

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

Annexe

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# **Chapter 2. Antimicrobial resistance**

### Methods and caveats annexe

#### Antibacterial resistance

Data on the antibiotic susceptibility of pathogens causing bacteraemia was obtained from SGSS (Second Generation Surveillance System), a national database maintained by UK Health Security Agency (UKHSA) that contains laboratory data supplied electronically by approximately 98% of hospital microbiology laboratories in England. SGSS comprises 2 modules, a communicable disease reporting (CDR; formerly CoSurv/LabBase2) module and an antimicrobial resistance (AMR; formerly AmSurv) module. The CDR module includes antimicrobial susceptibility test results for bloodstream isolates of the key pathogens being monitored as part of the UK 5-year AMR Strategy, although any test results suppressed from clinical reports by the sending laboratories are not captured when the data is submitted. In contrast, the AMR module contains more comprehensive antibiogram information as it includes results for all antibiotics tested (including results suppressed from clinical reports) for isolates from all clinical sources. For trends included within this report, resistance data between 1 January 2019 to 31 December 2023 are taken from the AMR module.

Hospital microbiology laboratories have reported antimicrobial susceptibility test results as 'susceptible', 'susceptible, increased exposure' or 'resistant'. These categories were defined as follows as per the European Committee on Antimicrobial Susceptibility Testing (<u>EUCAST</u>):

- 1. Susceptible, standard dosing regimen (S): a bacterial strain is said to be susceptible to a given antibiotic when there is a high likelihood of therapeutic success using a standard dosing regimen.
- 2. Susceptible, increased exposure (I): a bacterial strain is said to be susceptible, increased exposure' when there is a high likelihood of therapeutic success because exposure to the agent is increased by adjusting the dosing regimen or by its concentration at the site of infection.
- 3. Resistant (R): a bacterial strain is said to be resistant to a given antibiotic when there is a high likelihood of therapeutic failure even when there is increased exposure.

The breakpoint criteria for categorising clinical isolates as susceptible, susceptible increased exposure or resistant to individual antibiotics have changed over time. As noted in the <u>ESPAUR report 2019</u>, in 2019 the <u>EUCAST definitions</u> were amended to rename the 'intermediate' category to 'susceptible, increased exposure' (with an adjusted increased dose), as the antibiotic should still work for treatment. The definition changes cannot be retrospectively applied.

As patients may have more than one positive blood culture taken, blood cultures taken from the same patient that yielded growth of the same pathogen during a rolling 14-day period from the

initial positive blood culture were regarded as comprising the same episode of infection and were de-duplicated, retaining the worst-case scenario susceptibility result for each antibiotic tested (resistant > intermediate > susceptible).

Antibiotic groupings used in the bacteraemia antimicrobial susceptibility analyses within the report are shown in <u>Annexe Table 2.1</u>.

Antibiotic class groupings	Antibiotic
Third-generation cephalosporins	cefotaxime, ceftazidime, cefpodoxime or ceftriaxone, unless otherwise indicated
Carbapenems	meropenem or imipenem, except where neither were tested, in which cases results for ertapenem were used if available; the exception to this is for <i>Pseudomonas spp.</i> where ertapenem was not used
Aminoglycosides	gentamicin and amikacin
Fluoroquinolones	ciprofloxacin, unless otherwise defined
Glycopeptides	vancomycin or teicoplanin
Macrolide	azithromycin, clarithromycin or erythromycin

Annexe table 2.1. Antibiotic class groupings

Data on the incidence of *Escherichia coli* (*E. coli*) and *Staphylococcus aureus* (*S. aureus*) bacteraemia was from the <u>national mandatory surveillance schemes</u> while data on the incidence of other pathogens was derived from cases reported to the AMR module of SGSS. As the latter data was provided on a voluntary basis, case ascertainment will have been incomplete.

SGSS and the mandatory surveillance Data Capture System are live reporting databases, and therefore data is subject to change and may differ to other published outputs.

Data on additional bacterial pathogens causing hospital bacteraemia in England can be found in <u>Chapter 2 data tables</u>.

Incidence trends, age and sex distributions and antibiotic resistance trends are presented based on SGSS AMR module data. This data continues the series previously published in separate annual voluntary surveillance bacteraemia reports (published in the Health Protection Report series).

#### Limitations and caveats

In England, the mandatory surveillance scheme for *E. coli* bacteraemia does not include susceptibility testing data, which is collected through a parallel voluntary laboratory reporting system. Comparison of the incidence reported between the 2 systems indicated that the ascertainment achieved in the laboratory reporting system was 89% in 2023 (88% in 2022; <u>Annexe Table 2.2</u>) and varied by local geography across the country (ranging between 69% and 97%; <u>Annexe Table 2.3</u>).

# Annexe table 2.2. Ascertainment factor applied to estimate total number of resistant bloodstream infections

Year	Mandatory <i>E. coli</i> bacteraemia reports	SGSS AMR <i>E. coli</i> bacteraemia reports	% ascertainment	Ascertainment factor
2019	43,737	38,159	87%	1.146
2020	37,888	31,574	83%	1.200
2021	37,855	32,949	87%	1.149
2022	38,467	33,678	88%	1.142
2023	41,192	36,760	89%	1.121

# Annexe table 2.3. Regional ascertainment factor applied to estimate total number of resistant bloodstream infections 2023

Region	Mandatory <i>E. coli</i> bacteraemia reports	SGSS AMR <i>E. coli</i> bacteraemia reports	% ascertainment	Ascertainment factor
East Midlands	3,496	3,347	96%	1.045
East of England	4,479	3,906	87%	1.147
London	5,366	4,540	85%	1.182
North East	2,446	1,690	69%	1.447
North West	6,038	5,619	93%	1.075
South East	6,463	5,642	87%	1.146
South West	4,083	3,956	97%	1.032
West Midlands	4,273	4,104	96%	1.041
Yorkshire and Humber	4,548	3,909	86%	1.163

Since April 2017 reporting of bacteraemia caused by *Klebsiella spp.* and *Pseudomonas aeruginosa* is also <u>mandatory</u>. Initial reviews of ascertainment between the mandatory and voluntary surveillance schemes for each pathogen were assessed for 2021 as 83% (*Klebsiella spp.*) and 85%, for *P. aeruginosa*.

Rapid molecular techniques are used to identify the mecA gene (meticillin-resistant *S. aureus* (MRSA) indicator) avoiding the requirement to undertake susceptibility testing for isoxazolylpenicillins (such as oxacillin). This information is not captured in the SGSS data. Figure 2.1 and Figure 2.2 in the main report present the mandatory surveillance results for MRSA bacteraemia which represents a more accurate burden of MRSA in England. Whereas Figure 2.9 (resistance differences between MRSA and meticillin-susceptible *S. aureus* (MSSA)) is using SGSS AMR data, where MRSA is defined as resistant to meticillin, oxacillin, cefoxitin or flucloxacillin. The ascertainment factor for *S. aureus* reports in SGSS AMR was 1.124 in 2023.

EUCAST does not provide daptomycin clinical breakpoints for *E. faecium* and *E. faecalis*, but rather lists the breakpoint as 'Insufficient Evidence', in-part due to the dosing regimes which far exceed licensed doses. Although daptomycin is increasingly used for enterococcal bacteraemia and endocarditis, especially in the context of vancomycin resistance, uncertainties remain particularly with the inability of even the highest published doses to achieve adequate exposure against all wild-type enterococcal isolates (<u>1</u>). Although minimum inhibitory concentration (MIC) distributions and epidemiological cut-off values are frequently used to predict likelihood of clinical success, as the local method of susceptibility testing cannot be verified, daptomycin MIC cannot be categorised and therefore caution should be used when interpretating the results.

#### Estimating the burden of antibiotic-resistant bloodstream infections

Data used to update the pathogen and antimicrobial summaries in the ESPAUR report was utilised to generate a preliminary estimated burden of resistant bacteraemia in England. The total number of resistant infections is generated by calculating the proportion of each pathogen that were reported as resistant to one or more specific antibiotics and ensuring that that infection report is not counted in any subsequent antibiotic combinations to avoid double counting. A full list of pathogen and antibiotic combinations, including the reduced number of drug and bug combinations used within the National Action Plan (NAP) AMR burden monitoring, is shown in <u>Annexe Table 2.4</u>. Estimates of the burden reported in this report differ slightly from those calculated in some previous reports due to a methodological adjustment following the identification of a coding inconsistency in previous reports' methodology.

For each year, the ascertainment level of cases of *E. coli* bacteraemia reported on a voluntary basis to the AMR module of SGSS was estimated by comparison with mandatory surveillance reports (<u>Annexe Table 2.2</u>). This value was then applied to the other pathogens under surveillance to estimate the total number of bacteraemia for each pathogen each year (except for *S. aureus,* where the mandatory surveillance totals for both MRSA and MSSA were used). The same method with region-specific numbers was used to calculate the regional AMR burden (regional numbers and ascertainment factors are listed in the <u>data tables accompanying the report</u>.

For 2023, the AMR burden from bacteraemia was reported by ethnic group and by indices of multiple deprivation (IMD). As the mandatory surveillance scheme does not include ethnicity and deprivation information, incidence data of all pathogens was derived from cases reported to

the AMR module of SGSS. The 2023 ascertainment factor, as shown in <u>Annexe Table 2.2</u>, was applied to all pathogens to estimate the total number of bacteraemia for each pathogen, except for *S. aureus* where the number of reported mandatory cases of *S. aureus* bacteraemia was used.

Annexe table 2.4. Bacteria and antibiotic resistance categories included in the AMR burden analysis within the ESPAUR repo	rt;
ESPAUR AMR bacteraemia burden combinations and National Action Plan (NAP) estimate combinations	

Bacteria	Antibiotic resistance	ESPAUR AMR bacteraemia burden	NAP estimate AMR burden
Escherichia coli	Carbapenem-resistant	✓	✓
	Third-generation cephalosporin-resistant (excluding isolates also resistant to carbapenems)	~	~
	Aminoglycoside-resistant (excluding isolates also resistant to carbapenem and/or third-generation cephalosporin)	~	
	Fluoroquinolone-resistant (excluding isolates also resistant to carbapenem and/or third-generation cephalosporin and/or aminoglycoside)	~	
Klebsiella pneumoniae	Carbapenem-resistant	$\checkmark$	$\checkmark$
	Third-generation cephalosporin-resistant (excluding isolates also resistant to carbapenem)	~	~
	Aminoglycoside-resistant (excluding isolates also resistant to carbapenem and/or third-generation cephalosporin)	~	
	Fluoroquinolone-resistant (excluding isolates also resistant to carbapenem and/or third-generation cephalosporin and/or aminoglycoside)	~	
	Carbapenem-resistant	$\checkmark$	

Bacteria	Antibiotic resistance	ESPAUR AMR bacteraemia burden	NAP estimate AMR burden
Klebsiella oxytoca	Third-generation cephalosporin-resistant (excluding isolates also resistant to carbapenem)	~	
	Aminoglycoside-resistant (excluding isolates also resistant to carbapenem and/or third-generation cephalosporin)	~	
	Fluoroquinolone-resistant (excluding isolates also resistant to carbapenem and/or third-generation cephalosporin and/or aminoglycoside)	~	
Acinetobacter spp.	Carbapenem-resistant	~	$\checkmark$
	Aminoglycoside- and fluoroquinolone-resistant (excluding isolates also resistant to carbapenem)	~	$\checkmark$
Pseudomonas spp.	Carbapenem-resistant	~	✓ *
	Resistant to 3 or more antimicrobial groups (excluding isolates also resistant to carbapenem)	<ul> <li>✓</li> </ul>	$\checkmark_{\star}$
Enterococcus spp.	Glycopeptide-resistant	~	<b>√</b> **
Staphylococcus aureus	Methicillin-resistant	~	$\checkmark$
Streptococcus pneumoniae	Penicillin- and macrolide-resistant (excluding isolates only resistant to penicillin)	~	~
	Penicillin-resistant (excluding isolates also resistant to macrolides)	~	~

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\* The NAP estimate AMR burden includes *Pseudomonas aeruginosa* only and not other *Pseudomonas* species. \*\* The NAP estimate AMR burden includes *E. faecalis and E. faecium* only and not other *Enterococcus* species.

#### Acquired carbapenemase-producing Gram-negative bacteria

Acquired carbapenemase-producing Gram-negative organisms (CPO) continue to pose a significant public health concern in terms of threat to global health and economic stability ( $\underline{2}$ ).

Carbapenems constitute some of the most effective and broadest-spectrum antibiotics available and are typically reserved for severe and multi-drug-resistant infections. Acquired carbapenemases are enzymes which inactivate carbapenems and most other -lactam antibiotics, including penicillins and cephalosporins, and can result in infections with severely limited treatment options. Many carbapenemase genes are found on mobile genetic elements and are thus easily transferable between species.

The prominent carbapenemase families, termed the 'big 5', and constituting >98% of carbapenemase mechanisms overall, are KPC, NDM, OXA-48-like, VIM and IMP, and are increasingly found in species such as *E. coli*, *K. pneumoniae* and *Enterobacter cloacae* complex. However, novel mechanisms of resistance are increasingly being detected.

Preventing and controlling the spread of CPO in England is one of the deliverables of the 5-year NAP introduced in May 2019 (<u>3 to 6</u>). Developing local laboratory capacity to detect the 'big 5' carbapenemase families has been a key part of the national response, and a change in referral criteria to the Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit with a focus on invasive isolates and mechanistic uncertainty in the context of certain resistant determinants, has seen a decrease in nationally referred isolates (presented later in the Chapter).

Data on confirmed CPOs was obtained from both the Antimicrobial Resistance and Healthcare-Associated Infections (AMRHAI) Reference Unit and from the Antimicrobial Resistance (AMR) module of SGSS (see the <u>Antibacterial resistance methods</u> section for details).

As patients may have more than one positive specimen taken, specimens taken from the same patient that yielded growth of the same pathogen and carbapenem resistance mechanism within a 52-week period from the initial positive specimen were regarded as comprising the same episode of infection and were de-duplicated. CPO positive referred isolates and local laboratory isolates were combined for this de-duplication process, with resistance mechanism results from the AMRHAI Reference Unit retained preferentially where patient specimen overlap occurred. A summary of the distribution of the carbapenemase families covered by the AMRHAI Reference Unit (including those outside the 'big 5' families) is presented in <u>Annexe Table 2.5</u>, below. The local laboratory data presented only includes results from the 'big 5' carbapenemase families.

UKHSA strongly recommends that all diagnostic laboratories should be able to detect the 4 carbapenemase families in bold (the 'big 4'). The following table uses these symbols: ¥ = combinations of mechanism and species would not be considered as exceptional results. A = intrinsic to *A. baumannii* and only expressed when associated with an insertion element; B =

almost exclusively reported in *Enterobacter spp.* with less than a handful of reports in other genera; C = reported only in *Serratia marcescens*.

Where an 'exceptional' carbapenemase and species combination result (cells without a ¥ symbol in Annexe Table 2.5) has been identified, isolates should be sent to <u>AMRHAI Reference</u> <u>Unit</u> for confirmation.

