SUPPORTED BY

SPEAR

STI Prophylaxis and Emergence of Antimicrobial Resistance

FULL TITLE OF THE STUDY	STI Prophylaxis and Emergence of Antimicrobial Resistance
SHORT TITLE/ACRONYM	SPEAR
PROTOCOL VERSION AND DATE	V1.1 [16/DEC/2024]
SPONSOR	University College London (UCL)
SPONSOR REFERENCE NUMBER (EDGE)	174194
FUNDER(S)	British Infection Association (BIA), British HIV Association (BHIVA), National Institute for Health and Care Research (NIHR)
IRAS NUMBER	330315
CHIEF INVESTIGATOR	Dr Manik Kohli MBChB MSc MRCP Doctoral Research Fellow, Institute for Global Health, UCL
CO-INVESTIGATORS	Prof Nigel Field, Institute for Global Health, UCL Dr John Saunders, Institute for Global Health, UCL Dr Oliver Stirrup, Institute for Global Health, UCL Prof Samuel Sheppard, Dept of Biology, University of Oxford Dr Odile Harrison, Nuffield Dept of Population Health, University of Oxford

PROTOCOL VERSION HISTORY

Version Stage	Versions Number	Version Date	Protocol updated & finalised by;	Reasons for Update
	1.0	21/NOV/2024	Dr Manik Kohli	
Current	1.1	16/DEC/2024	Dr Manik Kohli	Response to REC

DECLARATIONS

The undersigned confirm that the following protocol has been agreed and accepted and that the investigator agrees to conduct the study in compliance with the approved protocol and will adhere to the U.K. Policy Framework for Health and Social Care Research 2017 (3rd edition) (as amended thereafter), the EU General Data Protection Regulation (2016/679) and the UK Data Protection Act (2018), Sponsor SOPs and applicable Trust policies and legal frameworks.

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

I (investigator) agree to ensure that no research activity or recruitment will commence at participating research sites until the appropriate regulatory approvals and NHS confirmations of Capacity and Capability have been issued, and Sponsor green light confirmed.

I (investigator) 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. Any deviations from the study as planned in this protocol will be explained and reported accordingly.

Chief Investigator:
Signature: ..... Date: 21/NOV/2024
Print Name (in full): .....Manik Kohli.....
Position: .....Doctoral Research Fellow.....

On behalf of the Study Sponsor:

Signature: Date: 07/11/2024
Print Name (in full): PUSHPSEN JOSHI
Position: RM&G MANAGER- UCLH& UCL JRO

STUDY SUMMARY

IDENTIFIERS	
IRAS Number	330315
REC Reference No.	24/EM/0282
Sponsor Reference No.	174194
Other research reference number(s)	UCL Data Protection: Z6364106/2023/09/15 ClinicalTrials.gov registration *insert*
Full (Scientific) title	STI Prophylaxis and Emergence of Antimicrobial Resistance
Health condition(s) or problem(s) studied	Antibiotic prophylaxis for bacterial sexually transmitted infections; antimicrobial resistance; gut and throat microbiomes
Study Type	Observational
Target sample size	108
STUDY TIMELINES	
Study Duration/length	28 months
Expected Start Date	January 2025
End of Study date	April 2027
Key Study milestones	03/2023 Funding awarded (British Infection Association) 08/2023 Funding awarded (British HIV Association) 05/2024 Funding awarded (NIHR) 01/2025 Aim for REC approval; Study site setup 01/2025 Recruit first participant 07/2025 Recruit final participant 07/2026 Final participant final follow-up visit 04/2027 NIHR funding ends; Complete study
FUNDING & OTHER	
Funding	National Institute for Health and Care Research (NIHR) Doctoral Fellowship £589,590 (NIHR303717); British Infection Association (BIA) £10,000 (2023/Manik Kohli); British HIV Association (BHIVA) £9,979.96 (BHIVA/5020/2023/Kohli)
STORAGE of SAMPLES / DATA (if applicable)	
Human tissue samples	Stool samples and oropharyngeal swabs. Collected and temporarily stored at the study site (Central and North West London NHS Foundation Trust). Study samples transferred to collaborating institution for processing and storage (Department of Biology, University of Oxford, South Parks Road, Oxford, OX1 3RB). Samples and extracted bacterial DNA will be stored at the Department of Biology, University of Oxford) for the duration of the study.
Data collected / Storage	Pseudonymised questionnaire responses will be stored at UCL
KEY STUDY CONTACTS	
Chief Investigator / Principal Investigator	Dr Manik Kohli Email: m.kohli@ucl.ac.uk, manik.kohli@nhs.net Telephone: 07837837096
Clinical Project Manager	Dr Emmi Suonpera

	Email: e.suonpera@ucl.ac.uk Telephone: 0203 108 2081
Other relevant study personnel	Prof Nigel Field – Co-investigator; Primary Supervisor Dr Odile Harrison – Co-investigator; Supervisor Dr John Saunders – Co-investigator; Supervisor Dr Oliver Stirrup – Co-investigator; Statistician; Supervisor Prof Samuel Sheppard – Co-investigator; Supervisor Prof Richard Gilson – Head of Research Centre Prof Magnus Unemo – Collaborator

KEY ROLES AND RESPONSIBILITIES

SPONSOR: The sponsor is responsible for ensuring before a study begins that arrangements are in place for the research team to access resources and support to deliver the research as proposed and allocate responsibilities for the management, monitoring and reporting of the research. The Sponsor also must be satisfied there is agreement on appropriate arrangements to record, report and review significant developments as the research proceeds, and approve any modifications to the design.

FUNDER: The funder is the entity that will provide the funds (financial support) for the conduction of the study. Funders are expected to provide assistance to any enquiry, audit or investigation related to the funded work.

CHIEF INVESTIGATOR (CI): The person who takes overall responsibility for the design, conduct and reporting of a study. If the study involves researchers at more than once site, the CI takes on the primary responsibility whether he/she is an investigator at any particular site.

The CI role is to complete and to ensure that all relevant regulatory approvals and confirmations of NHS Capacity and Capability are in place before the study begins. Ensure arrangements are in place for good study conduct, robust monitoring and reporting, including prompt reporting of incidents, this includes putting in place adequate training for study staff to conduct the study as per the protocol and relevant standards.

> The Chief Investigator is responsible for submission of annual reports as required. The Chief Investigator will notify the REC and JRO of the end of the study (including the reasons for premature termination, where applicable). Within one year after the end of study, the Chief Investigator will submit a final report with the results, including any publications/abstracts to the REC and JRO.

PRINCIPLE INVESTIGATOR (PI): Individually or as leader of the researchers at a site; ensuring that the study is conducted as per the approved study protocol, and report/notify the relevant parties – this includes the CI of any breaches or incidents related to the study.

KEY WORDS

Sexually transmitted infections; STI; antibiotic prophylaxis; antimicrobial resistance; microbiome.

