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Understanding the impact of resistant bugs on deaths in England

Submission date 28/05/2024	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [X] Statistical analysis plan [_] Results [_] Individual participant data [X] Record updated in last year
Registration date 02/06/2024	**Overall study status** Ongoing	
Last Edited 11/03/2025	**Condition category** Other	

Plain English summary of protocol

Background and study aims

Antimicrobial resistance refers to when bacteria, viruses, fungi and parasites (bugs) no longer respond to antibiotic medicines. It is usually caused by prolonged and repeated exposure of bugs to antibiotics, in people, animals or the environment, which helps bugs eventually build defence mechanisms against them. These bugs can then spread via contact from person to person, causing resistant infections to people who have not had antibiotics before. For this reason, previously effective treatments stop working due to antimicrobial resistance worldwide. Research has shown that infections from antibiotic resistant bugs are more likely to lead to death, disability, and additional stay in hospital. It has also been estimated that, by 2050, 10 million deaths a year will be caused by antimicrobial resistance.

Despite the importance of antimicrobial resistance, which has been characterised as a global health emergency by the World Health Organisation, we have limited information about how many people die every year due to infections resistant to antibiotics. This is because of a variety of factors. For example, studies have shown that doctors are more likely to record chronic health problems like cancer in the death certificate as the primary cause of death, and the contribution of infection is often underestimated. Another problem is that in order to find antibiotic resistant bugs, cultures from the patient need to be taken, which is not always performed. This leads to underestimation of true numbers of antibiotic resistant infections. Yet, knowing exactly how many people die due to antimicrobial resistance is important, as it drives political and public awareness about the problem, highlighting the need for better treatments.

Very few previous studies have tried to estimate the true numbers of deaths due to antibiotic resistant infections. They have primarily used a technique called modelling to do so. Modelling uses math to estimate the numbers of deaths, based on how groups of patients with antibiotic sensitive and antibiotic resistant infections behave, as well as total numbers of infections. Because modelling doesn’t look at individual patient cases though, it can lead to erroneous results and underestimation of the problem.

In this study, we will attempt for the first time to calculate the total number of deaths caused by antibiotic resistant infections in England in 2021, 2022 and 2023. We aim to do that by anonymously linking the cause of death of each patient as documented on the death certificate

with the bugs they were positive for in cultures and specimens up to 28 days before the date of death.

Who can participate?
Every patient who died in England in 2021, 2022 and 2023 will be included in the study but their data will be collected in a way that will not allow them to be identified. Participants who expressed their wish for their data not to be used for research purposes before they died will be excluded. We believe that with this approach we will get more accurate data on the total number of people in England, in whom antimicrobial resistance contributed to their death.

What does the study involve?
Retrospective analysis of patient records.

What are the possible benefits and risks of participating?
None

Where is the study run from?
University College London (UK)

When is the study starting and how long is it expected to run for?
March 2024 to December 2025

Who is funding the study?
UK Health Security Agency

Who is the main contact?
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Study website
https://www.ucl.ac.uk/child-health/research/infection-immunity-inflammation/infection/amr-dc-study-antimicrobial-resistance-death

Contact information

Type(s)
Principal Investigator

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Additional identifiers

EudraCT/CTIS number
Nil Known

IRAS number
340243

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
IRAS 340243, CPMS 61354

Study information

Scientific Title
Recording Antimicrobial Resistance during Death Certification in England

Acronym
AMR-DC

Study objectives
1. That it is possible to calculate AMR-associated deaths by linking death certification and patient-level microbiological data.
2. That AMR-associated mortality has been increasing in England during the study period.
3. That AMR was associated with a significant number of deaths (>2% of total deaths) in England in 2021-2023.