Carbapenemase	Associated with common 'host' organism			
family	Enterobacterales	Pseudomonas spp.	Acinetobacter spp.	
КРС	¥	<10	<10	
OXA-48-like	¥	<10	0	
NDM	¥	¥	¥	
VIM	¥	¥	<10	
IMP	¥	¥	¥	
IMI/NMC-A	В	0	0	
GES	¥	¥	0	
FRI	<10	0	0	
SME	<10 <sup>C</sup> ¥	0	0	
DIM	0	<10	0	
GIM	<10	0	0	
SIM	0	<10	0	
SPM	0	<10	0	
OXA-23-like	0	0	¥	
OXA-40-like	0	0	¥	
OXA-51-like <sup>A</sup>	0	0	¥	
OXA-58-like	0	0	¥	

Annexe table 2.5. Distribution of carbapenemase genes covered by AMRHAI Reference Unit molecular assay (based on AMRHAI data)

#### Notification data

Following the inclusion of carbapenemase screening in the notification schedule, a mechanism to combine reference laboratory referrals with local laboratory-confirmed carbapenemases was implemented. Data presented in the Antimicrobial resistance chapter in <u>the main ESPAUR</u> report includes analyses on counts of combined clinical infection and routine screening samples reported by laboratories using the recommended molecular or immunochromatographic methods to both SGSS and the AMRHAI Reference Unit. This differs slightly from the weekly case totals included within the causative agents of <u>notified diseases reports</u> which currently only include local laboratory reports.

For the purpose of the ESPAUR report and for the notification data, specimen reports of a positive CPO fall into 3 specimen type categories: sterile site, 'screening' and 'everything else'. A full list of the specimen types and how they are grouped is available in the <u>data tables</u> <u>accompanying this report</u>, but at a high level:

- sterile site group specimens include: blood, CSF and bone and joint specimens
- screening group specimens include: faecal, rectal swab, skin swab specimen
- the other specimens include: urine, upper respiratory, catheter and lower genital tract specimens

#### Timeline of CPE activities

#### The Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit

within UKHSA received and confirmed an increasing number of CPO year-on-year since 2006. Amongst Enterobacterales sent for referral in 2006, 4 were identified as carbapenemase producers compared to more than 4,000 identified in 2018. In response to the observed increase, UKHSA (then Public Health England (PHE)) established an incident control team in 2013 and implemented a number of initiatives aimed at preventing and controlling the spread of CPO.

The timeline of CPO activities included:

- October 2000: AMRHAI Reference Unit published 'Carbapenemases: a problem in waiting?'
- 2003: First VIM-producing Enterobacterales (*Klebsiella* sp.)
- 2003: First IMP-producing Enterobacterales (*Klebsiella* sp.)
- December 2005: Resistance alert issued: 'Carbapenem-resistant Enterobacteriaceae'
- November 2007: First OXA-48-producing Enterobacterales (K. pneumoniae)
- January 2008: First KPC-producing Enterobacterales (*K. pneumoniae*)
- October 2008: First NDM-producing Enterobacterales (K. pneumoniae)
- January 2009: Resistance alert issued: 'CPE in the UK: multi-faceted emergence'
- June 2009: First KPC-producing K. pneumoniae identified in Manchester
- July 2009: Resistance alert issued: 'CPE in the UK: NDM-β-lactamase: repeated importation from Indian subcontinent'
- mid-2009: Start of KPC outbreak in Manchester
- 2011: The Health Protection Agency (HPA; forerunner to PHE) and the Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infection (ARHAI) publish guidance on detection, control and treatment of carbapenem resistant infections
- March 2013: UK Standard for Microbiological Investigation (SMI) for detection of carbapenemases published
- November 2013: PHE Level 3 Incident Control Team established

- December 2013: Acute trust toolkit for CPE published
- March 2014: Patient Safety Alert: Addressing rising trends and outbreaks in CPE
- May 2015 Electronic Reporting System (ERS) for the enhanced surveillance of carbapenemase-producing Gram-negative bacteria launched
- June 2015: Non-acute and community settings CPE toolkit published
- July 2016: ERS upgraded to accept carbapenemase producers identified by diagnostic laboratories
- February 2017: UK component of ECDC-funded 'European Survey on Carbapenemase-producing Enterobacteriaceae (EuSCAPE)' project published
- April 2018: AMRHAI Reference Unit introduce charging for detection of KPC, NDM, OXA-48-like and VIM
- July 2018: PHE conducts national survey on carbapenemase testing methods performed by diagnostic laboratories
- August 2018: Evaluation of the acute trust toolkit for CPE published
- January 2019: AMRHAI requests diagnostic laboratories refer only locally-confirmed CPO from sterile sites
- January 2019: Evaluation of the ERS published
- 1 May 2019: ESR closed
- 1 October 2020: CPO was made notifiable
- April 2022: CPE point prevalence survey in intensive care units (ICUs) in England September 2022: Update of CPE Framework guidance

#### Paediatric bacteraemia data

Paediatric bacteraemia trends are presented based on SGSS CDR module data, without an ascertainment factor applied, and therefore, may differ from other results in the report that are based on SGSS AMR module data. Rates were calculated using age-specific mid-year population estimates from the Office of National Statistics. Some reports of coagulase-negative Staphylococcus (CoNS) and *Micrococcus* spp. may reflect the reporting of potential skin commensals or contaminants. The Streptococcus species group of anginosus, bovis, mitis, mutans, salivarius, and sanguin have been grouped into the viridans group streptococci.

#### Surveillance of antimicrobial resistance in *Neisseria gonorrhoeae*

Surveillance of antibiotic resistance 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 potential 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) and their 20 associated laboratories over a 2 to 3 month period each year. Gonococcal isolates are referred to the UKHSA sexually transmitted infection (STI) reference laboratory (STIRL)

for antimicrobial susceptibility testing and the results are linked to patient demographic, clinical and behavioural data for analysis of antimicrobial susceptibility trends in patient sub-groups.

#### Surveillance of antibiotic resistance in Mycoplasma genitalium

Surveillance of antimicrobial resistance in *M. genitalium* in England is monitored through the *M. genitalium* Antimicrobial Resistance Surveillance (MARS) Programme. Pilot collections for this programme were conducted in 2019 and 2020. The 2019 pilot included specimens from 17 sexual health services (SHSs) across England whilst the 2020 pilot included specimens from 15 SHSs across England.

From 1 March to 30 June 2023, *M. genitalium*-positive clinical specimens were collected from routine patient care at 28 participating SHSs and sent to the UKHSA Sexually Transmitted Infections Reference Laboratory. Specimens were tested for molecular markers predictive of macrolide and fluoroquinolone resistance in the *M. genitalium* 23S rRNA and parC genes, respectively.

Antimicrobial susceptibility data was combined with enhanced data including demographic data collected as part of routine STI surveillance from GUMCAD, as well as behavioural and clinical information provided by recruited SHS clinicians.

The MARS sentinel surveillance programme estimates the prevalence of macrolide and fluoroquinolone resistance and determines the demographic, behavioural and clinical factors associated with resistance.

928 specimens were included in the MARS 2023 sample. Macrolide resistance data was available for 90.6% (n=841) specimens; fluoroquinolone resistance data was available for 87.0% (n=807) specimens; and data for both was available for 83.1% (n=772) specimens.

#### Tuberculosis

Data for AMR in tuberculosis data for 2001 to 2023 was extracted from the Enhanced Tuberculosis Surveillance system (ETS). More detail on the methods and data sources are described in the <u>Tuberculosis in England annual report</u>.

#### Critical antibiotic resistance in foodborne bacteria

Surveillance of antibiotic resistance in foodborne bacteria is undertaken by the UKHSA <u>Gastrointestinal Bacterial Reference Unit</u>. Antibiotic resistance data for referred samples in England is derived through whole genome sequencing (WGS), identifying genes that confer resistance. Isolates were sequenced using Illumina technologies and antimicrobial resistance was profiled using a mapping-based approach using the in-house processor, <u>GeneFinder</u>. Specific genes that conferred resistance to tetracycline, carbapenems and colistin were investigated *in silico,* without phenotypic confirmation of expression of resistance. Single

nucleotide polymorphism (SNP) single linkage clusters were assigned using <u>SnapperDB</u>. SnapperDB.

Please see more detail regarding the specific findings of critical resistance determinants in the supplementary findings at the end of this chapter.

#### Salmonella Typhi

Confirmed *Salmonella* Typhi and *Salmonella* Paratyphi cases in England are diagnosed by the UKHSA Salmonella Reference Service (SRS), within GBRU. All *S*. Typhi and *S*. Paratyphi isolates referred to the SRS undergo WGS and SNP typing to detect clusters and genetic markers associated with antibiotic resistance. Data for laboratory-confirmed cases from 2019 to 2023, including markers for antibiotic resistance genes, was extracted from the reference laboratory database. The analysis focused on identifying *bla* <sub>CTX-M-15</sub> ESBL producers in *S*. Typhi, which are indicative of extensive drug resistance (XDR).

Epidemiological data, including travel and case details, was obtained from enhanced enteric fever surveillance and additional information was sourced from the UKHSA case management system (HPZone). This data was used to establish links between confirmed XDR *S*. Typhi cases and their travel history.

### Antifungal resistance

#### Routine surveillance

Data on the laboratory reports of yeast species from 2019 to 2023 was obtained from UKHSA's SGSS, as described in the <u>Antibacterial resistance section</u> of Chapter 2. The SGSS CDR module was used to obtain incidence trends of fungaemia (fungal bloodstream infections) and the species distribution of yeasts, the SGSS AMR module data was used for assessing the antifungal susceptibility.

As previously reported, several taxonomic revisions to species previously classified in *Candida* have been implemented in the period covered by this report. As a result, this report has expanded from *Candida* to include further yeast species causing fungaemia (Annexe Table 2.6). This may mean rates of fungaemia may not reflect what has been reported in previous reports. A full list of species causing fungaemia identified from SGSS can be found as part of the monomicrobial and polymicrobial data tables included in the <u>Chapter 2 data tables</u> accompanying this report.

Genus name	Species name	Previous name	New proposed name
Candida	C. africana		
Candida	C. albicans		
Candida	C. auris		Candidozyma auris
Candida	C. blankii		
Candida	C. dubliniensis		
Candida	C. haemulonis		
Candida	C. metapsilosis		
Candida	C. orthopsilosis		
Candida	Candida Other Named		
Candida	C. parapsilosis		
Candida	Candida Sp		
Candida	C. tropicalis		
Clavispora	C. lusitaniae	Candida lusitaniae	
Cryptococcus	C. neoformans		
Cryptococcus	Cryptococcus Sp		
Debaryomyces	D. hansenii	Candida famata	
Debaryomyces	D. polymorphus		
Kluyveromyces	K. lactis	Saccharomyces lactis	
Kluyveromyces	K. marxianus	Candida kefyr	
Meyerozyma	M caribbica		
Meyerozyma	M. guilliermondii	Candida guilliermondii	
Nakaseomyces	N. glabratus	Candida glabrata	
Nakaseomyces	N. nivariensis	Candida nivariensis	
Nakazawaea	N. peltata	Candida peltata	
Pichia	P. anomola		
Pichia	P. cactophila	Candida inconspicua	
Pichia	P. jadinii	Candida utilis	
Pichia	P. kudriavzevii	Candida krusei	
Pichia	P. norvegensis	Candida norvegensis	
Pichia	Pichia Sp		

Annexe table 2.6. Inclusion of yeast species causing fungal bloodstream infections

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Genus name	Species name	Previous name	New proposed name
Rhodotorula	R. dairenensis		
Rhodotorula	R. glutinis		
Rhodotorula	R. mucilaginosa		
Rhodotorula	Rhodotorula Other Named		
Rhodotorula	Rhodotorula Sp		
Saccharomyces	S. cerevisiae		
Saccharomyces	Saccharomyces Sp		
Starmerella	S. magnoliae	Candida magnoliae	
Starmerella	S. sorbosivorans	Candida sorbosivorans	

Recent taxonomic changes better reflect true lineages and is significant. For example, *Nakaseomyces glabratus,* unlike most *Candida* species, demonstrates reduced susceptibility to fluconazole. *P. kudriavzevii,* in common with other *Pichia species,* is innately resistant to fluconazole and *Clavispora lusitaniae* sometimes demonstrates the rare phenomenon amongst *Candida s*pecies of innate or emergent resistance to amphotericin B.

In previous <u>ESPAUR reports</u>, hospital microbiology laboratories antifungal susceptibility test results were grouped into 'reduced-susceptibility'. For the purpose of this report, antifungal susceptibility test results reported as 'susceptible', 'intermediate' or 'resistant', as determined locally, are presented alongside a proportion that are resistant.

The breakpoint criteria for categorising clinical isolates as susceptible, intermediate or resistant to individual antifungals have changed over time, the classification presented is the same as at the time of the specimen and has not subsequently been adjusted. Antifungal resistance for yeast species is focused on 3 antifungal drugs (amphotericin B, caspofungin and fluconazole). These drugs represent 3 different classes of antifungal drug and are the most frequently tested for and used.

As patients may have more than one positive blood culture taken, blood cultures taken from the same patient that yielded growth of the same pathogen during a rolling 14-day period from the initial positive blood culture were regarded as comprising the same episode of infection and were de-duplicated.

#### Reference laboratory surveillance

#### Perspective from the National Mycology Reference Laboratory

The UKHSA <u>National Mycology Reference Laboratory</u> (MRL) receives referred samples of fungal isolates from NHS trusts, regional mycology reference centres and private microbiology laboratories throughout the UK. In addition, the MRL provides a primary diagnostic service for

local laboratories. Samples are received for superficial, subcutaneous, deep-seated and disseminated fungal infections. Patient groups include those with dermatophytosis, chronic obstructive pulmonary disease (COPD) and cystic fibrosis, intensive care unit (ICU) patients and haematology and oncology patients including those who have received solid organ, stem cell and bone marrow transplants. The MRL is the UK coordinating centre for fungal outbreaks.

#### Candida auris

*Candida* (now *Candidozyma*) *auris*, the fluconazole- and sometimes multi-drug-resistant yeast which, unlike most *Candida* species, spreads readily from person to person, persists in the environment and has been responsible for multiple ICU outbreaks globally including several in the UK, continues to cause sporadic infections in the UK and has recently been responsible for 2 further outbreaks. Sporadic introductions are often precipitated by individuals who have recently travelled to areas of endemicity, most notably India, or who have been transferred from medical facilities in India or the Middle East where clade I (the South Asian clade) is widespread. However, with the list of countries reporting isolations ever increasing, hospitalisation in any overseas hospital is now a risk factor.

#### Candida parapsilosis

Globally, fluconazole resistance in isolates of *Candida parapsilosis* is emerging and is proving particularly problematic in South Africa, Turkey, India, Mexico, Brazil, and parts of Southern Europe, where resistance levels exceed 30 to 40% of isolates and in some areas 40 to 50%. This is definitely an emerging trend and we must be vigilant in the UK where fluconazole currently remains a first-line treatment for this species which frequently shows reduced susceptibility to the echinocandin class.