LIST OF ABBREVIATIONS

AE	Adverse Event
AMR	Antimicrobial Resistance
AR	Adverse Reaction
BHIVA	British HIV Association
BIA	British Infection Association
CI	Chief Investigator
CNWL	Central and North West London NHS Foundation Trust
CRO	Contract Research Organisation
DMC	Data Monitoring Committee
DSH	Data Safe Haven
HCP	Health Care Provider
HIV	Human Immunodeficiency Virus
ICF	Informed Consent Form
MMC	Mortimer Market Centre
MSM	Men who have sex with men
MTA	Material Transfer Agreement
NHS	National Health Service
NIHR	National Institute for Health and Care Research
PI	Principle Investigator
PIS	Participant Information Sheet
PEP	Post-exposure Prophylaxis
PPI(E)	Patient and Public Involvement (and Engagement)
PrEP	Pre-exposure Prophylaxis
QA	Quality Assurance
QC	Quality Control
R&D	Research and Development
REC	Research Ethics Committee
SAR	Serious Adverse Reaction
SAE	Serious Adverse Event
SDV	Source Data Verification
SHS	Sexual Health Service
SOP	Standard Operating Procedure
SSI	Site Specific Information
STI	Sexually Transmitted Infection
TMF	Trial Master File
WS	Workstream

CONTENTS

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1 INTRODUCTION

STI prophylaxis is the use of antibiotics before sex (pre-exposure-prophylaxis, or PrEP) or after sex (post-exposure prophylaxis, or PEP) to prevent acquisition of bacterial sexually transmitted infections (STIs). There is growing evidence that men who have sex with men (MSM), particularly MSM using HIV-PrEP or living with HIV, are buying antibiotics online to take as STI prophylaxis.[1,2] This is not currently endorsed by the British Association for Sexual Health and HIV (BASHH) or UK Health Security Agency (UKHSA), citing concerns about antimicrobial resistance (AMR) although new guidelines are in preparation and will likely recommend STI prophylaxis for some patient groups.[1] Recent trials demonstrated efficacy of doxycycline-PEP (commonly called 'DoxyPEP') in preventing chlamydia, syphilis, and gonorrhoea.[3,4] There is a need to understand the AMR risks to inform UK clinical guidance and STI prophylaxis implementation. Among MSM, high incidence of antibiotic resistant infections, altered microbiomes linked to sexual behaviours and living with HIV, and dense overlapping sexual networks, raise concerns about the possible impact of long-term antibiotic use. This study will develop the methodology needed to evaluate AMR emergence and microbiome changes in MSM who are using STI prophylaxis through bacterial genomics. These data will also inform further research on STI prophylaxis, AMR epidemiology, and microbiomes and subsequently clinical and public health decisions on STI prophylaxis.

2 BACKGROUND AND RATIONALE

Rates of bacterial STIs have been rising for the last decade and MSM are disproportionately impacted by STIs, particularly antibiotic resistant STIs. [5,6] This poses a serious public health threat and represents an increased burden on NHS sexual health services (SHS). Novel approaches are needed to halt and reverse these trends. HIV-PrEP provides an established, safe, and effective model for biomedical interventions to prevent STIs. There is growing interest in STI prophylaxis with small but significant numbers self-sourcing antibiotics, and very high levels of acceptability (up to 84%) among MSM if shown to be safe and effective.[7,8,9] There are concerns about the risk of AMR development in commensal and bystander organisms, as well as the impact on gut and other microbiomes. A debate is ongoing in the UK and elsewhere on the introduction of doxycycline-PEP for populations with high STI incidence where evidence of efficacy exists.[10,11] As MSM continue to self-source antibiotics for STI prophylaxis, and implementation by the NHS in the UK is planned – robust AMR and microbiome outcome data will be necessary to understand the risks and inform surveillance.

Efficacy of doxycycline prophylaxis

In 2022, the DOXYPEP randomised controlled trial (RCT) from the USA provided strong evidence for the efficacy of doxycycline-PEP to reduce bacterial STI incidence when taken within 72 hours of condomless sexual contact.[4] The study found a 65% reduction in STI incidence per quarter (RR0.35 (95%CI 0.27-0.46)), with significant reductions in gonorrhoea (*Neisseria gonorrhoeae*), chlamydia *(Chlamydia trachomatis*) and syphilis (*Treponema pallidum*) incidence among MSM and transgender women (TGW) on HIV-PrEP or living with HIV.[4] At study baseline tetracycline resistance among *N.gonorrhoeae* isolates was 20%, which limits generalisability to the UK where it is significantly higher (62%).[12] The French

DOXYVAC study of doxycycline-PEP and meningococcal B vaccine found significant reductions in chlamydia or syphilis (aHR0.17 (0.12-0.26)) and gonorrhoea (aHR0.67 (0.52-0.87)) with doxycycline-PEP.[4] Smaller RCTs from the USA, France and Canada also demonstrated efficacy of doxycycline-PEP and daily doxycycline-PrEP in reducing incidence of chlamydia and syphilis in MSM.[13-15] In 2023, a modelling study examined different doxycycline-PEP strategies, such as targeting all MSM/TGW, HIV-PrEP users, or only people with multiple STIs diagnosed.[16] Use of doxycycline-PEP in individuals with concurrent or repeated STIs could substantially reduce subsequent STIs.[16] However, an RCT in Kenya in cisgender women found doxycycline-PEP did not reduce incident bacterial STIs, which the study investigators believed to be adherence related.[17]

Use and acceptability

Surveys from the UK, Netherlands, and Australia estimate STI prophylaxis use among MSM using HIV-PrEP or living with HIV to be 3%-10%.[2,7,18] There was also very high levels of acceptability of STI prophylaxis among MSM (up to 84%).[8,9] Of concern is that up to 40% of STI prophylaxis users report using non-doxycycline antibiotics, such as azithromycin.[2] In recent survey by CNWL and UCL, we found that STI prophylaxis users continued to use non-doxycycline antibiotics, despite increased awareness and discussion about 'doxycycline-PEP' (Saunders, Kohli and Suonpera, unpublished). 80% of respondents (n=440) in this survey were 'somewhat' or 'very likely' to use doxycycline-PEP/PrEP if deemed safe and effective.

AMR

There are concerns about further development of AMR in MSM sexual networks that already have high rates of STIs with AMR.[12] Unregulated use of self-sourced antibiotics is a particular concern. Doxycycline (a tetracycline antibiotic) is needed as first-line treatment for STIs such as chlamydia, syphilis, and *Mycoplasma genitalium*, as well as respiratory, skin, and other infections. Overall, data on AMR associated with doxycycline prophylaxis from trials remains very limited, or focuses on specific organisms (*Staphylococcus aureus*, *Escherichia coli*, and *Neisseria* species); with no clear conclusions on AMR or the impact long-term doxycycline-PEP has on human microbiomes, although further analyses are expected.[3,4,15] In DOXYPEP, tetracycline resistant *N.gonorrhoeae* was higher in the doxycycline-PEP arm (38%) than at baseline (27%) and in the standard of care (SOC) arm (12%).[3] Additionally, although *S. aureus* carriage was lower in the doxycycline-PEP arm, a higher proportion had doxycycline resistance (16%) compared to SOC (8%).[3] In DOXYVAC, there was more high-level tetracycline resistance among incident gonorrhoea infections with resistance in the doxycycline-PEP arm (33.3%) compared to SOC (18.9%).[4]

Beyond standard microbiological approaches, including in the doxycycline-PEP/PrEP RCTs, there are limited data on genetic determinants of AMR in MSM. A study using residual rectal swab samples from MSM attending SHS in London estimated prevalence of the *mphA* gene (conferring azithromycin resistance) at 32.5%, and higher still (41.3%) among MSM with a diagnosed bacterial STI in the preceding 12 months.[19]

