



UK Health  
Security  
Agency

# **English surveillance programme for antimicrobial utilisation and resistance (ESPAUR)**

Report 2020 to 2021

# Contents

Executive summary .....	5
1. Introduction .....	10
2. Antibiotic resistance .....	13
Introduction.....	13
Trends in incidence of key pathogens from bloodstream infections .....	13
Trends in antibacterial resistance in bloodstream infections .....	15
Trends in antibiotic resistance in key pathogens in non-bloodstream infections .....	31
Discussion .....	42
Future actions.....	45
3. Acquired carbapenemase-producing Gram-negative bacteria .....	46
Introduction.....	46
Surveillance of acquired carbapenemase-producing Gram-negative bacteria .....	47
Impact survey: Royal College of Pathologists and professional bodies.....	57
CPE Mathematical Models .....	60
Discussion .....	61
Future actions.....	63
4. Antifungal resistance, prescribing and stewardship .....	65
Introduction.....	65
Antifungal resistance in Candidaemia .....	65
Antifungal prescribing .....	71
Antifungal stewardship .....	80
<i>Candida auris</i> update .....	82
Discussion .....	83
Future actions.....	85
5. Antibiotic consumption .....	86
Introduction.....	86
Total antibiotic consumption .....	86
Prescribing in primary care (in items) .....	95
Prescribing in secondary care (by admission).....	104
Total antibiotic use.....	104
Discussion .....	111
Future actions.....	115
6. Antimicrobial Stewardship.....	116
Introduction.....	116

Primary care .....	116
Newly developed TARGET UTI audits .....	123
NICE / PHE quick reference tools update.....	123
Implementation of the antibiotic checklist in community pharmacies.....	124
Assessing the impact of COVID-19 on secondary care AMS .....	127
Future actions.....	129
7. NHS England and NHS Improvement: improvement and assurance schemes.....	130
NHS Commissioning for Quality and Innovation (CQUIN) scheme 2020 to 2021 .....	130
Improving the management of lower urinary tract infection in older people in primary care .	131
Reducing antibiotic prescribing in primary care .....	131
8. Professional education, training and public engagement.....	134
PHE professional education and training: e-learning.....	134
PHE professional education and training: workshops.....	140
PHE professional education and training: conferences and programmes .....	141
e-Bug.....	146
Antibiotic Guardian (AG).....	149
World Antibiotic Awareness Week (WAAW) and European Antibiotic Awareness Day (EAAD) 2020 .....	152
Future actions.....	154
9. Keep Antibiotics Working evaluation .....	156
Introduction.....	156
Development of the campaign .....	157
Evaluation methods .....	159
Key performance indicators .....	160
Summary of findings.....	160
Performance against key metrics .....	161
Impact of the campaign on prescribers.....	162
Impact of the campaign on the public .....	163
How the campaign has evolved in response to the evidence .....	167
Impact of COVID-19 .....	168
Conclusion.....	169
10. Research.....	170
Introduction.....	170
Key research projects 2020 to 2021 .....	170
11. Stakeholder engagement .....	182
British Infection Association (BIA).....	182
British National Formulary (BNF).....	182

British Society for Antimicrobial Chemotherapy (BSAC).....	182
Care Quality Commission (CQC).....	184
Faculty of General Dental Practice UK (FGDP).....	184
Health Education England (HEE) .....	185
National Health Service England (NHSE).....	186
Specialist Pharmacy Service (SPS).....	187
Public Health Wales (PHW).....	188
Public Health Agency (Northern Ireland) .....	188
Scottish One Health Antimicrobial Use and Antimicrobial Resistance (SONAAR) .....	189
Royal College of Nursing (RCN).....	189
Royal Pharmaceutical Society (RPS) .....	189
Veterinary Medicines Directorate (VMD) and Department for Environment, Food and Rural Affairs (DEFRA).....	190
The National Institute for Health and Care Excellence (NICE) .....	191
References.....	195
Acknowledgements .....	207

## Executive summary

The incidence of most key organisms causing bloodstream infections (BSIs) (*Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca*, *Pseudomonas* spp., *Enterococcus* spp., *Staphylococcus aureus* and *Streptococcus pneumoniae*) increased between 2016 and 2019 but decreased in 2020. Reasons for the decline will vary for each pathogen related to differing transmission mechanisms, for example, less person-to-person contact may reduce some key pathogens, while less healthcare activity and procedures may reduce others.

Noteworthy trends in the proportions (percent) of BSIs between 2016 and 2020 caused by pathogens resistant to key antibiotics include increases in those due to *E. coli* resistant to co-amoxiclav and third-generation cephalosporins and those due to *K. pneumoniae* resistant to co-amoxiclav, third-generation cephalosporins, ciprofloxacin or piperacillin/tazobactam. Levels of resistance for other key drug/bug combinations remained relatively stable (albeit with minor fluctuations from year to year) or showed slight reductions (for example the percentage of *S. aureus* identified as MRSA which decreased by 1%).

Analysis of data on key bacterial pathogens causing lower respiratory tract infections (LRTI) (*S. pneumoniae*, *Haemophilus influenzae* and *Pseudomonas aeruginosa*) isolated between 2018 and 2020, showed increases in macrolide resistance in *S. pneumoniae*, co-amoxiclav resistance in *H. influenzae* and piperacillin/tazobactam resistance in *P. aeruginosa*.

The burden of antibiotic resistance (measured as the estimated total number of BSIs caused by pathogens resistant to one or more key antibiotics) increased year-on-year between 2016 and 2019, before declining in 2020. The reduction in the burden of antibiotic resistance in 2020 was mainly driven by the reductions in the incidence of *E. coli* BSIs.

The estimated number of deaths attributable to antibiotic-resistant bacteria (based on the antibiotic resistance burden) also increased year-on-year between 2016 and 2019, before declining in 2020 (estimated 2,596 deaths in England in 2019 versus 2,228 in 2020).

The reductions in both the burden of antibiotic resistance and the number of attributable deaths seen between 2019 and 2020 are likely to be multifactorial, including factors such as changes in treatment guidance, pandemic-associated restrictions, laboratory testing capacity, healthcare-seeking behaviour and antimicrobial usage.