#### Dermatophytes

A public health issue initially reported in India, but now spreading to many other countries including the UK, has been the emergence of the dermatophyte *Trichophyton indotineae* (part of the *Trichophyton mentagrophytes* group), that often, but not invariably, displays terbinafine resistance correlating with clinical failure of this drug, and is sometimes also resistant to one or more azole drugs. It is a cause of aggressive and recalcitrant groin infections (*tinea cruris*) in particular, although infection can quickly become more widespread leading to *tinea corporis*. It appears to spread most readily in close family or sexual contacts. This species currently accounts for more than 40% of the referred dermatophyte isolates sent to the UKHSA Mycology Reference Laboratory for identification and susceptibility testing.

#### Aspergillus

Sporadic cross-resistance of *Aspergillus fumigatus* to voriconazole in clinically azole naive patients is an issue associated with the emergence of resistance to environmental azoles, particularly tebuconazole, used in crop protection. This can be a cause of clinical failure in immunocompromised patients with serious invasive aspergillosis infections treated with the first line agent voriconazole. Currently about 5% of referred isolates in the UK exhibit resistance. There are also cases of emergent azole resistance due to multiple different mutations in patients on long-term azole therapy for more chronic pulmonary aspergillosis.

# Antiviral resistance

#### Influenza virus

UKHSA screens influenza virus positive samples for mutations in the virus neuraminidase (NA) and the cap-dependent endonuclease (PA) genes, which are known to confer neuraminidase inhibitor or baloxavir resistance, respectively. The samples are primarily obtained for surveillance; however, diagnostic testing is also performed on patient samples with a suspected antiviral-resistant strain.

Influenza virus susceptibility to the neuraminidase inhibitor class of antivirals has been monitored routinely in the UK since 2005 using a combination of phenotypic and genotypic testing. The current influenza antiviral susceptibility surveillance strategy is a genotypic only approach.

Results are reported in the <u>weekly national flu reports</u> during the active influenza season and summarised in the <u>influenza annual report</u> for each flu season.

#### Human immunodeficiency virus (HIV)

The detection of HIV resistance in drug-naïve people indicates the transmission of drugresistant variants, an important occurrence which limits first-line regimen options. Tracking drug resistance in the treatment-experienced population provides an insight into the causes of treatment failure. The prevalence of drug resistance mutations in the UK was tracked from 2001 to 2019 in both drug-naïve and treatment-experienced people with HIV by the National UK HIV Drug Resistance Database (UK-HDRD), which received results of resistance tests performed as part of routine care from 15 participating NHS and UKHSA virology laboratories. Support from the Medical Research Council for the UK-HDRD ended in 2020. However, it was relaunched by UKHSA in 2024, with the collection of data from 2020 to date still ongoing.

Within national HIV surveillance programs, samples from ~50% of individuals with newlydiagnosed HIV-1 are routinely submitted to UKHSA for recency testing as part of the Recent Infection Testing Algorithm (RITA) to determine whether the infection was recently acquired (<4 months) or longstanding. Those identified as recent are subjected to whole genome sequencing (WGS).

#### Hepatitis C virus (HCV)

Recommended first line Direct Acting Antiviral (DAA) combinations in the UK usually contain an NS5A inhibitor with either an NS5B polymerase inhibitor or NS3 protease inhibitor. Two antiviral combinations are available with activity against almost all viral strains common in the UK, sofosbuvir-velpatasvir and glecaprevir-pibrentasvir. The success of DAA drug roll-out underpins the UK's commitment to WHO HCV elimination targets.

Testing for HCV drug resistance is not universally recommended prior to initiating DAA therapy, as there is no or minimal impact of resistance on cure rates in DAA-naïve individuals in many scenarios. The European Association for the Study of the Liver (EASL) and the American Association for the Study of Liver Diseases (AASLD) have produced guidelines on particular scenarios when resistance testing may be considered or recommended. There is currently no role for phenotypic resistance testing in clinical management, as this is costly, laborious and available only within research contexts.

There is no national database of HCV resistance in the UK. However, the UKHSA Antiviral Unit provides a HCV genotyping and resistance testing service for the NHS. Since 2019, resistance testing has been carried out by whole genome sequencing, which identifies the viral genotype and subtype, as well as the resistance profile of the NS3, NS5A and NS5B genes, in a single test. UKHSA also coordinates the English HCV Treatment Registry which contains information on treatment status i.e. whether DAA-naïve or previously exposed to DAAs, and can be linked to HCV sequence data. The data used in this report includes subtype 1a NS5A samples from patients in England from years 2019 to 2023.

### Antiparasitic resistance

As part of the surveillance and resistance monitoring functions of the UKHSA Malaria Reference Laboratory (MRL) suspected treatment failure in cases of imported malaria is investigated by molecular genotyping of parasite genes implicated in reduced antimalarial susceptibility. Additional *in vitro* drug susceptibility testing of a subset of imported parasite infections is provided by colleagues in the malaria research laboratories at the London School of Hygiene and Tropical Medicine . Artemisinin combination therapy (ACT) consists of a member of the rapid-acting artemisinin family of compounds plus a partner drug from a different chemical class with a longer-half-life.

### Additional data sources

Population data used in the chapter was taken from the Office for National Statistics annual <u>mid-year population estimates</u> published data for the corresponding geographic region and year. Geographies were assigned to infection episodes based on patient postcode where available, where not available the reporting laboratory postcode was used. The postcodes were then assigned to <u>regions</u> and presented at this level.

A <u>SPINE trace</u> was performed on records of patient episodes to identify those with reported 30day all-cause mortality. Case fatality rates were calculated at 30 days in line with the <u>30 day all-</u> <u>cause mortality following MRSA, MSSA and Gram-negative bacteraemia and C. difficile</u> <u>infections, 2022 to 2023 report</u> protocol. CPO case fatality rates reported in this report differ slightly from those previously reported due to a methodological alignment following the identification of a coding inconsistency in previous reports' methodology. Gram-negative bacteraemia case fatality rates includes *K. pneumoniae* only and not other *Klebsiella* species. The <u>index of multiple deprivation</u> (IMD) is a way of summarising how deprived a particular geographical area is, based on a set of factors that includes levels of income, employment, education and levels of crime within that area. Episodes were linked to IMD using patient postcode (or GP or laboratory postcode where patient postcode was unavailable) and the IMD quintile score was identified by the lower super output area in which the patient resided.

The <u>Office for Health Improvements and Disparities</u> developed a method for <u>assigning ethnic</u> <u>group</u> based on hospital admissions data. As different ethnicities may be recorded in different treatment episodes, the method selected a single ethnic group from a patient's HES records. Episodes were linked to ethnic group using patient NHS number and date of birth.

### Statistical analyses

P-values were calculated to assess the change in resistance over time, these were generated using an unadjusted binomial regression model for each drug and bug combination. A significant change is defined by a p-value less than 0.05 (p<0.05).

Trends in incidence and resistance are shown at national, regional and IMD quintile level for England. Incidence rates are calculated per 100,000 population per year using the Office for National Statistics <u>mid-year population estimates</u>. At the time of writing, 2023 estimates were not yet available and therefore 2022 was used as a proxy for 2023.

Binomial confidence intervals were calculated to 95% for the percentage resistance for the ethnic group analysis.

Poisson regression models were used to examine the relationship between AMR burden rates and IMD quintile levels and years; the interaction between year and IMD quintile was tested using a likelihood ratio test.

Analyses were completed using Stata v15/v17 (StataCorp) and RStudio (R version 4.4.0).

### AMR resources

This will group together the locations and names of other AMR-relevant publications that UKHSA and others produce to help people know that there is more information available, including: MARS and GRASP report.

- <u>quarterly reports on acquired carbapenemase-producing organisms identified in</u> <u>human samples in England</u>
- notifications of infectious diseases (NOIDs)
- Escherichia coli (E. coli): guidance, data and analysis
- Pseudomonas aeruginosa: guidance, data and analysis
- <u>Klebsiella species: guidance, data and analysis</u>

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

- Clostridium difficile: guidance, data and analysis
- Staphylococcus aureus: guidance, data and analysis
- MRSA, MSSA, Gram-negative and CDI quarterly report (official statistics)
- MRSA, MSSA, Gram-negative bacteraemia and CDI; independent sector (annual official statistics)
- <u>Laboratory surveillance of paediatric bloodstream infections and antimicrobial</u> <u>resistance in England</u>
- pyogenic and non-pyogenic streptococcal bacteraemia annual data from voluntary surveillance
- Fingertips public health UKHSA data: AMR local indicators
- <u>Third UK One Health Report: joint report on antibiotic use, antibiotic sales and antibiotic resistance</u>
- Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2016 to 2017
- <u>Central Asian and European Surveillance of of Antimicrobial Resistance (CAESAR)</u>
   <u>data</u>
- <u>GLASS (Global Antimicrobial Resistance and Use Surveillance System) AMR routine</u> <u>data surveillance</u>
- podcast: Infection Control Matters on Apple Podcasts
- <u>the European Union Summary Report on Antimicrobial Resistance in zoonotic and</u> <u>indicator bacteria from humans, animals and food in 2021 to 2022</u>
- Tuberculosis in England: national quarterly reports
- <u>TB diagnosis, microbiology and drug resistance in England</u>
- Enteric fever (typhoid and paratyphoid) England, Wales and Northern Ireland
- <u>National flu and COVID-19 surveillance reports: 2022 to 2023 season</u>

### Supplementary analyses

#### Antibacterial resistance

#### Critical resistance in foodborne bacteria

The mobile colistin resistance (MCR) genes conferring resistance to colistin were present in *Salmonella* (n=15) and STEC (n=1). Within STEC, MCR-9 (n=1) was detected in one isolate and in *Salmonella* spp., MCR-1 was detected in *Salmonella* Heidelberg ST15 (n=1), *Salmonella* Java ST43 (n=1) and *Salmonella* Stanley ST29 (n=1). The gene MCR-3 was detected in *Salmonella* Typhimurium (monophasic) ST34 (n=2). The gene MCR-9 was detected in *Salmonella* Agona (n=6) (part of the same 25 SNP single-linkage human cluster), *Salmonella* Chester (n=1), *Salmonella* Minnesota (n=1), *Salmonella* Typhimurium (n=1) (although thought to be non-functional) and *Salmonella* Virchow (n=1).

Tetracycline resistance, specifically variants of the gene tet(X) were investigated. Within *Salmonella* spp, there were 2 variants of tet(X) detected in *Salmonella* Agona ST13 (n=1), *Salmonella* Infantis ST32 (n=2), *Salmonella* Kentucky ST198 (n=5) and *Salmonella* Stanley ST29 (n=2, as well as one (n=1) isolate of *Salmonella* Kentucky ST198 harbouring a third tet(X)

variant. Although at least one of the genes in each *Salmonella* profile is thought to be non-functional. The *Salmonella* Kentucky isolates were part of the same 25 SNP single-linkage human cluster, and the *Salmonella* Stanley were part of the same 10 SNP single-linkage human cluster. There was a variant of tet(X) detected in *Shigella flexneri* ST245 (n=1).

Within *Campylobacter* spp. there was no critical resistance conferring genes for carbapenems, and no MCR or tet(X) was detected.

#### Antifungal resistance

#### Incidence of candidaemia by region, and species frequency

<u>Annexe Figure 2.1</u>, below, shows *Candida albicans* was the most frequently isolated yeast species across the 5-year period, accounting for 40% of fungaemia in 2023 (848 out of 2,112). In common with many other surveillance studies the second most frequently reported species was *Nakaseomyces glabratus* (formerly *Candida glabrata*), which was identified in 27% (573) of fungaemia episodes in 2023.

Regionally, variation in incidence of fungaemia can be seen. The region with the highest rate of fungaemia in 2023 was the North West (4.4 per 100,000 population), closely followed by London and the North East (both 4.1 per 100,000 population). The lowest recorded rate was Yorkshire and Humber (2.8 per 100,000 population). Further regional data for incidence from 2019 to 2023 can be found in the 'Laboratory surveillance of fungaemia due to yeasts in England: 2023' Health Protection Report.





¥ Nakaseomyces glabratus (formerly Candida glabrata)

\* for all other yeast species and genera please see Annexe Table 2.6

# **Chapter 3. Antimicrobial consumption**

All data presented in this chapter in tables can be accessed in the 'Chapter 3 data tables' and all figures can be accessed via the downloadable slide set, both available from <u>the ESPAUR</u> <u>report web page</u>.

### Antimicrobial consumption: data sources

#### Primary care

Information on prescribing of antimicrobials in the community was obtained from the UKHSA Antibiotic Prescribing Data Warehouse, a project initiated by the ESPAUR Oversight Group. Data is sourced from the NHS Digital database and are extracted each month as a snapshot in time from the GP Payments system.

Age group data for primary care was obtained from ePACT2 from NHS BSA.

Primary care prescribing data includes antimicrobials prescribed from general practice and other community settings such as out-of-hours services and walk-in centres. The full list of primary care prescribing settings is provided in <u>Annex table 3.1</u>.

#### Secondary care

Information on the use of antimicrobials in secondary care was obtained from IQVIA (formerly QuintilesIMS, formed from the merger of IMS Health and Quintiles). The database held by IQVIA contains information from 99% of NHS hospital pharmacy systems for drugs dispensed to individual patients and wards.

Data from all NHS acute trusts was included and organisational changes is reflected up to the latest year of data provided in the report. Trusts can amend their prescribing data for up to a period of 2 years, hence data for the last 2 years is provisional and is subject to change.

All IQVIA data used retains IQVIA Solutions UK Limited and its affiliates Copyright. All rights reserved. Use of IQVIA data for sales. marketing or any other commercial purposes is not permitted without IQVIA Solutions UK Limited's approval, expressed by <u>IQVIA's Terms of Use</u>.

#### **Dental care**

Information on the use of antibiotics prescribed in NHS dental surgeries was obtained from NHS BSA through a data request.

### Classification of prescribing data

The classification of antimicrobials for this report is based on the Anatomical Therapeutic Chemical / Daily Defined Dose (ATC/DDD) index 2023 managed by the World Health Organization (WHO) at <u>Collaborating Centre for Drug Statistics Methodology</u>.

Data for antibiotics covered all agents in the ATC group 'J01', (antibiotics for systemic use) and 4 additional oral agents outside the 'J01' group used to treat *Clostridioides difficile* infections, fidaxomicin (A07AA12), metronidazole (P01AB01), tinidazole (P01AB02) and vancomycin (A07AA09).

Data for antifungals covered all agents in the ATC group 'J02', (antimycotics for systemic use) and one additional systemic antifungal outside the 'J02' group, terbinafine (D01BA02).

#### Third level pharmacological sub-grouping within ATC group 'J01'

Penicillins ('beta-lactam antibacterials, penicillins') include extended-spectrum penicillins, betalactamase sensitive and resistant penicillins, and beta-lactamase inhibitors either alone or in combination with penicillins.

'Other beta-lactam antibacterials' includes cephalosporins, carbapenems, and monobactams. Anti-*Clostridioides difficile* (formerly *Clostridium difficile*) agents include: oral vancomycin (ATC code: A07AA09) and fidaxomicin (ATC code: A07AA12). Oral metronidazole (ATC code: P01AB01) has been separated from this group, as opposed to previous years, following feedback from stakeholders.