Microbiomes

The impact of sexual behaviour and HIV on the gastrointestinal and oropharyngeal microbiota is of increasing interest.[20-22] Several studies identified differences in the gut microbiota between MSM and men who exclusively have sex with women, and sexual

behaviour and antibiotic exposure (given differences in STI risk, testing, and treatment) are important potential confounders when studying microbiomes in MSM and people living with HIV.[18] It has also been suggested that both macrolides and tetracyclines have greater impacts on gastrointestinal microbiota compared to other antibiotics.[19] Moreover, alterations in gastrointestinal microbiome have been associated with metabolic, mental health and autoimmune diseases.[23,24] An oropharyngeal microbiome study noted that prevalence of select AMR genes ('resistome') was lower in the general population compared to MSM (ratio 0.41(0.26-0.65)), but found no difference when comparing MSM with and without recent antibiotic exposure.[25] This small cross-sectional study did not assess antibiotic STI prophylaxis and was limited by the lack of data on sexual behaviour including oral sex and ano-oral sexual contact.[25] Microbiome disturbances are multifactorial and differences in the gastrointestinal and oropharyngeal microbiota require careful interpretation as findings may be confounded by sexual behaviour and living with HIV.[22,27] Despite this, a systematic review of human gut resistome studies included no discussion on the potential impact of sexual behaviour or HIV. [26]

While the evidence of STI prophylaxis efficacy in MSM is compelling, given the lack of data on AMR, global differences in baseline AMR, and the potential addition of long-term antibiotic prophylaxis as a recommended STI prevention strategy in MSM, further research is required in the UK on the risks associated with STI prophylaxis and methods for monitoring and mitigation, such as enhanced surveillance. This research will provide data to fill important evidence gaps and develop the methodologies for further AMR research and optimised surveillance.

3 AIM AND OBJECTIVES

Research Question
What are the risks of AMR and microbiome impacts of antibiotic prophylaxis for sexually transmitted infections (STI prophylaxis) in MSM, and how can we evaluate and mitigate these risks?

Aim
To evaluate AMR and microbiome changes through bacterial genomics, and generate UK-based evidence to inform clinical and public health decisions on STI prophylaxis, future AMR research, and AMR surveillance.

3.1 Primary Objective

To assess feasibility and acceptability of detecting AMR emergence and microbiome changes in the gastrointestinal tract and oropharynx of MSM who use antibiotic STI prophylaxis through bacterial genomics.

3.2 Secondary Objectives

A) To assess feasibility and acceptability of recruiting STI prophylaxis users via sexual health clinics versus online and obtaining appropriate samples.
B) To evaluate the use of shotgun metagenomic sequencing to identify AMR genes or gene mutations conferring resistance to tetracycline and other relevant antibiotic classes.
C) To evaluate the use of shotgun metagenomic sequencing to identify bacteria present in the gastrointestinal tract and oropharynx of MSM.
D) To estimate the prevalence of AMR genes/gene mutations of interest and describe changes over time in the gastrointestinal tract and oropharynx of MSM using and not using STI prophylaxis.
E) To characterise the gastrointestinal and oropharyngeal microbiomes and describe changes over time in MSM using and not using STI prophylaxis.
F) To develop the methodology for future AMR research and surveillance in MSM and other relevant population groups.

4 STUDY DESIGN & METHODS OF DATA COLLECTION

4.1 Study Design

Study design: Molecular epidemiology cohort study

Study site: Central and North West London (CNWL) NHS Foundation Trust Sexual Health Services (SHS). CNWL is one of the largest SHS in London, providing HIV PrEP to ~300 MSM each month, and routine care for ~3,000 MSM living with HIV.

Study population: MSM aged ≥ 18 years. Target of 108 participants, with minimum 40 participants living with HIV[1], distributed evenly across three antibiotic exposure groups at enrolment:

- Group A (n=36): recent[2] and recurrent[3] doxycycline STI prophylaxis use.
- Group B (n=36): recent[2] history of STI treatment with doxycycline.
- Group C (n=36): no recent[2] use of any antibiotic for any indication.

[1] 40 study places will be ring-fenced for MSM living with HIV, split evenly across the three groups (12-13 per group).
[2] recent is defined as within last 3 months.
[3] recurrent is defined as 2 or more doses taken.

Eligible individuals meeting the criteria for group A and B, will be allocated to group A.

4.2 Study Timeline

Aim for REC Approval	Jan 2025
Study site R&D approval and site setup	Jan 2025
Recruitment (Visit 1) window	Jan 2025 – Jul 2025
Sample processing starts	Oct 2024
Follow-up visit 2 window	Apr 2025 – Jan 2026
Visit 1 samples bacterial genomic sequencing & analysis	Jul 2025 – Sep 2025
Follow-up Visit 3 window	Oct 2025 – Jul 2026
Last participant last study visit	Jul 2026
Sample processing end	Jul 2026
Visits 2 & 3 sample sequencing & complete analysis	Jul 2026 – Apr 2027

See *Section 5 Study Schedule* for more information on study visits.

End of study: The end of the study is defined as once all study visits for every participant have been completed, all study samples processed and undergone bacterial genomic sequencing, and data has been checked and locked. Data analysis will be ongoing at the end of the study.

4.3 Sample Size

Target sample size 108. This assumes an overall prevalence of AMR in the gut of 32.5%.[19] Under this assumption, the proposed sample size for this study will allow the prevalence of

AMR genes of interest across all study participants to be estimated with 95% confidence intervals (CI) +/- 8.85%. The prevalence within the groups of 36 will be possible to estimate with 95%CI +/- 15.5%. This precision will be sufficient to inform the feasibility of larger AMR surveillance research and programmes in the same patient population. In each group of 36 participants, it is expected to observe 11 cases of AMR, with 99% probability of observing at least six cases in each subgroup. This will allow piloting all aspects of specimen processing, genome sequencing, data processing and transfer workflows.

4.4 Visit Activities and Samples

There are 3 planned visits for this study (see *Section 5 Study Schedule*). All data and samples will be pseudonymised. A unique identifier (participant ID) will be assigned to each participant enrolled in the study. The participant ID will be used for sample labelling and questionnaire completion. All study activities and procedures will be undertaken after eligibility has been confirmed and informed consent has been given (see *Sections 6 Eligibility Criteria* and *8 Consent* for more details).

At each of the study visits the following three steps will be undertaken:

Step 1: Questionnaire

Participants will self-complete an electronic questionnaire. This will be pseudonymised using the participant ID number, and obtain information on demographics, medical history, sexual activity, STI prophylaxis use, any other antibiotic use, and travel. This will be completed on a tablet or computer in a private clinic room with a member of the research team on hand in case of difficulty or queries. Where possible, the questionnaire incorporates validated questions from other research surveys. It will take approximately 15 minutes to complete.

Step 2: Oropharyngeal Swab

An oropharyngeal swab will be collected from participants by the member of the research team conducting the study visit. Prior to collecting each sample, the researcher will ask the participant for consent to proceed. All samples will be taken in a private clinic room. The swabs will be labelled with the date of collection, the participant ID, and a sample ID number.

Step 3: Stool Sample

Participants will be provided with a stool sample collection kit. For Visit 1, the kit will be provided during the study visit or posted to the participant prior to the visit if they have completed e-consent (see *Section 8 Consent*). Kits will include instructions on how to collect a stool sample and gloves for the collection. The researcher will explain the process of stool sample collection to the participant at the study visit or by telephone if collecting prior to the visit.

Participants will be offered a range of options for collecting stool samples:

- **In clinic at study visit:** participants providing stool samples during the study visit will be directed to a toilet to collect their own sample.
- **At home after study visit:** participants will be able to provide a stool sample collected at home within 7 days of the study visit and return the sample to the study site within 48 hours of collection.

