UK Health Security Agency

ESPAUR report 2025 to 2026

Abstracts

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Health disparities and inequalities

Health inequalities in *E. coli* bacteraemia and associated antibiotic resistance: a national surveillance study, 2018/2019 to 2023/2024

Authors

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NAP Outcome: 8 – Health disparities and health inequalities

Background

Health inequalities in *Escherichia coli* bacteraemia are increasingly recognised, with disadvantaged and minority groups disproportionately affected. Understanding intersecting inequality factors will clarify the poorly understood drivers of overall and resistant *E. coli* infections.

Methods

We retrospectively analysed English surveillance data (2018/2019 to 2023/2024) of *E. coli* bacteraemia and resistance. Multivariable logistic regression assessed healthcare- versus community-associated (HA versus CA) and resistant versus susceptible cases.

Findings

Between April 2018 and March 2024, 242,604 cases of *E. coli* bacteraemia were reported. Minority ethnic groups were disproportionately represented among patients aged <75 years, in both HA and CA categories. CA cases in females aged 30 to 44 were 2.7, 4.2, 4.4 and 4.0 times greater in Asian, Black, Mixed and Other ethnicities versus their White counterparts. Multivariable analysis showed odds of antibiotic-resistant *E. coli* bacteraemia were more than twice that in the Asian (OR 2.45, p<0.0001), and 51.0% greater in the Black (p<0.0001) ethnicities, respectively, compared to their White counterparts. Odds of resistance amongst the Asian ethnic group was twice the national average for 2nd (37.2 versus 18.3%) and 3rd generation cephalosporins (35.2 versus 16.1%) and ciprofloxacin (37.1 versus 17.9%). Residing within a care home more than doubled the odds of resistant infection (OR 2.28, p<0.0001).

Conclusions

Younger individuals of ethnic minorities particularly females experienced a disproportionate burden of infection, with resistance to key antibiotics particularly elevated in the Asian population. Care home residents had significantly higher rates of CA and resistant *E. coli* bacteraemia. A greater understanding of the source of infection in these groups is essential to inform targeted interventions.

The role of pharmacists and pharmacy teams in the prevention, preparedness, response and recovery of HIV and hepatitis C virus outbreaks: a rapid systematic review

Authors

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NAP Outcome: 8 – Health disparities and health inequalities

Introduction

Pharmacy professionals are accessible members of the public health workforce and serve as key contact points for populations disproportionately affected by HIV and hepatitis C virus (HCV) outbreaks. They possess public health competencies that can support outbreak management within the World Health Organisation (WHO) emergency cycle of prevention, preparedness, response and recovery. These interventions may be at micro (individual or patient-facing), meso (regional or organisational), and macro (national) levels. This sub-analysis of a rapid systematic review aimed to identify the contributions of pharmacy professionals globally to HIV and HCV outbreak management and classify them within the WHO emergency management cycle and by level of intervention.

Method

In February 2025, Embase, Medline, and SCOPUS were systematically searched for articles on pharmacy professionals' roles in non-COVID-19 outbreaks from 2014 onward. Papers were screened, extracted, and assessed risk of bias by one reviewer, with a minimum of 10% reviewed by a second reviewer. Risk of bias assessment was undertaken using the Mixed Methods Appraisal Tool. The protocol was registered on PROSPERO (CRD 42024617152). Subgroup analysis focused on articles relating to HIV and HCV outbreaks,

with findings synthesised thematically and reported narratively to account for study variability.

Results

Of the 1,489 articles identified, 161 underwent full-text extraction, of which 13 related to HIV and/or HCV outbreaks. Most papers (62%, n=8) were from the USA. Others were from the UK (2), Nigeria (1), Malaysia (1), and Cameroon (1). Twenty-six roles were identified: 53% in the prevention phase of the WHO emergency cycle, 37% in response, and one each in preparedness and recovery. Four papers reported roles spanning multiple phases.
When themed within the phases of the WHO emergency cycle, most identified roles (n=22) were related to micro level (individual or patient facing), the remainder (n=4) were meso level (regional or organisational roles), with no macro-level roles (national or international) reported.

Examples of roles identified included use of pharmacy data, for example tracking prescription refills (Response, Preparedness – Meso level), supply of syringes, preventive treatment, point of care testing (Prevention – Micro level), educating other healthcare professionals (Response – Micro level).

Conclusion

This review shows that pharmacy team members have key roles during the management of HIV and HCV outbreaks globally, with evidence of involvement in all stages of the WHO emergency cycle. However, it highlights an evidence gap for meso and macro level contributions and roles for pharmacy team members within preparedness and recovery phases. These findings underscore the need for strategic investment in workforce development (including strengthening public health competencies and outbreak response capability via education and training), as well as greater system-level integration of pharmacy professionals in HIV and HCV outbreak preparedness and response planning. Strengthening these capabilities across the global pharmacy workforce will help reduce variation in service delivery and improve equity of care for populations disproportionately affected by HIV and HCV outbreaks.

Pharmacist-led interventions for bacteraemia and antimicrobial-resistant bloodstream infections: a systematic scoping review

Authors

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NAP Outcome: 8 – Health disparities and health inequalities

Introduction

Bloodstream infections (BSIs) are severe infections usually diagnosed and managed within hospital settings. Pharmacy professionals are uniquely positioned within healthcare systems to influence antibiotic prescribing, educate patients, and implement stewardship interventions, making them vital in reducing antimicrobial resistance (AMR) and improving outcomes.

This scoping review aimed to synthesise evidence of pharmacist-led stewardship interventions for BSIs.

Method

The scoping review builds on a systematic search conducted across 5 online databases (Ovid Embase, Ovid MEDLINE, CINAHL, Scopus, Cochrane Central Register of Controlled Trials) in December 2024 to identify papers for BSIs and AMR BSIs. Search terms combined MeSH and free-text terms for antibiotic resistance, BSI risk factors, and health equity. No geographical or language restrictions were applied. Eligible studies included assessment of BSIs and listed pharmacy or pharmacist interventions in title or abstract. The Preferred Reporting Items for Systematic Reviews and Meta-Analyses-Scoping Review (PRISMA-ScR) abstract guidance was followed.

Results

From 7 586 articles, 17 articles were identified. Most of the studies (spanning 2017 to 2024), were conducted in the USA (n=7) and Japan (n=6), with one study each in Canada, Italy, and Spain. Study designs were predominantly retrospective pre-post (n=10), then cohort studies (n=4), observational(n=2) and matched cohort (n=1).

Intervention types were categorised into five: Rapid Diagnostic Testing (RDT) + pharmacist models(n=5), prospective audit and feedback (PAF) based interventions (n=4), BSI/ Staphylococcus aureus bacteraemia (SAB) bundles with pharmacist involvement(n=3), pharmacist directed therapeutic management such as vancomycin dosing or carbapenem deescalation (n=2), multifaceted ICU/system level AMS(n=2), and automation supported pharmacist workflows(n=2).

There were reported substantial reductions in process measures such as time to targeted therapy (for example, 22→2 h, 40→11 h, or 59.6→29.0 h), marked increases in bundle adherence (for example, 69%→92%, 79% versus 23%), also significant improvements in stewardship behaviours including deescalation, earlier step-down to oral therapy (6 days versus 8 days), culture before therapy, DOT/DDD reduction, and reductions in antipseudomonal antibiotic use (for example −42%). PAF and education models were particularly strong contributors to these antimicrobial use improvements.

Clinical outcome improvements were also reported. Pharmacist planned vancomycin dosing improved survival (82% versus 53%), MRSA stewardship bundles reduced 30-day mortality (41.8%→21.6%) and in hospital mortality (58.1%→27.5%), and pharmacist recommended carbapenem de-escalation lowered mortality (7.4% versus 29.3%) and LOS (−5days). Tele-ID plus pharmacist oversight improved SAB bundle adherence (79% versus 23%) and reduced readmissions (9% versus 17%). Pharmacist intervention in Italy's ICU was associated with a significant reduction in carbapenem resistant K. pneumoniae (94%→6%). No measurable clinical improvement was reported in a study that implemented an antimicrobial scoring system.

Discussion

Overall, the studies from the scoping review demonstrate that pharmacist- led or integrated stewardship, particularly when combined with RDT, PAF, care bundles, or targeted dosing drive measurable improvements in antimicrobial optimisation, patient survival and resistance outcomes. The findings of this study can contribute to the evidence base for developing pharmacy clinical services for sepsis and BSIs within hospital settings. In addition, these findings suggest that pharmacist-led stewardship operates not only as a quality improvement mechanism but as a clinical intervention influencing time-critical treatment pathways to improve patient outcomes.

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Assessing large language model performance in abstract screening for an infection-focused systematic review with >16,000 records

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NAP outcome: 8 – Health disparities and health inequalities

Background

The double screening abstracts for systematic review ensures rigour while demanding considerable time and resources. In a systematic review of risk factors for disparity or inequity in antibiotic-resistant bacteraemia in socioeconomically disadvantaged populations, our search generated 16,816 records (PROSPERO 601049). Large language models (LLM)

offer potential solutions to support screening large volumes of abstracts. LLMs automate classification through zero- or few-shot prompting, with studies reporting accuracies ranging from 40% to 92%.

The aims of this project were to determine the accuracy of LLMs as a second screener for a large infection-focused systematic review and contribute to a wider programme evaluating the role of LLMs in evidence synthesis.

Methods

Following initial screening by 5 evidence reviewers of a validation set of 100 abstracts (Fleiss' Kappa=0.35, fair agreement), we conducted a secondary screening using the Llama 3.3 70b LLM model. We instructed the LLM to assign abstracts as include or exclude per defined criteria using a free-text prompt. We optimised the prompt using an iterative prompt refinement process, comparing the LLM outputs to human reviewer assignments and calculating precision, recall, and F1 scores. We refined the prompt until the model's performance reached satisfactory alignment with expert judgement. We applied the finalised prompt to the full dataset of 16,816 abstracts.

Results

The LLM performance metrics improved when the prompt included concept key terms. The final prompt achieved precision, recall, and F1 scores of 0.61, 0.87, and 0.71, respectively. The LLM required approximately 8 hours to screen the 16,818 abstracts. The LLM agreed with majority human reviewer assignments for 13,349 abstracts and disagreed for 3,467. The Cohen's kappa score was 0.57 ($p<0.001$) suggesting moderate agreement.

Conclusions

These results support using LLMs as a second screener to improve the efficiency of evidence synthesis for systematic reviews, showing moderate agreement with human reviewers. Accuracy of the LLM improves with more explicit prompts, refined using a test-set of abstracts.

Acknowledgement

This project is funded by NIHR Senior Clinical and Practitioner Award (NIHR304553) award to DAO. The views expressed are those of the authors and not necessarily those of the NIHR, NHS England, UK Health Security Agency (UKHSA), the Department of Health and Social Care, or other funders.

Surveillance and epidemiology

Using network analysis and transmission modelling to design an efficient WGS surveillance system to rapidly detect emerging *Clostridioides difficile* strains in England

Authors

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NAP outcome: 3 – Strengthened surveillance

Whole genome sequencing (WGS) is being introduced in England to support national surveillance of key hospital-acquired pathogens, starting with *Clostridioides difficile*, to facilitate novel strain identification and enable timely interventions. However sequencing capacity is limited.