'Other antimicrobials' (ATC 3rd level pharmacological subgroup 'J01X') includes glycopeptides, polymyxins, steroid antibacterials, imidazole derivatives, nitrofuran derivatives, and other antimicrobials: fosfomycin, methenamine, linezolid, daptomycin and tedizolid.

The broad-spectrum antibiotics includes Co-amoxiclav J01CR02, Cefaclor J01DC04, Cefadroxil J01DB05, Cefalexin J01DB01, Cefixime J01DD08, Cefotaxime J01DD01, Cefoxitin J01DC01, Cefpodoxime J01DD13, Cefradine J01DB09, Ceftazidime J01DD02, Ceftriaxone J01DD04, Cefuroxime J01DC02, Cefazolin J01DB04, Cefotaxime J01DD01, Ceftazidime/avibactam J01DD52, Cefepime J01DE01, Ceftaroline fosamil J01DI02, Ceftobiprole medocaril J01DI01, Ceftolozane/tazobactam J01DI54, Ofloxacin J01MA01, Ciprofloxacin J01MA02, Norfloxacin J01MA06, Levofloxacin J01MA12, Moxifloxacin J01MA14

#### ATC and DDD methodology

The ATC system aims to identify the active therapeutic ingredient of all human medicines and assigns drugs a measure of use known as the DDD, which is the assumed average maintenance dose per day for a drug used for its main indication in adults. It is important to note however that while the DDD is used as a unit of measurement of drug use, it does not

necessarily reflect the recommended or prescribed daily doses used in practice as therapeutic doses for individual patients may vary depending on characteristics such as age, weight, ethnic differences, type and severity of disease and pharmacokinetic considerations.

### Denominators

Mid-year populations (inhabitants) for each year were extracted from the <u>Office National</u> <u>Statistics</u> (ONS). Hospital admission data for each year was extracted from <u>Hospital Episode</u> <u>Statistics</u> (HES) from NHS Digital. In addition, hospital admissions by speciality were extracted from NHS digital for the financial year 2022 to 2023. Where antibiotic use in NHS acute hospital trusts have been calculated by speciality, measured using hospital admissions as the denominator, data (both numerator and denominator data) has not been included for 11 trusts, as outline in the data quality section below. Please note that admissions by speciality are published annually by NHS Digital and 2022 to 2023 data was the latest available at the time of reporting.

### Trend analysis

National trends in the consumption of antibiotics were assessed using linear regression; the dependent variable was antibiotic consumption in DDD per 1,000 inhabitants per day and the explanatory variable being year. A statistically significant trend (p<0.05) is denoted with the inclusion of <sup>+</sup>. STATA 18 was used in all analysis.

### Other community settings categories

Other community settings	Setting category
Walk-in centre	Walk-in centre
Out-of-hours	Out-of-hours
WIC and OOH practice	Out-of-hours
Public health service	PH service
Community health service	Community service
Hospital service	Hospital
Optometry service	Other
Urgent and emergency care	Urgent care
Hospice	Hospice
Care home or nursing home	Nursing home
Border Force	No data reported

# Annexe Table 3.1. Mapping of community settings to the setting categories used within the report

Other community settings	Setting category
Young offender institution	Custody
Secure training centre	No data reported
Secure children's home	Custody
Immigration removal centre	Custody
Court	No data reported
Police custody	No data reported
Sexual assault referral centre	Other
Other: justice estate	No data reported
Prison	Custody
Secure Training Centre	Other
Other	Other

### Secondary care data quality

Data quality and completeness concerns originating from both the secondary care dispensing and hospital admission data have been identified. These data quality issues affect several trusts and will have an impact on the figures reported in this publication.

It is calculated that the 2019 to 2023 totals for England are missing data for approximately 2.6% of DDDs, and approximately 3.6% of hospital admissions. This should be taken into consideration when interpreting trends in this report.

Common issues affecting data quality and completeness include the migration to new electronic patient record systems affecting admissions and pharmacy dispensing data flow, other notable anomalies have resulted from changes to admission coding. An outline of the trust-specific issues that have been identified is provided below.

#### Dispensing data issues

The trends in dispensing data for one acute specialist trust are highly variable. Due to the uncertainty regarding the reliability of this data, this trust was removed from analysis for the report, equating to the removal of approximately 200,000 DDDs per year.

There are several trusts where data is largely incomplete in the pharmacy dispensing database. There is no data after 2019 for both an acute medium-sized trust (~97,000 DDDs/year) and an acute specialist trust (~67,000 DDDs/year). There is also no data for an acute teaching trust (~800,000 DDDs/year) since 2021, with a significant decrease in DDDs observed in 2021. As a result, all 3 of these trusts have been entirely removed from analysis for this report.

Another acute teaching trust and acute medium-sized trust both have incomplete periods of dispensing data that has subsequently resumed during the timeline of the report. There is no data for 2020 and 2021 for the acute teaching trust (~800,000 DDDs/year). There is no data for 2022 and there are concerns with the reliability of the data for 2021 for the acute medium-sized trust (~280,000 DDDs/year). As these are both large trusts accounting for a significant proportion of antimicrobial prescribing, the decision was made to include these trusts in this report. However, for those metrics calculated per 1,000 hospital admissions, the admissions data for these trusts has also been excluded for the affected period.

#### Dispensing and admissions data issues

Due to technical issues, one acute large-sized trust was unable to submit hospital admissions data between July 2022 and March 2023. Data is also missing from this trust in the pharmacy dispensing database for 2023. Proxy hospital admissions data has been calculated for this trust for the affected months, using the mean hospital admissions for each respective month from unaffected months across the 5-year period report period. Proxy hospital admissions data was calculated for this trust by averaging the admissions for each month from 2019 to present. The average for each month was then applied to the relevant month affected during the July 2022 to March 2023 period. Where the dispensing data for this trust is missing, the admissions data has been excluded during those months.

#### Admissions data issues

From April 2021, there was a change to how NHS Digital reported patient admissions data. This meant that day-case patients at an acute specialist trust were included in the admissions data, leading to a significant increase in the total number of admissions observed for this trust. Admissions subsequently returned to pre-April 2021 rates, as of April 2023. This had a significant effect on the trends for those metrics which are calculated per 1,000 hospital admissions for this trust, therefore a proxy measure was used for the affected period. This was calculated by averaging admissions for each month from 2019 to present (admissions for this trust remained stable throughout the COVID-19 pandemic and are thus included). The average for each month was then applied to the relevant month affected during the April 2021 to March 2023 period.

For secondary care metrics reporting admissions data by consultant speciality, the admissions data as provided by NHS Digital are aggregated across all trusts. This means that the exclusions described above are not applicable to these metrics and admissions will be higher than calculated for other metrics.

### **Trusts definitions**

<u>Trusts definitions</u> in the ESPAUR report are based on the <u>Estates Returns Information</u> <u>Collection</u> (ERIC).

#### Annex table 3.2. Definitions of trust type (source: ERIC)

Trust	Definition
Acute small, medium or large	Sites that provides a range of inpatient medical care and other related services for surgery, acute medical conditions or injuries (usually for short-term illnesses or conditions). Treatment centres providing inpatient facilities are classed as general acute hospitals.
Acute Teaching	Sites that are a hospital that provides clinical education and training to future and current health professionals. Teaching hospitals work closely with medical students throughout their period of matriculation, and especially during their clerkship (internship) years.
Acute Specialist	Sites that undertake a single specialist function, inclusive of Oncology, Orthopaedics, Dental Hospital, Maternity Hospital, Children's Hospital, and Cardio or Thoracic. This category excludes specialist hospitals in the Mental Health or Learning Disabilities sector.
Acute Multiservice	Sites where 2 or more functions are provided by the same provider. Such functions would include any combination of single speciality, acute services, community services, mental health services and learning disabilities services.

#### Department speciality

# Annex table 3.3. Department speciality to department group look-up table for antibiotic consumption

Department speciality	Department group
Mixed outpatient clinics	AE / Non-specific out-patient department
Aseptic unit	AE / Non-specific out-patient department
A12E	AE / Non-specific out-patient department
Psychogeriatric	Geriatrics
Geriatrics	Geriatrics
Intensive care	Intensive care unit
Dermatology	General medicine

Department speciality	Department group
Respiratory, chest or asthma clinic	General medicine
Cardiology	General medicine
Gastroenterology	General medicine
Coronary care	General medicine
Rheumatology	General medicine
Thoracic or chest medicine	General medicine
General medicine	General medicine
Endocrinology	General medicine
Obstetrics and gynaecology	Obstetrics and gynaecology
Fertility and genetics	Obstetrics and gynaecology
Orthopaedics	Orthopaedics
Trauma and Orthopaedics	Orthopaedics
Pain clinic	Other
Radiology	Other
Radiology and Imaging	Other
Physiotherapy	Other
Physically disabled	Other
Rehabilitation or long stay unit	Other
Pathology lab	Other
Mental handicap	Other
Occupational health	Other
Learning disabilities	Other
Child adolescent psychiatry	Other
Other wards or units	Other
Psychiatry and mental illness	Other
Psychiatric day Hospital	Other
Paediatric ICU	Paediatrics
Neonatal unit	Paediatrics
Paediatric or paediatric surgery	Paediatrics
Acute internal medicine	Specialist medicine
Medical oncology	Specialist medicine
Clinical oncology (Radiotherapy)	Specialist medicine
AIDS unit	Specialist medicine

Department speciality	Department group
Infectious disease or Isolation	Specialist medicine
Renal medicine	Specialist medicine
Liver or Pancreatic unit	Specialist medicine
Neurology	Specialist medicine
G.U.M	Specialist medicine
GU Medicine or HIV	Specialist medicine
G.U./ V.D./ S.T.D./ A.I.D.S.	Specialist medicine
Haematology	Specialist medicine
GUM medicine	Specialist medicine
Liver (failure) unit	Specialist medicine
Transplantation unit	Specialist surgery
ENT	Specialist surgery
Cardio-thoracic surgery	Specialist surgery
Plastic surgery	Specialist surgery
Burn and Plastic surgery	Specialist surgery
Oral surgery	Specialist surgery
Vascular surgery	Specialist surgery
Ophthalmology	Specialist surgery
Urology	Specialist surgery
Neurosurgery	Specialist surgery
General surgery	General surgery
Breast treatment and care	General surgery
Day case theatres	General surgery
Theatre and anaesthetics	General surgery

### Antiviral consumption

#### Data sources

COVID-19 therapeutics usage data for the primary care was obtained from ePACT2, and for the secondary care was sourced from IQVIA further details on IQVIA data is available on secondary care section of this annex. As data on the number of patients eligible to receive COVID-19 therapeutics was unavailable to UKHSA, COVID-19 case counts were used as the denominator and were sourced from the <u>UKHSA COVID-19 dashboard</u>.

#### Data analysis

Total DDDs from 1 January 2020 to 31 December 2023 by therapy were included for ( Molnupiravir (Lagevrio®), Nirmatrelvir plus ritonavir (Paxlovid®), Remdesivir (Veklury®) and Sotrovimab (Xevudy®). Rates of DDDs were estimated by dividing the number of DDDs by the COVID-19 case numbers (per 1,000) over the specified time period.

Rates by region were estimated by dividing the COVID-19 case numbers (per 1,000) which were extracted from the <u>UKHSA COVID-19 dashboard</u> by each region over the specified time period.

STATA 18 was used in all medicines supply data analysis.

### Antiparasitic consumption

#### Data sources

Antiparasitic usage data for the primary care was obtained from ePACT2, and for the secondary care was sourced from IQVIA further details on IQVIA data is available on secondary care section of this annex.

#### Data analysis

Total rates of antiparasitic consumption were calculated using the ONS Mid-year population (inhabitants) denominator, as above.

# **Chapter 5. Antimicrobial stewardship**

# Adaptation for the 2023 WHO AWaRE categories for stewardship in the UK

Annex table 5.1. Access, Watch and Reserve, and Other antibiotics consensus categories with comparison to WHO 2023 AWaRe categories, alphabetically presented by antibiotic

Antibiotic	Proposed 2024 UK AWaRe category	2023 WHO AWaRe category
Amikacin*	Watch	Access
Amoxicillin	Access	Access
Amoxicillin/ clavulanic-acid*	Watch	Access
Ampicillin	Access	Access
Azithromycin	Watch	Watch
Aztreonam	Reserve	Reserve
Benzathine-benzylpenicillin	Access	Access
Benzylpenicillin	Access	Access
Cefaclor	Watch	Watch
Cefadroxil	Access	Access
Cefalexin	Access	Access
Cefalotin	Access	Access
Cefamandole	Watch	Watch
Cefazolin	Access	Access
Cefepime	Watch	Watch
Cefiderocol	Reserve	Reserve
Cefixime	Watch	Watch
Cefotaxime	Watch	Watch
Cefoxitin	Watch	Watch
Cefradine	Access	Access
Ceftaroline-fosamil	Reserve	Reserve
Ceftazidime	Watch	Watch
Ceftazidime/avibactam	Reserve	Reserve
Ceftobiprole-medocaril	Reserve	Reserve
Ceftolozane/tazobactam	Reserve	Reserve

Antibiotic	Proposed 2024 UK AWaRe category	2023 WHO AWaRe category
Ceftriaxone	Watch	Watch
Cefuroxime	Watch	Watch
Chloramphenicol*	Watch	Access
Ciprofloxacin	Watch	Watch
Clarithromycin	Watch	Watch
Clindamycin*	Watch	Access
Colistin, intravenous	Reserve	Reserve
Colistin, oral	Reserve	Reserve
Dalbavancin	Reserve	Reserve
Dalfopristin/quinupristin	Reserve	Reserve
Daptomycin	Reserve	Reserve
Delafloxacin	Watch	Watch
Demeclocycline*	Other	Watch
Doripenem*	Reserve	Watch
Doxycycline	Access	Access
Eravacycline	Reserve	Reserve
Ertapenem*	Reserve	Watch
Erythromycin	Watch	Watch
Fidaxomicin	Watch	Watch
Flucloxacillin	Access	Access
Fosfomycin oral*	Access	Watch
Fosfomycin, intravenous	Reserve	Reserve
Fusidic acid	Watch	Watch
Gentamicin	Access	Access
Imipenem/cilastatin*	Reserve	Watch
Imipenem/cilastatin/ relebactam	Reserve	Reserve
Levofloxacin	Watch	Watch
Linezolid	Reserve	Reserve
Lymecycline	Watch	Watch
Meropenem*	Reserve	Watch
Meropenem/vaborbactam	Reserve	Reserve

Antibiotic	Proposed 2024 UK AWaRe category	2023 WHO AWaRe category
Methenamine	Other	Other
Metronidazole	Access	Access
Minocycline oral	Watch	Watch
Moxifloxacin	Watch	Watch
Nalidixic Acid	Other	Other
Neomycin	Watch	Watch
Nitrofurantoin	Access	Access
Norfloxacin	Watch	Watch
Ofloxacin	Watch	Watch
Oritavancin	Reserve	Reserve
Oxytetracycline	Watch	Watch
Phenoxymethylpenicillin	Access	Access
Piperacillin	Watch	Watch
Piperacillin/tazobactam	Watch	Watch
Pivmecillinam	Access	Access
Pristinamycin*	Other	Watch
Procaine-benzylpenicillin	Access	Access
Spectinomycin*	Other	Access
Spiramycin*	Other	Watch
Streptomycin, intravenous*	Other	Watch
Sulfadiazine*	Other	Access
Sulfamethoxazole/trimethop rim	Access	Access
Sulfamethoxypyridazine*	Other	Access
Sulfapyridine*	Other	Access
Tedizolid	Reserve	Reserve
Teicoplanin*	Watch	Watch
Telavancin	Reserve	Reserve
Temocillin	Watch	Watch
Tetracycline	Access	Access
Tigecycline	Reserve	Reserve
Tinidazole	Access	Access

Antibiotic	Proposed 2024 UK AWaRe category	2023 WHO AWaRe category
Tobramycin	Watch	Watch
Trimethoprim	Access	Access
Vancomycin	Watch	Watch

Note: Where categories between 2024 UK-adapted and 2023 WHO categories differ, these have been highlighted in red text and antibiotics referenced with an asterisk.

