using an encrypted recorder, transcribed verbatim by professional transcribers with established data security and confidentiality agreements with the University of Leicester, and will be pseudonymised prior to analysis.

Part 2a:

Co-design Workshops

The co-design workshops will run concurrently alongside all of Part 1, integrating findings from Part 1a, b and c into the design process as they become available. The co-design process will follow the Design Council's Double Diamond approach (33) consisting of iterative phases of discover, define, design, and develop.

The design researcher will integrate empirical findings from Part 1 of the study to inform a series of four co-design workshops which will be undertaken at each of the hospital sites for patients and healthcare staff. This will involve a series of 4 workshops through which the intervention(s) will be developed and refined into a testable product This work will give rise to a set of potential interventions which will be piloted (Part 2b) and evaluated (Part 2c).

Workshop 1 (Discover, Define) will involve maps of current pathways (actors, physical environment, prioritisation, and pain points of existing blood culture testing for acute medical patients), personas and visualising scenarios of the existing systems. Initial data from Part 1c will inform the development of archetypes - visual representations of key actors, including the experiences of patients and staff in blood sampling, daily struggles and pressures and their experiences of gaps in the current system, and will prompt discussion of perceived and actual barriers that impact the existing pathway. The visual, methodological tools will represent actors, physical environments, prioritisation, and pain points in existing practices for blood sampling for acute medical patients, and will be compared to identify points of convergence and divergence across sites. Workshop 2 (Define) will apply the use of storyboards and personas to ideate what and where interventions need to be placed, with key actors including healthcare staff and patients, to reconfigure the existing system and target behavioural factors to develop innovative approaches to more reliable blood sampling. Workshop 3 (Develop) will focus on prototyping and representing the previous co-design speculative interventions whilst reflecting

on developing theories of change and issues of implementation. Each of these workshops will be iteratively generated from the previous workshops' outputs, culminating in Workshop 4. Initial intervention prototypes may differ at each of the participating hospitals: during analysis we will compare initial interventions generated from across the three sites to identify shared solutions for collective action and improvement, for discussion in Workshop 4. Workshop 4 will be designed as a policy and practice workshop (Deliver) to reflect on the fit of intervention(s) to practice, and to guide wider implementation, dissemination, and plans for trial design including identifying key outcome measures. Implementation pathway co-design tools will be created to support this process.

For each workshop, we will offer participants the option to continue contributing to follow up workshops, to participate as a one-off, or to continue participating on an online iteration. Interested participants can attend any or all of the workshops as preferred. This approach will ensure that healthcare staff and patient participants have flexibility in their involvement. Each round of workshops will involve up to three identical in-person workshops, run at different times of the day (e.g., lunch and tea-time) and over several days (e.g., 3 days) at each trust site to maximise staff opportunity to participate. Each workshop will take approximately an hour. Each round of workshops will be held at around a 3-6 monthly frequency. On-line workshop spaces will mirror the in-person methods and tools, so that participants can choose to contribute on-line or if they have participated in-person and would like to further contribute they can have the option to do so digitally. The online spaces will be open for the duration of a week at each hospital and then closed.

Part 2c

Evaluation Interviews and Focus groups

The interventions will be piloted in each hospital over a three-month period (Part 2b) and evaluated using qualitative methods: interviews and focus groups:

Interviews: we will conduct interviews with 5-6 members of staff from each site to explore feasibility, uptake and usability. Interviews will be conducted face to face at the participating hospital sites during fieldwork, or via telephone/online if preferred for the participant's convenience. Interviews and fieldnotes will be audio-recorded using an encrypted recorder, transcribed verbatim by professional transcribers with established data security and confidentiality agreements with the University of Leicester, and will be pseudonymised prior to analysis. It is anticipated that the interview will last approximately 60 minutes.

Focus groups: we will hold a focus group with 6-8 staff from each site using vignettes and walkthroughs of the proposed bundle of interventions within the specific context of each site, to assess feasibility and considerations for implementation, using the NASSS-CAT interview guide (35).

We will offer participants a range of times and days over three days to maximise the feedback and provide flexibility to participants. Each focus group session will last for a maximum of one hour and will be held face-to-face at hospital sites. To support staff who are short of time we will also provide an online collaborative space (e.g. Miro) for further comments or reflections after the focus groups; this online space will be open during the week of the focus groups and then closed.

