

English surveillance programme for antimicrobial utilisation and resistance (ESPAUR)

Report 2023 to 2024

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Content has been divided into chapters with sub-sections, to allow the reader to navigate to the most relevant topics.

This report is accompanied by an annexe, infographics, data appendices in the form of spreadsheets and downloadable slide decks of the graphs. These can be all accessed from the <u>ESPAUR web page</u>.

Citation

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Executive summary

In 2023, the burden of antimicrobial resistance (AMR), calculated by determining the rates of resistance to antibiotics in organisms¹ selected for their public health importance, surpassed 2019 levels by 3.5%. This was largely due to changes in the rates of *Escherichia coli* (the most frequently reported cause of resistant bacteraemia within AMR burden pathogens at 68% in 2023). The rise in the AMR burden followed an initial reduction at the beginning of the pandemic, with year-on-year increases of resistant bacteraemia reported since 2020. In 2023, Enterobacterales (*E. coli, Klebsiella pneumoniae* and *K. oxytoca*) together comprised 83% of the AMR burden, followed by Gram-positive organisms (*Enterococcus* spp., *Staphylococcus aureus* and *Streptococcus pneumoniae*) at 14%.

As in previous years, the AMR burden in bacteraemia in 2023 varied markedly across the regions of England, with the rate of resistant bacteraemia highest in the London region (41.5 per 100,000), compared to the South West region (25.9 per 100,000). Variation in burden was also seen when patients were stratified by ethnicity, with the highest percentage resistant reported in the Asian or Asian ethnic groups (39.4%), almost double that seen when compared to White ethnic groups (20.1%).

In 2023, *E. coli* bacteraemia resistance to multiple antibiotics increased compared to 2019. In particular, 42.9% and 15.8% of isolates were resistant to co-amoxiclav and third-generation cephalosporins respectively, hence their role in empirical sepsis regimes requires careful consideration. Antibiotic resistance also increased across most major antibiotic classes in *Klebsiella pneumoniae* between 2019 and 2023.

In 2023, the overall crude case fatality rate for 30-day all-cause mortality in patients with selected² Gram-negative bacteraemia was 15.5%, with a statistically significant higher all-cause mortality rate for patients infected with a strain resistant to one or more AMR burden-defined antibiotics (16.9%), compared to those with a susceptible strain (15.1%). Thirty-day all-cause mortality in the context of a carbapenemase-producing organism (CPO) infection from a sterile site was 22.9% in 2023.

Since 2021, the rates of reported carbapenemase-producing organisms (CPO) from all sample types have doubled (2021: 4.7 per 100,000 versus 2023: 10.1 per 100,000).

In early 2024, the Global Antimicrobial Resistance Surveillance System on Emerging Antimicrobial Resistance Reporting (GLASS-EAR) issued a request for information to Antimicrobial Resistance (AMR) National Focal points enrolled in GLASS-EAR to rapidly assess the current global situation in view of the increased identification of isolates of hypervirulent Klebsiella *pneumoniae* (hvkp) ST23 carrying carbapenemase genes reported in several

¹ E. coli, K. pneumoniae, K. oxytoca, Pseudomonas spp., Acinetobacter spp., S. aureus, Enterococcus spp., S. pneumoniae

² E. coli, K. pneumoniae, Acinetobacter spp. and Pseudomonas spp.

countries. The <u>report</u> highlights the global spread of *K. pneumoniae* ST23 strains with diverse resistance profiles and virulence characteristics, posing challenges for healthcare systems worldwide, including an outline of the situation as applicable to Europe and the UK.

Rates of fungaemia increased by just over a fifth (22.3%) between 2019 and 2023, with *Candida albicans* having comprised 40% of all bloodstream infection reports due to yeast in 2023, however rates of resistance to key antifungals remained low. Although rates of *Candidozyma auris* (*C. auris*) fungaemia remained low, 2023 however saw increased reports of colonisations, infections and outbreaks in healthcare settings caused by this fluconazole-resistant pathogen, designated a critical priority fungal pathogen by the World Health Organization in 2022.

Total antibiotic consumption increased by 2.4% between 2022 and 2023 (in part linked to a national surge in group A *Streptococcus* (GAS) cases between September 2022 and March 2023), to 17.6 Daily Defined Dose (DDD) per 1,000 inhabitants per day (DID). In 2023, consumption increased in all primary and secondary care settings, except dental practices (6.9%). In 2023, penicillins remained the most frequently used antibiotic group in both primary and secondary care. Increases in consumption were observed for the majority of antibiotic groups between 2022 and 2023 with the highest proportional increase seen for anti-*Clostridioides difficile* agents.

In 2023, antibiotic consumption continued to be highest in general practice (71.7%) and increased by 2.4% since 2019 (2019:1.42 vs 2023: 1.46 items per 100,000 inhabitants per day).

In the past year, antibiotic use in secondary care decreased by 1.9% (from 4,781 to 4,690 DDDs per 1,000 admissions), with a 2.7% decrease observed in outpatient prescribing from 1,628 to 1,585 DDDs per 1,000 admissions) and a 1.5% decrease in inpatient prescribing from 3,153 to 3,105 DDDs per 1,000 admissions). Total antifungal consumption in 2023 was similar to that seen in 2019 (+0.06%).

In 2023, the sixth national point-prevalence survey (PPS) on healthcare-associated infection (HCAI) was carried out, providing a snapshot of the burden of HCAI and how this has changed over time. Data from 121 NHS trusts/independent sector organisations in England were submitted to the UKHSA. For the first time, mental health and community NHS trusts participated in the national PPS. Interim results show that the overall prevalence of HCAI was 7.6%, the most common types of HCAI being pneumonia or lower respiratory tract infections (29.6%), followed by urinary tract infections (17.5%) and sepsis and disseminated infections (10.6%). The 2 most used antimicrobials were the antibiotics co-amoxiclav (16.5%) and piperacillin/tazobactam (8.8%).

By the end of the 2023 to 2024 financial year, 24% of Integrated Care Boards (ICBs) had met the National Action Plan (NAP) targets (<u>1</u>) for reducing total antimicrobial prescribing in primary care, reflecting an overall improvement compared to the previous year. One-fifth of NHS trusts

(30 out of 132) achieved the NHS Standard Contract target to reduce 'Watch' and 'Reserve' prescribing by 10% from the 2017 baseline.

As in previous years, the <u>Treat Antibiotics Responsibly, Guidance, Education and Tools</u> (<u>TARGET</u>) website saw the number of views almost double in 2023 to 2024, compared to the previous year (2022 to 2023). TARGET has published updated diagnostic quick reference tools (for abnormal vaginal discharge and chlamydia) and knowledge mobilisation activities to action the <u>Start Smart Then Focus</u> framework were carried out including a training workshop.

The <u>national intravenous-to-oral switch (IVOS) in children and young people criteria</u> was published in June 2024, following a systematic review and a 2-step modified Delphi process. Following a 4-stage modified Delphi process, adapted AWaRe classifications were agreed with 16 antibiotics differing in classification when comparing classifications based on the 2023 WHO and the proposed UK adapted indexes, suggesting UK-AWaRe classifications are more stringent.

A wide range of new and ongoing research projects are reported in the field of HCAI and AMR in the last year, covering many of the major themes of the UK NAP for AMR, including stronger laboratory capacity and surveillance in AMR, human infection prevention and control, and optimal use of antimicrobials.

The <u>UK 2024 to 2029 AMR NAP</u> was announced in May 2024. It builds on the work of the earlier programme strengthening the UKs surveillance, guidance and IPC AMR associated activity. This report highlights the burden of infection, antimicrobial resistance and usage the new programme will need to address, a substantial challenge.

Infographics visualising the main findings from the report are available on the <u>ESPAUR report</u> <u>web page</u>.

This report details considerable challenges ahead – with rising numbers of infections and proportions that are drug resistant, and widening gaps in inequalities. The continued impact of the COVID-19 pandemic is likely to be profound, with returned global travel coinciding with residual effects of altered healthcare and changes in community vulnerability to seasonal pathogens. It also highlights key differences in burden by ethnicity and socio-economic class. All of these areas also represent avenues for change however, with the potential to further our understanding of trends and population differences, and in developing interventions to help redress these increases. This will be the focus of the early stage of the 2024-2029 AMR National Action Plan activity. The continued strengthening of our capabilities to monitor and mitigate AMR will be essential to the endeavour.

Chapter 1. Introduction

The 2023 to 2024 ESPAUR report offers a comprehensive analysis of the national data on antimicrobial prescribing, resistance and stewardship and highlights the pertinent development and trends.

Chapter 2 focuses on antimicrobial resistance (AMR) and describes the AMR trends in England. The chapter examines the increasing rates of resistant bacteraemia between 2019 and 2023, particularly among the most deprived populations. Notably, a 3.5% increase in the AMR burden was recorded between 2019 and 2023. The overall burden of resistance varied across geography, ethnic group and deprivation: with the highest burden observed in London and the North West. Notably, the highest rate of AMR burden was reported in the Asian or Asian British ethnic group (33.3 per 100,000 population; 39.4% resistant). Between 2019 and 2023 overall rates of reported bacteraemia for children aged 0 to 17 years also increased from 118.5 to 148.6 per 100,000 population. It includes a vignette on extensively-drug resistant *Salmonella* Typhi in travellers returning from Pakistan, where there is a large, multi-year ongoing outbreak, and a new section on resistance of *Mycoplasma genitalium*, focused on azithromycin and moxifloxacin resistance.

Chapter 3 provides trends on antimicrobial consumption. In 2023, England's total antibiotic consumption was 17.6 Daily Defined Doses (DDD) per 1,000 inhabitants per day (DID), a 2.4% increase from 2022 but 1.9% below pre-pandemic levels. Most primary and secondary care settings with the exception of dental practices saw increased antibiotic use compared to the preceding year. Antibiotic use in primary care settings accounted for 79.7% of all consumption, with penicillins representing the most used antimicrobials. Significant rises were observed in the usage of anti-*Clostridioides difficile* agents, reflecting higher *C. difficile* cases, and also in first and second-generation cephalosporins. Antibiotic use returned to or exceeded 2019 levels in all age groups, with the highest rates among those aged over 65 years old. Secondary care also saw increases, particularly in accident and emergency and orthopaedics. Antifungal and antiviral usage patterns shifted, with systemic antifungals rising steadily since a pandemic dip, and antiviral use dropping by 45% due to fewer COVID-19 cases. Antiparasitic consumption data included anthelmintics for the first time and provides a useful baseline to track.

Chapter 4 reports on the Point-Prevalence Survey (PPS) on healthcare-associated infection (HCAI), antimicrobial use (AMU) and antimicrobial stewardship. This was the sixth national PPS on HCAIs and the third national survey on AMU in England and aims to provide a snapshot of the burden of HCAI and describe AMU to allow meaningful comparisons between organisations over time. This will also provide an opportunity to understand the impact of changes to healthcare since the COVID-19 pandemic. The survey showed that in England the total prevalence of HCAIs in the PPS sample of patients was 7.6%. Acute NHS trusts had an overall prevalence of 8.0%. Pneumonia and lower respiratory tract infections were the most common type of HCAI (29.6%). A healthcare related COVID-19 infection was reported in 9.1% of patients.

Chapter 5 summaries antimicrobial stewardship (AMS) referencing several initiatives and findings aimed at improving antibiotic use and management. The TARGET antibiotics toolkit saw a significant increase in views, aided by the addition of antimicrobial prescribing summary tables and new diagnostic tools. Knowledge mobilisation activities using the knowledge-to-action framework identified barriers such as time constraints and limited resources, while emphasising the importance of engagement with microbiology consultants for effective implementation. A systematic review and Delphi process led to new national criteria for IV-to-oral switch in paediatrics and adapted WHO AWaRE classifications for paediatrics in the UK.

Chapter 6 of the report focuses on NHS England's improvement and assurance schemes. These are aimed at promoting the prudent use of antimicrobials across Integrated Care Systems (ICSs) to optimise patient outcomes and combat AMR. In the financial year 2023 to 2024 these schemes included the NHS Oversight Framework. Only 24% of Integrated Care Boards (ICBs) met the national target for total primary care antibiotic prescribing, but 95% met the target for broad-spectrum antibiotic prescribing. The National Medicines Optimisation Opportunities saw a significant increase in the prescribing of amoxicillin 5-day course packs. The Pharmacy Quality Scheme (PQS) continued to re-incentivise the TARGET resources, leading to widespread patient engagement and management of infections within pharmacies. The NHS Standard Contract target for reducing 'Watch' and 'Reserve' antibiotic prescribing was met by 20% of trusts, with a slight reduction in overall antibiotic consumption. Lastly, the Commissioning for Quality and Innovation (CQUIN) framework successfully promoted the prompt switching of intravenous to oral antimicrobial treatments, with 97% of participating trusts meeting the target.

Chapter 7 highlights professional education, training, and public engagement efforts in antimicrobial stewardship (AMS). TARGET collaborated with the Royal College of General Practitioners (RCGP) to deliver webinars and updated training resources, significantly increasing views of the TARGET toolkit. The UK Health Security Agency (UKHSA) and RCGP ran a campaign around World AMR Awareness Week, boosting toolkit engagement by 61%. The Antibiotic Guardian initiative saw 89 organizations register AMS activities, updated pledges, and expanded the Schools Ambassadors Programme. Public awareness campaigns and elearning courses were also developed and disseminated, addressing knowledge gaps in infection prevention and control (IPC) among teachers. Additionally, the 'Antimicrobial Prescribing and Stewardship' Competency Framework was updated using input from multidisciplinary professionals.

Chapter 8 outlines a broad range of new and ongoing research projects in HCAIs and AMR conducted by UKHSA with academic partners from April 2023 to March 2024. It highlights key contributions to the UK National Action Plan (NAP) for AMR 2019 to 2024 and how they align with the objectives of the latest NAP for 2024 to 2029, which has identified new research priorities. Over 100 peer-reviewed papers were published. Notable projects from the 2 NIHR-funded Health Protection Research Units (HPRUs) on AMR – long term collaborations with UKHSA and University of Oxford and Imperial College London are showcased, demonstrating significant impacts of these units on public health practice and policy.

The final chapters (Chapter 9 and 10) of the report focuses the attention on the ESPAUR's contributors and audience. Our thanks to all our contributing stakeholders whose broad breadth work and activities not only make up the report but influence policy in the face of the global health threat we are facing in AMR. Following on from the 10th ESPAUR report last year, user feedback was collated with surveys completed by a total of 797 attendees of the 2 most recent annual ESPAUR webinars in 2022 and 2023. Encouragingly the data showed that 75.7% in 2021 to 2022 and 96.5% in 2022 to 2023 endorsed the ESPAUR report to other stakeholders. We hope to keep building on the success of ESPAUR with stakeholder support whilst listening and adapting to our user feedback.

Chapter 2. Antimicrobial resistance (AMR)

Main messages

Bacteraemia: In 2023, the overall rates of bacteraemia due to the organisms used to calculate the burden of AMR (*Escherichia coli, Klebsiella pneumoniae, Klebsiella oxytoca, Pseudomonas* spp., *Acinetobacter* spp., *Staphylococcus aureus, Enterococcus* spp., and *Streptococcus pneumoniae*) were similar compared to 2019. This was largely due to the rates of *E. coli* (the most frequently reported cause of bacteraemia) remaining below pre-pandemic levels.

Fungaemia: Rates of fungaemia increased by 22.3% between 2019 and 2023. *Candida albicans* comprised 40% of all bloodstream infection reports due to yeast in 2023, however rates of resistance to key antifungals remained low. Rates of *C. auris* fungaemia remained low, however 2023 saw increased reports of colonisations, infections and outbreaks in healthcare settings caused by this multi-drug resistant pathogen.

Antimicrobial resistance within bacteraemia: The overall burden of resistance, estimated from cases of bacteraemia due to *E. coli, K. pneumoniae, K. oxytoca, Pseudomonas* spp., *Acinetobacter* spp., *S. aureus, Enterococcus* spp., and *S. pneumoniae* resistant to one or more critically important antibiotics (see Annexe table 2.4 for antibiotic list) increased by 3.5% between 2019 and 2023.

The AMR burden varied by region, patient age, ethnic group and indices of multiple deprivation. Nationally, the highest AMR burden rates were seen in: the London region, within the Asian or Asian British ethnic group, and in the most deprived populations of England. The difference between the most and least deprived widened between 2019 and 2023. The highest burdens in terms of number and rate of both bacteraemia and resistant bacteraemia were seen in the youngest and oldest age groups.

Enterobacterales dominated the burden of antibiotic-resistant bacteraemia, comprising 83.4% in 2023. *E. coli* was responsible for over 65% of antibiotic-resistant bacteraemia over the past 5 years, peaking in 2019 at 72.9%. Between 2019 and 2023, *E. coli* and *K. pneumoniae* resistance to multiple antibiotics increased, with significant rises reported for both organisms to third-generation cephalosporins, piperacillin with tazobactam, gentamicin and amikacin.

In 2023, the overall case fatality rate for 30-day all-cause mortality in patients with selected Gram-negative bacteraemia (*E. coli, K. pneumoniae, Acinetobacter* spp. and *Pseudomonas* spp.) was 15.5%. Thirty-day all-cause case fatality rates increased to 16.9% when caused by isolates resistant to one or more AMR-burden defined antibiotics.

The overall burden of antibiotic-resistant bacteraemia due to common Gram-positive pathogens (*Enterococcus* spp. (9.0%), *S. aureus* (4.7%), and *S. pneumoniae* (0.4%) remained relatively unchanged at 14.1% in 2023 compared to 14.3% in 2019.

Carbapenemase-producing organisms (CPOs): The rates of reported CPOs from all clinical sites per 100,000 population doubled since 2021 (4.7 per 100,000 in 2021 to 10.1 per 100,000 in 2023), with absolute numbers of episodes reported across all sample groups (screening, sterile site and other sample types) having increased. Thirty-day all-cause mortality in the context of a carbapenemase-producing organism (CPO) infection from a sterile site was 22.9% in 2023.

Since mandatory surveillance of CPO began in October 2020, New Delhi metallo-betalactamase (NDM) has now replaced OXA-48-like as the predominant resistance mechanism detected in England in 2023 when considering all CPO sample groups, although the distribution of carbapenem resistance genes varies geographically. When indicated, this has implications for treatment, as NDM-producing organisms have extremely limited treatment options.

Paediatrics: Between 2019 and 2023, rates of reported bacteraemia in children aged 0 to 17 years increased from 118.5 to 148.6 per 100,000 population (n=13,973 to 17,663), with approximately two-thirds of the rate rise due to coagulase-negative *Staphylococcus*, and *Micrococcus* species. Bacteraemia rates were highest in children under one year old (1,285.1 per 100,000 population in 2023). Between 2019 and 2023, rates of group A *Streptococcus* (GAS) increased in 0 to 17 year olds by 124.5%, reflecting the national GAS surge seen at this time. *S. aureus, S. pneumoniae* and *E. coli* are important pathogens in 1 to 17-year olds, and *E. coli, S. aureus*, Group B *Streptococcus* and *E. faecalis* in under one-year olds.

National Action Plan: The UK NAP ambition for AMR 2019 to 2024 aimed to reduce the estimated number of antibiotic-resistant infections in the UK by 10% from the 2018 baseline by 2025 (<u>1</u>), measured by a subset of antibiotic-resistant infections used to calculate the AMR burden for the ESPAUR report. In England, a 12.8% increase in estimated antibiotic-resistant infections (<u>2</u>) was recorded between 2018 and 2023 (from 59,171 to 66,730), driven by *E. coli* resistant to third-generation cephalosporins. Third-generation cephalosporin-resistant Enterobacterales are listed within the <u>WHO critical priority pathogen list</u> recognising their threat to public health due to limited treatment options, high disease burden, and need for targeted polices and interventions.

Other specialist disease areas: In 2023 the proportion of multi-drug resistant *Mycobacterium tuberculosis* peaked at 2.4% (n=71); the highest number since 2013.

In the Gonococcal Resistance to Antimicrobials Surveillance Programme, no cases of ceftriaxone resistance were observed. However the frequency of ceftriaxone-resistant cases reported outside the programme, including those with extensive drug-resistance, increased. Surveillance in *M. genitalium* indicated macrolide resistance declined to 62.2% in 2023 from 69.5% in 2019, however fluroquinolone resistance increased from 8.4% in 2019 to 12.1% in 2023. Dual resistance remained fairly stable over the period (10.3% in 2023).

There has been an increase in cases reported in England associated with a multi-year outbreak of extensively-drug resistant *Salmonella* Typhi in Pakistan; the highest number of cases to date was reported in 2023 (n=52).

Introduction to Chapter 2

This chapter presents findings from antimicrobial resistance (AMR) surveillance, predominately based on analysis of resistance in pathogens of public health importance causing bacteraemia and fungaemia, undertaken by the UK Health Security Agency (UKHSA). It reports bacteraemia resistance trends as recommended for surveillance by the Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare-Associated Infections (APRHAI) (<u>3</u>), and resistance related to *Mycobacterium tuberculosis, Neisseria gonorrhoeae,* and other common bacterial, fungal and parasitic infections. This chapter focuses predominately on organisms isolated from blood cultures (bacteraemia and fungaemia for bacteria and fungi respectively) due to the associated severity and impact of AMR on these clinical infections. However, evolving resistance in blood-borne viral infections, gastrointestinal infections, as well as Malaria are also covered, given the clinical impact. Antimicrobial consumption is detailed in <u>Chapter 3</u>.

Calculation of the 'AMR burden' was undertaken using previously described methodology (<u>4</u>) used to estimate the burden of antibiotic-resistant bacteria of public health importance, and this terminology is used throughout the chapter. In brief, the total number of resistant bacteraemia was estimated using the proportion of each pathogen that was reported as resistant to one or more specified antibiotics. These organisms and defined antibiotic combinations are listed in <u>Table 2.1</u>. Please see the <u>Annexe Table 2.1 and 2.4</u> for further details of specific pathogen-resistance combinations.

Pathogens	Antibiotic class resistance
Gram-negative bacteria	
Escherichia coli	carbapenems, third-generation cephalosporins,
Klebsiella pneumoniae	aminoglycosides, or fluoroquinolones
Klebsiella oxytoca	
Acinetobacter spp.	aminoglycosides and fluoroquinolones, or carbapenems
Pseudomonas spp.	3 or more antimicrobial groups, or carbapenems
Gram-positive bacteria	
<i>Enterococcus</i> spp	glycopeptides
Staphylococcus aureus	meticillin
Streptococcus pneumoniae	penicillin and macrolides, or penicillin alone

 Table 2.1. Bacteria of public health importance due to association with antibiotic

 resistance, and selected resistance profiles used to estimate AMR burden

Data on antimicrobial-resistant infections for the period 2019 to 2023 is presented as trends in either numbers of patient episodes (defined in the <u>Annexe accompanying this report</u>), percentage resistance or as a rate per 100,000 population. More detailed analysis of AMR burden pathogens, stratified by patient age group, biological sex, regional location within

England, 30-day all-cause case fatality rate (2023 data only), deprivation index, and ethnicity, are presented within the chapter or its appendices.

The primary data source used was the UKHSA's Second Generation Surveillance System (SGSS, described further in previous reports (<u>4</u>, <u>5</u>). Additional data sources, analytical methods, caveats, and additional resources are described in more detail in the <u>Annexe accompanying this</u> report. Data and figures are presented in the <u>data spreadsheets and downloadable slidedecks</u>, respectively.

Trends in incidence of priority pathogens causing bacteraemia

In 2023, there were 175,230 patient episodes of bacteria or fungi isolated from blood identified through reports received from laboratories in England (see <u>accompanying data tables</u>). This is a 13.6% increase compared to episodes reported in 2019 (n=154,245). The vast majority of this increase can be explained by increases in coagulase-negative staphylococci (CoNS) and *Micrococcus* sp. The factors surrounding the increased isolation of these organisms, as well as the clinical significance (which cannot be ascertained from routine linked data) requires further consideration at both local and national level.

In 2023, a reported 88.6% (n=155,298) of episodes were monomicrobial (a single organism isolated from blood). Similar to previous reports ($\underline{5}$, $\underline{6}$), the organisms most frequently isolated from monomicrobial bacteraemia were CoNS (29.4%), *E. coli* (21.1%) and *S. aureus* (7.4%). Among the 11.4% (n=19,932) of episodes that were polymicrobial (more than one bacterial or fungal species isolated from blood), the most frequently identified organisms were CoNS (15.8%), *E. coli* (13.5%), and *K. pneumoniae* (5.1%).

The AMR bacteraemia burden (<u>Table 2.1</u>) in 2023 was very similar to that reported in 2019, following a decline and subsequent increase during and after the COVID-19 pandemic. The incidence of bacteraemia due to *Acinetobacter* spp., *Enterococcus* spp., *K. pneumoniae, K. oxytoca*, and *S. aureus* increased between 2019 and 2023 from between 5.9% and 15.3% (<u>Figure 2.1</u>). In contrast, in 2023, the incidence of *E. coli* and *S. pneumoniae* bacteraemia remained below pre-pandemic levels, but have nonetheless risen since the declines seen during the COVID-19 pandemic.

More detail on the trends in incidence and mandatory national surveillance for *E. coli, S. aureus*, *K. pneumoniae and Pseudomonas aeruginosa* bacteraemia are available in the <u>annual</u> <u>epidemiological commentary</u>. In addition, incidence and resistance data for other Gramnegative organisms such as *Serratia* spp., *Enterobacter* spp., *Citrobacter* spp., *Proteus* spp., *Providencia* spp., *Morganella* spp. and *Stenotrophomonas* spp. are included in the <u>accompanying data tables</u>.

Figure 2.1. Annual incidence rate of selected pathogens** of public health importance causing bacteraemia, per 100,000 population, England 2019 to 2023



* Note in this graph, the asterisk denotes that data for *E. coli* and *S. aureus* incidence are based on mandatory surveillance data, while reporting of the other pathogens was voluntary. ** See <u>Table 2.1</u>

Box 2.1. Paediatric bacteraemia trends between 2019 and 2023

Trends in the incidence and causative agents of bacteraemia in the paediatric population differ from that of adults and warrant separate consideration. Data used for this analysis was taken from the communicable disease reporting module of UKHSA's Second Generation Surveillance System (SGSS) to best capture all causative agents, and may differ from data used to estimate the AMR burden which is used elsewhere in this report.

Between 2019 and 2023, overall rates of reported bacteraemia for children aged 0 to 17 years, increased from 118.5 to 148.6 per 100,000 population (n=13,973 to 17,663), (Box Figure 2.1.1). Box Figure 2.1.1). Bacteraemia rates were highest in children aged under 1-year (1,285.1 per 100,000 population in 2023; n=7,663), having risen 28.5% since the 5-year low in 2020 (1,000.4 per 100,000 population, n=5,996). In <1-year-olds in 2023, half of the bacteraemia episodes occurred in infants that were older than one month, and half in infants younger than one month (with 19.6% occurring in 0-to-3-day olds and 30.4% in 4-day- to one-month-olds). The number of bacteraemia episodes remained stable from 2019 to 2023 in 0-to-3-day olds and rose by around one quarter in the 4-day- to one-year-olds.



Box figure 2.1.1. Annual incidence of bloodstream infections, per 100,000 population by

Between 2019 and 2023, the incidence of CoNS and *Micrococcus* spp. increased across all paediatric age groups; approximately two-thirds of the 25.4% rate rise across the paediatric population is attributable to CoNS and Micrococcus spp. The highest rate of CoNS and Micrococcus spp. in 2023 was in those aged <1 year old, with a rate of 662.2 per 100,000 population; a rise of 33.5% compared to 2019 (476.2 per 100,000). The highest increase in rate of CoNS and *Micrococcus* spp. was in 5 to 17 year olds, rising by 53.4% from 2019 to 2023. The factors surrounding the increased isolation of these organisms, as well as the clinical significance (which cannot be ascertained from routine linked data) requires further consideration at both the local and national level.

In 2023, the majority of bacteraemia episodes in 1 to 4 year olds was attributable to CoNS and Micrococcus spp. (42.7%) and oral and other streptococci (10.3%). Rates of Group A Streptococcus (GAS) bacteraemia rose by 122.7% between 2019 and 2023 (3.7 to 8.3 per 100,000 population), corresponding with the national GAS surge which was seen at this time,

peaking in winter 2022/2023, and accounting for 4.4% of the bacteraemia episodes in the 1 to 4 year olds (n=206) in 2023 ($\underline{7}$). *S. pneumoniae* comprised a further 4.1% of the total bacteraemia counts, with rates increasing by 44.7% between 2019 and 2023 (5.5 to 7.9 per 100,000.

In the 5 to 17 year olds, CoNS and *Micrococcus* spp. comprised 43.6% of bacteraemia episodes, while 8.1% of bacteraemia episodes were attributable to *S. aureus*, increasing in rate by 21.1% from 2019 to 2023 4.0 to 4.9 per 100,000 population Increases were also seen in bacteraemia due to GAS (0.9 to 2.1 per 100,000 population, a 136.9% increase in rate) and *Salmonella* Typhi and Paratyphi (1.0 to 1.7 per 100,000 population, a 63.4% increase in rate) between 2019 and 2023. Predominately associated with travellers returning from regions with high endemicity, public health measures such as targeted messaging and vaccine uptake prior to travel may be helpful in reducing the number of *Salmonella* Typhi and Paratyphi infections. As seen with the other paediatric age groups, the majority of the rise in bacteraemia episodes in 5- to 17-year-olds was attributable to CoNS and *Micrococcus* spp. (60.3%).

In the under 1 year olds, *E. coli, S. aureus*, Group B *Streptococcus* (GBS) and *E. faecalis* remain important pathogens (comprising 18.1% of bacteraemia episodes in 2023), and bacteraemia rates (and counts) remained consistent or decreased between 2019 to 2023. The exception is *E. faecalis*, where the rate increased 10.0% during this period, to 34.9 per 100,000 in 2023. Excluding CoNS and *Micrococcus* spp., in the 0- to 3-day-olds, GBS predominated, followed by *E. coli*, and *S. aureus*, despite a 33.4% decrease in GBS counts (n = 317 in 2019 to n = 211 in 2023). In 2019 and 2023, the most frequently isolated pathogen from blood (after CoNS, *Micrococcus* and oral and other streptococci) in the 4-day- to <1-month-olds and 1-month- to <1-year-olds was *E. coli* (n = 172 and n = 256, respectively in 2023), followed by *S. aureus* (n = 114 and n = 159, respectively in 2023) and GBS (n = 68 in 2023) in the 4-day- to <1-month-olds and *E. faecalis* (n = 119 in 2023) in 1-month- to <1-year-olds (see data tables, accessory 18 and 19).



Box figure 2.1.2. Trends of the most commonly isolated pathogens in bacteraemia in 1 to 17 years old, in England between 2019 and 2023

The prevalence and trends of *E. faecalis* and *E. faecium* bacteraemia differ in the <1 year group compared to the >1 year groups (Box Figure 2.1.3). In <1-years-old, *E. faecalis* predominates. In the 1- to 17-years age groups, rates of *E. faecalis* and *E. faecium* are similar in 2023.





Note: The axes have different scales.

Supporting data can be found in the <u>data tables</u>, and further data on paediatric bacteraemia and resistance can be found in the latest <u>paediatric HPR</u>.

Antibacterial resistance

AMR burden

The burden of resistance, estimated by the total number of bacteraemia episodes due to bacteria of public health importance resistant to one or more defined antibiotics (<u>Table 2.1</u>), increased by 3.5% between 2019 (n=18,082) and 2023 (n=18,723; <u>Figure 2.2</u>). The methodology for this section can be found in <u>the accompanying Annexe</u>.





Enterobacterales (*E. coli, K. pneumoniae*, and *K. oxytoca*) dominated the burden of antibioticresistant bacteraemia, comprising 83.4% of the total number in 2023. *E. coli* was singularly responsible for over 65% of antibiotic-resistant bacteraemia over the past 5 years, peaking in 2019 at 72.9%. The relative contribution of *K. pneumoniae* increased from 11.1% in 2019 to 14.1% in 2023.

The burden of antibiotic-resistant bacteraemia due to common Gram-positive pathogens (*Enterococcus* spp. (9.0%), *S. aureus* (4.7%), *S. pneumoniae* (0.4%) remained relatively unchanged at 14.1% in 2023. Further detail is available in the <u>data tables accompanying this report</u>.

Box 2.2. UK AMR National Action Plan (NAP) in England

In November 2018, the European Centre for Disease Prevention and Control (ECDC) published a methodology for estimating incidence and attributable deaths due to severe antibiotic-resistant bacterial infections (2). This method calculated a ratio relating the number of antibiotic-resistant bacteraemia to the number of antibiotic-resistant surgical site infections, antibiotic-resistant urinary tract infections, and antibiotic-resistant respiratory infections, using point prevalence survey data alongside bacteraemia incidence data reported through ECDC surveillance schemes. A corresponding estimate of mortality was also calculated using the estimated case proportion deceased according to severe resistant infection type (site, organism, and resistance). Details on the derivation of the ratios are available in the ECDC publication (2). The organism-antibiotic combinations included in this methodology represent a sub-set of those used in the ESPAUR bacteraemia AMR burden estimates; further details are available in the <u>Annexe</u>.

The 2019 to 2024 UK NAP ambition for AMR was to reduce the estimated total number of antibiotic-resistant infections in the UK by 10% from the 2018 baseline by 2025 (<u>1</u>). The method of estimation used to monitor resistance was derived from the ECDC method described above. In England, a 12.8% increase in severe antibiotic-resistant infections was recorded between 2018 and 2023 (from 59,171 to 66,730; <u>Box Figure 2.2</u>), driven by *E. coli* resistant to third-generation cephalosporins (68.9% of estimated severe antibiotic infections in 2023). An initial increase occurred between 2018 and 2019 followed by a 15.1% decline between 2019 and 2020, primarily reflecting a decrease in *E. coli* cases during the COVID-19 pandemic, which has since increased by 26.1% between 2020 and 2023 to exceed the pre-pandemic peak in 2019 (<u>8</u>). The corresponding estimated number of deaths due to severe antibiotic-resistant infections in 2023 (n= 2,640) was higher than the 2019 estimate (n= 2,393) and has risen by 27.9% since the COVID-19 pandemic in 2020 (n= 2,064).



Box Figure 2.2. Estimated number of severe antibiotic-resistant infections by year

* The 2019 to 2024 AMR NAP was UK-wide; this figure depicts a calculation of the target based on data from England only and only includes estimates for England

The UK's 2024 to 2029 AMR NAP was published in May 2024. The 2024 to 2029 NAP includes 5 human health targets, one of which is to prevent any increase in a specified set of drug-resistant infections in humans compared to the 2019 or 2020 financial-year baseline; more details are available in the <u>Confronting antimicrobial resistance 2024 to 2029 Policy paper</u>.

Regional variation in the burden of AMR bacteraemia and the incidence of bacteraemia caused by resistant AMR burden pathogens is shown in <u>Figure 2.3</u>. The London region reported the highest AMR burden rate (41.5 per 100,000 population) followed by the North West (35.8 per 100,000 population) and Yorkshire and Humber (34.7 per 100,000 population). The lowest AMR bacteraemia burden rate was reported in the South West (25.9 per 100,000 population).

Whilst the North East had the highest incidence rate of bacteraemia (186.5 per 100,000 population), the resistance rate (30.0 per 100,000 population) was lower than that seen in many other regions. Similarly, London, which had the highest resistance rate, was the region with the lowest incidence rate of selected bacteraemia pathogens (139.0 per 100,000). However, variations in testing practice across trusts may impact regional bacteraemia rates.

Figure 2.3. Regional variation in rate per 100,000 population of a) the estimated burden of AMR and b) the estimated numbers of bacteraemia in England in 2023



Since 2021, variation in the AMR bacteraemia burden (<u>Table 2.2</u>) has been reported by ethnic group. Of those with a reported ethnicity, the highest number and rate per 100,000 population of bacteraemia episodes (as per AMR burden combinations described in <u>the Annexe</u> <u>accompanying this report</u>) was recorded in people reported as being in a white ethnic group (88.4% of AMR burden pathogen episodes; n=71,457) in 2023, of which 20.1% were recorded as resistant to at least one selected antibiotic. The highest percentage of resistance was reported in the Asian or Asian British ethnic group (39.4%; n=1,835), followed by the Black, African, Caribbean or black British ethnic group (26.5%; n=663).

Ethnic group	Rate of bacteraemia per 100,000Rate of resistant bacteraemia per 100,000 population (n)		Percent resistant (95% confidence intervals)
White	146.7 (71,457)	29.5 (14,365)	20.1% (19.8 to 20.4)
Asian or Asian British	84.5 (4,659)	33.3 (1,835)	39.4% (38.0 to 40.8)
Black, African, Caribbean or black British	104.0 (2,505)	27.5 (663)	26.5% (24.8 to 28.2)
Mixed or multiple ethnic groups	37.9 (651)	8.4 (145)	22.3% (19.1 to 25.5)

Ethnic group	Rate of bacteraemia per 100,000 population (n)		Percent resistant (95% confidence intervals)
Any other ethnic group	23.9 (300)	4.4 (55)	18.2% (13.9 to 22.6)
Not known or Not stated	N/A (1,304)	N/A (208)	16.0% (14.0 to 17.9)

* 6,130 (7.6%) bacteraemia episodes could not be linked to obtain ethnic group information. The percentage resistant in this group was 19.8% (n=1,212).

In 2023, the resistant bacteraemia burden differed according to indices of multiple deprivation (IMD), measured by quintile (where the first quintile represents the population in the most deprived 20% of areas in England and the fifth quintile represents the least deprived 20% of areas) (Table 2.3). From 2019 to 2023, the rate of resistant bacteraemia in the most deprived quintile rose by 9.5% (p<0.05), while the rate in the least deprived group decreased slightly but with no evidence of statistical difference (-0.6%, p>0.05).

In 2023, the rate of resistant bacteraemia was higher in the most deprived quintile (38.1 per 100,000) compared to the least deprived quintile (26.7 per 100,000) (p<0.05), representing a 42.6% higher rate in the most deprived compared to the least deprived; this increased from 2019 where the corresponding difference in resistant bacteraemia rate was 29.4%. The gap in AMR burden between the most and least deprived groups increased between 2019 and 2023 (p<0.05).

IMD quintile	Rate of bacteraemia per 100,000 population (n)	Rate of resistant bacteraemia per 100,000 population (n)	Percent resistant (95% confidence intervals)
1 (most deprived)	173.5 (19,601)	38.1 (4,301)	21.9% (21.4 to 22.5)
2	157.3 (18,299)	34.1 (3,963)	21.7% (21.1 to 22.3)
3	149.8 (17,201)	31.0 (3,559)	20.7% (20.1 to 21.3)
4	145.1 (16,219)	30.2 (3,376)	20.8% (20.2 to 21.4)
5 (least deprived)	130.9 (14,338)	26.7 (2,925)	20.4% (19.7 to 21.1)

Table 2.3. AMR bacteraemia burden by IMD quintile in England in 2023

The burden from all bacteraemia and resistant bacteraemia differed according to age group in 2023 (Table 2.4). The number and rate of both bacteraemia and resistant bacteraemia were highest in the >74 years old age group (bacteraemia rate = 830.0 per 100,000, with 22.1% resistant; resistant bacteraemia rate = 183.8 per 100,000), followed by the 65 to 74 age group and the youngest age group (<1 year old). The number and rate of bacteraemia and resistant bacteraemia were lowest in 5 to 9 year-olds (bacteraemia rate = 12.3 per 100,000, with 13.6% resistant; resistant bacteraemia rate = 1.7 per 100,000).

Age group (years)	Rate of bacteraemia per 100,000 population (n)	Rate of resistant bacteraemia per 100,000 population (n)	Percent resistant (95% confidence intervals)
Under 1	285.1 (1,652)	49.2 (285)	17.3% (15.4 to 19.1)
1 to 4	35.1 (870)	5.1 (128)	14.7% (12.3 to 17.0)
5 to 9	12.3 (411)	1.7 (56)	13.6% (10.3 to 16.9)
10 to 14	13.5 (462)	1.8 (62)	13.4% (10.3 to 16.5)
15 to 44	37.5 (8,122)	7.5 (1,619)	19.9% (19.1 to 20.8)
45 to 64	127.0 (18,506)	26.4 (3,845)	20.8% (20.2 to 21.4)
65 to 74	311.8 (17,359)	68.6 (3,819)	22.0% (21.4 to 22.6)
Over 74	830.0 (40,684)	183.8 (9,008)	22.1% (21.7 to 22.5)
Unknown	0.0 (19)	0.0 (6)	29.4% (9.0 to 49.9)

 Table 2.4. AMR burden from bacteraemia by age group in England in 2023

Gram-negative bacterial infections

Data presented in this section focuses on the most commonly isolated Gram-negative bacterial pathogens and their phenotypic susceptibility. More extensive pathogen and antibiotic combination analysis can be found in the <u>data and figure appendices accompanying this report</u>. Data on acquired carbapenemase-producing Gram-negative organisms (CPO) is presented later in the chapter.

Resistance trends in bacteraemia

Reports of *E. coli* resistance to multiple antibiotics increased between 2019 and 2023 (Figure 2.4). Significant rises (p<0.05) were reported for resistance to third-generation cephalosporins (from 14.5% to 15.8%), gentamicin (from 10.7% to 11.4%), and amikacin (0.9% to 3.1%). In 2023, *E. coli* resistance to co-amoxiclav, ciprofloxacin and carbapenems was 42.9%, 19.2% and 0.5% respectively (Figure 2.4).

Antibiotic resistance increased across most major antibiotic classes in *K. pneumoniae* between 2019 and 2023. (Figure 2.4). Significant increases were seen in resistance to third-generation cephalosporins (16.3% to 18.8%, p<0.05) gentamicin (9.0% to 10.6%, p<0.05), amikacin (1.1% to 2.1%; p<0.05), ciprofloxacin (15.5% to 18.3%, p<0.05) and carbapenems (1.0% to 1.5%, p<0.05).

Rates of resistance to piperacillin with tazobactam increased in both *E. coli* and *K. pneumoniae* from 2019 to 2023; in 2023 the rate in *K. pneumoniae* (23.8%) was nearly double that seen in *E. coli* (12.2%). The European Committee on Antimicrobial Susceptibility Testing (EUCAST) piperacillin with tazobactam breakpoints for Enterobacterales changed in 2021 (9) complicating the interpretation of resistance rate trends over time; this is discussed in more detail in Box 2.3.





* EUCAST piperacillin with tazobactam breakpoints for Enterobacterales changed in $2021(\underline{9})$; see <u>Box 2.3</u> for more details.

Further detail on antibiotic class groupings can be found in the <u>Annexe (Table 2.1)</u> accompanying this report.

Box 2.3. Exploring the effect of the 2021 EUCAST piperacillin with tazobactam breakpoint changes for Enterobacterales – implications for interpretation of national antibiotic resistance trends.

On the 1 January 2021, EUCAST amended the piperacillin with tazobactam clinical breakpoints for Enterobacterales following a public consultation (9). Pharmacokinetic and pharmacodynamic analyses and clinical studies suggested that the previous EUCAST 'R' category (clinically-resistant) was set too high and was associated with methodological testing issues (10, 11). As a result, the 'R' MIC breakpoint was reduced from >16 mg/L to >8 mg/L (susceptible, S ≤8 mg/l) with the 'I' (susceptible, increased exposure) category becoming obsolete (12).

Clinical breakpoint changes are adopted at different time points by local laboratories following their introduction and thus at a national surveillance level, there is a period of transition, sometimes spanning several years, where resistance rates will be reported to national surveillance systems, using both old and new clinical breakpoints. MIC values and disk zone of inhibition diameters are not typically accessible at a national level, with AST data reported

instead as 'S', 'I' or 'R' categories. As this ESPAUR reports spans the period 2019 to 2023, an analysis was performed to review the impact of the clinical breakpoint changes on piperacillin with tazobactam resistance trends against *K. pneumoniae and E. coli* bacteraemia. The impact was assessed by considering the proportion of 'R' *and* 'I' categories, versus only the 'R' category (ESPAUR methodology uses only the 'R' category) of all AST results for *K. pneumoniae and E. coli* over time.

Using the 'I' category as a proxy indicator of pre-version 11 EUCAST clinical breakpoint use, the percentage of bacteraemia episodes reported as 'I' against piperacillin with tazobactam decreased over time (from 2.8% of all tested *E. coli* bacteraemia in 2019 to 0.4% in 2023; see <u>Box Table 2.3.1</u>). In 2023, a small proportion of laboratories have still to transition to the amended clinical breakpoints as evidenced by continued reporting of the 'I' category.

Table 2.3.1. Number and percentage of bacteraemia episodes reported as 'l' by pathogenby year, 2019 to 2023

Year	E. coli n (%) K. pneumoniae n (%		
2019	961 (2.8%)	361 (5.3%)	
2020	606 (2.1%)	286 (4.7%)	
2021	543 (1.8%)	289 (4.2%)	
2022	323 (1.1%)	174 (2.5%)	
2023	145 (0.4%)	87 (1.1%)	

Between 2019 and 2023, resistance to piperacillin with tazobactam rose significantly (p<0.05) from 9.1% to 12.2% in *E. coli* and from 15.1% to 23.8% in *K. pneumoniae*. Retrospective application of version 11.0 clinical breakpoints to 2019 data increased previously-reported piperacillin with tazobactam resistance by 5.3% in *K. pneumoniae* and 2.7% in *E. coli* (Box Figure 2.3.1). Using the amended breakpoints to interpret piperacillin with tazobactam resistance trends between 2019 and 2023 (transformed data), demonstrated more moderate, but still significant (p<0.05) increases in resistance from 11.8% to 12.6% in *E. coli* and 20.4% to 24.9% in *K. pneumoniae*.

Box Figure 2.3.1. Comparison of resistance rates of piperacillin with tazobactam in *E. coli* and *K. pneumoniae* using data as reported to national surveillance versus transformed data, 2019 to 2023



Interpretating national antibiotic surveillance trends spanning clinical breakpoint transition periods requires additional consideration to avoid misinterpretation of data. As reporting laboratories transition to the amended breakpoints, the impact of the change decreases over time with less effect on national surveillance trends (Box Figure 2.3.1). Although a simplistic analysis, with several caveats, the impact of breakpoint changes on Enterobacterales resistance trends is clearly demonstrated for piperacillin with tazobactam. Although the non-transformed data is used within the body of this report (for consistency and in accordance with international surveillance methodology), local, regional and national policy makers should consider the impact of clinical breakpoint changes in their analysis of the report, and that these may not be uniform across affected organisms.

Pseudomonas spp. bacteraemia resistance remained stable from 2019 to 2023 across the major antibiotic classes (Figure 2.5a). Resistance to ciprofloxacin decreased from 8.1% in 2019 to 6.9% in 2023 (p<0.05), and carbapenem resistance in 2023 was 7.6%.

Resistance in *Acinetobacter* spp. bacteraemia also remained relatively stable over the 2019 to 2023 period, however, a decrease in resistance to ciprofloxacin (7.4% to 4.9%) was reported (p<0.05) (Figure 2.5b). In total, 34 (3.1%) carbapenem-resistant *Acinetobacter* spp. isolates were detected in 2023, of which 20 were *Acinetobacter baumannii*.



Figure 2.5a. Antibiotic resistance trends in *Pseudomonas* spp. bacteraemia, 2019 and 2023, England

Note: In this figure, 'carbapenems' refers only to meropenem or imipenem as ertapenem is intrinsically only weakly active against these species, as described in the <u>Annexe (Table 2.1) accompanying this report</u>.





Further detail on antibiotic class groupings can be found in the <u>Annexe (Table 2.1)</u> accompanying this report.

Figure 2.6 below highlights resistance to antibiotics commonly used empirically to treat *E. coli*, *K. pneumoniae*, and *Pseudomonas* spp. bacteraemia. The information may be useful when considering choice of empirical agent for the treatment of suspected Gram-negative infections prior to culture and susceptibility results. The combinations are used for illustrative purposes only and should not be interpreted as defined treatment regimes or as advocating for dual-therapy. Such information may also prove useful to policy makers or antimicrobial stewardship teams when considering and drafting local or regional antibiotic guidelines.

Antibiotic therapy should always be optimised for individual patients and guided by national, regional or local antibiotic policies or by specialist advice, taking into account the clinical scenario (including patient specific factors and allergies), the likelihood of a bacterial infection (and resistance), and weighing the benefits of treatment against harms of the antibiotic. The

antimicrobial prescribing and stewardship competency framework can be consulted for further information $(\underline{13})$.

The overall national resistance rates presented here may not be applicable on an individual level, as additional factors potentially impacting resistance should be considered; these include clinical scenario, prior antibiotic exposure, community versus hospital acquired, age, ethnicity, IMD and region.