Antibiotic	Survey findings were inconclusive	England adapted 2019 AWaRe category	WHO 2023 AWaRe category	Delphi workshop proposed 2024 UK AWaRe category	Rationale for final decision
Amikacin	Access or Watch	Watch	Access	Watch	Increasing gentamicin resistance makes it unclear why amikacin should be more reserved than gentamicin, particularly as this is an important first line treatment with increasing multidrug (MDR) gram-negative resistance. However, given the higher resistance to gentamicin and greater switch to amikacin, important to keep Watch.
Aztreonam	Watch or Reserve	Reserve	Reserve	Reserve	WHO have categorised as Reserve for the rationale that it is used in drug resistant-TB. It is an important alternative for Gram-negative infection in patients with severe penicillin allergy. However, caution should be used to prevent overprescribing for incorrect penicillin allergy records. Aztreonam is also currently used as an addition to ceftazidime and avibactam to overcome beta-lactam resistance. If use increases, then the treatment of more resistant infections will become increasingly challenging. Non-toxic, so prescribing may be encouraged if placed in a different category.

Annex table 5.2. Antibiotics which required further discussion to finalise placement of AWaRe category for the UK, and associated reasoning

Antibiotic	Survey findings were inconclusive	England adapted 2019 AWaRe category	WHO 2023 AWaRe category	Delphi workshop proposed 2024 UK AWaRe category	Rationale for final decision
Cefadroxil	Access or Watch	Watch	Access	Access	1st generation cephalosporins to be categorised as Access: much lower risk of <i>Clostridioides difficile</i> (CDI) than 2nd, 3rd and 4th. This will permit alternative options for penicillin allergies. Caveat: acknowledging CDI rates increasing in the UK and the importance of messaging of cephalosporins will need to be worked on.
Cefalexin	Access or Watch	Watch	Access	Access	As per comment above: 1st GC to move to Access. Growing evidence of lower CDI risk from 1st generation cephalosporins. Cefalexin is NICE first line for pyelonephritis.
Cefalotin	Access or Watch or Other	Access	Access	Access	As per comment above: 1st GC to move to Access. Proven to be useful alternatives for patients with non- severe or unverified penicillin allergy.
Cefamandole	Watch or Unsure	Watch	Watch	Watch	As per comment above: 1st GC to move to Access, 2nd and 3rd to move in line with WHO category. Associated with increased risk of CDI. WHO category is now in line with UK Watch category.
Cefazolin	Access or Watch or Other	Watch	Access	Access	As per comment above: 1st GC to move to Access. Associated with increased risk of CDI.

Antibiotic	Survey findings were inconclusive	England adapted 2019 AWaRe category	WHO 2023 AWaRe category	Delphi workshop proposed 2024 UK AWaRe category	Rationale for final decision
					Many hospitals now using cefazolin in preference to cefuroxime as first line for surgical prophylaxis. New endocarditis guidelines for penicillin allergy recommend cefazolin.
Cefradine	Access or Watch or Other	Watch	Access	Access	As per comment above: 1st GC to move to Access. Associated with increased risk of CDI.
Clarithromycin	Access or Watch	Watch	Watch	Watch	Macrolides are alternative for penicillin allergy, particularly in primary care but as ESPAUR report shows, there is more resistance to macrolides in common pathogens than there is to penicillins, so there is a case to preserve macrolides by categorising as Watch. Macrolide liquids are often considered to have a better taste than penicillin-based liquids, so often used in preference to improve adherence in children, keeping in Watch may help overcome this and help to drive using tablets at an earlier age in children.
Delafloxacin	Watch or Reserve	Watch	Watch	Watch	Consensus.
Demeclocycline	Access or Other	Watch	Watch	Other	Classified as uncategorised or other because of its use in hyponatremia; primarily used in correction of sodium levels, that is, non AMR use.

Antibiotic	Survey findings were inconclusive	England adapted 2019 AWaRe category	WHO 2023 AWaRe category	Delphi workshop proposed 2024 UK AWaRe category	Rationale for final decision
Erythromycin	Access or Watch	Watch	Watch	Watch	Linked with clarithromycin discussion: Case to preserve macrolide use.
Fusidic acid	Access or Watch	Access	Watch	Watch	A valuable antibiotic for confirmed Methicillin- sensitive and -resistant <i>Staphylococcus aureus</i> (MSSA and MRSA) systemic infection. Despite being narrow- spectrum, concerns were noted of increased reports of fusidic acid resistant strains or a high potential for resistance with inappropriate and increased use in the population. As resistance is rapidly acquired with this monotherapy (often given in combination with rifampicin for MSSA), it is for this reason used for limited indications and should be reserved once sensitivity results are available. As Fusidic acid is not a recommended first choice antibiotic, should therefore be Watch – in line with WHO categorisation.
Linezolid	Watch or Reserve	Reserve	Reserve	Reserve	Valuable and effective oral agent for gram-positive infections (MRSA), supports early or timely discharge from hospital (avoids the need for IV vancomycin and its associated complications or facilitates intravenous to oral switch (IVOS), is low cost, now off-patent and relatively narrow-spectrum.

Antibiotic	Survey findings were inconclusive	England adapted 2019 AWaRe category	WHO 2023 AWaRe category	Delphi workshop proposed 2024 UK AWaRe category	Rationale for final decision
					It's use in MDR-TB suggests better to maintain Reserve category.
Lymecycline	Access or Watch	Watch	Watch	Watch	Commonly used for acne, alternative non-antimicrobial drugs are available.
Methenamine	Access, Watch or Other	Other	Other	Other	Consensus.
Nalidixic Acid	Uncategorised or Other	Other	Other	Other	Consensus.
Oxytetracycline	Access or Watch	Watch	Watch	Watch	Used for acne, although not currently first line treatment. To discourage unnecessary oral antibiotic use for acne maintain in Watch.
Piperacillin	Watch or Other	Other	Watch	Watch	Resistance is increasing, to avoid overuse maintain Watch category.
Pristinamycin	Watch or Reserve or Other		Watch	Other	Unlicensed product, to be used when no other licensed version available. May present an opportunity to license in the UK if placed in Watch rather than Reserve.
Spectinomycin	Uncategorised or Other	Watch	Access	Other	Consensus.
Spiramycin	Uncategorised or Other	Other	Watch	Other	Not licensed in the UK. Not in high use.

Antibiotic	Survey findings were inconclusive	England adapted 2019 AWaRe category	WHO 2023 AWaRe category	Delphi workshop proposed 2024 UK AWaRe category	Rationale for final decision
Streptomycin, intravenous	Uncategorised or Other	Other	Watch	Other	Agent rarely used and for specific indications. Unlicensed in the UK
Sulfadiazine	Uncategorised or Other	Other	Access	Other	Prevention of rheumatic fever recurrence rather than infection. Will be skewing Access, hence uncategorised
Sulfamethoxyp- yridazine	Uncategorised or Other or Access	Other	Access	Other	Consensus.
Sulfapyridine	Uncategorised or Other	Other	Access	Other	Consensus.
Tinidazole	Access, Watch or Other	Other	Access	Access	Antiprotozoal agent, rarely see resistance. Rarely or no longer used. Maintained classification as per WHO
Vancomycin	Access or Watch	Other	Watch	Watch	Consensus.

# Annex 5.3 A rapid systematic review to assess interventions to tackle anti-microbial resistance and utilisation in adult social care.

**Introduction:** Adult social care involves a wide range of services beyond those provided by the NHS. These services support individuals who are elderly, living with disabilities, or have physical or mental health conditions, including those with learning disabilities, enabling them to live independently and safely. Maintaining high standards of hygiene and preventing the spread of infectious diseases are crucial for safeguarding the health of these individuals.

To effectively tackle AMR a thorough understanding of the existing evidence and gaps in both AMR and AMU within adult social care is crucial. While some primary studies have explored antimicrobial resistant infections there's a limited number of systematic reviews, none of which have covered the breadth of adult social care this review is aimed to do. Neither has any review assessed a range of interventions (as well as demographic factors, settings, and regional differences) within adult social care settings that are associated with different prevalence of AMR infections and levels of AMU.

#### Methods: A rapid systematic review (CRD42024494928

crd.york.ac.uk/prospero/display\_record.php?RecordID=494928) was conducted through electronic database searches, such as Embase, Medline and Scopus, from 1 January 2010 until 30 April 2024. Studies based in middle- or high-income countries (based on criteria from the World Bank) were included. Included studies assessed diverse interventions aimed at addressing AMR, encompassing educational and training programs, policy implementations, technological interventions and IPC, AMU and AMS strategies.

**Results:** Eighteen papers were included in the review from middle to high income countries around the world. The majority of the studies were based in North America, (United States n=10), (Canada n=3), with rest being from Denmark (n=2), UK (n=1), Sweden (n=1) and France (n=1). Across the 18 studies a total of 189 nursing homes, 8 long term care homes and 6 veteran homes were exposed to interventions to target antimicrobial resistance and utilisation.

A range of study designs were used: randomised control trials (RCT) (n = 2), cRCT (n = 2), quasi-experimental (n = 4), time series analysis (n = 1), pre-post-test designs (n = 4), observational (n = 2), interventional (n = 5).

AMS programmes, education and training was used most as interventions to target inappropriate antimicrobial prescribing and thereby tackling resistance. Sixteen studies had education and training elements including guidelines for prescribing, regular reviews of antibiotic use, and education and training for multidisciplinary teams. All these studies reported reductions in inappropriate antimicrobial prescribing ranging from 13% to 55.5%. Furthermore, increased adherence to guidelines and protocols was observed across studies with targeted staff training. One study conducted in France highlighted the importance of hand hygiene in conjunction with staff education. Even though the overall alcohol based anti-infective hand rub consumption was higher in the intervention group, the hospitalisations did not differ with the control group, but the

intervention group showed significantly lower mortality rate (2.10 vs 2.65 per 100 residents per month, respectively p-0.003) and antibiotic prescriptions (5.0 vs 5.8 defined daily doses per 100 resident days, respectively; P < .001).

Pharmacist (oversight in 2 long term care facilities spanning 94 residents suspected of having a UTI) oversight of antimicrobial prescribing didn't yield significant results on antibiotic prescribing practices. However, pharmacist oversight significantly improved correct treatment options being prescribed to patients with any symptoms.

**Conclusions:** Based on the review of these studies, interventions including a combination of staff education and training, standardised treatment protocols, pharmacist involvement, quality improvement initiatives and audits can significantly reduce inappropriate antibiotic use in adult social care settings. Multifaceted interventions that combine several strategies tend to be the most effective. These interventions can successfully tackle AMR without compromising patient safety or increased hospitalisation and mortality promoting AMS and tackling resistance in adult social care settings. To ensure sustainability of these interventions ongoing training and feedback is crucial. Further research is required to explore the adaptability of these interventions across different healthcare systems globally.

# 5.4 A rapid systematic review to determine AMS interventions targeted at individuals involved in sex work

**Introduction:** Individuals involved in sex work are particularly vulnerable to risky sexual practices, increasing their risk of sexually transmitted infections. Due to stigma, limited access to healthcare and socioeconomic barriers many sex workers do not seek treatment and guidance through proper healthcare channels, leading to misuse of antimicrobials which potentially contributes to the development and spread of AMR. This rapid systematic review aims to evaluate interventions addressing AMR and AMU among sex workers to identify effective strategies for mitigating the spread of antimicrobial resistant infections in this population.

**Method:** Three databases (Embase, Medline, and Scopus) were searched for studies published in English from 2010 onwards, without restrictions on study design or age. 265 articles were screened to identify studies for full-text review based on predefined criteria with 25 full-text articles to assessed for final inclusion.

**Results:** The review yielded no studies specifically addressing interventions for AMR or AMU in sex workers.

**Conclusion:** This review highlights a critical gap in research on interventions targeting AMR or AMU in sex workers despite the vulnerability of this population. Further research is urgently needed to develop and evaluate targeted interventions for this population.

# Annex 5.5 A rapid systematic review to determine AMR/AMU levels among those in contact with the criminal justice system in Europe and North America

**Background:** Individuals in contact with the criminal justice system may be especially vulnerable to resistant infections due to living conditions, work, behaviours and pre-existing health conditions. This review aims to assess the levels of bacterial antimicrobial resistance and antibiotic use among individuals in contact with the criminal justice system.

**Methods:** A rapid systematic review of Embase, Medline and Scopus electronic databases from 1 January 2010 up to 28 September 2023 was conducted (<u>OSF registration</u>). Included studies had to assess antimicrobial resistant bacteria or AMU among individuals in contact with the criminal justice system. Study quality was assessed using the Newcastle-Ottawa Scale and the STROBE AMS checklist.

**Results:** Sixteen papers were included in the review, 8 were at lower risk of bias. Three papers reported findings relating to antibiotic use. Inappropriate prescribing was found to be common in one study, and 2 studies found that recent antibiotic use was associated with a higher risk of a resistant infection.

Fourteen papers reported findings for bacterial antimicrobial resistance, the majority focused on TB and Staphylococcus aureus. Four papers assessed the prevalence of drug resistant TB amongst the prison population which ranged from 5.2% to 37%. Six papers assessed Staphylococcus aureus, with estimates of MRSA colonization ranging from 8.1% to 8.8% (4 papers). Resistance in Salmonella spp. Acinetobacter spp., Group A Streptococcus and Mycoplasma genitalium were assessed in 4 separate papers.

**Conclusions:** Individuals in contact with the criminal justice system are a marginalised population at risk of a range of resistant bacterial infections. As only 3 studies looked at antibiotic use, limited conclusions could be drawn. Collaborative, tailored approaches are needed to tackle this problem.

### **Chapter 7. Professional and public education and training**

### Antibiotic Guardian

Annexe table 7.1. Summary of Antibiotic Guardian pledges made on main pledge page by pharmacy teams each year, from 2014 to 2023, with breakdown of the sub-category of pledger

	Pharmacy	Pharmacy team pledge sub-category									
Year	teams pledges	Academic pharmacist	Community pharmacist	Pharmacy assistant	Pharmacy technician	Primary care pharmacist	Secondary care pharmacist	Unknown			
2014	1,300	N/A	N/A	N/A	N/A	N/A	N/A	0			
2015	1,338	30	0	85	270	398	551	0			
2016	2,111	75	0	145	409	654	756	0			
2017	3,021	81	0	357	544	861	901	0			
2018	1,627	30	245	163	317	350	496	0			
2019	2,410	42	807	242	403	299	574	0			
2020	28,701	125	10,145	13,214	3,166	1,359	394	0			
2021	27,684	47	8,856	13,900	2,885	1,223	392	0			
2022	9,747	43	3,059	4,755	965	547	378	0			
2023	14,896	84	4,063	8,010	1,454	717	325	243			

These sub-categories were not available in 2014 and the 'Community pharmacist' sub-category was introduced in 2018.

