UK Health Security Agency

English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 2022 to 2023

Annexe

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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 is taken from the AMR module.

In previous ESPAUR reports, hospital microbiology laboratories have reported antimicrobial susceptibility test results as ‘susceptible’, ‘intermediate’ or ‘resistant’. These categories were defined as follows:

1. Susceptible: a bacterial strain is said to be susceptible to a given antibiotic when its growth is inhibited in vitro by a concentration of the drug that is associated with a high likelihood of therapeutic success.
2. Intermediate: a bacterial strain is said to be intermediate when the concentration of antibiotic required to inhibit its growth in vitro is associated with an uncertain therapeutic outcome at standard antibiotic doses. It implies that an infection due to the isolate may be appropriately treated in body sites where the antibiotic is physically concentrated or when a high dosage of drug can be used.
3. Resistant: a bacterial strain is said to be resistant to a given antibiotic when the concentration required to inhibit its growth in vitro is associated with a high likelihood of therapeutic failure.

The breakpoint criteria for categorising clinical isolates as susceptible, intermediate or resistant to individual antibiotics have changed over time. As noted in the ESPAUR report 2019, in 2019 the EUCAST definitions 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 bloodstream infection (BSI) antimicrobial susceptibility analyses within the report are:

- third-generation cephalosporins comprised cefotaxime, ceftazidime, cefpodoxime and ceftriaxone, unless otherwise indicated
- carbapenems comprised meropenem or imipenem, except where neither were tested, in which cases results for ertapenem were used if available; the exception was for *Pseudomonas spp.* where ertapenem was excluded
- the only aminoglycoside included was gentamicin
- fluoroquinolones are ciprofloxacin, unless otherwise defined
- glycopeptides comprised vancomycin and/or teicoplanin
- colistin included results recorded as polymyxin

Data on the incidence of *Escherichia coli* (*E. coli*) and *Staphylococcus aureus* (*S. aureus)* bacteraemia was from the national mandatory surveillance schemes 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.

Data on additional bacterial pathogens causing hospital BSI in England can be found in Chapter 2 data tables.

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

Invasive group A streptococcal disease is notifiable in England and Wales under the Health Protection (Notification) Regulations 2010. Records of invasive group A streptococcal (GAS) based on isolates submitted to the UKHSA Antimicrobial Resistance and Hospital Associated Infections Reference Unit (AMRHAI, Colindale) were merged with SGSS laboratory reports (services have moved from the Respiratory and Vaccine Preventable Bacteria Reference Unit; RVPBRU). In this report, invasive specimens are defined as isolates from a normally sterile site, and include blood, cerebral-spinal fluid (CSF), bone, joint, brain and pleural fluid specimens.

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 87% in 2022 (84% in 2021; Annexe Table 2.1) and varied by local geography across the country (ranging between 82% and 93%; Annexe Table 2.2).

Annexe Table 2.1. Ascertainment factor applied to estimate total number of resistant bloodstream infections

Year	Mandatory *E. coli* bacteraemia reports	SGSS AMR *E. coli* bacteraemia reports	% ascertainment	Ascertainment factor
2018	42,557	36,686	86%	1.160
2019	43,715	37,996	87%	1.151
2020	37,823	31,012	82%	1.220
2021	37,889	31,838	84%	1.190
2022	38,639	33,599	87%	1.153

Annexe Table 2.2. Regional ascertainment factor applied to estimate total number of resistant bloodstream infections 2022:)

Region	Mandatory *E. coli* bacteraemia reports	SGSS AMR *E. coli* bacteraemia reports	% ascertainment	Ascertainment factor
London	5,128	4,197	82%	1.222
West Midlands	3,898	3,638	93%	1.071
East Midlands	3,327	3,104	93%	1.072
East of England	4,233	3,594	85%	1.178
North East	2,236	1,841	82%	1.215
Yorkshire and Humber	4,247	3,723	88%	1.141
North West	5,584	4,794	86%	1.648
South West	3,749	3,503	93%	1.070
South East	6,064	5,175	85%	1.172

Since April 2017 reporting of bacteraemia caused by *Klebsiella spp.* and *Pseudomonas aeruginosa* is also mandatory. 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 2.11 in the main report present the mandatory surveillance results for MRSA bacteraemia which represents a more accurate burden of MRSA in England. Whereas Figure 2.12 (resistance differences between MRSA and meticillin-susceptible *S. aureus* (MSSA)) is using SGSS AMR data. The ascertainment of *S. aureus* reports in SGSS AMR was 1.247.

In the absence of European Committee on Antimicrobial Susceptibility Testing (EUCAST) clinical breakpoints, daptomycin Minimum Inhibitory Concentrations (MICs) for enterococci were interpreted using ecological cut-offs (ECOFFs).

Estimating the burden of antibiotic-resistant bloodstream infections

Data used to update the pathogen and antibiotic 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 antibiotic and bacteria combinations used within the National Action Plan (NAP) AMR burden monitoring, is shown in Annexe Table 2.3. Estimates of the burden reported in this report differ slightly from those previously reported 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 (Annexe Table 2.1). This value was then applied to the other pathogens under surveillance to estimate the total number of BSIs 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 data tables accompanying the report.

For 2022, the AMR burden from BSI 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 2022 ascertainment factor, as shown in Annexe Table 2.1, was applied to all pathogens to estimate the total number of BSIs for each pathogen, except for *S. aureus* where the ascertainment factor of cases of *S. aureus* bacteraemia was used.

Annexe Table 2.3. Bacteria and antibiotic resistance categories included in the AMR burden analysis within the ESPAUR report; ESPAUR BSI AMR burden combinations and National Action Plan (NAP) estimate combinations

Bacteria	Antibiotic resistance	ESPAUR BSI AMR 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	✓	✓
	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)	✓	
Klebsiella oxytoca	Carbapenem-resistant	✓	
	Third-generation cephalosporin-resistant (excluding isolates also resistant to carbapenem)	✓	

Bacteria	Antibiotic resistance	ESPAUR BSI AMR burden	NAP estimate AMR burden
	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	✓	✓
	Aminoglycoside- and fluoroquinolone-resistant (excluding isolates also resistant to carbapenem)	✓	✓
Pseudomonas spp.	Carbapenem-resistant	✓	✓*
	Resistant to 3 or more antimicrobial groups (excluding isolates also resistant to carbapenem)	✓	✓*
Enterococcus spp.	Glycopeptide-resistant	✓	✓**
Staphylococcus aureus	Methicillin-resistant	✓	✓
Streptococcus pneumoniae	Penicillin- and macrolide-resistant (excluding isolates only resistant to penicillin)	✓	✓
	Penicillin-resistant (excluding isolates also resistant to macrolides)	✓	✓

* The NAP estimate AMR burden includes *Pseudomonas aeruginosa* only and not other *Pseudomonas* species.

** The NAP estimate AMR burden includes *E. faecalis and E. faecaium* only and not other *Enterococcus* species.

Acquired carbapenemase-producing Gram-negative bacteria

Acquired carbapenemase-producing Gram-negative bacteria continue to pose a significant public health concern in terms of threat to global health and economic stability (1).

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% 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 carbapenemase-producing Enterobacterales (CPE) in England, is one of the deliverables of the 5-year NAP introduced in May 2019 (2 to 5). 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 acquired carbapenemase-producing Gram-negative bacteria 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 Antibacterial resistance methods 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. Acquired carbapenemase-producing Gram-negative bacteria 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 Annexe Table 2.4, 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 2.4) has been identified, isolates should be sent to AMRHAI Reference Unit for confirmation.

Annexe Table 2.4. Distribution of carbapenemase genes covered by AMRHAI Reference Unit molecular assay (based on AMRHAI data)

Carbapenemase family	Associated with common 'host' organism		
	Enterobacterales	***Pseudomonas spp.***	***Acinetobacter spp.***
KPC	¥	<10	<10
OXA-48-like	¥	<10	0
NDM	¥	¥	¥
VIM	¥	¥	<10
IMP	¥	¥	¥
IMI/NMC-A	B	0	0
GES	¥	¥	0
FRI	<10	0	0
SME	<10[C]¥	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[A]	0	0	¥
OXA-58-like	0	0	¥

Quarterly mandatory laboratory returns data

National Health Service (NHS) acute trusts are required to complete quarterly mandatory laboratory returns (QMLR) for the 'total number of faecal specimens and rectal swabs taken for carbapenemase-producing Enterobacterales (CPE) screening' to the Healthcare-Associated Infections (HCAI) Data Capture System (DCS).

Reporting of quarterly totals of rectal swabs and faecal specimens taken for CPE screening was added to the mandatory quarterly laboratory returns section of the HCAI DCS in October 2019

but became mandatory in October 2020. (This was notified to all acute trusts through the HCAI DCS information cascade system in October 2020).

Trust-level CPE screening QMLR data was extracted from the HCAI-DCS on 26 May 2023. Acute trust codes were linked to the Estate Returns Information Collection (ERIC) data for 2019 to 2020 to establish acute trust type. A full list of QMLR CPE screening totals for the January to December 2021 period are included by acute trust by region in Annexe Table 2.5, below, and by acute trust in the data tables accompanying the report.

Annexe Table 2.5 QMLR returns for the total number of rectal swabs and faecal screening specimens taken for CPE screening by region*, England, 2022

	Number of trusts			Total screens reported	
Region	**Submitted screens***	**Did not submit screens**	**Submitted data for all 4 quarters (%)**	**Number**	**%**
East of England	11	4	10 (67)	22,037	5.2
East Midlands	5	3	4 (50)	37,726	9.0
London	19	3	15 (68)	198,083	47.1
North East	6	1	5 (71)	6,149	1.5
North West	15	10	11 (44)	34,126	8.1
South East	17	1	16 (89)	32,376	7.7
South West	13	1	10 (71)	10,682	2.5
West Midlands	13	2	12 (80)	62,232	14.8
Yorkshire and Humber	12	1	11 (85)	16,886	4.0
Total	111	26	84 (61)	420,297	100.0

* For at least one calendar quarter during 2022.

For previous number of screens reported, see the previous 2 ESPAUR reports.

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 the main ESPAUR 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 notified diseases reports which currently only include local laboratory reports.