Isolates were categorised as 'susceptible' to antibiotic combinations if they were susceptible to either one or both drugs, and as 'resistant' if they were resistant to both individual agents in the combination; only isolates with susceptibility test results for both antibiotics in each combination were included in the analysis. A total of 93.3% of reported *E. coli* bacteraemia isolates were tested for gentamicin susceptibility, compared with 67.7% against amikacin; this is likely due to local variation in testing Policies related to aminoglycoside use.

In *E. coli*, the addition of gentamicin in combination with either co-amoxiclav, ciprofloxacin or third-generation cephalosporins lowers the resistance in empirical treatment regimes from 42.9%, 19.2% and 15.8% respectively to less than 10%. Piperacillin with tazobactam combined with gentamicin lowers the resistance from 12.2% to < 3% which mirrors resistance rates for amikacin alone.

In *K. pneumoniae*, similar decreases to less than 10% resistance are achieved when either coamoxiclav, ciprofloxacin or third-generation cephalosporins are combined with gentamicin in empirical treatment regimes. Piperacillin with tazobactam resistance decreased from 23.8% to 8% when used in combination with gentamicin. This compares with amikacin resistance at <2%.

When gentamicin is combined with piperacillin with tazobactam, ceftazidime, ciprofloxacin or meropenem the resistance in empirical treatment regimens for *Pseudomonas* spp. drops below 2%.

For information on other less frequently reported Gram-negative pathogens, refer to the <u>health</u> <u>protection reports</u>.

Figure 2.6. Resistance to empirical combination regimes used for *E. coli*, *K. pneumoniae*, and *Pseudomonas* spp. bacteraemia in England, 2023



* Further detail on antibiotic class groupings can be found in the <u>Annexe (Table 2.1) accompanying this report.</u> **'Carbapenems' refers only to meropenem or imipenem as ertapenem is intrinsically only weakly active against *Pseudomonas* species, as described in the <u>Annexe (Table 2.1) accompanying this report.</u>

All-cause mortality in Gram-negative Bacteraemia

The overall case fatality rate for 30-day all-cause mortality in patients with selected Gramnegative bacteraemia (*E. coli, K. pneumoniae, Pseudomonas* spp., *Acinetobacter* spp.) was 15.5% in 2023 (estimated number of deaths=7,776); fatality was lowest in children aged 1 to 14 years (4.4%, est.=27) and highest in adults aged 85 years and over (21.8%, est.= 2,346). Male patients had a statistically significant (p<0.05) higher crude case fatality rate (17.1%, est.=4,541) than female patients (13.7%, est.=3,232). Patients infected with a strain resistant to one or more AMR burden-defined antibiotics had a statistically significant (p<0.05) higher crude case fatality rate (16.9%, est.=2,041) compared to those with a susceptible strain (15.1%, est.=5,689).

The case fatality rate varied by Gram-negative organism in 2023, where patients infected with *Pseudomonas* spp. had the highest crude case fatality rate (21.9%, est.=968) followed by *K. pneumoniae* (17.0%, est.=1,404), *E. coli* (14.6%, est.=5,280) and *Acinetobacter* spp. (10.9%, est.=124). Patients infected with an *E. coli* or *K. pneumoniae* strain resistant to one or more AMR burden-defined antibiotics had a statistically significant (p<0.05) higher crude case fatality rate (16.1%, est.=1,559; 19.5%, est.=394 respectively) compared to those with a susceptible strain (14.0%, est.= 3,703; 16.1%, est.=1,002 respectively).

Of those patients for whom ethnicity was reported, the crude case fatality rate was highest in the white ethnic group (16.2%, est.=6,713) and lowest in mixed or multiple ethnic groups (9.5%, est.=34). Case fatality rates in the most and least deprived IMD quintiles were the same (15.6%), however the estimated number of deaths was 30.8% higher in the most deprived quintile (est.=1,701) than in the least deprived quintile (est.=1,300).

Laboratories are reminded to send isolates with exceptional antibiotic resistant phenotypes to the AMRHAI Reference Unit for confirmation. This includes:

- Enterobacterales isolates with a meropenem MIC above the EUCAST screening cut-off (0.125 mg/L) but negative for the 'big' 4/5 carbapenemases, to rule out the presence of rarer carbapenemase families – isolates positive for the 'big 4/5' carbapenemase families and from invasive infections should also be referred for inclusion in the national strain archive
- Enterobacterales resistant to ceftazidime/avibactam, meropenem/vaborbactam or imipenem/relebactam and negative for class B (NDM, VIM or IMP) carbapenemases
- Enterobacterales (excluding *Serratia* spp., *Proteus* spp., *Hafnia* spp. and *Morganella* spp.), *Acinetobacter* spp. and *Pseudomonas aeruginosa* resistant to colistin by broth microdilution
- Acinetobacter spp. suspected to produce a metallo-carbapenemase
- Pseudomonas aeruginosa resistant to all of imipenem, meropenem, ceftazidime and piperacillin/tazobactam and exhibiting strong imipenem/EDTA synergy and positive for VIM, NDM and IMP carbapenemases should be referred for inclusion in the national strain archive – isolates negative for VIM, NDM or IMP carbapenemases and exhibiting strong imipenem/EDTA synergy and/or resistance to

ceftolozane/tazobactam should be referred to rule out presence of rarer carbapenemase families

Further referral criteria and guidance on how to do this is available in the <u>Bacteriology</u> <u>Reference Department user manual</u>.

Acquired carbapenemase-producing Gram-negative organisms (CPO)

Notification data

From 1 October 2020, diagnostic laboratories in England have had a statutory duty to report acquired CPO isolated from human samples, as well as the results of any antimicrobial susceptibility testing (including negative results) and resistance mechanisms to the UKHSA (<u>14</u>). Since October 2020, notifications of CPO have been published <u>weekly</u> and <u>quarterly</u> at national and regional levels, with the recent addition of data on ethnicity and IMD to the quarterly report. Details on notification definition, de-duplication and sample type categorisation are available in Chapter 2 of <u>the Annexe accompanying this report</u>.

In 2023, there were 5,753 notifications (from 4,437 persons) of CPO in England from all specimen types. The rates of reported CPO per 100,000 population have increased yearly since 2021, the first full year of mandatory CPO reporting; 4.7 per 100,000 in 2021 to 10.1 per 100,000 in 2023.

Whilst the proportion of screening (71.8% from 2021 to 2023), sterile site (4.5%) and other samples types (23.7%) has remained stable over the past 3 years, absolute numbers of infections across all categories are increasing, with an 85% and 130% increase in the number of CPOs isolated from sterile or non-screening sites respectively between 2021 and 2023 (Table 2.5).

Specimen type	Percentage of CPO episodes in 2021 (n)	Rate of CPO in 2021 per 100,000 population	Percentage of CPO episodes in 2022 (n)	Rate of CPO in 2022 per 100,000 population	Percentage of CPO episodes in 2023 (n)	Rate of CPO in 2023 per 100,000 population
Sterile site isolates	5.2% (139)	0.2	4.0% (163)	0.3	4.5% (258)	0.5
Screening samples	72.2% (1,930)	3.4	72.4% (2,920)	5.1	71.3% (4,101)	7.2
Other samples	22.6% (605)	1.1	23.6% (952)	1.7	24.2% (1,394)	2.4
Total	(2,674)	4.7	(4,035)	7.1	(5,753)	10.1

Table 2.5. Number and annual rate of CPO episodes by specimen type and year inEngland

Since surveillance of mandatory CPO reporting began in October 2020, New Delhi metallobeta-lactamase (NDM) has now replaced Oxacillinase-48-like (OXA-48-like) as the predominant CPO mechanism detected in England in 2023 (NDM: 2,004 out of 5,753, 34.8%; OXA-48: 1,961 out of 5,753, 34.1%; *Klebsiella pneumoniae* carbapenemase [KPC]: 1,311 out of 5,753, 22.8%). When indicated, this has implications for treatment, as NDM-producing organisms are some of the most resistant and challenging organisms to treat, with extremely limited treatment options. Rates of reported Verona Integron-Mediated Metallo-beta-lactamase (VIM) and Imipenemase Metallo-beta-lactamase (IMP) were low (<10% of reported CPOs; VIM: 184 out of 5,753, 3.2%; IMP: 273 out of 5,753, 4.8%). Of all 5,753 notifications in 2023, 6.1% reported dual mechanisms. For sterile site infections, 12 (4.7%) were dual mechanism, 9 of which were OXA-48-like and NDM.

In 2023, the North West and London continued (since October 2020) to report the highest number of CPOs, however, there is considerable regional variation in both the frequency and type of carbapenemases being recorded (Figure 2.7). It should be noted that CPO screening Policies vary across the country, which may affect the ascertainment of reports within these regions as well as the different CPO mechanisms having particular foci in certain areas, possibly linked to protracted outbreaks.




In 2023, the overall case fatality rate for 30-day all-cause mortality in patients with a CPO isolated from a sterile site specimen was 22.9% (estimated number of deaths =56), compared to the 15.5% (est.=7,814) observed in selected Gram-negative AMR burden pathogens (*E. coli, K. pneumoniae, Pseudomonas* spp., *Acinetobacter* spp.) isolated from blood mentioned in the previous section. The case fatality rate for patients with CPOs isolated from sterile sites varied by age-group and was highest in children aged <1 year, followed by adults aged over 85 years, however, numbers of deaths were low in each age group and limit meaningful interpretation.

Reference laboratory

In 2023, 958 (124 of which were isolated from blood cultures) Enterobacterales referred to the <u>AMRHAI Reference Unit</u> were confirmed as positive for at least one carbapenemase. The 'big 5' carbapenemase families (KPC, OXA-48-like, NDM, VIM and IMP) and combinations thereof, continue to dominate and account for >97% of carbapenemase-producing Enterobacterales (CPE). Of the referred carbapenemase-positive isolates in 2023, 7% harboured more than one carbapenemase gene (Figure 2.8a). In 2023, AMRHAI received the highest number of CPE submissions originating from blood (12.9% in 2023 compared to 9.5% in 2022) (Figure 2.8b). Data behind the graph is available in the <u>chapter 2 data table accompanying this report</u>.

AMRHAI has been screening all Enterobacterales sent for investigation of carbapenem resistance with a multiplex PCR targeting all carbapenemase gene families that have been identified amongst submissions (see <u>the Annexe accompanying this report</u>). Since 2020, this includes the OXA-23-like, OXA-40-like and OXA-58-like acquired carbapenemase genes consistently associated with resistance in *Acinetobacter* spp. In 2023, OXA-23 was detected in a further 4 *Proteus mirabilis* strains referred to AMRHAI by 4 laboratories (as reported in 2023 ESPAUR Report (<u>15</u>)). Other non-'big 5' families detected include GES (n=1), GIM (n=2) and IMI (n=13), highlighting the need to refer suspected carbapenemase-producing isolates negative for the 'big 5' families to AMRHAI for screening for rarer carbapenemase families. This multiplex PCR is also able to detect KPC genes that harbour a mutation leading to a D179Y amino acid substitution associated with ceftazidime/avibactam resistance (<u>16</u>). One *K. pneumoniae* isolated from a rectal swab was identified with this substitution in 2023, only the second identified since PCR screening was introduced by AMRHAI in 2019. However, most *K. pneumoniae* isolates identified as resistant to ceftazidime/avibactam by local laboratory testing have not undergone genomic investigation.

In early 2024, the Global Antimicrobial Resistance Surveillance System on Emerging Antimicrobial Resistance Reporting (GLASS-EAR) issued a request for information to the Global Antimicrobial Resistance and Surveillance System (GLASS) Antimicrobial Resistance (AMR) National Focal points enrolled in GLASS-EAR to rapidly assess the current global situation in view of the increased identification of isolates of hypervirulent Klebsiella *pneumoniae* (hvkp) ST23 carrying carbapenemase genes reported in several countries. The report, <u>Antimicrobial Resistance, Hypervirulent Klebsiella pneumoniae – Global situation</u>, highlights the global spread of *K. pneumoniae* ST23 strains with diverse resistance profiles and virulence characteristics, posing challenges for healthcare systems worldwide (<u>17 to 19</u>). Since 2019 in England, 3 ST23-K1 isolates have been detected associated with NDM-1 or OXA-48-like resistance mechanisms, with 80 susceptible ST23-K1 isolates, (approximately 10 to 20 patients per year). In addition, isolates of 'high-risk' clones with hybrid virulence plasmids carrying carbapenemase genes (usually NDM or OXA-48-like or both), particularly among representatives of ST147 (n=15) (from 21 patients in 2023) have also been detected in England.

There is currently no internationally agreed consensus definition of hypervirulent *K. pneumoniae* and the clinical presentation and extended disease spectrum of hypervirulent *K. pneumoniae* may not be familiar to most clinicians. Within England, there is currently no systematic surveillance that allows the routine identification and information gathering of hypervirulent *K. pneumoniae* strains and thus most hypervirulent *K. pneumoniae* strains are likely to go unnoticed. Whilst a presumptive clinical diagnosis would usually depend on the presentation of severe community-acquired infection in previously healthy individuals, the clinical picture may differ in vulnerable populations within healthcare settings, making the clinical diagnosis of healthcare-associated hypervirulent *K. pneumoniae* strains, there is the possibility of potentially untreatable infections in previously healthy adults with even higher morbidity and mortality expected in vulnerable patient populations.

Reference laboratory capacities for genomic sequencing and analyses of relevant virulence genes in addition to resistance genes is being expanded. Clinicians suspecting a possible hypervirulent *K. pneumoniae* strain with or without additional antimicrobial resistance should refer the isolate to the Opportunistic Pathogens Section of the AMRHAI Reference Unit for genomic sequencing.





* Following a change to the referral criteria in 2019, submission of confirmed CPE representing colonisation to the AMRHAI Reference Unit was no longer encouraged.



Figure 2.8 (b) Number of confirmed CPE blood culture isolates referred to the UKHSA's AMRHAI Reference Unit, 2014 to 2023

For *Pseudomonas* spp., the metallo-carbapenemase enzymes VIM and NDM continue to dominate but other metallo-carbapenemase enzymes (IMP, DIM and GIM) as well as non-metallo carbapenemase families (GES and KPC) have been identified (<u>Table 2.6</u>). Please review the <u>referral</u> <u>criteria</u> for when to suspect an acquired carbapenemase in a *Pseudomonas* spp. isolate.

Table 2.6. Distribution of carbapenemase gene families amongst *Pseudomonas* spp.referred to the UKHSA's AMRHAI Reference Unit from all sources

Year	VIM	IMP	NDM	GES	Other (number)
2017	111	22	19	8	DIM (1); OXA-48-like (2)
2018	99	17	41	9	DIM (2); KPC (3); OXA-48-like (2)
2019	86	11	27	11	DIM (1); KPC (1); OXA-48-like (1); SIM (1)
2020	33	10	19	8	DIM (2); KPC (1)
2021	33	4	13	9	-
2022	21	19	18	8	GIM (1), OXA-48-like (1)
2023	35	5	25	5	DIM (1); GIM (5); KPC (1)

Gram-positive bacterial infections

Resistance trends in bacteraemia

In 2023, meticillin-resistant *S. aureus* (MRSA) comprised 6.7% of the total number of *S. aureus* isolates from blood. As shown in Figure 2.9, resistance to a range of antibiotics was higher in MRSA compared with meticillin-susceptible *S. aureus* (MSSA), particularly macrolides (47.5% versus 20.5% in 2023), clindamycin (44.2% versus 18.3% in 2023) and tetracycline (25.7% versus 5.2% in 2023).

Whilst flucloxacillin remains the antibiotic of choice for MSSA infections, resistance to other relevant antibiotics continues to increase. Between 2019 and 2023, MSSA causing bacteraemia showed increased resistance to macrolides (17.9% to 20.5%; p<0.05), clindamycin (15.4% to 18.3%, p<0.05) and tetracycline (4.6% to 5.2%, p<0.05) (Figure 2.9), with resistance to fusidic acid (12.2% to 12.1%) and mupirocin (0.4% to 0.3%) remaining relatively stable. In MRSA bacteraemia, resistance to tetracycline also increased between 2019 and 2023 from 13.3% to 25.7% (p<0.05), whereas resistance to macrolides (47.5% resistance in 2023), clindamycin (44.2%), fusidic acid (23.5%) and mupirocin (3.1%) remained relatively stable.

Data on susceptibility of *S. pneumoniae* bacteraemia is shown in Figure 2.9. The percentage of isolates resistant to tetracycline and macrolides significantly increased between 2019 and 2023, from 6.8% to 9.0% and 5.9% to 7.1% (p<0.05); penicillin resistance increased slightly, however, this was not statistically significant (1.6% to 1.7%) from 2019 and 2023. Full 5-year trend tables are available in the Chapter 2 data tables accompanying this report.

Figure 2.9. Antibiotic resistance in meticillin-susceptible *S. aureus* (MSSA), meticillinresistant *S. aureus* (MRSA) (Note), and *Streptococcus pneumoniae* bacteraemia to selected antibiotics, England 2019 and 2023



Note: The *S. aureus* data in this chart is based on voluntary reports of meticillin resistance. Further detail on antibiotic class groupings can be found in the <u>Annexe (Table 2.1) accompanying this report</u>.

Enterococcus species

In 2023, *E. faecium* was the predominant *Enterococcus* species causing bacteraemia for a second year in a row, (45.4%, up from 41.8% in 2019), followed by *E. faecalis* (42.4%, compared to 43.0% in 2019), with most of the change occurring during the pandemic period. Overall, reporting rates of both *E. faecium and E. faecalis* have increased from 2019 to 2023 (Box 2.4.1).

E. faecium resistance to teicoplanin and vancomycin decreased from 2019 to 2020, but increased year-on-year from 2020 to 2023 with resistance to teicoplanin increasing from 21.4% in 2019 to 23.8% in 2023 (p<0.05), and vancomycin from 20.6% in 2019 to 22.4% in 2023 (p=0.07) (Figure 2.10). Teicoplanin and vancomycin resistance in *E. faecalis* remained low (<2.5%) in 2023. Resistance to linezolid remained low, however increased in *E. faecalis* from 0.4% to 0.9% from 2019 to 2023 (p<0.05), while linezolid resistance in *E. faecium* remained stable over this period (1.4% in 2023).

Figure 2.10. Antibiotic resistance in *Enterococcus faecalis* and *Enterococcus faecium* bacteraemia, England 2019 to 2023



There are no EUCAST breakpoints for daptomycin for *Enterococcus* spp. Clinicians wishing to treat enterococcal bacteraemia or endocarditis with daptomycin should be aware of the uncertainties around testing (please refer to the <u>Annexe</u>). Reported daptomycin resistance in *E. faecalis* and *E. faecium* remained low at 1.1% and 2.7% respectively in 2023.

Box 2.4. Trends in the incidence, distribution and antibiotic resistance in *Enterococcus* species

Incidence and distribution of Enterococcus species

Between 2015 and 2023, there have been sustained increases in the annual rates per 100,000 population of both *E. faecium* (3.8 per 100,000 population in 2015 vs 7.0 per 100,000 population in 2023) and *E. faecalis* bacteraemia (4.3 per 100,000 population in 2015 vs 6.6 per 100,000 population in 2023) (Box Table 2.4.1), with a marked spike in *E. faecium* rates during the COVID-19 pandemic (Box Figure 2.4.1).

The increases are seen in both males and females, across both enterococcal species, with men having higher rates of *E. faecium* and *E. faecalis* bacteraemia between 2015 and 2023, compared to females (<u>Box Figure 2.4.2</u>). The rates of bacteraemia due to other enterococcal species remained relatively stable (<u>Box Figure 2.4.1</u>).

	Rate (95% CI)			
Year	Enterococcus faecalis	Enterococcus faecium		
2015	4.3 (4.1 - 4.5)	3.8 (3.6 - 3.9)		
2016	5.1 (4.9 - 5.3)	4.8 (4.6 - 4.9)		
2017	5.6 (5.4 - 5.8)	4.8 (4.6 - 5.0)		
2018	5.7 (5.5 - 5.9)	5.3 (5.1 - 5.5)		
2019	5.8 (5.6 - 6.0)	5.7 (5.5 - 5.9)		
2020	5.6 (5.4 - 5.8)	5.8 (5.6 - 6.0)		
2021	6.4 (6.2 - 6.6)	7.0 (6.8 - 7.3)		
2022	6.2 (6.0 - 6.4)	6.9 (6.7 - 7.1)		
2023	6.6 (6.4 - 6.8)	7.0 (6.8 - 7.2)		

Box table 2.4.1. Annual rates per 100,000 population of *E. faecalis* and *E. faecium* bacteraemia with 95% confidence intervals, England 2015 to 2023

Between 2015 and 2023 there have been fluctuations in the dominant *Enterococcus* species causing bacteraemia with *E. faecium* dominating since 2022 (<u>Box Figure 2.4.1</u>). The shift is principally driven by changes in the species causing bacteraemia in females from 2022 onwards, with the rate of bacteraemia across *E. faecium* and *E. faecalis* remaining relatively similar in males (<u>Box Figure 2.4.2</u>).

Box figure 2.4.1. Monthly rates per 100,000 population of *Enterococcus* bacteraemia with a 3-month rolling average by species, England 2015 to 2023



Box Figure 2.4.2. Monthly rates per 100,000 population of *Enterococcus faecalis* and *Enterococcus faecium* bacteraemia per sex with a 3-month rolling average and 95% confidence intervals, England 2015 to 2023



Antibiotic resistance in Enterococcus species in 2023

Glycopeptide-resistant *E. faecium* rates are highest in older age groups overall. However, among individuals with *E. faecium* bacteraemia, the proportion of glycopeptide-resistant infections is highest in the 15 to 44 and 45 to 64 age groups, and lower at the youngest and oldest age extremes (Box Figure 2.4.3). This deviates from the general trend seen in overall AMR bacteraemia burden, with the oldest and youngest experiencing higher percentage of bacteraemia episodes that are resistant.

In *E. faecalis* bacteraemia, resistance to vancomycin (range, 1.2% to 2.3%), teicoplanin (range, 0.0% to 3.2%), and linezolid (range, 0.0% to 1.3%) remained very low across all age groups. Note that fewer than 100 sensitivity tests to a given antimicrobial were conducted for certain age groups due to low numbers of isolates (see <u>accompanying data tables</u>).





Laboratories are reminded to send isolates with exceptional antibiotic resistant phenotypes to the AMRHAI Reference Unit for confirmation. This includes:

- *S. aureus* isolates exhibiting resistance to ceftaroline, ceftobiprole, vancomycin, teicoplanin, telavancin, dalbavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin, or tigecycline
- E. faecalis exhibiting resistance to ampicillin/penicillin
- *Enterococcus* spp exhibiting resistance to daptomycin, tigecycline, linezolid or eravacycline, or omadacyline, or resistant to teicoplanin but not vancomycin
- *S. pneumoniae* exhibiting resistance to penicillin, cephalosporins, vancomycin, teicoplanin, telavancin, dalbavancin, daptomycin, linezolid, tedizolid, quinupristin-dalfopristin, fluoroquinolones, or tigecycline

Further referral criteria and guidance on how to do this is available in the <u>Bacteriology</u> <u>Reference Department user manual</u>.

Antibacterial resistance in specialist areas

Surveillance of antibiotic resistance in Neisseria gonorrhoeae

Surveillance of AMR in *Neisseria gonorrhoeae* is monitored through the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP), which comprises a suite of surveillance systems to detect and monitor AMR in *N. gonorrhoeae* and to record confirmed treatment failures. Trend data is derived from the national sentinel surveillance system which collects gonococcal isolates from consecutive patients attending a network of 25 participating sexual health services (SHSs) (23 in England, 2 in Wales) over a two-to-three-month period each year. Gonococcal isolates are referred to the UKHSA national STI reference laboratory (STIRL) for antimicrobial susceptibility testing and whole-genome sequencing, and the results are linked to patient demographic, clinical and behavioural data for analysis of antimicrobial susceptibility trends in patient sub-groups.

No cases of ceftriaxone resistance (MIC >0.125 mg/L) were observed in the sentinel programme. However, the frequency of ceftriaxone-resistant cases reported outside of the programme has been increasing. Twenty-two cases of ceftriaxone resistance have been detected since the start of 2022, totalling 31 cases detected in England since the first case detected in 2015. Concerningly, 6 of these recent cases were also extensively drug-resistant (XDR) with high levels of resistance to the second line treatment (azithromycin) as well as other antimicrobials. Most cases continue to have travel links with the Asia-Pacific region, which has been shown to have the highest prevalence of ceftriaxone-resistant *N. gonorrhoeae* globally ($\underline{20}$). However, as some cases appear to have acquired infection within the UK and as not all partners could be contacted, undetected transmission within England is possible.





* The 5% threshold (≥5% of infections resistant to the first-line therapy) at which the World Health Organisation (WHO) recommends that first-line monotherapy guidelines should be changed is indicated by the horizontal dashed red line. In 2021, pharyngeal isolates were prioritised ahead of all other sites for the first time, resulting in a substantial change in the distribution of specimen sites from 2021 onwards.

In 2023, EUCAST updated the resistance breakpoint for tetracycline against *N. gonorrhoeae* from 1.0 mg/L to 0.5mg/L. Breakpoint plates at 0.5 mg/L were introduced in 2022; therefore, no data for this breakpoint is available prior to 2022 and trend data is not presented.

Figure 2.11 describes the trends in azithromycin, cefixime, ciprofloxacin, penicillin and spectinomycin and ceftriaxone resistance. Penicillin resistance (MIC >1.0 mg/L or betalactamase positive) remained stable at 14.3%. As in previous years, no spectinomycin resistance (MIC >64 mg/L) was detected. Ciprofloxacin resistance (MIC >0.06 mg/L) remained stable at 58.6% relative to the year prior but has increased rapidly in recent years.

Cefixime resistance (MIC >0.125 mg/L) is currently at 5.6% following a likely underestimate in 2021 and 2022 due to a technical testing issue. Azithromycin resistance (MIC >0.5 mg/L) for 2023 is not available for presentation but remains above the 5% WHO threshold and continues to be unsuitable as first-line treatment. Tetracycline resistance (updated breakpoint of MIC >0.5 mg/L) remained high at 80.8%.

Prescribing data collected through the sentinel surveillance system demonstrate excellent compliance with the UK guidelines, with 97.9% of individuals receiving the recommended first-line therapy of ceftriaxone 1g IM monotherapy. One pharyngeal treatment failure with ceftriaxone (1g IM) was confirmed in 2024 (the first since 2018) and was eventually cleared with a single dose of ertapenem (1g IV) (<u>21</u>).

Further data on AMR in *N. gonorrhoeae*, as well as technical notes on the 2023 cefixime and azithromycin data, is available online in the <u>GRASP report</u>.

Surveillance of antibiotic resistance in Mycoplasma genitalium

Mycoplasma genitalium is a bacterial sexually transmitted pathogen which is associated with non-gonococcal urethritis in men and cervicitis and pelvic inflammatory disease in women. Azithromycin is recommended as the first-line treatment and moxifloxacin is the recommended second-line treatment. Doxycycline is commonly given as pre-treatment to lower the bacterial load and increase the effectiveness of the subsequent antibiotic prescribed. There is global public health concern about antimicrobial resistance to azithromycin and moxifloxacin in *M. genitalium*.

The *M. genitalium* Antimicrobial Resistance Surveillance (MARS) programme is a sentinel surveillance programme and aims to estimate the prevalence of macrolide and fluoroquinolone resistance and investigate the demographic, behavioural and clinical factors associated with resistance. Further details are available in the <u>Annexe</u>. Specimens were collected in pilots in 2019 and 2020, and in 2023 and tested for molecular markers predictive of macrolide and fluoroquinolone resistance.

A total of 62.2% (n=523/928) of sequenced specimens had mutations associated with macrolide resistance and 12.1% (n=98) had mutations predictive of fluoroquinolone resistance. Dual resistance was detected in 10.1% (n=78) of specimens.

<u>Figure 2.12</u> shows the percentage of specimens included in the pilots (2019, 2020) and 2023 MARS sample that had mutations associated with macrolide, fluoroquinolone, and dual resistance. In MARS 2023, macrolide resistance decreased compared to the pilots (69.5% in

2019 and 69.1% in 2020). Fluoroquinolone resistance increased in 2023, rising from 8.4% in 2019 and 11.1% in 2020. Dual resistance remained stable compared to the 2020 pilot, in which 10.3% of sequenced specimens carried mutations associated with both macrolide and fluoroquinolone resistance.

The complete results from the 2023 MARS Programme are available online in the MARS Report, which can be found at <u>Mycoplasma genitalium antimicrobial resistance surveillance</u>.





Surveillance of antibiotic resistance in *Mycobacterium tuberculosis* infections

The number of tuberculosis (TB) disease notifications has increased since the peak-pandemic year of 2020, a rebound effect seen globally (<u>World Health Organization Global TB report</u> 2023). England remains a low TB incidence country (less than 10 per 100,000 population) with a low incidence of multi-drug resistant (MDR) TB. However, the number of MDR TB increased in 2023 compared with 2022.

MDR TB is defined as TB resistant to both INH and rifampicin or rifampicin alone. Since 2011, MDR/rifampicin resistant (RR)-TB has been diagnosed in under 2% of culture-positive notifications apart from 2020 and 2023, with the peak observed in 2023 at 2.4% in 71 people. This compares with 44 people in 2022, the largest year on year increase observed over this period and similar to numbers reported pre-2014 (Figure 2.13).

Included in these numbers are people with acquired drug resistant strains after initially having tested sensitive at diagnosis. Numbers and proportions of acquired drug resistance are low and

have decreased in recent years. In 2023 no people acquired multi-drug, rifampicin or isoniazid resistance post-diagnosis.

Outcomes for patients with MDR TB are worse than for drug sensitive disease. The drugs used for treatment of MDR TB are often poorly tolerated and patients need careful monitoring because of toxicity. More detail on trends in drug resistance and treatment outcomes of MDR TB is presented in the most recent <u>Tuberculosis in England annual report</u>, and Official Statistics.

Figure 2.13. Number and proportion* of people ever diagnosed with drug-resistant *Mycobacterium tuberculosis*, England, 2011 to 2023



* Proportions are calculated as a proportion of TB notifications with a positive culture for MTB

Data underlying Figure 2.13 and additional data is available in the <u>chapter 2 data table</u> <u>accompanying this report</u>.

Critical antibiotic resistance in foodborne bacteria

UKHSA's <u>Gastrointestinal Bacteria Reference Unit</u> routinely performs whole genome sequencing (WGS) on referred isolates of food-borne or zoonotic bacteria. Overall, 9,304 isolates of *Salmonella* spp., 2,497 of Shiga toxin-producing *E. coli* (STEC), 1,695 *Shigella* spp., and 840 *Campylobacter* spp. from England underwent WGS in 2023. The vast majority of these (≥95%) were isolated from humans. Details on methodology can be found in the <u>Annexe</u>.

In 2023, genes encoding carbapenemases were detected in 3 *Salmonella* isolates; specifically, *bla* _{OXA-48-like} was detected in 2 *Salmonella* Kentucky (ST314) which were genetically indistinguishable using UKHSA's analysis pipeline, *bla* _{NDM-1} was found in an isolate of *Salmonella* Virchow ST181.

Mobile resistance genes conferring resistance to colistin (specifically *mcr-1*, *mcr-3* and *mcr-9*) have been found in STEC (n=1) and *Salmonella* sp. (n=15); 6 of these were part of the same genetically-related cluster.

Tetracycline resistance, specifically variants of the gene tet(X) have been found in *Salmonella* sp. (n=11), 7 of which fell into 2 closely genetically related clusters, and an additional 2 of which were *S*. Infantis; as well as *Shigella flexneri* (n=1). The tet(X) genes confer resistance to all tetracyclines, with some variants conferring additional resistance to tigecycline, eravacycline and omadacycline, which are drugs often used in last-line multidrug-resistant regimes.

Please see the <u>Annexe accompanying this report</u> for further detail regarding detected drug resistance and further characterisation of these isolates in foodborne bacteria.

Most foodborne bacteria cause self-limiting gastroenteritis and antibiotics are rarely necessary to treat these infections; various treatment options remain available despite critical resistance determinants. However, there is concern that mobile resistance determinants can be transferred from foodborne pathogens to healthy gut bacteria in the human host. Acquisition of resistance genes such as tet(X) or *mcr* by *E. coli* and other gut commensals could significantly reduce effective treatment options in individuals unwell from community-acquired infections such as urinary tract infections caused by gut commensals. Thorough cooking of food to piping hot temperatures and maintaining good kitchen hygiene is one way of reducing the acquisition of foodborne infections.

Box 2.5. Extensively drug-resistant (XDR) imported Salmonella Typhi cases in England

Salmonella Typhi and Salmonella Paratyphi infections are responsible for <u>enteric fever</u>, a clinical illness characterised by prolonged fever, abdominal pain, headache and malaise. Severe cases can lead to complications including intestinal bleeding and perforation (22). Enteric fever requires antibiotic treatment and has public health considerations due to the risk of onward transmission (Please see <u>public health guidance</u> for more details).

Enteric fever case numbers in England have fluctuated in recent years (see <u>enteric fever annual</u> <u>reports</u>), declining during the COVID-19 pandemic period in 2020 to 2021, and returning to prepandemic levels in 2022 (462 cases), with a peak of 631 cases in 2023. In addition to the increase in imported cases seen in England, there is a growing concern about the rise of antibiotic resistance in enteric fever.

A significant factor contributing to travel-associated cases of S. Typhi in England is an ongoing outbreak of extensively drug-resistant (XDR) S. Typhi in Pakistan which began in late 2016

(23,24). The first imported case in England was reported in 2017. <u>Box Figure 2.5.1</u> illustrates the trend in *S*. Typhi cases, highlighting the proportion attributed to this XDR strain.



Box Figure 2.5.1. Imported XDR S. Typhi cases in England: 2019 to 2023*

* In this graph, other XDR *S*. Typhi cases are those that reported travel to other countries, reported no travel, or cases where travel history was not available.

This XDR stain is resistant to most antibiotics used to treat enteric fever, including ampicillin, chloramphenicol, co-trimoxazole (which together define MDR *S*. Typhi), fluoroquinolones and third-generation cephalosporins (mediated by production of the extended-spectrum beta-lactamase [ESBL] *bla*_{CTX-M-15}).

Of the total 186 XDR *S*. Typhi cases reported between 2019 and 2023 in England, 93.0% were associated with travel to Pakistan, while other cases reported travel to Afghanistan, Iraq, and India. Six cases reported no travel abroad. Children under 18 years of age comprised 56% (n=104) of cases.

2023 saw the highest number of XDR *S*. Typhi cases reported to date (52), mainly linked to travel to Pakistan (47 cases); 3 cases travelled to Afghanistan, one to India, and the remaining case had no reported travel abroad.

Overall, these findings highlight a persistent and growing challenge posed by imported XDR *Salmonella* Typhi cases in England. The XDR profile of this strain means that these infections are harder to treat, posing a great risk to public health. This emphasises the need for targeted interventions and public health messaging, as well as improved travel health advice to address the spread of antibiotic-resistant strains seen in English travellers.

More information on S. Typhi can be found in UKHSA's 2023 annual report.

Antifungal resistance

Trends in incidence and antifungal resistance

The incidence of fungaemia (fungal bloodstream infection) was 3.7 per 100,000 population (n=2,112) in 2023, and has increased year on year since 2019, with an overall increase of 21.3% since 2019 (3.0 per 100,000, n=1,714). This is likely due to improved detection and reporting techniques.

Candida albicans was the most frequently isolated yeast species across the 5-year period followed by *Nakaseomyces glabratus* (formerly *Candida glabrata*), accounting for 40% and 27% of fungaemia episodes, respectively. Additional data on regional fungaemia incidence can be found in the 'Laboratory surveillance of fungaemia in England: 2023 health protection report'.

Box 2.6. Candidozyma auris (formerly Candida auris)

In 2024, *Candida auris* was proposed as the type species of the novel yeast genus *Candidozyma*, as *Candidozyma auris*, to reflect its distant relationship to the principal *Candida* species (*C. albicans* complex, *C. tropicalis* and *C. parapsilosis* complex).

Candidozyma auris (C. auris) is a rapidly emerging fungal pathogen with a global distribution. Designated a critical priority fungal pathogen by the World Health Organisation in 2022, it can cause severe invasive infection, mostly within healthcare settings. Resistance to the first-line antifungal agent fluconazole, combined with the ability to rapidly acquire resistance to other antifungal agents on therapy, complicates the management of invasive disease. In non-UK settings invasive disease has been associated with significant mortality. It has high outbreak potential due to its propensity to colonise skin and survive in the environment for prolonged periods. *C. auris* healthcare associated outbreaks can be disruptive, protracted and costly.

Following a period of decreased *C. auris* detection in 2020 during the COVID-19 pandemic, there have been year-on-year increases from 2020 to 2023 (Box Figure 2.6.1). There was a significant increase in the prevalence of *C. auris in* England in 2023 including protracted outbreaks in 2 large NHS trusts in London and the South-East. These regions reported the majority of *C. auris* detections in England. In 2023; 93 patients were reported to the UKHSA with first detections of *C. auris*, of whom 8 had bloodstream infections.

C. auris is not currently listed as a notifiable organism under schedule 2 of the Health Protection (Notification) Regulations 2010. There is known under-ascertainment of cases, particularly colonisation though possibly including clinical infections. This data was derived by review of the UKHSA SGSS and liaison with the Mycology Reference Laboratory (MRL), Bristol. Cross-referencing isolates reported to SGSS with data generated through other mycology reference laboratories has not occurred.





Further detail of *C. auris* epidemiology in England will be found in a UKHSA *C. auris* Health Protection Report which is due to be published together with updated guidance for the laboratory investigation, management and infection prevention and control of *C. auris* (in preparation at the time of ESPAUR report publication).

Routine laboratory surveillance reports submitted to the UKHSA's SGSS showed that in 2023, 64.7% (1,367 out of 2,112) of yeasts isolated from blood were subjected to susceptibility testing. This section will focus on susceptibility test results for 3 antifungals (amphotericin B, caspofungin and fluconazole, see Figure 2.14).

Further detailed trend data, including numbers reported as susceptible or resistant, is available in the <u>chapter 2 data table accompanying this report</u>.

Supplementary analyses on fungaemia cases are available in the <u>Chapter 2 data tables</u> which further outlines the rates of yeast isolated from blood cultures and regional breakdowns, along with an update from the <u>UKHSA National Mycology Reference Laboratory (MRL)</u> on antifungal susceptibilities in emerging fungal pathogens referred to the laboratory.



Figure 2.14 Percentage of a) *C. albicans* b) *N. glabratus* and c) *C. parapsilosis* isolates from blood displaying resistance to antifungals in England, 2019 and 2023

Figure 2.14 depicts the percentage of isolates resistant to 3 antifungals, comparing 2023 with 2019, for *C. albicans*, *N. glabratus* and *C. parapsilosis*. In 2023, resistance to fluconazole was detected in 1.3% of *C. albicans*, 16.6% of *N. glabratus* and 4.9% of *C. parapsilosis* isolates.

Antiviral resistance

Influenza virus

During the 2023 to 2024 influenza season (samples collected between week 40 2023 and week 20 2024) more than 2,500 viruses were screened by WGS for antiviral susceptibility. Analysis of 905 A(H3N2) viruses by sequencing found no virus with known markers of resistance to neuraminidase inhibitors (NAIs). Of 1162 A(H1N1)pdm09 NA sequences analysed, 5 oseltamivir-resistant viruses with the H275Y amino acid substitution were detected from 4 oseltamivir-treated individuals. One virus with a D199E amino acid substitution was detected from an immunocompromised adult patient known to have received oseltamivir treatment.

No virus with known markers of resistance to neuraminidase inhibitors were detected in 554 influenza B NA sequences analysed. One influenza B virus with a I221T mutation, previously known to result in reduced susceptibility to oseltamivir was detected.

No viruses with known markers of resistance to baloxavir marboxil were detected in 807 A(H3N2), 952 A(H1N1)pdm09 and 486 influenza B PA sequences analysed.

All A(H1N1)pdm09 NAI-resistant viruses emerged in immunocompromised individuals during NAI treatment, highlighting the vulnerable nature of these patients, and the need for close monitoring and low threshold of suspicion of resistance if viral load persists. Baloxavir has regulatory approval in the UK but is not marketed for use currently outside of an approved research protocol. There may be scope for compassionate use, against NAI-resistant viruses in specific clinical contexts.

This continues the ongoing trend of very low resistance to NAIs and baloxavir, globally as outlined in the 13th meeting short summary report by WHO-AVWG.

Further information on influenza virus trends and antiviral resistance testing for the 2022 to 2023 season can be found in the <u>annual influenza report</u>.

Human immunodeficiency virus (HIV)

Drug-naïve individuals

Two sources of data were used to ascertain the prevalence of transmitted resistance to HIV-1 antiretroviral drugs. First, the INITiO study (25), which aims to survey the prevalence of resistance to integrase strand transfer inhibitors (INSTIs) among treatment-naïve subjects in the UK. Samples from approximately 1,200 randomly selected patients with recently acquired (<4 months) HIV-1 and no history of antiretroviral drug treatment were submitted for HIV WGS in UKHSA's Antiviral Unit.

The second data source was HIV sequences generated as part of routine clinical care by the UKHSA and NHS laboratories collected by the UK HIV Drug Resistance Database at University College London until 2019. The UKHSA relaunched the HIV Drug Resistance Database in 2024, previously maintained at University College London, and aims to provide regular updates on HIV drug resistance after data from 2020 to date has been collected from the UKHSA and NHS laboratories. The HIV sequence data was linked to recency and treatment data held within the HIV and AIDS Reporting System (HARS) at the UKHSA. Where linkage was not possible, sequences collected within 90 days of first diagnosis were used. Overall, 1,694 individuals were included.

Drug resistance prevalence in the drug-naïve population increased from 8% in 2015 to 15% in 2020, reflecting an increase in resistance to nucleos(t)ide reverse transcriptase inhibitors (NRTIs): 4% to 6%, non-nucleoside reverse transcriptase inhibitors (NNRTIs): 2% to 4% and protease inhibitors (PIs) 3% to 6%. Drug resistance prevalence then declined to 9% in 2021, driven by a fall in PI and NNRTI resistance. INSTI resistance remained rare at \leq 1% throughout the period.

English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) Report 2023 to 2024

Drug-experienced individuals

Drug resistance prevalence in people exposed to therapy was ascertained by linkage of viral sequences from the UK HIV Drug Resistance Database to HARS, where the sample date was collected at least 90 days after initiation of antiretrovirals. Individuals were included for each year in which they were sampled from 2015 to 2019 (N=11,277).

Overall drug resistance prevalence was stable at 27 to 29% throughout the period. NRTI resistance prevalence was also stable at 17 to 18%. In contrast, NNRTI and INSTI resistance declined from 16% to 12% and from 8% to 5%, respectively. PI resistance remained rare at \leq 3% throughout the period.

The UKHSA is planning further analyses involving linkage of the HIV drug resistance database with <u>GUMCAD</u> (surveillance system for sexually transmitted infections (STIs) in England) to understand whether or not there has been any impact from the roll out of oral pre-exposure prophylaxis (PrEP) containing the NRTIs tenofovir and emtricitabine on the prevalence of K65R and M184V/I, as markers of resistance against these agents".

Hepatitis C virus (HCV)

Since 2019, the Antiviral Unit at the UKHSA has offered HCV WGS as a clinical service. This determines the HCV genotype/subtype and resistance pattern for the 3 HCV Direct Acting Antiviral (DAA) drug classes (NS3, NS5A and NS5B inhibitors).

HCV genomic data generated through this service was used to ascertain DAA drug resistance prevalence. For patients in England, data was linked to the English HCV Treatment Register to ascertain treatment status that is whether DAA-naïve or previously exposed to DAAs.

<u>Figure 2.15</u> shows the prevalence of resistance to HCV DAA drugs in the NS5A gene of subtype 1a in 934 samples received from England between 2019 and 2023.

In drug-naïve individuals, resistance prevalence was stable between 2019 and 2022, at 12% (13 out of 108) in 2019 and 16% (15 out of 93) respectively. However, resistance prevalence fell to 5% (2 out of 41) in 2023. It is unclear whether this trend reflects a true decline in transmitted resistance or an artefact due either to lower numbers of samples or a greater proportion where treatment history was not yet available.

The prevalence of NS5A resistance in treatment-experienced individuals remains high.

The UKHSA is in the process of establishing a national HCV genomics surveillance programme in support of HCV elimination goals, and has submitted an application to the UKHSA Research Ethics and Governance Group. The surveillance seeks to use leftover blood samples collected as part of routine care in patients with HCV infection for WGS. Results will be linked to treatment outcomes in the English HCV Register. Outputs will include monitoring of the prevalence of antiviral drug resistance, transmission networks and viral subtype distribution.





Antiparasitic resistance

Plasmodium falciparum accounts for 85% of all malaria cases (approximately 1,500 cases) imported into the UK annually. It causes the most clinically severe infection among the 5 *Plasmodium* species that infect humans and also accounts for the vast majority of drug-resistant malaria parasites

In the UK, clinical management of uncomplicated *P. falciparum* malaria is with oral artemisininbased combination therapies (ACT). Since their introduction from 2004, the efficacy of ACT in sub-Saharan Africa has remained high. In south-east Asia, however, waning efficacy of ACT, characterised by slow parasite clearance after treatment, has been reported since 2008 (<u>26</u>). This slow clearance is associated with certain mutations in the propeller domain of the *P. falciparum* kelch protein K13 (<u>27</u>).

The Malaria Reference Laboratory (MRL) has been routinely monitoring reports of ACT treatment failure in UK travellers since 2016. Three *P. falciparum* isolates among 49 genotypes evaluated during this period carried propeller domain mutations in the *pfk13* locus: C580Y (Cambodia, 2018), A675V (Uganda, 2022) and P443S (Namibia, 2023). A contemporary isolate also of Ugandan origin derived from a UK patient with malaria with post-artemether-lumefantrine recrudescence, but not harbouring a *pfk13* propeller domain mutation, showed equally significant reduction in susceptibility to both artemisinin and lumefantrine (28). The emergence of lumefantrine resistance in concert with the recently described increase in *pfk13* variants, poses a potential threat to therapeutic management of falciparum malaria in travellers returning from East Africa. It is assumed that mutations at additional parasite loci underly this reduced lumefantrine efficacy, but these are yet to be identified. Overall, however, artemether-

lumefantrine (Riamet[®]) retains good efficacy against the overwhelming majority of imported falciparum malaria infections in the UK.

In contrast to the overuse of antibiotics, there is significant underutilisation of antimalarial prophylactic drugs by travellers from the UK visiting malarious areas. In 2021, where the history of chemoprophylaxis was recorded, 89% of those diagnosed with imported malaria in the UK took no chemoprophylaxis, a similar pattern to previous years. Given that the regimens currently advised for UK travellers provide at least 90% protection, this represents a substantial failure of preventative advice. The MRL is actively engaging with relevant groups of travellers to develop better approaches to communicate the message and improve uptake. The following chapter on <u>antimicrobial consumption</u> discusses antimalarial consumption data in England in further detail.

UK participation in international surveillance of AMR

The fifth WHO <u>global antimicrobial resistance and use surveillance system (GLASS) report</u> was published in December 2022, and included data from the UK, covering blood and urine isolates from 2019, and a description of the current status of AMR surveillance nationally.

Long-term goals of GLASS include supporting the development of surveillance approaches that include epidemiological, clinical, and population-level data to allow calculation of AMR rates in the population, and the coordination of global surveillance systems on AMR in humans, animals, food, and the environment for the investigation of drivers of AMR development.

A submission was provided to the WHO Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR) network for 2021 UK data. This was included in its 2023 report, <u>Antimicrobial resistance surveillance in Europe 2023 to 2021 data</u>.