6.3 Data Analysis

Part 1c

Data will be analysed using NVivo software. Analysis approach will draw on the constant comparative approach (36) and will be theoretically-informed by our characterisation of antimicrobial stewardship as a problem of collective action (27), shaped by local contexts (24, 25). Analysis of data will be ongoing over the course of the fieldwork period. We will use techniques developed through our experience of conducting large scale ethnographic studies (38,39) to enable us to manage the large amounts of data generated, and to move quickly from data to interpretation. These include regular debriefs and the production of summaries of data by site and across sites, organised by research questions and emerging themes. We will conduct within- and cross-case analysis to build an understanding of influences on the pre-analytic pathway.

Part 2a

Co-design workshop outputs will be analysed and synthesised, and this will include, visual analysis of workshop outputs, discussions, and a summary of the developmental process of the design interventions.

Part 2c

Initial interventions generated from across the three sites will be compared to identify shared solutions for collective action and improvement. Evaluation interviews and focus groups will be analysed using a thematic analysis approach (40) using the NASSS framework as sensitising concepts.

6.4 Expenses

Patients involved in Part 2a will be remunerated for their time in the form of vouchers, in line with NIHR rates (https://www.nihr.ac.uk/documents/payment-guidance-for-researchers-and-professionals/27392#working-out-the-costs-for-your-study), e.g., £50 for an activity taking 2 hours of time. Any expenses such as travel will be reimbursed, in line with NIHR guidance, with a limit of the cost of a standard rail fare unless adjustments are required to allow participation (e.g. taxi required due to mobility issues). Original receipts will be required for all expenses. Health care staff will not be reimbursed for their time.

6.5 Access to Data

The Chief Investigator, Principal Investigators and members of the Research Team will have access to the full dataset.

Direct access will be granted to authorised representatives from the Sponsor, host institution and the regulatory authorities to permit project-related monitoring, audits and inspections.

7. SAFETY REPORTING

This study will not be subject to Safety Reporting and as such, adverse events will not be recorded and serious adverse events will not be reported to the sponsor.

8. ETHICAL AND REGULATORY CONSIDERATIONS

8.1 Assessment and management of risk

In the event of another pandemic, we would have to review the observation element of the project. It might be possible to observe remotely using digital video methods- for example, we could submit a substantial amendment to allow us to site cameras in key places along the pathway or to equip staff with body cameras.

We feel that any risk to staff/ PPI members from participating in our study is minimal. Nevertheless, we are conscious that sensitive issues could arise, especially in the focus groups. The moderator will be attuned to ensuring that the focus groups are conducted in an inclusive and respectful way. If a participant decides to withdraw, they will have a] the option to withdraw their data entirely in which case their voice will not be transcribed or b] to allow data already collected to be used.

All participants will have the contact details of members of the research team should they wish to contact them. The research team are not qualified to offer help or counselling but will be prepared to signpost staff to others who may be able to help them; for example, union representatives, well-being champions and Freedom to Speak Up guardians, the PPI lead [Krockow] and relevant patient safety organisations.

All data from the focus groups and interviews will be pseudonymised and identifying features will be removed. Participants will be asked how they would be preferred to be referred to in outputs.

If any safeguarding issues arise, the research team will report them to the appropriate authority.

8.2 Research Ethics Committee (REC), Regulatory review & Reports

Once the initial sponsor review process has been completed, a sponsor reference number allocated, indemnity received and all requested documentation have been reviewed and checked, authorisation from the University of Leicester's Research Governance Office will be given to book for further regulatory review of the proposed research. The NHS Research Ethics Committee and the Health Research Authority will then review the proposal.

Sponsor agreement is always in principle and is subject to the research receiving all relevant regulatory permissions. The Sponsor have a Green Light process and research activities will not commence at site(s) until this has been received.

Submission for regulatory approvals will be submitted via Integrated Research Application System (IRAS).

The Chief Investigator will ensure that all regulatory approvals, confirmation of capacity and capability from NHS sites and Sponsor Green Light are in place before any research activities start.

For any required amendments to the study, the Chief Investigator, in agreement with the sponsor will submit information to the appropriate body(ies) in order for them to issue approval for the amendment. NHS sites will be informed of any amendments. Amendments will not be implemented until the appropriate approvals/permissions are in place.