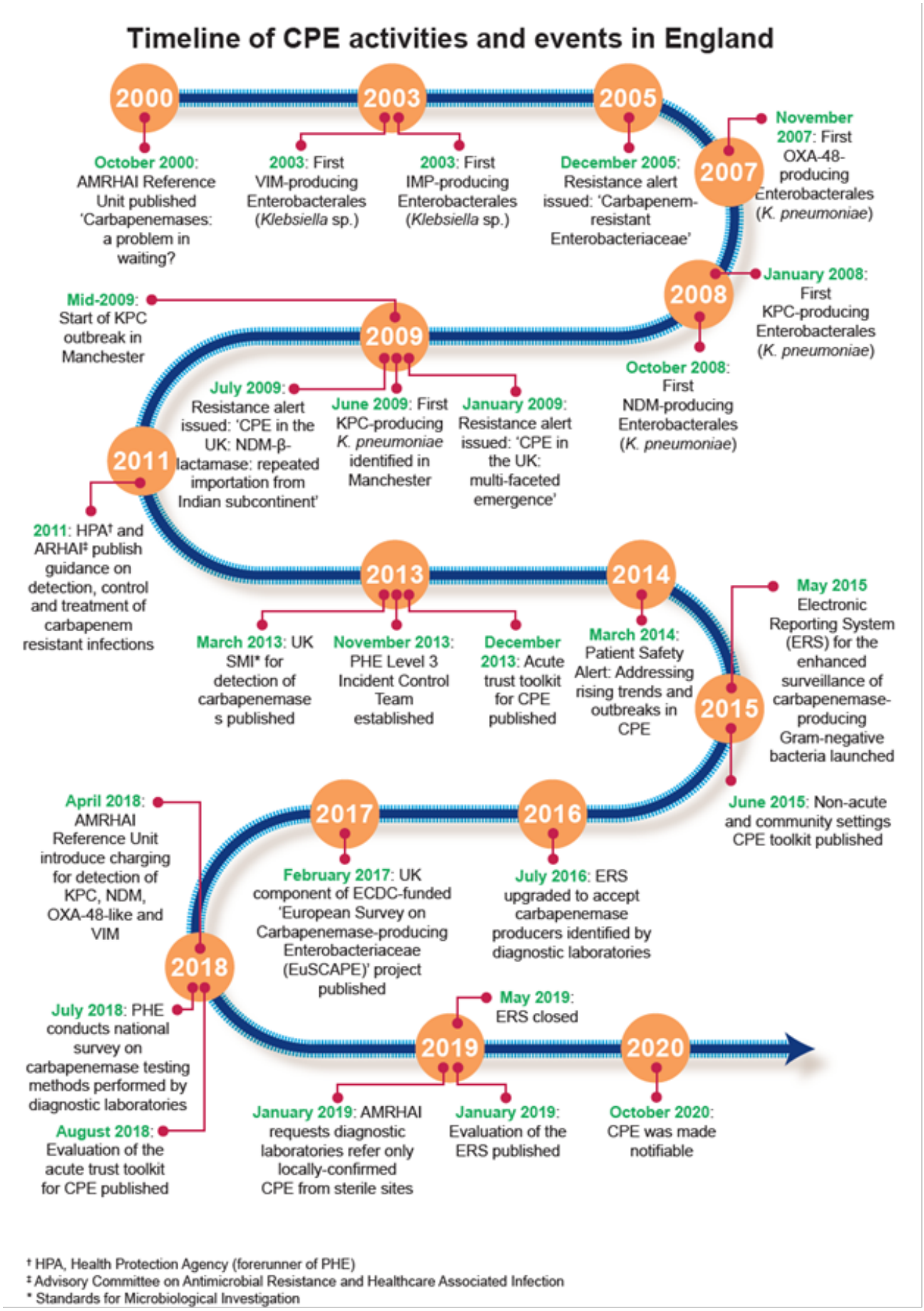
For the purpose of the ESPAUR report and for the notification data, specimen reports of a positive carbapenemase-producing Gram-negative bacteria fall into 3 specimen type categories: ‘invasive’, ‘screening’ and ‘everything else’. A full list of the specimen types and how they are grouped is available in the data tables accompanying this report, but at a high level:

- invasive 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, 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 carbapenemase-producing Gram-negative bacteria 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 CPE (Annexe Figure 2.1. An accessible text version of the figure is available below it).

Annexe Figure 2.1 Timeline of CPE activities and events in England



Text version of Annexe Figure 2.1

The timeline of CPE 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 CPE from sterile sites
- January 2019: Evaluation of the ERS published
- 1 May 2019: ESR closed
- 1 October 2020: CPE was made notifiable

- April 2022: CPE point prevalence survey in intensive care units (ICUs) in England
- September 2022: Update of CPE Framework guidance

End of text version of Annexe Figure 2.1

Critical antibiotic resistance in foodborne bacteria

Surveillance of antibiotic resistance in foodborne bacteria is undertaken by the UKHSA Gastrointestinal Bacterial Reference Unit. Antibiotic resistance data for referred samples in England is derived through whole genome sequencing (WGS), identifying genes that confer resistance. The antimicrobial resistance determinants were predicted using a validated bioinformatics tool 'Genefinder'.

Sexually transmitted infections

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 27 participating sexual health services (SHSs) (25 in England, 2 in Wales) and their 21 associated laboratories over a 2 to 3 month period each year. Gonococcal isolates are referred to the UKHSA AMR in Sexually Transmitted Infections (AMRSTI) national reference laboratory 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.

Tuberculosis

Data for AMR in tuberculosis data for 2001 to 2022 was extracted from the Enhanced Tuberculosis Surveillance system (ETS). More detail on the methods and data sources are described in the Tuberculosis in England annual report.

Antifungal resistance

Routine surveillance

Data on the laboratory reports of *Candida spp.* from 2018 to 2022 was obtained from UKHSA's SGSS, as described in the Antibacterial resistance section of Chapter 2. The SGSS CDR module was used to obtain incidence trends of candidaemia and the species distribution of *Candida spp.*, 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. These include *C. glabrata*, *C. kruseii* and *C. lusitaniae*, which have been reclassified as *Nakaseomyces glabratus, Pichia*

kudriavzveii and *Clavispora lusitaniae* respectively. The later 2 species had been excluded from contributing to the totals of the 2021 to 2022 ESPAUR report. However, this report includes species both currently and formerly defined as Candida. This may mean rates of candidaemia and species incidence reported may not reflect what has been reported in the previous report. A full list of species causing fungaemia (fungal bloodstream infections) identified from SGSS can be found as part of the monomicrobial and polymicrobial data tables included in the Chapter 3 data tables accompanying this report.

In previous ESPAUR reports, 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 *Candida* and former *Candida* species will focus on 3 antifungal drugs (amphotericin B, caspofungin and fluconazole). These drugs are focussed on as they 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 National Mycology Reference Laboratory (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 auris, the fluconazole-resistant 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. These are often in individuals who have recently travelled to areas where it is endemic, 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 also widespread. The marked association with travel is highlighted by the fact that we saw 31 isolates in 2019, down to 5 in 2020 when travel was not permitted rebounding to 24 in 2021 and 37 in 2022.

Dermatophytes

Another public health issue initially reported in India but now spreading to many other countries including the UK has been the emergence of a dermatophyte within the Trichophyton mentagrophytes/interdigitale group, now named as Trichophyton indotineae 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 has emerged as 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. With individual early cases in 2017 and 2018, since 2019 we have encountered more than 20 terbinafine-resistant clinical isolates per year of dermatophytes within this group in the UK, predominantly in the London area, which are either proven or suspected to be *T. indotineae*. This is almost certainly an underestimate as not all centres will refer such isolates to the UKHSA Mycology Reference Laboratory.

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. In some countries, notably The Netherlands, where levels of environmental resistance are high this has led to guidelines suggesting dual therapy at least initially in such patients until azole-susceptibility has been established. There are several commercial PCR tests to detect the 2 most common mutations associated with this phenomenon, but phenotypic testing is recommended when an isolate is available.
There is also the well-recognised emergence of resistance to one or more azole agents in patient who are receiving pro-longed or repeated azole therapy for chronic conditions due to Aspergillus. In these cases any one or more of a long list of mutations described to date may be present, or indeed a novel undocumented mutation, so there are no molecular tests currently available to detect these and the best approach, as always when an isolate is available, is to test it specifically with in vitro susceptibility tests.

Perspective from the Mycology Reference Centre, Manchester

The NHS Mycology Reference Centre Manchester (MRCM) offers a highly specialised diagnostic service primarily serving Manchester, north of England and Scotland but also receives daily referrals from throughout the UK and beyond. We provide a wide range of specialised mycological tests and have a considerable research and development portfolio. The Mycology Reference Centre Manchester is a well-established, UKAS/ISO 15189-accredited service providing an integrated conventional and molecular diagnostic service.

The NHS MRCM provides a specialist medical mycology reference service for patients attending the National Aspergillosis Centre, Wythenshawe Hospital, Manchester University Foundation Trust (MFT), and other specialist clinics, centres and hospitals throughout the UK and Europe. The MRCM, in partnership with the National Aspergillosis Centre, is the only UK Diamond level European Confederation of Medical Mycology (ECMM) Centre of Excellence for the diagnosis and treatment of fungal infections. The vision, scope and research activities can be viewed on the ECMM website.

The laboratory is an integral part of The Manchester Fungal Infection Network which unifies NHS services and University of Manchester research and teaching functions, creating one of the leading centres for medical mycology in Europe. The network is made up of over 100 NHS doctors, Clinical Scientists, Mycology Technologists, nurses and University of Manchester researchers. The MRCM laboratories are well equipped with a full range of analytical and automated platforms and enjoy the support of infectious diseases and respiratory clinical teams. The MRCM is a EUCAST Antifungal Susceptibility Testing Collaborative Laboratory and an European Fungal PCR Initiative Collaborative Centre. The MRCM aims to continue to deliver a patient-focussed service with an international reputation and be a premier supplier of mycology diagnostics in the NHS. We are implementing ambitious plans for modernising and improving service delivery, in particular rapid diagnosis of fungal infection and antifungal resistance.

The MRCM acts as a training and research centre in Medical Mycology in the UK, and it is a member of the UK Clinical Mycology Network. Furthermore, the MRCM provides undergraduate (University of Manchester Medical School) and post-graduate (PhD programmes in Medical Mycology) level education for the University of Manchester, and the European Society for Clinical Microbiology and Infectious Diseases. It also provides placements and training for registrars in infection training (Microbiology, Infectious Diseases, Respiratory Medicine). The MRCM is an integral component of the Manchester Fungal Infection Network which includes the National Aspergillosis Centre and the Manchester Fungal Infection Group.

MRCM total activity continued to increase in 2022, mainly due to high demand of the biomarker tests (galactomannan and Beta-D-glucan on serum and respiratory samples), return of normal clinical activities and centralisation of the processing of superficial fungal infection diagnostics (skin, hair, nails) in Manchester and North West. Over the last 4 years, the monthly activity has more than doubled. The MRCM team leads continuous auditing of the use of fungal diagnostics in critically ill patients with a focus on antifungal stewardship as well as resource management (for example, appropriate re-testing intervals).