Main AMR resources and reports

The UKHSA routinely publishes a range of reports on AMR and infections, a number of which are shown below. A longer list of AMR resources and reports is available in the 'Methods and caveats' section of <u>the Annexe accompanying this report</u>. Research-based outputs including peer reviewed publications using the data referred to in this report and the listed resources are documented in the Research chapter (<u>Chapter 8</u>) and include:

- <u>carbapenemase-producing Gram-negative bacteria laboratory surveillance quarterly</u>
 <u>reports</u>
- weekly carbapenemase Notifications of Infectious Diseases (NOIDs) reports
- annual epidemiological commentary: Gram-negative, MRSA, MSSA bacteraemia and *C. difficile* infections
- pyogenic and non-pyogenic Streptococcal bacteraemia annual data from voluntary surveillance
- Group A streptococcal infections <u>seasonal activity reports</u>

English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) Report 2023 to 2024

- Fingertips: AMR local indicators
- <u>UK One Health report: Joint report on antibiotic use, antibiotic sales and antibiotic resistance</u>
- <u>Tuberculosis in England: national quarterly reports</u>
- the gonococcal resistance to antimicrobials surveillance programme GRASP
- Enteric fever (typhoid and paratyphoid) England, Wales and Northern Ireland
- <u>laboratory surveillance of paediatric bacterial bloodstream infections and</u>
 <u>antimicrobial resistance in England</u>
- laboratory surveillance of Enterococcus spp. bacteraemia (England)

Future actions

Antibacterial resistance

- begin the implementation of the new 2024 to 2029 AMR NAP
- establish a multidisciplinary CPO strategy, encompassing surveillance, reference laboratory/medical microbiology, infection, prevention and control, guidance, modelling, collaboration or engagement, research, and genomics
- increase the capacity to process, analyse and interpret genomic data, ensuring the necessary resources are available to do so, with the aim of enabling better epidemiological understanding of AMR priority pathogens and resistance mechanisms in England to inform public health interventions

Antifungal resistance

- the focus of the ESPAUR antifungal sub-group is to strengthen the reporting of fungal infections, specifically: monitoring of *Aspergillus* and increased understanding of current fungal laboratory diagnostic capabilities
- further implement improved surveillance of *C. auris* to inform public health interventions
- undertake a review of fungal infections and antifungal resistance in different specimen groups

Antiviral resistance

- provision of data from 2020 onwards from UKHSA's relaunch of the HIV drug resistance database in 2024, previously maintained by University College London until 2020
- implementation of the national HCV genomics surveillance programme for England

Antiparasitic resistance

• inclusion of additional parasitic infections and AMR data routinely in ESPAUR

Chapter 3. Antimicrobial consumption

Main messages

Antibiotics: The UK's National Action Plan (NAP) for AMR 2019 to 2024 set a UK-wide target to reduce antimicrobial consumption from the 2014 baseline by 15% by 2024, to 16.9 defined daily doses (DDDs) (<u>29</u>) per 1,000 inhabitants per day (DID) (<u>29</u>). Total antibiotic consumption was 17.6 DID in England in 2023, 4.1% (+0.69 DID) above the NAP target.

This is an increase of 2.4% in 2023 compared with antibiotic consumption in 2022, in part linked to a national surge in group A *Streptococcus* (GAS) cases between September 2022 and March 2023 (further details can be found in <u>Chapter 2</u>), but 1.9% below the pre-pandemic 2019 consumption level. Increases in <u>antibiotic use</u> were observed across all primary and secondary care settings with the exception of dental practices, in which consumption was 6.9% (-0.01 DID) below the use in 2019.

Increases were observed across the majority of <u>antibiotic groups</u> between 2022 and 2023. The greatest proportional increase in antibiotic use was observed in anti-*Clostridioides difficile* agents, which exceeded pre-pandemic 2019 levels, reflecting the continuing rise in *C. difficile* infection (CDI).

In 2023, the rates of first and second-generation cephalosporins and 'other antibacterials' consumption increased beyond 2019 levels. Consumption of other groups stabilised at, or below, pre-pandemic levels.

Penicillins remained the most frequently used antibiotic group in both primary and secondary care. This group observed the greatest absolute increase in use between 2022 and 2023, followed by tetracyclines.

Over the past 5 years antibiotic use in the primary care setting accounted for approximately 80% of total consumption across the healthcare system. In 2023, 79.7% of all antibiotics used were consumed in primary care.

Antibiotic use in 2023 was at 2019 levels or above in all age groups in primary care, although children aged 0 to 4 years saw a slight decrease from 2022 levels, during which antibiotic use in this age group peaked in response to the surge in GAS cases (Figure 3.7). Within the paediatric age groups consumption of the most frequently prescribed antibiotics was highest amongst 1 to 4 year-olds (Figure 3.8).

The highest rate of antibiotic use in primary care in 2023 continued to be in older adults aged over 65 years.

Antibiotic use in secondary care surpassed 2019 levels in 2023, with increases in accident and emergency and 'other' secondary care.

A steady increase in consumption of cefiderocol has been noted since its launch in the UK in 2020. The increase was observed between 2021 and 2023, with the highest rate of use in London. Further details can be found in $\underline{Box 3.7}$.

Out-of-season infection transmission continued with delayed re-emergence of *Mycoplasma pneumoniae* in late 2023. This followed the surge in GAS infections witnessed in late 2022 that extended into 2023. Both infections can be associated with increased demand for antibiotics and increased prescribing in children aged 0 to 4 years old remained elevated in 2023.

Antifungals: Total use of systemic antifungals in 2023 was similar to that seen in 2019 (+0.06%). There was a large decrease in 2020 during the COVID-19 pandemic, with usage subsequently increasing year-on-year. Use of systemic antifungals in primary care and in NHS acute trusts increased by 30.8% and 11.8%, respectively, from 2020 to 2023.

Terbinafine, the most frequently prescribed antifungal in the community, demonstrated year-onyear increases in use between 2020 and 2023 (+44.0%, 0.60 to 0.87 DID), surpassing 'prepandemic' levels.

Posaconazole secondary care prescribing increased markedly from 2019 to 2020 (+46%, 28.6 to 41.8 DDDs per 1,000 admissions) and remains at an increased rate in 2023 (44.9 DDDs per 1,000 admissions).

Antivirals: The total usage of the COVID-19 therapeutic agents in England showed a decrease of 45.0% (591,974 to 325,676 DDDs) between 2022 and 2023. This decline reflected the reduction in the number of reported COVID-19 cases in 2023 and changes in testing and guidance.

Antiparasitic agents: Among agents used to treat malaria, the most frequently prescribed was quinine; its use has decreased since 2019. Note that it can be used for non-infectious indications.

Mebendazole, indicated for treatment of threadworm infections, was the most frequently used anthelmintic in 2023, and saw a declining trend in use from 2019 to 2023.

Albendazole, however, saw a notable increase in the rate of use by 75% between 2021 and 2023. Part of this may be due to the increasing echinococcosis caseload.

Additions to this year's chapter

An AWaRe section including 'Watch' and 'Reserve' categories has replaced 'the broadspectrum' section.

Paediatric primary care data is highlighted to reflect the unique challenges in this population.

Introduction to Chapter 3

This chapter presents data on antimicrobial consumption in England from 2019 to 2023 in primary and secondary care and includes surveillance data 2 years on from the easing of COVID-19 pandemic restrictions. Antimicrobial prescribing settings included in the analysis presented in this chapter comprise primary care, encompassing general practices (GP), dental practices, and out-of-hours services, and secondary care, encompassing hospital inpatient and outpatient services. Total antimicrobial consumption includes antibiotic use across the healthcare system, comprising both the primary and secondary care settings listed above. Private healthcare settings are excluded from the analysis (see Chapter 3 of the <u>Annexe</u> accompanying this report for more details of the settings included in this chapter).

Antimicrobials (which include antibiotics, antivirals, antifungals and antiparasitics) are medicines used to stop the growth and spread of microorganisms causing infection. Antimicrobials are fundamentally different to other medicines in that their use not only improves individual health outcomes, but also has implications to the population. While antimicrobial resistance (AMR) is a natural phenomenon, use of antimicrobials accelerates this process. Efforts have been focused on improving the use of antimicrobials to maintain the efficacy of the ones currently available.

The majority of antimicrobial consumption within England is community-based through primary care. The focus of antimicrobial consumption epidemiology is on treatments used for common and less severe infections accordingly, such as urinary and respiratory tract infections treated in the community. Efforts have, however, been made to align the epidemiological presentation of antimicrobial consumption with AMR (<u>Chapter 2</u>), where relevant, in this chapter.

The UK's 2024 to 2029 National Action Plan (NAP) to confront AMR ($\underline{30}$) has an ambition to reduce total UK antimicrobial consumption in humans by 5% by 2029, from a 2019 baseline, with an increase in the relative proportion of narrow-spectrum antibiotics used. 'Data for action' is required to mobilise public health engagement and ensure progress towards these national targets. Data enables us to understand antimicrobial consumption trends at a national level and identify which antimicrobial stewardship (AMS) interventions may have the greatest impact (further details found in <u>Chapter 4</u>). This chapter illustrates the importance of access to robust national data from sources across different prescribing settings, ensuring the timely evaluation of trends in antimicrobial use, including unusual periods, such as the COVID-19 pandemic and out-of-season trends in infection transmission across the healthcare system.

Methods can be found in the <u>Annexe</u>. Data and figures presented in this chapter are available in the <u>Chapter 3 data table spreadsheet</u> and the <u>downloadable infographics figures slide deck</u>.

Antibiotic consumption

Total antibiotic consumption

2023 was the first complete year without any COVID-19 measures since 2019. Antibiotic consumption increased by 2.4% compared to 2022, although overall consumption remained below 2019 levels (-1.9%; 17.61 defined daily doses (DDDs) (<u>29</u>) per 1,000 inhabitants per day (DIDs) in 2023 compared to 17.96 DIDs in 2019) (<u>Figure 3.1</u>).

The post-pandemic period also saw changes to previously observed transmission patterns and interactions within the healthcare system, which partially explain these trends. From mid-September 2022, there were out-of-season increases seen in Group A streptococcus (GAS) infections. The trend in unusual circulation of infections continued into 2023, including a reemergence of *Mycoplasma pneumoniae* reflecting a similar trend seen globally (<u>31</u>). Both infections are frequently associated with increased demand for antibiotics (<u>32</u>, <u>33</u>).

Most antibiotics in England are prescribed in general practice. This remained the case in 2023 (71.7% of overall consumption, 12.6 DID). The percentage of usage in other settings in 2023 comprised hospital inpatients 13.5% (2.4 DID), hospital outpatient 6.8% (1.2 DID), other community settings 4.6% (0.82 DID) and dental practices 3.4% (0.60 DID) (Figure 3.1).

Figure 3.1 shows antibiotic consumption across the healthcare system in 2019 to 2023. Following the COVID-19 pandemic, a rebound in antibiotic consumption was observed between 2021 and 2023. Dental practices are the exception to this trend, with high rates of use observed from 2020 (0.75 DID) to 2021 (0.69 DID). Antibiotic consumption in dental care returned to 2019 levels (0.60 DID in 2023 compared to 0.61 DID in 2019). Antibiotic use in 2023 remained slightly lower compared with 2019 rates across all settings, with the exception of other community settings (+12.1%, 0.73 DID in 2019 to 0.82 DID in 2023).



Figure 3.1. Total antibiotic consumption by setting, expressed as DID, England 2019 to 2023

General Practice Hospital Inpatient Hospital Outpatient Dentist Other Community

Box 3.1. Regional variation in antibiotic consumption in England

Total DIDs have consistently been greatest within the North East and North West of England, and lowest in London and, in 2023, the South East (<u>Box figure 3.1.1</u>). This may be the result of regional differences in access to healthcare services, particularly in London, where the use of antibiotics in primary care has remained the lowest across all regions since 2019.

Regional reductions in the rate of total DID across all UKHSA centres in England in both primary and secondary care DIDs were seen during the COVID-19 pandemic (Box figure 3.1.1). The rate of antibiotic consumption, however, increased in primary and secondary care between 2022 and 2023 for most regions, apart from the South East (-5.6%, 2.93 to 2.76 DID) and North West (-5.7%, 3.95 to 3.73 DID), which have both seen a slight decrease in secondary care DID during this period. Between 2022 and 2023, primary care and secondary care increases were greatest in London (+3.2% and +15.1% respectively).

In 2023, consumption levels by UKHSA regions in primary and secondary care have largely remained below 2019 levels, with 4 of 9 UKHSA centres maintaining sustained lower antibiotic consumption compared to 2019. Slight increases in the rate of consumption were observed beyond 2019 levels in London (+0.8% total DID and +1.3% primary care DID), West Midlands (+0.1% total DID and +0.2% primary care DID), East of England (+0.7% secondary care DID) and East Midlands (+0.4% secondary care DID), while the North East saw rates surpass 2019 levels across the healthcare sector (+2.0% total DID between 2019 and 2023, +1.4% and +4.6% in primary and secondary care, respectively).



Box figure 3.1.1. Total, primary and secondary care antibiotic consumption in UKHSA centres, expressed as DID, 2019 to 2023 (excludes dental practice data)

(Primary care data does not include dental care prescribing as dental data at the UKHSA region-level was not available at time of production for the entire duration assessed. The order of UKHSA centres presented is based on geographic location from North to South of England.)

Antibiotic group

Figure 3.2 displays the antibiotic groups with the highest total consumption in England. In 2023, penicillin, excluding beta-lactam/beta-lactamase-inhibitor combinations (BLIs), remained the most used antibiotics groups in England, accounting for 32.7% (5.76 DIDs) of total consumption. This was followed by tetracyclines (25.8%, 4.55 DIDs), and 'macrolides, lincosamides and streptogramins' (13.3%, 2.35 DIDs). These groups were similar across primary and secondary care settings, however greater representation of penicillins including BLIs was observed in secondary care settings (Figure 3.2).

The period between 2022 and 2023 saw an increase in the use of the majority of antibiotic groups (Figure 3.2). The greatest absolute increase in use was seen in penicillins (excluding BLIs), with an increase of 0.14 DID between 2022 and 2023; this was primarily related to increased use of flucloxacillin (+0.06 DID, 3.5%) and amoxicillin (+0.08 DID, + 2.8%). However, the increase in amoxicillin was to a much lower extent compared to 2022, when unprecedented levels of GAS infection led to increased demand for antibiotics and a significant operational impact on healthcare services ($\underline{7}$). Following a rise in consumption during the elevated GAS activity in <u>December 2022 to March 2023</u>, phenoxymethylpenicillin use decreased slightly from 2022 to 2023 (-0.008 DID, -0.8%).

Although widespread increases were seen across several antibiotic groups, these for the large part remained lower than 2019 levels. However, first and second-generation cephalosporins (increase of 13.2% between 2019 and 2023, p<0.01), anti-*C. difficile* agents (+81.4%, p<0.05) and other antibacterials (+17.2%, p<0.05) exceeded 2019 levels. Use of anti-*C. difficile* agents continued to rise in 2023, with the largest percentage increase across all antibiotic groups (+15.6% DID between 2022 and 2023), although these agents still comprise the group with the lowest consumption (0.008 DID in 2023). Increased use of anti-*C. difficile* agents is likely related to noted increases in *C. difficile* cases (<u>34</u>).

Total use of pivmecillinam increased by 22.3% (from 0.079 to 0.097 DID) between 2019 and 2023, accompanied by decreases in 'sulfonamides and trimethoprim' (-0.3%, -0.003 DID) and nitrofurantoin (-4.1%, -0.009 DID; included in 'other antibacterials' group). This trend may reflect the increasing recommendation for pivmecillinam as an alternative treatment to trimethoprim (-12.9% (-0.001 DID) between 2019 and 2023) and nitrofurantoin for urinary tract infection (UTI) in adults (<u>35</u>). Increases in sulfonamides and trimethoprim and nitrofurantoin use were, however, seen in the hospital inpatient setting during this period (+27.2% (+0.023 DID) and +9.6% (+0.005 DID), respectively).

In contrast, consumption of oral metronidazole, 'macrolides, lincosamides and streptogramins', and quinolone antibacterials decreased by 3.1% (*p*=0.02), 1.1% (*p*=0.28), and 0.2% (*p*=0.15), respectively from 2022 to 2023.

The top 3 antibiotics used in primary care in 2023 were amoxicillin (penicillin excluding BLIs; 2.72 DID), doxycycline (tetracycline; 2.41 DID) and lymecycline (tetracycline; 1.35 DID). High

levels of amoxicillin and doxycycline consumption highlight the importance of AMS programmes aiming to optimise the duration of treatment courses for these antibiotics. More detail on the optimisation of antibiotic course duration can be found in Box 3.5. There is a need to evaluate the appropriateness of continuing high use of lymecycline, predominantly prescribed for acne in primary care.

In secondary care, the 3 most widely used antibiotics were co-amoxiclav (penicillin with BLIs; 0.59 DID), doxycycline (tetracycline; 0.50 DID), and flucloxacillin (penicillin with BLIs; 0.46 DID), reflecting the high proportion of antibiotics used for respiratory infection in secondary care settings (<u>36</u>). Flucloxacillin is also indicated for skin and soft tissue infections (<u>37</u>).



Figure 3.2 Total antibiotic consumption by antibiotic group and setting, expressed as DID, England, 2019 to 2023

General Practice Hospital Inpatient Hospital Outpatient Dentist Other Community

AWaRe: Access, Watch and Reserve

The AWaRe classification was first introduced by the World Health Organization (WHO) in 2017 and has since been updated every 2 years, with the latest revision in 2023 (<u>38</u>). The AWaRe classification categorises antibiotics into 3 groups, designated Access, Watch and Reserve. The 'Access' group comprises antibiotics where there is a need to improve availability to patients, particularly in countries where availability is currently limited. The 'Watch' group comprises antibiotics that are considered to have higher toxicity concerns and/or a potential for an increase in resistance. Lastly, the 'Reserve' group comprises new and 'last resort' broad-spectrum antibiotics, where inappropriate use should be minimised to reduce selective pressure for emergence and spread of resistance. A nationally adapted AWaRe classification has been used in England since 2019 (<u>39</u>), with several national- and trust-level antibiotic consumption targets based on this (<u>30</u>, <u>40</u>).

Following the 2023 update to the WHO classification, representatives across the UK 4 nations reviewed the 2019 England-adapted AWaRe classifications, following a modified Delphi approach, to ensure the classifications remain relevant to current national context (<u>41</u>). The adapted 2024 UK-AWaRe classification will support national AMS (<u>Chapter 5</u>) and the UK's NAP for AMR 2024 to 2029 (<u>30</u>), which has set a target that aims to achieve 70% total use (DDDs) of antibiotics from the Access category across the healthcare system, that is in primary and secondary care combined.

Use of Access antibiotics as a proportion of total antimicrobial consumption decreased during the COVID-19 pandemic between 2019 and 2020 but has seen a gradual increase, beyond 2019 levels, since 2021 (Figure 3.3).





Access use in primary care has been consistently higher than in secondary care between 2019 and 2023. In 2023, 66.7% of antibiotics used in primary care were in the Access category, 53.4% of antibiotics in secondary care and 64.1% across both sectors. Figure 3.4 shows proportions of Access, Watch and Reserve antibiotics used in primary and secondary care, and the combined total proportions across the healthcare system in 2023. In 2023, the most frequently used Watch or Reserve antibiotics in primary care were lymecycline (1.35 DID; Watch), clarithromycin (1.18 DID; Watch) and azithromycin (0.49 DID; Watch), whilst the top Access antibiotics were amoxicillin (2.72 DID), doxycycline (2.41 DID) and flucloxacillin (1.24 DID).

In secondary care, the most frequently used Watch or Reserve antibiotics were co-amoxiclav (0.59 DID), clarithromycin (0.22 DID) and ciprofloxacin (0.15 DID), all within the Watch category. Co-amoxiclav was also the most frequently used antibiotic in secondary care, reflecting the contribution of this antibiotic to the overall proportion of Watch and Reserve use in these settings. The Access antibiotics doxycycline (0.50 DID), flucloxacillin (0.46 DID) and amoxicillin (0.24 DID) were also used at high rates when compared to overall consumption in secondary care.



Figure 3.4 Proportion of AWaRe antibiotic use across the healthcare system in 2023 (2024 UK AWaRe classification)
Box 3.2. Increase in antibiotic usage in the private sector in England, May 2019 to April 2024

Surveillance of antimicrobial consumption across all healthcare sectors is required to better understand total consumption trends in England, to monitor changes or shifts in prescriber settings, and to identify areas requiring focused AMS efforts.

Penicillins and tetracyclines are the most frequently used antibiotics in the NHS (<u>Box figure</u> <u>3.2.1</u>). Furthermore, the majority of private antibiotic dispensing is observed in the community, with UTI being one of the most common clinical presentations. The antibiotic groups comprising penicillins and tetracyclines, in addition to the most frequently prescribed antibiotics for UTI were included in the private sector data presented here.

IQVIA collects data on antimicrobial usage across the private sector covering sales to private hospitals and private pharmacies, private prescriptions dispensed in community pharmacies and private usage in NHS facilities. Volume data (number of packs) was extracted for penicillin, tetracycline, nitrofurantoin, trimethoprim, fosfomycin and pivmecillinam antibiotics between May 2019 and February 2024 for private prescriptions dispensed in community pharmacies and to private patients in the NHS, and between June 2021 and February 2024 for sales into private hospitals and private pharmacies.

Over this period, medicines dispensed via private prescriptions represented approximately 3% of total packs dispensed from NHS prescriptions over the same period (increased from 1% in the 2023 report). These figures have steadily increased over recent years.

Usage by private hospitals, private pharmacies and private patients in the NHS remained stable, however there has been a steadily increasing trend in private prescriptions dispensed by community pharmacies (Figure 3.2.1). This may reflect an increasing trend towards people opting to pay for swift access to primary care through the private sector.

Penicillins remain the most commonly dispensed antibiotic group within the community pharmacy setting, followed by tetracyclines, nitrofurantoin, trimethoprim, fosfomycin and pivmecillinam.

Source:

- Sales into private hospitals and private pharmacies IQVIA Supply Chain Manager (SCM), June 2024, volume (number of packs)
- Private prescriptions dispensed in community pharmacy IQVIA Prescription Based Services (PBS), June 2024, volume (number of packs)
- Private usage within NHS hospitals IQVIA Hospital Pharmacy Audit (HPA), June 2024, volume (number of packs)

Box figure 3.2.1. Private sector dispensing of antibiotics (penicillins, tetracyclines, trimethoprim, fosfomycin, nitrofurantoin, pivmecillinam) in England, May 2019 to April 2024



a) Total penicillin, tetracycline, nitrofurantoin, trimethoprim, fosfomycin and pivmecillinam dispensing

Box 3.3. Changes to indications for fluoroquinolone use

An EU-wide review of fluoroquinolone safety was undertaken by the European Medicines Agency in October 2018, following very rare reports of disabling and potentially long-lasting or irreversible side-effects associated with fluoroquinolone use (<u>42</u>). The UK Medicines and Healthcare products Regulatory Agency (MHRA) subsequently published a drug safety update in March 2019, alerting clinicians to the introduction of new restricted indications for fluoroquinolone use in the UK, with particular reference to the 4 most commonly used fluoroquinolones: ciprofloxacin, levofloxacin, moxifloxacin and ofloxacin (<u>43</u>).



Box figure 3.3.1. Total, primary and secondary care consumption of fluoroquinolones

Box figure 3.1.1 shows the trends in fluroquinolone use from 2019 to 2023, following the review of fluoroquinolone safety, ordered by decreasing frequency of use.

- Ciprofloxacin consumption decreased in primary (-22.3% in DID) and secondary care (-9.1% in DID) from 2019 to 2023.
- Moxifloxacin also decreased in both primary (-41.1% in DID) and secondary care (-12.1% in DID) from 2019 to 2023.
- Ofloxacin use decreased in secondary care (-28.5% in DID) but increased in primary care (+11.6% in DID) from 2019 to 2023.

- Levofloxacin consumption increased in both primary (+16.9% in DID) and secondary care (+9.1% in DID) from 2019 to 2023.
- Norfloxacin represents a much smaller proportion of fluoroquinolone consumption. The rate of total consumption (DID) of this antibiotic decreased by 98.5% from 2019 to 2023.

The smaller decrease in rate observed in secondary care for ciprofloxacin and moxifloxacin may reflect the difference in clinical severity between patients treated in secondary versus primary care. However, the increase in use of levofloxacin in primary and secondary care, and ofloxacin in primary care, may point to the ongoing dependence on fluoroquinolones for certain clinical indications.

An alert of the risks associated with fluoroquinolone use was re-issued by MHRA in September 2023, which was complemented by further restrictions published in January 2024, adding that fluoroquinolones must be prescribed only when other antibiotics that are commonly recommended for these infections are considered inappropriate (44, 45). It is, therefore, likely that the rate of fluoroquinolone consumption will decrease further in the upcoming years; although, possibly, at a much slower pace due to the limited number of antibiotic alternatives.

Further information on the response to the MHRA alert can be found in <u>Chapter 5</u>, the Antimicrobial Stewardship chapter.

Antibiotic use in primary care (items by population)

In 2023, the primary care setting accounted for 79.7% of all antibiotics prescribed, with over 35 million prescriptions dispensed. Antibiotic use in primary care continued to rise in 2023 (+2.3% increase in items per 1,000 inhabitants per day between 2022 and 2023). Between 2019 and 2023, antibiotic prescribing within primary care increased from 1.66 to 1.70 items per 1,000 inhabitants per day, an increase of 2.3% (Figure 3.5), emphasising the need for continued AMS efforts.

Within primary care the increase in antibiotic use between 2022 and 2023 is reflected in both GP and other community settings (2.6% increase from 1.42 to 1.46 items per 1,000 inhabitants per day, and 9.2% from 0.11 to 0.12 items per 1,000 inhabitants per day, respectively). These rates are slightly above those observed in 2019.

Conversely, dental antibiotic consumption decreased between 2022 and 2023, with a 6.7% decline in antibiotics used in dental practices between 2022 to 2023 (from 0.13 to 0.12 items per 1,000 inhabitants per day).





Box 3.4. Antibiotic consumption in primary care by level of deprivation





Index of Multiple Deprivation (IMD) is a measure of the relative level of disadvantage across small areas in England. The data is presented as IMD quintiles, where IMD 1 represents primary care providers in the 20% most deprived neighbourhoods in England through to IMD 5, which represents primary care providers in the 20% least deprived neighbourhoods in England.

There is a notable positive association between increasing level of deprivation and increasing rates of antibiotic use in primary care, as shown in <u>Box figure 3.4.1</u>. The rate of total antibiotic use for the most deprived quintile was 65.7% higher than the rate of use in the least deprived quintile in 2019. From 2019 to 2023, the greatest increase in the rate of total antibiotic use was observed in the most deprived quintile (IMD 1) (+4.0% compared to +2.0% in IMD 5). The disparity in total antibiotic use subsequently increased between 2019 and 2023, with the difference in antibiotic use between IMD 1 and IMD 5 rising to 69.1%.

Broad-spectrum antibiotic use by IMD between 2019 and 2023, reflects the trend shown for total antibiotic use. In 2023, broad-spectrum antibiotic use as a proportion of total antibiotic use in primary care increased in all IMD quintiles; however, the difference in the proportion of broad-spectrum antibiotic use between IMD 1 and IMD 5 marginally decreased compared to 2019 (2.4% in 2023 compared to 2.8% in 2019). The use of broad-spectrum antibiotics in primary care has been previously attributed to poorer health status in line with the Marmot Review of Health Inequalities in England (<u>46</u>, <u>47</u>). Although the disparity in broad-spectrum use across quintiles has seen a slight improvement between 2019 and 2023, the increasing rate of total antibiotic use, and increasing proportion of broad-spectrum use across IMD quintiles in primary care demonstrate the ongoing need to address health equity issues.

General practice (GP) use

There was an overall increase (+2.4%) in total antibiotic items dispensed in the GP setting between 2019 and 2023, from 1.42 to 1.46 items per 1,000 inhabitants per day. Following the marked decrease observed between 2019 and 2020, prescribing subsequently increased from 1.25 to 1.46 items per 1,000 inhabitants per day between 2021 and 2023 (+16.6%).

Penicillins remain the most commonly used antibiotic group (Figure 3.6) within the GP setting, accounting for 48.5% of all antibiotic consumption in 2023, followed by tetracyclines (16.2%), other antibacterials (13.8%), and 'macrolides, lincosamides and streptogramins' (10.2%). GP penicillin consumption increased by 3.9% between 2019 and 2023 (Figure 3.6). Following a large decrease in penicillin use between 2019 and 2020, the rate of consumption rebounded beyond 2019 levels in 2022 (+26.3% to 0.69 items per 1,000 inhabitants per day). The substantial increase in use during 2022 is likely related to the unusual increase in circulating GAS, however this trend of increased use has continued into 2023 (+2.3% items per 1,000 inhabitants per day).





The COVID-19 pandemic resulted in a large reduction in antibiotic use across all ages between 2019 and 2020. This was most evident in children aged 0 to 4 years and 5 to 14 years; -39.9% (from 1.56 to 0.94 items per 1,000 inhabitants per day) and -25.9% (0.78 to 0.57 items per 1,000 inhabitants per day), respectively (Figure 3.7 a). This was followed by a post-pandemic increase in antibiotic consumption for paediatric age categories from 2021 through to 2023, with the sharp increase in the rate of consumption in paediatric patients likely attributable to the GAS surge during late 2022.

All age groups saw an increase in the rate of consumption between 2022 and 2023, with the exception of 0 to 4 year olds in whom there was decrease of 2.8% in the number of items consumed per 1,000 inhabitants per day. The rate of antibiotic use was highest amongst the oldest age groups in 2023 (Figure 3.7 b) (1.07 items per 1,000 inhabitants per day in those aged 65 years and above compared to 0.46 items per 1,000 inhabitants per day in those aged 15 to 64 years). The rate of antibiotic consumption was at 2019 levels (in 65 to 74 year olds) or above (in all other age groups) in 2023. The most frequently used antibiotics in the 65 and over age groups largely reflect the trends observed in the total population, with the exception of penicillins (including BLIs), which were the fourth most frequently consumed antibiotic group amongst older adults.

The next section explores the use of the most frequently used antibiotics within the paediatric age groups in response to the call to '<u>close the gap</u>' in the evidence base for this specific age group.





■ 0-4 ■ 5-14 ■ 15-64 ■ 65-74 ■ 75+ ■ Unknown

English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) Report 2023 to 2024

General practice antibiotic use by paediatric age groups





As shown in Figure 3.8 in 2023, the most commonly used antibiotic groups in paediatric primary care ('penicillins excluding beta-lactamase inhibitor combinations' and 'macrolides, lincosamides and streptogramins') have the highest rate of consumption in those aged 1 to 4 years old (1.77 DID and 0.23 DID, respectively), highlighting the increased vulnerability of this age group to infections, particularly of the respiratory tract (48). These top 2 groups represent approximately 90% of total antibiotic use in those aged 0 to 9 years old. The group with the third highest consumption, tetracyclines, which are indicated for the treatment of acne (49) in addition to respiratory infections and some sexually-transmitted infections (50), demonstrate exception to this trend. The highest rate of tetracycline consumption was observed in those aged 15 to 17 years old, followed by those aged 10 to 14 years old (Figure 3.8). The National Institute for Health and Care Excellence (NICE) does not recommend the use of tetracyclines for children younger than 12 years old (51), which may also support the higher rate of use in teenage groups and observed absence of use in the younger age groups. 'Sulfonamides and trimethoprim' comprise the fourth most commonly used antibiotic group in paediatric primary care, representing between 3.2% and 7.3% of total antibiotic use in primary care across the paediatric age groups. Sulfonamides and trimethoprim antibiotics are commonly used for the treatment of UTIs in young children (35). By contrast, penicillins including BLIs represent a relatively low proportion of antibiotic use within the paediatric age groups, ranging from 2% (0.03 items per 1,000 inhabitants per day; infants under one year old) to 2.5% (0.05 items per 1,000 inhabitants per day; 1 to 4 year olds) of total antibiotic use.

The proportion of total antibiotic consumption comprising Access antibiotics within the paediatric age groups was similar to that observed in the general population for 15 to 17 year olds. However, the relative proportion of Access antibiotic use in the youngest age groups was notably higher, decreasing with increasing age (90.4% in infants under one year; 86.8% in 1 to 4 year olds; 86.3% in 5 to 9 year olds, and 80.7% in 10 to 14 year olds).

Box 3.5. Optimising the duration of antibiotic treatment courses in primary care

Significant efforts have been made towards implementing effective shorter treatment durations for specific antibiotic indications in a drive towards the ambition to reduce total antimicrobial prescribing. The optimisation of antibiotic course duration from 7 to 5 days for amoxicillin, flucloxacillin and phenoxymethylpenicillin would deliver a 29% reduction and, for doxycycline, a 25% reduction in DDDs per prescribed item, respectively (<u>52</u>).

In September 2019, NICE published a guideline for the treatment of community-acquired pneumonia, recommending an amoxicillin and doxycycline course duration of 5 instead of 7 days (<u>53</u>). For 500, 250 and 125 mg amoxicillin capsules, the proportion of prescriptions for a 5-day course duration increased steadily from 29.7% to 54.0% between 2019 and 2023 (<u>Box</u> figure 3.5.1a). A similar increase in the proportion of items prescribed for a 5-day course duration of was observed for 100 mg doxycycline capsules (+18.9% between 2019 and 2023; <u>Box figure 3.5.1 b</u>).

In the case of flucloxacillin, NICE recommends 5-day antibiotic courses for impetigo (54), and 5 to 7 days for cellulitis (37) and secondary bacterial infection of eczema (55), as published in February 2020, September 2019, and March 2021, respectively. Between January 2019 and January 2022, the share of 5-day course duration with 500 mg and 250 mg flucloxacillin capsules increased by 1.2% (from 7.3% to 8.5%), with an additional increase of 4.6% in December 2023, reaching 13.1% (Box figure 3.5.1 c).

NICE guidelines also recommend shorter duration courses of phenoxymethylpenicillin (Penicillin V) for acute sinusitis (56) and acute sore throat (57). Since the publication of the respective NICE guidelines in 2017 and 2018, The proportion of 5-day treatment regimens for 250 mg phenoxymethylpenicillin tablets increased, demonstrating a change of 18.2% (Box figure 3.5.1 d), consistent with trends observed for both amoxicillin and doxycycline.

In conclusion, the results highlight the positive impact of national guidelines on reducing antibiotic course durations where appropriate. While recommended antibiotic dose and duration vary with the severity of the medical condition and patient circumstances, continuous review of clinical guidelines at national, regional and local levels is essential to ensuring that guidelines support evidence-based practice, promote health and avoid unnecessary harm. More evidence is required to inform recommendations to reduce the duration of antibiotic courses. This will further assist in the delivery of national targets towards a reduced national antimicrobial usage.

Figure 3.5.1. Proportion of treatment courses represented by 5-day, 7-day, or other durations for a) amoxicillin, b) doxycycline, c) flucloxacillin, and d) phenoxymethylpenicillin, 2019 to 2023





Other community use

Antibiotic consumption in other community settings has shown a 9.2% increase between 2022 and 2023 (from 0.11 to 0.12 items per 1,000 inhabitants per day). The 2023 rate of use remains higher than 2019 levels within this setting (0.108 items per 1,000 inhabitants per day). The rise in antibiotic consumption seen both here and in general practice is suggestive of increased healthcare demands in 2023, rather than shifts in provision of services alone.

Items dispensed in out-of-hours primary care centres accounted for 49.3% of 'other community' consumption in 2023, with large regional differences ranging from the lowest proportion in the North East (20.8%) and London (29.1%) to the highest in the East of England (64.2%) and the South West (79.6%). Nationally, 'other community' consumption exhibited an increase of 5.0% between 2022 and 2023 (0.055 to 0.059 items per 1,000 inhabitants per day). In 2023, out-of-hours, urgent care, community hospitals, nursing homes and custody had higher rates of antibiotic use than 2019, although many of these setting contribute a small proportion of total consumption in other community settings.

Dental use

A year-on-year decrease in antibiotic use in the dental setting has been observed since 2020 (average decrease of -7.4% (0.06 items per 1,000 inhabitants per day) in consumption rate each year from 2020 to 2023). In 2023, the rate of antibiotic use within the dental setting fell below the 2019 rate for the first time since the COVID-19 pandemic (-2.7% from 0.61 items per 1,000 inhabitants per day in 2019 to 0.60 in 2019) (<u>58</u>).

The antibiotics most commonly used in dental care in 2023 remain amoxicillin (67.1%), metronidazole (27.7%) and erythromycin (2.0%), all 3 of which showed a declining trend in 2023. Between 2019 and 2023 there was, however, a notable increase in the use of 'other' antibiotics used in dental care (+85.3%, from 0.001 to 0.003 items per 1,000 inhabitants per day).

Box 3.6. Practice-level dental prescribing

A dental ESPAUR sub-group comprising dental professionals and representatives from wider system organisations, including NHS England (NHSE), academia, and the NHS Business Service Authority (NHBSA), was formed to identify and address the barriers to availability of practice-level prescribing data in dental settings.

Dental prescriptions are handwritten, with no current scope for e-prescribing. Once a patient receives a prescription from a dentist it is taken to a pharmacy where it is processed. The dispensed paper prescription is then forwarded to the NHSBSA. Thus, it is currently only feasible to collect dental prescribing data at pharmacy level.

Work is ongoing to explore the requirements that would enable greater visibility of dental prescribing to be similar to other primary care prescribers, including the impact of coding.

Antibiotic use in secondary care (DDDs by admissions)

Total antibiotic use in secondary care

Antibiotic use in NHS acute hospital trusts, measured using hospital admissions as the denominator, increased by 0.4% between 2019 and 2023 (from 4,671 to 4,690 DDDs per 1,000 admissions). During this period inpatient prescribing increased by 5.0% (from 2,956 to 3,105 DDDs per 1,000 admissions), whereas outpatient prescribing decreased (-7.6% from 1,715 to 1,585 DDDs per 1,000 admissions).

Between 2022 and 2023, overall antibiotic use in secondary care decreased by 1.9% (from 4,781 to 4,690 DDDs per 1,000 admissions). There was a 2.7% decrease in outpatient prescribing (from 1,628 to 1,585 DDDs per 1,000 admissions), with the prescribing rate in 2023 remaining lower than that seen in 2019 (1,715 DDDs per 1,000 admissions). Prescribing to inpatients showed a 1.5% decrease (from 3,153 to 3,105 DDDs per 1,000 admissions), however the rate in 2023 remained above that seen in in 2019 (2,956 DDDs per 1,000 admissions).

Figure 3.9. Antibiotic consumption, by trust type, expressed as DDDs per 1,000 admissions, England, 2019 to 2023



The decrease in antibiotic use between 2022 and 2023 was noticeable in all acute trust types apart from acute small trusts and acute specialist trusts, where prescribing increased by 1.3% (from 4,505 to 4,564 DDDs per 1,000 admissions) and 0.6% (from 4,660 to 4,690 DDDs per 1,000 admissions), respectively (Figure 3.9). This was converse to the trend seen in 2022, when acute specialist trusts saw a decrease (-2.0%), when compared to other trust types.

Antibiotic use in acute small trusts, acute multiservice trusts and acute teaching trusts remained above 2019 levels in 2023, whilst acute medium and acute large trust antibiotic use fell below 2019 levels. Antibiotic use in acute specialist trusts remained below 2019 levels, despite the

slight increase observed from 2022 to 2023. Due to missing or unreliable data between 2019 and 2023, information for 11 trusts (equivalent to an estimated 3.7 million DDDs) was removed. A section providing details on data quality can be found in the <u>Annexe</u>.

<u>Figure 3.10</u> shows antibiotic usage (DDDs per 1,000 admissions) by antibiotic group from 2019 to 2023. In 2023, penicillins had the highest use in secondary care, accounting for 42% of acute trust antibiotic consumption. This was followed by tetracyclines at 15%, macrolides at 10%, other antibacterials at 9%, with the remaining groups each comprising less than 10% of all antibiotics. This trend in prescribing remains unchanged from 2022.

Following widespread increases in antibiotic use across the majority of antibiotic groups in 2022, there were subsequent decreases in prescribing in 2023. The largest decreases were observed in aminoglycosides (-8.0%, 141.5 to 130.2 DDDs per 1,000 admissions), macrolides (-5.4%, 494.8 to 467.9 DDDs per 1,000 admissions) and third, fourth and fifth generation cephalosporins (-3.7%, 102.1 to 98.3 DDDs per 1,000 admissions). However, an absolute increase was observed in the use of tetracyclines (Figure 3.10), which increased by 12.0 DDDs per 1,000 admissions (+1.7%). Between 2019 and 2023 there was a notable increasing trend observed in prescribing for anti-*C. difficile* agents (+85.4%, absolute difference of 3.73 DDDs per 1,000 admissions). Anti-*C. difficile* agents also saw the largest proportional increase in 2023 year, with a 10.7% increase in use from 2022. Increased use of anti-*C. difficile* agents may be related to noted increases in hospital-onset *C. difficile* infections. The change in use of anti-*C. difficile* agents also coincides with new NICE guidelines for *C. difficile* prescribing (59) and a subsequent increase in access to fidaxomicin.



Figure 3.10. Antibiotic consumption in trusts by antibiotic group, expressed as DDDs per 1,000 admissions, England 2019 to 2023

Box 3.7. Antimicrobial Product Subscription Model: new antimicrobials

In the UK's NAP for AMR 2019 to 2024 ($\underline{30}$), NHSE committed to test new ways to pay for antimicrobial products. This recognised the challenge for the pharmaceutical sector to bring products to market due to restrictions that are placed on the use of new products.

NHSE and NICE formed a joint project team to pilot a payment model that estimated the benefit of new products to patients and the health system, determining payments based on the underlying value of the product rather than the volume sold.

The payment model agrees a fixed annual fee with the pharmaceutical company that is split into 2 parts: 1) sales revenue from the purchase of packs by hospitals, and 2) a top-up fee paid by NHS England. This ensures that hospitals can continue to purchase packs of antibiotics using their regular wholesaler channels, whilst the pharmaceutical company receives the pre-agreed level of payment.

The subscription model will enable participation of all nations of the UK with a view to launch the first tender under the scheme in 2024, following the pilot in 2022 that selected 2 products: ceftazidime/avibactam and cefiderocol (60). The model offers contracts for up to 16 years in length to cover the intellectual property exclusivity period. In exchange for the payments, companies must comply with several obligations, including maintaining market supply, ensuring timely delivery of products and adhering to manufacturing environmental standards.

New antimicrobials

In England, there are several new antimicrobials which have become available over the past 5 years, including cefiderocol, ceftolozane/tazobactam, ceftazidime/avibactam and eravacycline. IQVIA collects data on antimicrobial usage across the secondary care setting. <u>Box figure 3.7.1</u> displays the total DDDs for these new antimicrobials in England, by region, in 2023.

Cefiderocol, a cephalosporin antibiotic primarily used against multidrug-resistant Gram-negative bacteria, including carbapenem-resistant Enterobacteriaceae (CRE) and *Pseudomonas aeruginosa*, shows a gradual increase over the past 4 years, with an increase (58%) in usage from 2022 to 2023.

Ceftolozane/tazobactam is a combination antibiotic used to treat complicated UTIs, complicated intra-abdominal infections, and hospital-associated bacterial pneumonia. There has been fluctuation in the usage of DDDs for ceftolozane/tazobactam due to a drug shortage in 2021 (<u>61</u>).

Ceftazidime/avibactam is a relatively new combination antibiotic used to treat complicated infections including severe drug-resistant Gram-negative bacterial infections. Consumption of ceftazidime/avibactam increased by 71.5% between 2019 and 2023, although relative consumption of this antibiotic remains low. The rate of ceftazidime/avibactam consumption was

highest in 2021 (1.0 DDDs per 1,000 admissions) and a slight decrease in use has been observed in 2022 (-4.4%) and 2023 (-0.8%).

Eravacycline, belonging to the tetracycline class, is used to treat complicated intra-abdominal infections. The secondary care setting began using eravacycline in May 2023, and there is currently low DDDs usage.

Box figure 3.7.1. Regional consumption of new antimicrobials, expressed as total DDDs, England 2023 (a) cefiderocol (b) ceftolozane/tazobactam (c) eravacycline (d) ceftazidime/avibactam



Cefiderocol and ceftazidime/avibactam had the highest usage across all the regions. London had the highest total DDDs follow by North West. Eravacycline had the lowest DID usage, with consumption in 2 regions, London and North West (<u>Box figure 3.7.1</u>).

Note: Use of cefiderocol, ceftolozane/tazobactam, ceftazidime/avibactam and eravacycline is monitored within the metrics presented above.

Speciality prescribing

Consumption data for specialist groups in secondary care is presented in <u>Table 3.1</u>. Within the specialist groups, intensive care units (ICUs) continue to have the highest antibiotic usage, with 67.9 DDDs per ICU admission in 2023. The next highest antibiotic usage was observed in accident and emergency (A&E) and non-specified outpatient departments, with 29.5 DDDs per speciality admission.

Between 2019 and 2023, most speciality groups showed an increase in antibiotic use, with the exception of specialist surgery and 'other' specialties in which decreases of -9.0% (1.9 to 1.8 DDDs per admission) and -3.8% (5.9 to 5.7 DDDs per admission) below pre-pandemic levels were observed, respectively.

The greatest increase in antibiotic prescribing from 2022 was observed in A&E and non-specific outpatient departments (+32.1%, 22.3 to 29.5 DDDs per admission).

Table 3.1. Percentage of all antibiotic consumption attributed to piperacillin/tazobactam,
carbapenems and colistin in secondary care by speciality, expressed as DDDs per
speciality admission, England, 2022 to 2023

Specialist group	DDDs per admission	Piperacillin/ tazobactam	Carbapenems	Colistin*
Intensive Care Unit	67.6	5.0%	4.2%	0.1%
A&E/Non-specific Out-Patient Department	29.5	1.0%	0.3%	0.1%
Specialist Medicine	4.8	2.9%	2.1%	0.7%
General Surgery	3.8	2.6%	1.2%	0.0%
Geriatrics	3.5	4.7%	1.8%	0.0%
Orthopaedics	3.2	2.5%	1.4%	0.0%
Obstetrics and Gynaecology	2.5	0.6%	0.4%	0.0%
Paediatrics	2.2	1.4%	1.3%	1.0%
General Medicine	2.2	3.4%	1.5%	0.1%
Specialist Surgery	1.8	1.6%	1.3%	0.2%
Other	5.7	2.0%	1.2%	0.0%

* Colistin: parenteral route only, inhaled colistin was excluded

Antifungal consumption

Total antifungal consumption

Total consumption of systemic antifungals in England in 2023 was similar to that seen in 2019 (+0.06%, (Figure 3.11). As presented in previous ESPAUR reports, antifungal usage, expressed as DDDs per 1,000 population per day, decreased significantly in 2020, the first year of the COVID-19 pandemic. Usage has since increased to pre-pandemic levels, increasing by 28.3% from 2020 to 2023. Specifically, use of systemic antifungals in primary care and in NHS acute trusts has increased by 30.8% (0.84 to 1.10 DID) and 11.8% (0.12 to 0.14 DID) respectively between 2020 and 2023.

In 2023, 89% of systemic antifungals were used in the community setting. It is difficult to know whether this is a true representation of community use as several antifungal agents can be supplied as over the counter (OTC) medicines, which are not captured in this data set.





Box 3.8. Regional variation in antifungal consumption in England

There was marked regional variation in use of antifungals in England (<u>Box figure 3.8.1</u>). In 2023, the North West had the highest prescribing rate (1.56 DID); this is also the region with the highest reported incidence of fungaemia (see AMR Annex). The South East used the fewest antifungals (1.06 DID). Differences in the resident population characteristics and distribution of specialist care trusts may account for the variations seen between regions.

Box figure 3.8.1. Total consumption (primary and secondary care) of systemic antifungals for UKHSA centres, expressed as DDDs per 1,000 inhabitants per day (a) 2019 (b) 2023



Following a substantial reduction in antifungal use from 2019 to 2020, that is the first year of the COVID-19 pandemic, all regions have subsequently seen year-on-year increases. All regions are nearing or have surpassed 2019 prescribing in 2023, most markedly in the East of England and South East, by 5.9% (1.01 to 1.07 DID) and 3.6% (1.02 to 1.06 DID), respectively.

Antifungal prescribing in primary care

The total use of systemic antifungals in the community in 2023 was similar to 2019 (+0.3%, from 1.097 to 1.100 DID). Figure 3.11 shows a large decrease in total systemic antifungals prescribed in the community between 2019 and 2020 (-23.3%, 1.097 to 0.841 DID). There have been year-on-year increases from 2020 to 2023 (+30.8%, 0.841 to 1.100 DID).

<u>Figure 3.12</u> shows that the most frequently prescribed antifungal in the community was terbinafine (0.87 DID in 2023), an oral agent active against common dermatophyte infections of the skin, hair and nails. Usage of terbinafine decreased by 27.8% from 2019 to 2020 likely related to the COVID-19 pandemic 'lockdowns' where transmission of dermatophyte infections

were reduced. There has been a year-on-year increase in terbinafine use between 2020 and 2023 (+44.0%, 0.6 to 0.87 DID), surpassing 2019 levels.

Fluconazole usage has increased over the last 5 years (+10.3%, 0.081 to 0.089 DID). Oral fluconazole, most often used for cutaneous and mucosal yeast infections, is available over the counter, hence numbers presented may not reflect true use. Nystatin use has decreased year-on-year from 2019 to 2022 (-18.4%, from 0.072 to 0.059 DID), with a slight increase in 2023 (+6.7%, from 0.059 to 0.063 DID). Itraconazole and griseofulvin usage have decreased each year since 2019 (between 2019 and 2023, from 0.101 to 0.075 DID, and from 0.007 to 0.003 DID, respectively).

There are a limited number of drugs shown <u>Figure 3.12</u>, as there are limited types of antifungal prescribed for systemic use in the community setting; more variety can be seen in the hospital setting.





