ISRCTN17060051 https://doi.org/10.1186/ISRCTN17060051

Tracking anti-microbial resistance across care settings in Liverpool (TRACS-Liverpool) Part 2

Submission date 25/09/2022	**Recruitment status** No longer recruiting	[X] Prospectively registered [_] Protocol [_] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 28/09/2022	**Overall study status** Completed	
Last Edited 23/01/2024	**Condition category** Infections and Infestations	

Plain English summary of protocol

Background and study aims

This study is looking at the spread of drug-resistant infections across different care settings in Liverpool. Infections become drug-resistant when the bacteria that cause them adapt and change over time, developing the ability to resist the drugs designed to kill them. The result is that many antibiotics are becoming less effective at treating illnesses. Without working antibiotics, routine surgery like hip replacements, or common illnesses can become life-threatening. People are already dying from drug-resistant infections.

Previous research has shown that people in hospital or who live in care homes may be at increased risk of drug-resistant infection, but exactly why is unknown. Data also shows there are slightly higher rates of some types of drug-resistant bacteria in the northwest of England. These bacteria are called enterobacterales and include common disease-causing bacteria such as E. coli. Enterobacterales that produce substances called extended-spectrum beta-lactamases (ESBL) or carbapenemases (CPE) are resistant to many commonly used antibiotics and preventing their spread is a global priority.

Some resistant bacteria – like E. coli - are thought to live harmlessly in the gut in many people before they go on to cause illness in others. This suggests that spread happens when one person swallows bacteria from the gut of another. It could be that bacteria are transmitted from toilets to hands via sinks, and then swallowed for example; but at present, this is not known.

The aim of this study is to understand exactly how these bacteria are transmitted and if there is a difference in rates of transmission in different care settings in Liverpool. The researchers will visit two hospital wards, one intermediate care ward and three care homes for a fortnight every three months. During these site sampling visits they will collect swabs from the environment (e. g. toilets, sinks, door handles), anonymised hand swabs from staff and stool samples or rectal swabs from patients and residents. They will test all these samples for resistant Enterobacterales bacteria and, when they find them, they will use gene sequencing techniques to track where they may have come from. This information will allow them to identify places where people catch resistant bacteria, and to design interventions to block transmission.

Who can participate?

Any patient or resident aged 18 years and over who is present on the ward or in the care home at the time of the study sampling visit, and not receiving palliative care, is eligible to participate.

What does the study involve?
Patients and residents enrolled into the study will be asked to provide up to five stool samples or rectal swabs at each round of study site sampling. Therefore, if they are a patient on a hospital ward, and discharged prior to the next round of sampling they may only provide up to five samples. If they are in a care home, and resident at each sampling visit they may provide up to 20 samples, provided they are willing to do so. The researchers will also collect data from hospital and GP records about antibiotics participants have received and where they have been in the hospital.

What are the possible benefits and risks of participating?
There are no direct benefits to the participants from taking part in the study, although it is anticipated that the knowledge gained from the research will allow the researchers to identify how and where people catch resistant bacteria and to design interventions to stop this from happening. This would result in improved care and fewer infections in hospital and care home settings. The researchers do not anticipate any risks from taking part although participants may experience some discomfort from having a rectal swab taken.

Where is the study run from?
Liverpool School of Tropical Medicine (UK)

When is the study starting and how long is it expected to run for?
July 2022 to 2024

Who is funding the study?
1. UK Research and Innovation (UK)
2. Unilever (UK)

Who is the main contact?
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Contact information

Type(s)
Public

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Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

Integrated Research Application System (IRAS)
320804

Protocol serial number
22-066, IRAS 320804

Study information

Scientific Title
Tracking anti-microbial resistance across care settings in Liverpool (TRACS-Liverpool) Part 2: an observational cohort study

Acronym
TRACS - Liverpool Part 2

Study objectives
The study aims to track transmission of extended-spectrum beta-lactamase and carbapenemase-producing Enterobacterales (ESBL-E/CPE) in hospitals and care homes in Liverpool, to optimise approaches to interrupting transmission.

Primary Objective:
To detect differences in rates of acquisition of ESBL-E/CPE between patients in hospital and residents in care home settings.