Trends in resistance

Due to change of LIMS systems, antifungal susceptibility testing data were available only for 686 yeast and mould isolates (6,518 in 2021). These had been processed following the EUCAST standard.

In general, there were no radical changes in Candida or other ascomycetous yeast susceptibilities compared to previous years. There is a continued trend for decreased

fluconazole susceptibility in Candida albicans (84% ‘susceptible’ in 2021 versus 78% in 2022) whilst there was no significant change in Candida parapsilosis fluconazole susceptibility (95% ‘susceptible’ in 2021 versus 97% in 2022). Following the update of EUCAST breakpoints for echinocandins and interpretation change from 'intermediate' to 'susceptible, increased exposure', more Candida parapsilosis isolates were reported as 'susceptible, increased exposure’ rather than ‘resistant’ to echinocandins (85% of micafungin ‘susceptible, increased exposure’ in 2022 versus 94% ‘intermediate’ in 2021). One *Candida auris* isolate was identified in 2022 (fluconazole MIC 64mg/L, itraconazole MIC 0.03 mg/L, voriconazole 0.25 mg/L, micafungin MIC 0.125 mg/L, anidulafungin MIC 1 mg/L, amphotericin B MIC 0.5 mg/L).

Antifungal susceptibility profiles of Aspergillus spp strains tested at the MRCM did not change radically in 2022 compared to previous years. For example, 83% of the A. fumigatus isolates were susceptible to voriconazole in 2021 versus 82% in 2022. Also, in 2021 95% of A. fumigatus isolates were susceptible to Amphotericin B but this increased to 99.7% in 2022. We continue to see a spectrum of cryptic species of *Aspergillus fumigatus* isolated from patients with chronic and allergic aspergillosis with elevated MIC for azoles and other antifungals. In addition, there seems to be more cases of invasive infections caused by non-fumigatus Aspergillus, including resistant strains. These appear to be small numbers, but we are auditing this.

At MRCM, pyrosequencing of the *A. fumigatus* cyp51A gene of positive Aspergillus PCR products when parallel culture is negative is used to detect mutations associated with azole resistance. Fifty clinical specimens were processed in 2022. Mutations associated with resistance to one or more of the mould active azoles (including pan azole resistance) was detected in 54% of the samples. Mutations associated with environmentally acquired resistance (TR34/L98H) counted for 41% of these. The high prevalence of resistance detected with this method reflects the patient population and type of infection this test is used in (breakthrough infections whilst on prophylaxis or treatment).

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 weekly national flu reports during the active influenza season and summarised in the influenza annual report for each flu season.

Human immunodeficiency virus (HIV)

The detection of HIV resistance in drug-naïve people indicates the transmission of drug-resistant 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 2016 in both drug-naïve and treatment-experienced people with HIV by the UK National HIV Drug Resistance Database (DRD), which received results of resistance tests performed as part of routine care from 15 participating virology laboratories. The last available UK HIV DRD data is from 2016 and support from the Medical Research Council ended in 2020.

More recent data is available from the UKHSA's Antiviral Unit (AVU). Within national HIV surveillance programs, samples from individuals with newly-diagnosed HIV-1 are routinely submitted to UKHSA for recency testing as part of the Recent Infection Testing Algorithm (RITA).

Hepatitis C virus (HCV)

Recommended first line 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 direct-acting antiviral (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 AVU provides a HCV genotyping and resistance testing service for the NHS and receives approximately 1,500 samples per year. Prior to 2019, resistance testing was available for HCV subtype 1a only.

Subsequently, testing has been performed with 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. The data used in this report only includes subtype 1a NS5A samples from years 2016 to 2021, as prior to 2019 it was the only genotype with available data.

Herpes simplex virus (HSV)

The UKHSA AVU is the only laboratory in the UK offering a phenotypic drug susceptibility testing service for HSV. Through this service, the AVU has generated an archive of hundreds of phenotypically characterised clinical isolates over the past 13 years. Recently the archive has been sequenced and together with previously published data, this led to the development of a genotype-to-phenotype database called herPHEgen®. The database contains approximately 10% novel resistance-associated mutations and polymorphisms and this number continues to grow. This has proven to be an invaluable tool that has enabled us to offer a much faster antiviral resistance testing service to the NHS.

Parasitic 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. 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 mid-year population estimates 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 regions and presented at this level.

A SPINE trace was performed on records of patient episodes to identify those with reported 30-day all-cause mortality. Case fatality rates were calculated at 30 days in line with the 30-day all-cause fatality subsequent to MRSA, MSSA and Gram-negative bacteraemia and *C. difficile*, 2021 to 2022 report protocol.

The index of multiple deprivation (IMD) is a way of summarising how deprived people are within an area, based on a set of factors that includes their levels of income, employment, education and local levels of crime. Episodes were linked to IMD using patient postcode (and GP or laboratory postcode where patient postcode was unavailable) and the IMD decile score was identified by the lower super output area the patient resided in.

The Office for Health Improvements and Disparities developed a method for assigning ethnic group 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 decile level for England. Incidence rates are calculated per 100,000 population per year using the Office for National Statistics mid-year population estimates. At the time of publication, 2022 estimates were not yet available and therefore 2021 was used as a proxy for 2022.

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

Analyses were completed using Stata v15 and v17 (StataCorp).

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:

- quarterly reports on acquired carbapenemase-producing Gram-negative bacteria identified in human samples in England
- notifications of infectious diseases (NOIDs)
- *Escherichia coli* (*E. coli*): guidance, data and analysis
- *Pseudomonas aeruginosa*: guidance, data and analysis
- Klebsiella species: guidance, data and analysis
- *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)
- Laboratory surveillance of paediatric bloodstream infections and antimicrobial resistance in England
- pyogenic and non-pyogenic streptococcal bacteraemia annual data from voluntary surveillance
- group A streptococcal infections activity during the 2021 to 2022 season
- Fingertips public health UKHSA data: AMR local indicators
- UK One Health Report: antibiotic use and antibiotic resistance in animals and humans
- Point prevalence survey of healthcare-associated infections and antimicrobial use in European acute care hospitals 2016 to 2017

- EARS-Net (European Antimicrobial Resistance Surveillance Network) data
- Central Asian and European Surveillance of of Antimicrobial Resistance (CAESAR) data
- GLASS (Global Antimicrobial Resistance and Use Surveillance System) AMR routine data surveillance
- 'Infection control matters' on Apple Podcasts
- the European Union Summary Report on Antimicrobial Resistance in zoonotic and indicator bacteria from humans, animals and food in 2019 to 2020
- Tuberculosis in England: national quarterly reports
- National flu and COVID-19 surveillance reports: 2021 to 2022 season

Supplementary analyses

Antifungal resistance

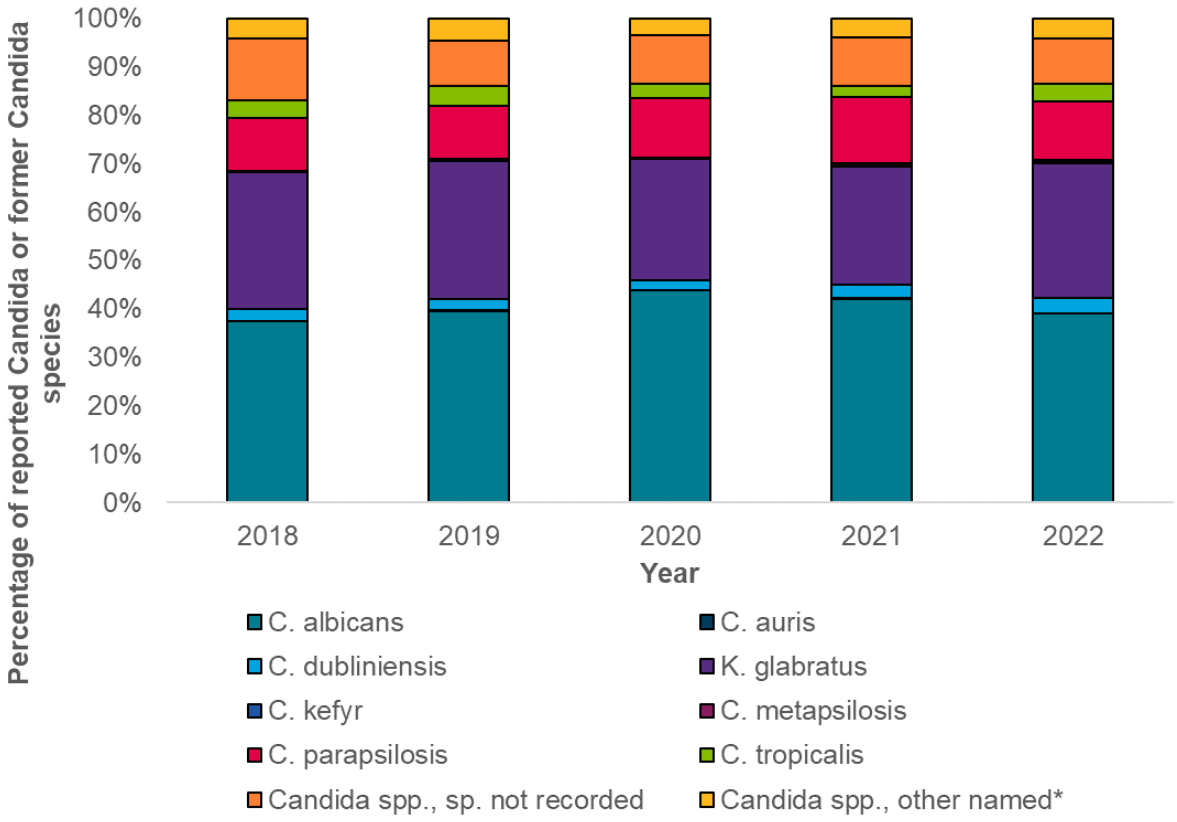
Incidence of candidaemia by region, and species frequency

Regionally, variation in incidence of candidaemia can be seen. The region with the highest rate of candidaemia in 2022 was the North East (4.8 per 100,000 population), closely followed by the North West (4.6 per 100,000 population). The lowest recorded rate continued to be in Yorkshire and Humber (3.0 per 100,000 population), as it has been for the past 5 years. Further regional data for incidence from 2018 to 2022 can be found in the Chapter 2 data tables.

Annexe Figure 2.2, below, shows *Candida albicans* was the most frequently isolated *Candida* species across the 5-year period, accounting for 40% of candidaemia in 2022 (883 out of 2,265). In common with many other surveillance studies the second most frequently reported species was *Nakaseomyces glabratus* (formerly *Candida glabrata*), which was identified in 29% (631) of candidaemia episodes in 2022.