Annual progress reports will be submitted to the Ethics Committee annually on the anniversary date of when favourable opinion is given by the Chief Investigator.

The Chief Investigator will notify the REC when the study has ended by completing the end of study notification form and will submit a final report of the results within one year after notifying REC.

A trial master file will be maintained for the duration of the study and will be stored for a minimum of 6 years after the study has ended

8.3 Regulatory Review & Compliance

Before any site can enrol patients into the study, the Chief Investigator/Principal Investigator or designee will ensure that appropriate approvals from participating organisations are in place.

The study will be conducted in accordance with the current approved protocol, ICH GCP, relevant regulations and standard operating procedures.

The Research will not commence until all regulatory approvals are in place, NHS confirmation of Capacity and Capability, and Sponsor Green Light are given.

The University of Leicester operate a risk-based audit programme to which this study will be subject to.

8.4 Peer review

This research has undergone extensive peer review during the course of the NIHR health and Sociual Care Delivery Research [HSDR] funding process.

8.5 Patient & Public Involvement

Acceptability and Design

We convened a PPI group (Oct 2022) comprising six patients with experience of severe infection and hospital care to advise on study design (2F, 4M; 5 White British, 1 Asian). Group members were recruited from existing local PPI groups, and through informal contacts by the local Research Design Service PPI lead. The PPI engagement event took place online to enable participation from PPIE members who were unable to travel. The meeting consisted of a project presentation, where we presented our research questions and ideas for study design and methods.

Following the presentation, we invited an open discussion, allowing PPI group members to comment on all aspects of the presentation. PPI members were provided with a series of questions about study value and study design, and how we could involve patients in research, co-design, and dissemination. These were discussed during the meeting, and also sent to participants by email following the meeting inviting further feedback. In addition, a further focused discussion was held online between Tarrant (PI) and Locke (PPI co-applicant). PPI feedback included the importance of considering patients from whom it is difficult to take

blood, and for studying inequalities in blood sampling across patient groups, suggestions for patient involvement and the potential for patient-facing interventions, and dissemination suggestions. All feedback was taken into account in preparing this application. This includes:

- ensuring PPI representatives are involved in study team meetings
- providing training to all PPI members on research methods and on specific topics e.g. sepsis, antimicrobial resistance
- involving PPI members in analysis of qualitative data and in giving presentations of the findings
- producing Plain English summaries and a video about findings aimed at the public
- ensuring that patients are fully involved in the co-design process and consider the potential for a patient held/led intervention
- paying costs for PPI member conference attendance.

Management and Support

The PPI lead [Krockow] will be responsible for collaborating with PPI members to develop PPI plans and identify training and support needs. They will provide support to the PPI co-applicant by co-chairing PPI advisory group meetings, liaising with the PPI group and organising, and attending regular PPI meetings and training (including the launch and end-of-project events). The PPI lead will also be available for informal enquiries by PPI members throughout the project.

The PPI co-applicant will act as main representative of the PPI advisory group, and will co-chair PPI advisory group meetings. They will represent the patient advisory group at the Study Management meetings. They will summarise PPI feedback, communicate it to the wider project team and ensure that feedback is integrated within the project design and analysis. They will help prepare lay summaries and patient-facing materials, contribute to analysis and report-writing, and be involved in the dissemination of findings.

PPI advisory group members will be remunerated for their time and expenses in line with NIHR guidance.

Undertaking, analysing and disseminating the research

Research methods training and training on the clinical context will be provided to the PPI participants. Training will take place in year 1, and include online research methods training, and additional bespoke training in specific topics e.g. sepsis and antimicrobial resistance.

PPI members will be involved in the analysis of findings, and in supporting dissemination. Members will also be asked to review and feedback on materials by email, with appropriate remuneration. Supporting dissemination will involve preparing Plain English summaries and social media materials, identifying dissemination routes, filming a video about the findings, participating in feedback presentations at participating hospitals, and attending national conferences (e.g., Health Services Research UK Conference).

At the end of the project, we will run a half-day face-to-face PPI event. This will include a debrief, where PPI members are invited to reflect on their experience of participating in the project. We will further explore their interest in future study involvement (e.g. in follow-up

research or separate projects). Finally, PPI members will be invited to attend the wider end-of-project workshop alongside clinical and academic collaborators and other relevant stakeholders.