The number of carbapenemase-producing Enterobacterales (CPE) isolates referred for confirmation to the Antimicrobial Resistance and Healthcare Associated Infections (AMRHA) Reference Unit decreased between 2018 and 2019 due to changes in referral criteria, with a further decrease in 2020.

Carbapenemase-producing Gram-negative bacteria (CPGNB) were added to the Health Protection (Notification) Regulations on 1 October 2020. There were 586 notifications of CPGNB between October and December 2020, 6% of which were from sterile sites. In the first quarter of notifications, OXA-48 was the most frequently (42.5%) identified carbapenemase (in both invasive and screening isolates), although this varied by organism and geographic region. The North West and London regions had the highest rates of carbapenemase producers, although they differed in terms of the distributions of resistance mechanisms, with NDM producers being more frequent in London compared to KPC producers in the North West.

In March 2020 the Royal College of Pathologists (RCPATH) recommended stopping CPE (and vancomycin-resistant enterococci; VRE) screening in 'low risk' settings to help preserve laboratory capacity during the pandemic. A survey was launched in March 2021 to try and ascertain from hospitals whether there had been a change in screening as a result. Only one-third of acute Trusts responded, therefore there is poor generalisability for the survey. Of those Trusts that responded, 44% (18 out of 41) indicated that there had been a reduction in CPE screening. Multiple reasons for the reduction were highlighted, with 17% indicating that the reduction was as a result of changes following the RCPATH recommendations, and 95% citing a reduction in the number of patients who would normally be screened.

The incidence of candidaemia decreased between 2016 and 2019, but then increased by 10.6% in 2020. This was potentially as a result of the coronavirus (COVID-19) pandemic with more people being admitted to Intensive Care Units.

In 2020 only 4 detections of *Candida auris* were recorded, compared with 163 in 2016. The low number recorded in 2020 is likely to be due, at least in part, to the lack of travel options due to the COVID-19 pandemic, as in recent years the predominant source of *C. auris* detection has been following international travel.

Between 2019 and 2020, community prescribing of antifungals decreases by 24% and hospital prescribing increased by 21%. Increased prescribing in hospitals is again highly likely as a result of the COVID-19 pandemic, with the prescribing rate increasing sharply in April 2020 (88.1% higher DDDs per 1,000 admissions per day in April 2020 than in February 2020), before falling again by August 2020, although not back to pre-2020 levels. With fewer hospital admissions and a different case-mix of patients, comparisons of 2020 to previous years should be done with caution.

During the pandemic, total consumption of antibiotics (defined daily doses [DDDs] per 1,000 inhabitants per day) continued to decline, with a larger decrease seen between 2019 and 2020 (10.9% reduction) than with previous average annual declines. All settings demonstrated decreases in prescribing between 2019 to 2020 (when using the metric DDDs per 1,000 inhabitants per day), apart from the dental setting which saw an increase in consumption by 17.6%. Increased antibiotic consumption in the dental setting has been associated with

restricted access to dental care and change in service delivery during the COVID-19 pandemic period.

Antibiotic prescribing continued to be greatest within the general practice setting (72.7%). The reduction in antibiotic prescribing in general practice between 2019 and 2020 was greater than the reduction seen between 2016 and 2019 (reduced 1.96 compared to 1.27 DID). The greatest percentage change in items prescribed per 1,000 inhabitants per day between 2019 and 2020 was amongst children aged 0 to 4 years (-39.9%) and children aged 5 to 9 (-25.9%). Penicillins showed the greatest decline in general practice antibiotic consumption between 2019 to 2020 (20.2%).

There were no significant changes in the proportions of consumption across different prescriber settings, suggesting that despite the pandemic there was no identifiable shift in antibiotic prescribing (for example, from GP to emergency department outpatient prescribing).

From 2016 to 2019 the rate of antibiotic use in secondary care increased by 1.9% (4,586 to 4,674 DDDs per 1,000 admissions). Between 2019 and 2020 there was a 4.8% increase in total prescribing rate (4,674 to 4,899 DDDs per 1,000 admissions). This increase was driven by a rise in the rate of inpatient hospital prescribing (using the metric DDDs per 1,000 admissions), thought to be largely related to reductions seen in hospital admissions (the denominator) and changes in hospital populations since the start of the pandemic. Increased inpatient prescribing rates may also be related to a shift in prescribing behaviour away from broad-spectrum antibiotics to narrow-spectrum antibiotics.

There were decreases in secondary care prescribing of 'macrolides, lincosamides and streptogramins' and oral metronidazole until 2019 to 2020, where prescribing subsequently increased by 0.4% and 1.6% respectively. Other notable increases between 2019 and 2020 included prescribing of anti-*Clostridioides difficile* agents (23.8%) and sulphonamides and trimethoprim (19.6%).

Prescribing of 'Watch' and 'Reserve' antibiotics decreased by 1.8% and 0.5% in 2019 compared to 2017; from 2,136 to 2,097 DDDs per 1,000 admissions, and 133 to 132 DDDs per 1,000 admissions, respectively. However, between 2019 to 2020 there was an increase of 7.2% in 'Watch' antibiotics (2020: 2,484 DDDs per 1,000 admissions), 16.6% in 'Reserve' antibiotics (154 DDDs per 1,000 admissions), and 2.1% in 'Access' antibiotics (2,487 DDDs per 1,000 admissions).

In the financial year (FY) 2020 to 2021, 133 out of 135 (99%) Clinical Commissioning Groups (CCGs) met or exceeded the national target to reduce antibacterial items per STAR-PU to the national target of 'at or below 0.965'. This is an improvement on financial year 2019 to 2020 when 96 out of 191 (50%) CCGs met or exceeded this target. However, this is a far larger reduction than expected, due to reduced primary care antibiotic use during the COVID-19 pandemic, particularly in children.

AMR improvement schemes for NHS providers of acute care were paused in financial year 2020 to 2021 due to the focus on managing the COVID-19 pandemic.

NHSEI released the RightCare urinary tract infection (UTI) data packs to enable local health systems to identify opportunities for further improvement in the safe and effective management of UTIs in older people in primary care.