- **At home before study visit:**
    - **Visit 1:** participants completing e-consent and opting to be posted a stool sample collection kit will collect the sample at home less than 48 hours before the study visit and to bring it with them.
    - **Visits 2 and 3:** At Visit 1, participants will be given kits for follow-up visits to take home and return when they attend for Visits 2 and 3. Participants will be asked to collect the sample at home less than 48 hours before the visit.

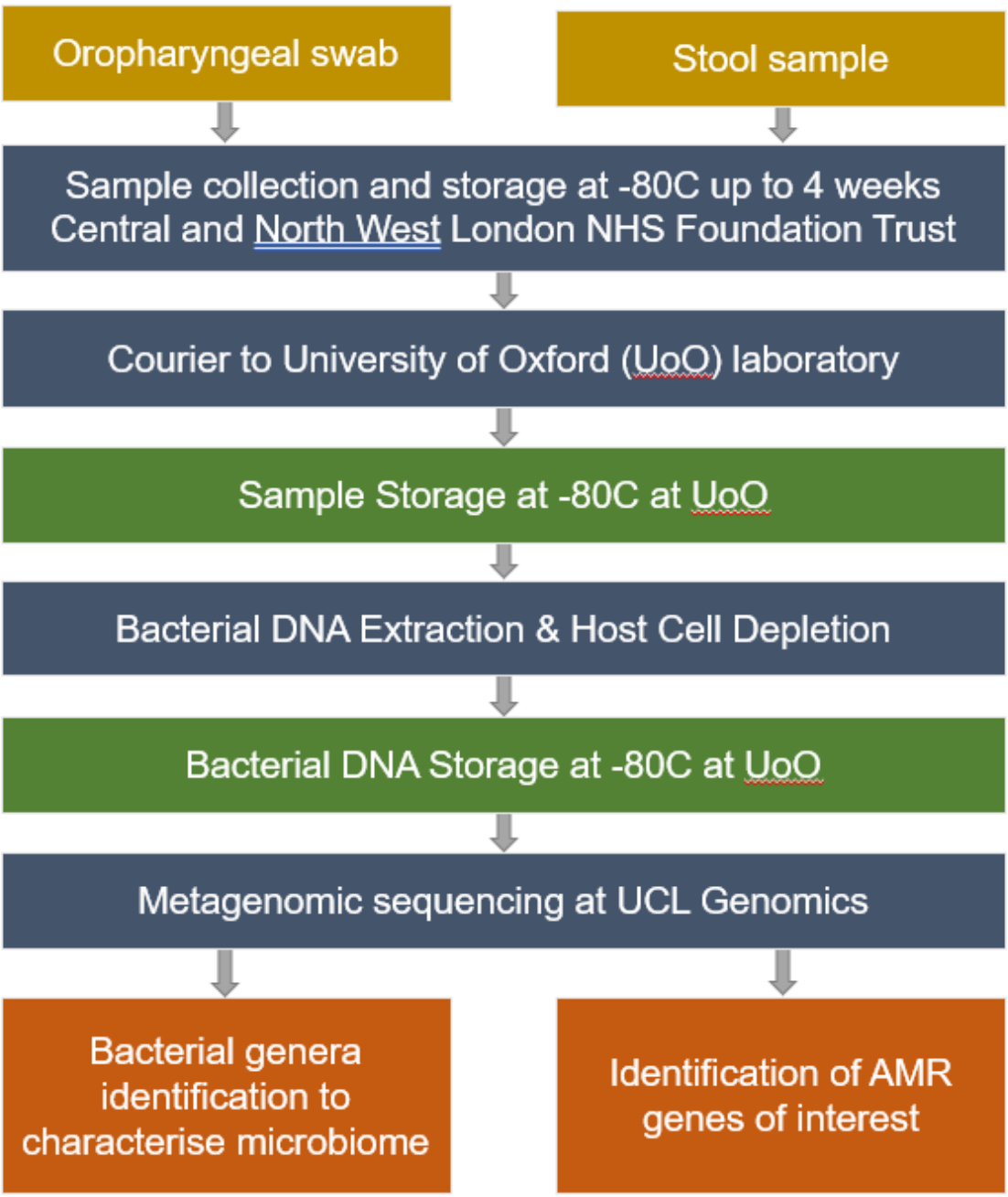
Stool samples will be labelled with the date of collection, the participant ID, and a sample ID number.

Sample Storage and Transport
Samples will be labelled with the date of collection, unique participant ID, and a sample ID number. Samples will be stored at the study site at -80C for a maximum of 28 days, before being couriered in an appropriate container for microbiology samples to the University of Oxford laboratory (Department of Biology, University of Oxford, South Parks Road, Oxford, OX1 3RB) for processing and storage until the end of the study (see **Figure 1** and *Section 13 Material/Sample Storage and Storage*). No study samples will be stored beyond the end of the expected study completion of April 2027.

Sample Processing and Sequencing
Sample specific microbial DNA extraction kits will be used. Extracted bacterial DNA will be stored at the Department of Biology, University of Oxford at -80C prior to metagenomic sequencing. Library preparation and metagenomic sequencing will be undertaken at UCL Genomics (20 Guildford Street, London, WC1N 1DZ).

Participants will remain in the study for a maximum of 13 months (360 +/ 30 days) (see *Section 5 Study Schedule*)

Figure 1: Sample workflow for Visits 1, 2, and 3.



5 STUDY SCHEDULE

All study visit activities will be conducted by a member of the clinical research team (research doctor, research nurse, or research assistant). For information on identification of potential participants and informed consent please see sections *7 Recruitment* and *8 Consent*. Participants receive a £30 voucher for each study visit. This will be given to participants at the end of each study visit. Participants will be able to withdraw from the study at any time. All data and samples collected prior to this will be retained by the research team.

Visit	Schedule (days)	Activities	Length (minutes)
1	0	Informed consent; questionnaire; oropharyngeal swab; stool sample	60
2	180 +/- 30	Questionnaire; oropharyngeal swab; stool sample	30-60
3	360 +/- 30	Questionnaire; oropharyngeal swab; stool sample	30-60

6 ELIGIBILITY CRITERIA

6.1 Inclusion Criteria

- Aged ≥ 18 years.
- Identifies as a man (cis or trans).
- Has sex with men.
- Able to provide informed consent.

6.2 Exclusion Criteria

- Use of an antibiotic other than doxycycline in the 3 months prior to enrolment
- Currently being treated for an STI with doxycycline
- Use of doxycycline within the prior 3 months for an indication other than STI treatment or STI prevention.

7 RECRUITMENT

Participant identification and recruitment will be through two distinct methods: clinic-based and community-based. The recruitment strategy has been co-developed with the SPEAR study community advisory group (see *Section 10 PPI*). The study includes online community-based recruitment through targeted adverts on social media and MSM-focused geospatial networking ('dating') apps to ensure the recruitment target for MSM using STI prophylaxis (group A) is met and allow recruitment of MSM not regularly attending in-person SHS or living outside London. Enrolment will be monitored in real-time to ensure targets for each antibiotic exposure group and MSM living with HIV are achieved.

7.1 Clinic-based: Patients attending CNWL SHS

Clinician referral

Clinicians seeing potentially eligible patients will refer them to the research team. The patient will be given the leaflet and PIS to read. If they wish to proceed and are eligible, they will be asked to provide informed consent (see *Section 8 Consent*) and booked for Visit 1 (*see Section 5 Study Schedule*).