The frequency of isolating these 2 species has not changed significantly in the last 5 years, with *C. albicans* and *C. glabrata* accounting for 38% (687 out of 1,828) and 28% (516 out of 1,828) of isolated species in 2018, respectively. This is not the case for all species, with *C. parapsilosis* increasing from 11% of isolated species in 2018 to 13% in 2022. The number of isolates also increased from 200 in 2018 to 274 in 2022 (37% increase). There was one *C. auris* bloodstream infection reported to SGSS in 2022. During 2022, 10% of *Candida* isolates were not identified to species level, a decrease from the 13% not recorded in 2018.

Annexe Figure 2.2. Reports of sterile site isolates of *Candida* and former *Candida* by species, 2018 to 2022



* including *C. africana*, *C. blankii*, *C. haemulonii*, *Pichia cactophila* (previously *C. inconspicua*), *Pichia kudriavzveii (C. kruseii) Clavispora lusitaniae* (*C. lusitaniae*), *Starmerella magnoliae* (*C. magnoliae*), *Nakaseomyces nivariensis* (*C. nivariensis*), *Pichia norvegensis* (*C. norvegensis*), *C. orthopsilosis*, *Nakazawaea peltata* (*C. peltata*), *C. sake*, *Starmerella sorbosivorans* (*C. sorbosivorans*), *Pichia jadinii* (*C. utilis*).

Bloodstream isolates from organisms previously classified as *Candida*

Candida glabrata, Candida kruseii and *Candida lusitaniae* have been reclassified as Nakaseomyces glabratus, *Pichia kudriavzveii* and *Clavispora lusitaniae* respectively. These changes better reflect their true lineage and is significant as *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* species of innate or emergent resistance to amphotericin B.

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 slideset, both available from the ESPAUR report web page.

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 the Annexe.

Secondary care

Information on the use of antibiotics 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.

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 antibiotics for this report is based on the Anatomical Therapeutic Chemical / Daily Defined Dose (ATC/DDD) index 2019 managed by the World Health Organization (WHO) at Collaborating Centre for Drug Statistics Methodology.

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

Third level pharmacological sub-grouping within ATC group ‘J01’

Penicillins (‘β-lactam antibacterials, penicillins’) include extended-spectrum penicillins, β-lactamase sensitive and resistant penicillins, and β-lactamase inhibitors either alone or in combination with penicillins.

‘Other β-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

The classification of antifungals for this report are also based on the ATC/DDD index 2021 managed by the WHO Collaborating Centre for Drug Statistics Methodology. Data covered all antifungals in the ATC group ‘J02’, (antimycotics for systemic use) and one additional systemic antifungal outside the 'J02' group, terbinafine (D01BA02).

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 Office National Statistics (ONS). Hospital admission data for each year was extracted from Hospital Episode Statistics (HES) from NHS Digital. In addition, hospital admissions by speciality were extracted from NHS digital for the financial year 2021 to 2022. 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) have not been included for 2 trusts: The Royal Marsden NHS Foundation Trust (acute specialist) and Frimley Health NHS Foundation Trust (acute large)

This was related to these trusts having incomplete HES data (the denominator) by specialty for the period between 2018 to 2022. Please note that admissions by speciality are published annually by NHS Digital and 2021 to 2022 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 $^{+}$. STATA 15 was used in all analysis.

Other community settings categories

A table defining how community settings have been mapped to the setting categories used within the report.

Other community settings	Setting category
Other	Other
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

Other community settings	Setting category
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
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	No data reported
Other: justice estate	No data reported
Prison	Custody

Trusts definitions

Trusts definitions in the ESPAUR report are based on the Estates Returns Information Collection (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.

Trust	Definition
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

Department speciality to department group look-up table.

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

Department speciality	Department group
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
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

Department speciality	Department group
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

Surveillance of the clinical use and supply of COVID-19 novel therapeutic agents utilises treatment request data from Blueteq, and medicines supply data from Rx-info.

Data sources

The Blueteq form was created as an output by the stewardship team within UKHSA's therapeutics programme. The most recent date of extraction for this report was 13 June 2023, and data was restricted to the period between 1 October 2021 and 31 December 2022.

The Blueteq system manages high-cost drugs for NHS England and as such contains clinical requests made for neutralising monoclonal antibodies (nMAB) and antiviral therapies used for the treatment of patients with COVID-19. Not all treatment requests may have resulted in patients receiving treatment with these drugs, but the electronic or patient prescribing data were not accessible. Requests for patient neutralising monoclonal antibodies (nMAB) and antiviral therapies of interest are recorded in the Blueteq system, with data extracts received by UKHSA on a weekly basis (with all cumulative treatment requests up to midnight of the previous Sunday included).

Data analysis

Total treatment requests from 1 January 2022 to 31 December 2022 by therapy were included for (Casirivimab with imdevimab (Ronapreve), Molnupiravir, Nirmatrelvir plus ritonavir (Paxlovid), Remdesivir and Sotrovimab). Rates of treatment requests by group (region, age group, ethnicity) were estimated by dividing the number of treatments by the COVID-19 case numbers (per 100,000) in that group over the specified time period.

Rates by region were estimated by dividing the COVID-19 case numbers (per 100,000) which were extracted from the UKHSA COVID-19 dashboard by each region over the specified time period.

STATA 17 was used in all medicines supply data analysis.

Chapter 4. Antimicrobial stewardship

Evaluation of the ‘How to…’ acne treatment resources in primary care and feasibility of implementation in community pharmacy

Annex Table 4.1 Mean 5-point Likert responses to COM-B survey components from pharmacy professionals working in general practice who completed both the initial and follow-up surveys

1. Capability

Capability	Mean (S.D.) n=141		p value
	Initial	Follow-up	
I have enough knowledge to manage people with acne	3.00 (1.21)	-	
I am confident in managing people with acne	2.79 (1.23)	-	
I am able to give self-care advice to people with acne	3.61 (1.14)	-	
I have enough knowledge to undertake reviews with patients with repeated or long-term use of antibiotics for acne management	2.96 (1.23)	-	
I am confident undertaking clinical review for patients with repeated or long-term use of antibiotics for acne management	2.82 (1.24)	-	
I understand the risks of long-term antibiotic treatment	4.28 (0.79)	-	
I have the skills to run searches on my clinical system	4.08 (1.16)	-	
I understand the review criteria for stepping up treatment for acne	2.89 (1.27)	-	
I understand the review criteria for a trial-off antibiotic treatment for acne	2.89 (1.29)	-	
I understand when onward referral is needed	3.01 (1.32)	-	
Capability mean	3.23 (0.52)	-	
Capability mean pharmacy technician respondents (n=20)	2.70 (0.94)	-	

Capability	Mean (S.D.) n=141		p value
	Initial	Follow-up	
Capability mean (respondents completing initial and follow-up n=19)	3.68 (0.40)	4.11 (0.29)	0.000

n = sample size; S.D, standard deviation

2. Opportunity

Opportunity	Mean (S.D.) n=141		p value
	Initial	Follow-up	
I have the opportunity to run searches on the practice's clinical system for quality improvement initiatives	3.48 (1.55)	-	
Antimicrobial stewardship and antibiotic prescribing review are a priority in the practices I work in	3.86 (0.90)	-	
Antimicrobial stewardship and antibiotic prescribing review are a PCN priority	3.61 (1.04)	-	
I am able to undertake quality improvement initiatives on areas of prescribing that I have an interest in	3.91 (1.02)	-	
There are support staff to run searches on my behalf	3.48 (1.19)	-	
Opportunity mean	3.67 (0.22)	-	
Opportunity mean (respondents completing initial and follow-up n=19)	3.85 (0.24)	4.08 (0.28)	0.007

n = sample size; S.D, standard deviation

3. Motivation

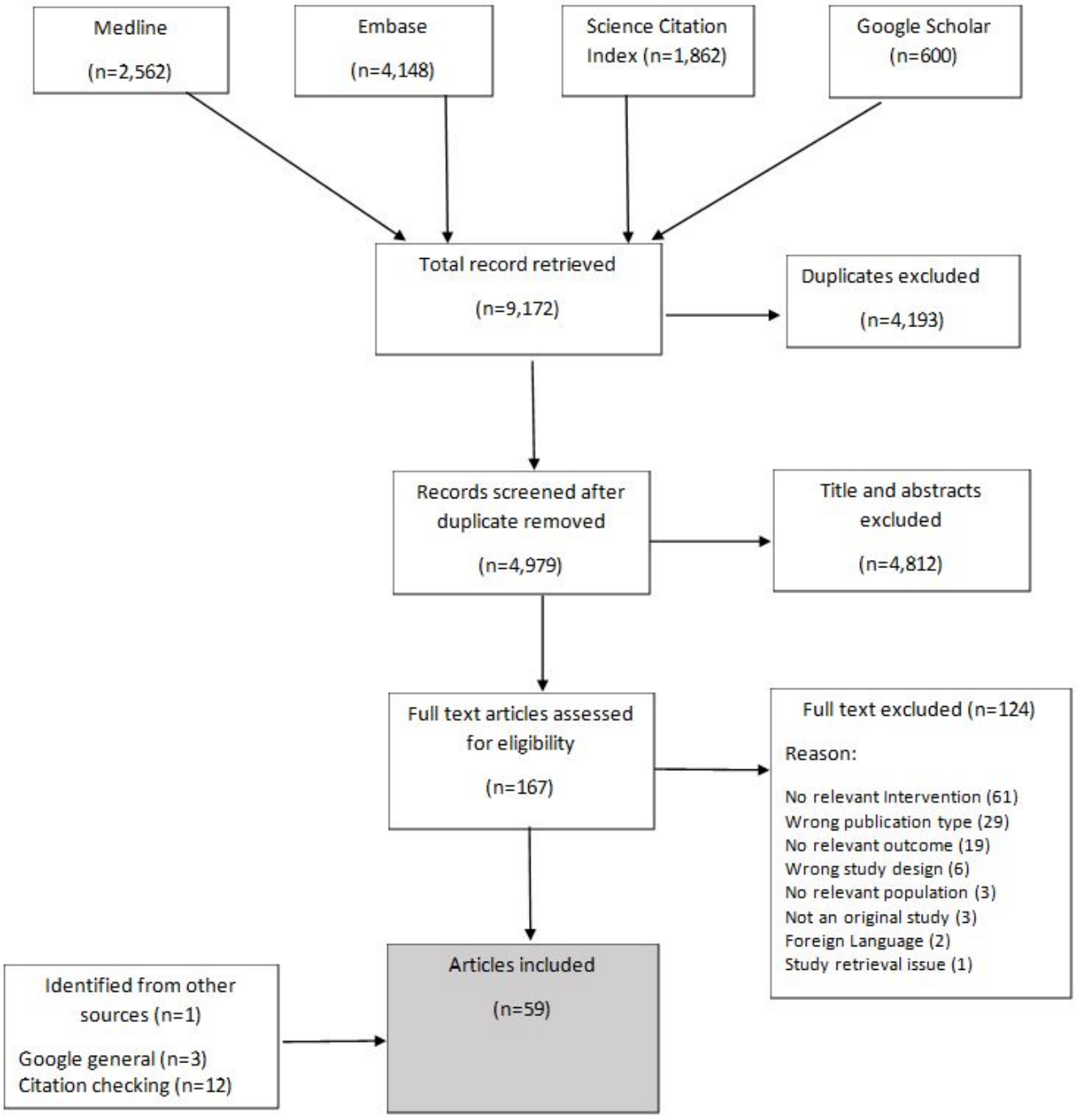
Opportunity	Mean (S.D.) n=141		p value
	Initial	Follow-up	
Appropriate prescribing of antibiotics is of high importance in the context of other competing NHS priorities	4.32 (0.79)	-	
Appropriate self-care advice is important to avoid unnecessary antibiotic use for acne	4.50 (0.82)	-	
Managing the prescribing of antibiotics for acne appropriately can impact on antibiotic resistance	4.54 (0.74)	-	
Managing acne appropriately is important for the patient's quality of life	4.72 (0.56)	-	