The TARGET antibiotics toolkit suite of antimicrobial stewardship (AMS) resources hosted on the Royal College of General Practitioners website remained the most accessed section of their website throughout FY 2019 to 2020. The 'UTI resource suite' and 'Leaflets to share with patients' were the most visited website sections. The TYI-UTI leaflet for under 65 year olds was the most downloaded item throughout the year.

The COVID-19 pandemic had a significant impact on the AMS activities undertaken across the UK. Of the AMS leads that responded to a UK-wide survey, most reported a reduction in AMS activity with 64% (61 out of 95) reporting that COVID-19 had a negative impact on routine AMS activities.

Negatively-impacted activities included audit, quality improvement initiatives, education, AMS meetings, and multidisciplinary working. Positive outcomes included the increased use of technology for example, virtual meetings and ward rounds and increased acceptance of using procalcitonin tests to distinguish between viral and bacterial infections.

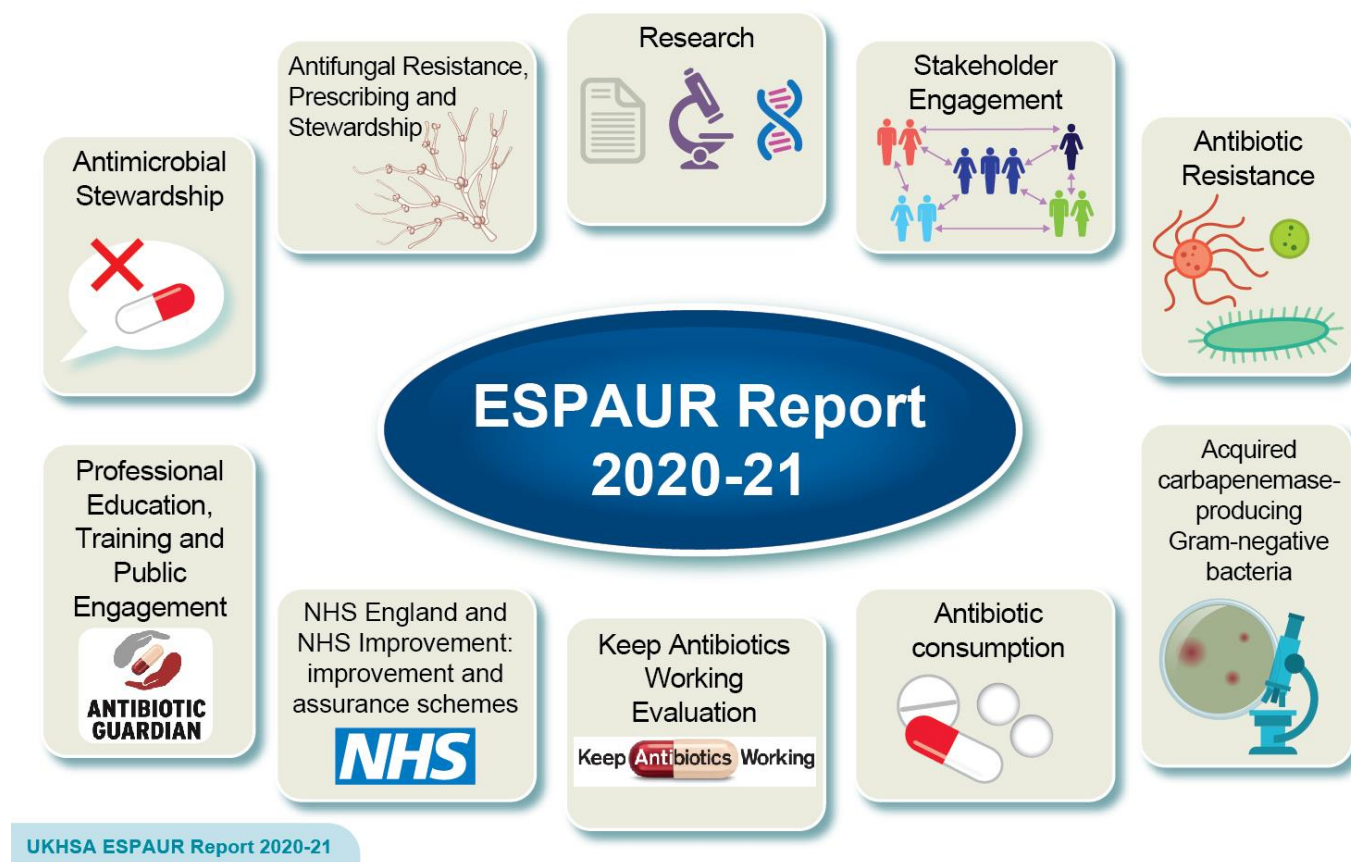
The Public Health England-developed e-learning training course, Preventing and Managing Infections in Childcare and Pre-school, ran from August 2020 through March 2021. During the first 4 runs 4,763 participants enrolled in the e-learning and participants signed up from 149 countries. This course was very positively received, scoring 4.8 out of 5 stars from the 123 reviewers.

Between April 2020 to March 2021, the e-Bug website received almost 2.8 million visits with UK users dominating at 43%.

During the year, Public Health England (PHE)'s education, training and engagement activities were delivered remotely, including TARGET and eBug training, the national One Health healthcare students conference, Antibiotic Guardian Shared learning event and awards, the national AMS training programme for pharmacists (in collaboration with Royal Pharmaceutical Society) and World Antimicrobial Awareness Week activities. During 2020, the Antibiotic Guardian campaign website was visited 86,581 times, resulting in 36,733 pledges from 118 countries. This is the highest number of pledges in one year since the campaign began in 2014 and more than double any other annual figure.