Several important nosocomial infections, including *C. difficile* and key antimicrobial resistance threats such as Carbapenemase-producing Enterobacterales (CPE) or methicillin resistant *Staphylococcus aureus* (MRSA), can be carried asymptomatically and these colonised individuals can be sources of transmission to other patients. Building on the insight that hospital inpatients who have nosocomially acquired *C. difficile* could act as inter-hospital vectors if they later attend another facility whilst still colonised, we simulated the inter-hospital spread of a hypothetical novel strain across a network formed by shared patients and modelled the strain's potential detection, via WGS, under a range of sampling protocols.

We used empirical networks of shared patients ascertained through analysis of all hospital admission data from all acute hospital organisations in England's National Health Service (NHS), with model parameterisation informed by data-linkage with mandatory case reports of *C. difficile* infection. Using these simulated outbreaks, we identified an optimised set of well-connected sentinel sites enabling early detection of novel strains, adapting the algorithm to incorporate real-world sequencing constraints, including total sequencing burden and site participation considerations.

The combination of an efficient case sampling protocol and optimised set of 20 sentinel sites detected a novel strain 27% faster than random sentinel selection, across all possible index case locations, whilst sequencing less than 15% *C. difficile* infection cases nationally. We conducted sensitivity and scenario analyses using plausible ranges of pathogen characteristics and prevalence, applied to current and historical networks which confirmed epidemiologically- and longitudinally robust sentinel selection and detection performance. These findings have informed the new WGS surveillance system for *C. difficile* in England, launched in 2025, and provide a design approach to enable to establish similar systems for other hospital-acquired pathogens facing similar real-world constraints.

Evaluation of UKHSA surveillance outputs related to the AMR NAP 2024 to 2029

Authors

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NAP outcome: 3 – Strengthened surveillance

Background

Effective surveillance underpins evidence-based decisions, policy, outbreak preparedness, and resource planning. UKHSA produces several antimicrobial resistance (AMR) and healthcare-associated infection (HCAI) surveillance outputs. The UK National Action Plan (NAP) on AMR 2024 to 2029 calls for a surveillance strategy review to optimise data usage and avoid duplications. We assessed usage, impact and potential gaps of UKHSA surveillance outputs to inform actions supporting AMR NAP objectives.

Methods

We conducted a cross-sectional mixed-methods study to assess the usage, accessibility, utility, and impact of 21 AMR/HCAI surveillance outputs. A survey was disseminated using a snowball approach across stakeholder groups (civil service, NHS, academia, local

authorities, industry, private healthcare, charities). Semi-structured interviews (n=19) across all stakeholder groups explored usage patterns, purposes and impacts in depth.

Results

A total of 269 participants completed the survey: NHS (50.7%), civil service (18.9%), other (30.4%). The most used outputs were the English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) (56.8% of respondents) and annual (52%) and quarterly (51%) reports on key HCAIs. However, more than 25% of participants were unaware of each of the 21 outputs. While broad outputs, such as Fingertips (46.6%) and ESPAUR (34.9%) were rated most valuable, topic-specific reports on critical care (90.9%) or surgical site infections (50%) received high impact ratings. Interviewees emphasised the need for better joined-up data, particularly between the NHS and civil service. Real-time, granular dashboards were most impactful and prioritised for local interventions, while annual reports provided context for broader policy development. In-depth analyses on patient risk factors were viewed as essential for targeted action. Numerous suggestions were made to improve usability and utility of outputs.

Conclusion

Surveillance outputs are valued but fragmented, with inconsistent awareness, and accessibility. Users requested improved granularity, integration across platforms, timely data and focus on actionable messages. Co-creation, collaboration, and knowledge mobilisation are essential to ensure usage and impact of outputs.

Genomic surveillance of bloodstream infections suggests occult transmission of invasive *E. coli* strains and plasmids in England.

How much is enough for genomic surveillance of *Escherichia* and *Klebsiella* bloodstream infections?

Authors

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NAP outcome: 3 – Strengthened surveillance

Background

Escherichia and *Klebsiella* are major causes of bloodstream infection (BSIs) and subject to national surveillance in England. However, surveillance currently lacks genomic inputs, and optimal sampling strategies to capture relevant regional genomic epidemiology are unclear. Using data from systematically sequenced *E. coli*/*Klebsiella* BSIs (NEKSUS study), we estimated how many isolates would need to be sequenced to capture a representative proportion of the genetic diversity present.

Methods

Ten regional NHS microbiology laboratories were asked to submit all *E. coli*/*Klebsiella* BSI, October 2023 to March 2024, for sequencing. Isolates were long-read sequenced (Oxford Nanopore Technologies), basecalled (Dorado v5.0.0 super-high accuracy), assembled (long-read consensus pipeline) and annotated (MLST v2.23.0, AMRFinderPlus v4.0.23), MOB-suite v3.1.9). Assembly quality was assessed using CheckM2 v1.1.0, species confirmed using Kraken2 v2.1.3, and plasmids clustered using PLING v2.0.0. To characterise the minimum number of sequences required to capture sequence type (ST), AMR gene (ARG) and plasmid diversity observed across the entire dataset, rarefaction was performed by sampling without replacement and counting unique STs, ARGs or plasmid groups.

Results

1,939 out of 2,382 (81%) non-duplicate isolates were collected and successfully sequenced and assembled (median: 179 [IQR: 123-269]] sequences/region, 1471 *E. coli*, 468 *Klebsiella*). Rarefaction showed that, to capture ≥90% of total observed diversity in *E. coli* STs, ARGs, plasmid Inc-types and plasmid subcommunities, at least 85% (95% CI:79% to 89%), 71% (60 to 81%), 81% (75 to 86%), and 87% (84 to 89%) of isolates, respectively, would have to be sequenced. For *Klebsiella*, this percentage was 1 to 5% higher (90% [85 to 90%] for STs, 74% [64 to 83%] for ARGs, 82% [74 to 88%] for Inc-types and 88% [84 to 90%] for plasmid subcommunities respectively).

Conclusions

Understanding how much genomic diversity is captured by sub-sampling or sequencing strategies is key to designing affordable surveillance. In England, 85%, 71%, 81% and 87% of *E. coli* BSI isolates need to be sequenced to capture ≥90% observed diversity at ST, ARG, plasmid Inc-type and plasmid subcommunity-levels respectively, whereas for *Klebsiella*, the sampling fraction is 1 to 5% higher.

Is mandatory surveillance of carbapenemase-producing Gram-negative organisms working? A surveillance evaluation, 2020 to 2023

Authors

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NAP outcome: 3 – Strengthened surveillance

Carbapenemase-producing organisms (CPOs) are an increasing public health threat. In October 2020, English laboratories were mandated to report acquired CPO detections in Gram-negative organisms from human clinical samples and screens to the existing national laboratory reporting system.

The aim of this study was to describe acquired CPO epidemiology and evaluate the laboratory coverage, data quality, timeliness, simplicity, and acceptability of the mandatory surveillance system.

Using a mixed-method approach, we extracted laboratory-confirmed CPO reports from 1 October 2020 to 31 December 2023 to assess laboratory coverage (proportion of laboratories reporting at least one CPO to the Second-Generation Surveillance System in 2023) and data quality (completeness of variables). We conducted semistructured interviews with stakeholders to assess simplicity, acceptability, and perceived timeliness via thematic analysis.

Reports of acquired CPO episodes in England doubled, from 2,670 (2021) to 5,759 (2023), with regional variation in rates (London 21.3 out of 100,000 population versus South-West 1.8 out of 100,000). In 2023, laboratory coverage was 72% (83 out of 115), from 38 to 100% by region. The data quality was high. Participants (N = 12) described laboratory reporting delays due to technical issues, limited staff capacity, or human error but were satisfied with the timeliness of surveillance outputs for monitoring longer-term trends. Mandatory reporting

was acceptable, and some participants experienced streamlined, automated reporting, whereas others noted complicated or manual workarounds using pre-existing systems. Reported CPO incidence is increasing, and CPO surveillance is perceived as efficient, valuable, and acceptable. However, despite being mandatory, laboratory reporting is still not comprehensive. We recommend investing in improvements to the existing surveillance system, ensuring that all laboratories have the capacity to report and optimise processes.

Rapid emergence of Trichophyton indotineae observed in the United Kingdom, up to August 2025

Authors

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NAP outcome: 7 – Using information for action

Trichophyton indotineae is an emerging dermatophyte increasingly detected in the United Kingdom, often with antifungal resistance. We identified 363 cases between January 2017 and August 2025, with 310 cases (85%) since January 2023. Cases were mostly concentrated in major urban centres, and most affected individuals were working-age adults, frequently reporting South Asian ethnicity. The importance of international importation versus domestic transmission remains unclear. Implementing enhanced surveillance would help to identify risk factors and transmission routes to focus prevention efforts.

Optimising genomic and molecular characterisation

Persistent cluster of NDM-1 carbapenemase-producing *K. pneumoniae* among patients attending a haematology ward in England

Authors

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NAP outcome: 3 – Strengthened surveillance

Background

Carbapenemase-producing Enterobacterales (CPE) are known to cause sporadic outbreaks in healthcare settings and can be challenging to manage due to environmental and human colonisation.

Our aim was to identify common exposures among a cluster of cases with NDM-1-producing *Klebsiella pneumoniae* in a single ward, using epidemiological, genomic and environmental investigation, to identify possible sources and inform targeted control measures.

Methods

Cases were patients on the ward with laboratory confirmed *K. pneumoniae* with NDM-1 sequence type 15 identified via variable number tandem repeat (VNTR) analysis and clustered by whole-genome sequencing. Case exposure information was collected through reviewing patient notes and hospital floor plans. Environmental samples were taken from ward surfaces on 2 occasions and cultured to isolate CPE.

Results

Twelve cases (4 infections and 8 colonisations) were identified over a 3.5-year period. Of the first 9 cases that occurred after the index case, 8 were inpatients on the ward at the same time as at least one other case, and 6 occupied a patient side-room after a positive case had occupied that room.

NDM-1-producing *K. pneumoniae* with the same VNTR profile as the clinical isolates were recovered from the ward environment, including from the drain of a handwash basin which had been installed to replace one that tested positive during the first environmental sampling.

Conclusion

We demonstrated that persistent, multi-year clusters of CPE in hospitals occur, and long-term environmental reservoirs may persist following remediation measures. Understanding the epidemiology, supplemented with targeted environmental sampling, can help to identify potential sources of CPE in healthcare settings.

Diversity of carbapenemase-producing Enterobacterales bloodstream isolates referred to the UK's national reference laboratory over a 10-year period.