Secondary Objectives:
1. To identify risk factors for acquisition of ESBL-E/CPE in people in health and social care settings, including location (e.g. acute hospital ward, intermediate care facility, long-term residential care).
2. To describe the movement of ESBL-E/CPE bacteria, ESBL and carbapenemase genes and mobile genetic elements within and between hospitals and care facilities.
3. Describe the distribution and within-host diversity of ESBL-E/CPE as people move through health and social care settings and are exposed to antimicrobials, and the implications for inferring transmission.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 17/11/2022, North West - Greater Manchester South Research Ethics Committee (3rd Floor, Barlow House, 4 Minshull Street, Manchester, M1 3DZ, UK; +44 (0)207 104 8079; gmsouth.rec@hra.nhs.uk), ref: 22/NW/0343

Study design
Multicentre longitudinal observational cohort study

Primary study design
Observational

Study type(s)
Other

Health condition(s) or problem(s) studied
Transmission of antimicrobial resistance within and between care settings in Liverpool including NHS wards, intermediate care and long term residential care

Interventions
Following consent and enrolment participants will be asked to provide up to five stool samples or rectal swabs over a 2-week period of site-specific sampling. Each site will be revisited approximately every 12 weeks. If participants remain at the site for the duration of the study they may be asked to provide a maximum of 20 samples.

Intervention Type
Other

Primary outcome(s)
The presence of ESBL-E/CPE will be defined by selective culture of stool or rectal swab. Samples will be collected from all residents of the sampling area (hospital ward or care home) at 5 time-points over the two week sampling period at that location. Sample areas will be visited 4 times over the course of the study at 12 week intervals. If participants are still present the sampling schedule will be repeated.
Hazard ratio of ESBL-E/CPE acquisition: The ESBL-E/CPE presence/absence data will be used to fit multistate Markov models. In these models participants can be either colonised or uncolonised with a transition rate between each state. The transition rate is governed by a linear combination of covariates, which can be included in such a way that the effect of the covariate can be interpreted as a hazard ratio. Hence by including care home (versus hospitalisation) as a covariate in the models this will generate a hazard ratio of ESBL acquisition for care home residency versus hospitalisation.

Key secondary outcome(s))
1. Parameter values for effect of covariates from multistate models including hazard of ESBL-E /CPE acquisition measured by including other covariates in the Markov multistate models, this will generate estimates of the effect of the included covariates, analogously to the hazard ratio of ESBL acquisition described above. The values of these parameters (i.e. estimated quantities from the model) will allow an understanding of the effect of the included covariates.
2. Description of putative transmission events (bacteria and mobile genetic elements and routes within and between hospitals and care facilities. We will sequence the genomes of cultures bacteria using short read whole genome sequencing and map them to a reference genome. We can then compare genomes using the number of single nucleotide polymorphisms (SNPs) between them. Very closely related bacteria (i.e., < 10 SNPs) are putative transmission events. We will describe these transmission events in terms of which compartments (patient, environment, staff) are most linked to allow an understanding of likely transmission routes). To describe mobile genetic elements we will use long read sequencing with a similar analysis.
3. Longitudinal description of within-host ESBL-E/CPE diversity. We will describe within-participant diversity by limited diversity metagenomics following selective culture of samples for ESBL-E/CPE. This technique allows sequencing of all ESBL-E/CPE organisms in a sample with subsequent computation reconstruction of the different bacteria present. We will present a

descriptive analysis of the diversity of ESBL-E/CPE strains within participants and the effect on the diversity of exposure to antimicrobials, hospitalisation, and residence in care homes.

Completion date
31/07/2024

Eligibility

Key inclusion criteria
All current adult (aged ≥18 years) residents of the study sampling location during the sampling period

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Key exclusion criteria
Residents being managed with palliative intent in whom active treatment has been withdrawn

Date of first enrolment
01/02/2023

Date of final enrolment
01/07/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Liverpool University Hospitals NHS Foundation Trust
Royal Liverpool University Hospital
Prescot Street
Liverpool

United Kingdom
L7 8XP

Study participating centre
Merseycare NHS Trust
V7 Building
Kings Business Park
Prescot
United Kingdom
L34 1PJ

Study participating centre
Mersey and West Lancashire Teaching Hospitals NHS Trust
Whiston Hospital
Warrington Road
Prescot
United Kingdom
L35 5DR

Sponsor information

Organisation
Liverpool School of Tropical Medicine

ROR
https://ror.org/03svjbs84

Funder(s)

Funder type
Industry

Funder Name
UK Research and Innovation Strength in Places fund

Alternative Name(s)
UKRI

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Funder Name
Unilever

Alternative Name(s)
Unilever Global, Unilever PLC, U

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
Following the publication of the results, anonymised data and code to reproduce results will be published in data and code repositories (e.g. zenodo, GitHub) without any preconditions for access.

IPD sharing plan summary
Stored in publicly available repository

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
HRA research summary			28/06/2023	No	No