Opportunity	Mean (S.D.) n=141		p value
	Initial	Follow-up	
I routinely share quality improvement outcomes with my colleagues	3.84 (1.07)	-	
The review of patients on treatment for acne gives me job satisfaction	3.52 (0.90)	-	
Motivation mean	4.24 (0.42)	-	
Motivation mean (respondents completing initial and follow-up n=19)	4.35 (0.47)	4.51 (0.32)	0.007

n = sample size; S.D, standard deviation

Improving healthcare professionals' interactions with patients to tackle antimicrobial resistance: a systematic review of interventions, barriers and facilitators

Annex Figure 4.1. PRISMA flowchart of study selection



Text version of Annexe Figure 4.1.

Figure 4.1 shows a PRISMA flow diagram of the study selection process for the systematic review on improving healthcare professionals' interactions with patients to tackle antimicrobial resistance.

Four boxes in a row at the top contain the texts 'Medline n= 2,562'; 'Embase n=4,148'; 'Science Citation Index n=1,862'; 'Google Scholar n=600'.

Four arrows link these boxes to a box below which records total record retrieved as n=9,172. An arrow links to a box the right which contains the text 'Duplicates excluded, n=4,193'. A second arrow links to a box below which contains the text 'Records screened after duplicates removed, n=4,979'.

An arrow links from this box to a box on the right of the image contains the text title and abstracts excluded, n=4,812.

A second arrow links to a box below which contains the text 'Full text articles assessed for eligibility, n=167'.

An arrow links to a third box on the right of the image which contains the text 'Full text excluded, n=124' and lists reasons, namely: No relevant intervention (61), wrong publication type (29), no relevant outcome (19), wrong study design (6), no relevant population (3), not an original study (3), foreign language (2), study retrieval issue (1).

A second arrow links to a box at the bottom of the image which contains the text 'Articles included, n=59'.

An arrow links from this box to one on the left which includes the text 'Identified from other sources, n=1; google general (n=3); citation checking (n=12)'.

End of text version of Annexe Figure 4.1.

Chapter 6. Professional and public education and training

Antibiotic Guardian

Pledges made on other country pages in 2022 included 131 from African, 100 from South African, 1 from Australian, 16 from the Dutch, 16 from French, and 4 from German pages respectively. See Table 6.6 for breakdown of pledges from pharmacy teams from 2014 to 2022.

Annexe Table 6.1. A summary of Antibiotic Guardian pledges made on the main pledge page by pharmacy teams each year, from 2014 to 2022, with breakdown of the sub-category of pledger. These sub-categories were not available in 2014 and the 'Community pharmacist' sub-category was introduced in 2018

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

Annexe Table 6.2. Summary of the organisational AMS pledge activity in 2022, broken down by the type of organisation, from across UK, Canda, India, Spain and South Africa

Organisation type	Number of registrations in 2022
Charity	2
Community pharmacy	13
Government (local)	2
GP practice	8
Hospital (secondary care)	18
National NHS organisation	6
NHS primary care	5
NHS trust or health and social care trust (NI)	12
Private healthcare	4
Regional NHS organisation (for example, CCG, local commissioning group)	4
Veterinary and animal care	1
Other	14
Total	89

Assessment of global AMR campaigns conducted to alter public awareness and antimicrobial use behaviours: a rapid review

Annexe Figure 6.1. PRISMA diagram outlining the study selection process

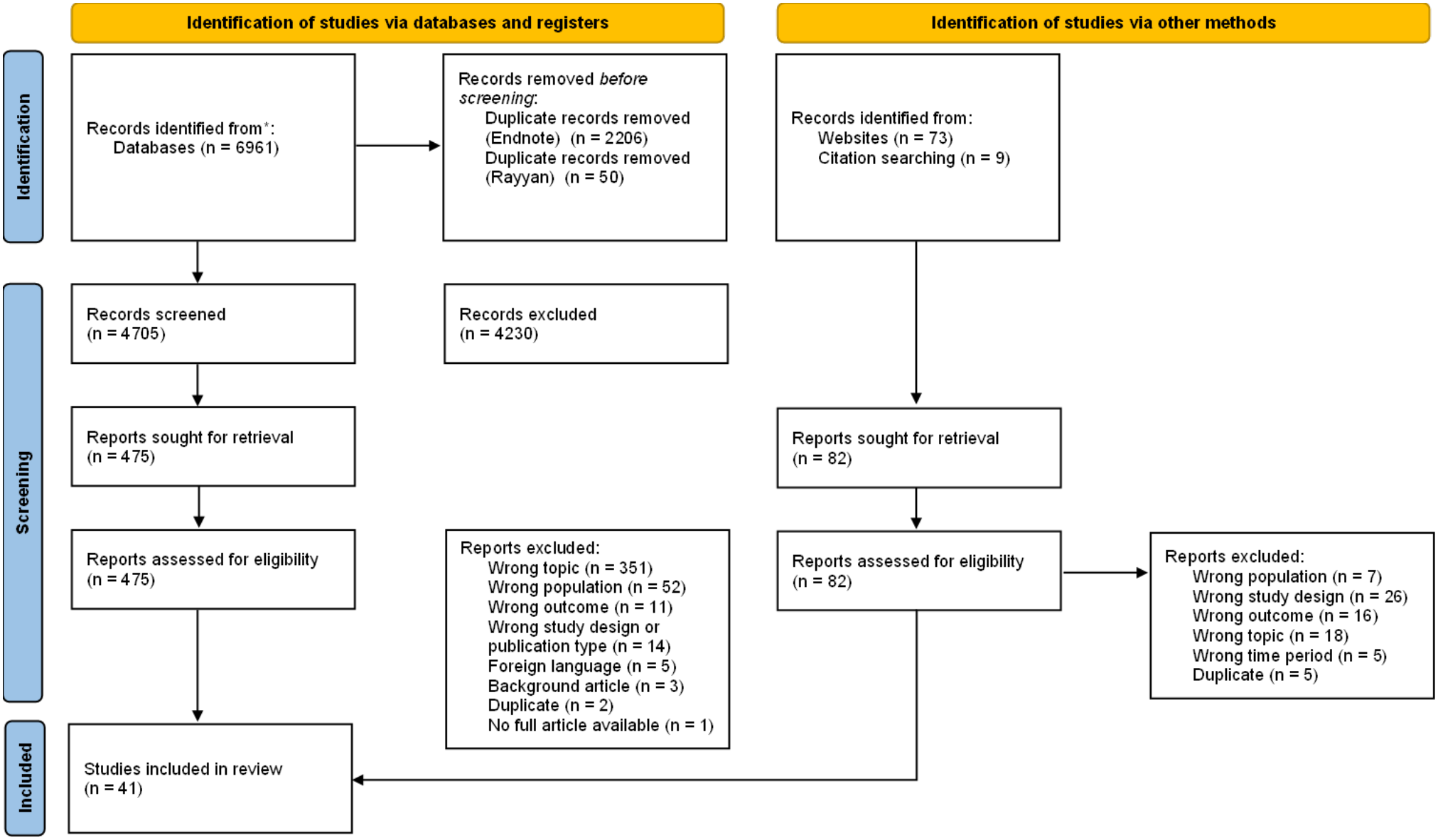
This diagram is from Page MJ, McKenzie JE, Bossuyt PM, Boutron I, Hoffmann TC, Mulrow CD and others. 'The PRISMA 2020 statement: an updated guideline for reporting systematic reviews' British Medical Journal 2021: volume 372, page n71. doi: 10.1136/bmj.n71

Text version of Annexe Figure 6.1.

This diagram shows the process for study selection, including (a) identification of studies via databases and registers and (b) identification of studies via other methods.
Identification of studies via databases and registers. There were 6961 records identified from databases. Duplicate records were removed before screening via EndNote (n=2206) and Rayyan (n=50). Of the 4705 remaining, 4230 records were excluded, yielding 475 records sought for retrieval. This led to the assessment of 475 reports assessed for eligibility, 439 of which were excluded for the following reasons: wrong topic (n=351); wrong population (n=52); wrong outcome (n=11); wrong study design or publication type (n=14); foreign language (n=5); background article (n=3); duplicate (n=2); and no full article available (n=1).

Identification of studies via other methods. There were 73 records identified from websites and 9 records identified from citation searching. As part of the screening process, these 82 reports were sought for retrieval and assessed for eligibility. Reports were excluded for the following reasons: wrong population (n=7); wrong study design (n=26); wrong outcome (n=16); wrong topic (n=18); wrong time period (n=5); and duplicate (n=5).
The process yielded a total of 41 studies included in the review.

End of text version of Annexe Figure 6.1.