Genomic and molecular characterisation of a KPC-producing *K. pneumoniae* clinical isolate resistant to multiple novel agents

Authors

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NAP outcome: 3 – Strengthened surveillance

Background

Resistance to carbapenems and third-generation cephalosporins is increasing in *Klebsiella pneumoniae* globally, restricting therapeutic options. The β-lactam/β-lactamase inhibitor combinations are widely used to circumvent β-lactamase-mediated resistance. In 2021, an unusual *K. pneumoniae* clinical isolate, KpMVR1, was recovered from a hospitalised patient in England, exhibiting resistance to meropenem-vaborbactam, imipenem-relebactam, and ceftazidime-avibactam. To investigate this phenomenon, we characterised the genome and antimicrobial susceptibility of KpMVR1 alongside 2 clonally related isolates susceptible to all 3 β-lactam/β-lactamase inhibitor combinations: KpMVS1, collected from the same patient 42 days earlier, and KpMVS2, from another patient in the same hospital.

Methods

Illumina and MinION whole-genome sequencing were conducted for these 3 isolates, followed by hybrid genome assembly. Annotated genome assemblies were compared to identify genetic variation. Mutagenesis experiments were performed to verify predicted functional alterations.

Results

All isolates belonged to clone ST8134 and carried blaKPC-2 alleles (KpMVR1: blaKPC-157, KpMVS1 and KpMVS2: blaKPC-2) in plasmids predicted to be conjugative. Insertion sequence ISEc68 caused a frameshift mutation in KpMVR1's ompK36 gene, reducing susceptibility to meropenem-vaborbactam and imipenem-relebactam. KPC-157 demonstrated decreased hydrolysis of imipenem and ceftazidime when compared with KPC-2. KpMVR1 also encoded a disrupted transcriptional repressor MarR and a destabilising mutation in AcrB, a component of the AcrAB-TolC multidrug efflux pump. An intact, iron-transporting fec operon was identified on a novel IncFII(pKP91)/IncFIB(K) plasmid unique to KpMVS2, possibly accounting for the cefiderocol resistance observed in this isolate.

Conclusions

KpMVR1 carried multiple resistance-associated genetic alterations and likely developed its resistance profile through within-patient evolution. This study highlights the importance of routine screening for resistant pathogens in vulnerable patients to guide antimicrobial chemotherapy and the need to characterise underlying resistance mechanisms to assess the risk of onward dissemination.

In-vitro activity of ceftazidime-avibactam against multidrug resistant clinical isolates from the UK

Authors

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NAP outcome: 3 – Strengthened surveillance

Background

Ceftazidime-avibactam is licenced in the UK for treating severe drug-resistant Gram-negative bacterial infections. We aimed to determine ceftazidime-avibactam MICs against WHO key bacterial priority pathogens: critical priority 3rd generation cephalosporin-resistant Enterobacterales and carbapenem-resistant Enterobacterales, and high-priority carbapenem-resistant *Pseudomonas aeruginosa*, and to determine cross-resistance to comparator antimicrobials.

Methods

The isolate panel comprised 352 Enterobacterales, including isolates with ESBL and/or AmpC or with carbapenem resistance due to impermeability (porin loss) or class A or D carbapenemases, 85 Pseudomonas aeruginosa, including isolates with AmpC, ESBL or carbapenem resistance due to efflux or/and OprD loss. MICs were determined by broth microdilution using cation-adjusted Mueller Hinton broth (CAMHB, iron depleted for cefiderocol) and interpreted using EUCAST breakpoints. The comparators were ceftazidime, ceftolozane-tazobactam, meropenem, meropenem-vaborbactam, imipenem-relebactam, colistin, tigecycline, amikacin and cefiderocol.

Results

Among the Enterobacterales, ceftazidime-avibactam was the most active agent tested, with only 3 out of 352 (<1%) isolates resistant. Two were *Klebsiella pneumoniae* with a D179Y amino acid substitution in their KPC carbapenemase, and both were also resistant to ceftazidime, ceftolozane-tazobactam and cefiderocol. The third was a Serratia marcescens inferred to have AmpC and impermeability, that was also resistant to ceftazidime, ceftolozane-tazobactam, imipenem-relebactam, cefiderocol and amikacin. The highest geometric mean MIC of ceftazidime-avibactam (breakpoint 8mg/L) was for isolates with (ESBL and/or AmpC)+impermeability (1.07 mg/L).

For P. aeruginosa, ceftazidime-avibactam was the fourth most active agent tested (after colistin, amikacin and cefiderocol) with 23 out of 85 (27%) isolates resistant. Resistance was seen most often in isolates with ESBLs, with 16 out of 20 (80%) resistant and a geometric mean of 21.1 mg/L. Cross-resistance was frequent to ceftolozane-tazobactam (82.6%), imipenem-relebactam (73.9%) and meropenem (73.9%).

Conclusions

Ceftazidime-avibactam was the most active agent tested against Enterobacterales with either 3rd generation cephalosporin resistance due to ESBL and/or AmpC, or carbapenem resistance due to impermeability, or class A or D carbapenemases. Ceftazidime-avibactam had good activity against *P. aeruginosa* with upregulated AmpC or with carbapenem

resistance due to efflux or/and OprD loss. Resistance to ceftazidime-avibactam was most common in *P. aeruginosa* with ESBLs.

Quantifying the association of resistance with antimicrobial resistance genes in *E. coli* for new β-lactam/β-lactamase-inhibitor/enhancer combinations

Authors

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NAP outcome: 3 – Strengthened surveillance

Background

An understanding of genotype-phenotype relationships is essential for genomics-based antimicrobial resistance (AMR) surveillance and diagnostics but is limited by the scarcity of high-quality representative phenotypic data. Current approaches often consider binary (susceptible/resistant) phenotypes rather than quantifying the degree of resistance, and interpretation is particularly limited for newer antimicrobials reserved for multi-drug resistant organisms. Here, we apply a recently described approach[1] to estimate the effect of known AMR mechanisms on minimum inhibitory concentrations (MICs) of 4 beta-lactam/beta-lactamase-inhibitor/enhancer (BL/BLI/E) combinations of clinical interest.

Methods

A total of 1,536 clinical E. coli isolates were collected from 10 NHS trusts across England, October 2023 to March 2024 (NEKSUS study). Isolates were sequenced (PromethION, Oxford Nanopore Technologies), basecalled (Dorado v5.0.0 super-high accuracy), assembled (with a long-read only pipeline) and annotated for AMR genes (AMRFinderPlus v4.0.23). MICs to 37 antimicrobials were determined for a selected subset using a custom 3-plate ThermoFisher Sensititre panel, incorporating extended dilution series versus existing diagnostic panels. The fold-change in MIC associated with the presence of AMR mechanisms was quantified for aztreonam-avibactam, cefepime-taniborbactam, cefepime-zidebactam and ceftazidime-avibactam using multivariable interval regression.

Results

Four hundred and eighty-two *E. coli* isolates have been phenotyped to date, selected to include isolates with a range of genetic mechanisms including 97 carbapenemase-positive isolates. 59 unique mechanisms associated with beta-lactam resistance were included. Phenotypic resistance was observed to 3 of the 4 antimicrobials considered here, with sub- or peri-breakpoint variation in MIC. Interval regression revealed heterogeneity in effect size associated with presence of different genes, including sub-breakpoint effects (for example $bla_{CTX\text{-}M}$/bla_{KPC}/bla_{OXA}/bla_{CMY}/ftsI), and for different alleles of the same gene family or the same gene to different antimicrobials (for example $bla_{NDM\text{-}1}$/$bla_{NDM\text{-}5}$). Importantly, we also identified known resistance-conferring mechanisms (for example bla_{NDM} conferring high-level resistance to ceftazidime-avibactam).

Conclusions

Resistance to newer BL/BLI/E antimicrobials is already present amongst *E. coli* in the UK, and known beta-lactam resistance mechanisms are associated with varying degrees of resistance. Our approach to quantifying MIC can serve as a biologically interpretable framework to predicting resistance in other drugs or species-drug combinations. Interactions and impact of genetic context or population structure still need to be explored.

IncHI2 plasmids drove dissemination of carbapenemase gene blaIMP among healthcare-associated Enterobacterales in the UK, 2014 to 2022

Authors

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NAP outcome: 3 – Strengthened surveillance

Background

Carbapenems are broad-spectrum beta-lactam antibiotics that are often considered the last line of treatment for severe multidrug-resistant bacterial infections. There has been an increasing rate of infections caused by carbapenemase-producing Enterobacterales (CPE) globally, particularly those with the most common carbapenemase genes *bla*NDM, *bla*OXA-48-like, *bla*VIM*, bla*KPC and *bla*IMP. These genes are commonly carried by plasmids, which facilitate their spread across bacterial genera or species. A regional network study in London, found that IMP carbapenemases have recently emerged as significant contributors to CPE infections locally, with IncHI2 plasmids carrying both *bla*IMP and colistin resistance gene *mcr-9* as the predominant vector across a wide range of Enterobacterales species1. We set out to characterise plasmids in a national CPE dataset to determine if IncHI2 plasmids carrying *bla*IMP and *mcr-9* are broadly disseminated in the UK.

Methods

Genomic data for 208 confirmed *bla*IMP-carrying CPE collected from patients and clinical environment between 2014 and 2022 in the UK was analysed. Species were confirmed using Kraken2 and Bracken. Genomes were genotyped (based on MLST) and presence or absence of antimicrobial resistance genes was determined using ABRicate. Reconstruction and characterisation of plasmids was completed using MOB-suite and reconstructed plasmids were visualised using Proksee. Phylogenetic analysis of bacterial species and reconstructed plasmids was completed using FastANI, Snippy, and IQ-TREE.

Results

Our analysis identified 18 species, with *Enterobacter hormaechei* (n=96), *Klebsiella pneumoniae* (n=52) and *Escherichia coli* (n=20) accounting for >80% of genomes. A total of 6 *bla*IMP alleles were identified in the dataset dominated by IMP-4 (n=93) and IMP-1 (n=88). Reconstruction of 189 plasmids harbouring *bla*IMP revealed the predominance of IncHI2 plasmids (n=99, 52%), which primarily carried IMP-4 (77 out of 99), 77%) followed by IncN (n=21), 11%) and IncC (n=13, 7%). Of the IncHI2 plasmids, 89% (89 out of 99) carried both *bla*IMP *and mcr-9 genes.*

Conclusion

IncHI2 plasmids were the main vector of *bla*IMP across CPEs in this national dataset, with IMP-4 being the most dominant allele. Our findings highlight that WGS is essential for understanding species-plasmid dynamics of CPE in different settings.

Identifying risk factors for mortality in *E. faecalis* and *E. faecium* bacteraemia: a retrospective cohort study, 2019 to 2024

Authors

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NAP outcome: 3 – Strengthening surveillance

The Enterococci bacteraemia burden is increasing in England and associated with high mortality. We explored risk factors for 30-day mortality in adults with Enterococcus faecalis (Efc) and faecium (Efm) bacteraemia in England, 2019 to 2024.

Laboratory-confirmed Enterococcus isolates from blood specimens from UKHSA's laboratory system were linked to ONS mortality and Hospital Episodes Statistics clinical data. We examined risk factors for 30-day all-cause mortality using Cox proportional hazards models, adjusting for sociodemographics, hospital or community onset, glycopeptide resistance, co-infections (+/−2 days), comorbidities and procedures.