Direct approach by the research team
Clinic appointment lists will be screened in advance by a member of the research team for potentially eligible participants. Members of the research team are also members of the clinical team involved in routine sexual health and HIV care alongside research. Patients will be contacted in advance of their appointment or approached in the waiting room. They will be given a copy of the PIS to read. If they wish to proceed and are eligible, they will be asked to provide informed consent (see *Section 8 Consent*) and booked for Visit 1 (see *Section 5 Study Schedule*).

Participant self-referral
Posters and leaflets describing the study will be available in clinical areas. These will include details of the study specific UCL webpage and contact details for the research team. Patients will be able to directly contact the research team by email. They will be sent the PIS to read. If they wish to proceed and are eligible, they will be asked to provide informed consent (see *Section 8 Consent*) and booked for Visit 1 (see *Section 5 Study Schedule*).

These recruitment strategies are used successfully for other studies within CNWL. Participation in the study does not impact the routine NHS sexual health or HIV care being provided to the participant by CNWL. Study visits and study sample collection are conducted independently of routine NHS care provided. The poster/leaflet have been co-designed by the community advisory group (see *Section 10 PPI*).

A log will be kept of potential participants approached in clinic but who decline to participate, alongside a reason for declining if given.

7.2 Community-based online

Social Media
Social media posts promoting the study will be shared on social media. This will include approved images/graphics and recruitment video. A study specific X™ account (formerly Twitter™) will be created to promote the study. Posts will also be shared on existing social media accounts (e.g. X™, Instagram™) associated with the UCL research team and CNWL. The research team have established links with professional organisations (e.g. BASHH) and is collaborating with the LGBTQ+ health focused community group The Love Tank who will promote the study.

MSM-focused geospatial networking ('dating') apps
Paid adverts will be placed on MSM-focused dating apps (e.g. Grindr, Scruff). This recruitment strategy is used successfully for cross-sectional surveys of MSM conducted by UCL.

Online posts/adverts will include a brief overview of the study, information on reimbursement for participation, and details of how to contact the research team. Online posts/adverts have been co-designed by the community advisory group (see Section 10 PPI). Individuals who contact the research team will be sent the PIS and then receive a phone call to discuss the study further and assess eligibility. If they wish to proceed and are eligible, they will be asked to provide informed consent (see *Section 8 Consent*) and booked in for Visit 1 (see Section 5 *Study Schedule*).

8 CONSENT

Informed consent will be gained from participants before any study activities are undertaken. Participants will be given and/or emailed the PIS to read prior to being asked to give informed consent. Participants will have three options for providing informed consent using the latest approved informed consent form (ICF):

1. E-consent prior to the first study visit.
2. E-consent at the start of the first study visit.
3. Written consent on paper ICF at the start of the first study visit.

E-consent will be provided using an online REDCap form. Completed e-consent forms will be stored in a study specific REDCap database within the UCL Data Safe Haven (see *Section 12 Data Handling and Management) 12*.[28] Participants opting for e-consent prior to the first study visit will receive a telephone call from a member of the research team (research doctor, research nurse, research assistant) to explain the study, confirm eligibility, and answer any questions. They will then be emailed a link to the e-consent form to complete and sign. The e-consent form will be signed by the member of the research team taking consent.

Participants opting to provide informed consent at the start of the first study visit will be offered to complete an e-consent or a written consent form. During the informed consent process, the study will be explained, participants will be given time to read the PIS again, and all questions will be answered. Participants opting for e-consent will complete the form online. The e-consent form will be signed by the member of the research team taking consent. Participants opting for written paper consent will sign two paper copies of the ICF. The person taking consent (research doctor, research nurse, research assistant) will also sign both ICFs. One signed ICF copy will be given to the participant and the second copy will be retained and stored securely at the study site (CNWL). A scanned copy of the written or e-consent form will be uploaded to the participant's CNWL-held medical records.

It will be clearly stated that the participant is free to withdraw from the study at any time for any reason without prejudice to current or future care, without affecting their legal rights, and with no obligation to give the reason for withdrawal. Participants will be informed that if they withdraw from the study, any study samples and data already collected will be retained and used in the final analysis. Participants will be asked for specific consent to review their study site medical records.

9 DATA ANALYSIS

9.1 Statistical Analysis

The planned statistical analysis is summarised here. The statistical analysis will be fully outlined in a statistical analysis plan (SAP). The SAP will be written by Dr Manik Kohli (Chief Investigator) and Dr Oliver Stirrup (Co-Investigator & Statistician). The SAP will be finalised before any analysis takes place. An analysis of baseline samples will be undertaken once all participants have completed Visit 1.

Sample characteristics, STI prophylaxis use, and questionnaire responses will be described using absolute numbers and proportions. A pooled prevalence estimate with 95% CI for AMR genes/gene mutations of interest will be produced. Chi-square tests will be used to evaluate evidence of differences in prevalence between subgroups, although findings will be presented with caution given the relatively small sample size. The association between detection of AMR genes/gene mutations of interest with demographic and sexual history variables will be described and investigated in exploratory univariable analyses.

Descriptive analyses of AMR detection over time within each group will be conducted. If adequate variation within individuals over time, then generalised estimating equations logistic regression will explore trends over time and consistency of AMR detection within each group.

Statistical analyses will be undertaken on the statistical programmes STATA and R.

9.2 Bioinformatic Analysis

The bioinformatic methodology and analysis is summarised here. The bioinformatic analysis will be fully outlined in a bioinformatic analysis plan (BAP). The BAP will be written by Dr Manik Kohli (Chief Investigator) and Prof Samuel Sheppard (Co-Investigator & Bioinformatician).

Bacterial taxonomic profiling will use both de novo assembly and read-mapping approaches. De novo assembly tools (e.g., MEGAHIT, metaSPAdes) will allow evaluation of taxonomy and AMR genetic diversity. Supervised binning methods will group assembled contigs (DNA sequences) by species using tools such as metaBAT, and the PubMLST/metaMLST reference databases which hosts assembled whole genome sequence data from over 480,000 bacterial isolates. Antibiotic resistance databases (e.g., Comprehensive Antibiotic Resistance Database) will be used to identify genes conferring resistance to tetracyclines (e.g., *tet(M)*, *tet(W)*, *tet(Q)*) and other important antibiotic classes (e.g., Macrolides *mphA*, *ermF*).

To mitigate potential assembly problems from low-abundance organisms, read mapping approaches will be undertaken using the pipeline CCMetagen which uses the National Centre for Biotechnology Information (NCBI) database as reference. Computationally intensive analyses will be carried out in a single in silico system that archives and integrates bacterial metagenomes and AMR genes with other rich metadata, and can organise and share genomes to allow integrated analyses and modelling.

Genome-wide association study analyses incorporating machine learning will identify core and accessory genome AMR elements (including plasmids) from complex samples. Genomic variation identified will include gene presence and absence; gene orthologs/alleles; insertions/deletions and single nucleotide polymorphisms (SNPs). These will be linked to AMR and other metadata.

Bacterial genera diversity (microbiome profiles) and AMR genes/gene mutations of interest ('resistome' profiles) will be compared between baseline study groups, and over time by use of doxycycline prophylaxis. Exploratory analysis of microbiome profiles by other characteristics including HIV status and sexual history will be undertaken.

This study does not analyse human DNA.

10 PATIENT AND PUBLIC INVOLVEMENT (PPI)

10.1 PPI for Funding Proposals and Study Design

Input was sought from:

- The Love Tank, who undertake advocacy work on LGBTQ+ health issues and provide information on STI/HIV prevention through their PrEPster and queerhealth.info programmes.
- The Terrence Higgins Trust and BASHH lay research panel.
- NIHR Research Design Service lay reviewers.
- Gay and bisexual men, through two workshops with six community members, funded by an NIHR PPI grant.