Identification of studies via databases and registers
Identification of studies via other methods
Identification
Screening
Included
Records identified from*:
Databases (n = 6961)
Records removed *before screening*:
Duplicate records removed (Endnote) (n = 2206)
Duplicate records removed (Rayyan) (n = 50)
Records identified from:
Websites (n = 73)
Citation searching (n = 9)
Records screened
(n = 4705)
Records excluded
(n = 4230)
Reports sought for retrieval
(n = 475)
Reports sought for retrieval
(n = 82)
Reports assessed for eligibility
(n = 475)
Reports excluded:
Wrong topic (n = 351)
Wrong population (n = 52)
Wrong outcome (n = 11)
Wrong study design or publication type (n = 14)
Foreign language (n = 5)
Background article (n = 3)
Duplicate (n = 2)
No full article available (n = 1)
Reports assessed for eligibility
(n = 82)
Reports excluded:
Wrong population (n = 7)
Wrong study design (n = 26)
Wrong outcome (n = 16)
Wrong topic (n = 18)
Wrong time period (n = 5)
Duplicate (n = 5)
Studies included in review
(n = 41)

Cost effectiveness of AMR campaigns

Annexe Table 6.3. Summary of included studies

Study 1: Dekker and colleagues (2019)

Country: Netherlands

Study design: CEA conducted alongside RCT

Model: No modelling. Bootstrap analysis using 5,000 samples conducted to address uncertainty

Time horizon: two weeks

Payer perspective: Societal

Population: Children under 18 years old with symptoms of RTI (and their parents) who consult GP

Interventions: Online training for GPs and a written information booklet of parents

Outcomes: Mean cost per patient in intervention and control groups. Percentage decrease in antibiotic prescribing. Incremental cost-effectiveness ratio (ICER) for cost per percentage decrease in antibiotic prescribing

Study 2: Mamum and colleagues (2019)

Country: Canada

Study design: Partial economic evaluation with cost analysis based on interrupted time series modelling

Model: Statistical model – interrupted time series regression of antibiotic prescription rates. No modelling of cost

Time horizon: 9 years (comparison from 2005 prior to intervention until end-2014)

Payer perspective: Limited societal perspective

Population: Population of British Columbia (BC), Canada

Interventions: DBND program: includes freely accessible guidelines and continuing health education for prescribers, direct outreach through schools, daycares and community care

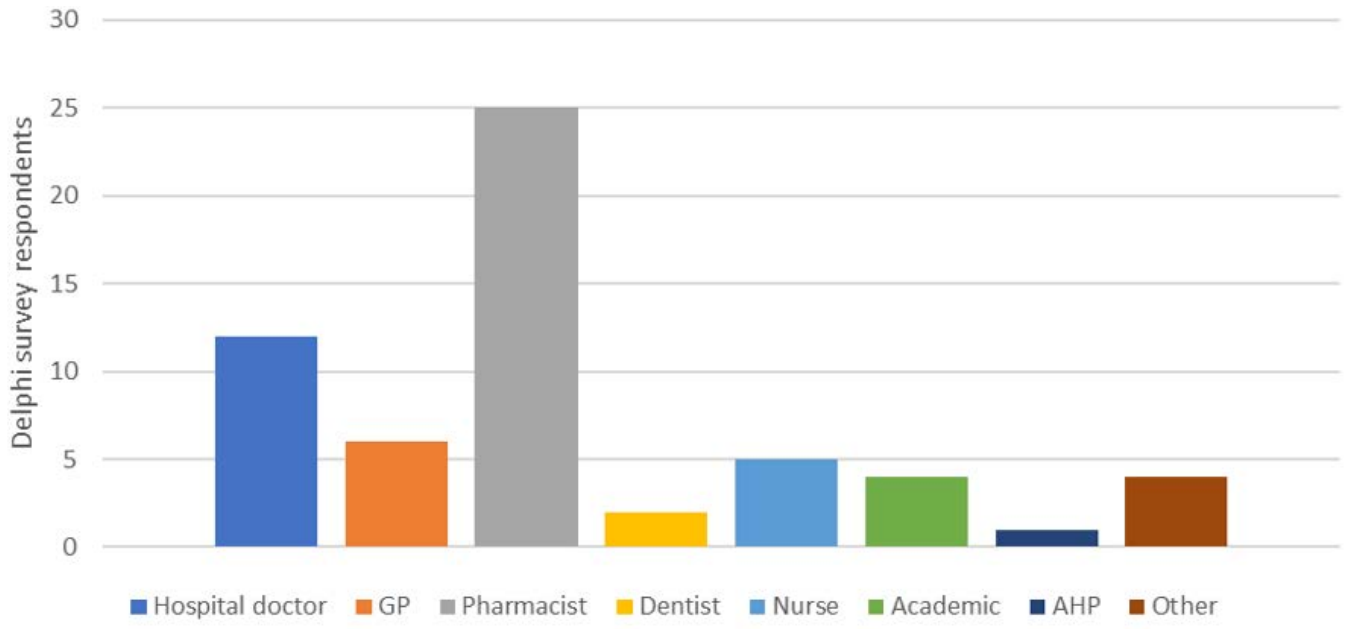
facilities using a workforce of volunteer health sciences, students and pharmacists, and public campaigns ranging from transit ads to social media

Outcomes: Average monthly prescription rates per 1,000 population, mean monthly prescription rates by antibiotic class, reduction in average monthly cost of antibiotics (adjusted for drug unit cost) before and after modelling, reduction in tottal cost of antibiotics during intervention period and cost savings per $1 invested

Updating the Antimicrobial Prescribing and Stewardship (APS) Competency Framework

To facilitate the the updating of the competency framework domains and their corresponding statements were assessed for their validity and the need for any potential edits. Descriptors were evaluated using a Likert scale to determine their level of essentialness. Additionally, feedback and comments on the list of potential domains, statements, and descriptors were collected. The results underwent statistical analysis, and the feedback was collated to incorporate relevant changes within the framework.

Annexe Figure 6.2. Illustrates the multidisciplinary professions of the Delphi survey respondents of which there were 59 in total



Chapter 7. Research

10-year overview of Health Protection Research Unit (HPRU) projects generating public health and patient impact

University of Oxford HPRU

HPRU1

2015 to 2016

Demonstration that fluoroquinolone prescribing, and not improved infection control, is the major driver of reductions in the incidence and transmissibility of *C. difficile* infection.

2017 to 2018

Identifying routes of transmission of a new ‘super-fungus’ *Candida auris*: Our research shows that environmental survival appears to be key to *Candida auris* persistence and transmission in healthcare settings, and led to successful infection control measures containing the outbreak. This reinforces the need to carefully investigate a patient’s environment and, in particular, the use of multi-use patient equipment.

What is driving increases in *Escherichia coli* (*E. coli*) bloodstream infections?: Our evidence indicates that the increase in number of *E. coli* bloodstream infections is largely occurring in the community (cases not associated with hospitals) and interventions need to be developed accordingly. The increase does not primarily appear to be due to patients with evidence of previous urinary tract infections.

Klebsiella pneumoniae carbapenamase outbreak: Our evidence indicates that the current interventions in place are insufficient to adequately control or eliminate KPC.

2018 to 2019

Real-Time Whole Genome Sequencing in Partner Notification and Management of Neisseria gonorrhoeae: We have developed a tool using whole genome sequencing which can track *Neisseria gonorrhoea* transmission and predict resistance processing a culture or direct from sample.

New technology can predict antibiotic resistance in *Mycobacterium tuberculosis*: Our research demonstrated that whole genome sequencing can accurately assess susceptibility of *M. tuberculosis* isolates to 4 first-line drugs, improving patient care and helping to reduce antibiotic resistance.

Predicting antibiotic resistance in *E. coli* via whole-genome sequencing: Our research shows that whole genome sequencing can accurately identify the causes of a particular type of

commonly used antibiotic (co-amoxiclav) resistance in *E. coli*, more precisely than phenotyping and most algorithms do this poorly and machine learning is still suboptimal.

2019 to 2020
Bash the Bug a citizen science project: The work of the people participating improves the precision of the phenotyping of tuberculosis so the work identifying the variation causing antituberculosis drug resistance is improved yielding a more accurate test for drug resistance.

HPRU COVID-19 Response: The work supported Pillar 1, Pillar 2, Pillar 3 and Pillar 4 of the government's COVID-19 response. The investigations addressed validation of swabs and transport medium, lateral flow antibody tests, ELISA development and evaluation, and leadership of the ONS Epidemiological survey.

HPRU2

2020 to 2021
Lateral Flow Devices detect the majority of infectious individuals with COVID-19, including asymptomatic cases: Our study enabled the use of COVID-19 lateral flow devices to detect asymptomatic infection in hospitals and work places, use of daily testing of COVID-19 contacts to avoid quarantine, and large scale pre-event testing to enhance safer attendance.

2021 to 2022
Providing SARS-CoV-2 bioinformatics the world: Global Pathogen Analysis Service (GPAS): An online platform that automates the process of turning jumbled, raw genome sequencer data into information that can directly drive public health decisions. The services is offered free of charge for SARS-CoV-2.

The SARS-CoV-2 Immunity and Reinfection Evaluation (SIREN) study: investigating immunity and vaccine effectiveness throughout the evolving COVID-19 pandemic: The SARS-CoV2 Immunity and Reinfection Evaluation (SIREN) study is a unique, large-scale partnership with NHS healthcare workers providing an agile response to an evolving pandemic. It is one of the national core studies established in response to COVID-19 and a National Institute for Health Research (NIHR) urgent priority study, providing vital research into immunity and vaccine effectiveness. The SIREN study was established early in the pandemic with participants undergoing regular testing for up to 2 years. Analysis of these testing samples helps the UK to evaluate the immune response to COVID-19, build understanding of the protection offered by vaccines and provide insight into COVID-19 reinfections.

2022 to 2023
National carbapenemase-producing Enterobacterales admission screening strategies informed by model-based evaluation.

Imperial College London HPRU

HPRU1

2016 to 2017
Applying social sciences methodologies to antimicrobial prescribing; our group was the first to conduct this work, finding that positive prescribing and infection prevention and control behaviours are determined by a number of social factors including individual, team and organisational norms, dynamics and culture, To be successful interventions to improve these behaviours must take these factors into account.

Assessment of strategies for carbapenemase-producing Enterobacterales control; we looked at national screening and isolation recommendations and provided economic analyses of the impact of outbreak control in the NHS; over EURO 1.1m over 10 months for one outbreak with reduced ability to perform elective surgical procedures due to bed closures representing the greatest cost. Research also demonstrated that antimicrobial consumption data can provide a potential tool for forecasting emergence of carbapenemase-producing Enterobacterales and how routine NHS data can be used for effective surveillance.

2017 to 2018
National Estimate of the burden of *E.coli* on patient in-hospital mortality and length of stay. Our Health and Cost estimate of Bacteraemia in the Hospital Setting was subsequently used by NHS Improvement to develop an indicative tool showing NHS providers and commissioners how many infections are occur on a local level. The tool provides trust-level costing and excess mortality due to these infections by utilising the estimates of excess length of stay and mortality from our work.

2017 to 2018
Assessment of the national antimicrobial stewardship programme. Overall the findings from our study showed that the Quality Premium: 2015 to 2016 guidance was associated with a significant reduction in all antibiotic items and broad-spectrum antibiotic items prescribed. Overall there were no significant unintended consequences, or association between the Quality Premium and clinical outcomes in primary and secondary care, except for a few specific infectious conditions.