Antifungal prescribing in secondary care

As can be seen in Figure 3.13, total consumption of systemic antifungals in NHS acute trusts in 2023 was 185 DDDs per 1,000 admissions. This represents a 4.6% increase in the rate of prescribing from 2019 (177 DDDs per 1,000 admissions) but an 8.4% decrease from 2020 (202 DDDs per 1,000 admissions). The decrease in prescribing rate from 2020 to 2023 suggests that in 2023 antifungal prescribing and acute trust admissions were returning to pre-pandemic levels.



0

2019

2020

Figure 3.13. Total consumption of systemic antifungals in NHS acute hospital trusts in England, expressed as DDDs per 1,000 admissions, 2019 to 2023

Year

2021

2022

2023

Figure 3.14 shows the prescribing of individual systemic antifungals in secondary care. Fluconazole was the most frequently prescribed antifungal (2023: 64 DDDs per 1,000 admissions). Prescribing of fluconazole in 2023 is similar to levels in 2019 (-0.02%) however it has decreased from a peak of 74 DDDs per 1,000 admissions in 2020 (-13.3%). The next highest antifungal prescribed was posaconazole (2023: 45 DDDs per 1,000 admissions). Posaconazole prescribing increased markedly in 2020 (+57% in comparison to 2019) and remains at the increased rate in 2023, most likely due to the reduced cost of this drug following its coming off patent in 2020. Itraconazole and voriconazole usage has decreased between 2019 and 2023, with 30.3% and 8.5% reductions respectively during this time period, possibly representing a switch to posaconazole.

Amphotericin B is a broad-spectrum agent suitable for most invasive yeast and mould infections. Usage of it increased year-on-year from 2019 to 2021, increasing by 18.5% over this period (from 26.7 to 31.6 DDDs per 1,000 admissions). Usage has since decreased by 27.5% from 2021 to 2023 (31.6 to 22.9 DDDs per 1,000 admissions).

In 2023, the rates of use of echinocandin antifungals were 5.1, 6.3 and 0.6 DDDs per 1,000 admissions for anidulafungin, caspofungin and micafungin, respectively. Since 2019 both anidulafungin and caspofungin usage have increased (2019 to 2023: +42% and +17% respectively), although rates are still small. Micafungin usage, however, decreased by 65%, from 1.8 to 0.6 DDDs per 1,000 admissions between 2019 and 2023.

Flucytosine, which is not prescribed as a sole agent but often in combination with Amphotericin B, has the lowest levels of prescribing at 0.2 DDDs per 1,000 admissions. Terbinafine usage decreased between 2019 and 2021 (9.9 to 9.4 DDDs per 1,000 admissions) but has since increased to 10.9 DDDs per 1,000 admissions.



Figure 3.14. Total antifungal consumption by drug in NHS acute trusts, 2019 to 2023

In 2023, the specialty with the highest systemic antifungal prescribing rate was 'Haematology' (11,658 DDDs per 1,000 admissions) followed by 'Intensive Care Medicine' (11,443 DDDs per 1,000 admissions).

Antiviral consumption

Influenza virus

Box 3.9. Use of influenza antivirals

Influenza admissions and use of oseltamivir and zanamivir in secondary care have the same trend and seasonality over time. Prescriptions and admissions both begin to increase during October, peak in December, and then decline to baseline levels in April (<u>Box figure 3.9.1</u>). The 2020 to 2021 and 2021 to 2022 influenza seasons were severely impacted by the COVID-19 pandemic and associated social distancing measures, resulting in relatively few influenza admissions and influenza antiviral prescriptions.

Box figure 3.9.1. Time series plot of monthly courses of influenza antivirals oseltamivir and zanamivir in primary and secondary care settings, compared to monthly influenza admissions, from January 2019 to December 2023 in England



Prescriptions of influenza antivirals in primary care settings through FP10 prescriptions are permitted only after the Chief Medical Officer and Chief Pharmaceutical Officer notification to primary care providers that influenza is circulating in the community. FP10 prescriptions of oseltamivir or zanamivir in primary care was not permitted during the periods 08 May 2019 to 03 December 2019, 18 May 2020 to 24 November 2022, and the 09 May 2023 to 14 December 2023. Primary care prescriptions typically peak within one month of the notification being issued and follow a similar trend to secondary care prescriptions.

Oseltamivir prescriptions in primary care peaked at 9,807 courses in December 2022, increasing from 7,199 in December 2019. From the 2019 to 2020 influenza season to the 2022 to 2023 influenza season, the peak number of oseltamivir courses in secondary care increased by approximately 50%, from 20,814 to 31,507. In contrast, the peak number of oseltamivir courses per influenza admission decreased, from 1.94 in the 2019 to 2020 season, to 1.06 in the 2022 to 2023 season. DDDs of oseltamivir per 1,000 influenza admissions decreased by over 37% from 2019 to 2023 (Box figure 3.9.2).

Prescriptions of zanamivir (often second line treatment) are of quantities much lower than oseltamivir in both primary and secondary care settings, peaking at approximately 68 courses in primary care in February 2019, and 1,290 courses in secondary care in December 2022, respectively (Box figure 3.9.2). Prescriptions of zanamivir in primary care are exclusively powder inhalation devices. DDDs of zanamivir per 1,000 influenza admissions peaked in 2021 at 0.63, before decreasing to 0.09 in 2023.



Box figure 3.9.2. Total oseltamivir consumption in secondary care, expressed as DDDs per 1,000 influenza admissions, 2019 to 2023 in England

SARS-CoV-2: COVID-19 therapeutics

This section discusses the use of antiviral agents against SARS-CoV-2. It includes epidemiological surveillance data on 4 direct-acting antiviral COVID-19 treatments use in England from 2020 to 2023 (62). Primary care data was obtained from NHSBSA ePACT2, and secondary data was sourced from IQVIA. The total usage of these therapeutic agents, measured in DDDs, in England showed a decrease of 45.0% from 591,974 to 325,676 DDDs between 2022 and 2023. This decline from 2022 to 2023 is in line with a reduction in the number of reported COVID-19 cases in 2023 (n=8,665,433; 593,963 respectively).

Figure 3.15 displays the rates (expressed as DDDs) in England for therapeutics for primary and the secondary care settings. As denominator data for individuals who were eligible, offered and accepted each treatment was unavailable, the number of COVID-19 cases were used. This is considered an exploratory analysis and may not directly reflect variations between care providers. Further work is planned to understand the use of COVID-19 therapeutics in people. Nirmatrelvir plus ritonavir was the most frequently dispensed within both primary and secondary care setting with the highest rate in 2023 (533 DDDs per 1,000 COVID-19 cases (69%). Followed by molnupiravir 202 DDDs per 1,000 COVID-19 cases (19%). Remdesivir and sotrovimab are only used within the secondary care setting which were 121 DDD per 1,000 COVID-19 cases (8%) and 39 DDD per 1,000 COVID-19 cases (3%), respectively. The period between November and December 2023 saw an increase in the use of DDDs per 1,000 COVID-19 cases with exception of remdesivir which saw a reduction of 21.5%. Rate were higher in 2023 compared to 2020 as COVID-19 cases as decreased and the rate fluctuated with transmission of SARS-CoV-2 in the population and changes in testing and guidance (Figure 3.15).



Figure 3.15. Total consumption of COVID-19 therapeutics, expressed as DDDs per 1,000 COVID-19 cases, England, 2020 to 2023

Rate of total DDDs per 1,000 COVID-19 cases between 2020 and 2023 varied by UKHSA region (Figure 3.16). London had the highest use of remdesivir (0.18 DDDs per 1,000 COVID-19 cases) compared to other regions, ranging from 0.03 in East Midlands to 0.09 in the North West (DDDs per 1,000 COVID-19 cases). The highest use of nirmatrelvir plus ritonavir, molnupiravir and sotrovimab was seen in the South East, whilst the lowest use was in the East Midlands and South West.

Figure 3.16. Regional consumption of COVID-19 therapeutics, expressed as DDDs per 1,000 COVID-19 cases, England, 2023 (a), remdesivir, (b), nirmatrelvir plus ritonavir (c), molnupiravir and (d) sotrovimab



Hepatitis B virus

Box 3.10. Antiviral prescribing for the treatment of hepatitis B virus (HBV)

Entecavir and tenofovir disoproxil are the primary recommended options for people in whom antiviral treatment is indicated. Surveillance of antiviral treatment coverage of individuals living with diagnosed chronic hepatitis B is required to monitor equity in access and outcome from treatments. The main aim of current treatment strategies is to prevent chronic liver disease progression through endpoints of long-term suppression of HBV replication with HBsAg loss being the optimal endpoint.

As treatment eligibility has historically been complex and can change over a person's life, with many people being monitored but not on treatment for years, attrition of retention in care can occur. Simplified treatment guidelines may improve patient engagement, require less specialist follow up, and expedite achievement of public health programme goals. European Association for the Study of the Liver (EASL) and WHO have recently simplified guidance on treatment eligibility to (i) those with HBV DNA >2,000 IU/ml, elevated alanine aminotransferase (ALT) and/or at least moderate histological lesions, and (ii) all cirrhotic patients with detectable HBV DNA. Additionally, all patients should be monitored for disease progression and hepatocellular carcinoma (HCC).

Although a national comprehensive treatment monitoring system has not yet been established, IQVIA collects data on antiviral prescriptions dispensed in secondary care pharmacies in England. Volume data (number of packs) was extracted from IQVIA for entecavir (0.5mg or 1mg once daily) and for tenofovir disoproxil (245mg once daily) between 2019 and 2022. The number of doses was estimated by number of packs provided by IQVIA. Tenofovir, in combination with other antiretroviral drugs, is also a treatment for HIV and is recorded as a combination treatment in IQVIA. We identified any single use of tenofovir disoproxil as indicating HBV treatment.

The average number of prescriptions (which equates to packs) per year between 2019 and 2022 was 60,363 units for entecavir and 115,817 units for tenofovir disoproxil. Numbers of prescriptions increased between 2019 and 2022 from 50,621 to 73,708 units for entecavir and from 114,769 to 120,469 units for tenofovir disoproxil. Between 2019 and 2022, an estimated annual average of 4,961 individuals were treated with entecavir and 9,519 individuals treated with tenofovir disoproxil (Box figure 3.10.1). Between 2019 and 2022, the estimated number of individuals treated with entecavir increased from 4,161 to 6,058 and from 9,433 to 9,902 for tenofovir disoproxil. For London, an estimated annual average of 2,370 individuals were treated with entecavir and 4,200 with tenofovir disoproxil; outside London the estimated numbers were 2,591 and 5,319 individuals, respectively.





Please refer to the <u>Hepatitis B annual report</u> for further information.

Antiparasitic consumption

Assessment of the consumption of antiparasitic drugs is included below and includes antimalarial and antihelminthic drugs, which are a new addition to the ESPAUR report this year. Consumption data is provided for the antiparasitics used in England, for which DDDs are available according to the WHO. Data is presented as DIDs, combined for primary and secondary care.

Antimalarial consumption

The UKHSA recently reported data showing a rise in travel-acquired malaria to pre-COVID-19 levels, with the number of imported cases diagnosed in 2023 exceeding 2000 cases for the first time in over 20 years (<u>63</u>). The rise is linked to an increase in overseas travel following removal of COVID-19 pandemic restrictions, combined with a global resurgence of malaria cases beyond pre-pandemic levels (<u>64</u>). Antimalarial consumption data in <u>Table 3.2</u> is reported for the treatment and prophylaxis against malaria.

Quinine is the mostly frequently prescribed antimalarial drug (0.500 DID in 2023). Consumption of quinine has seen a steady decline over the past 5 years (26.0% decrease in DIDs between 2019 and 2023) in contrast to the observed increase in travel-acquired malaria cases. This is likely to be due to the change from quinine to ACT as first line antimalarial therapy in the UK. Not all quinine prescribing can be attributed to malaria treatment and may include prescribing for other conditions, although the only indication for quinine apart from malaria listed in the British National Formulary is nocturnal night cramps.

Conversely, consumption of atovaquone-proguanil (A-P; commonly known as Malarone) showed an overall increase between 2019 and 2023 (+95.1% in DIDs). Prescribing remained stable over the formative years of the COVID-19 pandemic (0.0059 DIDs in 2020 and 2021), but a sustained increase in prescribing has been observed since the pandemic, continuing into 2023. A-P is used in both the prevention and treatment of malaria, but as ACTs are the first line for malaria treatment in the UK, most scripts for A-P are likely to be for chemoprophylaxis, especially in the community, as malaria is predominantly treated in secondary care. Therefore, it is most likely that the increase in A-P prescribing is a result of the increase in international travel post-pandemic.

Whilst some antimalarial drugs are also used to treat other conditions, or as chemoprophylaxis, ACT is only used in the treatment of malaria. Oral ACT is the first line treatment for *P. falciparum*, with severe or complicated cases receiving intravenous artesunate prior to oral ACT. Consumption data indicates that artemisinin compound prescriptions have remained stable over the 5 years to 2023, at 0.0002 DID, except for an observed decrease to 0.0001 DIDs, coinciding with the COVID-19 pandemic in 2020.

Antimalarials	2019	2020	2021	2022	2023	
Quinine*	0.6755	0.6051	0.5596	0.5286	0.5000	
Atovaquone/proguanil**	0.0041	0.0059	0.0059	0.0067	0.0080	
Chloroquine***	0.0011	0.0011	0.0007	0.0009	0.0006	
Primaquine	0.0010	0.0010	0.0008	0.0009	0.0011	
Mefloquine	0.0001	0.0000	0.0001	0.0001	0.0001	

Table 3.2. Total antimalarial consumption in England, expressed as DDDs per 1,000inhabitants per day, 2019 to 2023

Antimalarials	2019	2020	2021	2022	2023
Artemisinin compounds [^]	0.0002	0.0001	0.0002	0.0002	0.0002
Piperaquine phosphate/artenimol	0.0000	0.0000	0.0000	0.0000	0.0000

Notes to Table 3.2

* Quinine includes: quinine bisulfate, quinine dihydrochloride, quinine sulfate.

** Atovaquone/proguanil includes: proguanil, proguanil/atovaquone, atovaquone. (Atovaquone alongside use as antimalarial may also be used for treatment of *Pneumocystis* pneumonia).

*** Chloroquine includes: chloroquine and chloroquine phosphate.

^ Artemisinin compounds includes: artemether/lumefantrine, artesunate.

Anthelmintic consumption

Consumption of anthelmintics can be seen in <u>Table 3.3</u>. The data indicates that mebendazole is the most frequently used anthelmintic drug in England (0.0108 DID in 2023). The rate of mebendazole consumption has decreased over the previous 5 years (-29.0% in DIDs between 2019 and 2023). Mebendazole is indicated for the treatment of several helminth infections, including threadworm (*Enterobius vermicularis*), the most common parasitic worm infection in the UK, particularly in children aged between 4 and 11 years old (<u>NICE, 2023</u>).

Mebendazole is available as an over the counter (OTC) medication (<u>following a public</u> <u>consultation in 2018</u>), without prescription, for certain indications (for example, threadworm), and whilst the data includes community pharmacy consumption, the data does not capture anthelmintics dispensed OTC, which may be influencing the observed reduction. The data is therefore likely to underestimate mebendazole consumption. Furthermore, mebendazole is also indicated for the treatment of whipworm (trichuriasis), hookworm and roundworm (ascariasis) and, whilst these infections are not endemic to England, previous reports by the UKHSA suggest that helminth infections may affect up to 20% of migrants from endemic countries (<u>OHID, 2021</u>). Unfortunately, as with the antimalarial data, we are not able to distinguish prescribing by indication in the presented anthelmintic consumption data.

Consumption of albendazole was relatively stable between 2019 and 2021 but has seen a more notable increase of 75% DID between 2021 and 2023. Part of this may be due to the increasing echinococcosis caseload. Likewise, ivermectin and praziquantel consumption have increased since the COVID-19 pandemic, these anthelmintics are indicated for the travel-associated helminth infections strongyloidiasis and schistosomiasis, respectively, and contribute a small proportion of the overall anthelmintic DIDs.

Table 3.3 Total anthelmintic consu	mption in E	ngland, e	expresse	d as DDDs	per 1,000
inhabitants per day, 2019 to 2023					

Antihelminthics	2019	2020	2021	2022	2023
Mebendazole	0.0152	0.0126	0.0110	0.0104	0.0108
Albendazole	0.0014	0.0016	0.0016	0.0023	0.0028

Antihelminthics	2019	2020	2021	2022	2023
Ivermectin	0.0002	0.0002	0.0002	0.0003	0.0007
Praziquantel	0.0001	0.0001	0.0001	0.0002	0.0002
Diethylcarbamazine	0.0000	0.0001	0.0000	0.0000	0.0000



Progress against the National Action Plan

The 2019 to 2024 UK NAP has concluded and the UK's progress against the ambition to reduce total antibiotic use to below 16.92 DDDs per 1,000 inhabitants per day (DID) by 2024 will be evaluated. The NAP ambitions apply to the UK as a whole, whilst this report presents data for England only.

The COVID-19 pandemic had a significant impact on total antibiotic consumption in England, supressing antibiotic use during the peak pandemic years (16.11 DID in 2020 and 15.98 DID in 2021). However, subsequent increases in total antibiotic use were seen in 2022 (17.22 DID) and 2023 (17.61 DID). A reduction in the proportion of total antibiotic use that comprises Watch and Reserve antibiotics was observed between 2019 and 2024 in England, decreasing by 4.8%. Although total antibiotic consumption in 2023 remained below 2019 levels (17.96 DID), the post-pandemic increases emphasise the requirement for continued improvement in AMS to progress towards reaching the new NAP ambitions.

New NAP targets have been set for the 5-year period 2024 to 2029 (<u>30</u>), with the main consumption ambition being to reduce UK antimicrobial total use in humans by 5% from the 2019 baseline, the most recent pre-COVID-19 pandemic period, by 2029.

Following revision of the WHO AWaRe categorisations in 2021, the UKHSA has, in the past year, led a review of the respective AWaRe classifications of antibiotics used across the UK, involving the 4 devolved administrations of the UK. A new nationally-adapted AWaRe classification has been produced following a modified-Delphi consensus seeking process, further details of which can be found in <u>Chapter 5</u>, the Antimicrobial stewardship chapter.

Updates to the categorisation will be implemented for the 2024 to 2029 NAP, with a new target aiming to achieve 70% of total use of antibiotics from the Access category (UK 2024 categorisation) across the healthcare system.

The preceding NAP targets, concluding in 2024, continue to be measured against the England 2019 categorisation, and progress towards Ambition 2B: a 10% reduction in use of Reserve and Watch antibiotics in hospital from 2017 baseline, are not therefore affected by the latest AWaRe re-classification.

Current UK collaboration (4 nations) and participation in international surveillance

Consumption data for England continues to be monitored and collated alongside those of the devolved administrations (Northern Ireland, Scotland, and Wales) to understand the UK-wide picture of total primary and secondary care consumption and progress made towards the UK AMR 5-year NAP for antimicrobial reduction targets.

England, alongside the UK devolved administrations, submit and validate data (for England and Scotland, for the years covering 2016 to 2023) to the WHO Global AMR and Use Surveillance System (GLASS) <u>antimicrobial consumption module</u>.

Future actions

As highlighted in this chapter, access to data sources from across the healthcare system enriches the epidemiological analysis that can be performed and the relevant questions that can answered. It is expected that, in the next year, for the first time data will be accessible from an historical patient-level secondary care dataset, which will enable prescribing data to be linked to data on AMR trends and hospital admissions information. Increased granularity of primary care data, specifically clinical indication, is also anticipated. The availability of this data will substantially increase the scope of our epidemiological research.

Furthermore, access to independent sector antibiotic prescribing data is being pursued. This would assist in fully understanding the role of private sector prescribing in current trends and provide a more accurate picture of total antimicrobial consumption across the country and by setting. Finally, we also hope to enrich the antibiotic consumption data that is available from primary care dental practices, where there are current barriers to availability.

The ways in which people access to healthcare continue to change and adapt. Work is underway to explore the role that the continued high level of remote versus face-to-face prescribing may have on antibiotic consumption trends in general practice. This will build upon previously published work exploring the impact national restrictions on dental antibiotic use during COVID-19 pandemic, to inform on the appropriateness of antibiotic use and drive future AMS interventions.

2024 also saw the introduction of the <u>Pharmacy First</u> scheme, which enables community pharmacies to supply prescription-only medicines, including antibiotics and antivirals, for a defined list of 7 common health conditions, where clinically appropriate. The UKHSA will explore the scope to monitor the impact of Pharmacy First on trends in antimicrobial use in the community in England, in the context of national surveillance.

Future work is also planned to expand on the variations seen in antimicrobial consumption across the country, exploring regional differences in antimicrobial use and possible correlations with AMR profiles and sociodemographic characteristics, particularly by level of deprivation, which has been associated with higher prescribing and healthcare seeking behaviour, in more deprived areas ($65 ext{ to } 67$).

Antifungal use data was included in the UK submission to the WHO GLASS antimicrobial consumption module for the first time in 2024. The UKHSA has engaged and re-established the ESPAUR antifungal sub-group, hence future antifungal collaboration should inform antifungal prescribing and resistance surveillance. Initial work of the subgroup includes a survey of NHS acute trusts to determine the extent to which antifungal stewardship (AFS) is embedded in clinical practice and barriers to increasing AFS in secondary care. Further information can be found in the AMS chapter.

It is important to continue to monitor usage of newer antibiotics in England, to assess changes in consumption and indications for their clinical use, alongside implications resistance to these drugs. This will inform clinical guidance and national roll-out of stewardship interventions.

Work on assessing potential unintended consequences following changes in antibiotic use in England will continue. Furthermore, we will engage in cross-disciplinary work to producing an update on the current One Health challenges that threaten antimicrobial consumption in humans.

AMR knows no borders in an increasingly connected world. We hope to build on previous collaborative work between the UKHSA and the Health Protection Research Units in Healthcare-Associated Infections and Antimicrobial Resistance, as we look to develop new international research collaborations. We will also continue to develop international relations through our Global AMR Surveillance workstream. This will facilitate knowledge mobilisation around a shared challenge; the importance of which was made clear in lessons learned through the COVID-19 pandemic.

Chapter 4. Point-Prevalence Survey on Healthcare-Associated Infections, Antimicrobial Use and Antimicrobial Stewardship in England, 2023

Introduction

The Point-Prevalence Survey (PPS) on healthcare-associated infection (HCAI), antimicrobial use (AMU) and antimicrobial stewardship (AMS) was the sixth national PPS on HCAIs and the third national survey on AMU in England.

The survey was aimed at providing a snapshot of the burden of HCAI and describe AMU to allow meaningful comparisons between organisations and over time. This will also provide an opportunity to understand impact of changes to healthcare since the COVID-19 pandemic.

The results of the survey will:

- support development of local and national policies and interventions to better understand and reduce HCAIs and inappropriate antimicrobial use
- facilitate comparisons of HCAI and AMU across organisations in England and in an international context
- contribute to efforts to address antimicrobial resistance nationally and internationally through National and Global Action Plans
- allow benchmarking with peer group hospitals in England to identify opportunities for improvement

Coordination of the PPS was led by the UKHSA's HCAI and AMR Division with support from UKHSA Regional Leads and NHS England (NHSE) National and Regional AMS and Infection Prevention and Control (IPC) Leads.

Methods

Inclusion criteria

All NHS and independent acute-care hospitals, NHS Community and Mental Health trusts in England were eligible for inclusion in the 2023 PPS. Hospitals caring for exclusively day case patients were excluded, further details can be found at the <u>point prevalence survey on HCAI</u>, <u>AMU and AMS in England page</u>.
Protocol

The protocol for the 2023 PPS on HCAI and AMU in England was based on the protocol version 6.1 of the third EU-wide PPS in acute care hospitals (PPS 2022 to 2023) (68). This ensured alignment with data captured in the national PPSs on HCAI and AMU in England in 2011 and 2016 which were coordinated by the European Centre for Disease Prevention and Control (ECDC) and allows meaningful comparisons with the contemporaneous ECDC survey. In contrast to previous national PPSs, Community and Mental Health trusts were eligible to participate and indicators for compliance with AMU guidelines and appropriateness of prescribing – adapted from the <u>Australian National Antimicrobial Prescribing Survey</u> – were added.

Survey materials

Materials and tools were developed to assist hospitals in carrying out the 2023 PPS, which were:

- data entry forms
- study codebook, including case definitions of HCAI
- standardised training material
- web-based software to enter or upload data (including user guides)
- PPS email inbox with short turnaround time for queries
- drop-in sessions for PPS participants organised by regional NHSE AMS leads

The UKHSA's data capture system (DCS) was used for capturing hospital, ward and patient data. The DCS allowed participants to collect and enter data directly onto the system in real-time or retrospectively.

Training

More than 600 participants were trained in preparation for the PPS via a series of webinars and online training sessions.

Statistical analysis

Single-variable analysis was conducted to provide an overall description of the data. 95% confidence intervals (CI) were determined as appropriate. Prevalence was compared using estimations to assess overlapping CIs.

Results

This section presents an overview of the interim findings, for more detailed analyses, please refer to <u>national PPS Report</u>.

Participation

Data from 121 NHS trusts and independent sector organisations in England was submitted to the UKHSA. Of these, 113 trusts and organisations, 293 hospital sites (85.7%) and 44,372 (80.3%) patients fulfilled the eligibility criteria outlined in the survey protocol and were included in the Standard Protocol Dataset for the national analysis of the PPS (Table 4.1).

The PPS was conducted between 18 September and 30 November 2023.

Organisation type	Number of trusts or organisations	Number of hospitals	Number of patients	Average number of beds
Acute – large	10	18	7,139	1,077
Acute – medium	14	20	7,088	687
Acute – small	9	9	3,705	495
Acute – teaching	25	38	19,053	1,119
Acute – specialist	9	25	1,251	215
Mental health	21	90	3,540	386
Community	9	48	1,451	210
Independent sector	16	61	1,145	41
Total	113	293	44,372	-

Table 4.1. Trust type and size, PPS on HCAI and AMU, England, 2023

Definitions

Acute – large: general acute trust, gross internal area 500m² or more

Acute – medium: general acute trust, gross internal area 151 to 500m²

Acute – small: general acute trust, gross internal area up to 150m²

Acute – specialist: specialist trust (acute only)

Acute - teaching: teaching trust

Community: community trust (with inpatient beds)

Mental health: mental health trust (including specialist services)

Independent sector: hospital from the independent sector

Patient demographics

Overall, there were 44,372 patients included in the analysis. An overview of the main patient demographics is shown in <u>Table 4.2</u>.

Table 4.2 Demographics of	patients included in PPS on HCAI and AMU, England 2023
Table 4.2. Demographics of	patients included in 110 on noAl and Amo, England 2020

Patient demographics	Number of patients (n)	Percent total (%)
Sex		
Female	22,852	51.5
Male	21,139	47.6
Unknown	370	0.8
Missing	11	0
Age group		
Under 1 month	1,231	2.8
1-11 months	612	1.4
1 to 9	732	1.6
10 to 15	451	1.0
16 to 18	344	0.8
19 to 29	2,079	4.7
30 to 49	5,175	11.7
50 to 64	7,000	15.8
65 to 79	12,703	28.6
80 and over	14,045	31.7
Ethnicity		
Asian or Asian British	2,351	5.3
Black, African, Caribbean or Black British	1,594	3.6
Mixed or multiple ethnic groups	506	1.1
Other ethnic group	3,171	7.1
Unknown	1,717	3.9
White	32,173	72.5
Missing	2,860	6.4
Total	44,372	100

An overview of important risk factors for HCAI is presented in <u>Table 4.3</u>.

Risk factors	Number of	Percent total (%)
	patients (n)	
Total	44,372	100.0
Central venous catheter		
Yes	3,103	7.0
No	40,898	92.2
Unknown	371	0.8
Intubation		
Yes	687	1.5
No	43,367	97.7
Unknown	318	0.7
Peripheral venous catheter		
Yes	18,476	41.6
No	24,625	55.5
Unknown	1,271	2.9
Urinary catheter		
Yes	8,516	19.2
No	35,498	80.0
Unknown	358	0.8
Surgery		
No	36,058	81.3
Unknown/Missing	462	1.0
Yes (NHSN)*	6,531	14.7
Yes (Non-NHSN)	1,321	3.0
COVID-19 vaccination		
No	4,522	10.2
Unknown	14,789	33.3
Yes, patient received 1-2 doses	4,176	9.4
Yes, patient received 3 doses	5,337	12.0
Yes, patient received 4 or more doses	15,548	35.0

Table 4.3. Patient risk factors.	PPS on HCAI and AMU, England 2023

* National Healthcare Safety Network (NHSN) operative procedures

The distribution of patients across medical specialities by organisation type is presented in Figure 4.1.





Healthcare-associated infections

Prevalence of healthcare associated infections

The total prevalence of HCAIs in the PPS sample of patients in England in 2023 was 7.6% (95% CI: 7.3 to 7.8) (Figure 4.2). This comprised a total of 3,493 reported HCAIs, with 3,359 patients having had at least one HCAI.

Acute NHS trusts had an overall HCAI prevalence of 8.0% (95% CI: 7.7 to 8.3; within Acute NHS trusts, Acute specialist trusts had the highest HCAI prevalence (16.6%; 95% CI: 14.6 to 18.7). Mental health and community trusts had the lowest HCAI prevalences (5.1%; 95% CI: 4.4 to 5.8, and 5.0%; 95% CI: 3.8 to 6.1), respectively. Figure 4.2 shows HCAI prevalence by organisation and infection type.

The most common types of HCAI were pneumonia or lower respiratory tract infections (29.6%), affecting 962 (2.2%, 95% CI: 2.0 to 2.3) patients, followed by urinary tract infections (UTIs) (568 patients; 17.5%) and sepsis and disseminated infections (343 patients; 10.6%). Laboratory-confirmed bloodstream infections (BSIs) accounted for 7.6% of reported HCAIs (<u>Table 4.4</u>). A healthcare-related COVID-19 infection was reported for 296 patients (9.1%).



Figure 4.2. National prevalence of HCAI by organisation and infection type, PPS on HCAI and AMU, England 2023

*Labels above indicate the number of patients, prevalence of AMU and 95% confidence intervals

Table 4.4. Site of diagnosis of HCAI, PPS England 2023

Site of diagnosis	No. of patients with HCAI*	Prevalence (95% CI)	No. of HCAIs	Percent of total number of HCAIs (%)
Surgical site infections	286	0.6 (0.6 – 0.7)	288	8.9
Pneumonia/LRI	960	2.2 (2.0 – 2.3)	962	29.6
COVID-19 infections	296	0.7 (0.6 – 0.7)	296	9.1
Urinary tract infections	568	1.3 (1.2 – 1.4)	569	17.5
Bloodstream infections (laboratory or microbiologically confirmed)	242	0.6 (0.5 – 0.6)	247	7.6
CVC or PVC-related infection (no positive blood culture)	21	0.0 (0.0 – 0.1)	21	0.6
Cardiovascular infections	25	0.1 (0.0 – 0.1)	25	0.8
Central nervous system infections	23	0.0 (0.0 – 0.1)	23	0.7
Eye, ear, nose or mouth infections	139	0.3 (0.3 – 0.4)	139	4.3
Gastro-intestinal tract infections	278	0.6 (0.6 – 0.7)	280	8.6
Reproductive tract infections	19	0.0 (0.0 – 0.1)	19	0.6
Skin and soft tissue infections	180	0.4 (0.3 – 0.5)	180	5.5
Bone and joint infections	52	0.1 (0.1 – 0.1)	53	1.6
Sepsis and disseminated infections	343	0.8 (0.7 – 0.8)	343	10.6
Other healthcare-associated infection/unspecified HCAI	48	0.1 (0.1 – 0.1)	48	1.5
Total	3,359	7.6 (7.3 – 7.8)	3,493	100

* Patients may have more than one HCAI

Of the 3,493 reported HCAIs, 1,309 (37.5%) had at least one positive microorganism result with a total of 1,513 microorganisms identified. The 5 most commonly identified microorganisms were *Escherichia coli* (16.5%), SARS-CoV-2 (10.7%), *Staphylococcus aureus* (10.6%), *Clostridioides difficile* (7.4%) and *Pseudomonas aeruginosa* (7.2%). Antibiotic resistance for the most frequently reported bacterial microorganisms is shown in <u>Table 4.5</u>.

Table 4.5. Antibiotic resistance of HCAIs for the most frequently reported bacterial microorganisms, PPS on HCAI and AMU, England 2023

Organism	Total	Number tested*	Number resistant
Antimicrobial		(% of total)	(% of tested)
Enterobacterales	·······		
Third-generation cephalosporins	509	249 (48.9)	59 (23.7)
Carbapenems	509	214 (42.0)	8 (3.7)
E. coli			
Third-generation cephalosporins	249	119 (47.8)	27 (22.7)
Carbapenems	249	87 (34.9)	3 (3.4)
S.aureus			
Meticillin/oxacillin	160	92 (57.5)	13 (14.1)
Glycopeptides	160	36 (22.5)	0 (0.0)
P. aeruginosa	·······		
Carbapenems	109	74 (67.9)	9 (12.2)
K. pneumoniae			
Third-generation cephalosporins	80	38 (47.5)	10 (26.3)
Carbapenems	80	38 (47.5)	2 (5.3)
Other Klebsiella spp.			
Third-generation cephalosporins	38	15 (39.5)	3 (20.0)
Carbapenems	38	16 (42.1)	1 (6.2)
E. faecium			
Glycopeptides	60	48 (80.0)	26 (54.2)
E. faecalis		· · · · ·	· · · · · ·
Glycopeptides	30	16 (53.3)	0 (0.0)
		. ,	

* Information available at the time of the survey.

Antimicrobial use

The prevalence of AMU in the 2023 PPS in England was 34.1% (33.7 to 34.5) (Figure 4.4). When comparing the AMU prevalence in acute NHS trusts only, the prevalence in 2023 (37.3%, 36.8 to 37.8) was similar to 2016 (36.7%, 36.3 to 37.2).

The number of patients receiving at least one antimicrobial was 15,134 patients, that is more than a third of the patients captured by the PPS were receiving at least one antimicrobial.

In 2023, the highest AMU prevalence was reported by NHS Acute Specialist trusts (46.8%, 95% CI: 44.0 to 49.5) and independent sector organisations (43.7%, 95% CI: 40.8 to 46.5). Mental health and community trusts, which participated for the first time in the survey and do not provide acute care, had the lowest AMU prevalences when compared to the other organisation types with 7.2% (95% CI: 6.3 to 8.1) and 8.6% (95% CI: 7.2 to 10.1) respectively.

More than half (57.5%) of patients receiving antimicrobials were treated for community-acquired infections, 21.1% were for hospital-associated infections, and 1.7% were to treat long-term care infections or chronic-care hospital infections (Figure 4.4).



Figure 4.4. National prevalence of AMU by organisation type and treatment intention, PPS on HCAI and AMU, England 2023

*Labels above indicate the number of patients, prevalence of AMU and 95% confidence intervals

Distribution of antimicrobials

The 2 most commonly used antimicrobials were 'Watch' antimicrobials: amoxicillin/clavulanic acid accounted for 16.5% of AMU and piperacillin/tazobactam for 8.8% of AMU (<u>Table 4.6</u>). Meropenem was the only 'Reserve' antibiotic in the top 10, representing 3.8% of AMU.

Antimicrobial	AWaRe Count category		t Percentage of	Percentage of patients on	Percentage of total number of				
			antimicrobial courses (%)	antimicrobials (%)	patients (%)	Parenteral	Oral	Other	
J01CR02 – Amoxicillin/clavulanic acid	Watch	3,380	16.5	22.3	7.6	1,972 (58.3)	1,407 (41.6)	5 (0.1)	
J01CR05 – Piperacillin/tazobacta m	Watch	1,814	8.8	12	4.1	1,799 (99.2)	11 (0.6)	4 (0.2)	
J01CA04 – Amoxicillin	Access	1,070	5.2	7.1	2.4	517 (48.3)	551 (51.5)	2 (0.2)	
J01CF05 – Flucloxacillin	Access	1,061	5.2	7.0	2.4	706 (66.5)	356 (33.6)	1 (0.1)	
J01XD01 – Metronidazole (parenteral)	Access	986	4.8	6.5	2.2	967 (98.1)	16 (1.6)	3 (0.3)	
J01AA02 – Doxycycline	Access	882	4.3	5.8	2.0	26 (2.9)	855 (96.9)	1 (0.1)	
J01DH02 – Meropenem	Reserve	782	3.8	5.2	1.8	778 (99.5)	3 (0.4)	2 (0.3)	

Table 4.6. Top 10 antimicrobials used, PPS England 2023

Antimicrobial			Percentage of total number of					
			antimicrobial courses (%)	antimicrobials (%)	patients (%)	Parenteral	Oral	Other
J01FA09 – Clarithromycin	Watch	664	3.2	4.4	1.5	137 (20.6)	528 (79.5)	0 (0.0)
J01GB03 – Gentamicin	Access	659	3.2	4.4	1.5	653 (99.1)	3 (0.5)	4 (0.6)
J01MA02 – Ciprofloxacin	Watch	648	3.2	4.3	1.5	186 (28.7)	462 (71.3)	0 (0.0)
Total number of patients	-	44,372	-	-	-	-	-	-
Total number of patients on antimicrobials	-	15,134	-	-	-	-	-	-
Total number of antimicrobial courses	-	20,543	-	-	-	11,887 (57.9)	8,548 (41.6)	108 (0.5)



Figure 4.5. Antibacterials for systemic use (J01) by treatment intention and class, PPS on HCAI and AMU, England 2023



Appropriateness of antibiotic use

The reason for initiating antimicrobial treatment had been documented for more than 92% of all antimicrobial courses captured by the PPS.

More than a third of courses had been started less than 72 hours before the time of survey so did not qualify for a review. For those courses that had been started 72+ hours before the time of the survey, 80% had been reviewed Figure 4.6).

When using AWaRe categories (<u>41</u>) to classify antibiotic use, 31.3% of all antibiotics used were from the 'Access' category, 49.0% from the 'Watch' category, and 6.0 from the 'Reserve' category.

Questions on the quality of local antimicrobial prescribing showed that 68% of AMU was compliant with national or local guidelines and 86% fulfilled the criteria for optimal or adequate prescribing.

Figure 4.6. Overview of antimicrobial stewardship, PPS on HCAI and AMU, England 2023



Future actions

The PPS has identified a need to continue support for hospitals and other care providers to reduce HCAIs and review AMU. Its results will help to focus these activities, particularly related to the Government's National Action Plan (NAP) on targets to reduce Gram-negative infections, reduce AMU and increase the proportion of Access antibiotics used across the healthcare system.

- UKHSA will work with the Government's advisory group on Antimicrobial Prescribing, Resistance and Healthcare-associated infections (APRHAI) to consider interventions based on the PPS findings.
- Publish the PPS protocol and forms to allow hospitals to repeat local PPS at regular intervals, develop and measure quality improvement actions.
- Identify methods to improve data capture to reduce time and resource pressures of data collection for future PPS.
- Present regional and national PPS results at relevant scientific meetings and conferences to encourage ownership of IPC and AMS actions.
- Engage with international partners to present and discuss findings, fostering mutual feedback and knowledge exchange.

Chapter 5. Antimicrobial stewardship

Main messages

TARGET (Treat Antibiotics Responsibly, Guidance, Education and Tools) antibiotics toolkit

The TARGET antibiotics toolkit now hosts the summary tables on antimicrobial prescribing for common infections, which has contributed to the toolkit receiving over double the number of website views in 2023 to 2024 (397,185) than in 2022 to 2023 (193,093). TARGET have published updated diagnostic quick reference tools for abnormal vaginal discharge and chlamydia and have piloted a communication tool for use in care homes to aid in the management of suspected urinary tract infections.

Knowledge mobilisation of the Start Smart then Focus

Knowledge mobilisation activities used the knowledge to action framework and included a training workshop for healthcare professionals to raise awareness about the updated toolkit. The main barriers identified to implementation of the updated toolkit were limited time and capacity, competing departmental priorities, data complexity, insufficient organisational support, and limited dedicated resources. Additionally, some felt it was not their role to lead the implementation. Key facilitators for enhancing implementation included engagement with microbiology consultants and the Electronic Prescribing and Medicine Administration team to ensure a consistent approach to antimicrobial prescribing.

IV-to-oral (IVOS) switch in children and young people

A systematic review evaluating IVOS criteria for paediatric patients and a 2-step modified-Delphi were undertaken. The <u>new national criteria</u> and <u>sample decision aid</u> were published in June 2024.

Adaptation of the 2023 WHO AWaRE categories

Following the 4-stage modified Delphi process, adapted AWaRe classifications were agreed for the UK. Sixteen antibiotics differed in classification when comparing classifications based on the 2023 WHO and the proposed UK adapted indexes. Further discussions are underway to consider the policy implications from the proposed list.

Antimicrobial stewardship (AMS) awareness in domiciliary care

Carers understand the importance of and undertake a wide range of infection prevention and control (IPC) measures. However, a lack of time, habits, and challenging working environments are barriers to this. Carers associate certain symptoms with infection. However, they do not see

themselves as having a medical role and will not formally diagnose infections. Carers routinely administer and monitor antibiotic use by clients, in line with medical advice and if recorded on the client's Care Plan. Carers said they would return unused antibiotics to a pharmacy.

Survey of UK healthcare professional (HCP) knowledge, attitudes and behaviour on antibiotics

Over half of HCPs answered all 7 knowledge questions correctly (62%, 1,876 out of 2,996) which was slightly higher than was found in the previous survey of HCP knowledge which was conducted in 2018 (59%). Medical doctors had the highest percentage of respondents answering all knowledge questions correctly (75%, 626 out of 831), followed by pharmacists (72%, 546 out of 762) and dentists (58%, 61 out of 104).

Rapid systematic review of antimicrobial resistance (AMR) burden and interventions to tackle AMR in inclusion health groups (prisons and sex workers) and adult social care

No studies of relevant interventions for sex workers were identified.

Individuals in contact with the justice system are at higher risk of resistant bacterial infection, particularly tuberculosis and MRSA.

Interventions including education and training reduced inappropriate antibiotic use in adult social care settings.

Introduction to Chapter 5

Tackling antimicrobial resistance (AMR) requires action on multiple fronts to optimise antimicrobial use (AMU) and reduce the emergence and transmission of resistance. An important element of this approach is the implementation of antimicrobial stewardship (AMS) interventions. AMS enables healthcare workers to choose the most appropriate drug, dosage and duration of treatment, whilst limiting the microbe's ability to develop or acquire resistance. Optimising prescribing in this way is a focus of the UK's 5-year National Action Plan on tackling AMR (<u>1</u>) which includes a target to reduce total antibiotic use in human populations by 5% from the 2019 baseline and to achieve 70% of total use of antibiotics from the Access category (new UK category) across the human healthcare system.

In this chapter we provide a summary of national primary and secondary care AMS interventions led by the UKHSA between April 2023 and March 2024. In addition, we outline ongoing work to tackle health inequalities associated with AMR and prescribing.

Professional and public education and training is an important part of AMS. Further information about World AMR Awareness Week (WAAW) AMS resources, such as the <u>Antibiotic awareness</u>

toolkit for healthcare professionals in England, is available in the Professional and Public Education and Training (PPET) chapter.

Primary care AMS

TARGET antibiotics toolkit, programme objectives and introduction

The TARGET (Treat Antibiotics Responsibly, Guidance, Education and Tools) antibiotics toolkit is a collection of resources and tools for primary care clinicians. The toolkit aims to support a practice-based approach to AMS and improve how antibiotics are used in primary care. By providing information and resources for patients and healthcare staff, TARGET supports shared decision-making around AMU. The UKHSA collaborates with NHS England (NHSE), other healthcare stakeholders and patients to develop and maintain the toolkit, which is hosted on the Royal College of General Practitioners (RCGP) website. Between April 2023 and March 2024, TARGET was the third most accessed resource in the RCGP e-Learning hub. Throughout 2023 to 2024 several toolkit resources have been developed or reviewed against the latest evidence base:

'How to ...?' resources

Antibiotic stewardship tools, audits and other resources

The addition of two worked example slide decks supports clinicians to review patients on long term or repeat antibiotic prescriptions for acne vulgaris and chronic obstructive pulmonary disease (COPD), to help guide them in decisions about stopping unnecessary prescriptions and to set appropriate durations for treatment.

Quick reference tools

Antibiotic and diagnostic quick reference tools

To assist primary care clinicians in diagnosing and managing infections, TARGET published updated diagnostic quick reference tools (QRTs) for <u>abnormal vaginal discharge (AVD)</u> and <u>*Chlamydia*</u> in May 2023 (Figure 5.1). Endorsed by the <u>British Association for Sexual Health and HIV (BASHH)</u>, the QRTs summarise BASHH diagnostic guidance specific to the management of six infections. This helps users follow recommended national prescribing guidance in primary care. From their launch in May 2023 up to April 2024, the QRT's have been downloaded more than 500 times.





TARGET webinar series

Learning resources for prescribers

Three TARGET/RCGP webinars were held between April 2023 and March 2024 (see <u>chapter 7</u>) focusing on evidence and tools to support management of acne vulgaris and COPD, urinary tract infections (UTIs) and respiratory tract infections (RTIs).

Management of common infections antimicrobial summary tables

Summary of antimicrobial guidance

Previously published on the British National Formulary (BNF) website, these summary tables have now been moved to the TARGET website. The table currently summarises 26 common infections covered under the NICE antimicrobial prescribing guidance, and links to guidance that underpins 24 infections (Figure 5.2). The landing page summary also has a quick-link list of infections that take users to NICE Clinical Knowledge Summaries (CKS) and BASHH guidance underpinning 50 common infections clinicians may see in primary care. Between April 2023 and March 2024, users have accessed national guidance 66,490 times through the quick-link list and accessed the summary table 16,564 times. The table and quick-link list allow clinicians to check recommended first and second line antibiotics, and the table is frequently used by commissioning groups to develop local formularies for infection management in primary care.

This supports AMS efforts to optimise first line use of antibiotics in primary care settings, with the aim of reducing resistance and improving patient outcomes.

Figure 5.2. Screenshot of the UKHSA/NICE summary table of antimicrobial prescribing guidance



UK Health Security Agency

Summary of antimicrobial prescribing guidance - managing common infections

- Fluoroquinolone antibiotics: In January 2024, the MHRA published a <u>Drug Safety Update</u> on fluoroquinolone antibiotics. These must now only be prescribed when other commonly recommended antibiotics are inappropriate. Stakeholders are assessing the impact of this warning on recommendations in the relevant guidance.
- See BNF for appropriate use and dosing in specific populations, for example, hepatic impairment, renal impairment, pregnancy and breastfeeding



		Madiaina					
Infection	Key points	Medicine	Adult	Child	Length	summary	
Upper res	piratory tract infections						
Acute sore throat	Advise paracetamol, or if preferred and suitable, ibuprofen for pain.	First choice: phenoxymethylpenicillin	500mg QDS or 1000mg BD		5 to 10 days*		
	Medicated lozenges may help pain in adults.	Penicillin allergy:	250mg to 500mg	1	5 days	1	
NICE	Use <u>FeverPAIN</u> or <u>Centor</u> to assess symptoms:	clarithromycin OR	BD				
UK Health	FeverPAIN 0-1 or Centor 0-2: no antibiotic; FeverPAIN 2-3: no or back-up antibiotic; FeverPAIN 4-5 or Centor 3-4: immediate or back-up antibiotic.	erythromycin (if macrolide needed in pregnancy; consider benefit/harm)	250mg to 500mg QDS or 500mg to 1000mg BD		5 days		
Security Agency	Systemically very unwell or high risk of complications: immediate antibiotic.		60	in interv.			
Last updated: Feb 2023	*5 days of phenoxymethylpenicillin may be enough for symptomatic cure; but a 10-day course may increase the chance of microbiological cure.						
	For detailed information click the visual summary icon.						

UTI care home management aid

A draft tool to support recognition and communication around suspected UTIs for care assistants and nurses in care home settings has been developed through collaboration with care home staff and other experts in the field. The tool directs care staff to prepare, escalate and encourage (PEE) and aims to improve the initial assessment of care homes residents with suspected UTI and facilitate communication, monitoring and action planning between the primary care clinician and care home staff by following these 3 steps. The tool has been piloted in 6 care homes across England and a wider evaluation is planned with more care homes to inform further iterations and implementation.

Engagement with TARGET

There was a total of 397,185 views for the TARGET antibiotics toolkit website between April 2023 and March 2024 (Figure 5.3) s. The addition of the national antimicrobial prescribing guidance for common infections in June 2023 contributed to a large increase in views to the website. The most viewed toolkit sections, 'Leaflets to discuss with patients' (90,595 views) and 'Resources for the community pharmacy' (61,565 views), both saw large increases in views over January 2024 (17,936 and 17,688 views, respectively) and February 2024 (20,121 and 14,972 views, respectively) from the previous highest month in November (8,289 and 5,406 views, respectively). This coincided with the Pharmacy Quality Scheme, which ran from June

2023 until March 2024 and incentivised use of the TARGET Antibiotic Checklist and TARGET patient information leaflets for the community pharmacy setting (see Chapter 6). The Pharmacy First scheme was also officially launched on 31 January 2024 which enables community pharmacies to provide care for 7 common conditions following defined clinical pathways (see Chapter 6) (<u>69</u>).