Efm had higher 30-day mortality than Efc bacteraemia (32%, N=21,333 versus 20.6%, N=19,172). Older age increased mortality risk in both species while glycopeptide resistance (%GRE, Efc:2.0%, Efm:20.6%) did not. Over 90% had at least one comorbidity (median Charlson Cormorbidity Index, Efc:3, Efm:4), with lower gastrointestinal disease the most prevalent (Efc:57.5%, Efm:67.3%). Moderate or severe liver disease (aHR, Efc:1.99, 1.73-2.29, Efm:1.84, 1.70-2.00), metastatic solid tumor (Efc:2.32, 2.10-2.57, Efm:2.15, 2.01-2.31), hospital onset (Efc:1.17, 1.08-1.27, Efm:1.39, 1.27-1.53), and critical care onset (Efc:2.07, 1.77-2.41, Efm:2.87, 2.56-3.22) increased mortality risk. Nearly a third were polymicrobial (Efc:32.3%, Efm:28.5%), with *Escherichia coli* the predominant co-infection (Efc:10.9%, Efm:10.5%), followed by *Klebsiella pneumoniae* (Efc:3.8%, Efm:4.1%) and Proteus mirabilis (Efc:4.4%, Efm:0.8%). Co-infections with *Staphylococcus aureus, P. mirabilis*, and *K. pneumoniae* increased mortality risk in both Enterococcus species.

Co-infections and comorbidities, rather than glycopeptide resistance, significantly contribute to mortality in Enterococcus bacteraemia. The differing epidemiology and mortality risk profiles of Efc and Efm highlight the need for a species-specific approach to clinical management, with targeted interventions to improve outcomes.

The importance of monitoring a new antibiotic: ceftazidime/avibactam usage and resistance experience from England, 2016 to 2020

Authors

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NAP outcome: 7 – Using information for action

Background

Ceftazidime/avibactam, launched in the United Kingdom (UK) in March 2017, is an antibiotic against multidrug-resistant Gram-negative pathogens. It was selected for the government's subscription model pilot, for incentivising new antibiotic development, which began in December 2020. Ahead of the pilot, we assessed ceftazidime/avibactam testing, resistance (2016 to 2020) and usage (2017 to 2020) levels in England, as baselines for future surveillance.

Methods

From routine surveillance samples, we retrieved reported ceftazidime/avibactam resistance categorisation. From reference laboratory samples, we reviewed minimum inhibitory concentration (MICs) and molecular data. Among surveillance samples, the percentage of resistance was estimated. Referred samples' MICs, by carbapenemase gene presence, were investigated. Ceftazidime/avibactam hospital use was measured in defined daily doses (DDDs).

Results

Overall, 6.3% (4,200 out of 66,914, 95% confidence interval (95%CI): 6.1 to 6.4%) of surveillance-reported ceftazidime/avibactam-tested Gram-negative bacteria were resistant. Percentage resistance per bacterial species varied over time, somewhat stabilising as testing was established, with between April 2019 and March 2020, 1.3% *Escherichia coli* (288 out of 22,736, 95%CI: 1.1 to 1.4%), 12.6% *Pseudomonas aeruginosa* (690 out of

5,495, 95%CI: 11.7 to 13.5%) and 6.1% of *Klebsiella pneumoniae* (314 out of 5,179, 95%CI: 5.4 to 6.7%) being resistant. For 8,437 referred Enterobacterales, MIC determination found 11.5% (968 out of 8,437, 95%CI: 10.8 to 12.2%) resistant. Among resistant isolates, 89.3% (864 out of 968, 95%CI: 87.1 to 91.1%) had metallo-β-lactamase (MBL) genes. Of 908 MBL-negative isolates, producing ≥ 1 non-metallo-carbapenemase(s), 2.1% (19 out of 908, 95%CI: 1.3 to 3.2%) were resistant. Since March 2017, 69.5% (105 out of 151) of English NHS trusts used ceftazidime/avibactam. Monthly usage progressed from 21 to 744 DDDs in March 2020.

Conclusion

For appropriate treatment, carbapenemase gene detection and variant identification in ceftazidime/avibactam surveillance matters. Detecting emerging resistant pathogens and preventing spread within healthcare settings requires vigilance.

Antimicrobial stewardship, prescribing and primary care

An impact and implementation evaluation of the Pharmacy First Services for management of common conditions in England

Authors

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NAP outcome: 4 – Antimicrobial stewardship and disposal

In January 2024, Pharmacy First (PF) was launched across England. This NHS service enables community pharmacists to supply prescription-only medicines, including antibiotics, to treat 7 common health conditions. The programme aims to ensure faster access to medical care and reduce pressure on general practitioners (GPs).

The public, patients, healthcare, and public health professionals and policymakers need to know whether and how current policy initiatives aimed at widening the range of access to antimicrobials impact AMR and patient outcomes.

The aim of the National Institute for Health and Care Research (NIHR) funded Pharmacy First Evaluation is to perform a mixed-method study to answer the following questions: how are the 7 PF minor illness Patient Group Directives (PGDs) being implemented across England, what explains this pattern, and what are their impacts on volume of prescribing, patient case-mix of GP consultations, Accident and Emergency (A&E) and hospital use, equity of access and cost for different groups of patients in different contexts?

The research, which is in its third year, is led by Dr Rebecca Glover and Professor Nicholas Mays at London School of Hygiene and Tropical Medicine (LSHTM), working in collaboration with the Universities of Nottingham, Manchester and the Bennett Institute at the University of Oxford, as well as the UKHSA. The mixed methods evaluation includes impact, economic and process components.

Publications to date

1. Details of the design and methods of the evaluation were published in March 2025 in the mixed methods protocol.
2. The UKHSA's work on antibiotic prescribing changes in the first year of the service was published in the 2025 ESPAUR report.
3. A health policy paper describing and explaining the factors affecting the development and early implementation of Pharmacy First was also published in May 2026.
4. In June 2026, the study team published a descriptive quantitative output describing the coding of Pharmacy First consultations.

More publications are expected in the final year of the evaluation.

Exploring community pharmacy and general practice views on primary care communication and pathways to access antibiotics

Authors

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NAP outcome: 4 – Antimicrobial stewardship and disposal

Background

With most antimicrobials in England being prescribed in primary care, collaboration on antimicrobial stewardship (AMS) between general practitioners (GPs) and community pharmacists (CPs) is important. Previous research identified barriers to communication between GPs and CPs across England.

The objective was to explore experiences of communication between GPs and CPs in relation to AMS and the pathways to access antibiotics in primary care.

Methods

Five qualitative focus groups and 9 semi-structured interviews were conducted with GP and community pharmacy professionals (CPPs) independently. Two reconvened focus groups with GPs and CPPs present together provided a holistic discussion on initial findings and practical solutions. Data was analysed thematically.

Results

Nine CPs, 3 pharmacy technicians and 12 GPs participated. Four themes emerged: nature of GP-CP interactions, role recognition, barriers to AMS and overcoming barriers. Many CPs, particularly those not co-located with a GP surgery, reported challenges in contacting GPs. Proximity of location between CPs and GPs influences ease of communication and relationship management. GPs highlighted having limited or no awareness of the availability of medicines at the point of prescription. Suggested solutions to optimise collaborative working on AMS included providing functionality to share topline patient notes with prescriptions, a system that tracks and summarises stock levels and having central points of contact between CPs and GPs.

Conclusion

The challenges reported have implications on the collaborative relationship between GPs and CPs and solutions are needed to optimise AMS between primary care health professionals. The appetite for digital transformation suggests that strategic conversations with senior stakeholders are needed.

Implementing a cycle of AMS in primary care: a qualitative study

Authors

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NAP outcome: 4 – Antimicrobial stewardship and disposal

Background
In England, over 70% of antibiotics are prescribed in primary care. Although antimicrobial stewardship (AMS) is a priority for reaching policy targets and requires a continuous, whole-practice approach, its practical implementation remains unclear. This qualitative study explores how primary care professionals perceive the implementation of existing AMS activities, such as audits, training and patient education, within their practice. The insights will be used to support the development of a practical visual aid ('The Cycle of Antimicrobial Stewardship') to guide a consistent approach to AMS delivery through the TARGET toolkit and other relevant AMS resources.

Method
Three focus groups (FGs) involving 17 professionals from general practices across England were conducted, and data was analysed thematically.

Results
AMS in primary care is often reactive and linear, typically limited to audit and intervention due to time and resource constraints. Nonetheless, participants supported a more continuous, team-wide approach and viewed the proposed 4-step cycle as a practical visual aid to support this. Key enablers to AMS included incentive schemes, Pharmacy First and strategies to manage patient expectations. The evolving role of administrative staff and non-GP prescribers in delivering AMS messaging was highlighted, with a need for tailored training and resources. A real-world example illustrates how a cyclical AMS approach improved urinary tract infection (UTI) management in a busy practice.

Conclusion
The 'Cycle of Antimicrobial Stewardship' was positively received but requires consistent implementation across teams and external groups, including out-of-hours (OOH) services and community pharmacies. Further work is needed to support a unified approach across the wider primary care system. Strengthening stewardship efforts requires coordinated collaboration that acknowledges the diverse roles of professionals and settings.

Exploring factors affecting the national implementation and uptake of an AMS training programme to primary care providers in England

Authors

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NAP outcome: 5 – AMR workforce

Background
Most antibiotics are prescribed in the primary care setting. In response to the global threat of antimicrobial resistance (AMR), the TARGET (Treat Antibiotics Responsibly, Guidance, Education and Tools) antimicrobial stewardship (AMS) training toolkit for primary care clinicians was rolled out in England in 2022. This study aimed to understand preconceived, as well as actual, factors influencing the roll out of training to improve and inform implementation strategies of this and future initiatives.

Methods
Two workshops were held: one at the launch (22 participants) in 2022 and another 18 months (14 participants) into intervention roll out, in 2024. Qualitative data was collected using the Theoretical Domains Framework to identify barriers and facilitators, and the Expert Recommendations for Implementing Change Framework to identify strategies for supporting change.

Results
Anticipated barriers, at launch, included lack of secure knowledge and, at a national level, confidence in presenting training content. Anticipated enablers were appointing regional champions and linking training to continuing professional development. Eighteen months later, barriers related to the effort needed to both implement the training and maintaining knowledge of evolving AMR evidence. Promoting the benefits of the training and financial incentives were cited as facilitators. Across both workshops, barriers were a lack of capacity and time. Purposive strategies most employed concentrated on educating stakeholders, providing support and development of stakeholder relationships. Strategies least employed were financial strategies and changing the regional level infrastructure.

Conclusions

Overall, the implementation of a national training programme requires support, both centrally and regionally, to be successful. Regional variation in priorities and practical issues should be acknowledged when implementing interventions nationwide.