2017 to 2018
Group B streptococcus (GBS) late onset disease (LOD) arising in the Neonatal Intensive Care Unit (NICU): our work showed these are clusters, resulting from nosocomial horizontal transmission and were not necessarily sporadic or isolated events. These findings lead toa national-level genomic study of nosocomial GBS infections, in order to further inform national guidance.

2018 to 2019

‘Off-guideline’ antibiotic prescriptions for UTI: Our research on antibiotic prescriptions for UTI in comparison with the UKHSA national antibiotic prescribing guideline found that 64% of antibiotic prescriptions for uncomplicated UTI over the previous 9 years were not in line with guidance, although this was not found to put patients at risk of a subsequent BSI.

2020

Strain-specific link between Scarlet fever and invasive GAS infection rates; we identified that the increased proportion of pharyngitis and Scarlet fever strains in 2016, was the result of emm1/M1 strains. Our prospective, observational study in children attending schools and nurseries in London showed an intense level of transmission peaking at week 2 after initial case ascertainment, with infection in up to 50% of classroom contacts with a genomically identical strain. 20% of asymptomatic carriers were heavy shedders of GAS, and airborne transmission was identified as a major transmission route.

HPRU II

2020 to 2021

Hospital onset COVID infection (HOCI) Surveillance: We developed pragmatic case definitions for HOCI prior to national definition development and used data routinely collected through electronic healthcare systems to develop a novel surveillance system, which linked with national surveillance systems, to identify, monitor and reporting HOCI providing daily reports on incidence and trends over time to support HOCI investigation and geo-temporal reports using network analysis to interrogate admission pathways for common epidemiological links to infer transmission chains

Outbreak of GES-5–positive *Klebsiella oxytoca*, revealing nationwide circulation of a GES-5 carbapenemas encoding plasmid vector. This work demonstrated the translational potential of WGS to facilitate the development of rapid detection assays to produce clinically actionable information for routine use.

Bacterial and fungal co-infection of patients with COVID-19 research, helped to inform and was cited by, the WHO in their Interim Guidance on Clinical Management of COVID-19. It showed that only 8% of patients were reported as experiencing bacterial or fungal coinfection during hospital admission. Secondary analysis demonstrated wide use of broad-spectrum antibacterials, despite a paucity of evidence for bacterial coinfection. On secondary analysis, 1,450 out of 2,010 (72%) of patients reported received antimicrobial therapy. Our research showed that there was a lack of evidence to support frequent prescription of broad-spectrum empirical antimicrobials in patients with coronavirus associated respiratory infections.

2021 to 2022

The impact of COVID-19 on antimicrobial use, infection, and AMR. We investigated the pandemic’s impact on primary and secondary care antimicrobial prescribing and the resulting patient outcomes associated with observed changes in prescribing patterns and changes in methods of healthcare delivery. In primary care, were the first research team to report the

significant reduction in GP antibiotic during wave 1 and 2 of the pandemic (up to March 2021). This has led to further investigation of whether there have been any unintended consequences associated with reduced antibiotic use and delayed or missed treatment. In acute care, we assessed the incidence of healthcare associated bloodstream infections in both COVID-19 and non-COVID-19 patients, the results suggested that despite the rapid expansion of intensive care capacity during the COVID-19 surges, more patients acquired bloodstream infections, including those ones without COVID-19.

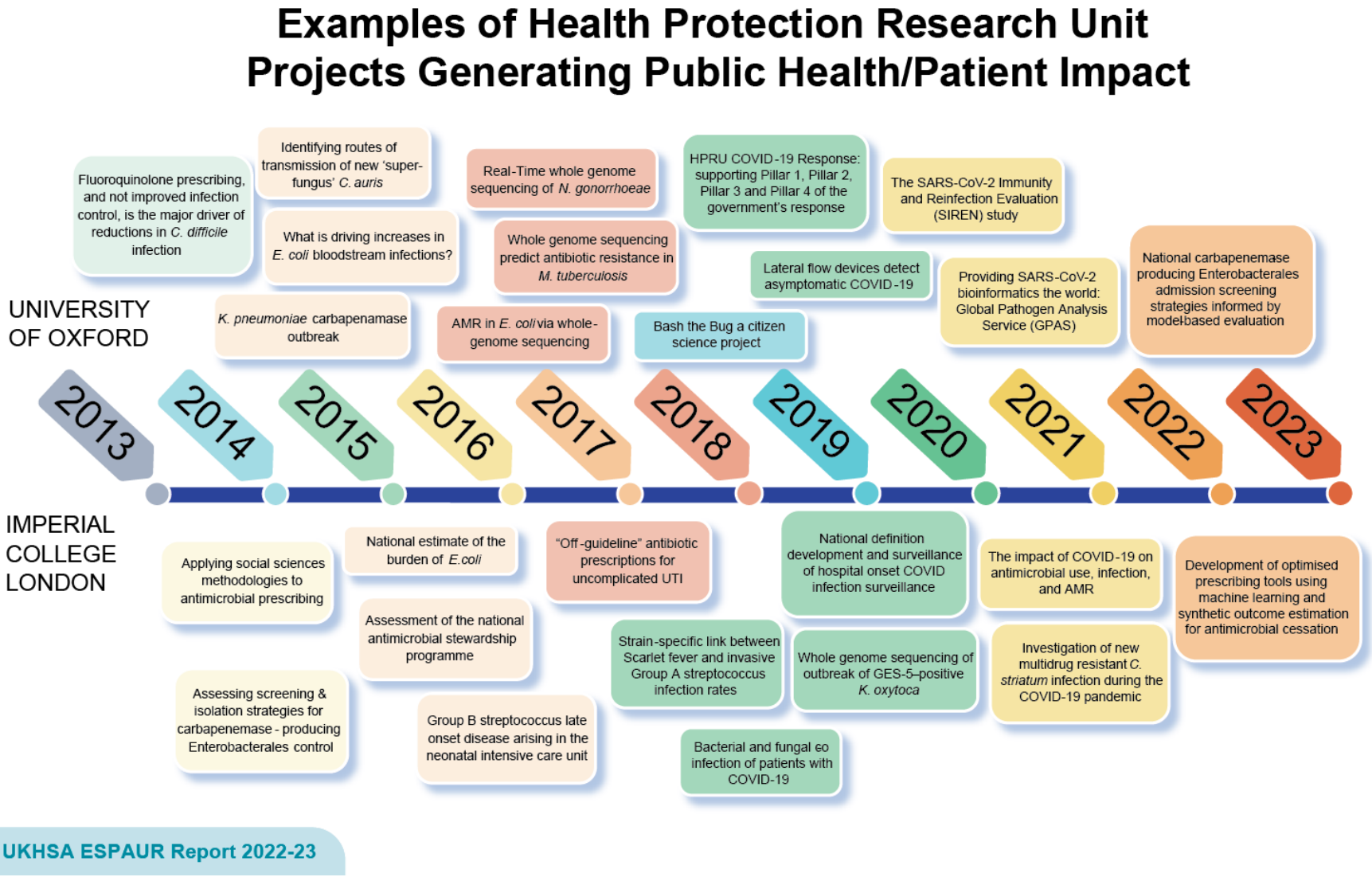
New multidrug resistant *Corynebacterium striatum* infection during the 2 COVID-19 waves was investigated within our NHS hospital network. Genomic analysis characterised the 2 genetically distinct clones of *C. striatum* circulating at the same time during the 1st COVID wave which emerged in intensive care patients during the first COVID-19 wave in the UK as a result of sudden changes in the healthcare system due to the pandemic.National surveillance has subsequently commenced to further characterise *C. striatum* isolates across different hospital networks nationally.

2022 to 2023

Optimised prescribing tools have been developed, including a triple quadrupole (LC/MS) method for the simultaneous quantitative measurement of cefiderocol and meropenem in serum, the development of machine learning and synthetic outcome estimation tool for individualised antimicrobial cessation and closed-loop control of continuous piperacillin delivery.

This timeline of research is shown in the following infographic.

Infographic showing examples of Health Protection Research Unit projects generating public health or patient impact 2013 to 2023



List of publications

A list of peer-reviewed publications from April 2022 to March 2023:

1. Agnew E, Kerrie KA, Viprey VF, Evans S, Davis GL, Hope R and others. ‘Impact of testing on Clostridioides difficile infection in hospitals across Europe: a mathematical model’ Clinical Microbiology and Infection 29 2023: number 6, issue 796, pages e1 to e96
2. Agnew E and Robotham JV. ‘Research on Antimicrobial Utilization and Resistance in England 2021 to 2022 (Espaur Report).’ Medical Sciences Forum 2022: volume 15, issue 1, page 17
3. Frances A, Brunt E, Humphries H, Cavell B, Leung S, Allen L and others. ‘Generation of a universal human complement source by large-scale depletion of Igg and Igm from pooled human plasma.’ Bacterial Vaccines: Methods and Protocols 2022: pages 341 to 362
4. Ashiru-Oredope D, Garraghan F, Olaoye O, Krockow EM, Matuluko M, Nambatya W and others. ‘Development and implementation of an antimicrobial stewardship checklist in Sub-Saharan Africa: a co-creation consensus approach’ Healthcare 2022: volume 10, issue 9, page 1,706
5. Ashiru-Oredope D, Nabiryo M, Yeoman A, Bell M, Cavanagh S, D’arcy N and others. ‘Development of and user feedback on a board and online game to educate on antimicrobial resistance and stewardship’ Antibiotics 2022: volume 11, issue 5, page 611
6. Bacon J, Waddell SJ, and Flores-Valdez MA. ‘Biofilms in tuberculosis: what have we learnt in the past decade and what is still unexplored?’ Tuberculosis 2022: volume 132, page 102,153
7. Benkő R, Matuz M, Pető Z, Weist K, Heuer O, Vlahović-Palčevski V and others. ‘Trends in the hospital-sector consumption of the who aware reserve group antibiotics in Eu/Eea countries and the United Kingdom, 2010 to 2018’ Eurosurveillance 2022: volume 27, issue 41, page 2,101,058
8. Bennet, KF, Guy RL, Gerver SM, Hopkins KL, Puleston R, Brown CS, 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 2023: volume 5, issue 2, page 100,281
9. Boles JE, Bennett C, Baker J, Hilton KLF, Kotak HA, Clark ER and others. ‘Establishing the selective phospholipid membrane coordination, permeation and lysis properties for a series of ‘druggable’ supramolecular self-associating antimicrobial amphiphiles’ Chemical Science 2022: volume 13, issue 33, pages 9,761 to 9,773
10. Bou-Antoun S, Falola A, Fountain H, Squire H, Brown CS, Hopkins S and others. ‘Antimicrobial consumption in England 2017 to 2021’ Medical Sciences Forum 2022: volume 15, issue 1, page 1
11. Casale E, Hayes CV, Lecky D, O’Neil L, Sides E, Cooper E, Pursey F and others. ‘National Antimicrobial Stewardship activities in primary and secondary care in England 2021 to 2022 (Espaur Report)’ Medical Sciences Forum 2022: volume 15, issue 1, page 14