Overall, feedback was extremely supportive of the research and participants were clear that this was an important topic.

Changes made to the study on the advice of the PPI groups included:

- Revision of the research objectives to include changes in microbiome over time.
- Mechanisms to ensure ongoing PPI involvement in the study.
- Recruitment: dual strategy from sexual health clinics (to increase likelihood of participating) and online (to ensure inclusion opportunities for participants not attending clinics and from a wider geographical area).
- Study documents, promotional materials, and dissemination: to include clear understandable information about AMR, to use sensitive language to avoid contributing to stigma, and for information on STI prophylaxis should be balanced discussing both benefits and risks
- Co-production and collaboration: inclusion of co-production group and collaboration with trusted community organisations (see below).
- Stool samples: Collection of stool samples in clinic was acceptable, with provision options for participants to collect samples at home if they unable to provide a sample in clinic.

10.2 Community Advisory Group

The study includes a community advisory group. The group will meet regularly throughout study (online and/or in-person); and includes patients and community members. To date, the group have given input on the PIS and questionnaire; co-designed the online adverts/poster; and co-developed the recruitment strategies (see *Section 7 Recruitment*). Throughout the study, the group will monitor enrolment and advise on recruitment strategies as needed; co-analyse questionnaire data; co-develop dissemination plans; review the overall study findings; and co-produce community-focused outputs.

10.3 Collaboration with The Love Tank

The Love Tank is an LGBTQ+ and sexual health focused community organisation which runs the community programmes PrEPster and queerhealth.info. The Love Tank will be involved with online study promotion for community-based recruitment and community dissemination of the study findings.

11 FUNDING AND SUPPLY OF EQUIPMENT

The study funding has been reviewed by the UCLH/UCL Joint Research Office and deemed sufficient to cover the requirements of the study.

The research costs for the study have been supported by the National Institute for Health and Care Research (NIHR) Doctoral Fellowship £589,590 (NIHR303717), the British Infection Association (BIA) £10,000 (2023/Manik Kohli), and the British HIV Association (BHIVA) £9,979.96 (BHIVA/5020/2023/Kohli).

12 DATA HANDLING AND MANAGEMENT

The study is compliant with the requirements of General Data Protection Regulation (2016/679) and the UK Data Protection Act (2018). All investigators and study site staff will comply with the requirements of the General Data Protection Regulation (2016/679) with regards to the collection, storage, processing and disclosure of personal information, and will uphold the Act's core principles. UCL is the data controller; the UCL Data Protection Officer is data-protection@ucl.ac.uk. The data processors are Central and North West London NHS Foundation Trust.

The project will collect data on age, gender, ethnicity, sexual orientation, sexual history, and medical history as part of the research. Data will be collected through participant questionnaires and medical records. **Figure 2** below summarises the study team organisation and data flow.

All participants will be assigned a unique pseudonymised identifier (participant ID). Questionnaire responses and all study samples will be pseudonymised using this participant ID. Questionnaire responses will be collected via a secure REDCap form and all data will be stored in a REDCap database within the UCL Data Safe Haven.(28) The UCL Data Safe Haven

is a secure and protected environment for storing, handling, and analysing sensitive or identifiable data.(28) The collection of medical and sexual history information is necessary for the aims of the research. Only members of the research team will have access to the database. Participants opting for e-consent, this will be completed using a REDCap form and stored with the study specific REDCap database within the UCL Data Safe Haven.

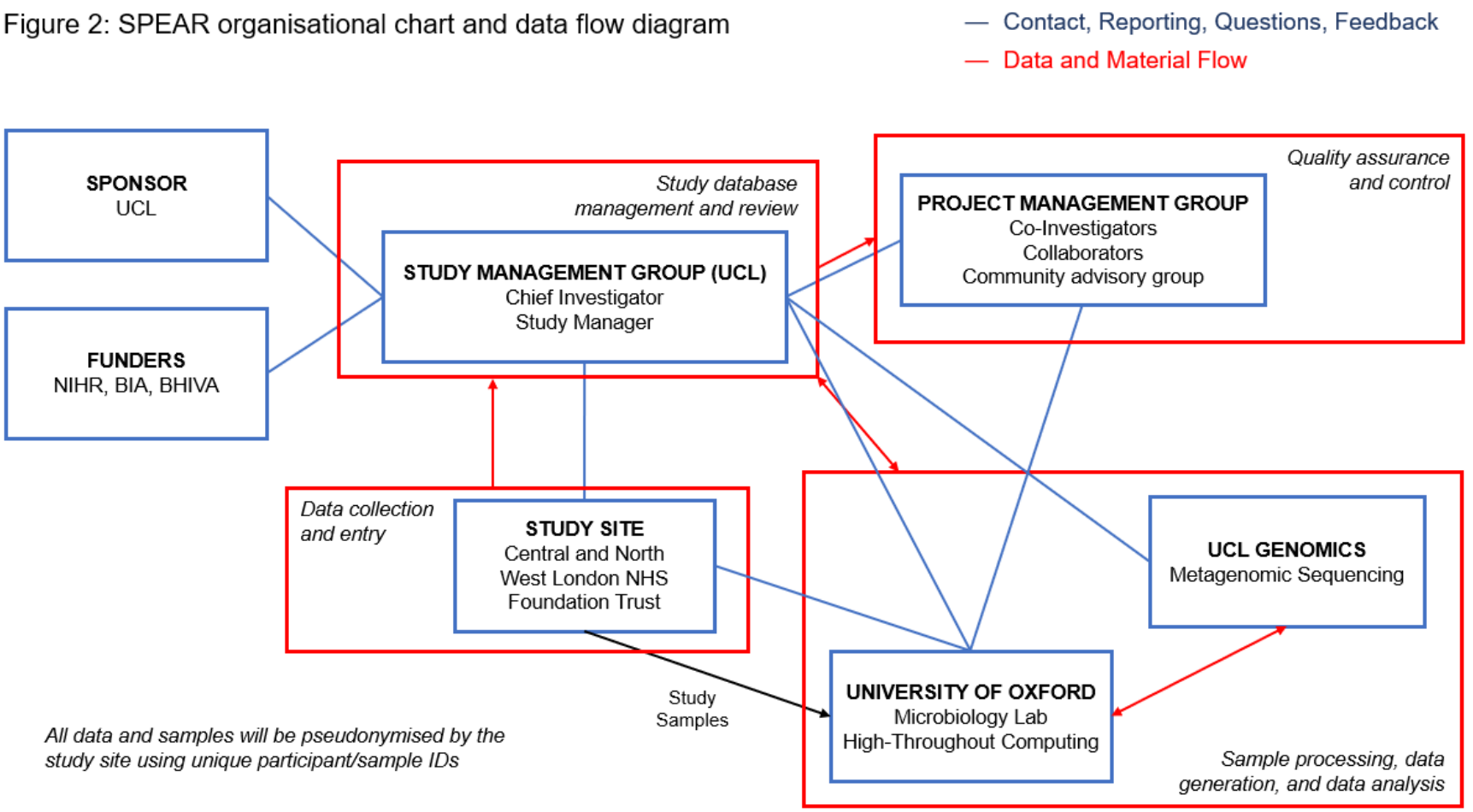
This research is a collaboration between UCL and the University of Oxford. Study samples collected at the study site will be labelled with the participant ID, sample ID number, and date of collection. No identifiable information will be shared outside the study site (Central and North West London NHS Foundation Trust, CNWL). A collaboration agreement covering material and data transfers will be in place between UCL and the University of Oxford. Bacterial genomic sequencing will take place at UCL Genomics. If additional metagenomic sequencing of bacterial DNA samples occurs at a third-party organisation (not UCL or University of Oxford), a separate MTA will be instituted for the transfer.