## Infographic 1. The ESPAUR Report



### Accessible text explanation of infographic 1. The ESPAUR Report

A graphic showing a central text box surrounded by 11 others. The one in the centre reads: 'ESPAUR Report 2020 to 2021'. Each of the 11 surrounding text boxes contains a chapter name, being:

- antibiotic resistance
- acquired carbapenemase-producing gram-negative bacteria
- antibiotic consumption
- Keep Antibiotics Working evaluation
- NHS England and NHS Improvement: improvement and assurance schemes
- professional education, training and public engagement
- antimicrobial stewardship
- antifungal resistance, prescribing and stewardship
- research
- stakeholder engagement

The full set of [infographics visualising the main findings from the report is available on the ESPAUR report page.](#)

# 1. Introduction

This is the eighth English Surveillance Programme for Antimicrobial Use and Resistance (ESPAUR) report and the last report based on activities whilst at PHE. The ESPAUR programme and oversight group continued to work across the healthcare system to ensure that surveillance is optimised for antimicrobial use and resistance and that interventions related to AMS including public and professional education and training are delivered.

This report highlights the changes in incidence of bloodstream infections (BSIs), antibiotic-resistant infections, and the burden of resistant infection and subsequent mortality between 2019 and 2020. For each of the key pathogens in the report, the incidence of BSI decreased between 2019 and 2020, with the largest relative decrease noted for *Streptococcus pneumoniae*, which decreased by 59% and *Escherichia coli* which decreased by 14%. The decreased rates of BSI seen for all key organisms in 2020 is likely due, at least in part, to the COVID-19 pandemic, which resulted in reduced contact between individuals and overall fewer interactions with the healthcare system (both related to infection presentations and reductions in healthcare associated infections due to decreased procedures and inpatients), although the underlying causes of reductions in BSI rates are likely to be complex and multifactorial.

It is also a pivotal moment with antimicrobial resistance (AMR) (specifically carbapenemase-producing Gram-negative bacteria (CPGNB)) added to the Health Protection (Notification) Regulations on the 1 October 2020. There were 586 notifications of CPGNB between October and December 2020, 6% of which were from sterile sites. This statutory obligation to laboratories aims to improve the robustness of reporting for these AMR pathogens and will be critical in measuring the impact of interventions in controlling the spread of these resistant pathogens in our population.

PHE continued to calculate the burden of antibiotic resistance using the methodology developed by the European Centre for Disease prevention and Control (ECDC) for estimating incidence and attributable deaths due to antibiotic-resistant bacteria. The reduction in incidence of bacterial BSIs between 2019 and 2020, reduced the estimation of total resistant infections and deaths by 15% and 17% respectively, in 2020 compared to 2019. However, should community and hospital healthcare return to previous methods of delivery in 2021 and beyond, the burden of antibiotic-resistant infections could be expected to return to pre-COVID levels.

This report extends AMR data to include resistance in tuberculosis, sexually-transmitted infections, as well infections due to viruses and fungi. Between 2019 and 2020, there was a decrease in reduced susceptibility to ceftriaxone in *Neisseria gonorrhoea* (the current first-line therapy), from 2.9% to 1.4%, potentially related to differing sexual networks and reduced imported cases in 2020. In addition, the second *Mycoplasma genitalium* resistance pilot study indicated that 1 in 10 isolates are resistant to macrolides and quinolones.

With the changes in healthcare delivery and in healthcare-seeking behaviour, one of the most pronounced changes was the reduction in antibiotic prescribing, especially in primary care, where the reductions observed between 2019 and 2020 were greater than the reductions seen between 2016 and 2019. However, it should also be noted that unlike the H1N1 2009 pandemic, antibiotics were not routinely recommended as part of the community care pathway. Nonetheless community antibiotic prescribing in England is now lower than it has been for more than 15 years and if maintained post-pandemic would highlight England as being one of the lowest community prescribing countries in Europe.

While community prescribing decreased across all age groups between 2016 and 2020, it is highly likely that the lack of seasonal uncomplicated respiratory infections in 2020 effectively reduced demand for antibiotics. Most notably, between 2019 and 2020, there were dramatic reductions in general practice antibiotic prescriptions dispensed for children aged 0 to 4 years (40% reduction) and 5 to 14 years (26% reduction).

Reductions in primary care prescribing were matched by reductions in antibiotic use for hospital outpatients and inpatients when population-level consumption rates were assessed (DDDs per 1,000 inhabitants per day [DID]). However, When secondary care consumption rates were assessed as DDDs per 1,000 hospital admissions, a greater increase compared to previous years was seen between 2019 and 2020, driven by an increase in inpatient prescribing (6%). Given the similarities between the clinical features of severe respiratory infection syndrome caused by SARS-COV-2 and bacterial respiratory tract infections, changes in prescribing during COVID-19 pandemic were expected. That said, increases in hospital inpatient consumption (DDDs per 1,000 hospital admissions) were thought to be largely related to changes in hospital populations (with cancellations of elective procedures) and reductions in hospital admissions during the COVID-19 pandemic. AMS teams will need to work tirelessly with prescribers in the coming 12 months to reverse this trend. Hospital prescribing of antifungals also increased, most likely related to increased numbers of individuals with COVID-19 requiring high dependency and Intensive Care Unit (ICU) care.

The report also highlights that there was reduced AMS activities, especially audit, quality improvement and stewardship meetings. However, despite this, for primary care, the TARGET antibiotics toolkit suite hosted on the Royal College of General Practitioners website remained the most accessed section of their website.

PHE developed an e-learning training course, 'Preventing and Managing Infections in Childcare and Pre-school', which was delivered 4 times from August 2020 through to March 2021, with 4,763 participants enrolled from 149 countries. Alongside this course, the E-Bug website has continued to have large numbers of visitors (2.8 million), ensuring that the materials developed by the team continue to support the education of children.

The Keep Antibiotics Working (KAW) social marketing campaign supported a range of actions across the healthcare system. The percentage of GPs reporting that 'the advertising makes me

more confident to say no to patients asking for antibiotics' was high at launch in 2017 and has been maintained over the 3 years. Campaign recognition among the general public also improved over the 3 years, rising from 56% (n=1,201) of participants recognising the campaign in 2017 to 71% (n=1,350) in 2019.

PHE continued to lead on the development of a range of tools for World Antimicrobial Awareness Week (WAAW). For 2020, a variety of digital resources were developed for healthcare workers, designed to standardise and de-duplicate efforts in disseminating AMR messages in 2020 and mitigate challenges in running local campaigns due to the COVID-19 pandemic.