Development of biomarker-based diagnostics to support early infection detection and AMS

Authors

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NAP outcome: 6 – Innovation and influence

The UK government's 20-year vision for antimicrobial resistance (AMR), ‘Contained and Controlled: the UK's 20-Year Vision for Antimicrobial Resistance’, sets out a long-term strategy to reduce the burden of infection, improve prevention and treatment of resistant infections, support optimal antimicrobial use, and accelerate the development and adoption of innovative diagnostics, therapeutics, vaccines and other interventions. These ambitions align closely with UKHSA's mission to strengthen health security through innovation, preparedness and evidence-based public health action.

Rapid and accurate diagnosis remains a major challenge in infectious disease management and AMR control. Conventional microbiological methods can require up to 48 hours to generate results, often necessitating empirical antimicrobial treatment while awaiting confirmation. There is a recognised need for novel diagnostic approaches that can rapidly distinguish bacterial from viral infections, differentiate pathogenic from commensal organisms, and support timely clinical decision-making. Recent advances in host-response profiling have demonstrated the potential of circulatory biomarkers and multi-marker diagnostic signatures to provide earlier and more precise information on infection aetiology and disease progression, supporting a transition from empirical treatment towards precision antimicrobial stewardship. To address these challenges, we are developing biomarker-based diagnostic tests for 2 difficult-to-diagnose conditions: sepsis and tuberculosis (TB). These technologies are currently being developed as laboratory-based quantitative PCR (qPCR) assays and point-of-care lateral flow devices (LFDs). Our TB LFD programme, funded through the Knowledge Asset Grant Fund, is progressing towards clinical evaluation during 2026 to 2027 through collaboration with partners in India.

Our approach reflects growing international interest in host-response biomarkers that can support diagnosis, treatment monitoring and prognostic assessment. Emerging evidence suggests that biomarker panels may enable earlier identification of serious bacterial

infections, improve differentiation between infectious and non-infectious causes of inflammation, and provide clinically actionable information within the critical early stages of patient assessment. Such advances have the potential to improve antimicrobial stewardship by reducing unnecessary antimicrobial prescribing while ensuring that patients with severe infections receive timely and appropriate treatment. These projects support national priorities for diagnostics innovation, AMR mitigation and health preparedness by enabling earlier and more accurate diagnosis across both acute and community healthcare settings. In addition to improving diagnostic certainty, these biomarker-based approaches have the potential to support treatment monitoring, predict disease severity and guide more targeted antimicrobial use. Through improved clinical decision-making and antimicrobial stewardship, these technologies aim to enhance patient outcomes, strengthen preparedness for infectious disease threats, and contribute to efforts to address the growing challenge of AMR.

Adaptation of the WHO AWaRe antibiotic classification to support national AMS priorities in the UK

Authors

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NAP outcome: 7 – Using information for action

This manuscript describes the adaptation of the WHO AWaRe (Access, Watch, Reserve) classification for the UK context, to better support antimicrobial stewardship and inform national antibiotic prescribing targets. Using a 4-stage modified Delphi process with 61 experts across the UK, antibiotic classifications were reviewed in light of national resistance patterns, prescribing data, and stewardship practices.

The resulting UK-adapted AWaRe classification differed from the WHO 2023 version for 17 antibiotics, with the strongest consensus achieved for the Access category. A key change was the reclassification of first-generation cephalosporins into the Access group, representing a shift from previous England categorisation where all cephalosporins were classified as Watch. Analysis of national antibiotic consumption data in England showed that Access antibiotics accounted for over 60% of use (63.7% under the UK-adapted classification compared with 69.7% using the WHO classification).

The adapted UK-AWaRe list is intended to support national antimicrobial stewardship efforts and guide antibiotic usage targets within the UK's 2024 to 2029 AMR National Action Plan.

Improving primary care antibiotic prescribing to reduce antibiotic resistant urine infections

Authors

Improving primary care antibiotic prescribing to reduce antibiotic resistant urine infections: the IPAP-UTI programme

NAP outcome: 7 – Using information for action

Urinary tract infections (UTIs) are among the most common infections managed in primary care. Antimicrobial-resistant UTIs are associated with worse patient outcomes than antimicrobial-sensitive UTIs, including longer infection duration, increased primary care re-

consultations, additional antibiotic courses, and higher rates of hospital admission and mortality.

The IPAP-UTI programme aims to tackle the growing problem of antimicrobial resistance (AMR) by generating evidence to inform UK policy on how UTIs should be treated in primary care in response to local AMR challenges. The programme involves a series of randomised controlled trials (RCTs), each addressing the primary question: Does an intervention that encourages primary care prescribing of alternative antibiotics for UTI, rather than an antibiotic with high local resistance (‘target antibiotic’), reduce resistance to the target antibiotic in routinely submitted urine samples?

The programme includes multiple workstreams:

- statistical analyses evaluating the impact of the intervention on patient outcomes (including UTI AMR, antibiotic dispensing, treatment failure, and bloodstream infection admissions)
- a qualitative process evaluation exploring the acceptability and feasibility of the intervention
- a health economic evaluation assessing cost-effectiveness
- a comprehensive investigation of AMR patterns across IPAP-UTI trial areas using standardised antibiogram testing and whole genome sequencing

The programme is led by researchers at the University of Bristol, in collaboration with clinicians and epidemiologists at the UKHSA, antimicrobial stewardship leads at NHS England, medicines optimisation pharmacists at Bristol North Somerset and South Gloucestershire Integrated Care Board, and Patient and Public Involvement (PPI) contributors. This 5-year programme is funded by the National Institute for Health and Care Research (NIHR) and is scheduled to end in June 2028.

Public engagement, behaviour and communication

The role and needs of teachers/schools in IPC post COVID-19

Authors

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NAP outcome: 1 – Infection prevention and control and infection management

Objectives
COVID-19 highlighted the importance of infection prevention and control (IPC) across all settings. This study aimed to understand current teacher IPC knowledge and measures in schools, the teacher's role in infectious disease outbreaks in schools, school or teachers' needs around IPC, and how all these may have changed since the COVID-19 pandemic.

Methods
This was a mixed-method cross-sectional study with teachers from England. Quantitative data was collected via an online survey and qualitative data via focus group interviews. Survey questions were reviewed using descriptive analysis, and thematic analysis was used for the open-ended survey questions and focus group interviews.

Results
A total of 1,000 teachers completed the survey across a range of teaching roles. Eight headteachers participated in the workshops. Respondents reported that IPC measures are now less frequently implemented during an infectious disease outbreak than during the pandemic. About 71% of respondents who have been teaching for at least 2 years (at the time of the survey) said their role has changed since the pandemic, now having more responsibility for pupil health and hygiene, and 72% of them reported feeling better prepared to deal with a public health outbreak compared to pre-pandemic. Furthermore, around 84% reported they had no IPC training, and 1-in-3 (35%) had unmet IPC needs.

Conclusion

Schools and teachers play a pivotal role in preventing the spread of communicable disease as highlighted during the COVID-19 pandemic. Training and updated policies would support the educational workforce who feel their needs are not being met.

Social media as a means of sharing information on AMR and appropriate antibiotic use: a systematic review

Authors

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NAP outcome: 2 – Public engagement and education

Background

Use of social media to access health information is increasing. This systematic review aims to assess the availability of social media-based information related to AMR and antibiotic use aimed at members of the public. It also looked to determine whether sharing information related to AMR and antibiotic use on social media improves public knowledge.

Methods

MEDLINE, Embase and PsycINFO were searched on 24 May 2024. Google Scholar was searched on 4 October 2024. All primary studies published between January 2013 and May 2024 that outlined AMR or antibiotic-related information on social media or assessed the effectiveness of social media at improving knowledge and attitudes towards AMR and antibiotic use were eligible for inclusion. Risk of bias assessment was conducted using the Mixed-Methods Appraisal Tool. A narrative synthesis was used to describe the studies.

Results

624 papers were identified with 607 records removed during de-duplication and screening. Identified papers assessed the reach of and engagement with social media posts (n=7), attitudes towards antibiotic use (n=4), learning materials (n=3) and the effectiveness of social media at increasing public knowledge (n=2). Common misconceptions were identified, including how AMR develops and the conditions that antibiotics can be used to treat.

Conclusions

This review highlights that a range of information relating to AMR and antibiotic use is available on social media, including false information. However, the impact of exposure to

social media content on knowledge, attitudes and behaviours towards AMR and appropriate antibiotic use remains unclear.

A systematic review of research methodologies to inform the study of AMR misinformation on social media

Authors

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NAP outcome: 2 – Public engagement and education

Background
There is a lack of published research assessing the prevalence of AMR misinformation on social media. A range of methodologies are used for social media research. This systematic review aims to identify different methodologies used and their strengths and limitations to inform future research into AMR misinformation.

Methods
Embase, MEDLINE and Global Health were systematically searched in February 2025. Studies published between January 2020 and February 2025 assessing health information on social media aimed at the public or patients were eligible for inclusion. Studies reporting on COVID-19 were excluded. A narrative synthesis was used to describe the results.

Results
3503 articles were identified with 38 articles included in the review. Two main methodologies were identified. One used a search term or specific hashtag to manually search for information that met an inclusion/exclusion criterion (n=10). A search limit was then applied, often the top 100 to 200 most liked posts. This methodology was applied to YouTube (n=3), Facebook (n=2), Twitter (n=2), Instagram (n=1), Reddit (n=1), Pinterest (n=1) and TikTok (n=1). Two studies implemented precautionary measures to reduce selection bias associated with this research methodology. One study collected data using a newly created Instagram account and the other used a cache-clearing web browser in private mode with all available updates.

Alternatively, methodologies implemented web scrapping tools which use specific hashtags or key words to search for content posted within a specific period (n=28). They then applied a selection criterion to the identified content to refine the sample used for data analysis. This methodology was most frequently applied to Twitter (now called X) (n=21), as well as to

Facebook (n=5), Instagram (n=4), Reddit (n=2), TikTok (n=1), YouTube (n=2) and Pinterest (n=1). A total of 18 web scrapping tools were used within the identified studies.

A range of methodologies and tools are currently used in social media research. Although manual searching to identify relevant social media posts is a low-cost approach and does not require any specialist software, the search results may be biased due to the algorithms that are applied to social media channels. It may also create issues in misinformation studies due to challenges with accessing deleted and archived posts. The use of web scrapping tools facilitate access to a large quantity of data generating a more representative sample. However, the reliance on keyword searches may lead to selection biases. Furthermore, this is a fast-evolving field with changes frequently being made to data access and methods of analysing data, such as the introduction of large language models.

The review highlights a need to implement more standardised methodologies for social media research due to the challenges that occur when looking to collate evidence and make comparisons between studies.

Parental awareness and management of antibiotic side effects and allergies in children and young people: a UK survey

Authors

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NAP outcome: 2 – Public engagement and education

Background

Antibiotic use in children and young people is common, however, the associated short- and long-term effects are often unknown. Inappropriate prescribing and misdiagnosed allergies contribute to antimicrobial resistance (AMR) and poorer health outcomes. To explore parental awareness, experiences and management of antibiotic side effects and allergies in children and young people, to inform strategies for improved antimicrobial stewardship and communication.

Methods

An online survey was conducted in April 2024 with 1205 UK parents of children aged 16 years or under. The survey assessed experiences of side effects, knowledge of antibiotic

risks, and allergy management. Descriptive statistics and chi-squared tests were used to analyse responses, with weighting applied to ensure representativeness of the UK population.