* Data captured using previous version of Google Analytics and so may not be accurately comparable to 2023 to 2024 data

A total of 115,226 patient information leaflets were accessed over the year; 80,601 downloaded as printable documents (56,158 in PDF, 24,454 in Word) and 34,614 accessed as a digital leaflet through a weblink. Figure 5.4 shows the breakdown of downloads by format for each leaflet.



Figure 5.4. Downloads of the TARGET patient information leaflets by format, between April 2023 and March 2024

AccuRx is a software company who develop software which facilitates digital communication between patients and healthcare professionals. In collaboration with TARGET, AccuRx have integrated six of the TARGET patient leaflets into SMS text messaging templates. From April 2023 to March 2024, a total of 12,253 leaflets have been shared nationally through the SMS messaging templates. The most shared leaflet was the UTI leaflet for women under 65 years of age, accounting for 39% of all leaflets shared.

TARGET have also developed a UTI florey³ (70) in collaboration with AccuRx. The UTI florey aligns with UKHSA UTI diagnostic guidance and supports clinicians in the management of prescribing antibiotics for UTI. Between April 2023 and March 2024, the UTI florey was issued on average 13,721 times per month, doubling the monthly average of 6,930 from the previous year. This data suggests that digital resources are increasingly used in primary care and should be considered in the development of future resources.

Community pharmacy and general practice communication pathways to support AMS

General practitioners and community pharmacists have complementary roles in AMS making inter-professional collaboration an important aspect in primary care. The Pharmacy Antimicrobial Stewardship Intervention (PAMSI) consists of the TARGET Antibiotic Checklist,

³ Florey is a questionnaire, sent via text message link, designed to collect information about patients' symptoms prior to consultation

the 'AMS for Community Pharmacy' e-Learning, Antibiotic Guardian pledge, and TARGET information leaflets for patients with common infections. A previous evaluation of PAMSI revealed concerns about AMS continuity. Many patients were not being reached through the intervention due to communication difficulties between prescribers and pharmacy teams about antibiotic prescriptions (71). Therefore, there is a need for further work to explore the communication pathway between prescribers in general practice and community pharmacy teams, with emphasis on the impact of AMS.

Secondary care AMS

Knowledge mobilisation of 'Start SMART then Focus' toolkit

AMS involves optimising prescribing practices, promoting education, and fostering healthcare collaboration to enhance patient outcomes and reduce resistance. The 'Start Smart Then Focus' (SSTF) toolkit, developed in 2011 (72) and updated in August 2023, implements a 2-stage approach: 'Start Smart' ensures accurate diagnosis and initial treatment, while 'Then Focus' reassesses and adjusts therapy based on patient response. This toolkit is tailored to inpatient care and provides guidance for secondary care clinicians and leaders to reduce the risk of AMR while safeguarding the quality of care for patients with infection.

During 2023 to 2024, the focus has been on knowledge mobilisation activities for the toolkit using the knowledge to action framework, and identification of barriers and facilitators to implementation of the updated toolkit in organisational antimicrobial guidelines.

Knowledge mobilisation activities involved a training workshop for healthcare professionals nationally, to raise awareness about the updated toolkit. Pre-workshop surveys, the workshop itself, and a post-workshop survey were conducted online. Collaboration with NHSE and UKHSA behavioural scientists was essential to ensure the importance of co-production, teamwork, and behaviour change in implementing the SSTF toolkit.

Seventy-one participants registered for the workshop, with 57 attending the training workshop on teams. The workshop covered SSTF updates, shared different case studies, and introduced the COM-B model for behaviour change. Participants engaged in breakout sessions to apply their knowledge and improve antimicrobial prescribing practices. A post-workshop survey was distributed to capture lessons learnt and next steps to evaluate the success of knowledge mobilisation. In addition to this workshop the summary of this was also presented at an AMS workshop organised by NHSE with 209 registered participants from community health services, mental health services and the health and justice system.

Following the knowledge mobilisation workshop, a post-survey was sent to participants to gather feedback. Of the 57 attendees, 16 responded, with the majority being pharmacists, doctors, and nurses from across England. 87.5% (14 out of 16) of the respondents expressed high satisfaction with the workshop. Participants found the changes to SSTF, case studies on e-

prescribing implementation, the introduction to barriers and facilitators, and breakout sessions with behavioural scientists to be the most useful aspects.

However, feedback highlighted that the introduction to SSTF and its history were less useful. Suggestions for future workshops included more real-life examples of implementation, including understanding barriers and facilitators to implementation, how other trusts incorporated the toolkit into their guidelines, and resources available for prescribing antimicrobials.

Participants identified significant barriers to the implementation of the SSTF toolkit, with lack of time and capacity being the most frequently mentioned. Other barriers included competing departmental priorities, data complexity, insufficient organisational support, and limited resources. Additionally, some felt it was not their role to lead the implementation. When asked about their ability to identify barriers within their organisations, only 2 participants felt fully capable, while the rest were partially or not yet able to identify them.

Key facilitators for enhancing implementation included engagement with microbiology consultants and the Electronic Prescribing and Medicines Administration (ePMA) team to ensure a consistent approach to antimicrobial prescribing. Raising awareness of the SSTF toolkit among multidisciplinary teams and building relationships through AMS ward rounds were also emphasised. Embedding the toolkit into existing guidelines, audits, prescriber teaching, and ePMA systems, as well as extending these principles into nurse education with scenario-based learning, were seen as crucial steps.

Participants suggested that the UKHSA and NHSE could support implementation by increasing teaching sessions and workshops aimed at consultants and registrars, providing educational materials in accessible formats, and developing e-learning resources. Practical tools like infographics and downloadable images were valued for promoting AMS and high-quality prescribing practices.

In conclusion, the updated SSTF toolkit offers a comprehensive, evidence-based framework for AMS in secondary healthcare settings. Its successful implementation relies on a diverse approach involving education, stakeholder engagement, and robust support systems to overcome barriers and promote prudent antimicrobial prescribing.

Developing national criteria to facilitate prompt intravenous-to-oral antimicrobial switch in children and young people: a modified-Delphi approach

Antimicrobial intravenous-to-oral switch (IVOS) is recognised as an important hospital AMS intervention, associated with patient safety and economic benefits, including the decreased risk of bloodstream and intravenous catheter-associated infections, reduced equipment costs, reduced carbon footprint and earlier discharge from hospital, as well as increased patient mobility and comfort and reduced nursing time to care for patients (<u>73 to 75</u>).

IVOS criteria for national adoption were developed to inform clinical decision making in hospitalised adults in 2023, however there remained a need to validate IVOS criteria for paediatric patients.

A study aimed to complete a systematic rapid review of the literature to evaluate these criteria; undertake a 2-step modified-Delphi to achieve multidisciplinary expert agreement on evidencebased, nationwide IVOS criteria for hospitalised paediatric patients, and to design an IVOS decision aid to operationalise agreed IVOS criteria in the hospital setting (Figure 5.5). Paediatric antibiotic IVOS interventions were selected through a rapid review literature search, undertaken in Ovid Embase and Medline databases for articles published between January 2014 and January 2024.

Articles without IVOS criteria and those focusing on a specific antimicrobial were excluded, to limit the results to generalisable IVOS criteria. Articles were also limited to those including populations under 18 years of age.

Of 158 papers identified, 32 papers reported IVOS criteria. The IVOS criteria from the literature were extracted and synthesised into a 5-section framework, aligned with the process followed for development of the adult criteria ($\underline{4}$): 1) timing of IV antimicrobial review; 2) clinical signs and symptoms; 3) infection markers; 4) enteral route, and 5) special considerations.

Figure 5.5. Overview of process for development of paediatric IVOS criteria



Sample decision aid

Accessible text for Figure 5.5

Flow diagram for the modified Delphi approach used to develop IV to oral switch guidance in children and young people.

Literature data: Rapid review of 32 out of 158 papers.

Delphi process:

Step 1: Web-based questionnaire with 170 respondents.

Step 2: Virtual meeting with 8 participants.

There is a split arrow from the second box to an image of the published criteria and an image of the sample decision aid.

End of Accessible text for Figure 5.5

The 29 identified IVOS criteria were then formatted into 5-point Likert scale questions to inform the 2-step modified-Delphi process:

Step 1 – web-based questionnaire for UK-wide cascade to assess opinions of safety, relevance and effectiveness of criteria.

Step 2 – workshop to reach consensus on final criteria wording.

Criteria were accepted if greater than 60% of respondents agreed, or strongly agreed with the criterion on a 5-point Likert scale. When more than one criterion under a category reached this cutoff, the highest scoring criterion was accepted, as shown in <u>Figure 5.6</u>.

Figure 5.6. Consensus agreement on the timing of antimicrobial review. Criterion achieving highest positive agreement score (strongly agree or agree) greater than or equal to 60%, highlighted by orange box



Note: Criterion achieving highest positive agreement score (strongly agree or agree) greater than or equal to 60%, highlighted by orange box

Consensus (defined as \geq 60% agreement) was achieved for IVOS criteria from 170 multidisciplinary experts from across the UK (including 40 pharmacists, 112 doctors, and 18 nurses). The new national criteria and sample decision aid have been published alongside the adult criteria and are available at <u>Antimicrobial intravenous-to-oral switch</u>: <u>criteria for prompt</u> <u>switch</u>.

NHSE regional teams are pivotal in promoting implementation of the national IVOS criteria in clinical practice. The nationally agreed paediatric IVOS criteria were incorporated into an NHSE IVOS <u>Commissioning for Quality and Innovation (CQUIN) indicator</u> from April 2024, to complement the adult IVOS criteria that were introduced in 2023. Although the mandatory CQUIN scheme has been paused for 2024 to 2025, non-mandatory indicators have been made available to enable trusts to operate local quality incentivisation processes in 2024 to 2025. A full set of resources developed by NHSE are also available on the <u>FutureNHS Collaboration</u> <u>Platform</u>.

Adaptation for the 2023 WHO AWaRE Categories for Stewardship in the UK

Following updates to the WHO Access, Watch and Reserve antibiotic medicines classifications in 2023 categories ($\underline{76}$), a modified Delphi process was implemented to update the adapted England-specific AWaRe categories so they remain relevant for the needs of healthcare professionals in the UK ($\underline{38}$).

Modified Delphi process

Stage 1: A pilot survey was sent to members of an AWaRe working group, followed by a virtual meeting. This stage provided an understanding of whether there was a requirement for review of the AWaRe index for the UK context and piloted the format and questions on which antibiotics required review.

Stage 2: A survey was sent to experts across the UK 4 nations, cascading through the AWaRe working group and ESPAUR oversight group members' contacts. These experts were asked which AWaRe category they felt the 85 antibiotics should be placed in for the UK, and their rationale. Collated responses determined whether a consensus was reached on categorisation for each antibiotic (deemed as 70% or over agreement) and provided the reasoning accompanying any re-categorisation of antibiotics.

Stages 3 and 4: Two national remote workshops were held to reach consensus for antibiotics where categorisation was inconclusive following the stage 2 survey. Invites were limited to the AWaRe working group to better manage participants and structure discussions at these stages. Sixty-one experts contributed and completed the national survey (stage 2), with good representation from across the 4 UK nations (72% from England, 10% Scotland, 8% Wales, and 10% Northern Ireland). The types of organisations that participants were predominately associated with were teaching hospitals (30%), district or general hospitals (20%), and acute

trusts with multiple types of hospitals (18%). The majority of participants had expertise in AMS (49%) or microbiology (31%). The most common primary professions reported were pharmacist (48%), microbiologist (27%) or hospital doctor (14%).

For stages 3 and 4, 20 experts attended across both workshops: 55% from England, 20% from Scotland, 20% from Northern Ireland and 5% from Wales.

Responses to the survey seeking views on UK-adapted AWaRe classifications by antibiotic (stage 2) resulted in consensus for all but 28 antibiotics (see Supplementary tables 1 and 2). The 2 national workshops (stages 3 and 4), which discussed and aimed to build consensus for these 28 antibiotics, resulted in agreed classifications at a consensus level.

Following the 4-stage modified Delphi process sixteen antibiotics differed in classification when comparing classifications based on the 2023 WHO and the proposed UK adapted indexes (Annex Table 5.1 and 5.2).

Contention around cephalosporin categorisations

As a change from the 2019 UK categories which placed all cephalosporin generations in Watch, first-generation cephalosporins have now been placed in the Access category which aligns with the 2023 WHO AWaRe categorisation.

After the modified Delphi process, concerns were raised following the category change of firstgeneration cephalosporins that messaging and health education would be difficult with cephalosporins placed in different categories, especially considering the current clinical guidelines in place.

Subsequently, the following supporting points were raised by the ESPAUR Oversight group. Firstly, moving first-generation cephalosporins to Access does not mandate changes to guidelines and it is still reasonable to advise avoidance of these antibiotics for patients at risk of *Clostridioides difficile* infections. Secondly, aminoglycosides straddle 2 AWaRe categories (gentamicin is in Access, while amikacin is in Watch) which has been manageable for clinicians and from a guidance perspective. Thirdly, this change is deemed useful in terms of providing an oral option particularly for treating UTIs in the community. Finally, the hospital setting has seen increased use of cefazolin, which is useful for patients who are penicillin allergic, and which is generally narrower in spectrum than other potential alternatives to penicillin.

Full details of the project have been submitted for peer review.

Stewardship of antivirals, antifungals and paediatrics

Stewardship of antivirals

AMS has mostly focussed on the judicious use of antibiotics and less on the use of antiviral, antifungal or anti-parasitic drugs. This is partly because antibiotic use is more widespread with an associated increase in resistance, alongside a lack of new effective antibiotics in the pipeline. However, antifungal stewardship, and more recently antiviral stewardship are increasingly recognised.

The goal of antiviral stewardship is to avoid the unnecessary use of antivirals, prevent the emergence of antiviral resistance, optimise treatment effectiveness and safety, and reduce healthcare costs, while optimising patient care.

Antiviral stewardship can advocate for better awareness of the potential risks of the simultaneous use of a drug or drug class for both prophylaxis and first-line treatment for example acyclovir for Herpes Simplex Virus (HSV), tenofovir/emtricitabine or cabotegravir for HIV and oseltamivir for influenza. This has the potential to drive the emergence of resistance that reduces options for first-line therapy. The consequences could be life threatening in some scenarios such as immunocompromised patients undergoing bone marrow transplants where second-line therapies against HSV have severe side effects.

Antiviral stewardship should also advocate for holistic patient management with a better understanding of other factors such as the role of host immunity in viral suppression and drugdrug interactions considering that most individuals receiving antivirals have co-morbidities. Immunosuppression and failure to optimise therapies can lead to adverse effects including treatment failure and development of resistance (77, 78). A study at a UK hospital showed that antiviral stewardship can optimise healthcare outcomes and reduce costs. Antiviral stewardship was therefore embedded into routine care, with the authors suggesting the model could be adopted by other hospitals Thus, regular antiviral stewardship has been introduced with plans to roll it out in other hospitals (79). Finally, antiviral stewardship is likely to underpin therapeutic approaches for responding to future viral pandemics (80).

Future work will include developing a toolkit for antivirals similar to SSTF that will encompass these key principles:

- virological diagnosis
- antiviral drug
- antiviral dose
- antiviral administration route
- discontinuation of therapy or prophylaxis when not clinically required

Antifungal stewardship

The ESPAUR antifungal use and resistance subgroup formed a task and finish group in 2023 to develop and launch an antifungal stewardship (AFS) survey of UK secondary care providers. A follow up to a similar survey performed in 2016, this latest survey was designed to gain an understanding of the current challenges of implementing AFS in hospitals.

The survey was launched in May 2024 and closed with 49 responses, 46 of which were from NHS trusts in England. Most respondents were antimicrobial pharmacists. A full analysis will be made available in a peer reviewed publication.

Data for action in children and young people – closing the gap

Children and young people are particularly vulnerable to infections, and their long-term health outcomes are disproportionately affected by AMU. However, this age group is underrepresented in research and policy initiatives, creating gaps in evidence and implementation of interventions aimed at reducing AMR and improving AMU in this population.

Closing these gaps is necessary to achieve positive and equitable health outcomes, and to create comprehensive and effective AMR solutions that protect all age groups.

The following list highlights work done by UKHSA's healthcare-associated infections and AMR division and aiming to close these gaps. The UKHSA work on vaccine-preventable illness, acute respiratory infections, and other paediatric conditions is covered elsewhere.

Data for action

The epidemiology of bloodstream infections and AMR in England (2017 to 2021) was first described in this age group by the UKHSA, with yearly updates published in parallel with the ESPAUR report. Earlier ESPAUR reports also included paediatric-focussed analyses.

Infection data has been contributed to the National Child Mortality Database's publication of a thematic report investigating infection-related deaths in children and young people; an extension of this work into routine activity is being planned:

- analysed data for children and young people separately from the rest of the population in the 2023 national point-prevalence survey of healthcare-associated infections and AMR, to inform bespoke interventions
- reviewed historical trends and described the population trends in Gram-negative bacterial infections in infants in England, 2011 to 2019
- assessed the variation in neonatal sepsis screening across England and assessed the impact of the use of different risk calculators (ongoing work)
- measured the impact of ethnicity on rates of invasive group B streptococcal disease in neonates in England, 2016 to 2020

 evaluated the effect of paediatric live attenuated influenza vaccine in reducing risk of group A streptococcal infection

Outbreak response

- led on the response to an increased incidence of Staphylococcus capitis in neonatal units in England and shared the results of epidemiological and environmental investigations, as well as an infection prevention and control statement; work on optimising vancomycin use is ongoing
- investigated an increase in invasive group A streptococcal infections in England, 2022, and the unusual lower respiratory tract presentations
- responded to an increase in paediatric acute hepatitis of unknown aetiology in England in 2022
- described a surge of SARS-CoV-2 transmission in school-aged children during the COVID-19 pandemic

Guidance and policy

- conducted a UK-wide consensus process involving 170 multidisciplinary participants to list national criteria and designed a decision aid for antimicrobial IVOS in children and young people to support NHSE's quality improvement work
- included paediatric-specific content in the World AMR Awareness Week toolkit and actively promotes the Antibiotic Guardian School Ambassadors programme
- held conversations with the Medicines and Healthcare products Regulatory Agency (MHRA) to improve the communication of safety alerts related to antimicrobials used in children and young people
- collaborated with the Specialist Pharmacy Service on a paediatric-specific podcast for the Pharmacy First scheme
- considered children and young people while supporting the drafting and implementation of the UK action plan to confront antimicrobial resistance (most recently in the 2024 to 2029 iteration)
- met on a regular basis with colleagues from NHSE, the Royal College for Paediatric and Child Health, and the Department for Education to discuss matters arising and strengthen communications on topics related to children and young people
- collaborated with the UK Paediatric Antimicrobial Stewardship network in wide consultations and a call to action to participate in national initiatives

Changes to indications for fluoroquinolone use

The MHRA published their sixth fluoroquinolone drug safety update in 6 years in January 2024 stating that fluoroquinolones antibiotics must only be prescribed when other commonly recommended antibiotics are inappropriate (<u>45</u>). Fluoroquinolones are the only oral antibiotic with *Pseudomonas* cover. The UK are the second lowest users in Europe (after Norway) mainly

due to low primary care use with 450,000 prescriptions per year. Hospital use is similar to the European average with 5 million DDDs per year. NHSE worked with the UKHSA, NICE, BASHH and the MHRA to update existing guidelines, and to ensure that patients received a copy of the MHRA fluoroquinolone information leaflet. Resources were made available via the Future NHS AMR antimicrobial medicines safety pages to support primary care and hospitals with implementation. A number of webinars were run on the subject.

Monthly usage reduced by 13% in primary care to May 2024 and 15% in hospitals to July 2024. This is likely due to changes in antibiotic choice for pyelonephritis (especially where a penicillin allergy is present), lower empiric use for chronic bacterial prostatitis where urologists have ruled out other causes for chronic pelvic pain with urinary symptoms in older men, review of repeat prescriptions for exacerbations of bronchiectasis where previous Pseudomonal infection, less use in catheter-associated UTI after previous failures, less oral treatment of pseudomonal skin or wound infections, review of prophylaxis against febrile neutropenia related to chemotherapy or haematological conditions.

AMR awareness and opportunity for AMS in domiciliary care

Most antibiotics in England are used in the community, therefore all community health and care professionals have a role in AMS. There is very little evidence defining the role of domiciliary care workers in AMS and how to best engage the workforce in this agenda. Domiciliary care workers need to be considered separately from other Adult Social Care workforces, as the carers have a greater degree of independence, travelling between the homes of their clients. This context provides distinct challenges and opportunities for promoting AMS behaviours.

In collaboration with <u>Basis Social</u> (a social insights research agency), a qualitative study was conducted to determine domiciliary care workers understanding of and their opportunity for AMS. Qualitative interviews were conducted with 30 domiciliary carers working for CQC-registered agencies to explore their behaviours and perceived responsibilities around AMS. It also explored their understanding of how they can prevent AMR in the context of their work.

As part of their day-to-day role, domiciliary carers may contribute to AMS by preventing infection through cleanliness and hygiene practices, identifying symptoms of infection in their clients, managing the administration and disposal of medicines, and educating clients and their families on AMS behaviours.

Taking each of these in turn, the study highlighted the following findings:

Preventing infection

Carers understood the importance of and mostly undertake a wide range of infection prevention and control (IPC) measures. However, a lack of time, habits, and challenges working in clients' homes are barriers to this.

Identifying symptoms of infection

Carers associate certain symptoms with infection – for example a burning sensation being associated with UTIs. However, they do not see themselves as having a medical role and will not formally diagnose infections. Instead, carers see themselves as playing an important role in encouraging clients to seek medical advice. They will also signpost to, and reinforce information from, health professionals.

Medicines management

Carers routinely administer and monitor antibiotic use by clients, in line with medical advice and if recorded on the client's Care Plan. Carers said they would return unused antibiotics to a pharmacy. There were rare instances of carers not adopting AMS behaviours, which included using existing antibiotics to treat infections or disposing of unused antibiotics in a bin.

Educating clients or a clients' families on AMS behaviours

Carers do not provide medical advice to clients or their families but will reinforce instructions for antibiotic use. Despite adopting many AMS behaviours, and seeing these as "common sense", carers displayed a limited awareness and understanding of how their behaviours related to AMR. Carers mostly believed they had an important role in contributing to AMS and were open to learning more about AMR.

Underpinning these findings, the research found that there was a strong compliance culture in care agencies, with practices dictated by a care plan drawn up by the agency. This, together with the close monitoring of drug administration by carers, was the main factor influencing AMS. While this culture of compliance generally supports AMS, there were instances of unintended consequences arising – such as a client not being given a prescribed antibiotic as it was yet to be registered on the care plan. Some inconsistency also emerged in terms of whether carers see it as their responsibility to dispose of unused antibiotics to a pharmacy as this is rarely recorded on a care plan. The research findings suggest that care agencies may have different guidelines and expectations of their carers in this regard.

Recommendations

In summary, domiciliary care workers have a unique position in communities to make an impact on AMR and to promote good AMS with their clients and families. The research identified 4 key areas to help carers promote AMS behaviours:

- strengthening carers' ability to notice and act on early signs of infection by having conversations with their clients and signposting them to seek healthcare appropriately
- formalising carers' role in reinforcing AMS practices with clients and their families
- tailoring care plans and associated procedures to support and empower carers' role in AMS

 training carers on AMR to strengthen their AMS practices – educating carers on how their actions directly impact on AMR may mean that that when a carer needs to make a judgement call in the unpredictable context of a client's home that they are more likely to make a decision that supports AMS

UK Healthcare workers' knowledge, attitudes and behaviour on antibiotics to influence antimicrobial stewardship

Self-reported knowledge, attitude and practice of healthcare professionals in the management of infection and AMS: a systematic review

Health and social care professionals, including students and leaders, play a crucial role in reducing AMR and promoting the responsible use of antimicrobial agents. Understanding their knowledge, attitudes, and practices (KAP) related to AMR is vital for identifying gaps and developing effective improvement strategies. The systematic review aimed to assess health and social care professionals, students and leaders' KAP related to infection management – including infection control, prevention, AMS, and resistance.

In January 2024, a literature search across 4 electronic databases – Medline, Embase, Web of Science, and CINAHL – was conducted. Any type of study involving health and social care professionals or students who are expected to have prescribing, dispensing or administration responsibilities were included if they examined self-reported KAP about managing infections, infection prevention and control, AMU, AMS, and AMR. A 10-item quality appraisal tool covering external validity (4 items) and internal validity (6 items) was used. Due to significant heterogeneity of data, we conducted a narrative synthesis (PROSPERO 2024 CRD42024510775).

The search identified 10,990 studies, of which 113 met the inclusion criteria. The final synthesis incorporated all relevant studies, irrespective of their quality appraisal scores. The included studies were from 21 different countries, encompassing a diverse range of health and social care professionals (such as doctors, nurses, pharmacists, dentists, veterinarians), students (medical, dental, nursing and pharmacy), and allied healthcare personnel (such as researchers, technicians).

The studies used a range of questionnaires to capture the self-reported KAP on infection management, AMS, AMR, and AMU. The response rate of the questionnaires, where reported, ranged from 5.1% (in a study among medical students) to 97% (in a study among nurses). Instruments used to measure KAP varied significantly between studies. The familiarity with AMS reported ranged from 31.4% (in a study among a mix of different healthcare providers) to 77%

(in a study among critical care physicians). The proportion of samples who perceived they had adequate knowledge about AMR varied between 59% and 96%.

All the studies which examined knowledge and perceived knowledge about the purpose of hand hygiene regarding infection prevention and control among health and social care students reported that they had sufficient knowledge. Where measured, all studies reported positive attitudes towards participation in AMS across all health and social care personnel. Many studies (n=28) reported that most participants (range 83% to 99%) believe that AMR is a concern and many participants (ranged 64.5% to 97%) agree that inappropriate AMU increases AMR. Many studies (n=32) reported that about 50% to 95% of prescribers were motivated to use antibiotics appropriately. About half of the health and social care professionals were involved in providing verbal education on AMU. The most cited influence on antibiotic prescribing practice was adherence to guidelines. However, one study reported 37.1% of community pharmacists being involved in dispensing antibiotics without prescription. The proportion of participants that practiced good hand hygiene varied between studies and professions.

This systematic review provides a comprehensive summary of KAP among healthcare professionals (HCPs) regarding infection management, AMR, AMS and AMU. Although there is a strong endorsement of AMS programs, there is gap in appropriate practice. The review also highlights the need for a more consistent approach in measuring KAP to facilitate understanding of trends and comparisons between settings.

Assessment of UK healthcare workers' knowledge, attitudes and behaviour on antibiotics to influence antimicrobial stewardship

UK healthcare workers knowledge, attitudes and behaviour on antibiotic resistance and antibiotic use was last assessed in 2018 (<u>81</u>). One of the human health targets included in the 2024 to 2029 National Action Plan aims to increase UK public and HCPs' knowledge on AMR by 10%, using 2018 and 2019 baselines respectively, by 2029.

Therefore, a survey which aimed to assess current knowledge, attitudes and behaviours of HCPs regarding AMR and antibiotic prescribing was conducted to measure progress towards achieving the NAP Outcome 2 target.

An online survey using COM-B framework (<u>81</u>) was deployed in collaboration with Basis Market Research (an insights consultancy) between 1 and 18 March 2024. Individuals surveyed included patient facing HCPs in community, primary and secondary care and workers in long-term care facilities (doctors, nurses and pharmacists, dentists).
Key findings

A total of 2,996 HCPs completed the survey. The highest response rates were seen in nursing professionals (nurses, nursing assistants and midwives (31%, 932 out of 2,996), followed by medical doctors (28%, 831 out of 2,996) and pharmacists (25%, 762 out of 2,996).

Knowledge of antibiotic resistance

Nearly all HCPs correctly answered that antibiotics are not effective against viruses (99%, 2,951 out of 2,996) or against cold and flu (98%, 2,945 out of 2,996), they have associated side effects (99%, 2,979 out of 2,996), unnecessary use makes antibiotics ineffective (99%, 2,794 out of 2,996), and that healthy people can carry antibiotic resistant bacteria (94%, 2,802 out of 2,996). However, fewer HCPs knew that individuals treated with antibiotics are at an increased risk of an antibiotic resistant infection (86%, 2,580 out of 2,996), and that antibiotic resistant bacteria can spread from person to person (76%, 2,273 out of 2,996). Compared to the 2018 survey, knowledge had increased for 5 out of the 7 questions. It had remained the same for the question relating to effectiveness of antibiotics at treating colds and flu and had decreased by 2% for the question relating to the spread of resistant bacteria between people.

Over half of HCPs answered all 7 knowledge questions correctly (62%, 1,876 out of 2,996) with medical doctors having the highest level of knowledge (Figure 5.7). This was 3% higher than the 2018 survey.



Figure 5.7. Percentage of healthcare professionals who correctly answered all 7 knowledge questions correctly by healthcare profession

Attitudes towards antibiotic use and resistance

Almost all medical professionals have a good understanding of antibiotic resistance (96%, 2,880 out of 2,996). However, only 84% (2,517 out of 2,996) of HCPs felt they had a key role in helping control antibiotic resistance, this proportion was lowest in nurses (78%, 728 out of 932) and pharmacy technicians (63%, 162 out of 258).

Most medical professionals surveyed prescribe/dispense prescriptions at least weekly (84%, 1,623 out of 2,996). A lack of available resources (29%, 865 out of 2,996) and insufficient time (28%, 845 out of 2,996) were the main barriers to providing patients with advice on AMR and appropriate antibiotic use. Reporting of a lack of resources as a major barrier to providing advice to patients was especially predominant in dentists (63%, 66 out of 104) compared to other HCPs (Table 5.1).

	Total population	Medical doctor	Nurse	Dentist	Pharmacist	Pharmacy technician	Allied health professional
Patient did not require information	22%	25%	19%	24%	23%	16%	16%
Patient uninterested in information	25%	26%	23%	20%	26%	23%	26%
Insufficient time	28%	41%	17%	25%	34%	19%	13%
Difficulty getting patient to understand diagnosis	10%	11%	12%	7%	7%	5%	11%
Language barriers	8%	8%	8%	6%	10%	9%	6%
No resources available	29%	37%	28%	63%	21%	13%	38%
I was not sure what advice to provide	9%	13%	10%	8%	5%	5%	14%

Table 5.1 Reasons for not giving out advice or resources by healthcare profession

	Total population		Nurse	Dentist	Pharmacist	-	Allied health professional
I was able to give out advice or resources as needed	15%	10%	17%	17%	17%	17%	7%

Rapid systematic review of AMR burden and interventions to tackle AMR in inclusion health groups (prisons and sex workers) and adult social care

Systematic reviews focused on inclusion health groups and adult social care

The impact of resistant infections may be particularly significant for those in vulnerable populations who often experience barriers to healthcare access and disparities in health outcomes. Inclusion health groups include people who experience homelessness, drug and alcohol dependence, vulnerable migrants, Gypsy, Roma and Traveller communities, sex workers, people in contact with the justice system, and victims of modern slavery.

A series of reviews are being undertaken to understand the risks and potential actions that can be undertaken to support these groups. The reviews aim to systematically identify and assess the levels of antimicrobial-resistant infections and AMU focusing on specific inclusion health groups and adult social care populations. This information will inform and guide the development of effective, targeted interventions to reduce AMR and optimise AMU among these populations.

We acknowledge that individuals in these groups may overlap and therefore AMR prevalence may be due to experiences when an individual was a member of a former group (for example individuals experiencing homelessness may become a prisoner). However, the populations will be assessed separately. This is because the interventions are likely to differ depending on the population they are a member of (for example, access to prison healthcare, versus using night shelters).

Protocols for the reviews have been submitted to PROSPERO or registered to Open Science Framework (OSF). Electronic databases Embase, Medline and Scopus were searched for relevant publications. Three of these reviews, focusing on adult social care, individuals involved in sex work and those in contact with the criminal justice system, are nearing completion and, the abstracts for these can be found in the annex (Annex 5.3 to 5.5).

Future actions

TARGET antibiotics toolkit

Research

The TARGET toolkit will undergo a resource analysis with focus groups consisting of key users and stakeholders to identify areas of improvement with regards to availability, relevance, and effectiveness. Findings will inform future updates to the toolkit and resource development plans.

TARGET will work with NHSE and other stakeholders to evaluate the UTI Care Home Communication Tool.

Resources and website

TARGET are planning the development and/or update of a number of AMS tools including:

- a full review of the patient information leaflets updated versions of the leaflets are expected to be published on the TARGET toolkit in November 2024
- a 'How to...?' guide for recurrent UTI will be developed in collaboration with NHSE and other key stakeholders experienced in research and clinical management of recurrent UTI
- updating and incorporating the bacterial vaginosis, chlamydia, epididymitis, gonorrhoea, herpes (genital), pelvic inflammatory disease, scabies (website update pending), trichomoniasis and vaginal candidiasis infection rows covered by BASHH guidance in the 'Management of common infection' summary table
- publishing updated UTI diagnostic quick reference tools that will be co-branded with NHSE
- launching a digital AMS self-reflection questionnaire (self-assessment checklist) relevant for GP clinical staff, community pharmacy staff and commissioners across the UK in November 2024

Adaptation for the 2023 WHO AWaRE Categories for Stewardship in the UK

Following the update of the AWaRE categories knowledge mobilisation activities will be undertaken to promote awareness among HCPs. Further discussions are also underway to consider the policy implications from the proposed list.

UK Healthcare workers' knowledge, attitudes and behaviour on antibiotics to influence antimicrobial stewardship

Following the systematic review to assess healthcare workers' (HCWs) knowledge, attitudes and behaviour, information on the measurement tools used will be collated and used to develop a comprehensive measure of knowledge, attitudes and practice. The draft questionnaire will undergo a Delphi-process in order to gain consensus on the included questions. This will allow for the routine collection of data, meaning changes over time in HCWs knowledge, attitudes and practice can be monitored and compared to targets included within the 2024 to 2029 National Action Plan for AMR.

Health inequalities

In addition to the 3 near-complete reviews, another review will be undertaken in 2024 to 2025 titled "A Rapid Systematic Review to Assess Antimicrobial Use, Antimicrobial Resistance, and Relevant Antimicrobial Stewardship Interventions in People Who Use Drugs". This review will evaluate the levels of AMR and AMU among people who use drugs and identify relevant AMS interventions. The findings will provide crucial insights into tailoring strategies for this high-risk group. Additional reviews covering the remaining factors associated with health inequalities are due to be completed over the next 2 years. Please note: a relevant review of refugees and asylum seekers is already underway.

Furthermore, to support local and regional UKHSA teams, NHS colleagues and public health teams identify and address health inequalities in access, infection incidence, clinical outcomes, vaccine uptake and antimicrobial exposure, a toolkit will be collated and published. Interventions to tackle AMR in inclusion health groups and adult social care will also be identified.

In addition to this work which supports Commitment 8.3 of the 2024 to 2029 National Action Plan work is ongoing to further improve reporting on infection incidence and antimicrobial resistance by age, sex, ethnicity, deprivation, geography, and high-risk settings including adult social care and prisons.

Chapter 6. NHS England: improvement and assurance schemes

Main messages

NHS England (NHSE) designs and administers improvement and assurance schemes including elements to incentivise prudent use of antimicrobials across the Integrated Care Systems (ICSs), to optimise patient outcomes, minimise avoidable exposure to antimicrobials and reduce selection pressure for antimicrobial resistance (AMR). During the financial year 2023 to 2024, NHSE improvement and assurance schemes have included the following:

NHS Oversight Framework. The number of Integrated Care Boards (ICBs) meeting the national target for total primary care prescribing of antibiotics 'at or less than 0.871 items per STAR-PU' was 10 out of 42 (24%) and the number of ICBs meeting the national target for primary care broad-spectrum antibiotic prescribing 'at or less than 10%' was 40 out of 42 (95%).

National Medicines Optimisation Opportunities. There was a 36% relative increase in the proportion of 5-day prescriptions for amoxicillin capsules. This shows continued year-on-year improvement, with 38% of total amoxicillin prescriptions prescribed as 5-day course by March 2022, 42% by March 2023 and 57% by March 2024.

Pharmacy Quality Scheme (PQS). The PQS continued the re-incentivisation of the TARGET resources. 7,927 community pharmacies submitted data from 197,475 TARGET Antibiotic Checklist where 70,612 patient information leaflets were provided and an additional 11,273 influenza vaccinations were delivered prompted by discussions using the checklist. Community pharmacies reviewed patients presenting with urinary tract infection symptoms (98,836) and respiratory tract infection symptoms (111,521) and managed 83,166 (84%) and 102,271 (93%) of these, respectively, within the pharmacy without the need to escalate to another healthcare setting.

NHS Standard Contract. Thirty out of 132 (20%) trusts achieved the NHS Standard Contract target to reduce 'Watch' and 'Reserve' antimicrobials prescribing by 10% from the 2017 baseline. The antibiotic consumption for antibiotics from the 'Watch' and 'Reserve' categories across all participating trusts at financial year end was 2,307 DDD per 1,000 admissions, which is 0.2% lower than the 2017 baseline of 2,311 DDD per 1,000 admissions.

Commissioning for Quality and Innovation (CQUIN) framework. A total of 46,340 audit cases were submitted across 117 trusts participating in the CQUIN03: Prompt switching of intravenous antimicrobial treatment to the oral route of administration as soon as patients meet switch criteria. All but 2 participating trusts (97% of 117) met the 40% or lower threshold by Q4, and a quarterly reduction was observed from 23% in Q1 to 18% by end of Q4.

An overview of NHS England Improvement and Assurance Schemes and antibiotic prescribing performance for financial year 2023 to 2024 is presented in <u>Figure 6.1</u>.

Figure 6.1. Overview of NHS England Improvement and Assurance Schemes and antibiotic prescribing performance for financial year 2023 to 2024



NHS England Improvement & Assurance Schemes: prescribing in primary and secondary care

Performance in 2023 to 2024

This section covers the following policies and initiatives: NHS Oversight Framework, National Medicines Optimisation Opportunities, Pharmacy Quality Scheme, NHS Standard Contract and NHS Commissioning for Quality and Innovation (CQUIN) scheme.

NHS Oversight Framework

The NHS Oversight Framework (NOF) aims to ensure the alignment of priorities across the NHS and with wider system partners. It provides clarity to ICBs and NHS providers on how NHSE will work with and through ICBs to monitor performance, based on objective measures of system performance and quality of care outcomes, and supports the ICBs' and NHS providers' goals.

The NOF 2023 to 2024 is a continuation of the NOF 2022 to 2023, which is aligned with the ambitions set out in the NHS Long Term Plan and the 2022 to 2023 NHS operational planning and contracting guidance.

The NOF contains 2 AMR-related indicators with set targets for ICBs that have been used in NHS improvement and assurance schemes since 2015. The metrics and associated national targets are set out in Table 6.1. The national target for total prescribing of antibiotics is aligned with the <u>UK AMR National Action Plan (NAP) (2019 to 2024)</u> ambition to reduce community antibiotic prescribing by 25% from a 2013 baseline.

Code	AMR metric description	Target
SO44a	AMR: total prescribing of antibiotics in primary care. The number of antibiotic (antibacterial) items prescribed in primary care, divided by the item-based Specific Therapeutic group Age-Sex Related Prescribing Unit (STAR-PU) per annum.	At or less than 0.871 items per STAR-PU
SO44b	AMR: proportion of broad-spectrum antibiotic prescribing in primary care. The number of broad-spectrum antibiotic (antibacterial) items from co-amoxiclav, cephalosporin class and fluoroquinolone class drugs as a percentage of the total number of antibacterial items prescribed in primary care.	At or less than 10%

Table 6.1. NHS Oversight metrics and targets (March 2024) for antibiotic prescribing

NHSE in collaboration with the NHS Business Services Authority (NHSBSA) produce monthly reports of ICB and sub-ICB location (SICBL) performance for both AMR indicators to monitor antibiotic prescribing in primary care and report ICB progress towards the NOF targets. The

NHSE AMR NOF 2023 to 2024 dashboard is published in the <u>AMR Programme FutureNHS</u> workspace.

For the 12 months to 31 March 2024, the number of ICBs meeting the national target for total primary care prescribing of antibiotics 'at or less than 0.871 items per STAR-PU' was 10 out of 42 (24%) and the number of ICBs meeting the national target for primary care broad-spectrum antibiotic prescribing 'at or less than 10%' was 40 out of 42 (95%). The number of ICBs meeting both targets was 10 out of 42 (24%). This reflects an overall improvement in ICB performance compared to the previous year (44a up from 17%, 44b down from 98%, 44a and 44b combined up from 17% in the 12 months to March 2023).

For England as a whole, total primary care antibiotic prescribing for the 12 months to 31 March 2024 was 0.938 items per STAR-PU, exceeding the national target of 0.871 items per STAR-PU. This represents a decrease of around one million primary care antibiotic prescriptions in the 12 months to 31 March 2024 compared to the previous 12 months to 31 March 2023. Meanwhile primary care prescribing of broad-spectrum antibiotics as a proportion of total antibiotics met the target of 'at or less than 10%' with 7.8% of prescriptions being for broad-spectrum agents, and a reduction of over 84,000 prescriptions compared to the previous 12 months to March 2023.

Overall, 0.938 items per STAR-PU is 19% below the 2013 to 2014 baseline of 1.161 on which the UK AMR NAP ambition to reduce community use of antibiotics by 25% by 2024 is based. This was in the context of the COVID-19 pandemic and increased antibiotic prescribing during the Group A Streptococcus infection outbreak in winter 2022 to 2023, which saw around <u>10</u> times more scarlet fever GP consultations (in hours) than baseline. During the financial year 2023 to 2024, primary care antibiotic prescribing remains impacted by sustained <u>high levels of consultations for respiratory tract infections</u> resulting in a relatively high volume of antibiotic prescribing previously reported for the same months prior to the COVID-19 pandemic.

National Medicines Optimisation Opportunities

The inaugural <u>National Medicines Optimisation Opportunities 2023 to 2024</u> was launched by NHSE to provide guidance on 16 optimisation opportunities for ICBs and signposts to resources to help with their implementation. ICBs are recommended to choose at least 5 medicines optimisation opportunities to focus and deliver on, alongside their local medicines optimisation priorities.

For 2023 to 2024, there were 2 AMR-related national medicines optimisation opportunities: (1) reducing course length of antimicrobial prescribing and (2) switching intravenous antibiotics to oral. Performance for both these opportunities are available via the NHSBSA <u>national medicines</u> <u>optimisation opportunities dashboard</u>. PrescQIPP publish the <u>Optimising antimicrobial duration</u>

<u>dashboards</u> which report metrics that can be used to optimise duration of antibiotic use in primary care.

During the financial year 2023 to 2024, there was a 36% relative increase in the proportion of amoxicillin 500 mg capsule 5-day courses prescribed across England. This shows continued year on year improvement with 38% of total amoxicillin 500 mg capsule prescriptions prescribed as 5-day courses by March 2022, 42% by March 2023 and 57% by March 2024.

Performance for the national medicines optimisation opportunity on switching intravenous antibiotics to oral is reported in the subsection NHS Commissioning for Quality and Innovation Scheme of this chapter.

Pharmacy Quality Scheme

The <u>NHS England Pharmacy Quality Scheme (PQS)</u> forms part of the <u>Community Pharmacy</u> <u>Contractual Framework (CPCF)</u>. It supports delivery of the NHS Long Term Plan and rewards community pharmacy contractors that deliver quality criteria in 3 quality dimensions: clinical effectiveness, patient safety and patient experience. This section summarises community pharmacy activities that were carried out prior to the introduction of the national Pharmacy First service that was introduced on 31 January 2024.

The AMS criteria of the PQS Scheme 2023 to 2024 included the re-incentivisation of the TARGET resources for use in community pharmacies in England: (1) TARGET Antibiotic Checklist and (2) TARGET Treating Your Infection (TYI) <u>leaflets</u> for urinary tract infections (UTIs) and respiratory tract infections (RTIs).

TARGET antibiotic checklist

Community pharmacy teams were required to have implemented the recommendations from the TARGET antibiotic checklist review 2021 to 2022 found in the <u>Findings from the</u> <u>antimicrobial stewardship initiatives report</u>. They were required to submit evidence that they had reviewed their current AMS practice using the TARGET Antibiotic Checklist over 4 weeks with a minimum of 25 patients, or up to 4 weeks if the minimum number of patients was not achieved within 8 weeks.

Data was submitted by 7,927 community pharmacies who claimed for the AMS criteria of and collectively submitted data from 197,475 TARGET Antibiotic Checklists. In total, 70,612 patient information leaflets were provided to patients to aid in the knowledge about their condition and treatment. A total of 67,616 checklists were completed for patients with an RTI; 43,644 for UTI; and 24,440 for dental infections. An additional 11,273 influenza vaccinations were delivered by community pharmacies prompted by discussions whilst using the antibiotic checklist.

TARGET 'Treating your infection' leaflets

Community pharmacy teams were required to have implemented the recommendations from the <u>Community Pharmacy Quality Scheme 2022-23</u>: findings and recommendations from the <u>TARGET treating your infection leaflets initiatives</u>. They were also required to have reviewed their practice to include the 2 TARGET leaflets (for UTI and RTI). The purpose of this was to help them assess walk-in or community pharmacist consultation service (CPCS) patients and provide tailored advice to patients and promote awareness of AMR and AMS. Eligible patients are those presenting to the pharmacy for advice and/or requesting antibiotics with suspected UTIs or RTIs without a prescription, who have not already seen a GP or other healthcare professional for their current illness.

Pharmacy teams were required to submit evidence that they had reviewed their current AMS practice using the TARGET TYI leaflets over 4 weeks with a minimum of 15 patients for each condition, or up to 4 weeks if the minimum number of patients was not achieved within 8 weeks.

Urinary tract infections

Data was submitted by 7,537 community pharmacies for 98,836 patients presenting with UTI symptoms. Most, 69,713 (71%), (non-pregnant) women presented with none or only one of the 3 strongly predictive symptoms of dysuria, new nocturia, cloudy urine, and/or vaginal discharge, and therefore were less likely to have a UTI, as outlined in UTI diagnostic guidance. Conversely, 29,123 (29%) of women presented with 2 or more symptoms of dysuria, new nocturia, cloudy urine and with no vaginal discharge, and therefore they were more likely to have a UTI.

Around a quarter of patients were managed by community pharmacy team members without the need for escalation to a pharmacist and 83,166 (84%) patients were managed within the pharmacy, by the pharmacist and pharmacy team without the need to escalate to another healthcare setting. Most women 93,625 (95%) received self-care advice, of whom 37,398 (35%) were also provided with patient information leaflets.

Respiratory tract infections

Data was submitted by 7,525 community pharmacies for 110,521 RTI patients. Of patients with suspected RTIs, 59,148 (54%) were managed by the pharmacy team without the need to escalate to the pharmacist. Most of the 102,271 (93%) patients were managed within the pharmacy, by the pharmacist and pharmacy team without the need to escalate to another healthcare setting.

From the other 8,250 (7%) of patients 4,075 (4%) presented with symptoms suggesting that urgent medical advice was required. Of these, 4,075 (4% of all patients) were signposted to other healthcare services, with most (3,333, 3%) of all patients) referred to their GP. Of these patients, 3,949 (4%) were advised to seek medical advice if symptoms did not improve within 48 hours or got worse.

106,770 (97%) of patients were provided with self-care advice, of whom 34,242, (31%) were also provided with patient information leaflets to support the verbal advice provided.

NHS Standard Contract

Since 2019, the NHS Standard Contract has required acute providers to make year-on-year reductions in their per-patient usage of antibiotics, in line with the ambition for a 10% cumulative reduction set out in the UK 5-year NAP for AMR 2019 to 2024. Previously, the NHS Standard Contract requirement for annual reductions was expressed against the 2018 baseline of actual usage. To align with the NAP, the NHS Standard Contract 2023 to 2024 was changed to be expressed as a 10% cumulative reduction by 31 March 2024 against the 2017 baseline (instead of a 6.5% reduction against a 2018 baseline).

NHS Standard Contract final performance data by trust for the antibiotic consumption targets for 2023 to 2024 are available within the NHSE <u>AMR Programme FutureNHS workspace</u>. Table 6.2 shows antibiotic consumption for 2019 to 2024. For 2023 to 2024, antibiotic consumption from the 'Watch' and 'Reserve' categories across all participating trusts at financial year end was 0.2% lower than the 2017 baseline of 2,311 DDD per 1,000 admissions.