In addition to the core PPI, we have a commitment from The Sepsis Trust and Antibiotic Research UK for support with some of our PPI activities, including helping us to engage with a wider group of patients with experience of infection to feed into latter stages of the co-design process, and to support public and patient dissemination of the outputs from our project.

8.6 Protocol compliance

If a protocol breach occurs, then the CI will document this in adherence to the University's Standard Operational Procedure SOP Identifying and Reporting Deviations and Serious Breaches of GCP and/or the Protocol for Trials. The CI will seek advice from the research supervisors and the sponsor.

8.7 Data protection and patient confidentiality

The study is compliant with the requirements of the Data Protection Act 2018/GDPR.

Participants will be made aware that the interviews/focus groups will be recorded, that we are using an encrypted Digital Recorder, and their permission will be granted before the discussions commence. We will state a participant number (in place of a participant's name) at the beginning of the interviews and in the case of all interview/observation/focus group recordings, all recordings will be pseudonymised during transcription with any names, places or other identifying information mentioned removed during transcription. In the case of field notes, the researcher will not note down any personal identifiers. The recordings will be deleted from the audio recorder as soon as they are transferred to the University of Leicester secure servers, where they will be stored in restricted access folders. Digital/audio recordings will be deleted from the server following transcription. Any printed confidential material will be kept in a folder in a locked drawer in a secured room in a secure office environment office at the University of Leicester.

Contact details of participants will be stored electronically and deleted as soon possible within the duration of the study. Access to the contact details will be restricted to the PI [the data custodian] and the researchers. All investigators and study site staff must comply with the requirements of the Data Protection Act 1998 with regards to the collection, storage, processing and disclosure of personal information and will uphold the Act's core principles.

In the context of the workshops, participants will provide their names and email address on a data collection sheet and a space for them to describe their role in the blood culture pathway next to a code – this code will then be matched to a pack of post-it notes which the participant will use to engage in the co-design activities. The facilitators will not note down any personal identifiers during the co-design session and any mention of names places and or other identifying information will be removed from worksheets. Digital / audio recordings of

workshop conversations will be deleted following transcription. Participants will be made aware that discussions will be recorded and that we are using an encrypted Digital Recorder, and their permission will be sought before the co-design starts. Photographs taken during the co-design session will focus on hands and the writing and completion of the templates. No photographs will be taken that will identify individuals. The digital images will be deleted once they are uploaded on to University of Leicester's secure server.

For the digital on-line activities, the digital board author will have the 'Make Names Anonymous' option switched on for the duration of the online activities so that none of the participants will be identifiable. Once the board is closed to the participants, the identifier toggle will be switched-on for the researchers to record the roles of the contributors, and these will be coded. The 'Make Names Anonymous' option will then be switched back on and locked. PDFs will be downloaded in this confidential mode, and the digital images uploaded on to the University of Leicester's secure server.

For the feedback focus groups, the coding identification will be the same for those who attended earlier workshops, their codes will remain the same. New participants will be given a code using the same process applied to the in-person workshops to maintain confidentiality.

While participants are taking part in the study their contact details will be available to the researchers so that they can contact the participant to arrange the details of their research involvement. Where individuals have consented to receive a copy of the research findings, contact details will be retained until this time. Contact details will be stored securely and separately from participants research data and clinical information. Consent forms, enrolment logs and details of record linkage (i.e., participant ID numbers/pseudonyms) will be kept for a minimum of six years after the study has ended as part of the research data so that in the event of the data being challenged, this will allow for verification of the quality of the data. At the end of this period approval from the Sponsor will be requested for the destruction of the data.

The Trial Master File will be kept a folder in a locked cabinet/drawer in a secured room in a secure office environment office at the University of Leicester by the Chief Investigator. The site file will be at the NHS organisation also to be stored in a secure environment. Storage will comply with each organisation's policy on storage and archiving.

The TMF/ISF will be maintained for the duration of the study and will be stored for a minimum of six years after the study has ended.

Long-term storing will comply with the University of Leicester archiving Standard Operating Procedure and local policies.

Research data will be pseudonymised by transcribers before being transferred to the University of Leicester. Pseudonymised research data will be stored for six years after the study has ended, unless there is explicit consent for the data to be retained beyond the scope of the original research project.

8.8 Indemnity

The University of Leicester insurance applies for this study.