Results

Among respondents, 64% (n = 770) reported their child had taken oral antibiotics, with 9% (n = 72) reporting side effects and 7% (n = 53) reporting allergies. Skin infections were the most common antibiotic indication that led to side effects (23%, n = 16). Skin irritation was the most frequently reported side effect (26%, n = 19) and allergic reaction (58%, n = 30). Side effects often disrupted daily activities and led to 64% (n = 46) stopping the antibiotic course early, of which 24% (n = 11) did so without professional advice. Following their experience, many parents would seek professional advice on side effects (64%, n = 46) and allergic reactions (76%, n = 40) for future infections in their children.

Conclusion

Improved communication can facilitate appropriate recognition, assessment and management of antibiotic adverse reactions in children and young people, potentially reducing incorrect penicillin allergy labelling.

A survey of parental health-seeking behaviour, knowledge, and expectations around ear infection symptoms in children

Authors

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NAP outcome: 2 – Public engagement and education

Background

An estimated half a million UK primary care consultations are due to middle ear infections annually. In children, ear infections are one of the most common reasons for antibiotic use.

Aim

To describe parents' experiences and actions for their child's ear infection symptoms.

Method

Online survey with parents of children aged ≤10 years who had suspected ear infection symptoms in the previous 12 months in England. Data was collected retrospectively and through self-report. Multivariable logistic regression explored association of variables with consulting and reported prescription of antibiotics.

Results

In total, 503 parents participated. Most parents perceived their child's symptoms as mild (25.8%) or moderate (64.6%). Consulting healthcare was the most reported action (90.3%) – 74% consulted within 1 to 2 days. Perceived severity and duration of symptoms were associated with consulting. Parents were concerned about serious illness and the need for treatment. Other factors associated with consulting were missing work (adjusted odds ratio [aOR] 4.8, 95% confidence interval [CI] = 1.6 to 14.8), childcare impacts (aOR 3.1, 95% CI = 1.0 to 9.5), and fluid in child's ear (aOR 3.9, 95% CI = 1.48 to 10.5). Of consultors, 55.7% (253 out of 454) reported receiving an antibiotic. Of all parents (503), 36.4% believed children always require antibiotics for ear infections.

Conclusion

Most parents consult for their child's ear infection symptoms and are prompted by impacts on daily life and perceptions of risk and treatment needs. There are knowledge gaps that, if addressed, may help to reduce primary care consultations and antibiotic use by supporting parents to manage self-limiting ear infections in children.

Women’s experiences of the assessment and management of UTIs during the COVID-19 pandemic

Authors

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NAP outcome: 4 – Antimicrobial stewardship and disposal

Background

Urinary tract infections (UTIs) are one of the most common bacterial infections affecting women. The COVID-19 pandemic altered how healthcare was accessed and resulted in the rapid adoption of remote technologies. This study explored patients' experiences of consultations for UTIs in general practice during the pandemic.

Methods

Women included in this study were ≥16 years, recruited via Ipsos's online panels in England, reporting at least one episode of UTI symptoms in the previous year, and had sought a consultation with a healthcare professional. We analysed 799 responses to a free-text questions, using inductive thematic analysis, regarding their experiences.

Results

We identified key themes related to (i) the consultation mode and healthcare professional consulted, (ii) UTI assessment and management, (iii) validation of UTI symptoms and experience and (iv) concerns due to the COVID-19 pandemic. Positive aspects of care related to prompt and thorough assessment and treatment, consulting a healthcare professional (HCP) who validated their experience, while encouraging discussions about prevention and self-care. Negative aspects of care were related to long appointment waiting times, a lack of in-person consultation if desired and patients feeling uninformed and unvalidated about their UTIs.

Conclusion

This study presents evidence that positive patient experience on UTI assessment and management is determined by the HCP involved, the mode of consultation and the application of shared decision-making to determine treatment. To improve satisfaction, systems and consultations should account for these patient preferences with shared decision-making approaches, adapted for remote consultations, to support discussions around UTI investigation and management.

Modelling, health economics and policy evaluation

Cost of Gram-negative bloodstream infection admissions in English NHS trusts: an analysis using health resource groups

Authors

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NAP outcome: 3 – Strengthening surveillance

Background

Estimating the economic cost of antimicrobial resistance is a research priority in the UK, essential for justifying investment and identifying interventions that offer value for money. We provide an initial estimate for England of the cost burden of hospital admissions linked to reported Gram-negative bloodstream infections (GNBSIs) and explore how costs per admission vary by infection and patient characteristics.

Methods

We linked data on *Escherichia coli*, *Klebsiella spp.,* and *Pseudomonas aeruginosa* BSIs from the UKHSA's surveillance systems to the Hospital Episode Statistics database to identify a cohort of patients admitted to hospital in England during the 2023 to 2024 financial year who had a reported GNBSI during admission or in the 14 days prior.

To estimate hospitalisation costs for this cohort we assigned Healthcare Resource Groups to each admission using the NHS 2023/24 Reference Costs Grouper software and valued using costs from the 2023/24 National Cost Collection.

The cost burden of GNBSI-linked hospitalisations was examined across groups defined by infection characteristics, including onset type (community onset (CO), hospital onset (HO)), causative pathogen (*E. coli*, *Klebsiella spp.*, *P. aeruginosa*) and resistance status

(susceptible, resistant), and additionally by patient characteristics, including sex (male, female), age group (<1, 1 to 14, 15 to 44, 45 to 64, 65 to 74, 75 to 84, 85+), comorbidity (measured with the Charlson Comorbidity Index and grouped into quartiles), ethnicity (White, Asian, Black, Mixed, Other, Not known), and deprivation (Index of Multiple Deprivation quintile).

Log-linear regression models with hospital-level fixed effects and robust standard errors, stratified by infection onset type, assessed associations between cost per admission and infection characteristics (pathogen was interacted with resistance status), controlling for patient characteristics (age group was interacted with comorbidity).

Results

Our cohort comprised of 55,074 GNBSIs linked to 53,410 hospital admissions (3.1% of admissions were linked to more than one infecting pathogen). Five extreme cost outliers were removed from the cohort due to data quality issues. The total cost of the remaining 53,405 GNBSI-linked hospital admissions beginning in financial year 2023 to 2024 was estimated at £841,876,420.

Overall, admissions linked to CO infections accounted for a greater share of the cost burden than admissions linked to HO infections (55.5% versus 44.5%). Admissions linked to *E. coli, Klebsiella spp.* and *P. aeruginosa* infections accounted for 64.1%, 26.3%, and 9.5% costs respectively. Susceptible and resistant infections made up 73% and 27% of costs respectively. Susceptible CO *E. coli* infections accounted for the largest share of both cases and costs (41.8% and 29.5% respectively).

Men made up 53.8% of cases and 56.8% of costs. Age groups <1, 1 to 14, 15 to 44, 45 to 64, 65 to 74, 75 to 84, and 85+, made up 5.3%, 1.7%, 7.1%, 19.5%, 20%, 27.4%, and 18.9% of the cost burden respectively.

The average cost per admission linked to a CO infection was £10,842 (SD 10,028), compared with £26,611 (SD 32,371) per admission linked to HO infections. For both infection onset types, costs per admission were higher for *Klebsiella spp.* and *P. aeruginosa* compared to *E. coli* infections and higher for resistant compared to susceptible infections, after controlling for patient characteristics.

Conclusion

We estimated the full cost burden of hospital admissions linked to CO- and HO-GNBSIs. Cost burden was highest in infection groups with low costs per admission but high case numbers (for example CO, susceptible, *E. coli* linked admissions).

In the case of admissions linked to HO infections, much of the cost is generally incurred due to the original reason for admission and only a portion of costs are caused by the infection itself. Further work will use causal inference to estimate costs attributable to both infection and antimicrobial resistance.

GNBSIM: Modelling the impact of point-of-care susceptibility testing on *E. coli* bloodstream infections

Authors

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NAP outcome: 3 – Strengthening surveillance

Background

Escherichia coli causes 59% of Gram-negative BSIs in England and is a critical antimicrobial resistance (AMR) concern. Of these, 51% originate in the urinary tract, thus the pathway from urinary tract infections (UTI) to BSI for *E. coli* infections is important to reduce Gram-negative BSIs and meet the UK's 2019 to 2024 AMR National Action Plan targets. This study aims to investigate effective interventions to reduce BSI, particularly those with antibiotic resistance.

Methods

An individual-based model was developed, of hospital patients and their pathways from colonisation with antibiotic-susceptible and -resistant strains of *E. coli*, through to developing UTI and BSI. Key patient characteristics have been defined, such as age, sex, provenance (from care home or wider community) and all parameterisation of variables across the model determined from national (England) data (hospital data linked with laboratory results, mortality data and care home records). Patients are admitted with either a community-acquired infection (UTI or BSI) or with the potential to develop a hospital-acquired infection, with the infections being susceptible or resistant to antibiotics. Point-of-care testing (POCT) for antibiotic susceptibility is introduced in the model and the results of which are compared to the baseline of the current standard of care, to determine the potential reduction in length of stay and mortality for patients with resistant infections.

Results

The model results show that the length of stay for patients with a resistant infection could be reduced from 17.9 days (95% CIs:17.5 to 18.3) to 14.1 days (95% CIs:13.8 to 14.4) with the introduction of a POCT for antibiotic susceptibility. The probability of mortality could be reduced from 0.14 (95% CIs:0.14 to 0.15) to 0.11 (95% CIs:0.10 to 0.11). Further analysis has investigated the variation in these reductions by age and sex. Sensitivity analysis has

assessed the influence of parameter variations on the model behaviour and to elucidate the parameters most responsive to perturbations.

Conclusion

Modelling the transmission dynamics of antibiotic-susceptible and -resistant strains of *E. coli* improves understanding of the pathways to severe infection and has identified the potential of POCT for susceptibility to improve care and outcomes for patients.

Estimating the impact on patient mortality of antibiotic-resistant bloodstream infections in England

Authors

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NAP outcome: 3 – Strengthening surveillance

Introduction

Understanding the mortality burden of antimicrobial resistance (AMR) is critical to assessing its public health impact. We estimated the number of deaths due to antibiotic-resistant bloodstream infections across 4 key pathogens: *E. coli*, Klebsiella spp., Pseudomonas spp. and *S. aureus* in England for the year April 2023 to March 2024.

Methods

We linked microbiology data from reported bloodstream infections (BSIs) in England with hospital admissions and mortality data. Antibiotics were considered eligible if we assessed that they could be used for treatment of bloodstream infections. Patients under palliative care were excluded from the analysis.

We considered 2 scenarios, corresponding to estimates of deaths which could have been averted: firstly, if infections that were resistant to key antibiotics had not occurred, secondly, if these resistant infections had instead been susceptible.

We used different models, using causal inference methods, according to whether the BSIs were community or hospital onset and ran models separately for each pathogen. Models were adjusted for confounding due to patient characteristics.