The ESPAUR oversight group and the members from a wide variety of organisations continued to support and challenge the core delivery team with many organisations continuing to run alongside PHE to deliver the important objectives.

PHE has transferred all of its health protection functions into the UK Health Security Agency (UKHSA). Health improvement and healthcare public health functions have moved into the Office for Health Improvement and Disparities, NHS England and Improvement, and NHS Digital. ESPAUR will continue to support the UKHSA to deliver on the national objectives in the UK AMR 5 year plan and will continue to deliver annual reports on achievements.

## 2. Antibiotic resistance

### Introduction

This chapter presents updates on antibiotic resistance surveillance activities undertaken at PHE and trends in resistance for the drug/bug combinations recommended for surveillance by the Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare-Associated Infections (APRHAI). The estimated burden of antibiotic resistance is also presented to indicate progress against the Government's national action plan (NAP) target of reducing antimicrobial-resistant infections by 10% by 2025 ([1](#), [2](#)).

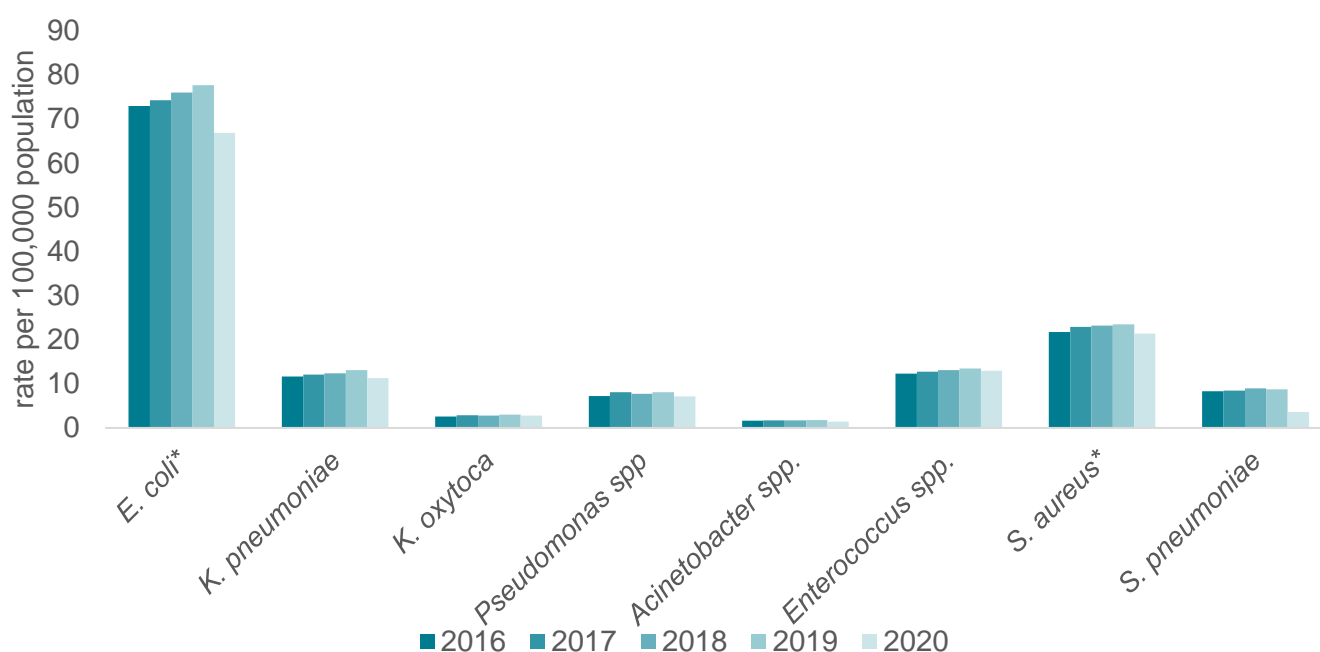
The data presented covers the period 2016 to 2020 for bloodstream infection (BSI) data analysis, and 2018 to 2020 (inclusive) for lower respiratory tract infection (LRTI) data analysis. The primary data source used in this chapter is PHE's Second Generation Surveillance System (SGSS) which is described further in the [Methods and caveats annexe for Chapter 2](#), which was also used in last year's report ([3](#), [4](#)).

The number of reports of BSIs for 2020 presented in this chapter is lower than would be expected based on prior years' reports. When considering this data, the broader context of the global Sars-CoV-2 (COVID-19) pandemic needs to be kept in mind. The potential effects of the COVID-19 pandemic on the number of reported BSIs for the key pathogens outlined in this report are highlighted throughout the chapter and expanded on further in the [Discussion](#).

The data sources, analytical methods, clinical breakpoints and caveats are described in more detail in the [Methods and caveats annexe for Chapter 2](#) of this report. Data and figures are presented in the [data tables and figures appendices](#).

### Trends in incidence of key pathogens from bloodstream infections

The incidence of BSI increased between 2016 and 2019 for all key pathogens apart from *Acinetobacter* spp., which stayed level (1.6 per 100,000 population in 2016 versus 1.8 per 100,000 population in 2019). For each of the key pathogens in the report, the incidence of BSI decreased between 2019 and 2020, with the largest relative decrease noted for *Streptococcus pneumoniae*, which decreased by 59% from 8.7 cases per 100,000 population in 2019 to 3.6 per 100,000 in 2020 ([Figure 2.1](#)). This large decrease was most likely due to the COVID-19-associated reduction in person-to-person contact from March 2020 onwards, when the seasonal increases in infection would have normally been seen ([5](#)), whereas the declines noted in other key pathogens may be more multifactorial.

**Figure 2.1 Incidence per 100,000 population for key pathogen bloodstream infections in England, 2016 to 2020**

\* *Escherichia coli* and *Staphylococcus aureus* incidence is based on mandatory surveillance data.