Genomic data will be stored at the University of Oxford in line with their data protection and data management policies. Pseudonymised questionnaire responses with only participant ID numbers will be securely transferred to the University of Oxford for analysis alongside the bacterial genomic data. A data flow diagram is included below (Figure 2).

A site agreement will be in place between UCL and the study site (CNWL). For participants opting for written paper consent, signed paper consent forms will be stored the study site. A copy of the consent form (paper or e-consent) will be uploaded to the participant's CNWL-held medical records. A secure password protected log will be kept at the study site which will include participant ID numbers alongside identifiable information: name, date of birth, medical records number, and contact information (phone number and/or email). This will be stored separately to the questionnaire responses at the study site on NHS computers. Contact information will be needed to arrange follow-up visits and to invite participants to dissemination events at the end of the study.

Data will be retained until the end of study and for up to 20 years (see *Section 21 Archiving)*.

Figure 2: SPEAR organisational chart and data flow diagram



13 MATERIAL/SAMPLE TRANSPORT AND STORAGE

Stool samples and oropharyngeal swabs will be collected from patients in accordance with the patient consent form and patient information sheet and shall include all tissue samples or other biological materials and any derivatives, portions, progeny or improvements as well as all patient information and documentation supplied in relation to them. Samples will be processed, stored and disposed in accordance with all applicable legal and regulatory requirements, including the Human Tissue Act 2004 and any amendments thereafter, and the applicable HTA Codes of Practice Departmental SOPs will be followed to facilitate regulatory compliance.

Samples will be labelled with the unique participant ID, a sample ID number, and date of collection. Study site sample collection, storage and storage SOPs will be written by Dr Manik Kohli (CI/PI). Samples will be stored at the study site in a freezer (lowest temperature -80C) for a maximum of 28 days, before being couriered in an appropriate container for microbiology samples to the University of Oxford laboratory (Department of Biology, University of Oxford, South Parks Road, Oxford, OX1 3RB) for processing and storage at -80C until the end of the study. Samples will be processed as quickly as possible after collection and courier. An MTA will be in place prior to any sample collection and transfer. A study specific laboratory SOP, adapted from existing local SOPs and DNA extraction kit protocols, will be written by Dr Manik Kohli (Chief Investigator) and Dr Odile Harrison (Co-Investigator and Microbiologist) prior to any sample processing. No study samples will be stored beyond the end of the expected study completion of April 2027 and will be destroyed in line with local health and safety protocols.

Samples will be processed at the University of Oxford, Department of Biology laboratory. Samples will undergo bacterial DNA extraction. Extracted bacterial DNA will be stored at the University of Oxford Department of Biology at -80C prior to metagenomic sequencing. Metagenomic sequencing will be undertaken at UCL Genomics (20 Guildford Street, London, WC1N 1DZ).

14 PEER AND REGULATORY REVIEW

The study has been peer reviewed in accordance with the requirements outlined by UCL.

Choose either (having discussed with the UCLH/UCL Joint Research Office):

The Sponsor considers the procedure for obtaining funding from National Institute for Health and Care Research, NIHR to be of sufficient rigour and independence to be considered an adequate peer review.

The study was deemed to require regulatory approval from the following bodies REC Favourable Opinion and HRA Approval). **Before any site can enrol patients into the study,**

the Chief Investigator/Principal Investigator or designee will ensure that the appropriate regulatory approvals have been issued, and NHS Confirmations of Capacity and Capability and Sponsor green lights are in place.

For any amendments to the study, the Chief Investigator or designee, in agreement with the Sponsor, will submit information to the appropriate body in order for them to issue approval for the amendment. The Chief Investigator or designee will work with sites (R&D departments as well as the study delivery team) to confirm ongoing Capacity and Capability for the study.

All correspondence with the Sponsor, REC and HRA will be retained. The Chief Investigator will notify the Sponsor and REC of the end of the study.

It is the Chief Investigator's responsibility to produce the annual progress reports when required; an annual progress report (APR) will be submitted to the Sponsor and REC within 30 days of the anniversary date on which the favourable opinion was issued, and annually until the study is declared ended.

If the study is ended prematurely, the Chief Investigator will notify the Sponsor and REC, including the reasons for the premature termination. Within one year after the end of the study, the Chief Investigator will submit a final report with the results, including any publications/abstracts, to the Sponsor and to the REC and HRA.

15 ASSESSMENT AND MANAGEMENT OF RISK

This is a minimal risk observational study. The following potential risks have been identified and strategies to mitigate these potential risks are outlines below.

Potential risk
Emotional distress related to questionnaire completion.
Plan to minimise this risk
To minimise this risk, questions have been adapted from validated sources such as the National Survey of Sexual Attitudes and Lifestyles (Natsal) and other UCL-sponsored surveys, which have been developed with extensive user feedback to be acceptable and easily understood. PPI input and feedback has been sought on the questionnaire to ensure questions are appropriate and inclusive. If any participants are distressed on questionnaire completion, they will be signposted to appropriate support.

Potential risk
Loss of confidentiality.
Plan to minimise this risk
All data will be pseudonymised, with each participant being assigned a unique identifier to be recorded on all questionnaires and samples. Study-specific data will be captured electronically using a computer or tablet. The data management system for these will be based on a mature, secure web application REDcap. All data will be stored in the UCL Data Safe Haven. A study log linking the participant ID with the clinic medical records number will

be kept securely on NHS computers at the study site (CNWL). Only members of the study site research team will have access to the password protected study log and patient identifiable information. These will be stored separately on NHS computers and can only be accessed by the relevant person(s) on the study research team. All email correspondence with potential and enrolled participants will be via NHS email.

Potential risk
Contamination of clean surroundings when collecting a stool sample.
Plan to minimise the risk
Participants will be provided stool sample collection kits. Kits will include how to collect a stool sample safely and correctly. Kits will also include gloves for collection of the sample.

Potential risk
Discomfort from oropharyngeal swabbing
Plan to minimise the risk
All member of the research team will undertake training on oropharyngeal swab collection to minimise discomfort.

16 RECORDING AND REPORTING OF EVENTS AND INCIDENTS

All events and incidents (and near misses) that occur to participants and/ or staff that are **unexpected** and directly **related** to the research study will be reported to the Sponsor via research-incidents@ucl.ac.uk or UCL REDCAP incident reporting form) and host sites via their Trust reporting systems, and documented in the Trial Master File/Investigator Site File via study-specific incident logs (and related correspondence). This will be completed by the CI or PI. The Sponsor will be responsible for investigating, reviewing, or escalating to a serious breach if required.

16.1 Personal Data Breaches

Any personal data breaches will be immediately reported to the UCL Information Security Group (ISG) and the UCL Data Protection Officer [data-proection@ucl.ac.uk], (as per form and guidance: https://www.ucl.ac.uk/data-protection/guidance-staff-students-and-researchers/practical-data-protection-guidance-notices/report-breach), and to the Sponsor via the UCL REDCAP incident reporting form (https://redcap.slms.ucl.ac.uk/surveys/?s=NE5dypTdFo). The following information will be provided: full details as to the nature of the breach, an indication as to the volume of material involved, and the sensitivity of the breach (and any timeframes that apply). Sites will additionally follow their Trust incident reporting mechanisms and will document this within their TMF/ISFs.