Results

For the year 2023 to 2024 we identified 55,323 resistant BSI cases, with 6,769 (12.2%) all-cause deaths within 30 days of infection. Of these, we estimated that 74.9% (95% confidence interval: 63.9%, 85.9%) could have been avoided if the infections had not occurred, and that 14.5% (3.1%, 27.2%) could have been avoided if the infections had been susceptible.

Conclusions

We estimated that three quarters of deaths occurring within 30 days of an antibiotic-resistant BSI caused by one of these 4 pathogens could be avoided if the infections could have been prevented altogether. We found that approximately 1 in 7 deaths were attributable to the resistance of these infections.

Model-based economic evaluation of IPC measures to address carbapenemase producing Enterobacterales in hospitals across Europe (REVERSE)

Authors

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NAP outcome: 3 – Strengthening surveillance

The pREVention and management tools for rEducing antibiotic Resistance in high prevalence Settings (REVERSE) project aims to develop and implement cost-effective interventions for the prevention and clinical management of multidrug-resistant healthcare associated infections. REVERSE is an EU-funded mixed-method project across 24 acute care hospitals in 4 European countries (Greece, Italy, Romania, Spain) with high a prevalence of multidrug-resistant organisms.

A dynamic transmission model has been developed to simulate patient movement between and within hospital and community settings, including nosocomial and environmental

carbapenemase-producing Enterobacterales (CPE) transmission in a typical hospital in England. Preliminary results suggest targeted admission screening is cost-effective, although with considerable uncertainty. Sensitivity analysis indicates universal admission screening becomes cost-effective when nosocomial transmission is high.

Work is under way to adapt the England model to the 4 REVERSE countries, to explore the cost-effectiveness of the infection prevention and control interventions being trialled. The updated model framework will incorporate country-specific parameters and account for heterogeneity across settings, including prevalence and transmission, healthcare provider, intervention uptake and effectiveness, unit costs, and willingness-to-pay for health gains. The country-specific models will be parameterised using primary data from the REVERSE trial, national-level administrative data and estimates from the literature. The model output will be validated using trial data.

In summary, preliminary results indicate targeted admission screening of CPE in England is cost-effective, although uncertainty is high. The dynamic transmission model is being adapted to explore the cost-effectiveness of the REVERSE interventions.

Predicting the impact of monoclonal antibodies and vaccines on AMR (PrIMAVeRa)

Authors

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NAP outcome: 3 – Strengthening surveillance

Predicting the Impact of Monoclonal Antibodies and Vaccines on Antimicrobial Resistance (PrIMAVeRa) is an EU-funded project aiming to support evidence-based decision-making for AMR interventions through the development of integrated transmission and cost-effectiveness modelling evaluating the potential impact of vaccines and monoclonal antibodies (mAbs) across healthcare settings. The project focuses on multiple high-priority pathogen-infection combinations, including *Staphylococcus aureus*, *Escherichia coli*, and *Klebsiella pneumoniae*.

Within PrIMAVeRa, a major workstream centres on developing pathogen-specific and generic modelling frameworks that capture infection dynamics, healthcare pathways, and intervention effects, linked to detailed health economic (HE) modules. These models incorporate both clinical outcomes (for example infections, hospitalisations, mortality, antibiotic use) and economic consequences (for example healthcare costs, quality-adjusted

life years (QALYs)), enabling estimation of cost-effectiveness across a range of intervention scenarios.

Current modelling work includes:

- a compartmental transmission model for *S. aureus* capturing ward-level dynamics (general ward, intensive care unit (ICU), haemodialysis), colonisation, and progression to bloodstream infection (BSI) and ventilator-associated pneumonia (VAP), used to evaluate decolonisation strategies and mAbs
- a population-based model and individual-based model (IBM) evaluating vaccination scenarios targeting *E. coli* urinary tract infections (UTIs), incorporating uncomplicated and complicated infections and subsequent progression to bloodstream infections
- an IBM for *Klebsiella pneumoniae* VAP in ICU settings, linking patient-level infection and clinical trajectories to economic outputs
- a generic compartmental transmission model developed to be applicable to multiple bug-drug-infection syndromes for evaluation of vaccines including HE impacts evaluated across the patient pathway

Health economic modules have been developed to incorporate key drivers of cost-effectiveness, including general ward and ICU length of stay, diagnostic testing, antibiotic treatment, and illness- and mortality-related QALY losses. Scenario analyses explore intervention characteristics (for example efficacy, target population), healthcare pathways (for example ward-to-ICU transitions), and implementation strategies such as screening and isolation.

Preliminary results suggest that intervention impact varies substantially by target setting and population. For example, *S. aureus* analyses indicate that targeting general wards yields the largest reduction in infections, while ICU-focused strategies avert a greater proportion of resistant cases. Early *E. coli* vaccine analyses suggest that targeting older adults (for example ≥60 years) with higher efficacy vaccines may offer favourable cost-effectiveness profiles, although results remain provisional pending model refinement.

A key element of the project will be to conduct value of information (VOI) analyses to understand how uncertainty in model inputs affects the results and identify where additional evidence would be most useful for future policy decisions. Planned outputs include detailed reports and manuscripts capturing model development and cost-effectiveness analysis (CEA) results, and deployment of an online, user-friendly dashboard presenting modelling and CEA results. This dashboard is currently under development and incorporates feedback from a diverse range of stakeholders (including industry and healthcare professionals, policymakers and researchers) to facilitate data-driven decision-making.

In summary, PrIMAVeRa is developing a comprehensive and flexible modelling and economic evaluation platform to assess interventions targeting AMR and provide a strong foundation for generating policy-relevant cost-effectiveness evidence across pathogens and healthcare systems.

Innovative solutions for the treatment and prevention of AMR infections

Open Innovation model to support Pathways to Antimicrobial Clinical Efficacy (PACE)

Authors

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NAP outcome: 6 – Innovation and influence

This case study describes the utilisation and continued development of a platform set up by UKHSA to support and encourage the research community to discover and develop new drugs against infectious diseases, including infections that are difficult to treat, through partnership with the ‘Pathways to Antimicrobial Clinical Efficacy’ (PACE) initiative. The lack of a healthy pipeline of new antimicrobials has resulted in predictions that by 2050, AMR will be the cause of at least 10 million deaths each year, overtaking cancer at 8.2 million. Additionally, modern healthcare relies on antimicrobials, which have saved billions of lives. If antimicrobials fail, cancer treatment, routine surgeries, birth and all healthcare where antimicrobials are supporting mechanisms, will become increasingly risky, if not impossible. It is extremely important to invest in the discovery and development of new antimicrobials to fight this global public health threat. At UKHSA Porton Down, we have developed an ‘Open Innovation’ model for the discovery and development of novel antimicrobials against World Health Organization (WHO) priority pathogens. We work openly with academics, small and 2 medium entities and larger biotech companies to share resources and knowledge and to evaluate new therapies against our large library of clinical isolates of bacteria and fungi. We test both traditional style antimicrobials (small molecules) and non-traditional therapies such as bacteriophage, antimicrobial peptides, lysins, immune modulators, microbiome modulators, and delivery vehicles for antimicrobial warheads. Over the last 8 years, we have worked with >70 collaborators, including medicinal chemists, supramolecular chemists, engineers, microbiologists, pharmacologists, materials scientists, and synthetic biologists. In

2023, the £30million PACE initiative was launched by LifeArc, Medicines Discovery Catapult and Innovate UK to invest in early-stage antimicrobial development. PACE works to remove barriers and connect the AMR research and development (R&D) ecosystem to accelerate and strengthen the pre-clinical pipeline. Through its funding rounds, PACE is supporting 11 novel and diverse antimicrobial projects targeting the most critical microbes and resistance mechanisms. Further diagnostic and therapeutic projects will be added to the PACE portfolio in the future. UKHSA's Open Innovation platform provides the wrap-around microbiological support for this exciting initiative. PACE portfolio projects have access to the UKHSA expertise to test their antimicrobial candidates against panels of reference and clinically relevant strains of bacteria. As part of the collaboration, collections of contemporary clinically relevant bacterial strains are being developed, incorporating geographically and infection-site diverse clinical isolates. These isolates are being provided by the UKHSA Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit at the UKHSA Colindale. They will be made available to the wider research community through the National Culture Type Collections as fully characterised panels with whole genome sequencing and phenotypic testing to illustrate the antimicrobial resistance traits for each strain. The Open Innovation in AMR platform at UKHSA was highlighted as a case study in supporting innovation as part of the National Action Plan for AMR published in May 2024. In uniting two key national assets, the UKHSA Open Innovation Platform and PACE, the partnership illustrates how UK innovation can be mobilised to meet national priorities and strengthen global health security. To date, 8 out of the 11 PACE portfolio projects have used the Open Innovation service to test a range of novel antimicrobial modalities. Central to the ethos of the Open Innovation platform and PACE is the training and support of the next generation of AMR researchers, to help replace the 'brain drain' of researchers moving away from this area. Because UKHSA is also a member of the PACE Delivery Partner Network, portfolio projects can tap into these wider services and collaborate across the community to deliver strong outputs. In addition to its work with PACE, multiple patents have been filed by the UKHSA with research partners and we are actively exploring commercialisation of key assets in improving the efficacy of antibacterial and antifungal agents by stopping them being pumped out (effluxed) from the target pathogen, and rapid phage susceptibility tests, based on the iFAST platform.

Impedance-based Fast Antimicrobial Susceptibility Tests (iFAST)

Authors

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NAP outcome: 6 – Innovation and influence

Most antibiotics are currently prescribed without evidence that they will be effective for the specific infection. This means that an ineffective antibiotic may be prescribed, leading to poor treatment outcomes and increased risk of antibiotic resistance developing. One of the reasons for prescribing without evidence is that current antibiotic susceptibility tests (ASTs) take at least 2-3 days, which is too long to wait for treatment initiation. In this project, supported by an Invention for Innovation (i4i) award from the National Institute for Health and Care Research, we developed a new technology, which can measure antibiotic susceptibility in around 4 hours. We worked with engineers from the University of Southampton to measure small electrical changes to individual bacterial cells that are affected after 2 hours of antibiotic exposure. A multi-disciplinary project team involving microbiologists and Health Care Economists from UKHSA, Engineers from the University of Southampton, Biomedical Scientists from Southampton General Hospital and an engaged Public Advisory Group, developed the technology ready for commercialisation via spin-out company iFAST Diagnostics. As an original proof-of-concept, we tested how our technology matched susceptibility results as currently measured in a diagnostic laboratory for 58 E. coli and K. pneumoniae strains exposed to 8 different antibiotics. Agreement between the 2 methods was very high (>95%), showing the promise of this technology to speed up antimicrobial susceptibility testing. A concordance study carried out at Southampton General Hospital by Biomedical Scientists, in parallel with standard ASTs, confirmed this high level of concordance. A health care economics study on the cost savings of introducing this technology to urinary tract infection (UTI) ASTs, showed that it would save a significant number of lives, quality adjusted life years and money. The project has resulted in the establishment of a commercial vehicle, iFAST Diagnostics, to develop the technology and move it into clinical use. The company identified that UKCA marked products will be available in 2026, as they enter a formal clinical trial. Impacts delivered and anticipated. The technology offers the potential to speed up the selection of antibiotics which work against drug resistant infections, offering the potential for improved treatment and better patient outcomes (by avoiding the use of antibiotics that don't work) as well as helping to reduce the use of ineffective antibiotics that promote drug resistance. This work aligns with UKHSA strategic priorities on AMR. The work has generated new intellectual property (know-how and patents), as well as supporting the establishment of a company to develop the technology. The company, based in Southampton, has raised over £12million in initial investment and currently employs 14 people. The technology is potentially disruptive as it provides rapid results to support clinical decision making. By measuring the responses of individual bacteria, the approach can see responses that are difficult to measure using classical culture-based methods, and this may support a range of new applications as well as underpinning discovery science and innovation. The technology has been evaluated by the company in a series of applied studies in UK hospitals, looking at increasing the speed of antimicrobial susceptibility data generation for bloodstream infection. The data is strongly supportive of the technology being further developed and implemented in this area, with independent health economic assessment supporting the case for development and implementation.

