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A hospital study testing whether more tailored antibiotic treatment for patients with sepsis can improve recovery while also helping reduce antibiotic resistance

Submission date
25/06/2026

Recruitment status
Not yet recruiting

Registration date
14/08/2026

Overall study status
Ongoing

Last Edited
25/09/2026

Condition category
Infections and Infestations

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English summary of protocol

Background and study aims
The PATH Sepsis trial (Precision Antimicrobial Treatment in Hospitals for Sepsis) is a UK hospital study for people who come to A&E with sepsis, a life-threatening reaction to infection. Sepsis must be treated quickly with antibiotics, but doctors do not always know which antibiotic is best to start first. This is becoming more difficult because some bacteria are now resistant to commonly used antibiotics. As it is vital to treat patients quickly, a deferred consent approach will be used. The aim of the PATH trial is to find the best initial antibiotic treatment for sepsis while also helping to reduce unnecessary use of very broad-spectrum antibiotics. The study compares different antibiotic strategies that are already routinely used in NHS hospitals.

Who can participate?
Adult (18 years or older) inpatients with newly suspected bacterial infection with moderate to high risk of deterioration.

What does the study involve?
Patients are placed into groups based on how likely they are to have an infection caused by resistant bacteria; these groups are called 'at risk' and 'low risk'. Within each group, patients are randomly allocated to one of two antibiotic approaches. In the at-risk group, treatment compares a carbapenem strategy with a carbapenem-sparing strategy. In the low-risk group, treatment compares WATCH antibiotics with ACCESS antibiotics" based on the REC meeting: In the low-risk group, treatment compares the World Health Organization (WHO) categorised "WATCH" list antibiotics (higher risk antibiotics recommended for specific infections) with WHO categorised "ACCESS" (first and second choice antibiotics for common infections) list antibiotics. The trial plans to recruit up to 1,452 participants across the UK. Researchers will collect information during the hospital stay and for up to 28 days after the trial starts, including blood test results, microbiology findings, vital signs and length of stay. If treatment needs to change, patients may be randomised a second time to compare whether adding or switching antibiotics works better. Taking part does not change the rest of a patient's care, and all antibiotics used

are standard NHS treatments. The trial will use two delivery models, a traditional trial (e-consent and randomisation completed in the trial database and the research team entering data collected routinely in medical notes) and an embedded trial (the randomisation is completed in the electronic patient medical notes and data is accessed from routine secure data environments).

What are the possible benefits and risks of participating?
Taking part in the PATH study is not expected to directly benefit you. However, the information we get may help improve the treatment of patients with sepsis in the future and reduce drug-resistant infections across the UK
It is possible that the antibiotic given to participants will be different to what they would have received if they were not taking part in the trial. However all antibiotics are used routinely across hospitals so no risks are foreseen.
There is no increased burden for participants as all data is collected routinely, no additional procedures or assessments are required.

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

When is the study starting and how long is it expected to run for?
October 2026 to December 2027

Who is funding the study?
GlaxoSmithKline (UK)

Who is the main contact?
pathtrial@imperial.ac.uk

Contact information

Type(s)
Scientific, Public

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Type(s)
Principal investigator

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Additional identifiers

Integrated Research Application System (IRAS)
1011638

Central Portfolio Management System (CPMS)
66631

Sponsor's protocol code number
177467

Study information

Scientific Title
A parallelarm, openlabel, randomised feasibility and proof-of-concept trial of precision antimicrobial prescribing in hospitalised patients with sepsis to improve clinical outcomes whilst minimising antimicrobial resistance

Acronym
PATH Sepsis Trial

Study objectives
Primary objective:
To obtain proof-of-concept data for the best first treatment of sepsis comparing both how well it works and the safety

Secondary objectives:
1. Investigate whether using the electronic health record system to run a trial makes the process easier and more efficient, including finding eligible patients, signing them up, checking their risk level, assigning them to groups, and collecting data, than the usual way of doing things
2. Investigate whether it’s practical to use a step-by-step, tailored random assignment process for hospital patients with sepsis, and collect information that will help plan a larger future study