NHS Standard Contract	Target reduction in antibiotic consumption from calendar year 2018 baseline (except 2023 to 2024)	Number of trusts that met requirement	Antibiotic consumption value at year end
2019 to 2020	1% reduction in total DDD per 1,000 admissions (cf. 2018)	43/145 (30%)	4,612 DDD per 1,000 admissions
2020 to 2021	Suspended due to COVID-19 pandemic	N/A	N/A
2021 to 2022	2% reduction in total DDD per 1,000 admissions (cf. 2018)	69/138 (50%)	4,465 DDD per 1,000 admissions
2022 to 2023	4.5% reduction in DDD per 1,000 admissions for antibiotics from the WHO 'Watch' and 'Reserve' categories (adapted for use in England) (cf. 2018)	40/137 (29%)	2,397 'Watch' and 'Reserve' categories DDD per 1,000 admissions
2023 to 2024	10% cumulative reduction in DDD per 1,000 admissions for antibiotics from the WHO 'Watch' and 'Reserve' categories (adapted for use in England) (cf. 2017)	30/132 (20%)	2,307 'Watch' and 'Reserve' categories DDD per 1,000 admissions

 Table 6.2. Summary of changes to antibiotic consumption targets and achievement, 2019

 to 2024

NHS Commissioning for Quality and Innovation (CQUIN) scheme

CQUIN03 prompt switching of intravenous antimicrobial treatment to the oral route of administration as soon as patients meet switch criteria

During the financial year 2023 to 2024, 117 of 135 (87%) NHS hospital trusts providing acute care services participated in the NHS Commissioning for Quality and Innovation (CQUIN) scheme: CQUIN03: Prompt switching of intravenous antimicrobial treatment to the oral route of administration as soon as patients meet switch criteria.

This evidence-based scheme aimed to promote timely intravenous to oral switch (IVOS) in line with the <u>National antimicrobial intravenous-to-oral switch (IVOS) criteria for prompt switch for</u> <u>adults</u> and was intended to improve a range of patient outcomes and resource utilisations including: reducing healthcare-associated infections, reducing length of stay, reducing exposure to broad-spectrum antibiotics, increasing nursing workforce capacity, reducing drug expenditure, and reducing carbon footprint of medicines.

This CQUIN scheme required submission of a minimum sample of 100 patient cases meeting the inclusion criteria of adult inpatients (16+ years of age) with active prescriptions for IV antibiotics each quarter. Quarterly reporting was submitted to the UKHSA using a standard data capture tool, and quarterly performance was published on the Office for Health Improvement and Disparities Fingertips <u>AMR portal</u>, and on the <u>NHS England AMR FutureNHS workspace</u>. Optional questions were included in the standard reporting tool inviting trusts to share information on their rationale in the IV to oral switch decision making; findings from this data will be published separately once analysis is complete.

Trusts received full payment for achieving 40% (or fewer) patients continuing to receive IV antibiotics past the point at which they meet switching criteria, and partial payment for achieving 41 to 60% case compliance. <u>CQUIN scheme details</u> are published by NHSE. Resources to support implementation of the CQUIN scheme are published on the <u>AMR Programme</u> <u>FutureNHS workspace</u>. A webinar titled 'Nursing the problem of AMR using the 5 R's of Medicines Management' was delivered in October 2023 by the NHSE AMR programme in collaboration with pharmacy and nursing colleagues from 4 acute hospital trusts, highlighting successful antimicrobial stewardship (AMS) practices with a focus on timely IVOS.

Overall, 46,340 audit cases were submitted across 117 trusts (see Table 6.3). The majority (101 of 117, 85%) of participating trusts submitted audit data for all 4 quarters. All submitted data was included in the analysis. All but two2 participating trusts (97% of 117) met the 40% or lower threshold by Q4. There was a quarterly reduction in the percentage of adult inpatients with an active IV antibiotic prescription past the point at which they meet switching criteria from 23% in Q1 to 18% by end of Q4. Table 6.3 shows data submitted each quarter.

Table 6.3. CQUIN scheme 2023 to 2024: CQUIN03 Prompt switching of intravenous
antimicrobial treatment to the oral route of administration as soon as patients meet
switch criteria

	Q1	Q2	Q3	Q4	Total	Trusts submitting all 4 quarters
Number of cases audited by Quarter	11,038	11,953	11,508	11,841	46,340	41,895
Number of cases with active IV antibiotic prescription past the point at which they meet switching criteria (%)	2,580 (23%)	2,462 (21%)	2,216 (19%)	2,167 (18%)	9,425 (20%)	8,257 (20%)
Number of acute trusts submitting audit data	109	113	111	116	117	101
Number of trusts achieving partial CQUIN compliance (41% to 60%)	9 (8%)	5 (5%)	3 (3%)	2 (2%)	2 (2%)	1 (1%)
Number of trusts achieving full CQUIN compliance (40% or less)	99 (91%)	107 (95%)	108 (97%)	114 (98%)	115 (97%)	99 (98%)

Other activities during 2023 to 2024

AMR Programme FutureNHS workspace

The NHSE AMR Programme workspace was launched on the <u>FutureNHS</u> collaboration platform in March 2022. The workspace is designed to support local, regional and national stakeholders to access guidance, resources and performance data for national improvement and assurance schemes and these are all regularly updated. Additional information is provided to support the AMR/AMS workforce to enhance their knowledge and capabilities through provision of recorded webinars, updates on antimicrobial issues and management, summaries of key research through the AMS Evidence Observatory and case studies to illustrate improvement opportunities in practice.

The FutureNHS platform, upon registration, is open to all staff working within the NHS, and those providing or supporting NHS-funded services, at the discretion of the workspace manager. The platform provides registered users with the opportunity to network, collaborate,

and share learning via dedicated discussion forums. There are now over 1,300 registered users with approximately 500 members visiting the workspace each month.

Pharmacy First

In May 2023, NHSE and the Department of Health and Social Care announced a <u>Delivery plan</u> for recovering access to primary care. Part of the plan includes enabling patients to get certain prescription medications directly from a community pharmacy, without a GP appointment. This new service is expected to free up GP appointments for patients who need them most and will give people quicker and more convenient access to safe and high-quality healthcare.

NHSE launched the new <u>Pharmacy First service</u> on 31 January 2024. The Pharmacy First service builds on the <u>NHS Community Pharmacist Consultation Service</u> which has run since October 2019. The consultation service enables patients to be referred into community pharmacy for a minor illness or an urgent repeat medicine supply. The Pharmacy First service enables community pharmacies to complete episodes of care for 7 common conditions following defined clinical pathways:

- acute otitis media (age 1 to 17 years)
- impetigo (age one year and over)
- infected insect bites (age one year and over)
- shingles (age 18 years and over)
- sinusitis (age 12 years and over)
- sore throat (age 5 years and over)
- uncomplicated urinary tract infections (women aged 16 to 64 years)

Led by the NHSE Primary Care Pharmacy team, these pathways were developed with a wide range of stakeholders including substantial contributions from members of the NHSE AMR Programme, Specialist Pharmacy Services (led on the patient group directions), NICE, the UKHSA, ICB representatives, Community Pharmacy England, clinical academics, practising clinicians, and NHS111.

Patients will be able to access the 7 clinical pathways element via referrals from referring organisations including general practice, urgent and emergency care settings, and NHS 111 (online and via telephone). In addition, for the 7 common conditions clinical pathway consultations only, patients can access the service by attending or contacting the pharmacy directly without the need for referral. The NHSE AMR Programme in collaboration with NHSBSA are developing the ePACT2 AMS Pharmacy First Dashboard to support AMS in ICSs.

Plans for 2024 to 2025

NHS Oversight Framework

The consultation for the NHS Oversight and Assessment Framework 2024 to 2025 closed on 13 June 2024 and the final framework will replace the NOF 2022 to 2023 that was continued for 2023 to 2024. For the financial year 2024 to 2025, the focus will be on sustaining improvement against the NOF 2023 to 2024 metrics.

NHS Standard Contract

The NHS Standard Contract 2024 to 2025 will focus on sustained improvement against the NHS Standard Contract 2023 to 2024 metrics, in line with the new <u>UK 5-year action plan for</u> <u>AMR: Confronting antimicrobial resistance 2024 to 2029</u> targets.

NHS Commissioning for Quality and Innovation (CQUIN) Framework

The mandatory CQUIN scheme has been paused for 2024 to 2025. However, an optional list of 20 indicators has been published that can be used by any systems that have agreed to operate a local quality scheme during the financial year 2024 to 2025. The NHSE AMR Programme is responsible for the non-mandatory CQUIN indicator for 'Prompt switching of intravenous to oral antibiotic'. This indicator builds on and extends the 2023 to 2024 CQUIN03: 'Prompt switching of intravenous (IV) antimicrobial treatment to the oral route of administration as soon as patients meet switch criteria'.

For financial year 2024 to 2025, the non-mandatory CQUIN 'Prompt switching of intravenous to oral antibiotic' has been extended to paediatric patients in alignment with the <u>UK PAS paediatric</u> <u>antimicrobial intravenous-to-oral switch (IVOS) decision aid.</u> The suggested thresholds are 15% (or fewer) patients still receiving IV antibiotics past the point at which they meet switching criteria as full achievement and 25% for partial achievement.

National support from the NHSE AMR programme continues to be available to support the implementation of the non-mandatory CQUIN scheme via dedicated resources on the <u>AMR</u> <u>Programme FutureNHS workspace</u>. In April 2024 the NHSE AMR Programme delivered a national webinar titled 'IVOS CQUIN: What's new for 2024-25?' to outline the new requirements and highlight the improvement work that was undertaken in 2 NHS trusts (Epsom and St Helier and West Suffolk NHS trusts) for the 2023 to 2024 CQUIN.

Chapter 7. Professional and public education, engagement, and training

Main messages

TARGET professional education, training and promotional campaigns

TARGET collaborated with the Royal College of General Practitioners (RCGP) to deliver 3 webinars between 2023 and 2024, presented live to a combined total of 922 viewers and subsequently hosted on the TARGET website for future use by healthcare professionals. Training resources have been reviewed, updated, and cascaded regionally to primary care teams through the TARGET Train-the-Trainer programme. A total of 1,331 healthcare professionals across England have received training through the programme.

The UKHSA and RCGP ran a joint campaign to promote awareness of the TARGET toolkit and use of their resources. Focused around World AMR Awareness Week (WAAW), the campaign lasted 7 months and included emails and bulletins to RCGP members, paid digital advertising and social media posts.

The national roll out of TARGET training and WAAW campaign activities contributed to a 61% increase in total views to the TARGET toolkit during this year's campaign period (September 2023 to March 2024), compared to 2022 to 2023.

Antibiotic Guardian

The Antibiotic Guardian campaign website's main page received 19,321 AMS pledges in 2023, totalling 177,681 since inception of the campaign in 2014. Over 80 organisations registered their AMS activities on the Antibiotic Guardian website in 2023.

The sixth Antibiotic Guardian shared learning and awards event took place in person on 2 May 2023, attended by 108 delegates from organisations the UK and internationally. Sixty-two projects and case studies were submitted across all 11 categories and 31 were shortlisted, with shortlisted posters and video presentations shared on the Antibiotic Guardian webpage.

Antibiotic Guardian Schools Ambassadors Programme: Since 2021, the programme has aimed to target regions with the most deprived areas. A total of 26 colleagues registered to become an Antibiotic Guardian Schools Ambassador in 2023 (189 in 2022, 110 in 2021 and 79 in 2019). In 2023, the programme was expanded to include strengthened veterinary content, in collaboration with the Veterinary Medicines Directorate (VMD), to share learning with young people who may be pet or animal owners.

World Antimicrobial Awareness Week (WAAW) and European Antimicrobial Awareness Day (EAAD) 2023

Digital resources were developed and shared through a toolkit for healthcare professionals in England to support the NHS and others to lead activities. The webpage hosting the toolkit was visited 4,488 times between publication in October 2023 and the end of 2023.

Digital notes remain one of the most shared resources during WAAW.

Public education and engagement with e-Bug

The e-Bug team has reviewed and updated their 'Health Educator' and 'Preventing and Managing Infections in Childcare and Pre-School' e-learning courses hosted on FutureLearn.

In a survey of 1,036 teachers across England, the majority (84%) have not received training on infection prevention and control (IPC) and over a third (35%) have unmet needs in regard to IPC. This knowledge gap will be addressed in a national cascade of IPC training through e-Bug's Train the Trainer programme.

Introduction to Chapter 7

Public and professional engagement and education is a crucial antimicrobial stewardship (AMS) activity, as outlined in both the UK's 20-year vision and 5-year national action plan (NAP) on controlling antimicrobial resistance (AMR) (<u>1,82</u>). It calls for a collaborative approach from professionals, patients or service users, consumers and the public to help develop, promote and deliver strategies that promote knowledge gain and behaviour change around AMR. Behaviour change is not a quick process, it requires sustained efforts by multiple stakeholders working at various levels. But if successful, education and training can ensure that best practices and strategies are followed by professionals who are sufficiently competent to be able to deliver these, and that the public are empowered to be agents of change with a key role to play in the fight against AMR.

The behaviour change wheel (BCW) is a framework which explains the mechanisms by which interventions bring about behaviour change. Training, defined as the process of imparting skills to others, is included in the BCW as an intervention that can achieve the physical and psychological capability to change behaviour (<u>83</u>). The NAP highlights the importance of an open and learning culture within healthcare settings by supporting the implantation of learning strategies that are most likely to bring about behavioural change on AMR.

The BCW also includes education, defined as increasing knowledge or understanding, as an intervention that can achieve the psychological capability and reflective motivation to change behaviour (83). The NAP highlights several commitments to promoting better IPC practices among the public. These include targeting interventions to improve hand hygiene, conducting

surveillance of the public's awareness and attitudes to AMR and focusing attention on educators and local authorities to ensure that school leavers understand appropriate IPC practices and use of antimicrobials.

Interventions tend to have a specific focus, for example training, education and awareness raising, therefore a wraparound approach is required if we wish to see sustained positive behaviours towards antibiotic use and AMR. In this chapter we share a range of professional and public education, engagement, and training initiatives which all work together to provide this wraparound service.

Healthcare professional education and training

TARGET webinars

TARGET (Treat Antibiotics Responsibly, Treatment, Education and Tools) webinars are aimed towards primary care health professionals and focus on improving the management of common infections in primary care settings by optimising the use of antibiotics, according to national guidance. The webinar format comprises a main topic presentation followed by a question and answer (Q&A) session with a panel of experts. All webinars are recorded, and recordings, slides and Q&A sheets can be viewed on the <u>TARGET website</u>.

The TARGET webinar series has proved to be the most popular on the Royal College of General Practitioners (RCGP) platform, with webinars consistently being oversubscribed and over 90% of attendees stating that they would recommend the webinars to a colleague. Three live webinars took place between November 2023 and March 2024 (Table 7.1). All participants were asked to complete an evaluation form following the event. Respondents rated webinars 1 and 2 an average of 8.2 and 8.7 out of 10, respectively, and 80% of respondents rated webinar 3 as "excellent" or "very good". Healthcare professionals (HCPs) from across primary care attended the webinars and responded to the evaluation: GPs (n=156, 39%), trainee GPs (n=95, 24%), pharmacists (n=57, 14%), nurses (n=51, 13%) and other HCPs (n=47, 12%). The webinars have proven to be a successful means of delivering key information directly to HCPs, with the evaluation feedback guiding the delivery of future webinars that optimises user needs.

Table 7.1. TARGET webinar statistics for 2023 to 2024	

Webinar title and date	Registrations	Attendees	Online views	Evaluation response rate
Webinar 1 – Reviewing antibiotic prescribing for patients with acne and COPD exacerbations (November 2023)	751	241	117	76/241 (32%)
Webinar 2 – Improving antibiotic management of respiratory tract infections (January 2024)	800	396	139	227/396 (57%)

Webinar title and date	Registrations	Attendees	Online views	Evaluation response rate
Webinar 3 – Applying diagnostic and prescribing guidance of urinary tract infections in practice (March 2024)	1,024	285	180	97/285 (34%)
Totals	2575	922	436	400/922 (43%)

TARGET training roll out

Workshop: TARGET Antimicrobial Stewardship Training - A year on

The TARGET AMS Train-the-Trainer cascade model (84) was launched at a workshop in 2022 involving AMS and IPC staff from the UKHSA and NHS England (NHSE). The realist approach provides regional AMS leads with the autonomy to modify the suggested delivery to suit their regional and local needs. In March 2024, a follow-up workshop was held with representatives from regional AMR and IPC teams within the UKHSA and NHSE to elicit lessons learned across the regions following the 18 months of delivery.

Facilitated discussions, following the principles of the BCW, were led by the UKHSA Behavioural Science and Insights Unit (BSIU) and the HPRU in Healthcare Associated Infections and Antimicrobial Resistance, where each region identified barriers and facilitators to their implementation of training (Table 7.2).

Table 7.2. Feedback given by workshop attendees on the case	scade of TARGET training
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Facilitators	Barriers
Running dedicated meetings and webinars for the training Improving patient and public knowledge of AMR Improving perceived behaviour control relating to prescribing behaviour and the sharing of best practice	Competing demands within the service Limited available resources Constantly changing AMS evidence base Ability and confidence to translate and apply AMR knowledge into practice Worries about misdiagnosis and treatment Focus on long-term goals instead of shorter, more attainable goals

Regions that had not implemented TARGET training reported their barriers: a lack of need for TARGET, perceived difficulty of sustaining behaviour, and discrepancies between the management of illness decided by the patient and clinician, which was incongruent to guidance following the completion of risk assessment. These demonstrate further work that the team aims to address for the national implementation of TARGET training.

Regions that had implemented TARGET training planned strategies to support their continued implementation: to provide support to clinicians, to adapt and tailor the training to fit the context of their region or health setting, and to train and educate stakeholders.

Summary of training (April 2023 to March 2024)

Between April 2023 and March 2024, TARGET training was delivered to 1,331 primary HCPs across NHSE regions. The TARGET training toolkit is accompanied by pre- and post-session surveys which measure attendees' AMS attitudes and behaviours, knowledge and use of TARGET resources, intention to implement actions and their feedback on the training. Attendees found TARGET training to be a good use of their time, where they were able to understand (n=348/353, 99%) and relate (n=341/353, 97%) to the objectives and content of the training.

Following the training, there was an increase in attendees' knowledge of the resources and tools available to support their stewardship actions. Although attendees demonstrated high baseline knowledge towards AMS, there was a positive shift in their understanding that their prescribing is linked to antibiotic resistance (pre-training: n=362/432, 84%; post-training: 314/353, 89%) and an understanding of the collective effort required to tackle AMR in their area (pre-training: n=351/430, 82%; post-training: 321/353, 91%). Attendees indicated that they are most likely to implement practice and individual-level AMS actions, specifically to discuss AMS at their practice or pharmacy meetings (n=325/347, 94%), keep AMS on the agenda (n=324/347, 93%) and to use appropriate coding to support research into AMR (n=281/347, 81%). Over half of attendees (n=128/205, 62%) planned to implement AMS within 6 months of completing the training, and 71% (n=145/205) do not anticipate any barriers to implementing actions from the training sessions.

TARGET FutureLearn

The <u>TARGET Antibiotics: Prescribing in Primary Care</u> e-learning course, developed in collaboration with the British Society for Antimicrobial Chemotherapy (BSAC), is a free course hosted on the FutureLearn platform. Comprising of 6 weekly one-hour modules aimed at HCPs, the course covers AMS topics related to management of common infections. The course ran from 24 March 2023 to 25 March 2024 and just under half (n=82/137, 43%) of registered learners actively participated during that period. All survey respondents (n=7/7, 100%) reported that the course met or exceeded their expectation and that they had acquired new knowledge or skills.

Public and professional engagement activities

TARGET AMS campaign with RCGP

The UKHSA and the RCGP ran a joint AMS campaign aimed at general practice prescribers to promote awareness of AMR and engagement with the TARGET antibiotics toolkit. Campaign

activities were concentrated around WAAW in November 2023, although the campaign period continued throughout the winter months (September 2023 to March 2024). The campaign focused on encouraging GP staff to:

- update their knowledge on the best practice approach to managing common infections while optimising antibiotic use in primary care (signposted to the toolkit hub)
- sign up and attend free webinars to understand the importance of reviewing patients on long term or repeat antibiotics, and AMS in RTIs and UTIs (signposted to 'free webinars' page or specific events listing)

Promotional campaign activity included:

- a promotional email to RCGP members, targeting over 28,000 members
- regular content (features and listings) across all RCGP member bulletins, that is Learning Bulletin and Chair's News and the RCGP Primary Care Development Newsletter aimed at practices and key decision makers
- paid digital advertising including search advertising via Google and Bing and social media advertising on META (Facebook and Instagram) – targeting RCGP members and bespoke audiences
- social media posts on Facebook and X (formerly Twitter), and a separate Instagram Stories campaign, promoting TARGET resources and upcoming webinars

The results through paid search advertising (Google and Bing) were significantly higher compared to previous years' campaigns, achieving more than 72,000 impressions. This is a result of running paid search advertising across a 6-month period, tightening messaging and creative assets, as well as key search terms. The TARGET toolkit featured more regularly across the RCGP bulletins as there were 'new' messages, and therefore opportunities, to remind members to register for the free webinars.

The campaign achieved strong and positive engagement over the 7-month campaign, with increased visits to the TARGET website and spikes during WAAW. During the WAAW campaign period, total views of the TARGET toolkit reached over 19,000, an uplift of 61% (7,324 views) compared to last year. TARGET and RCGP will take learning on the success of earlier implementation and tighter key messaging in the campaign for 2024.

Engagement with TARGET

X (formerly Twitter)

TARGET posted 67 times between April 2023 and March 2024, with an average of 855 impressions (the number of people who have seen a post) per post and an engagement rate (level of interaction a post receives per view) of 5.3% from 36 posts. This is an increase in average impressions from 217 in the previous year, but with a slightly reduced engagement

rate, down from 6.8%. With almost double the amount of posts this year, this suggests that increasing the quantity of posts can help to increase the audience that the content reaches.

TARGET newsletters

Bi-annual newsletters are distributed to stakeholders who have signed up to the TARGET mailing list, to provide updates on recent developments and to promote new and updated resources and upcoming events. The open rates (percentage of recipients that opened the newsletter) for the spring and autumn newsletters sent out over 2023 were 28.6% (n=218/762) and 26.6% (n=268/1,006), respectively, and the click rates (percentage of recipients that engaged with the newsletter through clicks) were 15.9% (n=121/762) and 24.5% (n=246/1,006), respectively. Stakeholder engagement was higher with the autumn newsletter, where the content is primarily targeted towards the promotion of the WAAW campaign, showing that this is an effective method of communication for increasing engagement during promotional campaigns.

Other avenues of engagement

TARGET was promoted at 4 major conferences in the UK. This allowed for the promotion and dissemination of new and updated resources to stakeholders, further building the public and professional engagement with TARGET. The conferences also allowed the opportunity to share recent research and for delegates to provide feedback on the toolkit and suggestions for future projects. TARGET website statistics for 2023 to 2024 can be found in chapter 5.

World Antimicrobial Resistance Awareness Week (WAAW) and European Antibiotic Awareness Day (EAAD) 2023

WAAW took place between 18 and 24 November 2023 and European Antibiotic Awareness Day (EAAD) on 18 November 2023. The World Health Organisation (WHO) rebranded the 2023 campaign to World Antimicrobial Resistance Awareness Week, formerly World Antimicrobial Awareness Week, after global consultations to better represent the challenges being faced. The digital resources from 2022 were reviewed and updated. Resources aligned with 5 daily themes that were unchanged from the 2022 campaign:

- Day 1 'Prevention' theme (including IPC measures and vaccination)
- Day 2 'Antimicrobials in clinical practice' theme (antibiotic course length, promoting shorter course length, empiric prescribing, intravenous-oral switch, promotion of current clinical guidelines)
- Day 3 'Optimising diagnostics' theme (increasing understanding of established and innovative methods of detection of infection, antibiotic-resistant or otherwise)
- Day 4 'Antimicrobials and untrue or spurious allergy' theme (including issues such as untrue penicillin allergy labels and de-labelling spurious antibiotic allergy labels)

 Day 5 – 'AMR and the environment and research' theme, linking AMR with environmental considerations, such as disposal of antibiotics and environmental contamination (One Health approaches to tackling AMR through research were also highlighted on this day)

For the 2023 campaign there were 3 cross-cutting themes underpinning all 5 days: children, sustainability, and inequalities. New digital notes for 2023 reflected these underpinning themes, examples of which are shown in Figure 7.1.

Resources were shared through a toolkit for healthcare professionals in England to support the NHS, local authorities and others to lead activities and encourage responsible use of antibiotics.

The toolkit was updated and made evergreen to reflect changes in COVID-19 practices and to strengthen the One Health message and impacts of Health Inequalities.

The webpage hosting the toolkit was visited 3,098 times between its publication in October 2023 and the end of 2023, and 2,704 visits within WAAW week. Digital notes were introduced in 2020, and new messages were designed for 2023, with digital notes remaining one of the most shared resources during WAAW.

Figure 7.1. Selection of digital notes that were promoted for use during WAAW 2023

Prescribe the correct amount to avoid waste #AntibioticGuardian #KeepAntibioticsWorking	Stomach upset isn't allergy. Don't wrongly label your child with allergy #AntibioticGuardian #KeepAntibioticsWorking	Antibiotics are spent, act to prevent #AntibioticGuardian #KeepAntibioticsWorking
Antibiotic waste is for pharmacies, NOT rivers #AntibioticGuardian #KeepAntibioticsWorking	7 out of 10 children with a cough will feel better within 3 weeks, whether or not they take antibiotics #AntibioticGuardian #KeepAntibioticsWorking	Vaccinations help us to develop immunity against infections and helps to fight off the infection <u>https://www.e-bug.eu/ks4- vaccinations</u> #AntibioticGuardian #KeepAntibioticsWorking

A range of custom teleconference backgrounds and screensavers were created in 2021 and redesigned to incorporate the rebranding of the campaign in 2023, for colleagues to use during WAAW and the WHO 'Go Blue for AMR' campaign was promoted and supported by designing blue versions of these resources. <u>Figure 7.2</u>shows examples of these backgrounds, which included messages aligned with the digital notes for each day and editable versions were created for colleagues to include their own wording or institutional logos. The designs of these backgrounds were based around the 2-tone pill motif used in both 'Keep Antibiotics Working' and 'Antibiotic Guardian' campaign materials.

Two new blogs were published on the <u>Antibiotic Guardian website for WAAW 2023</u>. To highlight the focus on the children's theme for the 2023 campaign, a blog written by the Chair of the UK Paediatric Antimicrobial Stewardship (UK-PAS) network was published. UK-PAS network aims to improve antibiotic use in children and young people, and in their blog they shared several achievements and reflections.

Figure 7.2. Teleconference backgrounds designed for use during World Antimicrobial Awareness Week 2023



WAAW and EAAD social media activity

During WAAW 2023 there were a total of 3,114 tweets using the WAAW, Antibiotic Guardian or Keep Antibiotics Working hashtags. WAAW was the most frequently used hashtag (n=2,315/3,114, 74%), followed by the Keep Antibiotic Working (n=510/3,114, 16%) and Antibiotic Guardian hashtags (n=287/3,114, 9%). Between 18 and 24 November 2023, WAAW

was mentioned 5,256 times on social media and was also included within 2 news articles. During WAAW 2023, sentiment of social media posts relating to WAAW was predominately neutral (n=3,663/5,055, 72%), 16% (n=830/3,663) of posts were positive and 11% (n=562/3,663) were negative.

Ten-year review of the Antibiotic Guardian Campaign

Public Health England (PHE, now the UKHSA) launched the pledge-based <u>Antibiotic Guardian</u> campaign in 2014, with the aim of transitioning from raising awareness to increasing engagement. The campaign uses an online pledge-based approach among human and animal health professionals, scientists and educators and the public. In the 10 years since inception, the campaign had surpassed 100,000 pledges in 2020 and approached 200,000 pledges by the end of 2023, ending 2023 with 177,681 pledges made via the main website page and over 200,000 including all the Antibiotic Guardian collaboration pages (Table 7.3).

After launching in 2014, the Antibiotic Guardian campaign received over 10,000 pledges in the first year. Engagement and reach were increased worldwide in 2016/17, the campaign was rebranded in September 2017, ensuring the campaign aligned with other AMR activities from PHE under the Keep Antibiotics Working brand. In 2018, the campaign worked with university students to organise a national healthcare student AMS conference, extending engagement and shared learning opportunity with students and in 2019, the Antibiotic Guardian schools ambassadors programme was developed to empower Antibiotic Guardians to act as ambassadors in the local community by sharing learning with local schools and community groups. Finally, the introduction of the Antibiotic Guardian pledge as part of the Pharmacy Quality Scheme (PQS) in 2020/21 led to a vast increase in UK pledges from pharmacy teams in 2020 (28,369 pledges), which was sustained in 2021 (27,334 pledges).

Year	НСР	Public	Students	Unknown
	n (%)	n (%)	n (%)	n (%)
2014	8,501 (69)	3,725 (30)	0 (0)	89 (1)
2015	7,979 (53)	4,542 (30)	2,322 (15)	159 (1)
2016	6,928 (46)	4,727 (31)	3,392 (22)	92 (1)
2017	8,494 (56)	3,518 (23)	3,028 (20)	130 (1)
2018	4,570 (55)	1,293 (15)	2,359 (28)	151 (2)
2019	5,899 (64)	1,234 (13)	2,022 (22)	134 (1)
2020	30,940 (84)	643 (2)	4,337 (12)	814 (2)
2021	29,608 (90)	627 (2)	1,571 (5)	617 (2)

Table 7.3. Number and proportion of pledges annually from the main pledge page bypledge groups from the start of the campaign in 2014 to December 2023

Year	НСР	Public	Students	Unknown
	n (%)	n (%)	n (%)	n (%)
2022	11,746 (84)	502 (4)	1,388 (10)	279 (2)
2023	16,486 (85)	438 (2)	1,950 (10)	447 (2)
Total	131,151 (74)	21,249 (12)	22,369 (13)	2,912 (2)

During 2023, the campaign received 19,321 pledges (<u>3</u>). Between 1 January 2019 and 31 December 2023, – aligning with the 5-year UK AMR NAP, 112,303 pledges were made, with the number of pledges exceeding 100,000 in 2020 and, reaching 177,681 by the end of 2023. The majority of all pledges were made by those identifying as a health or social care professional or leader (74%, n=131,151/177,681 pledges). Of these, 93,021 were made by those belonging to 'pharmacy teams', including those from primary and secondary care and community pharmacy. Annexe Table 7.1 has a breakdown of pharmacy team pledges from 2014 to the end of 2022. Furthermore, 12% of pledges made by the public has declined in recent years. Between 2014 and the end of 2023, 52,620 users stated finding out about Antibiotic Guardian through community pharmacy. 2023 saw the third-highest number of annual pledges since inception of the campaign, and a 39% increase on the pledges seen in the previous year. The increase in pledges in 2023 may be related to an update of Antibiotic Guardian pledges and the Antibiotic Guardian website, which was completed and publicised in 2023.

A total of 82 organisations registered their AMS activities on the Antibiotic Guardian website in 2023, between the update of the Antibiotic Guardian webpage in April 2023 and the end of the calendar year. The total number of organisational registrations is likely to be higher, which likely represents an increase on the annual number compared to 83 in 2022.





Antibiotic Guardian Shared Learning and Awards

The sixth Antibiotic Guardian shared learning and awards event took place in person, with hybrid virtual participation option, on 2 May 2023. Keynote speeches were delivered by honorary guests David Webb (Chief Pharmaceutical Officer for the UK), Professor Susan Hopkins (Chief Medical Adviser, UKHSA), and Dr Richard Irving (Chief Veterinary Officer for Wales). A patient story was shared by Vanessa Carter (Patient advocate and lay member for the Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection).

The event was attended by 108 delegates from organisations in the UK and internationally. Several projects which started locally and have won or been highly commended at the Antibiotic Guardian awards have gone on to become national projects and/or feature in the UK AMR NAP. A full list of shortlisted entries across all years can be viewed on the <u>Antibiotic Guardian</u> <u>website</u>. The 'COVID-19 Learning' category was introduced for the 2022/2023 awards cycle, aiming to highlight projects that have utilised learning from the COVID-19 pandemic to help tackle AMR, or unique interventions to mitigate against AMR during the COVID-19 pandemic. Thirteen entries from across the categories were received from international organisations. Annex Table 7.3 presents the number of entries per category in 2023. Shortlisted entries were given the opportunity to adapt their project entries into abstracts, several of which were published in <u>Medical Sciences Forum</u> on 24 March 2023, as a collection alongside insights from the 2022 ESPAUR report. In publishing in an academic journal, alongside poster presentations and publishing videos from shortlisted projects online, the Antibiotic Guardian Shared Learning and Awards event represents a strong example of knowledge mobilisation in the space of tackling AMR.

Antibiotic Guardian Schools Ambassadors programme

The Antibiotic Guardian Schools Ambassadors programme, first piloted in 2019, aims to connect healthcare professionals with local schools and community groups, to share information about antibiotic use, AMR and IPC. The programme aligns with the 5-year UK AMR NAP (2019 to 2024) and in this time, over 400 individuals have registered to become an Antibiotic Guardian Schools Ambassador and spread awareness to young people in their local community. Since 2021, the programme has aimed to target the regions with the most deprived lower-layer super output areas (LSOAs) (55) through cascading information through regional AMS pharmacy leads and the regional AMS pharmacy network. In 2023, the Antibiotic Guardian Schools Ambassadors programme was expanded to include strengthened veterinary content, in collaboration with the Veterinary Medicines Directorate (VMD), to share learning with young people who may be pet or animal owners.

A total of 26 colleagues registered to become an Antibiotic Guardian Schools Ambassador in 2023 (compared to 189 in 2022, 110 in 2021 and 79 in 2019). Of the 13 registrants from England that provided information on which region they live, the largest proportion were from the South East (n=13, 23%), with the East Midlands, North West and South West each accounting for 15% respectively (n=13). Although the small number of registrants hinders interpretation, the fact that registrations were seen from across 8 of the 9 regions in England (no registrations were received from Yorkshire and the Humber) suggests broad reach of the campaign. A sharp decline in registrants may suggest that promotion in 2023 was ineffective, or that those that had registered across the first 4 years of the campaign had not registered again, although they may continue to be using the teaching resources. In 2022, registrations were received for the first time from international colleagues, and in 2023, 31% of registrants (n=26) registered from outside of the UK, all based in Uganda.

The Antibiotic Guardian Schools Ambassadors programme highlights the dedication of HCPs to engage with schools around AMR including antibiotic use and infection prevention and control, even during the pandemic, and the utility of regional AMS lead networks in increasing engagement in areas of deprivation. The international reach of Antibiotic Guardian materials was demonstrated in 2022 and beyond, suggesting that use of translated e-Bug materials in future versions of the Antibiotic Guardian Schools Ambassadors lesson-planning toolkit may be

helpful. Future work will focus on strengthening this focused regional approach and designing robust indicators of impact.

Public education and engagement with e-Bug

The e-Bug programme, operated by the UKHSA, aims to target children and young people in all communities with messaging on IPC and AMS. To do this, e-Bug provides free educational resources to support and empower children and young people to contribute to the prevention of AMR, through the teaching of correct IPC practices.

The e-Bug website welcomed 336,792 page views between April 2023 and March 2024 (Figure 7.4). Unsurprisingly, website views were at their lowest during the summer months and school holidays, increasing again in September in line with the beginning of the new school year. Website views peaked in November, coinciding with e-Bug's social media campaign for WAAW, in which they posted 19 times on X (formerly Twitter), totalling 71,906 impressions and 903 engagements. It is clear from the website views that ongoing promotion is vital to reinvigorate engagement.



Figure 7.4. e-Bug monthly page views between April 2023 and March 2024

Social media

e-Bug utilises a variety of social media platforms to promote resources and inform on public health campaigns, reaching their audience of teachers and educators. Between April 2023 and March 2024, e-Bug received over 283,000 views on YouTube and an additional 486 subscribers. Total impressions per post on X (formerly Twitter) for the months April 2023 to July 2023 varied between 169 and 27,256, and highlighted improvements for October 2023 to March 2024, with impressions between 14,990 and 71,882. Engagement rates per post between April 2023 to March 2023 to March 2024 varied between 0.01% and 0.72%. Social media can be an effective method of communicating information and resources to teachers and educators.

Newsletter

e-Bug also distributes a quarterly newsletter to inform subscribers of any approaching campaigns, ongoing public health advice tailored towards educational settings and any upcoming research and evaluation projects. The open rate for the most recent edition, published in March 2024, was 43.3% (n=2,822/6,515), with 6.4% (n=416/6,515) engaging by clicking the contained links.

Training

e-Bug has developed 2 free courses, in collaboration with the British Society for Antimicrobial Chemotherapy (BSAC), which are hosted on e-learning platform FutureLearn. The courses, titled 'e-Bug Health Educator Training' and 'Preventing and Managing Infections in Childcare and Pre-School' ran from 24 March 2023 to 25 March 2024. In April 2023, following a review of the content, e-Bug relaunched their updated FutureLearn courses. Both courses inform behavioural change tactics to be used in the fight against AMR, which closely follows the teaching resources created by e-Bug that were developed for use in classrooms for children and young people aged 3 to 16 years.

Topics in the 'e-Bug Health Educator Training' course include an introduction to microbes, the application of behavioural changes to prevent infection spread and teachings on how to use antibiotics responsibly. With this training, individuals should feel confident in their knowledge and skill to educate children and young people. This first course is primarily tailored towards child educators and teachers in the UK but is also appropriate for medical professionals working with children.

The 'Preventing and Managing Infection in Childcare and Pre-school' course is designed for those who care for children under the age of 4 years. It provides training to inform students with an understanding of microorganisms, infectious diseases and knowledge on how to prevent and control this in childcare environments.

Survey

As the COVID-19 pandemic emphasised the significance of IPC across all settings, especially educational settings, a study was carried out to understand attitudes towards, and knowledge of IPC in schools following the pandemic, and highlight any gaps in the training and resources needed. An online survey of 1,036 primary and secondary school teachers was carried out across England. Respondents reported that IPC measures are now less frequently implemented than during the pandemic, whilst 71% reported that they now have more responsibility for student health and hygiene. This was higher in primary school teachers (31%) versus secondary school teachers (25%), and one-third felt that this change was permanent. 72% of teachers stated that they felt better prepared to deal with a public health outbreak compared to before the COVID-19 pandemic. Some gaps in knowledge and needs were also identified as 84% of respondents said they had no IPC training, 22% do not have an updated IPC policy, and 35% had unmet needs as regards IPC. This survey showed the need for IPC training, clear and evidence-based information, and policies to support the educational workforce.

Framework for developing an engagement guide on antimicrobial resistance

The role of the public in reducing AMR has been greatly emphasised. However, existing evidence has highlighted gaps in public knowledge about appropriate antimicrobial use, and differences between groups in knowledge, attitudes and health seeking behaviour towards antimicrobials. There is a need for consistent AMR-related messages across various organisations to improve public understanding of the scale and nature of the risk and the individual actions that they can take to reduce the spread of infection. To address this, the UKHSA and the University of Warwick collaborated to co-develop a framework by and for government, civil societies (non-profit voluntary groups and other non-governmental organisations) and local partners to develop a comprehensive guide on communicating and conducting engagement activities relating to AMR.

We employed a participatory and iterative approach, including a stakeholder co-design workshop, email correspondence, and refining. To provide a foundation for the framework, we conducted a scoping review to identify existing communication and engagement guides across several topic areas. This included topics relating to infection, as well as other public health topics, such as physical activities, loneliness and climate change. We examined the main components of these guides to gain ideas of structure and useful sections to be included in AMR engagement guides. Based on the insight obtained from these guides, we drafted an initial framework. We then conducted a stakeholder engagement workshop involving 18 people; with 14 people attending in person (of which 7 were project team members) and 4 others joining online. This group represented a range of perspectives and was made up of public contributors, including people with experience of AMR infection and chronic conditions, as well as academic researchers, policymakers and experts in health protection.

During the stakeholder engagement workshop, we first allowed participants to share insights on AMR, before providing suggestions for an AMR engagement guide. This allowed us to capture any ideas that we may not have covered in the initial draft. We then gave the attendees the initial draft of the framework to discuss and comment on. We also sent the initial draft to colleagues at UKHSA who were unable to attend, as well as the UKHSA communication team, to receive further input by email.

Based on the workshop feedback and email responses, we revised the framework, incorporating valuable insights from contributors and refining its content. The final version was reviewed by workshop attendees, ensuring input from all stakeholders.

The framework comprises 11 key sections which the stakeholders agreed should be included in an engagement guide: (1) defining AMR, (2) expressing the scale and nature of the risk, (3) providing information on how AMR happens, (4) explaining individual actions which can prevent the problem, (5) improving communication about AMR between healthcare providers and the public, (6) policy actions to tackle the problem, (7) engagement strategies, (8) considering

factors associated with health inequalities (inclusive communications), (9) other features to consider, (10) feedback, evaluation and continuous improvement, and (11) sources of additional information. Each section contains details of what should be considered by those developing engagement guides relating to AMR.

In the finalisation phase, we worked with graphic design and communication experts to ensure the engagement guide is visually appealing and accessible.

Future actions

TARGET Antibiotics programme

TARGET/RCGP campaign and webinars

TARGET will implement a joint campaign with the RCGP in the autumn of 2024, focusing on promotion of the toolkit to improve prescribing in primary care. TARGET and RCGP will continue to implement their collaborative webinar series, with another 3 webinars planned for late 2024 to early 2025.

Roll out of TARGET training

TARGET will continue to evaluate the implementation and reach of their training roll out across England with additional process and impact evaluations. A mixed-methods approach will assess if TARGET training affects clinician behaviour and prescribing rates, as well as investigating any barriers and facilitators for the implementation of the training.

e-Bug programme

Implement e-Bug in UKOTS and develop vector-borne disease lesson plans

e-Bug are currently working with the UK Overseas Territories (UKOTS) and the UKHSA UKOTS Programme Global Operations team to implement their resources in the territories and to develop a module or lesson plans about vector-borne diseases.

Incorporate MRNA vaccine information into vaccine lesson plans

e-Bug are updating their vaccinations lesson plans for Key Stage 2 to Key Stage 4 to include information about MRNA and HPV vaccines. The aim of this is to ensure children receive evidence-based information about MRNA and HPV vaccines and their benefits.

Promote the Antibiotic Guardian Youth Badge resource

A key part of e-Bug's work this year is to update and promote the Antibiotic Guardian Youth Badge (AGYB) resource. The AGYB was developed for use in various community settings to teach young people about microbes, IPC and AMR.

Review and update the Beat the Bugs pack

Beat the Bugs is a 6-week community hygiene course aimed at equipping young people with knowledge of self-care, microbes, and correct food, hand, respiratory and oral hygiene practices. This year, e-Bug will begin to update and adapt the course to suit a varied audience of young people (16 to 25 years), focusing on those who are transitioning from supported living and those with learning difficulties.

Antibiotic Guardian and World AMR Awareness Week (WAAW)

Antibiotic Guardian Shared Learning and Awards (AGSLA)

The next iteration of the AGSLA event is planned to take place in 2025, with a call for entries being launched in 2024, giving sufficient time for high-quality projects to be submitted.

Antibiotic Guardian Schools Ambassadors scheme

The Antibiotic Guardian Schools Ambassadors scheme will run for its sixth year in 2024, strengthening focus on areas of deprivation, in a commitment to tackling inequalities. Further promotional activity will be included to increase engagement from 2023 levels.

World AMR Awareness Week (WAAW)

National planning for the 2024 WAAW campaign will focus on incorporating key messages from the new UK AMR NAP and helping frontline workers to incorporate them into their practices. Digital resources will be consolidated, and changes will be made to how WAAW toolkit resources are accessed, to make them more accessible.

Chapter 8. Research

Main messages

A wide range of new and ongoing research projects were undertaken in the fields of healthcareassociated infection (HCAI) and antimicrobial resistance (AMR) in the last year, with the publication of over 100 peer-reviewed papers from across the UKHSA.

This chapter showcases key AMR and HCAI research projects within the UKHSA and jointly with external stakeholders, undertaken from April 2023 to March 2024, highlighting the contributions to the goals of the UK National Action Plan (NAP) for AMR 2019 to 2024 (<u>1</u>), as well as looking at how the work will align with the objectives of the latest UK NAP for AMR 2024 to 2029 (<u>30</u>).

The publication of the UK NAP for 2024 to 2029 (<u>30</u>) has identified key research priority areas and provided example research questions. Many of the projects showcased in the Research Chapter have alignments to these priorities as well as the new NAP commitments for 2024 to 2029.

The 2 National Institute for Health Research (NIHR)-funded Health Protection Research Units (HPRUs) working on HCAI and AMR (University of Oxford and Imperial College London) continue to produce a wealth of translational research aiming to impact public health practice and policy. An overview of the research of the HPRUs is provided and impactful projects highlighted.

Introduction to Chapter 8

Within and in collaboration with the UKHSA, there are a wide range of new and ongoing research projects in the fields of healthcare-associated infections (HCAIs) and antimicrobial resistance (AMR), undertaken in the last financial year.

These projects cover many priorities in innovation, research, and development, including studies to improve our understanding of behaviours around antimicrobial usage, as well as contributing to evidence about new and existing control strategies, including infection prevention and control (IPC), antimicrobial stewardship (AMS), and the development of novel vaccines, immunotherapeutics, and antibiotics. There is work to understand the risk factors for patients and to elucidate the characteristics that are predisposed to infection, resistance, or poor outcomes.

The work is focused on supporting the achievement of the goals and commitments of the UK National Action Plan (NAP) for AMR 2019 to 2024. This is demonstrated in <u>Figure 8.1</u>, which illustrates the breadth of peer-reviewed publications resulting from research undertaken by the
UKHSA against the 2019 to 2024 NAP major themes. A complete list of these AMR-related publications from April 2023 to March 2024 is provided in the <u>Annexe accompanying this report</u> (Chapter 8).





The recent publication of the latest UK AMR NAP for 2024 to 2029 ($\underline{30}$) has introduced the focus for research priorities over the next 5 years. Priority AMR research questions for the UK in the next 5 years are described in Appendix C of the NAP (2024 to 2029) and include:

- What is the cost of AMR?
- What is the relationship between AMR and health disparities?
- How to influence public awareness and behaviour on AMR?
- How to address AMR in international settings?
- What are the basic drivers and effects of AMR, and how does it spread?
- How can we prevent AMR from spreading?
- How can we optimise the use of antimicrobials?
- What methods can be used to prevent, treat and manage infections without antimicrobial medicines?
- How can we drive innovation of new products for tackling AMR?

• How can we ensure what is known to work is implemented?

This chapter outlines examples of AMR and HCAI research projects undertaken by the UKHSA from April 2023 to March 2024. The projects showcase research across many fields within AMR, and are organised according to the following themes of the NAP 2019 to 2024:

- human IPC
- clean water and sanitation
- optimal use of antimicrobials in humans
- stronger laboratory capacity and surveillance of AMR in humans
- development of new therapeutics
- wider access to therapeutics for those who need them
- development and access to vaccines
- development and access to diagnostics

We have categorised the projects by the major theme from the 2019 to 2024 NAP, additionally for ongoing research projects and where applicable, we have included the key outcome that the work aligns to in the latest NAP (2024 to 2029). Projects that were completed during the timescales of the report (April 2023 to March 2024), have not been mapped to the outcomes of the latest NAP.

Many projects report against several of the outcomes of the latest NAP 2024 to 2029 and as is often the case, the projects cut across several fields, objectives, and disciplines. The key outcomes described here, demonstrate the breadth of research as it aligns under the latest NAP 2024 to 2029.

We also provide an overview of the research from the 2 National Institute for Health Research (NIHR) Health Protection Research Units (HPRUs) in the topic area of HCAI and AMR, led by Imperial College London and the University of Oxford, in partnership with the UKHSA.

Research projects

Human infection prevention and control

The laboratory investigation, management, and infection prevention and control of *Candida auris*: a narrative review to inform the 2024 national guidance update in England

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NAP 2024 to 2029 outcome: using information for action

The emergent fungal pathogen Candida auris is increasingly recognised as an important cause of healthcare-associated infections globally. It is highly transmissible, adaptable, and persistent, resulting in an organism with significant outbreak potential that risks devastating consequences. Progress in the ability to identify C. auris in clinical specimens is encouraging, but laboratory diagnostic capacity and surveillance systems are lacking in many countries. Intrinsic resistance to commonly used antifungals, combined with the ability to rapidly acquire resistance to therapy, substantially restricts treatment options, and novel agents are desperately needed. Despite this, outbreaks can be interrupted, and mortality avoided or minimised, through the application of rigorous infection prevention and control measures with an increasing evidence base. This review provides an update on epidemiology, the impact of the COVID-19 pandemic, risk factors, identification and typing, resistance profiles, treatment, detection of colonisation, and infection prevention and control measures for C. auris. This review has informed a planned 2024 update to the UKHSA guidance on the laboratory investigation, management, and infection prevention and control of C. auris. A multidisciplinary response is needed to control C. auris transmission in a healthcare setting and should emphasise outbreak preparedness and response, rapid contact tracing and isolation or cohorting of patients and staff, strict hand hygiene and other infection prevention and control measures, dedicated or single-use equipment, appropriate disinfection, and effective communication concerning patient transfers and discharge.