4. That a significant proportion of deaths (>10%) due to infection in England in 2021, 2022 and 2023 were AMR-associated.
5. That ESBLs were the AMR resistance mechanism with the highest number of AMR-associated deaths in England during the study period.
6. That most AMR-associated deaths (>90%) occur in hospital, disproportionately affect patients in Intensive Care and patients under Haematology and Oncology.
7. That patients recording AMR-associated deaths have longer hospital length of stays, are more likely to be admitted to Intensive Care and require more prolonged organ support.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 20/03/2024, North West - Haydock Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 (0)207 104 8032; haydock.rec@hra.nhs.uk), ref: 24/NW/0084

Study design
Retrospective observational cohort

Primary study design
Observational

Secondary study design
Cohort study

Study setting(s)
Medical and other records

Study type(s)
Other

Participant information sheet
Not applicable (retrospective study)

Health condition(s) or problem(s) studied
Antimicrobial resistance effect on mortality

Interventions
This will be a retrospective observational cohort study. Eligible patients will be identified through the Civil Registrations of Death database provided by NHS England and will be linked to the HES database, also held by NHS England, to obtain additional clinical metadata. Pseudonymised cases will be subsequently linked to the SGSS database (AMR module) held by UKHSA in order to detect clinical samples with AMR pathogens of interest within 28 days of the patient's death. Anonymised results will be analysed using a standardized pathway to determine whether each death was AMR-associated. The rate and total number of deaths associated with AMR in this cohort, the most important pathogens, pathogen drug-combinations and resistance mechanisms will be described.

Intervention Type
Other

Primary outcome measure
Measured using clinical databases:
The total number of patients with AMR-associated deaths in England in 2021-2023

Secondary outcome measures
Measured using clinical databases:
1. The percentage of AMR-associated deaths in 2021, 2022 and 2023, including the monthly trend of totals numbers.
2. The total number and percentage of AMR-associated deaths for each site of infection, AMR pathogen of interest, pathogen-drug combination, and resistance mechanism.
3. Underlying cause of death (UCODs) and Multiple cause of death (MCDs) groupings percentages for the entire study cohort.
4. The total number and percentage of UCOD and MCDs that were AMR-associated.
5. The total number and percentage of patients with AMR-associated deaths who die in hospital versus in the community.
6. The percentage of AMR-associated deaths per medical specialty for patients who died in hospital.
7. The association between AMR and healthcare utilisation (mode of admission, duration of stay in hospital, ICU admission rates and duration of stay, life-support duration).
8. The total number and percentage of patients with AMR pathogens of interest in sterile sites within 28 days of death without infection being recorded in the pathway that led to death in the MCCD.
9. The total number of patients who had AMR documented in their death certificate (by using the ICD-10 codes U82-84).

Overall study start date
20/03/2024

Completion date
31/12/2025

Eligibility

Key inclusion criteria
All patients who had their death registered in England between 01/01/2021 and 31/12/2023 will be included in this study.

Participant type(s)
Patient

Age group
All

Lower age limit
0 Years

Upper age limit
150 Years

Sex

Both

Target number of participants
1,600,000

Total final enrolment
1520000

Key exclusion criteria
Only patients who had expressed the wish for their data not to be used for research purposes under the National Data Opt-Out (DOO) will be excluded.

Date of first enrolment
01/07/2024

Date of final enrolment
31/10/2025

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
UCL Great Ormond Street Institute of Child Health
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Sponsor information

Organisation
University College London

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Sponsor type
University/education

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https://www.uclh.nhs.uk/Pages/home.aspx

ROR
https://ror.org/02jx3x895

Funder(s)

Funder type
Government

Funder Name
UK Health Security Agency

Results and Publications

Publication and dissemination plan
Planned publication in peer reviewed journal

Intention to publish date
01/06/2025

Individual participant data (IPD) sharing plan
The datasets generated during and/or analysed during the current study will be stored for 3 years and may be available upon request from Dr Louis Grandjean (l.grandjean@ucl.ac.uk)

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol file	version 1.1	25/05/2024	29/05/2024	Yes	No
Statistical Analysis Plan	Section 5.8 of the protocol version 1.1	25/05/2024	10/06/2024	No	No
Protocol file	version 1.2	08/10/2024	30/10/2024	No	No