Ethics approval required
Ethics approval required

Ethics approval(s)
Submitted 24/06/2026, to be confirmed (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; no telephone number provided; -), ref: 26/WS/0104

Primary study design
Interventional

Allocation
Randomized controlled trial

Masking
Open (masking not used)

Control
Active

Assignment
Parallel

Purpose
Treatment, Feasibility

Study type(s)

Health condition(s) or problem(s) studied
Sepsis

Interventions
Parallel-group, open-label randomised feasibility and proof-of-concept trial of empiric antibiotic treatment strategies for adult inpatients with suspected bacterial sepsis, stratified by ESBL-infection risk.
Randomisation: 1:1 within ESBL-risk stratum using permuted blocks stratified by site and severity. At St Mary's Hospital and Charing Cross Hospital, randomisation is completed directly within the electronic health record (Cerner). At the other hospitals, randomisation is completed using Sealed Envelope.
Arm 1: At-risk ESBL group - carbapenem-based strategy
Arm 2: At-risk ESBL group - carbapenem-sparing strategy
Arm 3: Low-risk ESBL group - WHO WATCH antibiotic strategy
Arm 4: Low-risk ESBL group - WHO ACCESS antibiotic strategy

Specific antibiotic, dose/dose range, frequency, route, and duration are determined by local hospital guidelines and the treating clinician. Antibiotics are prescribed from routine hospital stock and given as standard care. Intermittent aminoglycoside use may be allowed in the first 48 hours; additional clinically indicated cover may also be given. Participants are randomised within 8 hours of meeting eligibility criteria. Subsequent antibiotic changes and total duration are at clinician discretion. A nested feasibility component allows a second 1:1 randomisation in participants with treatment failure by 120 hours and no definitive microbiology: augment (add second agent) or switch (change to broader/new agent).

Follow-up: routine clinical data to 120 hours and 28 days or discharge.

Intervention Type
Drug

Phase
Phase IV

Drug/device/biological/vaccine name(s)

amikacin, amoxicillin, cefazolin, ciprofloxacin, clarithromycin, co-amoxiclav, co-trimoxazole, doxycycline, ertapenem, levofloxacin, meropenem, Negaban [temocillin disodium] , teicoplanin, ceftriaxone, gentamicin, cefuroxime, piperacillin/tazobactam, vancomycin

Primary outcome(s)

Occurrence of treatment failure is measured as a binary composite outcome using routine clinical records, microbiological culture and susceptibility results, prescribing records, and independent assessment against pre-defined criteria, by 120 hours post-randomisation. Treatment failure is defined as any of the following occurring within 120 hours of randomisation: death; antibiotic change due to confirmed resistance on microbiological culture; or antibiotic change/addition of broader-spectrum cover (including extension of regular aminoglycoside use beyond 48 hours) due to clinical failure.

Key secondary outcome(s)