Annexe Table 7.2. Summary of the organisational AMS pledge activity from April to December 2023, broken down by the type of organisation, from across UK

Organisation type	Number of registrations in 2023
Charity	2
Community pharmacy	6
GP practice	26
Hospital (secondary care)	10
National NHS organisation	5
NHS primary care	10
Other primary care (for example hospice, community hospital and so on)	4
NHS trust or health and social care trust (NI)	10
Private healthcare	5
Regional NHS organisation (for example CCG, local commissioning group)	1
Professional organisation	2
University	1
Total	82

# Antibiotic Guardian Shared Learning and Awards – held May 2023

Annexe table 7.3. Summary of number of entries received per category for Antibiotic Guardian Shared Learning and Awards event 2022 to 2023 and number shortlisted

Category	Number of entries	Number of shortlisted entries
Animal health, agriculture and food supply	4	4
Children and family	1	1
Community communications	5	3
COVID-19 learning	3	3
Diagnostic stewardship	3	2
Innovation and technology	6	3
Multi-country collaboration	4	2
Prescribing stewardship	18	3
Public engagement	7	5
Research	5	3

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

Category	Number of entries	Number of shortlisted entries
Das Pillay antimicrobial stewardship memorial award	6	3
Total	62	32

# **Chapter 8. Research**

## List of publications

A list of peer-reviewed publications from April 2023 to March 2024:

Aggarwal, Dinesh, Diana Rajan, Katherine L Bellis, Emma Betteridge, Joe Brennan, Catarina de Sousa, CARRIAGE Study Team‡, Julian Parkhill, Sharon J Peacock, and Marcus C de Goffau. 'Optimization of High-Throughput 16s Rrna Gene Amplicon Sequencing: An Assessment of Pcr Pooling, Mastermix Use and Contamination.' Microbial Genomics 9, no. 10 (2023): 001115.

Agnew, Emily, Kerrie A Davies, Virginie F Viprey, Stephanie Evans, Georgina L Davis, Russell Hope, Mark H Wilcox, Sebastian M Wingen-Heimann, and Julie V Robotham. 'Impact of Testing on Clostridioides Difficile Infection in Hospitals across Europe: A Mathematical Model.' Clinical Microbiology and Infection 29, no. 6 (2023): 796. e1-96. e6.

Ashiru-Oredope, Diane, Neil Cunningham, Ella Casale, Berit Muller-Pebody, Russell Hope, Colin S Brown, and Susan Hopkins. 'Reporting England's Progress Towards the Ambitions in the Uk Action Plan for Antimicrobial Resistance: The English Surveillance Programme for Antimicrobial Utilisation and Resistance (Espaur).' Journal of Antimicrobial Chemotherapy 78, no. 10 (2023): 2387-91.

Ashiru-Oredope, Diane, Bradley J Langford, Candice Bonaconsa, Vrinda Nampoothiri, Esmita Charani, and Debra A Goff. 'Global Collaborations in Antimicrobial Stewardship: All Hands on Deck.' Antimicrobial Stewardship 12 Healthcare Epidemiology 3, no. 1 (2023): e66.

Ashiru-Oredope, Diane, Maxencia Nabiryo, Lisa Zengeni, Nduta Kamere, Alexia Makotose, Omotayo Olaoye, William Townsend, Beatrice Waddingham, Ayodeji Matuluko, and Winnie Nambatya. 'Tackling Antimicrobial Resistance: Developing and Implementing Antimicrobial Stewardship Interventions in Four African Commonwealth Countries through a Health Partnership Model.' Journal of Public Health in Africa 14, no. 6 (2023).

Ashiru-Oredope, Diane, Roeann Osman, Christina Narh, Uju Okereke, Eleanor J Harvey, Christopher Garland, Cecilia Pyper, Marion Bennie, and Andrew Evans. 'Public Health Qualifications, Motivation, and Experience of Pharmacy Professionals: Exploratory Cross-Sectional Surveys of Pharmacy and Public Health Professionals.' The Lancet 402 (2023): S24.

Ayorinde, Abimbola, Iman Ghosh, Junaid Shaikh, Victoria Adetunji, Anna Brown, Mary Jordan, Ellie Gilham, Daniel Todkill, and Diane Ashiru-Oredope. 'Consideration of Factors Associated with Inequalities in Interventions That Support Health-Care Professionals' Interaction with Patients to Reduce Inappropriate Antimicrobial Use: A Systematic Review.' The Lancet 402 (2023): S25.

Baker, Kate S, Elita Jauneikaite, Katie L Hopkins, Stephanie W Lo, Leonor Sánchez-Busó, Maria Getino, Benjamin P Howden, Kathryn E Holt, Lillian A Musila, and Rene S Hendriksen. 'Genomics for Public Health and International Surveillance of Antimicrobial Resistance.' The Lancet Microbe 4, no. 12 (2023): e1047-e55.

Baker, Kate S, Elita Jauneikaite, Jamie G Nunn, Janet T Midega, Rifat Atun, Kathryn E Holt, Kamini Walia, Benjamin P Howden, Heather Tate, and Iruka N Okeke. 'Evidence Review and Recommendations for the Implementation of Genomics for Antimicrobial Resistance Surveillance: Reports from an International Expert Group.' The Lancet Microbe (2023).

Bashir, Shazia, Maria Wilson, Diane Ashiru-Oredope, and Sudaxshina Murdan. 'Tailoring Vaccines for Older Individuals: Aging of the Immune System and the Impact on Vaccine Efficacy.' In Pharmaceutical Formulations for Older Patients: Springer, 2023.

Beale, Mathew A, Louise Thorn, Michelle J Cole, Rachel Pitt, Hannah Charles, Michael Ewens, Patrick French, Malcolm Guiver, Emma E Page, and Erasmus Smit. 'Genomic Epidemiology of Syphilis in England: A Population-Based Study.' The Lancet Microbe 4, no. 10 (2023): e770-e80.

Bennet, Kirsty F, Rebecca L Guy, Sarah M Gerver, Katie L Hopkins, Richard Puleston, Colin S Brown, and Katherine L Henderson. 'Determining the Impact of Professional Body Recommendations on the Screening of Acquired Carbapenemase-Producing Enterobacterales in England.' Infection Prevention in Practice 5, no. 2 (2023): 100281.

Bladon, Siân, Diane Ashiru-Oredope, Neil Cunningham, Alexander Pate, Glen P Martin,
Xiaomin Zhong, Ellie L Gilham, Colin S Brown, Mariyam Mirfenderesky, and Victoria Palin.
'Rapid Systematic Review on Risks and Outcomes of Sepsis: The Influence of Risk Factors
Associated with Health Inequalities.' International Journal for Equity in Health 23, no. 1 (2024):
34.

Bou-Antoun, Sabine, Sakib Rokadiya, Diane Ashiru-Oredope, Alicia Demirjian, Emma Sherwood, Nicholas Ellaby, Sarah Gerver, Carlota Grossi, Katie Harman, and Hassan Hartman. 'Covid-19 Therapeutics: Stewardship in England and Considerations for Antimicrobial Resistance.' Journal of Antimicrobial Chemotherapy 78, no. Supplement\_2 (2023): ii37-ii42.

Bristowe, Henrietta, Michaela Day, Helen Fifer, and Mauricio Arias. 'Gonococcal Pericarditis with Tamponade-Use of Molecular Technology to Improve Diagnosis and Management.' International Journal of Infectious Diseases 134 (2023): 150-52.

Clarke, Maria, Charlotte K Hind, Philip M Ferguson, Giorgia Manzo, Bhumil Mistry, Bingkun Yue, Janis Romanopulos, Melanie Clifford, Tam T Bui, and Alex F Drake. 'Synergy between Winter Flounder Antimicrobial Peptides.' npj Antimicrobials and Resistance 1, no. 1 (2023): 8. Clarke, OE, H Pelling, V Bennett, T Matsumoto, GE Gregory, J Nzakizwanayo, AJ Slate, A Preston, M Laabei, and LJ Bock. 'Lipopolysaccharide Structure Modulates Cationic Biocide Susceptibility and Crystalline Biofilm Formation in Proteus Mirabilis.' Frontiers in Microbiology 14 (2023): 1150625.

Cooper, Emily, Brieze Read, Leigh Sanyaolu, Haroon Ahmed, and Donna Lecky. 'Impact of Sociodemographic Status and Uti Symptoms on Women's Health-Care Seeking and Management in England: Findings from an E-Survey Conducted During the First Year of the Covid-19 Pandemic.' BJGP open 7, no. 4 (2023).

Cui, Yixin, Alice Lanne, Xudan Peng, Edward Browne, Apoorva Bhatt, Nicholas J Coltman, Philip Craven, Liam R Cox, Nicholas J Cundy, and Katie Dale. 'Azetidines Kill Multidrug-Resistant Mycobacterium Tuberculosis without Detectable Resistance by Blocking Mycolate Assembly.' Journal of Medicinal Chemistry (2024).

Davies, Timothy J, Jeremy Swann, Anna E Sheppard, Hayleigh Pickford, Samuel Lipworth, Manal AbuOun, Matthew J Ellington, Philip W Fowler, Susan Hopkins, and Katie L Hopkins. 'Discordance between Different Bioinformatic Methods for Identifying Resistance Genes from Short-Read Genomic Data, with a Focus on Escherichia Coli.' Microbial Genomics 9, no. 12 (2023): 001151.

Dewé, Tamsin, Fraser Broadfoot, Diane Ashiru-Oredope, Colin Brown, and William Malcolm. 'Taking a One Health Approach to Antibiotic Stewardship.' Veterinary Record 192, no. 7 (2023): 298-99.

Evans, Stephanie, James Stimson, Diane Pople, Mark H Wilcox, Russell Hope, and Julie V Robotham. 'Evaluating the Impact of Testing Strategies for the Detection of Nosocomial Covid-19 in English Hospitals through Data-Driven Modelling.' Frontiers in Medicine 10 (2023): 1166074.

Falola, Angela, Alicia Demirjian, Wendy Thompson, Colin S Brown, Sarah Gerver, and Sabine Bou-Antoun. 'The Impact of Covid-19 National Restrictions on Dental Antibiotic Dispensing Trends and Treatment Activity in England: January 2016 to July 2021.' JAC-Antimicrobial Resistance 5, no. 4 (2023): dlad081.

Findlay-Wilson, Stephen, Linda Easterbrook, Sandra Smith, Neville Pope, Matthew Aldridge, Gareth Humphries, Holger Schuhmann, Didier Ngabo, Emma Rayner, and Ashley Otter. 'Refinement of an Ovine-Based Immunoglobulin Therapy against Sars-Cov-2, with Comparison of Whole Igg Versus F (Ab') 2 Fragments.' Scientific Reports 13, no. 1 (2023): 13912.

Findlay-Wilson, Stephen, Linda Easterbrook, Sandra Smith, Neville Pope, Gareth Humphries, Holger Schuhmann, Didier Ngabo, Emma Rayner, Ashley David Otter, and Tom Coleman. 'Development of a Cost-Effective Ovine Antibody-Based Therapy against Sars-Cov-2 Infection and Contribution of Antibodies Specific to the Spike Subunit Proteins.' Antiviral Research 203 (2022): 105332.

Fwoloshi, Sombo, Uchizi Chola, Ruth Nakazwe, Timothy Tatila, Tebuho Mateele, Mwewa Kabaso, Theresa Muzyamba, Ilunga Mutwale, Anja St Clair Jones, and Jasmin Islam. 'Why Local Antibiotic Resistance Data Matters–Informing Empiric Prescribing through Local Data Collation, App Design and Engagement in Zambia.' Journal of Infection and Public Health 16 (2023): 69-77.

Gilham, Ellie L, Ella Casale, Alison Hardy, Adeola H Ayeni, Ella Sunyer, Tori Harris, Rachel Feechan, Anna Heltmann, Malcolm Fawcett, and Susan Hopkins. 'Assessing the Impact of a National Social Marketing Campaign for Antimicrobial Resistance on Public Awareness, Attitudes, and Behaviour, and as a Supportive Tool for Healthcare Professionals, England, 2017 to 2019.' Eurosurveillance 28, no. 47 (2023): 2300100.

Gilham, Ellie L, Nicola Pearce-Smith, Vanessa Carter, and Diane Ashiru-Oredope. 'Assessment of Global Antimicrobial Resistance Campaigns Conducted to Improve Public Awareness and Antimicrobial Use Behaviours: A Rapid Systematic Review.' BMC Public Health 24, no. 1 (2024): 396.

Guimond, Scott E, Courtney J Mycroft-West, Neha S Gandhi, Julia A Tree, Thuy T Le, C Mirella Spalluto, Maria V Humbert, Karen R Buttigieg, Naomi Coombes, and Michael J Elmore. 'Synthetic Heparan Sulfate Mimetic Pixatimod (Pg545) Potently Inhibits Sars-Cov-2 by Disrupting the Spike–Ace2 Interaction.' ACS central science 8, no. 5 (2022): 527-45.

Guy, Rebecca L, Jamie Rudman, Hannah Higgins, Emma Carter, Katherine L Henderson, Alicia Demirjian, and Sarah M Gerver. 'Nitrofurantoin Resistance as an Indicator for Multidrug Resistance: An Assessment of Escherichia Coli Urinary Tract Specimens in England, 2015–19.' JAC-Antimicrobial Resistance 5, no. 6 (2023): dlad122.

Hallmaier-Wacker, Luisa K, Amelia Andrews, Russell Hope, Alicia Demirjian, Theresa L Lamagni, and Simon M Collin. 'Incidence of Infant Gram-Negative Invasive Bacterial Infections in England, 2011–2019: An Observational Study Using Population-Wide Surveillance Data.' Archives of Disease in Childhood 108, no. 9 (2023): 762-67.

Hamilton, Ryan A, Molly Courtenay, Kevin J Frost, Roger Harrison, Helen Root, David G Allison, Antonella P Tonna, Diane Ashiru-Oredope, Mamoon A Aldeyab, and Katherine Shemilt. 'Implementation of the National Antimicrobial Stewardship Competencies for Uk Undergraduate Healthcare Professional Education within Undergraduate Pharmacy Programmes: A Survey of UK Schools of Pharmacy.' JAC-Antimicrobial Resistance 5, no. 4 (2023): dlad095.

Harvey, Eleanor J, Caroline De Brún, Ella Casale, Viviana Finistrella, and Diane Ashiru-Oredope. 'Influence of Factors Commonly Known to Be Associated with Health Inequalities on Antibiotic Use in High-Income Countries: A Systematic Scoping Review.' Journal of Antimicrobial Chemotherapy 78, no. 4 (2023): 861-70.