Figure 2.1. shows the incidence per 100,000 population of BSIs in England caused by the 8 main pathogens, for the period 2016 to 2020. *Escherichia coli* was the most common cause of BSI in this period, with an incidence in 2016 of 73.0 per 100,000 population, increasing to 77.7 per 100,000 population in 2019. Of particular note, in 2020 the incidence decreased to the lowest rate during this period, at 66.9 per 100,000 population, likely due to the reduction in community-onset cases ([6](#)). *Staphylococcus aureus* was the second most common cause of BSI in 2016 to 2020, with an incidence in 2016 of 21.8 per 100,000 population, increasing in 2017 and staying relatively stable at around 23 per 100,000 up to and including 2019, before declining to 21.4 per 100,000 population in 2020.

*Klebsiella pneumoniae*, *Pseudomonas* spp. and *S. pneumoniae* also followed a similar trend with year-on-year increases in BSI incidence between 2016 and 2019, followed by a reduction in 2020 to an incidence that was lower than that seen in 2016 ([Figure 2.1](#)). Although *Enterococcus* spp. BSI rates also increased annually between 2016 and 2019 with a reduction in 2020, the 2020 rate did not fall below that seen in 2016 (2020: 12.9 versus 2016: 12.3 per 100,000 population). *Klebsiella oxytoca* and *Acinetobacter* spp. BSI were the least frequently reported key pathogen BSIs across all years, with neither exceeding 3.0 per 100,000 population annually between 2016 and 2020. Declines in reporting for these pathogens were also observed in 2020, with rates of *K. oxytoca* and *Acinetobacter* spp. BSI at 2.8 and 1.5 per 100,000 respectively in this year.

The decreased rates of BSI seen for all key organisms in 2020 is likely due, at least in part, to the COVID-19 pandemic. This resulted in reduced contact between individuals and overall
























fewer interactions with the healthcare system, although the underlying causes of reductions in BSI rates are likely to be complex and multifactorial. In 2020, there were significant changes in hospital patient admissions such as the cancellation of elective surgery, which may have resulted in a possible decline in surgical site and other hospital-onset infections. Potential changes in healthcare presentation behaviours may also account for the change in incidences, with less people presenting with non-COVID-19 infections ([7](#)). Changes in the incidence of pathogens that are part of the mandatory surveillance scheme (*E. coli*, *Klebsiella* spp., *Pseudomonas aeruginosa*, and *S. aureus*) are discussed in more detail in the latest mandatory surveillance annual report ([8](#)).

## Trends in antibacterial resistance in bloodstream infections

In the following table the phrase ‘third-generation cephalosporins’ refers to cefotaxime, ceftazidime, cefpodoxime and ceftriaxone. ‘Carbapenems’ refers to meropenem and/or imipenem. *S. aureus* data presented comes from mandatory reports.



**Table 2.1 Trends in resistance in key drug/bug combinations in bacteraemia, 2016 to 2020, England**

Bacteria	Antibiotics	% Resistant		P value	Trend
		2016	2020		
<i>Escherichia coli</i>	ciprofloxacin	18.2	18.4	0.566	
	third-generation cephalosporins	11.9	14.0	<0.001	
	gentamicin	9.8	10.4	0.022	
	carbapenems	0.1	0.2	<0.001	
	co-amoxiclav	40.0	43.7	<0.001	
	piperacillin/tazobactam	9.2	9.3	0.874	
<i>Klebsiella pneumoniae</i>	ciprofloxacin	9.9	14.2	<0.001	
	third-generation cephalosporins	11.1	15.2	<0.001	
	gentamicin	8.3	8.4	0.825	
	carbapenems	0.5	0.8	0.077	
	co-amoxiclav	26.1	30.5	<0.001	
	piperacillin/tazobactam	13.6	16.4	<0.001	
<i>Klebsiella oxytoca</i>	ciprofloxacin	2.0	1.9	0.956	
	third-generation cephalosporins	5.9	6.2	0.727	
	gentamicin	1.4	1.2	0.655	
	carbapenems	0.4	0.1	0.223	
	piperacillin/tazobactam	11.8	9.0	0.013	
<i>Pseudomonas</i> spp.	ceftazidime	6.4	6.8	0.530	
	carbapenems	7.9	7.6	0.614	
<i>Acinetobacter</i> spp.	colistin	1.7	12.2	0.294	
<i>Streptococcus pneumoniae</i>	penicillin	1.7	2.4	0.065	
	erythromycin	6.0	6.8	0.305	
<i>Enterococcus</i> spp.	glycopeptides	15.1	15.0	0.878	

Trends in resistance for the key drug and bug combinations grouped by pathogen are presented in [Table 2.1](#), along with the result of statistical tests of the differences in the percentage of resistant isolates reported in 2020 compared to 2016. Many of the specific drug or bug combination changes are described later in the chapter. Trendlines are also presented to provide a visual summary of the year-on-year changes in percentage resistant for each key drug and bug combination over the 5-year period 2016 to 2020. Detailed graphs for each combination are described in this chapter and are also available in the Figure appendix accompanying the report.

Very few of the changes in resistance were assessed as being statistically significant (p-value less than 0.05), with only minor changes in resistance noted for most of the drug and bug combinations. An exception was colistin resistance in *Acinetobacter* spp., where the percentage of resistant isolates increased from 1.7% in 2016 to 12.2% in 2020; although this change was



not statistically significant ( $p=0.294$ ), this is likely due to low numbers of *Acinetobacter* spp. isolates and the low number tested for colistin resistance (41 isolates in 2020 due to selective testing). Full details on the numbers and percentages of BSIs that were tested for and found resistant to each combination are available in the [data table appendix](#).