Clinical characteristics of patients with reported acquired carbapenemase-producing Gramnegative bacteria in England, October 2020 to April 2023

Authors

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¹ HCAI, Fungal, AMR, AMU and Sepsis Division, UK Health Security Agency Conference abstract: European Congress of Clinical Microbiology and Infectious Diseases (ECCMID) 2024

NAP 2024 to 2029 outcome: using information for action Introduction:

Acquired carbapenemase-producing Gram-negative bacterial (aCPNGB) infections are an increasing global health concern and associated with poor patient outcomes. However, little is known about the clinical characteristics of patients with an aCPNGB positive screen or infection in England since reporting became mandatory on 1 October 2020.

Methods:

Laboratory confirmed aCPNGB isolates from all specimen-site samples in England between October 2020 and April 2023 were extracted from the UKHSA's Second Generation Surveillance System and the Antimicrobial Resistance and Healthcare-Associated Infections Reference Unit database. Data was deterministically linked to inpatient Hospital Episode Statistics (HES) to obtain patient comorbidities, including a 6-month lookback period. Charlson comorbidities were defined using International Classification of Diseases 10th revision (ICD-10) codes in HES using the <u>comorbidity</u> R package by Gasparini.

Results:

Between October 2020 and April 2023, 5,621 patients with an aCPNGB positive screen or infection were linked to a hospital admission record (out of a total of 6,422 linkable patients). Of these patients, 88.3% (4,963 out of 5,621) had \geq 1 comorbidity. The most common comorbidity reported, regardless of specimen-site and England region, was diabetes without complications, accounting for 32.1% of sterile site samples (Table 1) and was reported more often in male patients (59.6%). The most reported comorbidity in patients with the detected IMP and VIM mechanisms was chronic pulmonary disease (32.3% and 29.2%, respectively), for NDM and OXA-48-like it was diabetes without complications (35.7% and 35.0%, respectively) and for KPC it was renal disease (35.7%).

Conclusions:

Most patients with, or at risk of developing, aCPNGB infections had a comorbidity, with diabetes (without complications) frequently reported across all specimen-sites and geographical regions in England. There was some variation in the most frequently reported comorbidities by carbapenem-resistance mechanisms. The result of this study supports evidence that recommended at-risk patient groups (for example those on dialysis) are being screened for aCPNGB as recommended by the UKHSA framework. However, forthcoming multivariate risk factor analysis will enhance the understanding of the epidemiology in patients with no comorbidities, to inform screening and diagnostic testing strategies.

Comorbidities associated with increased odds of antibiotic resistance in *Enterococcus faecium* bacteraemia in England, 2023

Authors

Cindy Leung Soo¹, Jacquelyn McCormick¹, Emily Mason¹, Katherine Henderson¹ ¹ HCAI, Fungal, AMR, AMU and Sepsis Division, UK Health Security Agency Conference abstract: European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) 2024

NAP 2024 to 2029 outcome: using information for action

Introduction:

Understanding the epidemiology of resistant *Enterococcus faecium* bacteremia is crucial for preventing nosocomial infections. Therefore, we aim to characterise the comorbidities associated with resistant *E. faecium* bacteremia.

Methods:

Laboratory-confirmed *E. faecium* isolates from blood specimens in England 2023 were extracted from the UKHSA's national laboratory system and deduplicated using a 14-day rolling episode. Data was linked with Hospital Episode Statistics data (2018 to 2023) and mapped using the Charlson comorbidity score. The likelihood of *E. faecium* resistance to teicoplanin and/or vancomycin was examined using multivariate logistic regression, adjusting for region, age, sex, ethnicity, and Index of Multiple Deprivation (IMD).

Results:

In *E. faecium*, resistance to teicoplanin was 24.5% (N=3,616), to vancomycin 22.8% (N=3,737), or to both was 22.9% (N=3,359). In our adjusted analyses, peripheral vascular disease and cancer were associated with higher odds of teicoplanin (aOR, 95%CI: 1.5, 1.2-1.9 and 1.3, 1.0-1.6) and vancomycin (1.5, 1.2-1.9 and 1.3, 1.0-1.5) resistance in *E. faecium* bacteraemia. Rheumatoid disease and dementia were associated with lower odds of combined teicoplanin and vancomycin resistance (0.6, 0.4-1.0 and 0.5, 0.3-1.0). In 2023, compared to London, the East of England had higher odds of teicoplanin, vancomycin and combined resistance in *E. faecium* bacteremia, whereas North East and East Midlands had lower odds of resistance. There was no statistically significant difference in resistance across sex, ethnic groups or IMD quintile. \leq 14 year olds and \geq 75 year olds had lower odds of *E. faecium* resistance compared to 45 to 64 year olds.

Conclusion:

Our results indicate that patients with peripheral vascular disease and cancer have increased odds of resistant *E. faecium* bacteremia in England. Better understanding the epidemiology of resistant bacteraemia can help target screening and improve patient outcomes.

Research to better understand the role of the built environment in transmission of AMR

Authors

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NAP 2024 to 2029 outcome: Infection prevention and control and infection management

The UK National Action Plan for AMR (2019 to 2024) (<u>1</u>) recognised the need to better understand how the built environment contributes to the spread of AMR (Lower burden of human infection; Ambition 3). It also acknowledged that to support healthcare professionals, more research on how to design and optimise our use of the built environment is required, and the findings used to inform action and investment (Improve the professional capacity and

capability for IPC). To this end, the UKHSA has designed and built a full-scale, fully functional, model hospital ward in which to study the built environment and its impact on AMR. This unique facility allows the Biosafety Group to carry out applied microbiology research without impacting patients or disrupting clinical practice.

Over the past year (2023 to 2024), and in collaboration with the UKHSA colleagues, the NHS and academic partners, we have continued to investigate the colonisation of sinks, showers and drains, and the dispersal of waterborne pathogens. Surfaces and fomite transmission are another area of interest, and we performed work to study the type of surfaces that become contaminated during patient care, how easily pathogens are transferred from non-porous surfaces to hands, and how people choose to launder clothes and other linen.

This work will continue throughout the next 5-year National Action Plan (2024 to 2029) and will support the UK's commitment to prioritise infection prevention and control, the management of infections, and biosecurity in the built environment.

Changes in public health-seeking behaviours for self-limiting respiratory tract infections across England during the COVID-19 pandemic

Authors

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¹ Clinical and Public Health Group, UK Health Security Agency

NAP 2024 to 2029 outcome: public engagement and education

Introduction:

The NHS guidance for acute respiratory tract infections (RTIs) advocates self-care, encourages utilisation of local pharmacies, and recommends consulting general practitioners (GPs) primarily for the vulnerable or those with persistent symptoms. COVID-19 exerted a substantial strain on the English NHS, affecting public access to primary care services.

Methods:

For 3 years, public surveys assessed RTI incidences in the previous 12 months and associated health-seeking behaviours. Telephone surveys of 1,676 respondents across England were conducted in March 2021 and 1,663 respondents in March 2022. Findings were compared with a face-to-face baseline survey of 2,022 respondents from March 2020. Key demographics were representative of the population.

Results:

In 2021, the proportion of respondents who reported an RTI (51%) significantly declined from 2020 (70%, P < 0.05), then returned to pre-pandemic rates in 2022 (67%). Respondents reported more proactive symptom management in both 2021 and 2022 compared to 2020: there were greater reports of seeking over-the-counter treatments (55% vs. 35%, P < 0.05) and use of alternative remedies (38% vs. 21%, P < 0.05). In 2022 it was observed that there was a reduction in those who reported consulting their GP for their most recent RTI (15%) compared

to 2021 (25%, P < 0.05) and 2020 (23%), which was not accounted for through greater consultation rates with other healthcare services.

Conclusions:

Public health bodies should consider how pandemic-related changes may have facilitated increased self-care for self-limiting infections such as RTIs. Resources and support must include safety-netting advice to safeguard against unintentional consequences of increased self-care.

The impact of appropriateness of urinary tract infection diagnoses and treatment on hospital patient outcomes

Authors

Rebecca Oettle¹, Sabine Bou-Antoun¹, Hannah Higgins¹, Alicia Demirjian¹, Elizabeth Beech, Kieran Hand, Berit Pebody-Muller¹.

¹ HCAI, Fungal, AMR, AMU and Sepsis Division, UK Health Security Agency Conference abstract: ESCMID Global, April 2024

NAP 2024 to 2029 outcome: infection prevention and control and infection management Introduction:

Last year 147,285 patients were admitted to hospital with a primary diagnosis of urinary tract infection (UTI). As a leading cause of Gram-negative bloodstream infections and a major contributor to the burden of antimicrobial resistance, UTIs place a substantial burden on healthcare resources. In 2022 to 2023, National Health Service (NHS) England consequently targeted the improvement of UTI diagnosis and treatment with a Commissioning for QUality and INnovation (CQUIN) indicator to monitor and incentivise improvement in compliance with national clinical guidelines for the management of UTI in patients aged 16 years and older. We aim to: i) determine whether patients were diagnosed appropriately, according to National Institute of Health and Care Excellence (NICE) UTI guidelines, and ii) identify whether patient outcomes varied according to appropriate or inappropriate diagnosis and treatment for UTI.

Methods:

This study utilised the CQUIN retrospective audit data, collected from 84 Acute NHS Trusts in England. Patient-level CQUIN data is being deterministically linked to hospital admissions and laboratory antimicrobial resistance database systems, to evaluate the association between adherence to UTI clinical guidelines and patient outcomes, including length of hospital stay, and prevalence of serious sequelae such as *Escherichia coli* bacteraemia and mortality.

Results:

Data was reported for n = 28,171 UTI cases. In 85% of cases, patient management followed NICE guidelines (61.4%), local guidelines (14.6%) or was guided by susceptibility testing (8.7%). UTI diagnosis was empirically informed by microbiological urine analysis in 71.4% of cases. Adherence to clinical guidelines varied by patient age, with greater adherence to NICE guidelines seen in the younger age groups. Conversely, a higher proportion of older patients had treatment guided by antimicrobial sensitivity reporting.

Conclusions:

This study has identified variation in adherence to national and local guidelines for the management of UTI by patient age group, that may have implications for clinical outcomes. This will be explored in future work using linked data to specifically investigate whether guideline-adherent management of acute UTI in adults can reduce avoidable healthcare associated infection rates, reduce length of hospital stay, and in turn, release bed capacity.

Clean water and sanitation

A pilot of methodology to inform surveillance of antimicrobial resistance in river catchments in England

Authors

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NAP 2024 to 2029 outcome: strengthened surveillance

Introduction:

The environment plays an important role in the development and transmission of antimicrobial resistance (AMR). As part of the 'PATHogen Surveillance in Agriculture, Food, and the Environment (PATH-SAFE)' programme, the aims were to: i) to test a range of methodologies for detection of AMR organisms and associated AMR genes, and ii) to report on water quality within 3 pilot river catchments with respect to presence of AMR microorganisms.

Methods:

Water samples were taken along 3 river catchments reflecting different surrounding land use settings. *Escherichia coli* (including ESBL-*E. coli*), Enterococcus spp. (including vancomycin-resistant enterococci, VRE), yeasts and moulds were sought using selective and differential media. ESBL-*E. coli*, VRE and fungal antimicrobial MICs were determined by broth microdilution. Whole-genome sequencing (WGS) was performed on ESBL-*E. coli* and VRE to derive sequence types (STs) and AMR gene complement. Short- and long-read shotgun untargeted metagenomic sequencing and 16S rRNA metabarcoding was performed to determine presence of AMR genes and microbial community composition. High-throughput chip array qPCR (HT-qPCR) sought relative abundance of a selected set of up to 384 AMR genes.

Results:

Significant differences were observed in the yield of total *E. coli*, Enterococcus spp. and yeasts but not of VRE or moulds, across the 3 river catchments. Putative ESBL-*E. coli* was isolated from 53% of the water samples with significant differences (p <= 0.001) in yield observed across the 3 river catchments. VRE was only detected in 22% of samples with no difference in yield

across the 3 catchments. WGS revealed greater diversity in bla_{CTX-M} variants amongst ESBL-*E. coli* from urban vs. rural catchments. STs 131 (16%), 38 (13%), 10 (7%), 69 (6%) and 1193 (5%) dominated amongst ESBL-*E. coli* and were reflective of human and animal sources contributing to the ecosystem. Catchments were broadly similar in the AMR genes detected by HT-qPCR but relative abundance varied widely across time. Metagenomics revealed that more diverse microbial communities were associated with potentially more polluted river ecosystems.

Conclusion:

This study informs methodology to inform future surveillance approaches and provides initial baseline data on AMR prevalence and levels in the riverine environment in England.

Optimal use of antimicrobials in humans

Consumption of antibiotics in response to invasive group A streptococcus outbreak and changed clinical guidelines in England, winter 2022

Authors

Emma L Budd¹, Sabine Bou-Antoun¹, Berit Muller-Pebody¹, Alicia Demirjian¹ ¹HCAI, Fungal, AMR, AMU, and Sepsis Division, UK Health Security Agency Conference abstract: European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) 2023 (Antimicrobial use theme)

NAP 2024 to 2029 outcome: antimicrobial stewardship and disposal

Introduction:

Between November and December 2022, England experienced a surge in group A streptococcus (GAS) infections in children under 15 years. On December 9th (week 49) 2022 interim clinical guidance was introduced for the diagnosis and treatment of children with suspected GAS infections. On 15 December, a serious shortage protocol was introduced for phenoxymethylpenicillin (penV), which allowed pharmacists to dispense alternative antibiotics. This study aims to describe the trends in national community prescribing of respiratory antibiotics by age, during this period.

Methods:

Antibiotic prescribing data in Defined Daily Doses (DDDs) for primary care in England 2017 to 2022 was provided by the NHS Business Services Authority. Assessment of antibiotic trends were completed for antibiotics commonly prescribed for respiratory-tract infections (RTI): amoxicillin, azithromycin, cefalexin, clarithromycin, clindamycin, co-amoxiclav, erythromycin, and penV.

Results:

Prescribing of all the respiratory antibiotics increased in all age groups from week 46 in 2022; with a peak in prescribing at week 49 in ages 0 to 14 and at week 51 in those aged 14 to 75+. Prescribing of penV for ages 0 to 14 peaked in week 49 and was 388% and 514% higher than the same week in 2019 and 2021 respectively. Prescribing of amoxicillin for ages 0 to 14

peaked at week 50 and was 150% and 221% higher than week 50 in 2019 and 2021, respectively.

Conclusions:

Prescribing of respiratory antibiotics for children, and more specifically, penV, was substantially higher during the winter of 2022 compared to previous seasons in England, coinciding with a national GAS outbreak and changed clinical guidelines advising a lower threshold for antibiotic treatment of sore throat and recommending penV. Reported stock shortages led to subsequent increases in alternate RTI antibiotics. This study highlights the need for timely antibiotic surveillance data to inform medicines supplies and antibiotic stewardship initiatives.

Appropriateness of acute-care antibiotic prescriptions for community-acquired infections and surgical antibiotic prophylaxis in England: analysis of 2016 national point prevalence survey data

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Introduction:

Estimates of inappropriate prescribing can highlight key target areas for antimicrobial stewardship (AMS) and inform national targets. The objectives were to define and produce estimates of inappropriate antibiotic prescribing levels within acute hospital trusts in England.

Methods:

The 2016 national Healthcare-Associated Infections (HAI), Antimicrobial Use (AMU) and AMS point prevalence survey (PPS) was used to derive estimates of inappropriate prescribing, focusing on the 4 most reported community-acquired antibiotic indications (CAIs) in the PPS and surgical prophylaxis. Definitions of appropriate antibiotic therapy for each indication were developed through the compilation of national treatment guidelines. A Likert-scale system of appropriateness coding was validated and refined through a 2-stage expert review process.

Results:

Antimicrobial usage prevalence data was collected for 25,741 individual antibiotic prescriptions, representing 17,884 patients and 213 hospitals in England. 30.4% of prescriptions for the 4 CAIs of interest were estimated to be inappropriate (2054 prescriptions). The highest percentage of inappropriate prescribing occurred in uncomplicated cystitis prescriptions (62.5%), followed by bronchitis (48%). For surgical prophylaxis, 30.8% of prescriptions were inappropriate in terms of dose number, and 21.3% in terms of excess prophylaxis duration.

Conclusions:

In 2016, the prevalence of inappropriate antibiotic prescribing in hospitals in England was approximated to be 30.4%; this establishes a prevalence baseline and provides indications of where AMS interventions should be prioritised. Our definitions appraised antibiotic choice, treatment duration, and dose number (surgical prophylaxis only). However, they did not consider other aspects of appropriateness, such as combination therapy, which is an important area for future work.

The impact of side effects and allergies on patients' attitudes and adherence to prescribed antibiotic use

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NAP 2024 to 2029 outcome: antimicrobial stewardship and disposal

Overuse and misuse of antibiotics are known contributing factors for antibiotic resistance. The experience of adverse reactions to antibiotics is well documented. However, little is known about how this can impact patients' adherence to recommended use. This study aimed to explore the impact of side effects (SE) and allergies on users' attitudes and behaviours towards prescribed antibiotic use. The mixed methods study included an online survey (n=1,059) and focus groups (n=21), for adults who had previously experienced SE to antibiotics.

Respondents identified many antibiotic SE, usually presenting mild (37%; 397 out of 1,059) or moderate (45%; 474 out of 1,059) effects, shortly after consumption. 31% (325 out of 1,059) were not aware of the possibility of SE prior to use, barriers included inaccessibility of patient information leaflets and lack of information about SE shared by healthcare professionals (HCPs). 42% (440 out of 1,059) of respondents did not complete the course; 61% (269 out of 440) of which sought HCP advice and 32% (142 out of 440) personally decided to stop, many due to the SE impacting their life more than the infection being treated. Those with antibiotic allergies usually had this confirmed by a HCP (89%; 275 out of 308), but 49% (152 out of 308) had not experienced a reaction for over 10 years.

Providing accessible information on SE prior to taking antibiotics may help to manage patient expectations, which could reduce subsequent consultations and improve antibiotic adherence. Patients diagnosed with an antibiotic allergy should be encouraged to have their allergy reassessed to potentially de-label inaccurate allergies. Future research should involve parents whose children have experienced adverse reactions to antibiotics.

The impact of COVID-19 national restrictions on dental antibiotic dispensing trends and treatment activity in England: January 2016 to July 2021

Authors

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Introduction:

Reducing inappropriate antibiotic prescribing can temper the growing threat of antimicrobial resistance. The aim was to quantify the associated impact of COVID-19-related national restrictions in England on dental antibiotic dispensing and to describe the changes in appointments and modes of delivery of care.

Methods:

Interrupted time-series analyses were completed using NHS Business Service Authority (NHSBSA) ePACT2 data to measure the associated changes in antibiotic dispensing in England following COVID-19-related restrictions (which began March 2020). For face-to-face dental consultations, the NHS dental treatment plan (FP17) data was used. For remote consultations during the COVID-19 period, the NHSBSA Compass system remote management data was used.

Results:

Between January 2016 and February 2020, there was a decrease in the trend in antibiotic dispensing (-0.02 per 1000 population per month, P<0.05). In contrast, there was an increase of 0.98 per 1000 population (P<0.05) in March. The peak in antibiotic use occurred between June 2020 and July 2020, once the restrictions were eased. At the end of the study period (July 2021), the elevated prescribing trend had not returned to pre-pandemic counterfactual levels, despite exhibiting a declining trend. A stable trend in dental treatment plans was seen pre-COVID-19, with a sharp decline coinciding with the restrictions. Dental treatment plans had not yet returned to the higher pre-pandemic levels.

Conclusions:

Dental antibiotic prescribing significantly increased with the national COVID-19 restrictions when service delivery was altered, with the closure of dental practices and the introduction of remote consultations. Teledentistry was likely associated with inappropriate antibiotic prescribing. Continued antimicrobial stewardship and the prudent use of antibiotics in dentistry, is important.

COVID-19 therapeutics: stewardship in England and considerations for antimicrobial resistance Authors:

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The COVID-19 pandemic saw unprecedented resources and funds driven into research for the development, and subsequent rapid distribution, of vaccines, diagnostics, and directly acting antivirals (DAAs). DAAs have undeniably prevented progression and life-threatening conditions in patients with SARS-CoV-2 infection. However, there are concerns for antimicrobial resistance (AMR), and, more specifically, antiviral resistance, for DAAs. To preserve activity of DAAs for COVID-19 therapy, as well as detecting possible mutations conferring resistance, antimicrobial stewardship and surveillance were rapidly implemented in England. This work expands on the ubiquitous ongoing public health activities carried out in England, including, epidemiologic, virologic, and genomic surveillance, to support the stewardship of DAAs and to assess the deployment, safety, effectiveness, and resistance potential of these novel and repurposed therapeutics.

The changing aetiology of paediatric bacteraemia and associated antimicrobial resistance in England, 2008 to 2022

Authors

Benjamin Simmons¹, Hannah Higgins¹, Jacquelyn McCormick¹, Katherine L. Henderson¹, Rebecca Guy¹, Theresa Lamagni¹, Mariyam Mirfenderesky¹, Alicia Demirjian¹ ¹ HCAI, Fungal, AMR, AMU and Sepsis Division, UK Health Security Agency Conference abstract: European Society for Paediatric Infectious Diseases (ESPID) 2024

NAP 2024 to 2029 outcome: health disparities and health inequalities

This study investigates the epidemiological factors that have changed the incidence of bacteraemia in zero to 17 year-olds and associated antimicrobial resistance (AMR), in England. Retrospective surveillance was performed on paediatric bacteraemia in England between 2008 and 2022. Reports of positive bacterial blood isolates and associated AMR were extracted from the UKHSA's voluntary national laboratory database and deterministically linked to inpatient Hospital Episode Statistics using patient identifiers to determine ethnicity and location of infection onset (community or hospital).

Between 2008 and 2022, reported incidences of annual positive blood cultures increased by 48.3% (n=9,248 to 19,149) in 0 to 17 year-olds in England. In all age groups, this was predominantly driven by increases in reports of Coagulase-Negative Staphylococcus (CoNS) and Micrococcus spp.

Aside from CoNS, there have been changes in the organisms that are isolated the most. For example, in 2008, *Staphylococcus aureus* was the second most dominant organism, whereas in 2022 the second most dominant organism was *Escherichia coli*. *Klebsiella pneumoniae* increased in the ranking and was among the top 5 reported isolated organisms in children aged 4 days to one month and one month to one year, in 2022. Despite a decrease in Group A Streptococci incidence between 2018 and 2021, in age groups more than one month old it ranked among the top 5 organisms in these age groups, in 2022. Reports of *Neisseria meningitidis* decreased across all age groups.

The increase in positive blood cultures between 2008 and 2022 is concerning. With a large proportion of the cultures being potential contaminants, discussion is needed for the development of guidelines to avoid inappropriate prescribing and prevent harm to patients.

Mixed-method impact and implementation evaluation of the 'Pharmacy First' services for management of common conditions

Authors

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NAP 2024 to 2029 outcome: using information for action

Under the Government's NHS Primary Care Recovery Plan, NHS England (NHSE) is commissioning the Pharmacy First (PF) service. From February 2024, pharmacies participating in PF can supply prescription-only medicines for 7 common conditions: earache, uncomplicated urinary tract infections in women, sore throat, sinusitis, impetigo, shingles, and infected insect bites, after consultation with a community pharmacist. The aim of the <u>National Institute for</u> <u>Health and Care Research (NIHR) Health and Social Care Delivery Research (HSDR)</u> <u>Programme</u> is to perform a mixed-method evaluation 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 casemix 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 team at UKHSA will evaluate how antimicrobial use and antimicrobial resistance (AMR) change following the introduction of PF.

We plan to analyse the impact of PF on trends in:

- the number and type of antibiotics dispensed in the community in England (total and by patient age, per 1,000 population), with sub-group analysis by region or ICS, age group, and antibiotic class (in the context of national surveillance), including antimicrobials approved for use in the 7 PF conditions using UKHSA's routine antimicrobial use surveillance data (obtained from ePACT2 from NHS BSA)
- the number of positive community-associated urine samples (by causative organism, age group, sex, ethnicity and deprivation) and the urine isolate AMR rates (by causative organism) using UKHSA's Second Generation Surveillance System (SGSS) data
- the number of positive bacterial community-associated respiratory samples (by causative organism, age group, sex, ethnicity and deprivation) and the respiratory isolate AMR rates (by causative organism) using SGSS data

Quasi-experimental analyses will be conducted using interrupted time-series analysis at 2 timepoints: one-year and 2-years after PF introduction, comparing monthly data up to 2 years after roll-out of PF with 2 years pre-PF, and by the 7 PF conditions and the total.

The project started in February 2024. Results are pending and work is ongoing. Capturing information related to national antimicrobial use and resistance following the roll-out of the PF service in England is crucial to identify and respond to any impact of those changes on AMR. 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.

Are there unintended consequences of lower antibiotic prescribing for respiratory tract infections in primary care?

Authors

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NAP 2024 to 2029 outcome: strengthened surveillance

Introduction:

About 60% of antibiotic prescribing in primary care is for respiratory tract infections (RTIs), some of which is likely to be unnecessary. There is limited evidence on the association between reduced antibiotic prescribing and adverse events. We aimed to identify associations between practice-level prescribing rates for RTIs in general practice, and patient-level adverse outcomes.

Methods:

We included 1,471 English General Practitioner (GP) practices, linked to hospital admissions in England, from the Clinical Practice Research Datalink for 2005 to 2019. Outcomes were hospitalisation, RTI-related re-consultations, and additional antibiotic prescriptions; adjusted for practice level case-mix prescribing.

Results:

Prescribing rates for practices falling within the lowest and highest-prescribing quintiles were 52 and 139 prescriptions per 1000 RTI-related consultations. Patients from practices in the lowest prescribing quintile did not have a significantly higher risk of hospitalisation, and an adjusted odds ratio 0.99 (95% CI 0.96 to 1.02). Re-consultations within 30 days were significantly higher for the lowest prescribing practices, with an adjusted odds ratio of 1.209 (1.206 to 1.212). Additional antibiotic prescriptions, and subsequent prescriptions upon re-consultation, were significantly lower for the lowest prescribing practices, with adjusted odds ratio of 0.317 (0.314 to 0.321) and 0.706 (0.699 to 0.712), respectively.

Conclusions:

Our results contribute to evidence on the safety of reduced antibiotic prescribing for RTIs in primary care. Results suggest that for the majority of practices further reductions in RTI-related antibiotic prescribing should be possible without an increase in hospitalisation for pneumonia.

Community-onset urinary tract infection in females in the context of COVID-19: a longitudinal population cohort study exploring case presentation, management, and outcomes

Authors

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Introduction:

COVID-19 affected the epidemiology of other infectious diseases and how they were managed. Urinary tract infection (UTI) is one of the most common infections treated in the community in England. We investigated the impact of the COVID-19 pandemic on UTI primary care consultations and outcomes in female patients.

Methods:

We analysed General Practice (GP) consultation and hospital admission records using the Whole Systems Integrated Care (WSIC) data in North West London between January 2016 and December 2021. We quantified the changes in UTI GP consultation rates using time-series analysis before and during the pandemic. We assessed the outcomes of UTI, measured by subsequent bacteraemia and sepsis within 60 days, for consultations delivered face-to-face or remotely, with or without diagnostic tests, and with or without antibiotic treatment.

Results:

This study identified 375,859 UTI episodes in 233,450 female patients. Before the pandemic (to February 2020), the UTI GP consultation rate stayed level at 522.8 cases per 100,000 population per month, with a seasonal pattern of peaking in October. Since COVID-19, (March 2020 to December 2021), monthly UTI GP consultations declined when COVID-19 cases surged and rose when COVID-19 cases fell. During the pandemic, the UTI consultations delivered face-to-face were reduced (72.0% to 29.4%), consultations with appropriate

diagnostic tests, including urine culture and urinalysis, were reduced (17.3% to 10.4%), and cases treated with antibiotics were reduced (52.0% to 47.8%). The likelihood of antibiotics being prescribed was not affected by consultation type (face-to-face vs. remotely) but was associated with administration of a diagnostic test. The percentage of non-prophylactic acute UTI antibiotic prescriptions with durations that exceeded the guideline recommendations decreased during the pandemic (58.7% to 49.4%). This led to 830,522 total excess days of treatment, accounting for 63.3% of all non-prophylactic acute antibiotics prescribed for UTI. Before the pandemic, excess antibiotic days of UTI drugs had been reducing consistently. However, this decline slowed down during the pandemic. Having a diagnostic test was associated with 0.6 fewer excess days of antibiotic treatment.

Conclusions:

This analysis provides a comprehensive examination of management and outcomes of community-onset UTI in female patients, considering the changes in GP consultations during the COVID-19 pandemic. Our findings highlight the importance of appropriate urine testing to support UTI diagnosis in symptomatic patients and initiation of antibiotic treatment with appropriate course duration. Continued monitoring is required to assess the overall impact on patients and health systems in the changed landscape of primary care delivery.

Stronger laboratory capacity and surveillance in humans

REVERSE: pREVention and management tools for rEducing antibiotic Resistance in high prevalence SEttings

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NAP 2024 to 2029 outcome: strengthened 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 (HCAIs). REVERSE is an EU-funded mixed-method project across 24 acute care hospitals in 4 European countries (Greece, Italy, Romania, Spain) with a high prevalence of multidrug-resistant organisms.

As part of the REVERSE economic effectiveness work package, an umbrella review is being conducted (that is systematic review of systematic reviews) of economic evaluations of interventions for the prevention and clinical management of healthcare-associated infections in hospitals, with a particular focus on infections that are resistant to antibiotics. The objective of the review is to provide an up-to-date overview of the evidence for cost-effectiveness of these interventions, to help decision makers identify which interventions provide best value for money,

and to inform specific parameters and modelling approaches for the cost-effectiveness analysis that will be undertaken as part of the REVERSE project.

A systematic review of MEDLINE (Ovid), Embase (Ovid) and Econlit was conducted using a variety of 'HCAI' or 'antimicrobial resistance (AMR)' and 'economic evaluation' and 'systematic review' search terms. All studies were synthesised qualitatively, with quality assessment using the JBI Checklist for Systematic Reviews and Research Synthesis.

The search strategy identified 668 unique studies, 23 of which met the inclusion criteria and were synthesised narratively. Preliminary results suggest most of the current evidence is focused on screening followed by contact precautions, and isolation and/or decolonisation. While selective screening in high-risk settings was demonstrated to be, most likely cost-effective, results are highly context specific. There was also evidence that hand hygiene interventions are cost-effective when compared to standard practice; as is environmental cleaning. However, economic evidence for other types of interventions, such as antimicrobial stewardship and microbiology and diagnostic stewardship, is sparse and largely focuses on high-income countries.

In summary, where evidence exists for interventions, the cost-effectiveness results are highly context-dependent. Evidence for many other interventions is sparse. Further economic evaluations of all interventions are needed, explicitly accounting for different implementation contexts. The REVERSE project aims to address some of these knowledge gaps by assessing the cost-effectiveness of various interventions, including analysing how the results vary according to setting, and how the results can be extrapolated across countries.

Carbapenemase-producing Enterobacterales in intensive care units: England 2022 pointprevalence survey

Authors

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Conference abstract: European Scientific Conference on Applied Infectious Disease Epidemiology (ESCAIDE) 2023

NAP 2024 to 2029 outcome: using information for action

Introduction:

Hospital outbreaks associated with carbapenemase-producing Enterobacterales (CPE) have been identified increasingly in England. In site-specific studies, hospitals have assessed CPE prevalence at 0 to 11%. No CPE prevalence studies have been conducted in national intensive care units (ICU). We therefore aimed to generate CPE prevalence estimates among patients in England ICUs.

Methods:

A prospective, randomly selected, cross-sectional cluster survey was used to estimate CPE prevalence. From randomly selected acute-care providers in England, ≤20 eligible patients were randomly selected per ICU, with trust-level, ICU-level and patient-level data collected on a single date (between 18 April 2022 and 2 May 2022) by ICU staff using existing medical notes. Estimates were determined by adult, paediatric and neonatal ICU prevalence.

Results:

Seventy-four hospital Trusts participated (66 invited; 8 voluntary), with data from 94 adult ICUs, 13 paediatric ICUs (PICUs) and 49 neonatal ICUs (NICUs). Non-participation from invited Trusts was 25 out of 62 (40%) for adults, 10 out of 19 (53%) for paediatrics, and 54 out of 92 (59%) for neonates.

56.3% (n=424 out of 753) of adults, 74.7% (n=68 out of 91) of paediatrics, and 36.1% (n=145 out of 402) of neonates were tested for CPE. Screening accounted for 95.3% of adult CPE tests (versus 4.7% clinical investigation); this was higher for paediatrics (100% (n=68 out of 68) and lower for neonates (93.7% (n=136 out of 145).

CPE prevalence in tested adults was 1.2% (n=5 out of 424), and 2.8% in tested neonates (n=4 out of 145). No CPE were detected in paediatric patients tested. More than 80% of trusts had CPE screening policies, varying by age range (adults:95.6% n=43 out of 45; paediatrics:100% n=10 out of 10; neonates:82.1% n=32 out of 39).

Conclusions:

The first national CPE point-prevalence survey identified low prevalence (<3%) in ICUs in England, although such low numbers make risk factor elucidation a challenging prospect. While a high proportion of trusts operate a CPE screening policy, improvements can be made, particularly in NICUs.

Intermittent point prevalence surveys on healthcare-associated infections, 2011 and 2016, in England: what are the surveillance and intervention priorities?

Authors

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Introduction:

Point prevalence surveys are an important surveillance method for determining the burden of healthcare-associated infections (HCAIs). The aim was to outline the key results of 2-point prevalence surveys in England (2011 and 2016).

Methods:

All National Health Service and independent sector hospitals in England were eligible to participate. Data was collected between September and November in both 2011 and 2016 based on the protocol and codebook devised by the European Centre for Disease Prevention and Control. A mixed-effects model was applied, which allowed estimation of organisation-specific means and accounted for the heterogeneity in the responses from different organisations.

Results:

A total of 100,755 case records were included (52,433 in 2011 and 48,312 in 2016). The estimated prevalence of HCAIs was slightly higher in 2016 [6.89%, 95% confidence interval (CI) 6.21 to 7.57%] than in 2011 (6.41%, 95% CI 5.75 to 7.06%). In both surveys, the prevalence of HCAIs was highest in adult intensive care units (23.1% in 2011, 21.2% in 2016), and pneumonia or lower respiratory tract infections were the most common causes of HCAIs (22.7% in 2011 vs 29.2% in 2016). Inpatients in acute hospitals were older and had a higher risk of dying in 2016 compared with 2011. However, the proportion of inpatients with HCAIs or on antibiotics did not differ significantly.

Conclusion:

The burden of HCAIs in English hospitals increased slightly between 2011 and 2016. However, the proportion of inpatients with HCAIs or on antibiotics did not differ significantly.

Nitrofurantoin resistance as an indicator for multidrug resistance: an assessment of Escherichia coli urinary tract specimens in England, 2015 to 2019

Authors

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Introduction:

The aim was to determine whether multidrug resistance (MDR) occurs more frequently in nitrofurantoin-resistant *Escherichia coli* urinary isolates in England, compared to nitrofurantoin-susceptible isolates.

Methods:

Using routine antibiotic susceptibility laboratory surveillance data for *E.coli* isolated from urine for England, from 2015 to 2019 inclusive, the percentage of MDR or extensively drug resistant (XDR) phenotype was estimated for nitrofurantoin-susceptible or nitrofurantoin-resistant; as reported by region, patient sex and age group for laboratory-reported urinary tract samples.

Results:

Resistance to nitrofurantoin among *E. coli* urinary samples decreased slightly year on year from 2.9% in 2015 to 2.3% in 2019. Among *E. coli* UTIs tested for nitrofurantoin susceptibility and \geq 3 additional antibiotics, the percentage that were MDR was consistently 15% to 20% percentage points higher for nitrofurantoin-resistant isolates compared to nitrofurantoin-susceptible isolates. Similarly, the percentage of isolates with an XDR phenotype was higher among nitrofurantoin-resistant versus -susceptible isolates (8.7% versus 1.4%, respectively, in 2019); this disparity was greater in male patients, although variation was seen by age group in both sexes. Regional variation was also noted, with the highest MDR percentage amongst nitrofurantoin-resistant *E. coli* urinary samples in the London region (36.7% in 2019); the lowest was in the North East (2019: 16.9%).

Conclusions:

MDR and XDR phenotypes occur more frequently in nitrofurantoin-resistant *E. coli* urinary isolates in England, compared with nitrofurantoin-susceptible isolates. However, nitrofurantoin resistance is low (<3%) overall. This latest study provides important insights into the trends in nitrofurantoin resistance and MDR, which are of particular concern for patients ≥75 years old and those who are male. This study also emphasises geographical heterogeneities within England in nitrofurantoin resistance and MDR.

Genotypic determinants of macrolide resistance in Group A Streptococcus

Authors

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Conference abstract: European Congress of Clinical Microbiology and Infectious Diseases, 2023

NAP 2024 to 2029 outcome: using information for action

Introduction:

Year to year there are varying patterns of resistance to second line treatment agents for group A Streptococcus (GAS). Since 2022 there has been a move to whole genome sequence referred isolates, potentially allowing for a greater level of understanding of antimicrobial resistance.

Methods:

During 2023 a preliminary assessment of the antimicrobial resistance genes identified in a randomly selected subset of 372 macrolide and/or clindamycin phenotypically resistant isolates (between 2003 and 2022) was undertaken, identifying a range of resistance genes as well as variation of resistance by emm type.

Results:

Of note was *ermB* accounting for 51.2% (n=88 out of 171) detected resistance genes, followed by *ermA* with 33.9% (n=58 out of 171; clindamycin and macrolide resistance phenotype). For those harbouring ermB, emm11.0 was the most frequently identified type (n=15 out of 88; 17.0%), followed by emm82.0 (n=9 out of 88; 10.2%). For those harbouring *ermA*, emm77.0 was the most frequently identified type (n=7 out of 58; 12.1%), followed by emm12.0 and emm44.0 (both 8.6%; n=5 out of 58). Inducible clindamycin resistance was found in 24.2% (n=36 out of 149) of isolates harbouring *erm* genes. Overall, where a resistance gene was detected, phenotypic resistance was also identified. However, there were 16 isolates that were phenotypically macrolide resistant where no resistance gene was detected.

Discussion:

Further work to understand the 16 genotypically false negative isolates is underway. These may be as a result of known resistance genes and flagged as false-negative as a result of poor coverage of Streptococcus species resistance genes in AMR gene databases worldwide. The results of this study are of particular importance given the recent decision by the World Health Organization to include macrolide resistance in GAS in the <u>priority AMR pathogens list</u>. This is part of a wider piece of work looking at AMR patterns by emm type and improving referral of beta-haemolytic streptococci to UKHSA for monitoring circulating strain types and emerging resistance.

A similar study is underway for group B Streptococcus. The increasing trend in resistance to second line agents (macrolides, clindamycin) has led to a change in guidance. However, investigations to see whether the mechanisms of resistance have remained consistent over time are underway.

Acquired carbapenemase-producing Gram-negative organisms (CPOs) in England: surveillance of antibiotic resistance from 2020 to 2023

Authors

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NAP 2024 to 2029 outcome: strengthened surveillance

Introduction:

Acquired carbapenemase-producing Gram-negative organisms (CPOs) threaten viable antibiotic treatment options. This is the first national look at CPO phenotypic antimicrobial resistance (AMR) rates since becoming statutorily notifiable in England from October 2020.

Methods:

All acquired big-5 (NDM, KPC, OXA-48-like, VIM, IMP) CPO reported specimens and antibiotic susceptibilities were extracted from national laboratory surveillance databases between October 2020 and December 2023. Records were deduplicated by patient, specimen group (invasive,

screening or other), bacterial species, and CPO mechanism, per year. Regional big-5 CPO population rates were calculated; 2023 AMR data was assessed by mechanism and species.

Results:

In total, 13,022 episodes from 9,945 patients were reported; median age was 70 years old, 54% were male. The dominant mechanisms were OXA-48-like (n=4,884; 37.6%), NDM (n=3,927; 30.2%), and KPC (n=3,045; 23.4%). NDMs became more dominant in 2023 than OXA-48-like. Screening samples accounting for 72% (n=9,378), and < 5% (n=591) were from invasive samples. Thirty-three patients with invasive samples had dual-mechanisms detected: 61% were NDM and OXA-48-like; *Klebsiella pneumoniae* was the dominant species (patients=21). In 2023, the lowest reported resistance for the most frequently isolated species (n=5,535 out of 5,711) was for colistin (4 to 7%) for all big-5 mechanisms in *Escherichia coli, Enterobacter* spp., *Citrobacter* spp., whilst higher for *Klebsiella* spp. and *Pseudomonas* spp. (10 to 17%). Similarly, lower *Enterobacterales* resistance was observed for KPC and OXA-48-like to ceftazidime/avibactam (9 to 12%) and amikacin (7 to 8%), except for *Klebsiella* spp., which was higher (22%). Ciprofloxacin and gentamicin had ≥ 35% resistance. Fosfomycin resistance in *E. coli* was low (≤ 9%).

Conclusion:

Continued national CPO and associated AMR surveillance is crucial, particularly for new antimicrobials, to inform guidance and local, empiric prescribing by region, given the geographical variation in CPO mechanism. Further enhancement via data linkage to ethnicity and clinical characteristics to identify risk factors, and tracking changes in patients' antibiograms over time would help further target national guidance.

Pre- and post-COVID-19 pandemic trends of Gram-negative bloodstream infections in England

Authors

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NAP 2024 to 2029 outcome: strengthened surveillance

Introduction:

Gram-negative bloodstream infections (GNBSIs) pose a significant health burden and are associated with high antimicrobial resistance rates. This study aims to estimate the burden of GNBSIs in England to guide informed decision making around the targeted implementation of interventions aimed at reducing GNBSIs. We analysed data from pre- and post-COVID-19 pandemic time periods to examine its impact on the epidemiology of GNBSIs.

Methods:

This study was conducted using the Hospital Episode Statistics Admitted Patient Care database. All patient records with an admission date in 2019 or 2022 were extracted. Patients that experienced GNBSI were identified using ICD-10 diagnostic codes. Descriptive statistics were produced to summarise GNBSI cases by patient demographics, admission pathways, and clinical characteristics.

Results:

A total of 58,066 GNBSI cases were identified in 2019, compared to 51,588 cases in 2022. Across both study periods a slightly higher number of cases occurred in males (52.22% in 2019 and 53.43% in 2022) and the median age remained consistent at 74 years (IQR: 60 to 83). There was a slight decrease in the number of cases as patient deprivation scores improved. Similar patterns in admission pathways were also observed, with 85% of cases admitted from home and 89% of cases entering hospital via emergency routes. Across both study periods, 84% of cases also experienced a urinary tract infection (UTI), respiratory tract infection, surgical site infection and/or hepatobiliary infection, indicating the potential source of GNBSI. While the number of cases with each infection type decreased following the pandemic period, this was disproportional with a 17% reduction observed in cases that experienced a UTI compared to a 3 to 5% reduction across the other infection types.

Conclusion:

The COVID-19 pandemic led to a substantial decrease in GNBSIs, particularly those associated with UTIs, highlighting a need for further investigation. This study has identified key populations, such as the elderly and patients that experienced a UTI and who may benefit from targeted GNBSI interventions. Future research will involve linking GNSBI surveillance data to explore additional risk factors such as the source of infection, onset of infection, causative pathogen, and resistance to key antimicrobials.

Basic research

Molecular detection of ceftriaxone resistance in Neisseria gonorrhoeae

Authors

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NAP 2024 to 2029 outcome: strengthened surveillance

Introduction:

We validated and implemented a reverse transcription polymerase chain reaction method (RT-PCR) for the molecular detection of *penA* alleles associated with ceftriaxone resistance in *Neisseria gonorrhoeae*.

Methods:

A modified *N. gonorrhoeae penA* RT-PCR was developed and validated using clinical specimens, isolate lysates, and ceftriaxone-resistant samples. The feasibility of using the PCR for molecular surveillance was assessed using residual *N. gonorrhoeae* positive clinical specimens linked to *N. gonorrhoeae* isolates in the 2020 Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP).

Results:

The assay achieved 100% sensitivity, specificity, positive predictive value (PPV), and negative predictive value (NPV) for the *penA* target. No cross-reactivity with other Neisseria species or urogenital pathogens was detected. *N. gonorrhoeae* was detected in 73 out of 78 *N. gonorrhoeae*-positive specimens, resulting in 92.6% sensitivity, 100% specificity and PPV, and 89.4% NPV. No *penA* alleles were detected in clinical specimens from the GRASP 2020 molecular surveillance study (n=54).

Conclusion:

Implementing this PCR assay for patient management, public health, and surveillance purposes enables the rapid detection of gonococcal ceftriaxone resistance.

Development of new therapeutics

An immunotherapeutic for *Clostridioides Difficile* infection

Authors

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NAP 2024 to 2029 outcome: innovation and influence

The Antigen Research Team based at UKHSA Porton has an ongoing programme of *Clostridioides difficile* work. This pathogen disproportionately affects people taking antibiotics which disrupt the microbiome and is a significant cause of morbidity and mortality in the UK. Relapse rates from the current treatments of Vancomycin, Metronidazole, and Fidaxomicin are unacceptably high. The objective of the programme is to develop immunotherapeutics for the treatment of *Clostridioides difficile* infection. Ovine antibody formulations and the underpinning antigens have been developed and patented. This year the work programme received Wellcome Trust funding, alongside our commercial partners, to carry out clinical trials up to Phase 2 for our orally delivered therapeutic 'OraCab'.

Professor Isabel Oliver, Chief Scientific Officer at UKHSA commented: "With drug-resistant infections on the rise, the development and evaluation of new therapeutic approaches, such as OraCAb, are key to reduce antimicrobial resistance as it avoids the use of antibiotics. It's really exciting that, as part of our long-standing scientific collaboration with MicroPharm, OraCAb is now moving into the clinical trial phase."

Open Innovation in AMR Research (NIHR200658, EU MSCA, DHSC CoVID Research Programme, MRC MR/W018594/1 and UKHSA)

Authors

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NAP 2024 to 2029 outcome: innovation and influence

The Open Innovation in AMR platform was established with support from DHSC (NIHR200658) to support the evaluation of novel therapeutic agents against a range of WHO priority pathogens (bacterial and fungal) and high consequence viruses, including SARS CoV-2. The platform supports a range of studies with external researchers, underpinning early-stage discovery and evaluation of new antimicrobials developed in the academic research community and by SMEs. More than 35 visiting researchers, including PhD students and post-doctoral scientists have spent time in the labs at UKHSA Porton Down, learning how to carry out microbiological evaluation of new therapeutics. Aside from the research aspects, this supports much-needed interdisciplinary skills development in an area recognised as internationally scarce. The impact of the Open Innovation in AMR platform is evidenced by the selection of UKHSA as the first partner with a new funding call, administered through the Pathways to Antimicrobial Clinical Efficacy consortium <u>UKHSA PACE Collaboration (paceamr.org.uk)</u>. Studies to evaluate a range of new antimicrobials from award holders will start in October 2024, with the Open Innovation team working in collaboration with colleagues from the AMR Reference lab.

The Open Innovation platform was discussed as a case study within the National Action Plan for AMR (2024 to 2029), as an example of new approaches to stimulate innovation and to advance the development of non-traditional therapeutic agents. This emphasis on novel types of therapeutic agent led to a request for UKHSA to give evidence to the Parliamentary Inquiry on the antimicrobial potential of bacteriophage. The <u>report and government response</u> detail the ongoing support which UKHSA gives to the advancement of phage research and pre-clinical studies in the UK.

Wider access to therapeutics for those who need them

Resources Available for Addressing Inequalities in Antimicrobial Use and Antimicrobial Resistance in the UK: Scoping Review

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NAP 2024 to 2029 outcome: health disparities and health inequalities

Introduction:

Increased reporting by factors associated with health inequalities (HI) has highlighted the significant differences in antimicrobial resistance (AMR) and antimicrobial use (AMU) within these HI compared to the general population. Addressing HI has since become a focus for the UK National Action Plan (NAP) for AMR (2024 to 2029). However, while data is beginning to highlight the extent of the issue, there is limited information regarding what actions can be taken at a local and regional level to address these inequalities. Preliminary searches of PubMed and Google Scholar databases have indicated the presence of a body of literature addressing various aspects of AMU and AMR in the UK. However, a comprehensive synthesis of evidence on the available resources addressing these inequalities is lacking. We therefore conducted a review which sought to map out and evaluate the resources available for healthcare professionals (HCPs) to address these disparities.