Harvey, Eleanor J, Monsey McLeod, Caroline De Brún, and Diane Ashiru-Oredope. 'Criteria to Achieve Safe Antimicrobial Intravenous-to-Oral Switch in Hospitalised Adult Populations: A Systematic Rapid Review.' BMJ open 13, no. 7 (2023): e068299.

Hassoun-Kheir, Nasreen, Mariana Guedes, Marie-Therese Ngo Nsoga, Lorenzo Argante, Fabiana Arieti, Beryl P Gladstone, Rhys Kingston, Nichola R Naylor, Maria D Pezzani, and Koen B Pouwels. 'A Systematic Review on the Excess Health Risk of Antibiotic-Resistant Bloodstream Infections for Six Key Pathogens in Europe.' Clinical Microbiology and Infection (2023).

Hayes, Catherine V, Sejal Parekh, Donna M Lecky, Jill Loader, Carry Triggs-Hodge, and Diane Ashiru-Oredope. 'The National Implementation of a Community Pharmacy Antimicrobial Stewardship Intervention (Pamsi) through the English Pharmacy Quality Scheme 2020 to 2022.' Antibiotics 12, no. 4 (2023): 793.

Heath, Bethany, Stephanie Evans, David S Robertson, Julie V Robotham, Sofía S Villar, and Anne M Presanis. 'Evaluating Pooled Testing for Asymptomatic Screening of Healthcare Workers in Hospitals.' BMC Infectious Diseases 23, no. 1 (2023): 900.

Henderson, Katherine L, Ayoub Saei, Rachel Freeman, AP Johnson, Diane Ashiru-Oredope, Sarah M Gerver, and Susan Hopkins. 'Intermittent Point Prevalence Surveys on Healthcare-Associated Infections, 2011 and 2016, in England: What Are the Surveillance and Intervention Priorities?', Journal of Hospital Infection 140 (2023): 24-33.

Higgins, H, R Freeman, A Doble, G Hood, J Islam, S Gerver, KL Henderson, A Demirjian, S Hopkins, and D Ashiru-Oredope. 'Appropriateness of Acute-Care Antibiotic Prescriptions for Community-Acquired Infections and Surgical Antibiotic Prophylaxis in England: Analysis of 2016 National Point Prevalence Survey Data.' Journal of Hospital Infection 142 (2023): 115-29.

Hilton, Kira LF, Antonis A Karamalegkos, Nyasha Allen, Lauren Gwynne, Bree Streather, Lisa J White, Karen B Baker, Samantha A Henry, George T Williams, and Helena J Shepherd. 'Controlling the Structure of Supramolecular Fibre Formation for Benzothiazole Based Hydrogels with Antimicrobial Activity against Methicillin Resistant Staphylococcus Aureus.' Journal of Materials Chemistry B 11, no. 17 (2023): 3958-68.

Hilton, Kira LF, Howard Tolley, Jose L Ortega-Roldan, Gary S Thompson, J Mark Sutton, Charlotte K Hind, and Jennifer R Hiscock. 'Phospholipid Headgroup Composition Modulates the Molecular Interactions and Antimicrobial Effects of Sulfobetaine Zwitterionic Detergents against the 'Eskape' Pathogen Pseudomonas Aeruginosa.' Chemical Communications 59, no. 70 (2023): 10504-07. Hyams, Catherine, David T Arnold, Robyn Heath, Zahin Amin-Chowdhury, David Hettle, Gabriella Ruffino, Paul North, Charli Grimes, Norman K Fry, and Philip Williams. 'Parapneumonic Effusions Related to Streptococcus Pneumoniae: Serotype and Disease Severity Trends from 2006 to 2018 in Bristol, UK.' BMJ Open Respiratory Research 10, no. 1 (2023): e001440.

Hyams, Catherine, Robert Challen, David Hettle, Zahin Amin-Chowdhury, Charli Grimes, Gabriella Ruffino, Rauri Conway, Robyn Heath, Paul North, and Adam Malin. 'Serotype Distribution and Disease Severity in Adults Hospitalized with Streptococcus Pneumoniae Infection, Bristol and Bath, UK, 2006–2022.' Emerging Infectious Diseases 29, no. 10 (2023): 1953.

Jamrozy, Dorota, Guduru Gopal Rao, Theresa Feltwell, Theresa Lamagni, Priya Khanna, Androulla Efstratiou, Julian Parkhill, and Stephen D Bentley. 'Population Genetics of Group B Streptococcus from Maternal Carriage in an Ethnically Diverse Community in London.' Frontiers in Microbiology 14 (2023): 1185753.

Jauneikaite, Elita, Kate S Baker, Jamie G Nunn, Janet T Midega, Li Yang Hsu, Shweta R Singh, Alison L Halpin, Katie L Hopkins, James R Price, and Padmini Srikantiah. 'Genomics for Antimicrobial Resistance Surveillance to Support Infection Prevention and Control in Health-Care Facilities.' The Lancet Microbe 4, no. 12 (2023): e1040-e46.

Jones, Annie SK, Amy HY Chan, Kebede Beyene, Chloe Tuck, Diane Ashiru-Oredope, Victoria Rutter, and Rob Horne. 'Beliefs About Antibiotics, Perceptions of Antimicrobial Resistance, and Antibiotic Use: Initial Findings from a Multi-Country Survey.' International Journal of Pharmacy Practice 32, no. 1 (2024): 21-28.

Kamere, Nduta, Victoria Rutter, Derick Munkombwe, Dorothy Atieno Aywak, Eva Prosper Muro, Felix Kaminyoghe, Kalidi Rajab, Mashood Oluku Lawal, Naomi Muriithi, and Ndinda Kusu. 'Supply-Chain Factors and Antimicrobial Stewardship.' Bulletin of the World Health Organization 101, no. 6 (2023): 403.

Kim, Seong-Heun, Charlotte K Hind, Guilherme FS Fernandes, Jingyue Wu, Dorothy Semenya, Melanie Clifford, Caleb Marsh, Silvia Anselmi, A James Mason, and Kenneth D Bruce. 'Development of Novel Membrane Disrupting Lipoguanidine Compounds Sensitizing Gram-Negative Bacteria to Antibiotics.' ACS Medicinal Chemistry Letters 15, no. 2 (2024): 239-49.

Kingston, Rhys, Venanzio Vella, Koen B Pouwels, Johannes E Schmidt, Radwa A Abdelatif El-Abasiri, Eduardo Reyna-Villasmil, Nasreen Hassoun-Kheir, Stephan Harbarth, Jesús Rodríguez-Baño, and Evelina Tacconelli. 'Excess Resource Use and Cost of Drug-Resistant Infections for Six Key Pathogens in Europe: A Systematic Review and Bayesian Meta-Analysis.' Clinical Microbiology and Infection (2023). Lakha, Alishah, Naomi Fleming, Kimberly Sonnex, Tracey Thornley, Claire Anderson, Kieran Hand, and Diane Ashiru-Oredope. 'Evaluating the Role of Primary Care Pharmacy Technicians in Antimicrobial Stewardship (Ams) and Acne Management Using Target Resources.' JAC-Antimicrobial Resistance 6, no. 1 (2024): dlae011.

Lamagni, Theresa, Rebecca L Guy, Shiranee Sriskandan, Valérie Decraene, and Colin S Brown. 'Improving Maternal Outcomes through Early Recognition, Rapid Notification, and Investigation of Invasive Gas Infection.' The Lancet Microbe 4, no. 10 (2023): e766.

Larenas-Muñoz, Fernanda, Inés Ruedas-Torres, Laura Hunter, Alison Bird, Irene Agulló-Ros, Rebecca Winsbury, Simon Clark, Emma Rayner, and Francisco J Salguero. 'Characterisation and Development of Histopathological Lesions in a Guinea Pig Model of Mycobacterium Tuberculosis Infection.' Frontiers in Veterinary Science 10 (2023).

Leung, Stephanie, Clare F Collett, Lauren Allen, Suzanna Lim, Pete Maniatis, Shanna J Bolcen, Bailey Alston, Palak Y Patel, Gaurav Kwatra, and Tom Hall. 'Development of a Standardized Opsonophagocytosis Killing Assay for Group B Streptococcus and Assessment in an Interlaboratory Study.' Vaccines 11, no. 11 (2023): 1703.

Li, Ho Kwong, Xiangyun Zhi, Ana Vieira, Harry J Whitwell, Amelia Schricker, Elita Jauneikaite, Hanqi Li, Ahmed Yosef, Ivan Andrew, and Laurence Game. 'Characterization of Emergent Toxigenic M1uk Streptococcus Pyogenes and Associated Sublineages.' Microbial Genomics 9, no. 4 (2023): 000994.

Livermore, David M, Shazad Mushtaq, Anna Vickers, and Neil Woodford. 'Activity of Aztreonam/Avibactam against Metallo-B-Lactamase-Producing Enterobacterales from the Uk: Impact of Penicillin-Binding Protein-3 Inserts and Cmy-42 B-Lactamase in Escherichia Coli.' International Journal of Antimicrobial Agents 61, no. 5 (2023): 106776.

Mason, E, O Nsonwu, J Elmes, D Chudasama, C Pearson, L Hasan, R Hope, and SM Gerver. 'Increased Rates of Hospital-Onset Staphylococcus Aureus Bacteraemia in National Health Service Acute Trusts in England between June 2020 and March 2021: A National Surveillance Review.' Journal of Hospital Infection 143 (2024): 33-37.

McGuire, Emma, Ang Li, Simon M Collin, Valerie Decraene, Michael Cook, Simon Padfield, Shiranee Sriskandan, Chris Van Beneden, Theresa Lamagni, and Colin S Brown. 'Time to Negative Throat Culture Following Initiation of Antibiotics for Pharyngeal Group a Streptococcus: A Systematic Review and Meta-Analysis up to October 2021 to Inform Public Health Control Measures.' Eurosurveillance 28, no. 15 (2023): 2200573.

McGuire, Emma, Claire Neill, Simon M Collin, Hannah Higgins, Rebecca Guy, Mark Ganner, Juliana Coelho, Bruno Pichon, Russell Hope, and Colin S Brown. 'Is Panton–Valentine Leucocidin (PvI) Toxin Associated with Poor Clinical Outcomes in Patients with Community-

Acquired Staphylococcus Aureus Bacteraemia?', Journal of Medical Microbiology 72, no. 4 (2023): 001683.

Mehra, R, M Meda, B Pichon, V Gentry, A Smith, M Nicholls, Y Ryan, J Woods, and S Tote. 'Whole-Genome Sequencing Links Cases Dispersed in Time, Place, and Person While Supporting Healthcare Worker Management in an Outbreak of Panton–Valentine Leucocidin Meticillin-Resistant Staphylococcus Aureus; and a Review of Literature.' Journal of Hospital Infection 141 (2023): 88-98.

Mentasti, Massimo, Sophia David, Jane Turton, Mari Morgan, Luke Turner, Joseph Westlake, Jonathan Jenkins, Catie Williams, Sara Rey, and Joanne Watkins. 'Clonal Expansion and Rapid Characterization of Klebsiella Pneumoniae St1788, an Otherwise Uncommon Strain Spreading in Wales, UK.' Microbial Genomics 9, no. 9 (2023): 001104.

Michalsen, Benedikte Olsen, Alice XT Xu, Sarah L Alderson, Lars Bjerrum, Jamie Brehaut, Heiner C Bucher, Janet Clarkson, Eilidh Duncan, Jeremy Grimshaw, and Ronny Gunnarsson. 'Regional and National Antimicrobial Stewardship Activities: A Survey from the Joint Programming Initiative on Antimicrobial Resistance—Primary Care Antibiotic Audit and Feedback Network (Jpiamr-Paan).' JAC-Antimicrobial Resistance 5, no. 2 (2023): dlad048.

Miliani, K, B Migueres, D Verjat-Trannoy, JM Thiolet, S Vaux, P Astagneau, and collective the French Prevalence Survey Study Group. 'National Point Prevalence Survey of Healthcare-Associated Infections and Antimicrobial Use in French Home Care Settings, May to June 2012.' Eurosurveillance 20, no. 27 (2015).

Moon, Christopher, Eleanor Porges, Adam Roberts, and Joanna Bacon. 'A Combination of Nirmatrelvir and Ombitasvir Boosts Inhibition of Sars-Cov-2 Replication.' Antiviral Research 225 (2024): 105859.

Moore, Ginny, Ailbhe Barry, Jennifer Carter, Joseph Ready, Yu Wan, Mustafa Elsayed, Claire Haill, Minesh Khashu, O Martin Williams, and Colin S Brown. 'Detection, Survival, and Persistence of Staphylococcus Capitis Nrcs-a in Neonatal Units in England.' Journal of Hospital Infection 140 (2023): 8-14.

Moore, Hannah L, Cheryl Battersby, Chinthika Piyasena, Alicia Demirjian, and Theresa Lamagni. 'Assessing Variation in Neonatal Sepsis Screening across England.' Archives of Disease in Childhood-Fetal and Neonatal Edition 108, no. 4 (2023): 430-31.

Murdan, S, N Ali, J Darlow, E Christopher, F Tolani, and D Ashiru-Oredope. 'Enhancing the Training of Community Engagement Officers to Address Vaccine Hesitancy: A University and Local Authority Collaboration.' Perspectives in Public Health 143, no. 4 (2023): 190-92.

Mushtaq, Shazad, Anna Vickers, Neil Woodford, and David M Livermore. 'Activity of Aztreonam/Avibactam and Ceftazidime/Avibactam against Enterobacterales with

Carbapenemase-Independent Carbapenem Resistance.' International Journal of Antimicrobial Agents 63, no. 3 (2024): 107081.

Pagnossin, Davide, William Weir, Andrew Smith, Manuel Fuentes, Juliana Coelho, and Katarina Oravcova. 'Streptococcus Canis Genomic Epidemiology Reveals the Potential for Zoonotic Transfer.' Microbial Genomics 9, no. 3 (2023): 000974.

Parekh, Sejal, Kieran Hand, Lingqian Xu, Victoria Roberts, Fionna Pursey, Diane Ashiru-Oredope, and Donna M Lecky. 'Responding to Urinary Tract Infection Symptoms in England's Community Pharmacies.' Antibiotics 12, no. 9 (2023): 1383.

Parekh, Sejal, Catherine V Hayes, Jill Loader, Diane Ashiru-Oredope, Kieran Hand, Gemma Hicks, and Donna Lecky. 'The Use of the Target Antibiotic Checklist to Support Antimicrobial Stewardship in England's Community Pharmacies.' Antibiotics 12, no. 4 (2023): 647.

Perry-Duxbury, Meg, Sebastian Himmler, Job van Exel, and Werner Brouwer. 'Willingness to Pay for Health Gains from an International Integrated Early Warning System for Infectious Disease Outbreaks.' The European Journal of Health Economics 24, no. 6 (2023): 967-86.

Pitt-Kendall, Rachel, Clare Foster, Michael Rayment, Beata Orzechowska, Rufat Mammadov, Suneeta Soni, Simon Mortlock, Jodie Owen, Luke Uglow, and Michaela Joanne Day. 'Retrospective Testing for Mpox Virus in Routine Sti Screens from Men Who Have Sex with Men in England, August–October 2022.' Sexually Transmitted Infections 99, no. 8 (2023): 548-51.