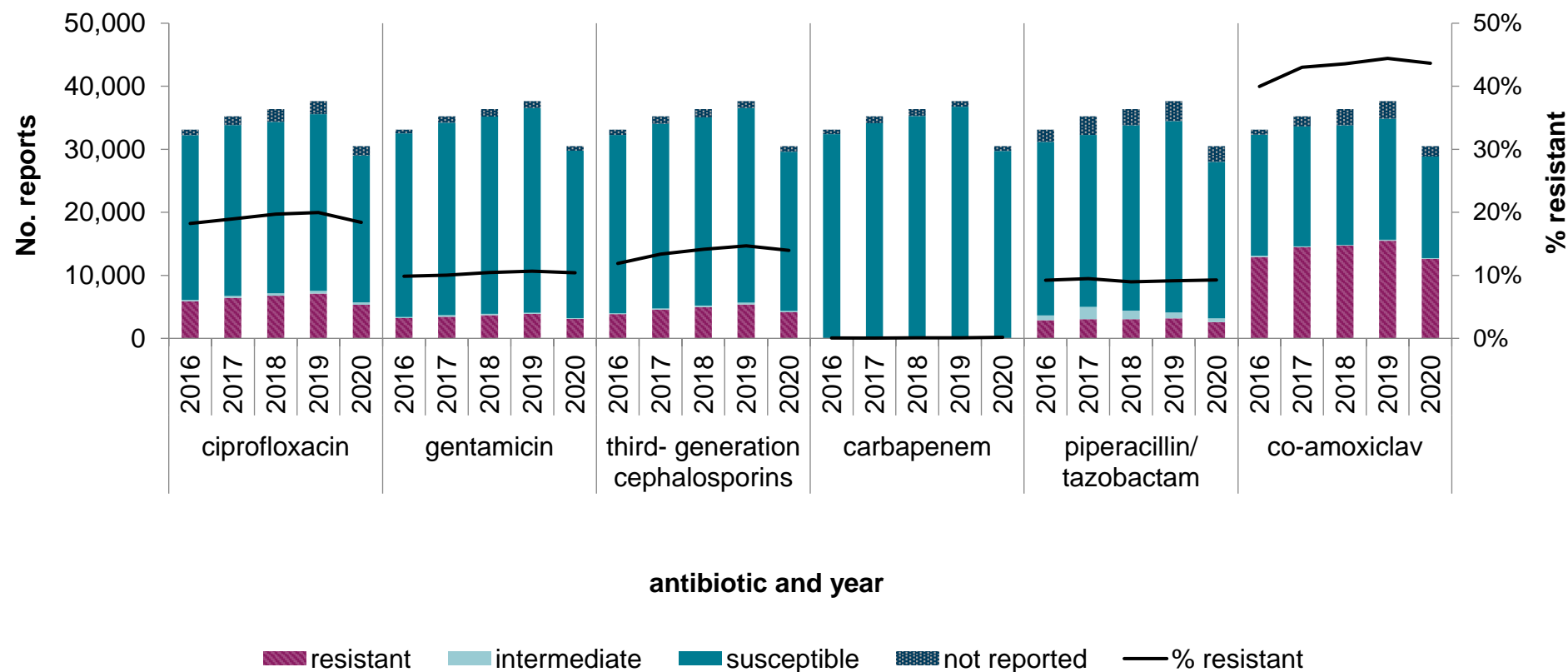
## Gram-negative bacterial infections

Between 2016 and 2020, resistance in *E. coli* isolated from blood increased significantly to third-generation cephalosporins (from 11.9% to 14.0% ( $p$  less than 0.001)), and co-amoxiclav (from 40.0% to 43.7% ( $p$  less than 0.001)), while ciprofloxacin, gentamicin, piperacillin/tazobactam and carbapenem resistance remained similar between the 2 time points (Figure 2.2a). However, of note, resistance of *E. coli* to each of ciprofloxacin, gentamicin, third-generation cephalosporins and co-amoxiclav (each antibiotic is considered separately), decreased in 2020 compared with 2019, with a percentage resistance from 20.0% to 18.4%, 10.7% to 10.4%, 14.7% to 14.0% and 44.4% to 43.7%, respectively (Figure 2.2a). The reduction noted in 2020 is likely to be associated to changes in the types of patients in hospital settings, as well as the changes in behaviour associated with the pandemic (such as healthcare seeking behaviours, hand hygiene and social distancing).

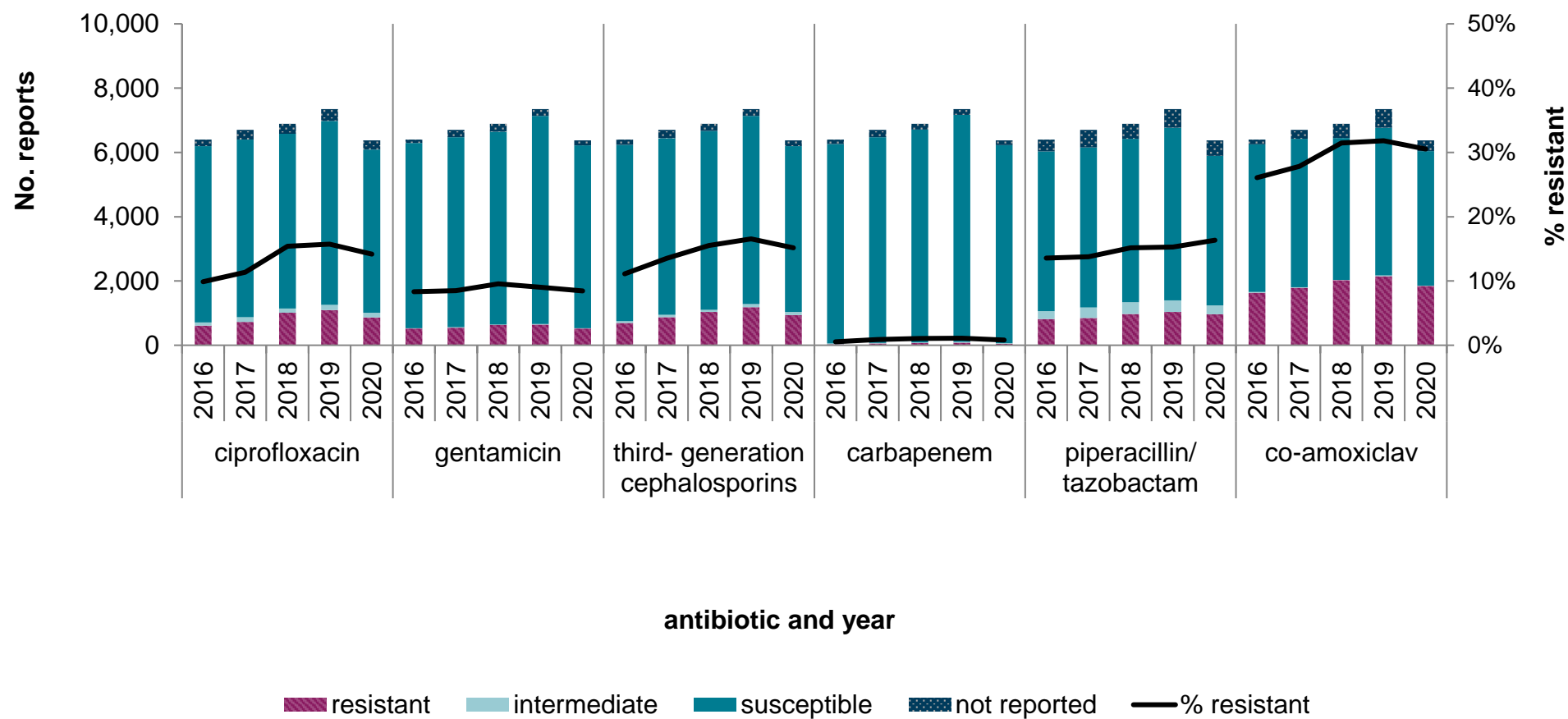
Figures [2.2a](#), [2.2b](#) and [2.2c](#) show the percentage of *E. coli*, *K. pneumoniae* and *K. oxytoca* from BSI that are resistant to key antibiotics in 2016 compared to 2020. For each of these pathogens and in every year, the highest percentage resistance was to co-amoxiclav and the lowest was to carbapenems.