TBVAC-HORIZON (EU Horizon Europe/UKRI)

Authors

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NAP outcome: 6 – Innovation and influence

TBVAC-HORIZON is a research project in the Horizon Europe (HE) program of the European Union (EU). It aims to increase understanding of immune protection in the lung in *Mycobacterium tuberculosis* infection and to develop mucosal vaccination strategies for translation towards clinical evaluation. The Consortium's activities range from pre-clinical research to aligned studies with humans, non-human primates (NHP) and mice. The goal is to fill the vaccine pipeline to accelerate availability of more effective TB vaccines. The project is linking 19 institutions and builds upon over 25 years of EU-funded collaboration. UKHSA provides a unique head-to-head evaluation of efficacy of vaccine candidates being developed within the TB field contributing to acceleration to towards human clinical trials.

ITHEMYC (EU Horizon Europe/UKRI)

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NAP outcome: 6 – Innovation and influence

The ITHEMYC project, coordinated by TBVI, advances beyond the current state-of-the-art by combining existing TB drug treatment regimens and immunotherapies to develop novel therapeutic options with the potential to shorten treatment duration, improve outcomes and prevent relapse. This multidisciplinary consortium brings together leading expertise and capacity to tackle the challenges of working in new scientific areas to combat the global burden of tuberculosis. UKHSA provides a unique head-to-head evaluation of efficacy of therapeutic candidates being developed within the TB field, contributing to acceleration towards human clinical trials.

IMPAc-TB (NIH)

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NAP outcome: 6 – Innovation and influence

The IMPAc-TB program aims to develop a comprehensive understanding of the immune responses required to prevent initial infection with *Mycobacterium tuberculosis*, the establishment of latent infection, and transition to active TB disease. This consortium will identify the complex immune responses required to prevent *M. tuberculosis* infection or active TB disease by comparing and examining protective immune responses induced by natural mycobacterial infection or vaccines. The research team evaluates recombinant protein vaccines combined with adjuvants to identify and validate common protective correlates of immunity in well-established animal models for TB and human challenge clinical studies where participants are deliberately exposed to BCG (as a controlled human infection model) under carefully controlled conditions. The investigational vaccines being evaluated are ID93 and M72 formulated with GLA-SE and other adjuvants developed by Access to Advanced Health Institute (AAHI) and contractors supported by NIAID's Division of Allergy, Immunology, and Transplantation's (DAIT) adjuvant program. The studies also address how immunity from previous BCG vaccination and natural nontuberculous mycobacteria (NTM) infection affects the investigational vaccines' effectiveness and ability to generate an immune response across species. The studies will provide crucial insights into the development of candidate vaccines that generate robust levels of durable, protective immunity against TB. UKHSA contributes by using established models designed to identify the key immune responses needed for protection against *M. tuberculosis*, determine immunologic targets that can be used to improve TB vaccine strategies, and to identify how bacterial immune evasion mechanisms subvert immune responses to *M. tuberculosis*.

Systematic unbiased mapping of an antibiotic interaction landscape identifies novel combinations in high-risk *E. coli* lineages

Authors

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NAP outcome: 6 – Innovation and influence

Combination antibiotic therapy offers a strategy to overcome resistance, yet systematic profiling of the complete landscape of possible antibiotic combinations remains limited by the throughput constraints of classical methods. We applied the DiaMOND (Diagonal Measurement of N-Way Drug Interactions) platform to quantify 253 unique pairwise interactions arising from 23 licensed antibiotics, representing clinically relevant antimicrobial classes (aminoglycoside, tetracycline, oxazolidinone, macrolide, dihydrofolate reductase inhibitor, sulphonamide, fluoroquinolone, ansamycin, nitrofuran, penam, carbapenem, cephalosporin, monobactam, β-lactamase inhibitor, diazabicyclooctane β-lactamase inhibitors, glycopeptide, lipopeptide, polymyxin and phosphonic acid derivative), against 3 *Escherichia coli* strains with different resistance profiles: *E. coli* ATCC 25922 is an antibiotic susceptible reference strain, *E. coli* EC958 from the global ST131 clone is characterised by resistance to fluoroquinolones and third-generation cephalosporins, and *E. coli* EC511 a clinical isolate representative of the global ST410 clone that is carbapenem resistant.

E. coli EC958 exhibited a larger number of additive or synergistic combinations than *E. coli* EC511. Clinically relevant combinations, ceftazidime/avibactam in EC958 and aztreonam/avibactam in EC511, generated strong synergistic scores in the DiaMOND assay and bactericidal activity in time-kill experiments, demonstrating the capacity of our methodology to confirm established resistance and synergy patterns. Unbiased screening identified new, previously unidentified, additive interactions between pairs of antibiotics, including clavulanic acid/avibactam, a dual β-lactamase inhibitor pairing producing bactericidal killing in EC958, and nitrofurantoin/tigecycline, which achieved sustained bactericidal activity in EC511 and suppressed the emergence of *nfsA*-mediated nitrofurantoin resistance. These findings demonstrate that systematic, unbiased combination screening can identify combinations that slow the development of antimicrobial resistance with potential therapeutic relevance in multi-drug resistant (MDR) *E. coli*.

A novel nitroaromatic scaffold: nitrofuran isoxazolines bypass Ddn activation

Authors

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NAP outcome: 6 – Innovation and influence

The rise of multidrug-resistant (MDR) and extensively drug-resistant (XDR) tuberculosis necessitates new antimycobacterial agents. We report on the development of modified nitrofuran isoxazolines, a novel nitroaromatic class with potent activity against Mycobacterium tuberculosis and non-tuberculous mycobacteria. Lead compound 3.27 exhibited low nanomolar MICs, bactericidal activity that surpasses pretomanid and delamanid, favourable pharmacokinetics, and low toxicity *in vitro* and *in vivo*. Mechanistic studies indicate activity independent of Ddn-mediated activation, with no nitric oxide release and minimal metabolic conversion, suggesting a distinct mode of action. Collectively, these findings establish nitrofuran isoxazolines as a mechanistically distinct chemical class for antimycobacterial drug discovery.

Expanded screening of under-utilised novel compounds against AMR pathogen panels

Authors

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NAP outcome: 6 – Innovation and influence

Drug discovery laboratories often harbour a plethora of under-utilised small compounds, which had been identified as possessing activity against a specific pathogen but had not been taken further outside of this scope. To utilise this missed potential, the 'Idler' compound library was created by the Todd Group at UCL to collate an open-source collection of small molecules, not being actively pursued in group projects in their host labs, that could be screened against a panel of different pathogens. Utilising the unique drug screening capabilities at UKHSA Porton, the Idler compounds were dispensed into plates at working concentrations of 100 µM or 10 µM and tested against a wide range of organisms including *Staphylococcus aureus, Acinetobacter Baumannii, Escherichia coli, Candida albicans* and the mycobacterial species*, M. abscessus* and *M. avium,* to ascertain their impacts on viability. The screen identified that there were multiple compounds which showed good activity against *E. coli*, *S. aureus,* and *A. Baumannii*, with one antimalarial compound, WEL2.76 showing cross-specificity against all these strains. The screen also identified compounds with antifungal properties, where there were 10 compounds with activity against *C. albicans*, 3 of which were specific only to the organism. Finally, a tRNA synthetase-targeting antimalarial compound, YNW5-2, was found to have specific activity against the intrinsically resistant mycobacterial strain, *M. avium*, in addition to *E. coli*. To supplement this data, the cytotoxicity was also tested in a haemolysis assay to show that none of the compounds exuded a lysis effect. Taken all together, the data collected from the Idler screen has shown the strength of repurposing compounds that have promise against specific pathogens. As a result, there are now promising leads being followed up to confirm the activity of these compounds and ascertain their mode of action. The work on the Idler compounds truly highlights the wide variety of drug screening capabilities and fundamental microbiology residing at UKHSA Porton and how this can be used to catalyse effective partnerships with academia to combat AMR.

Generation of outer membrane vesicles from representative *Neisseria gonorrhoeae* isolates for standard assay development

Authors

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NAP outcome: 6 – Innovation and influence

UKHSA-Porton has been engaged to generate, purify and characterise outer membrane vesicles from relevant clinical strains of *N. gonorrhoeae* for MHRA-NIBSC to develop a

standardised Luminex-based multiplex assay to assess protective responses to Bexsero and other new gonorrhoeae vaccines.

Analysing case-control samples for predicting defined correlates of protection for Group B Streptococcus vaccines

Authors

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NAP outcome: 6 – Innovation and influence

Using the standardised Opsonophagocytic Killing Assay (OPKA) developed by UKHSA-Porton, the Pathogen Immunology Group have been testing samples from 2 critical case-control studies in newborn infants. The ability to find a protective risk-reduction threshold in the OPKA is important for understanding the level of immunity required by candidate maternal vaccines to protect infants from infection by Group B Streptococcus.

Antibiotic mitigation process for removing antibiotics from clinical samples to allow for testing in bacterial killing assays

Authors

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NAP outcome: 6 – Innovation and influence

The presence of antibiotics in serum samples from natural immunity and clinical vaccine studies is complicated by the presence of antibiotics in many samples. This is particularly important in case-control studies, especially in newborn infants, where the presence of numerous antibiotics is very common. These contaminating antibiotics prevent the use of these samples in bacterial killing assays that are crucial for assessing immune responses.

Using Group B Streptococcus as a target, The Pathogen Immunology Group at UKHSA-Porton have developed a process to easily remove all types of antibiotics from these samples, making killing immune assays possible. This process, using commercially available products, is fast, reproducible, and can process 96 samples at a time. This work will also be critical for future studies to measure immune responses to other important bacterial pathogens of AMR concern (*Klebsiella pneumoniae*, Group A Streptococcus, *Escherichia coli* and so on).

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UK Health Security Agency (UKHSA) prevents, prepares for and responds to infectious diseases, and environmental hazards, to keep all our communities safe, save lives and protect livelihoods. We provide scientific and operational leadership, working with local, national and international partners to protect the public's health and build the nation's health security capability.

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