Piyasena, Chinthika, Sorana Galu, Rie Yoshida, Devangi Thakkar, Joanna O'Sullivan, Catherine Longley, Katie Evans, Suzanne Sweeney, Giles Kendall, and Khadija Ben-Sasi. 'Comparison of Diagnoses of Early-Onset Sepsis Associated with Use of Sepsis Risk Calculator Versus Nice Cg149: A Prospective, Population-Wide Cohort Study in London, UK, 2020–2021.' BMJ open 13, no. 7 (2023): e072708.

Pople, Diane, Theodore Kypraios, Tjibbe Donker, Nicole Stoesser, Anna C Seale, Ryan George, Andrew Dodgson, Rachel Freeman, Russell Hope, and Ann Sarah Walker. 'Model-Based Evaluation of Admission Screening Strategies for the Detection and Control of Carbapenemase-Producing Enterobacterales in the English Hospital Setting.' BMC medicine 21, no. 1 (2023): 492.

Ragonnet-Cronin, Manon, Rungtiwa Nutalai, Jiandong Huo, Aiste Dijokaite-Guraliuc, Raksha Das, Aekkachai Tuekprakhon, Piyada Supasa, Chang Liu, Muneeswaran Selvaraj, and Natalie Groves. 'Generation of Sars-Cov-2 Escape Mutations by Monoclonal Antibody Therapy.' Nature Communications 14, no. 1 (2023): 3334.

Ramos, Celia, Kairi Lorenz, Marta Putrinš, Charlotte K Hind, Andres Meos, Ivo Laidmäe, Tanel Tenson, J Mark Sutton, A James Mason, and Karin Kogermann. 'Fibrous Matrices Facilitate

Pleurocidin Killing of Wound Associated Bacterial Pathogens.' European Journal of Pharmaceutical Sciences 192 (2024): 106648.

Read, Brieze, Monsey McLeod, Sarah Tonkin-Crine, Diane Ashiru-Oredope, Anna Quigley, Colin S Brown, and Donna M Lecky. 'Changes in Public Health-Seeking Behaviours for Self-Limiting Respiratory Tract Infections across England During the Covid-19 Pandemic.' European Journal of Public Health 33, no. 6 (2023): 987-93.

Riou, Julien, Christian L Althaus, Hester Allen, Michelle J Cole, Yonatan H Grad, Janneke CM Heijne, Magnus Unemo, and Nicola Low. 'Projecting the Development of Antimicrobial Resistance in Neisseria Gonorrhoeae from Antimicrobial Surveillance Data: A Mathematical Modelling Study.' BMC Infectious Diseases 23, no. 1 (2023): 252.

Robotham, Julie V, Evelina Tacconelli, Venanzio Vella, and Marlieke EA de Kraker. 'Synthesizing Pathogen-and Infection-Specific Estimates of the Burden of Antimicrobial Resistance in Europe for Health-Technology Assessment: Gaps, Heterogeneity, and Bias.' Clinical Microbiology and Infection 30 (2024): S1-S3.

Rodger, Gillian, Kevin Chau, Paz Aranega-Bou, Aysha Roohi, Ginny Moore, Katie L Hopkins, Susan Hopkins, A Sarah Walker, and Nicole Stoesser. 'A Workflow for the Detection of Antibiotic Residues, Measurement of Water Chemistry and Preservation of Hospital Sink Drain Samples for Metagenomic Sequencing.' Journal of Hospital Infection 144 (2024): 128-36.

Sanyaolu, Leigh N, Emily Cooper, Brieze Read, Haroon Ahmed, and Donna M Lecky. 'Impact of Menopausal Status and Recurrent Utis on Symptoms, Severity, and Daily Life: Findings from an Online Survey of Women Reporting a Recent UTI.' Antibiotics 12, no. 7 (2023): 1150.

Schwartz, Kevin L, Alice XT Xu, Sarah Alderson, Lars Bjerrum, Jamie Brehaut, Benjamin C Brown, Heiner C Bucher, An De Sutter, Nick Francis, and Jeremy Grimshaw. 'Best Practice Guidance for Antibiotic Audit and Feedback Interventions in Primary Care: A Modified Delphi Study from the Joint Programming Initiative on Antimicrobial Resistance: Primary Care Antibiotic Audit and Feedback Network (Jpiamr-Paan).' Antimicrobial Resistance and Infection Control 12, no. 1 (2023): 72.

Shamas, Nour, Elizabeth Stokle, Diane Ashiru-Oredope, and Evelyn Wesangula. 'Challenges of Implementing Antimicrobial Stewardship Tools in Low to Middle Income Countries (Lmics).' Infection Prevention in Practice 5, no. 4 (2023): 100315.

Shaw, David, Raquel Abad, Zahin Amin-Chowdhury, Adriana Bautista, Desiree Bennett, Karen Broughton, Bin Cao, Carlo Casanova, Eun Hwa Choi, and Yiu-Wai Chu. 'Trends in Invasive Bacterial Diseases During the First 2 Years of the Covid-19 Pandemic: Analyses of Prospective Surveillance Data from 30 Countries and Territories in the Iris Consortium.' The Lancet Digital Health 5, no. 9 (2023): e582-e93.

Sinnathamby, Mary A, Fiona Warburton, Rebecca Guy, Nick Andrews, Theresa Lamagni, Conall Watson, and Jamie Lopez Bernal. Epidemiological Impact of the Pediatric Live Attenuated Influenza Vaccine (Laiv) Program on Group a Streptococcus (Gas) Infection in England. Vol. 10. Open Forum Infectious Diseases: Oxford University Press US, 2023.

Słoczyńska, Alicja, Matthew E Wand, Lucy J Bock, Stefan Tyski, and Agnieszka E Laudy. 'Efflux-Related Carbapenem Resistance in Acinetobacter Baumannii Is Associated with Two-Component Regulatory Efflux Systems' Alteration and Insertion of Δabar25-Type Island Fragment.' International Journal of Molecular Sciences 24, no. 11 (2023): 9525.

Sonnex, Kimberley, Tracey Thornley, Naomi Fleming, Alishah Lakha, Donna M Lecky, Indira Pillay, Shazia Patel, Claire Anderson, Matthew Boyd, and Diane Ashiru-Oredope. 'Perceived Current and Future Roles of Uk-Based Community Pharmacy Professionals in the Long-Term Management of Acne.' Exploratory Research in Clinical and Social Pharmacy 11 (2023): 100310.

Spencer, Daniel, Yuetao Li, Yiling Zhu, J Mark Sutton, and Hywel Morgan. 'Electrical Broth Micro-Dilution for Rapid Antibiotic Resistance Testing.' ACS sensors 8, no. 3 (2023): 1101-08.

Stimson, J, Y Chen, R Hope, JV Robotham, S Ahmad, J Eddleston, and S Evans. 'Hospital Onset Sars-Cov-2 Infections in the Omicron Wave: Patterns of Infection in the Context of Asymptomatic Testing.' Journal of Hospital Infection 139 (2023): 158-60.

Szakmany, Tamas, Eleanor Fitzgerald, Harriet N Garlant, Tony Whitehouse, Tamas Molnar, Sanjoy Shah, Dong Ling Tong, Judith E Hall, Graham R Ball, and Karen E Kempsell. 'The 'Analysis of Gene Expression and Biomarkers for Point-of-Care Decision Support in Sepsis 'Study; Temporal Clinical Parameter Analysis and Validation of Early Diagnostic Biomarker Signatures for Severe Inflammation Andsepsis-Sirs Discrimination.' Frontiers in Immunology 14 (2024): 1308530.

Tanner, Judith, L Brierley Jones, Melissa Rochon, Nigel Westwood, Catherine Wloch, Ricky Vaja, Luke Rogers, Jeremy Dearling, Keith Wilson, and Rosalie Magboo. 'Barriers and Facilitators for Surgical Site Infection Surveillance for Adult Cardiac Surgery in a High-Income Setting: An in-Depth Exploration.' Journal of Hospital Infection 141 (2023): 112-18.

Thursz, Mark, Fuzia Sadiq, Julia A Tree, Peter Karayiannis, David WC Beasley, Wanwissa Dejnirattisai, Juthathip Mongkolsapaya, Gavin Screaton, Matthew Wand, and Michael J Elmore. 'Inhibition of Phosphodiesterase 12 Results in Antiviral Activity against Several Rna Viruses Including Sars-Cov-2.' Journal of General Virology 104, no. 7 (2023): 001865.

Turner, Rebecca, Jo Hart, Diane Ashiru-Oredope, Lou Atkins, Christopher Eades, Tim Felton, Emily Howlett, Stephen Rice, Laura Shallcross, and Fabiana Lorencatto. 'A Qualitative Interview Study Applying the Com-B Model to Explore How Hospital-Based Trainers Implement Antimicrobial Stewardship Education and Training in UK Hospital-Based Care.' BMC Health Services Research 23, no. 1 (2023): 770.

Turton, Jane F, Claire Perry, Kim McGowan, Jack A Turton, and Russell Hope. 'Klebsiella Pneumoniae Sequence Type 147: A High-Risk Clone Increasingly Associated with Plasmids Carrying Both Resistance and Virulence Elements.' Journal of Medical Microbiology 73, no. 4 (2024): 001823.

Unemo, Magnus, Michelle J Cole, Csaba Kodmon, Michaela Day, Susanne Jacobsson, Eszter Balla, Beatrice Bercot, Maria José Borrego, Dominique Caugant, and Michelle Cole. 'High Tetracycline Resistance Percentages in Neisseria Gonorrhoeae in Europe: Is Doxycycline Post-Exposure Prophylaxis Unlikely to Reduce the Incident Gonorrhoea Cases?', The Lancet Regional Health–Europe (2024).

van Tonder, Andries J, Frances McCullagh, Hanan McKeand, Sue Thaw, Katie Bellis, Claire Raisen, Liz Lay, Dinesh Aggarwal, Mark Holmes, and Julian Parkhill. 'Colonization and Transmission of Staphylococcus Aureus in Schools: A Citizen Science Project.' Microbial Genomics 9, no. 4 (2023): 000993.

Verma, Renu, Kalaiarasan Ellappan, Karen E Kempsell, and Noyal Mariya Joseph. 'Triage Test to Diagnose Presumptive Pulmonary Tuberculosis.' The Lancet Global Health 12, no. 2 (2024): e175-e76.

Wan, Yu, Ashleigh C Myall, Adhiratha Boonyasiri, Frances Bolt, Alice Ledda, Siddharth Mookerjee, Andrea Y Weiße, Maria Getino, Jane F Turton, and Hala Abbas. 'Integrated Analysis of Patient Networks and Plasmid Genomes to Investigate a Regional, Multispecies Outbreak of Carbapenemase-Producing Enterobacterales Carrying Both Bla Imp and Mcr-9 Genes.' The Journal of Infectious Diseases (2024): jiae019.

Wan, Yu, Akshay Sabnis, Zaynab Mumin, Isabelle Potterill, Elita Jauneikaite, Colin S Brown, Matthew J Ellington, Andrew Edwards, and Shiranee Sriskandan. 'Is 1-Related Large-Scale Deletion of Chromosomal Regions Harbouring the Oxygen-Insensitive Nitroreductase Gene Nfsb Causes Nitrofurantoin Heter resistance in Escherichia Coli.' Microbial Genomics 9, no. 9 (2023): 001102.

Waterlow, Naomi R, Ben S Cooper, Julie V Robotham, and Gwenan Mary Knight. 'Antimicrobial Resistance Prevalence in Bloodstream Infection in 29 European Countries by Age and Sex: An Observational Study.' Plops Medicine 21, no. 3 (2024): e1004301.

White, Andrew D, Andy C Tran, Laura Sibley, Charlotte Sarfas, Alexandra L Morrison, Steve Lawrence, Mike Dennis, Simon Clark, Sirine Zadi, and Faye Lanni. 'Spore-Fp1 Tuberculosis Mucosal Vaccine Candidate Is Highly Protective in Guinea Pigs but Fails to Improve on Bcg-Conferred Protection in Non-Human Primates.' Frontiers in Immunology 14 (2023): 1246826.

Zhi, Xiangyun, Ho Kwong Li, Hanqi Li, Zuzanna Loboda, Samson Charles, Ana Vieira, Kristin Huse, Elita Jauneikaite, Lucy Reeves, and Kai Yi Mok. 'Emerging Invasive Group a Streptococcus M1uk Lineage Detected by Allele-Specific PR, England, 2020.' Emerging Infectious Diseases 29, no. 5 (2023): 1007.

Zhong, Xiaomin, Diane Ashiru-Oredope, Alexander Pate, Glen P Martin, Anita Sharma, Paul Dark, Tim Felton, Claire Lake, Brian MacKenna, and Amir Mehrkar. 'Clinical and Health Inequality Risk Factors for Non-Covid-Related Sepsis During the Global Covid-19 Pandemic: A National Case-Control and Cohort Study.' EClinicalMedicine 66 (2023).

# **Chapter 9. Stakeholder engagement**

The ESPAUR Oversight Group is made up of a consortium of stakeholders. The following organisations are represented on the Oversight Group:

- Department of Health and Social Care (DHSC), including Dental Public Health, Office for Health Improvement and Disparities (OHID)
- DHSC Expert Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection (APRHAI)
- British National Formulary (BNF)
- British Society for Antimicrobial Chemotherapy (BSAC)
- Care Quality Commission (CQC)
- College of General Dentistry
- Health and Social Care Information Centre
- Independent or private sector healthcare
- IQVIA
- National Pharmaceutical Advisers Group
- National Institute of Health and Care Excellence (NICE)
- NHS England (NHSE)
- Patient representation
- 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
- Speicalist Pharmacy Service (SPS)
- UK Clinical Pharmacy Association: Pharmacy Infection Network (UKCPA PIN)
- Veterinary Medicines Directorate DEFRA
- Antimicrobial Resistance and Healthcare Associated Infectio (ARHAI) Scotland, NHS National Services Scotland
- Public Health Scotland
- Public Health Wales
- Public Health Agency Northern Ireland (Health and Social Care Northern Ireland -HSCNI)
- UKHSA (represented by individuals with appropriate expertise from HCAI, antimicrobial utilisation (AMU), AMR, Fungal and Sepsis Division, Behavioural Insights, Regions, Field Service and Communications teams)

# References

- 1. European Committee on Antimicrobial Susceptibility Testing (EUCAST). <u>Clinical</u> <u>breakpoints and dosing of antibiotics</u> 2024
- 2. O'Neill J. <u>Tackling drug-resistant infections globally: final report and recommendations</u> 2016
- 3. Department of Health and Social Care. <u>Tackling antimicrobial resistance 2019 to 2024:</u> <u>the UK's 5-year national action plan</u> 2019
- 4. UKHSA. English surveillance programme for antimicrobial utilisation and resistance (ESPAUR): Report 2020 to 2021 2021
- 5. UKHSA. English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 2021 to 2022 2022
- 6. UKHSA. English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 2022 to 2023 2023

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UKHSA is responsible for protecting every member of every community from the impact of infectious diseases, chemical, biological, radiological and nuclear incidents and other health threats. We provide intellectual, scientific and operational leadership at national and local level, as well as on the global stage, to make the nation's health secure.

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