16.2 Adverse Events and Serious Adverse Events Sponsor Reporting Requirements

Adverse events are any untoward medical occurrence in a patient or study participant, which does not necessarily have a causal relationship with any study activities. These do not require reporting to the Sponsor, but the severity, causality and expectedness will be

recorded in the participant's medical records, REDCap entry, and AE log, with a description of clinical symptoms and the event, including dates as appropriate.

In some instances, **unexpected and related SAEs** may occur in observational research. All reportable SAEs will be recorded in the medical records and CRF, and reported to the Sponsor via the JRO REDCAP research incident reporting form or research-incidents@ucl.ac.uk, within 5 working days of becoming aware of the event. The CI/PI will respond to any SAE queries raised by the Sponsor as soon as possible.

16.3 Incidental Findings in Research

All research staff will follow participating sites' incidental findings policies, and training on this will be provided as part of initiation to the research study.

16.4 Protocol deviations and notification of protocol violations

Protocol deviations are usually an unintended departure from the expected conduct of the study protocol/SOPs, which does not need to be reported to the Sponsor. The CI will monitor protocol deviations, and if found to frequently recur, will discuss in the first instance with the Sponsor to determine re-classification and reporting requirements.

A protocol violation is a breach which is likely to effect to a significant degree: –
(a) the safety or physical or mental integrity of the participants of the study; or
(b) the scientific value of the study
The CI and Sponsor will be notified immediately of any case where the above definition applies via research-incidents@ucl.ac.uk or UCL REDCap incident reporting form.

16.5 NHS Serious Incidents and near misses

A serious incident or near miss is any unintended or unexpected event that could have or did lead to harm, loss or damage that contains one or more of the following components:
a. It is an accident or other incident which results in injury or ill health.
b. It is contrary to specified or expected standard of patient care or service.
c. It places patients, staff members, visitors, contractors or members of the public at unnecessary risk.
d. It puts the Trust in an adverse position with potential loss of reputation.
e. It puts Trust property or assets in an adverse position or at risk.
Serious Incidents and near misses will be reported to the Sponsor and Trust Quality & Safety department as soon as the study team becomes aware of them.

16.6 Complaints from research participants

In the first instance, research participant complaints will be reported to the CI/PI to investigate, as documented in the patient information sheet(s), and to the Sponsor [via research-incidents@ucl.ac.uk, following the *UCL Complaints from Research Subjects about UCL Sponsored Studies and Trials* policy]. For participants who are NHS patients, complaints will be reported to the NHS Complaints Manager at the Trust where the recruitment and study procedures was undertaken. Complaints from NHS patients are handled under NHS

complaints policies and procedures, with involvement from PALS and the Sponsor where necessary.

17 MONITORING AND AUDITING

The CI will ensure there are adequate quality and number of monitoring activities conducted by the study team. This will include adherence to the protocol, procedures for consenting and ensure adequate data quality.

The CI will inform the Sponsor should he/she have concerns which have arisen from monitoring activities, and/or if there are problems with oversight/monitoring procedures.

18 TRAINING

The Chief Investigator will review and provide assurances of the training and experience of all staff working on this study. Appropriate training records will be maintained in the study files.

All staff working on this study will be required to have undertaken GCP training within the last two years. Study specific training with regards to the protocol and procedures will be undertaken by all staff.

19 INTELLECTUAL PROPERTY

All background intellectual property rights (including licences) and know-how used in connection with the study shall remain the property of the party introducing the same and the exercise of such rights for purposes of the study shall not infringe any third party's rights.

All intellectual property rights and know-how in the protocol, the study data and in the results arising directly from the study, but excluding all improvements thereto or clinical procedures developed or used independently of the study by each participating site, shall belong to UCL. All intellectual property rights deriving or arising from the material or any derivations of the material provided to UCL by the participating site shall belong to UCL. Each participating site agrees that by giving approval to conduct the study at its respective site, effectively assigns all such intellectual property rights ("IPR") to UCL and discloses all such know-how to UCL.

Nothing in this section shall be construed so as to prevent or hinder the participating sites from using its own know how or clinical data gained during the performance of the study, as its own risk, in the furtherance of its normal activities or providing clinical care to the extent that such use does not result in the disclosure or misuse of confidential information of the infringement of an intellectual property rights of UCL, or their funder. This section does not

permit the disclosure of any of the study data, all of which remain confidential until publication of the results of the study.

20 INDEMNITY ARRANGEMENTS

UCL holds insurance against claims from participants for harm caused by their participation in this clinical study. Participants may be able to claim compensation if they can prove that UCL has been negligent. However, as this clinical study is being carried out in a hospital, the hospital continues to have a duty of care to the participants of the clinical study. UCL does not accept liability for any breach in the hospital's duty of care, or any negligence on the part of hospital employees. This applies whether the hospital is an NHS Trust or otherwise.

Participants may also be able to claim compensation for injury caused by participation in this clinical study without the need to prove negligence on the part of UCL or another party. Participants who sustain injury and wish to make a claim for compensation should be advised to do so in writing in the first instance to the Chief Investigator, who will pass the claim to the Sponsor's Insurers, via the Sponsor's office.

Hospitals selected to participate in this clinical study shall provide clinical negligence insurance cover for harm caused by their employees and a copy of the relevant insurance policy or summary shall be provided to UCL upon request.

21 ARCHIVING

UCL and each participating site recognise that there is an obligation to archive study-related documents at the end of the study (as such end is defined within this protocol). The Chief Investigator confirms that they will archive the study master file at UCL for the period stipulated in the protocol and in line with all relevant legal and statutory requirements.

The Trial Master File will be archived at UCL, in accordance with the UCL Retentions Schedule and Policy. It will be archived for a minimum of 5 years from the study end, and no longer than 20 years from study end.

22 PUBLICATION AND DISSEMINATION

A dissemination plan will be co-produced with the community advisory group (see *Section 10.2 Community Advisory Group*) covering academic and community dissemination. The strategy will include, but not be limited to:

- Abstract submission for presentation at national and international conferences, such as those organised by BASHH, BHIVA, BIA, and the European Congress of Clinical Microbiology and Infectious Diseases (ECCMID).
- Manuscript submission to key peer-reviewed academic journals.
- Public and community focused lay summaries of the research, co-written with the community advisory group and community collaborator The Love Thank (see *Section*

10 PPI). These will be shared by on online. Lay summaries will be sent to all participants.

- Dissemination event for clinicians, academics, community organisations, public health officials, policymakers. Participants will be invited to attend the event, and this will be promoted on social media.

Individual level findings will not be reported back to participants.

The investigators and academic collaborators will be involved in reviewing drafts of academic manuscripts, abstracts, press releases and any other publication arising from this study. Authorship will be determined in accordance with the ICMJE guidelines and other contributors will be acknowledged. All outputs will acknowledge that the research was funded by BIA, BHIVA, and NIHR. Community advisory group members will be acknowledged in all outputs (anonymously if preferred), and where appropriate included in authorship.

23 REFERENCES

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24 APPENDICES

Include here **a list** of the supplementary information and documents that will support the protocol and information contained therein, e.g. PIS, ICF, schedule visit, assessment tools, delegation log, case report forms, questionnaires, scales, tables, charts, diagrams, manufacturer's brochures.

It is not advisable to insert copies of documents such as the PIS and ICF due to version control and document management issues. You may wish to list the document titles here or delete if unnecessary.

24.1 Associated Documents

Include here supplementary information and documents that will support the protocol and information contained therein.
E.g. data dictionary

Document Name	Document Version	Document Date