Methods:

Between March and April 2024 searches were performed in MEDLINE and EMBASE databases for studies that outlined tools or resources for HCPs to reduce the impact of factors associated with HI on AMR and AMU. The search strategy was developed using a PCC (population, concept, context) framework and included terms which fell under the following concepts 'healthcare professionals', 'antimicrobial resistance or use', 'health inequalities' and 'resources'. Studies conducted outside the United Kingdom or prior to 2019 were excluded. A grey literature search was also conducted using an advanced Google search; data from both searches was then extracted for narrative synthesis.

Results:

Out of 403 articles retrieved from the databases and 50 grey records, 10 were included in the final review. Six out of 10 of the identified literature were from grey literature, obtained from key organisational websites, including the NHS and the UKHSA, Public Health England (now the UKHSA), Royal Collage of General Practitioners, UK Teratology Information Service (UKTIS), Specialist Pharmacy Service (SPS). Four resources were identified from empirical studies; of which 2 used qualitative methodology, one employed a mixed methods study design, and one was a perspective study.

Target populations included the elderly (4 out of 10), pregnant women (2 out of 10), Black, Asian, and Minority Ethnic groups (BAME) (1 out of 10), children (1 out of 10), and inclusion health groups, including but not limited to people experiencing homelessness, vulnerable migrants, sex workers, Gypsies, Roma and traveller groups, people in contract with the justice system and people with learning disabilities (1 out of 10). Identified resources were intended for primary care, care homes, and community pharmacies.

The identified resources were grouped into 3 themes; resources that facilitate consultation by clinicians, resources that guide best practices, and those that guide antibiotic prescriptions. Resources that facilitate consultation include an information leaflet, a toolkit, and a diagnostic flow chart. The resources aimed to support clinicians in prescribing appropriate dosages of

antibiotics thereby minimising the risk of misuse and resistance, and some resources guide the clinicians in how to stimulate good conversations during consultation.

Resources to encourage best practices by HCPs included halting urine dipstick testing for UTI in elderly patients in care homes and taking cultural competency tests by HCPs to improve their sensitivity when communicating with the BAME population. Finally, prescribing guidance comprises of online resources that suggest appropriate antibiotic dosages for patients from the most vulnerable groups. These are the <u>UKTIS</u> and <u>SPS</u>, which help HCPs prescribe appropriate antibiotic dosages to pregnant women because of some physiological changes related to the pregnancy.

Conclusion:

This review highlights the scarcity of published and evaluated resources in the literature addressing factors associated with HI related to AMU/AMR, especially for inequalities associated socioeconomic factors. More work is required to aid HCPs in addressing these disparities.

Development and access to vaccines

Predicting the Impact of Monoclonal Antibodies and Vaccines on Antimicrobial Resistance (PrIMAVeRA)

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NAP 2024 to 2029 outcome: innovation and influence

PrIMAVeRA is a European-funded project involving 18 partners across the EU and UK, including academic institutions, public health bodies, small and medium enterprises and industry. The project aims to develop mathematical models and a comprehensive epidemiological repository to assess the impact of vaccines and monoclonal antibodies (mAB) on antimicrobial resistance (AMR) to support decision-makers in prioritising the most promising new vaccines and mABs.

Work packages (1 and 3) aimed to assess the availability and quality of published evidence surrounding the healthcare burden of drug-resistant bacterial infections and the availability of individual level data on such infections across Europe. UKHSA led the third in a set of 3 systematic literature reviews, published as a collection in Clinical Microbiology and Infection, providing an in-depth synthesis of the current evidence on the i) frequency, ii) excess health risk, and iii) excess resource use and cost of bloodstream infections (BSI) caused by 6 key antibiotic-resistant pathogens in Europe (Excess resource use and cost of drug-resistant infections for 6 key pathogens in Europe: a systematic review and Bayesian meta-analysis – Clinical Microbiology and Infection). A repository of health and outcomes data was created. This evidence will inform mathematical models under development that aim to assess the potential

effectiveness of vaccines/ monoclonal antibodies (work package 2), as well as individual-based models of selected programmes enabling cost-effectiveness evaluation; led by UKHSA (work package 4).

The aim is to complete all work by October 2026. A sustainability plan (work package 5) will also be designed to ensure continued data collection and monitoring of AMR in selected pilot countries and long-term model calibration, validation, and accessibility after the project is complete. A key deliverable will be an open-access web-based user interface to support access and continued use of epidemiological repositories and models.

Development of Standardised Functional Assays for Evaluation of Group A Streptococcus Vaccines

Authors

Clare Collett¹, Stephen Thomas¹, Stephen Taylor¹, Andrew Gorringe¹ ¹ Pathogen Immunology Group, Vaccine Development and Evaluation Centre, UKHSA Porton Down

NAP 2024 to 2029 outcome: innovation and influence

The Pathogen Immunology Group, at UKHSA, Porton Down has begun developing and optimising opsonophagocytic killing (OPK) and flow cytometric antibody-independent complement deposition (ADCD) assays for Group A *Streptococcus* (GAS). Based on the success of the Bill and Melinda Gates Foundation funded GASTON consortium, a package of work will develop standardised assays and reagents for Group B *Streptococcus*. The team will focus their expertise in producing standardised assays for GAS that will be freely available to the wider scientific community. It is hoped these assays will play an important role in standardising laboratory correlates of protection to aid in the licensure of new GAS vaccines. Licensure of a GAS vaccine will have a direct impact on reducing the burden of a bacteria that is listed in the WHO Bacterial Priority Pathogen List for AMR, as well as directly reducing the need for antibiotics in the treatment of GAS disease.

A BCG Skin Challenge Model for Assessing TB Vaccines

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NAP 2024 to 2029 outcome: innovation and influence

A human challenge model for tuberculosis could be used to assess the efficacy of candidate vaccines at an early stage and prioritise those that should proceed to larger scale efficacy trials. However, deliberate infection of humans with *Mycobacterium tuberculosis* would be unacceptable due to the 6-month multidrug treatment regimen and potential for latent infection. Others have demonstrated the potential of using the current BCG vaccine administered intradermally in humans as a surrogate for *M. tuberculosis* infection that can detect differences in anti-mycobacterial immunity in the skin induced by vaccination with different doses and strains of a novel TB vaccine candidate. However, application of the published model is limited

by the need for skin biopsies to sample the BCG load at the site of injection, making serial sampling challenging.

To facilitate development of a human challenge model for tuberculosis TB researchers at Imperial College London have constructed an improved version of the BCG challenge organism, expressing fluorescent reporter proteins that can be measured non-invasively through the skin using a digital camera equipped with LEDs to excite the fluorophores. This provides an indicator of bacterial survival over time as the fluorescent signal decreases when bacteria die because of vaccine-induced immune responses.

Through a collaborative project between the Discovery Group at UKHSA Porton Down and Imperial College London, UKHSA has used its expertise in bacterial fermentation under defined and controlled conditions, to produce a fully characterised seed stock of the BCG reporter strain, that will be used in the human challenge studies. The fermentation facilities within the Discovery Group are also being applied to the production of defined biomass for other bacterial human challenge studies or as challenge stocks for vaccine and drug evaluation *in vivo* for large EU consortia.

Novel vaccines for Tuberculosis and other Mycobacterial Diseases

Authors

Rebecca Winsbury and Simon Clark Aerosol Infection Microbiology and Pathology groups, UKHSA Porton Down

NAP 2024 to 2029 outcome: innovation and influence

It is widely accepted that strategies to vaccinate individuals from specific diseases in many circumstances will combat the threat of multi-drug resistance. The Aerosol Infection Microbiology Group are a partner in the international consortium with an aim of diversifying the vaccine development pipeline, recognised as a priority area in the Global TB Vaccine research and development roadmap, to treat tuberculosis more effectively. NEWTBVAC-HORIZON is a new project, which has nineteen partners, worldwide, and is funded by the Horizon Europe programme. The consortium aims to improve understanding of lung immunity in tuberculosis in order to establish a diverse and innovative global TB vaccine pipeline that targets mucosal immunity. The group at UKHSA is providing the guinea pig model to evaluate new vaccine candidates in this consortium.

Development and access to diagnostics

Impedance-based Fast Antimicrobial Susceptibility Tests – iFAST (NIHR Invention for Innovation-NIHR200968, Innovate UK Biomedical Catalyst, LifeArc/NIHR Biomedical Research Centre, University of Southampton and UKHSA)

Authors

Lucy Bock, Bethany Martin, Caitlin Daniels, Rebecca Hodges, Lara Titkova, Ann Varghese, J. Mark Sutton

Antimicrobial Discovery, Development and Diagnostics Team, Vaccine Development and Evaluation Centre, UKHSA Porton Down

NAP 2024 to 2029 outcome: innovation and influence

The UKHSA has developed a novel, rapid microbiology platform, with the University of Southampton and applied it to the rapid evaluation of antimicrobial susceptibility. The technology termed Impedance-based Fast Antimicrobial Susceptibility Tests (iFAST), can rapidly determine the susceptibility of a range of bacterial species to all antibiotics tested to date and the technology is being developed for clinical use by a spin-out company, <u>iFAST</u> <u>Diagnostics</u>. The work, which was initiated as an Open Innovation case study and subsequently funded by NIHR Invention for Innovation, has completed a hospital concordance study at University Hospital Southampton, looking at Urinary Tract Infections. Ongoing work has also looked at its application for bacteraemia, with funding through Innovate UK's Biomedical Catalyst scheme.

Aside from the applications of iFAST to rapid antibiotic susceptibility testing, the team at UKHSA continue to use the technology to understand bacterial responses to other types of "biologics", including bacteriophage and peptide antimicrobials. The work is currently focused on supporting rapid phage susceptibility testing to enable more rapid selection of phage therapies in future clinical studies.

Health protection research units (HPRUs)

The NIHR-funded HPRUs in HCAI and AMR, led by Imperial College London and the University of Oxford, both in partnership with the UKHSA, have continued to produce translational research outputs intended to impact public health policy and practice.

Research within the HCAI and AMR HPRU at Imperial College London covers 4 themes of: priority pathogens; precision prescribing; practice, design and engineering and population health and policy. The HPRU at the University of Oxford also consists of 4 research themes which are:

- populations
- interventions
- contexts
- sequencing

An exemplar piece of research from the HPRUs with public health impact is the development of a model simulating the network of patient movements across NHS acute trusts in England. Through modelling every patient hospital admission across all acute NHS trusts, the model determines the extent of 'sharing' of patients between trusts and therefore quantifies the 'connectedness' of all acute English NHS trusts across the country. This allows identification of which trusts pose greatest risk to one another in terms of spread of HCAI and nosocomial AMR.

Two key translational pieces of work made possible with this model are:

- during a recent *Clostridioides difficile* infection (CDI) incident, the simulated patientreferral network was used to identify 'at risk' sites most closely connected to those affected by the outbreak – through close working with the Incident Management Team this enabled early warning for those sites at greatest risk of spread
- the network was also used to support the design of a novel surveillance system for *C. difficile*

Clostridioides difficile genomic surveillance: selection of sentinel sites using network analysis **Authors**

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⁶ Nuffield Department of Medicine, University of Oxford

NAP 2024 to 2029 outcome: using information for action

C. difficile surveillance in England has been based on ribotyping since 2007. National surveillance will migrate to a whole genome sequence-based system in 2024. To maximise efficiency, we have explored whether using a network of sentinel laboratories can provide information on the range of *C. difficile* strain types across England.

Network analysis has been used to inform selection of these sentinel sites for *C. difficile* surveillance; optimising sentinel selection to detect a novel strain, arising anywhere within England, as rapidly and efficiently as practical.

Records of hospital admissions from Hospital Episode Statistics (HES) were analysed, from periods before and after the COVID-19 pandemic, to understand the underlying network of patient movements between acute NHS hospitals in England. A network of links between acute hospital trusts in England was determined; the network links joined trusts which had inpatients in common, within a 6-month period. Weighted, directed networks were built for all patients and linked surveillance data was used to assess movements of CDI patients.

The project built on <u>previous work</u> to develop a mathematical model simulating the inter-hospital pathogen spread across the network. Using these simulated outbreaks and empirical hospital networks, an optimised set of well-connected sentinel hospitals were determined, minimizing the time to detection of novel strains, adapting the algorithm to incorporate real-world

sequencing constraints, for example by capping or excluding specified hospitals as sentinel sites.

Selection of 20 sentinel sites (out of the approximately 150 trusts in England), determined through this novel analysis, are together expected to deliver an average detection time that is 36% faster than 20 randomly selected sentinels. These results were cross-referenced against those using networks restricted to CDI patients only or adjusted for past and future trust mergers to confirm epidemiologically and longitudinally robust sentinel selection.

This novel approach to national surveillance enables the selection of sentinel sites to efficiently provide rapid identification of novel *C. difficile* strains within real-world logistical constraints. The networks provide insight on relationships between hospitals across England which is also potentially applicable to interventions to control inter-hospital spread of other healthcare-acquired infection pathogens.

Future HPRUs

The NIHR have launched a new open competition to designate and fund HPRUs in England for 5 years from April 2025. Again, the HPRUs will act as centres of excellence in multi-disciplinary health protection research in key priority areas, including one HPRU in the topic area of HCAI and AMR. As previously, the purpose of the NIHR HPRU scheme is to support the UKHSA in delivering its functions and objectives for public health protection, including an immediate response to emerging priorities and by building an evidence base for public health protection policy and practice.

The objective of the successfully funded HCAI and AMR HPRU will be to conduct multidisciplinary research to inform the prevention and control of HCAIs and of AMR and support the delivery and accelerate progress towards the AMR NAP.

Chapter 9. ESPAUR oversight group members' actions to tackle AMR

Main messages

The ESPAUR Oversight Group comprises over 30 stakeholder organisations including the UK nations and national organisations, professional and educational bodies, healthcare providers and regulators.

A total of 13 stakeholders have contributed to this year's ESPAUR report.

Stakeholders have undertaken a range of activities, including but not limited to: ongoing antimicrobial stewardship (AMS) programmes promoting appropriate use of antimicrobials; publishing evidence-based guidance, guidelines and articles; producing workshops, conferences and educational resources; providing support to national and international networks; public and political engagement; promoting pharmacy resources such as the TARGET antibiotics toolkit.

The ESPAUR Oversight Group comprises over 30 stakeholder organisations including the UK nations and national organisations, professional and educational bodies, healthcare providers, regulators and has the following members (<u>85</u>):

- Department of Health and Social Care (DHSC), including AMR Policy Team
- Dental Public Health, Office for Health Improvement and Disparities (OHID)
- DHSC Expert Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection (APRHAI)
- British Infection Association (BIA)
- Bennet Institute for Applied Data Scient (OpenPrescribing/OpenSAFELY)
- British National Formulary (BNF)
- British Society for Antimicrobial Chemotherapy (BSAC)
- Care Quality Commission (CQC)
- College of General Dentistry
- Health and Social Care Information Centre (HSCI)
- Independent Healthcare Providers Network (IHPN)
- IQVIA
- Microbiology Society National Pharmaceutical Advisers Group
- National Institute of Health and Care Excellence (NICE)
- NHS England (NHSE)
- Primary Care Pharmacy Association (PCPA)
- Royal College of Nursing (RCN)
- Royal College of Pathologists
- Royal College of Physicians (RCP)

- Royal College of General Practitioners (RCGP)
- Royal College of Surgeons (RCS)
- Royal College of Paediatrics and Child Health (RCPCH)
- Royal Pharmaceutical Society (RPS)
- Rx-Info Ltd
- UK Clinical Pharmacy Association: Pharmacy Infection Network (UKCPA PIN)
- Veterinary Medicines Directorate (VMD DEFRA)
- Antimicrobial Resistance and Healthcare Associated Infection (ARHAI) Scotland
- NHS National Services Scotland
- Public Health Scotland
- Public Health Wales
- Public Health Agency Northern Ireland (Health and Social Care Northern Ireland HSCNI)
- public partner/patient representation
- UKHSA (previously PHE) (represented by individuals with appropriate expertise from HCAI, antimicrobial utilisation (AMU), AMR, Fungal and Sepsis Division, Behavioural Insights, regions, Field Service, microbiology services and communications teams)

Stakeholders have continued to contribute to tackling antimicrobial resistance (AMR) and promote good antimicrobial stewardship (AMS), with details listed below.

British Dental Association (BDA)

The British Dental Association (BDA) continues to work nationally and internationally to address the role of dentistry in AMR.

The BDA supported the joint statement by the Association of Clinical Oral Microbiologists and the College of General Dentistry, published for World AMR Awareness Week (WAAW), and hosted a CPD webinar on prescribing antibiotics appropriately. The BDA plays a key role in the AMS work of the Council of European Dentists and World Dental Federation (FDI). Led by Dr Wendy Thompson, member of the BDA's Health and Science Committee, the FDI Task Team on Preventing AMR and Infections continue to strongly advocate for the role of dentistry within the AMR agenda, part of the FDI Science Committee programme of work. Dr Thompson also delivered various international CPD sessions at the FDI World Dental Congress in Sydney 2023.

The BDA contributed to consultations on the UK 5-year action plan for AMR 2024 to 2029 and on legislation to enable dental hygienists and dental therapists to supply and administer specific medicines under exemptions, raising concerns that one of the medicines is not recommended in any national clinical guidelines and is not included in the Dental Practitioners' Formulary. The BDA engaged with the Chief Dental Officer for England regarding recommendations around remote prescribing of prescription-only medication, including antibiotics, in the recently updated NHS Clinical Standard for Urgent Dental Care. The BDA highlighted the need for consistency
with dental AMS, and appropriate access to face-face care to ensure optimal treatment for acute pain and infection.

British Infection Association (BIA)

The <u>British Infection Association</u> (BIA) is a professional, member-led, organisation that represents a multidisciplinary group of NHS and academic professionals who deliver clinical infection services in the UK. BIA works closely with the Royal Colleges of Physicians and Pathologists through representation on specialist training committees. We highlight workforce issues and are working towards supporting a sustainable infection workforce through <u>information gathering</u> and publishing <u>guidance</u>.

BIA publishes 2 open-access journals that support the publications relevant to the aims of ESPAUR. The <u>Journal of Infection</u> is ranked within the top 15 of worldwide infectious diseases journals with an impact factor 28.2. <u>Clinical Infection in Practice</u> (CLIP) focuses on the advancement of knowledge and discussion of clinical infection practice.

The Association's work includes providing expert opinion to the governments of the 4 UK nations, the Royal Colleges, NICE, statutory medical and other professional bodies; setting and reviewing standards; supporting good practice. In the past year the membership has responded to 7 NICE consultations. We have produced guidance in collaboration with the Hospital Infection Society (Norovirus) and British HIV Association (Opt-out blood borne virus testing).

BIA are in the process of updating guidance on the management of encephalitis and malaria. Further Infection Quick Reference Guides, produced in collaboration with the UKHSA's Standards for Microbiology Investigations, on urinary tract infections (UTIs), central nervous system infections and fever in returning traveller are due to be published shortly. We continue to provide educational meetings to keep the profession up to date and support networking and collaboration. We support the ID:IOTS podcast and LearnInfection which provide resources for infection trainees.

British Society for Antimicrobial Chemotherapy (BSAC)

The <u>British Society for Antimicrobial Chemotherapy (BSAC)</u> represents one of the world's most influential networks of infection specialists. Membership includes, but is not limited to, infectious disease physicians, microbiologists, pharmacists, researchers and, more recently, individuals engaged across One Health sectors in veterinary practice, environmental science, animal husbandry and aquaculture.

It provides high-quality open access support to the global antimicrobial chemotherapy community which takes many forms: free membership, workshops, conferences, and research

publications via its <u>Journal of Antimicrobial Chemotherapy</u>, and the online open access education and research journal <u>JAC-Antimicrobial Resistance</u>.

The society has a rich portfolio of activities that support both the UK National Action Plan (NAP) and global initiatives to combat AMR and throughout 2023 to 2024 this included:

- the <u>UK Antimicrobial Registry</u> which developed in partnership with the University of Aberdeen to capture real-world usage of antimicrobial agents and identify where the clinical unmet need lies
- a national <u>susceptibility testing programme</u>, supporting laboratories using EUCAST methodologies and serving as the national susceptibility testing committee for the UK
- the <u>Global Antimicrobial Stewardship Accreditation Scheme (GAMSAS)</u>, a continuous quality improvement programme seeking to identify barriers to successful stewardship practice, and build a global community of accredited AMS Centres of Excellence – the GAMSAS scheme has been included as a case study in the UK AMR NAP
- the <u>Global AMS Partnership Hub</u>, (GASPh) bringing organisations together to collaborate on initiatives that support effective prescribing and reduce the burden of AMR
- the <u>UK Outpatient Parenteral Antimicrobial Therapy (OPAT)</u> programme, bringing care closer to home; BSAC supported NHSE in developing a cost calculator to support the establishment of new services and an expansion of existing services
- the <u>Drug Stability Testing Programme</u> providing an expanding repository of open access data on drug and device stability compliant with UK NHS standards as provided by the Yellow Covered Document
- an <u>open access Infection Learning Hub</u> which includes over 60 open access e-learning courses with translations into 6 languages for some courses
- publication of evidence-based guidelines and good practice recommendations
- operating a <u>PhD Parliamentary Internship programme</u> in parliament through the office of Baroness Natalie Bennett
- providing the secretariat for the <u>All-Party Parliamentary Group on Antibiotics</u>, meetings with UK Government representatives and the NHS, public engagement through a musical <u>The Mould that Changed the World</u>, and global campaign partnerships through <u>Stop Superbugs</u> and <u>Wounds That Won't Heal</u>

The society is a registered NIHR partner and serves, and is available to serve, as an implementation partner on large consortia research projects and RCTs.

BSAC also hosts the UK-Paediatric Antimicrobial Stewardship (UK-PAS) network, a network of over 850 colleagues exchanging lessons learned on judicious antimicrobial use. A paediatric antimicrobial prescribing guideline is available on the website and on the Micro Guide mobile application. A webinar is held monthly. To join the network, please visit the <u>UK-PAS website</u>.

Care Quality Commission (CQC)

The Care Quality Commission makes sure health and social care services provide people with safe, effective, compassionate, high-quality care and encourages care services to improve. We regulate against the Health and Social Care Act 2008.

Since January 2024 we have been assessing services against our new Single Assessment Framework which includes Quality Statements about <u>infection</u>, <u>prevention and control</u> and <u>medicines optimisation</u> in the safe domain. The CQC website contains information to support providers including updated <u>GP</u> and <u>dental</u> mythbusters relating to IPC. To support our work in understanding and assessing services' antimicrobial assurance we met with <u>GAMSAS</u> to discuss their accreditation scheme.

In 2022 CQC was given the regulatory power to assess Integrated Care Systems. As part of the initial planning for these assessments we have been working with Regional NHSE leads on how systems may be able to demonstrate AMR assurance.

Internally, the CQC Medicines Optimisation Team plans to use the new NAP as a lever to raise the profile of AMS among colleagues in operational and regulatory leadership roles to strengthen this aspect of our assessments of services.

College of General Dentistry (CGDent)

For WAAW 2023, the CGDent produced the annual joint statement with the Association of Clinical Oral Microbiologists and 12 other oral and dental organisations across the UK: <u>Preventing antimicrobial resistance together – College of General Dentistry (cgdent.uk)</u>.

Over the year, CGDent contributed to refresh of the UK AMR NAP, highlighting the importance of AMS at all levels of healthcare systems. NHS policy makers and commissioners are as important as prescribers in optimising the use of antimicrobials across healthcare. CGDent is pleased to see dentistry recognised within the published NAP, such as in relation to the important issue of electronic prescribing.

CGDent also contributed to consultations on a change in legislation which was designed to facilitate allied healthcare professionals in dentistry to maximise their scope of practice. Whilst being supportive of this overall aim, the legislation enabled the supply of antimicrobial medication directly to patients for conditions which are neither included in the BNF's dental practitioners' formulary, nor indicated in UK clinical guidance. Disappointingly responses from Government indicated that the onus would be placed on clinicians not to use these drugs inappropriately rather than on the system to facilitate the use of antimicrobials only when strictly appropriate. CGDent continues to press for dental AMS efforts to place the onus on healthcare systems to design in appropriate use of antimicrobial prescribing. Access to healthcare services

which prevent infections and avoid the need for antimicrobials is CGDent's preferred solution to optimising antimicrobial use.'

National Institute for Health and Care Excellence (NICE)

During 2023 to 2024 NICE has continued to work with NHSE to design the expansion to the Antimicrobial Products Subscription Model which is due to launch in summer 2024, following a successful pilot project which awarded subscription contracts for 2 antimicrobials in 2022. Under the delinked payment model, companies will be paid a fixed annual fee for eligible antibiotics based on their value to patients and the NHS, rather than on the volumes used. Initially, the scheme will be open to antibiotics that target pathogens designated as critical priority by the World Health Organization, according to their 2024 list. NICE has been commissioned to provide expert clinical input to the assessment of product eligibility and establish a standing panel of clinical experts to assess each product against the evaluation criteria. The model is the first of its kind and, if widely adopted internationally, has the potential to provide the 'market pull' incentive to stimulate increased global investment in new antimicrobials.

In addition to work on the subscription model, NICE has continued to publish new guidelines, health technology evaluations and guideline updates to support AMS including: Meningitis (bacterial) and meningococcal disease (NG240), Suspected acute respiratory infection in over 16s (NG237), Neonatal infection: antibiotics for prevention and treatment (NG195), Suspected sepsis (NG51), Genedrive MT-RNR1 ID Kit for detecting a genetic variant to guide antibiotic use and prevent hearing loss in babies: early value assessment (HTE6) and Point-of-care tests for UTIs to improve antimicrobial prescribing: early value assessment (HTE7). NICE is also developing guidelines relating to antimicrobial use on: Topical antimicrobial dressings for wound care, Pneumonia in adults, Suspected sepsis and Urinary tract infection (recurrent).

For 2024 to 2025, NICE has a centralised approach to prioritising its guidance topics. This will ensure NICE continues to produce guidance that is relevant, timely, accessible and has demonstrable impact. More information about the new approach is available on the <u>NICE</u> <u>website</u>. This includes information on how to suggest a topic for guidance development.

Royal Pharmaceutical Society (RPS)

The Royal Pharmaceutical Society's vision is to become the world leader in the safe and effective use of medicine, and we remain committed to the global strategy for AMR through the recently released UK NAP and the 20 year vision. Our mission is to put pharmacy at the forefront of healthcare.

Advisory group activity

During April 2023 to March 2024 RPS Antimicrobial Expert Advisory Group (AmEAG) met on 4 occasions. Its role is to advise RPS on AMR, AMS, infection prevention and management, and any other antimicrobial issues that affect the pharmacy profession and the public. It provides a central point for requests for antimicrobial advice, expertise, sharing best practice and input and comment from government and other organisations.

Key topics around AMR advocacy have been:

- a joint statement with the BSAC around how AMS principles should be an integral part of virtual wards
- advised on service specifications for Pharmacy First in England
- advocated that RPS rejoin the International Pharmaceutical Federation (FIP) which is affiliated with WHO in order to strengthen and promote AMR/AMS related activity
- promotion of the RPS online antibiotic resource centre
- strengthening the relationship between RPS and its communication team to proactively respond to AMR issues
- introducing the concept of pharmacogenomics within the AMR/AMS space

One of the major AMR health topics that AmEAG has focused on has been to support the need to demystifying penicillin labels that patients may have acquired during their healthcare journey. This has included:

- FIP case study penicillin allergy labels
- a communication and media campaign aimed at increasing public awareness about penicillin allergy to support delabelling initiatives as part of efforts to reduce AMR (see case vignette) – the result of the campaign were far reaching with abstract selection for an oral presentation at the 34th Congress of European Society of Clinical Microbiology and Infectious Disease in Barcelona

AmEAG continues to work with colleagues and national or international partners around:

- World Antibiotic Awareness Week as part of 2023 WAAW/EAAD, the RPS updated its antibiotic resource centre to proactively support and promote the range of resources available to the pharmacy profession and public. Central messages and a blog were released as part of the week
- Antibiotic Amnesty updated pages to promote this campaign and include areas on setting up and running an antibiotic amnesty, plus videos and content to download for ease of promotion; in 2023 to 204 we introduced multilingual resources into the campaign
- pharmacy consultations we continue to respond to consultations relevant to AMR and AMS: NICE acute respiratory infection

Case vignette: debunking the myths around penicillin allergies – specialists raising awareness through a media campaign

In summer 2023, AmEAG planned to raise public awareness about penicillin allergy to support delabelling initiatives as part of efforts to reduce AMR. This study aimed to assess the interest, reach and potential impact of the communications and media campaign.

Two press releases were created, one aimed at national print and broadcast journalists, and one for pharmacy, medical, nursing and health policy media. Alongside these a public-facing blog was issued explaining more about the consequences of mislabelling. A checklist for pharmacists was developed to support pharmacists and enable informed conversations with patients. Social media posts were created across platforms and the news story was posted on the RPS website.

The media story launched 28 September 2023 and created widespread coverage including 130 broadcast mentions on radio and television and 717 national and international online stories on the day (Figure 9.1). For all media outlets – online, broadcast and print, the total potential reach online was 775.17 million people between 28 and 30 September; the reach for broadcast media was 73.78 million; for consumer media it was 54 million. The website story amassed 435 views between 28 and 30 September, with another 432 between 1 and 31 October. The number of views of the checklist for pharmacists was 1,759 between 28 and 30 September, with a further 3,067 between 1 and 31 October. Additionally a leading allergy charity reported 20% of calls to their helpline that day were about penicillin allergy, their members reported patients asking them about penicillin allergy (highlighting impact of the campaign). The expert group were contacted by senior national healthcare and public health agencies with the government requesting a briefing on the campaign.

Figure 9.1. Statistics showing how many people were reached by the campaign through media channels

1.	2.	3.	4.	
Online media	Broadcast media	Consumer media	News stor	ry views
Mentions: 717	Mentions:	130 React	h: 54 million	28 - 30 Sept: 435 views
Reach: 775.17 million	Reach: 73.	78 million		1 - 31 Oct: 432 views
5.	6.	7.		
Checklist views	Social media	Prompted a Reposts: 143	actions	
28 - 30 Sept: 1,759 view	s 🔀 🗗	Likes: 316	 20% of calls to helpline patients asking about p 	
1 - 31 Oct: 3,067 views	in 🞯	Views: 34k	 promotion of campaign briefing request from G 	

Specialist Pharmacy Service (SPS)

The SPS worked closely with NHSE colleagues and national subject matter experts to develop a suite of PGDs to support the supply of antimicrobials required within the following 7 common clinical conditions: sinusitis; sore throat; earache; infected insect bites; impetigo; shingles; and uncomplicated UTIs in women. The <u>Community Pharmacy advanced service specification: NHS</u> <u>Pharmacy First Service</u> has the final version of these PGDs.

We are aware that other NHS services are using PGDs in these care pathways provided by other clinicians, for example Urgent Care Centres. We, therefore, also published them as <u>PGD</u> <u>templates</u> which can be authorised locally.

As part of our ongoing review programme we reviewed, revised and published the following <u>PGD templates</u>:

- supply of azithromycin for the treatment of uncomplicated *Chlamydia trachomatis*, uncomplicated *Mycoplasma genitalium* and non-gonococcal/non-specific urethritis
- supply of oral metronidazole for the treatment of bacterial vaginosis (BV) or *Trichomonas vaginalis* (TV)
- supply of doxycycline for the treatment of uncomplicated *C. trachomatis*, uncomplicated *M. genitalium* or non-gonococcal/non-specific urethritis
- administration of ceftriaxone injection (reconstituted with lidocaine 1% w/v injection) by intramuscular (IM) injection for the treatment of uncomplicated *Neisseria* gonorrhoeae infection

SPS has published advice on using antimicrobials and antivirals when breast feeding:

- using tetracycline antibiotics during breastfeeding
- using macrolide antibiotics during breastfeeding
- using penicillin antibiotics during breastfeeding
- using nitrofurantoin during breastfeeding
- <u>using metronidazole during breastfeeding</u>
- using oseltamivir and zanamivir during breastfeeding
- managing COVID-19 and breastfeeding
- treating impetigo topically during breastfeeding
- treating herpes virus infections during breastfeeding

We have also published or updated advice on:

- <u>managing interactions between macrolides and statins</u>
- implementing pharmacogenomic testing for aminoglycosides
- using dental antibiotic prophylaxis for hydrocephalus shunts
- <u>using miconazole oral gel with statins</u>

Veterinary Medicines Directorate (VMD) and Department for Environment, Food and Rural Affairs (DEFRA)

Over the last 2 years, VMD has worked across the Defra group to coordinate the development of the Animal, Plant, Food and Environmental elements of recently published 2024 to 2029 AMR NAP. The new One Health AMR NAP sets out our national and international ambitions and the work we will do over the next 5 years to ensure we achieve these. In the agri-food sector, this includes ensuring robust surveillance of antibiotic use and resistance (including developing one health integrated surveillance), working with the veterinary and farming industries in the UK to ensure antibiotics are used responsibly and sustainably, filling key research gaps, and working internationally to advocate for the responsible use of antibiotics in animals and plants globally.

The <u>UK-Veterinary Antibiotic Resistance Sales and Surveillance (UK-VARSS) Report 2022</u> (2023) was published in November last year and showed that the UK has reduced its sales of antibiotics in food-producing animals by 59% since 2014 and sales of highest priority critically important antibiotics have fallen by 82%. This is reflected in the overall reducing levels of resistance in bacteria isolated from healthy UK livestock. The third <u>One Health report</u>, a joint report between UKHSA and the VMD was also published in November 2023. This unique report brings together antibiotic consumption and resistance data from human, animals, food and environment between 2014 and 2019 and showed that over a 5-year period (2014 to 2019) antibiotics fell by 51% in animals and 18% in animals. This report highlighted that in 2019, approximately two-thirds of antibiotics were prescribed in people and one-third in animals. By comparing data across all sectors, it allows us to gain and share insights across the one health spectrum to inform future work.

Under Pathogenic Surveillance in Agriculture, Food and Environment (PATH-SAFE) Programme we completed AMR projects which have generated representative data on AMR for species outside our established harmonised monitoring programmes, working collaboratively with stakeholder organisations in the process. PATH-SAFE led by the Food Standards Agency, is cross-government programme which aims to develop a model national genomic surveillance network and includes several projects on AMR across agri-food systems. These projects focussed on the surveillance of healthy ruminants through testing for resistant bacteria in healthy sheep and cattle in England and Wales, testing of bulk milk and investigating AMR levels in livestock and feed ingredients. The results of these projects will be published in this year's UK-VARSS report. PATH-SAFE has been a brilliant vehicle to expand our surveillance, one of the key outcomes of the new NAP.

The VMD have also been feeding into the National Biosurveillance Network (NBN) which forms part of the UK's refreshed Biological Security Strategy (BSS). Alongside Animal Plant Health

Agency (APHA), VMD are leading a pilot to assess the feasibility of accessing AMR data from private veterinary diagnostic laboratories.

We have revised our UK legislation on veterinary medicines, the Veterinary Medicines Regulations, and in doing so we have strengthened our law on antibiotic use in animals in a way which will support responsible antibiotic stewardship in order to tackle AMR. Throughout this process we worked closely with a wider range of stakeholders with an interest in the AMR provisions.

We maintained our engagement with the veterinary profession and livestock sectors, working together to promote good AMS and collection of antimicrobial usage data, with 2023 seeing the Medicines Hub for ruminants (run by AHDB) reporting data to us for inclusion in the VARSS report for the first time.

Meanwhile, our focus on AMS in companion animals has been increasing. This includes the launch in June 2023 by RCVS knowledge of the VMD funded Companion Animal and Equine VetTeamAMR training initiative, which provides over 20 hours of Continuous Professional Development (CPD) to vets in practical and bitesize modules. In addition, the RUMA companion animal and equine group continue to meet regularly and once again coordinated a successful antibiotic amnesty campaign in November 2023.

Internationally, we have been working with colleagues in other countries to progress global action on AMR in animals through bilateral and multilateral engagement, particularly in the preparation for the AMR High Level Meeting at the UN General Assembly held in September 2024. We are working to ensure our work includes advocating for reliable and harmonised systems of surveillance to monitor trends and evaluate the effectiveness of interventions in reducing AMR in animals, reducing the need for antibiotics and ensuring prudent and responsible use of antibiotics in animals and plants globally. The VMD continued its collaboration with the Fleming Fund to enhance capacity-building efforts in countries tackling AMR. A major milestone was initiating a postgraduate programme to facilitate research on antimicrobial resistance and antimicrobial use within the animal health industry.

Public Health Wales (PHW)

The HCAI, AMR and Prescribing (HARP) Programme provides professional support to the NHS to reduce the burden of HCAIs and AMR across Wales. This is delivered through the publication of reports including antimicrobial usage and resistance, and feedback against Welsh Health Circular targets and UK AMR NAP ambitions. The HARP team also provides surveillance data for antimicrobial usage, resistance and HCAI via NHS facing data portals and dashboards. Finally, HARP supports the Health Boards and Welsh Government by providing technical expertise in microbiology, AMS and Infection Prevention and Control (IPC).

National AMS activities in 2023 to 2024 included publication of a range of empirical infection treatment guidelines, specialist drug dosing guidelines and a suite of prescriber audits; collaboration with Health Education and Improvement Wales (HEIW) to develop and deliver a range of AMS and infection related e-learning modules and webinars; the specialist infection management course run in collaboration with Swansea University each November; the annual national Point Prevalence Survey (PPS) of secondary care antimicrobial prescribing, which this year focused on the management of UTIs; a national care home PPS; delivery of a national dental AMS training event; bi-annual AMS and IP&C national conferences; and a 2 day national *Clostridioides difficile* Infection (CDI) conference.

European Antibiotic Awareness Day (EAAD) / WAAW this year focused on a social media campaign aimed at 18 to 34 year-olds, with themes including 'what is AMR', 'how does AMR spread', 'how to prevent AMR' and 'what would a world without antibiotics look like?'. We provided media briefs and interviews, illuminated Welsh Government buildings and the National Library for Wales in blue to highlight AMR, and provided an extensive campaign asset library for use by the NHS and local government. The health boards carried out multi-disciplinary team IV to oral switch ward rounds, provided information to staff and visitors at stands in public places in acute hospitals as well as a one-health display in Cardiff Central Station, and performed an in-patient knowledge survey to assess patients' knowledge of the antibiotics they had been prescribed.

For more information on our activities, including our published reports and guidelines, please visit the <u>HARP programme webpage</u>.

Public Health Agency Northern Ireland

The Northern Ireland Public Health Agency (PHA) continues to support efforts to decrease MRSA bloodstream infections, CDI, Gram-negative blood stream infections and promote appropriate use of antimicrobials. New AMR governance structures were established to support the development of the Northern Ireland Implementation plan of the UK NAP 2024 to 2029. The HCAI/AMR surveillance team continued routine surveillance including providing information about incidence of HCA infections and antimicrobial use to local healthcare trusts. The Strategic Planning and Performance Group (SPPG) continued to promote responsible use of antibiotics as a priority. Specifically, around WAAW, sharing messages surrounding antibiotic resistance with SPPG staff and Family Practitioner Services (general practice, community pharmacy, dental and optometry). Messages included AMR, AMS, the importance of not treating common self-limiting conditions with an antibiotic, encouraging safe disposal of antibiotics and raising awareness of appropriate penicillin allergy labelling. In secondary care, work was undertaken to raise the profile of AMS and support the rollout of a single electronic healthcare record (known as Encompass). SPPG continued providing education and training to FPS on antimicrobial stewardship, appropriate use of antimicrobials and antimicrobial resistance. Other engagement work included encouraging primary care practices to address antibiotic prescribing using the NI antimicrobial formulary and TARGET resources as an action point in their annual SPPG

pharmacy adviser prescribing meetings. All antimicrobial newsletter supplements and links to resources were uploaded to the NI Formulary website to improve accessibility for FPS and the public.

Scottish One Health Antimicrobial Use and Antimicrobial Resistance (SONAAR)

In recognition of the importance of the 'One Health' ethos to the sustainable control of AMR, the SONAAR programme within <u>ARHAI Scotland</u> monitors trends in antimicrobial use and resistance. The SONAAR annual report contains information on use of antibiotics in humans across primary care and in acute hospitals along with small animal veterinary practices, and the levels of antibiotic resistance found in a range of important human and animal infections. This data is used by organisations such as the Scottish Antimicrobial Prescribing Group (SAPG) to inform antimicrobial prescribing policy and develop initiatives for AMS; the Scottish Microbiology and Virology Network (SMVN) to support the development of testing strategies for NHS diagnostic laboratories in Scotland; and a range of animal stakeholder groups to support development and delivery of a co-ordinated quality-driven approach to veterinary prescribing practice, education and surveillance data.

The SONAAR 2023 report will be published in November 2024 and will be available <u>NHS</u> <u>National Services Scotland</u>.

NHS England (NHSE)

The NHSE Antimicrobial Prescribing and Medicines Optimisation (APMO) workstream provides leadership to the NHS in England to deliver high quality, equitable, antimicrobial prescribing, and medicines optimisation for all. During 2023 to 2024 good progress has been made across all 3 areas of the APMO behaviour change strategy: capability, opportunity and motivation. These are enablers for national, regional, system, and place level improvements for the optimised use of antimicrobial medicines.

Some highlights of activities delivered by the team during 2023 to 2024 are:

- the indicative curriculum for AMR and AMS for <u>pharmacists</u> was published with supportive resources – pharmacy undergraduate <u>competency framework</u> and <u>practice-based assessment framework</u>
- continued expansion of TARGET 'train the trainer' sessions to AMS leads within integrated care systems (ICS) and integrated care boards (ICB)
- WAAW webinars, in collaboration with RCGP and PrescQIPP, had 200 to 500 attendees at each session and combined WAAW recordings and resources on FutureNHS AMR workspace were accessed over 2,000 times – a co-signed letter

from NHSE and the UKHSA was sent to healthcare leaders in all care sectors to share key messages and actions to support AMS

- a one-day workshop was held with AMS teams from health and justice, community and mental health trusts to share innovative ideas to facilitate AMS – there are now ongoing quarterly meetings with stakeholders to develop workstreams and showcase their AMS work
- the COPD Prevention of Exacerbation Toolkit (COPD-PET) to support the review of patients prescribed long term, or repeated courses, of antibiotics was piloted in East of England and findings were incorporated into prescribing incentive schemes by several ICBs
- PrescQIPP Optimising Antimicrobial Use dashboard now reporting 4 antibiotic metrics down to GP practice level – these metrics are also reported in the NHS Model Health System AMR dashboard at ICS organisational level which continues to provide data on a variety of metrics for 3 infection pathways (UTI, skin and soft tissue infection, and gastrointestinal infection)
- supportive oversight the 7 regional AMS leads continue to provide active and visible leadership within regional AMS committees and some also in Regional Medicines Optimisation Committee (RMOC), and multi-professional regional AMR committees in collaboration with regional medical directors and chief pharmacists, regional IPC leads and regional healthcare scientist diagnostics leads (monthly AMS and IPC data packs to highlight performance against national AMS metrics have been produced for ICB AMS leads nationwide since January 2023)
- guidance for ICBs and providers on OPAT services is due to be published later in 2024 to 2025
- 'A Digital Vision for Antimicrobial Stewardship', setting out priorities and what good looks like, is due to published later in 2024 to 2025
- NHS England policy and commissioning schemes are described in detail within Chapter 6 of this report

Chapter 10. Knowledge mobilisation of ESPAUR report: feedback from stakeholders and report users

The annual ESPAUR report and its collation of surveillance and stewardship efforts is used widely in the UK. Since its inception, the report has persistently broadened and diversified its content, extending beyond antibiotic resistance, in response to the escalating threat of antimicrobial resistance (AMR) over the past decade. To accompany the annual publication of the ESPAUR report, a webinar is hosted by the UKHSA to explore key insights and features of the new report to stakeholders.

2021 to 2022 and 2022 to 2023 webinar survey feedback

Recently, a report was compiled to understand the usage of the ESPAUR report, the professional backgrounds of those who use the ESAPUR report, and to summarise their feedback. The analysis was based on data gathered from 2 surveys completed by attendees of the 2 most recent annual ESPAUR webinars in 2022 and 2023. 393 and 404 respondents participated in the 2021 to 2022 and 2022 to 2023 ESPAUR webinar surveys. Descriptive analysis was carried out to summarise responses from report users. Most of the questions and their respective answers were structured in a categorical manner, with some allowing for free text responses. The response rate varied per question in both surveys, with data analysed for each question out of 'known' answers.

The majority of the feedback received from the users of the report was positive, with 75.7% (159 out of 210) in 2021 to 2022 and 96.5% (390 out of 404) in 2022 to 2023 endorsing the ESPAUR report to other stakeholders. The most reported job role of respondents in both surveys was pharmacist, accounting for 36.8% (137 out of 372) of responses in 2021 to 2022 and 28.6% (116 out of 406) in 2022 to 2023. Doctors (2021 to 2022: n=55, 2022 to 2023: n=48) and nurses (2021 to 2022: n=48, 2022 to 2023: n=76) were also among the top 3 roles reported in both surveys. Infographics, which were used to highlight key messages and statistics in the report, were found to be useful by the majority of respondents, with 83.6% (178 out of 213) in 2021 to 2022 and 86.4% (261 out of 302) in 2022 to 2023. The 3 most frequently used chapters in the report remained the same in both surveys (2021 to 2022: N=205 and 2022 to 2023: N=235): antimicrobial resistance (2021 to 2022: 46.8%, n=96 and 2022 to 2023: 85.5%, n=201), antimicrobial stewardship (2021 to 2022: 40.8%, n=84 and 2022 to 2023: 63.8%, n=154), and antimicrobial consumption (2021 to 2022: 40.8%, n=84 and 2022 to 2023: 63.8%, n=150). The primary reason for accessing the report, as reported in both surveys (2021 to 2022: N=243 and 2022 to 2023: N=356), was to gather information, with 77.0% (187) in 2021 to 2022 and 50.3%

(179) in 2022 to 2023. The second most common reason was to share with others, reported by 51.4% (125) of respondents in 2021 to 2022 and 19.4% (69) in 2022 to 2023.

Some free text responses suggested some improvements to the report including shortening the report, developing a more accessible colour scheme, and addressing the high reading age of the report. Additionally, several improvements to the survey design itself have been suggested following the analysis, allowing for deeper future insights and facilitating more efficient analysis.

ESPAUR oversight group members 2023 survey on knowledge mobilisation

In 2023, a survey was distributed to ESPAUR oversight group (OG) members to ascertain utilisation of the ESPAUR report and its impact on knowledge mobilisation activities within organisations. A total of 13 responses were received from dental subgroup, CGDent, CQC, DHSC, DCSO, RCGP, UKHSA, Public Health Agency Northern Ireland, regional AMS leads, VMD and NHSE. Members were asked to define how they identified themselves in relation to ESPAUR, with most relating to being a 'partner' (8 out of 13), followed by 'collaborator or stakeholder' (5 out of 13), and 'user or AMS Champion' (2 out of 13).

The AMR chapter was identified as the most relevant and used chapter (11), followed closely by the antimicrobial consumption chapter (9) and the infographics slide set (7). Most respondents found the ESPAUR helpful to generate awareness or interest (12), knowledge (9) and engaging with other stakeholders (8) (Figure 10.1).

Figure 10.1. Summary of responses and feedback received from ESPAUR OG members survey, 2023



"I use the report in ministerial briefings and also circulate it to colleagues working on AMR across DHSC. It is valuable for everyone to have consistent information about the England picture." "the report is used internally to inform regulatory leadership about current issues and progress and could be used to Set inspection priorities. It is also a resource for colleagues when giving presentations or training." "The ESPAUR report is Core literature for various reports and presentations. It underpins most recommendations we make on AMR/AMS across the dental profession." "I don't disseminate the whole report, but I have Used messages & infographics in teaching, generally to primary care clinicians, but also this year to medical students & Westminster forum "

Feedback received

for England, Wales and the UK as a whole to what we observe in NI. We also find the format and content of the report useful for informing the shape of our own annual reporting."

"the AMR surveillance team at VMD uses the resistance chapters for reference, and also providing context and background for the new NAP."

When reporting on knowledge mobilisation methods being used for the ESPAUR report, most selected the webinar (5), social media (3) and the press release (3). With respect to knowledge mobilisation activities carried out within organisations, text comments were received with many reporting using the report for briefings, AMR/AMS priorities, reports and presentations, teaching and to compare trends. Examples of these are shown in Figure 10.1.

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Executive summary

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Chapter 9. ESPAUR oversight group members' actions to tackle AMR

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Chapter 10. Knowledge mobilisation of ESPAUR report: feedback from stakeholders and report users

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Chapter 9. ESPAUR oversight group members' actions to tackle AMR

None.

Chapter 10. Knowledge mobilisation of ESPAUR report: feedback from stakeholders and report users

None.

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