8.9 Access to the final study dataset

Only, the Chief Investigator, researcher and co- investigators will have access to the full dataset. Direct access will be granted to authorised representatives from the Sponsor, host institutions and regulatory authorities for monitoring and/or audit of the study to ensure compliance with regulations.

9. DISSEMINATION POLICY

9.1 Dissemination policy

Our approach to dissemination will aim for significant reach across diverse stakeholders. We will share knowledge about our findings, generate learning to drive improvements in practices along the pre-analytic blood sampling pathway, provide initial evidence of feasibility and effectiveness of interventions to support applications for future research, inform ongoing NHSE work on optimising the blood culture pathway, and promote wider engagement and understanding of the research by patients and the public.

Dissemination will target: 1) Policy makers, national bodies including health professional organisations, and national interest groups; 2) Clinicians and healthcare professionals including microbiology staff and antimicrobials stewardship leads; 3) Academic audiences; 4) Patients and the public.

We will work closely with our patient and public contributors to develop and implement our dissemination plan, create appropriate outputs, and involve them in dissemination. The PPI co-applicant will lead on this. This will include the development of outputs, including creative outputs (infographics, short videos for hospital staff and the public) tailored to the needs and interests of patients and the public, and frontline healthcare staff. We will produce posters, videos that could be played in participating hospitals, and our PPI group members will attend presentations and external dissemination events to ensure that patient voice is heard.

We have strong links with the NHS England leads for improving the blood culture pathway across England (29), and will work with the NHSE Blood Cultures team to ensure we develop outputs that meet the needs of policy-makers. These connections will ensure the outputs have a direct pathway to impact for the national agenda. We will generate policy recommendations and disseminate through presentations at national AMR diagnostics policy board meetings and NHSE blood culture steering group. Through these connections we will reach influential national organisations including the UK Sepsis Trust and Antibiotic Research UK. We will also work through Coats, the emergency medicine project lead, to engage with the Emergency Medicine (the NIHR Emergency Medicine Incubator, the Royal College of Emergency Medicine and Health Education England Deanery leads for Emergency Medicine).

We have access to the international platform provided by BSAC via Jenkins to support dissemination of, and engagement with our research findings, and we will disseminate our findings through the network of regional antimicrobial stewardship leads.

We will reach academic audiences by presenting findings at key national and international academic conferences, and we will contribute to the current evidence on optimising the blood sampling pathway through papers in high impact journals. This will include publications in both clinical and social science journals, allowing us to make an important contribution to the body of social science research in antimicrobial resistance (41). We will publicise key academic

outputs through press releases, media interviews and through our research group Twitter feed. We will hold an end of project round table workshop for academics, and healthcare and policy stakeholders.

The study will produce the following outputs:

- A bundle of interventions to optimise blood sampling practices for patients with suspected severe infection in acute care, which will be implemented across diverse health care settings; implementation guidance, and supporting materials including service blueprints.
- Presentations at participating hospital sites, 3 national conferences (e.g., BSAC annual conference, Health Services Research conferences (HSRUK), and the UK society for Behavioural Medicine Annual Scientific Meeting), and 1 international conference (e.g., European Congress of Clinical Microbiology & Infectious Diseases, European Health Psychology Symposium (EHPS)).
- Policy recommendations and presentations to regional and national leads, policy-makers and national healthcare and infection organisations at the National AMR Diagnostics board and the NHSE blood culture task and finish group.
- Four open access publications in high impact peer-reviewed journals
- Plain English summaries of research findings.
- Creative outputs to disseminate findings to patients and the public, and frontline hospital staff. This will include videos, mixed-media outputs and infographics, similar to outputs previously developed by members of the team: https://antimicrobialsinsociety.org/commentary/re-envisaging-infection-practice-ecologies-in-nursing-ripen/; https://vimeo.com/368059130?login=true)
- A dedicated project website
- Blogs and social media, including a publication in The Conversation, to publicise findings more widely.
- A final report to the NIHR HSDR programme board, which will synthesise the findings across the stages of the study, and will set out recommendations for future evaluation of the intervention bundle.

Publications and outputs will be available on open access via the University's Library database

9.2 Authorship eligibility

All members of the research team in its current form will be given authorship on the final study report and other outputs as appropriate.

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APPENDICIES

Appendix 1 – Amendment History

Amendment No.	Protocol version no.	Date issued	Author(s) of changes	Details of changes made

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 REC.