1. All-cause mortality is measured as a binary outcome using routine clinical records, within 120 hours post-randomisation
2. Antibiotic change due to microbiological resistance is measured as a binary outcome using routine microbiological culture and susceptibility results and prescribing records, within 120 hours post-randomisation
3. Antibiotic change due to clinical failure is measured as a binary outcome using routine clinical records, prescribing records and assessment against pre-defined criteria, within 120 hours post-randomisation
4. A binary composite of treatment failure or pre-specified adverse events is measured as a binary composite outcome using routine clinical records, prescribing records, microbiology results and laboratory results, within 120 hours post-randomisation
5. Time to treatment failure is measured as a time-to-event outcome using routine clinical records, prescribing records, microbiology results and assessment against pre-defined criteria, from randomisation to 120 hours post-randomisation
6. 28-day all-cause mortality is measured as a binary outcome using routine clinical records, at 28 days post-randomisation
7. Clinical and microbiological cure is measured as a binary outcome using routine clinical records and microbiology results, at 28 days post-randomisation
8. Length of hospital stay is measured as a continuous outcome in days using hospital admission and discharge records, up to 28 days post-randomisation
9. Total duration of antimicrobial therapy is measured as a continuous outcome in days using prescribing and administration records, up to day 28
10. Time to IV to oral switch (IVOS) of antibiotics is measured as a time-to-event outcome using prescribing and administration records, up to day 28 post-randomisation
11. Appropriate empiric backbone antimicrobial selection is measured as a binary outcome using comparison with subsequent significant microbiology results, up to day 28 post-randomisation
12. Antimicrobial spectrum/exposure (empiric versus total treatment) is measured using prescribing records, up to day 28 post-randomisation
13. Antimicrobial consumption stratified by WHO AWaRe classification is measured using prescribing records classified by WHO AWaRe, up to day 28 post-randomisation
14. C. difficile infection is measured as a binary adverse event outcome using routine clinical records and microbiology results, within 28 days of randomisation
15. Acute kidney injury is measured as a binary adverse event outcome using RIFLE criteria and routine clinical/laboratory records, within 28 days of randomisation
16. Drug-induced liver injury is measured as a binary adverse event outcome using routine liver function tests, defined as greater than 5 times the upper limit of normal, within 28 days of randomisation

17. Severe allergic reaction to beta-lactam antibiotics is measured as a binary adverse event outcome using routine clinical records, within 28 days of randomisation
18. Significant blood dyscrasias is measured as a binary adverse event outcome using routine full blood count results and clinical records, within 28 days of randomisation
19. Observed colonisation or infection with a drug-resistant organism is measured as a binary microbiological outcome using routinely available clinical specimen results, within 28 days of randomisation
20. Isolation of a drug-resistant organism on routine clinical screening isolates is measured as a binary microbiological outcome using routine clinical screening isolate results, up to 28 days of randomisation

Completion date
31/12/2027

Eligibility

Key inclusion criteria
1. Adult inpatient (≥18 years)
2. Newly suspected bacterial infection with moderate to high risk of deterioration as defined by meeting any one of the following: Total National Early Warning Score 2 (NEWS2) ≥5, Any single NEWS2 parameter = 3, Blood lactate level of >2.0 mmol/L, Evidence of acute kidney injury, as defined by RIFLE criteria
3. Expected to remain in hospital for at least two calendar days (i.e. expected to still be in hospital the day after tomorrow)

Healthy volunteers allowed
No

Age group
Mixed

Lower age limit
18 Years

Upper age limit
120 Years

Sex
All

Total final enrolment
0

Key exclusion criteria
1. Allergy status does not permit randomisation to both arms according to local treatment strategies
2. Received more than 8-hours of inpatient antibiotic treatment for current infection
3. Unsuitable suspected or confirmed infective syndrome (e.g. meningitis/encephalitis, endocarditis, or febrile neutropenia)
4. Medical condition, co-morbidity, or social circumstance that the treating clinician determines,

and documents, that could compromise patient safety or protocol adherence (e.g. receiving end-of-life care, high risk of self-discharge against medical advice, or potential drug interaction)
5. Pregnant or breastfeeding women

Date of first enrolment
01/10/2026

Date of final enrolment
31/12/2027

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
St. Marys Hospital
Praed Street
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England
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Study participating centre
Charing Cross Hospital
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Study participating centre
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Sponsor information

Organisation
Imperial College London

ROR
https://ror.org/041kmwe10

Funder(s)

Funder type
Industry

Funder Name
GlaxoSmithKline

Alternative Name(s)
GlaxoSmithKline plc., GSK plc., GlaxoSmithKline plc, GSK

Funding Body Type
Government organisation

Funding Body Subtype
For-profit companies (industry)

Location
United Kingdom

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study will be included in the subsequent results publication. Data will only be shared after study has ended and the results have been published. Data sharing requests can be directed to the PATH Sepsis trial team at pathtrial@imperial.ac.uk.

IPD sharing plan summary
Published as a supplement to the results publication