12. Chan AHY, Beyene K, Tuck C, Rutter V, and Ashiru-Oredope D. ‘Pharmacist beliefs about antimicrobial resistance and impacts on antibiotic supply: a multinational survey’ JAC-Antimicrobial Resistance 2022: volume 4, issue 4, page 62
13. Cleary DW, Jones J, Gladstone RA, Osman KL, Devine VT, Jefferies JM, and others. ‘Changes in serotype prevalence of *Streptococcus pneumoniae* in Southampton, UK between 2006 and 2018’ Scientific Reports 2022: volume 12,issue 1, page 13,332
14. Coia JE, Wilson JA, Bak A, Marsden GL, Shimonovich M, Loveday HP and others. ‘Corrigendum to Joint Healthcare Infection Society (HIS) and Infection Prevention Society (IPS) guidelines for the prevention and control of meticillin-resistant *Staphylococcus aureus* (MRSA) in healthcare facilities’ The Journal of Hospital Infection 2022: volume 125, pages 92 to 93
15. Cunningham N, Casale E, Triggs-Hodge C, Brown CS, Hope R, Ashiru-Oredope D, and Hopkins S. ‘Introduction to the Espaur webinar and report 2021 to 2022: key findings and stakeholder engagement’ Medical Sciences Forum 2022, volume 15, issue 1, page 18
16. Davies H, Russell J, Varghese A, Holmes H, Soares MO, Woods B, Puig-Peiro R and others. ‘Developing a modeling framework for quantifying the health and cost implications of antibiotic resistance for surgical procedures’ MDM Policy and Practice 2023: volume 8, issue 1
17. Di Blasio S, Clarke M, Hind CK, Asai M, Laurence L, Benvenuti A, Hassan M and others. ‘Bolaamphiphile Analogues of 12-bis-THA Cl_2 are potent antimicrobial therapeutics with distinct mechanisms of action against bacterial, mycobacterial, and fungal pathogens’ Msphere 2023: volume 8, issue 1, page 00508
18. Euden J, Pallmann P, Grozeva D, Albur M, Stuart E Bond, Brookes-Howell L, Dark P and others. ‘Procalcitonin evaluation of antibiotic use in COVID-19 hospitalised patients (Peach): protocol for a retrospective observational study’ Methods and Protocols 2022: volume 5, issue 6, page 95
19. EvangelopoulosD, Shoen CM, Honeyborne I, Clark S, Williams A, Mukamolova GV and others. ‘Culture-free enumeration of mycobacterium tuberculosis in mouse tissues using the molecular bacterial load assay for preclinical drug development’ Microorganisms 2022: volume 10, issue 2, page 460
20. Ferguson PM, Clarke M, Manzo G, Hind CK, Clifford M, Sutton JM and others. ‘Temporin B forms hetero-oligomers with Temporin L, modifies its membrane activity, and increases the cooperativity of its antibacterial pharmacodynamic profile’ Biochemistry 2022: volume 61, issue 11, pages 1,029 to 1,040
21. Flintham L, Ashiru-Oredope D, Charlesworth J, Harrison R, and Dalgarno E. ‘A qualitative investigation of perceptions towards antibiotics by members of the public after choosing to pledge as an Antibiotic Guardian’ Health Expectations 2023: volume 26, issue 1, pages 440 to 451
22. Giles J and Roberts A. ‘*Clostridioides Difficile*: current overview and future perspectives’ Immunotherapeutics 2022: pages 215 to 245
23. Guy R, Higgins H, Rudman J, Fountain H, Bennet KF, Hopkins KL, Demirjian A and others. ‘Antimicrobial Resistance in England 2017 to 2021 (Espaur Report 2021 to 2022)’ Medical Sciences Forum 2022: volume 15, issue 13

24. Hand K, Ashiru-Oredope D, Beech E, Bou-Antoun S, Damant G, Fleming N, Hayes C and others. ‘Espaur Report 2021 to 2022 Chapter 5: NHS England Improvement and Assurance Schemes’ Medical Sciences Forum 2022: volume 15, issue 1, page 16
25. Hann M, Rosalie Allison, Mónica Truninger, Luís Junqueira, Alexandre Silva, Pia Touboul Lundgren, Virginie Lacroix Hugues and others. ‘Educating young consumers about food hygiene and safety with Safeconsume: a multi-centre mixed methods evaluation’ Education Sciences 2022: volume 12, issue 10, page 657
26. Harvey EJ, Hand K, Weston D, and Ashiru-Oredope D. ‘Development of national antimicrobial intravenous-to-oral switch criteria and decision aid’ Journal of Clinical Medicine 2023: volume 12, issue 6, page 2,086
27. Hayes CV, Lecky DM, Pursey F, Thomas A, Ashiru-Oredope D, Saei A, Thornley T and others. ‘Mixed-method evaluation of a community pharmacy antimicrobial stewardship intervention (Pamsi)’ Paper presented at the Healthcare, 2022
28. Hind C, Clifford M, Woolley C, Harmer J, McGee LMC, Tyson-Hirst I, Tait HJ and others. ‘Insights into the spectrum of activity and mechanism of action of MGb-BP-3’ ACS Infectious Diseases 2022: volume 8, issue 12, pages 2,552 to 2,563
29. Hopkins KL, Ellaby N, Ellington MJ, Doumith M, Mustafa N, Meunier D, and Woodford N. ‘Diversity of Carbapenemase-producing Enterobacterales in England as revealed by whole-genome sequencing of isolates referred to a national reference laboratory over a 30-month period’ Journal of Medical Microbiology 2022: volume 71, issue 5, page 001518
30. Horrocks V, Hind CK, Wand ME, Fady P, Chan J, Hopkins JC, Houston GL and others. ‘Nuclear magnetic resonance metabolomics of symbioses between bacterial vaginosis-associated bacteria’ Msphere 2022: volume 7, issue 3, pages e00166 to e00122
31. Kamere N, Garwe ST, Oluwatosin Olugbenga Akinwotu, Chloe Tuck, Eva M Krockow, Sara Yadav, Agbaje Ganiyu Olawale and others. ‘Scoping review of national antimicrobial stewardship activities in 8 African countries and adaptable recommendations’ Antibiotics 2022: volume 11, issue 9, page 1,149
32. Keating, Thomas, Samuel Lethbridge, Jon C Allnutt, Charlotte L Hendon-Dunn, Stephen R Thomas, Luke J Alderwick, Stephen C Taylor and Joanna Bacon. ‘Mycobacterium tuberculosis modifies cell wall carbohydrates during biofilm growth with a concomitant reduction in complement activation’ The Cell Surface 2021: volume 7, page 100,065
33. Ledda, Alice, Martina Cummins, Liam P Shaw, Elita Jauneikaite, Kevin Cole, Florent Lasalle, Deborah Barry and others. ‘Hospital outbreak of carbapenem-resistant enterobacteriales associated with an Oxa-48 plasmid carried mostly by *Escherichia coli* St399’ Microbial Genomics 2022: volume 8, issue 4, page 00675
34. Llewelyn MJ, Grozeva D, Howard P, Euden J, Gerver SM, Hope R, Heginbothom M, and others. ‘Impact of introducing Procalcitonin testing on antibiotic usage in acute NHS hospitals during the first wave of COVID-19 in the UK: a controlled interrupted time series analysis of organization-level data’ Journal of Antimicrobial Chemotherapy 2022: volume 77, issue 4, pages 1,189 to 1,196
35. Løchen A, Squire H, Ashiru-Oredope D, Hand KS, Hassan Hartman, Carry Triggs-Hodge, Holly Fountain and others. ‘Surveillance and stewardship approaches for COVID-19 novel therapeutics in England from 2021 to 2022 (Espaur Report)’ Medical Sciences Forum 2022: volume 15, issue 12

36. LuTheryn G, Hind C, Campbell C, Crowther A, Wu Q, Keller SB, Glynne-Jones P and others. ‘Bactericidal and anti-biofilm effects of uncharged and cationic ultrasound-responsive nitric oxide microbubbles on *Pseudomonas aeruginosa* biofilms’ Frontiers in Cellular and Infection Microbiology 2022: volume, page 1,130
37. MacDonald L, Keenan S, Lorenzo FD, Adade NE, Kenna DTD, Millar BC, Moore JE and others. ‘Polymyxin resistance and heteroresistance are common in clinical isolates of Achromobacter species and correlate with modifications of the lipid a moiety of lipopolysaccharide’ Microbiology Spectrum 2023: volume 11, issue 1, pages e03729 to e03722
38. McHugh MP, Parcell BJ, Pettigrew KA, Toner G, Khatamzas E, Sakka NE, Karcher AM and others. ‘Presence of optra-mediated linezolid resistance in multiple lineages and plasmids of *Enterococcus faecalis* revealed by long read sequencing’ Microbiology 2022: volume 168, issue 2
39. Miah T, Charlesworth J, Thornley T, Solanki K, Dunne R, and Ashiru-Oredope D. ‘How trainee pharmacists are tackling AMR through a schools outreach scheme’ Pharmaceutical Journal 2022: volume 309, issue 7,967
40. Morris DE, Osman KL, Cleary DW, and Clarke SC. ‘The characterization of *Moraxella catarrhalis* carried in the general population’ Microbial Genomics 2022: volume 8, issue 5, page 000820
41. Naylor NR, Evans S, Pouwels KB, Troughton R, Lamagni T, Muller-Pebody B, Knight GM, Atun R, and Robotham JV. ‘Quantifying the primary and secondary effects of antimicrobial resistance on surgery patients: methods and data sources for empirical estimation in England’ Frontiers in Public Health 2022: volume 10
42. Omotola O, Nabiryo M, Atteh M, Muringu E, Olaitan OJ, Rutter V, and Ashiru-Oredope D. ‘Exploring the antimicrobial stewardship educational needs of healthcare students and the potential of an antimicrobial prescribing app as an educational tool in selected African countries’ Antibiotics 2022: volume 11, issue 5, page 691
43. Patel S, Jhass A, Hopkins S, and Shallcross L. ‘Enhancing antimicrobial surveillance in hospitals in England: a Rand-Modified Delphi’ JAC-Antimicrobial Resistance 2022: volume 4, issue 5, page dlac092
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8. 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)

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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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