**Figure 2.2 Number of bloodstream isolates of (a) *E. coli* (b) *K. pneumoniae* and (c) *K. oxytoca* reported and the percentage resistant to key antibiotics, England, 2016 and 2020**

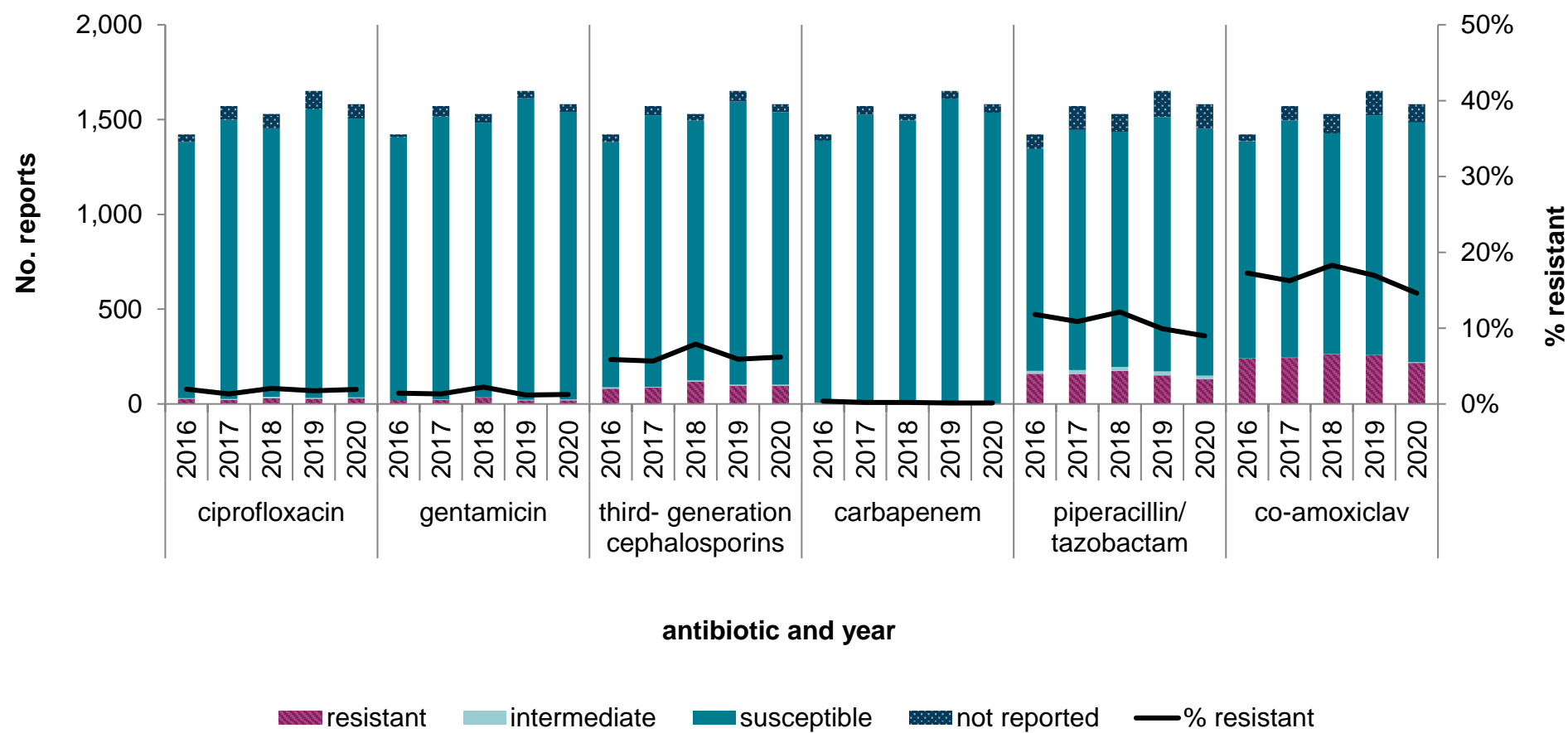
(a) *E. coli*



(b) *K. pneumoniae*



(c) *K. oxytoca*



In *K. pneumoniae* BSI, resistance increased between 2016 and 2020 for each of the key antibiotics ([Figure 2.2b](#)), with increases to each of ciprofloxacin, third-generation cephalosporins, co-amoxiclav and piperacillin/tazobactam being significant ( $p$  less than 0.001). As with *E. coli*, the percentage of isolates resistant to ciprofloxacin, gentamicin, third-generation cephalosporins, carbapenems and co-amoxiclav reported in 2020 was lower than in 2019. Resistance to ciprofloxacin increased from 9.9% in 2016 to 15.7% in 2019 and decreased to 14.2% in 2020; gentamicin resistance was 8.3% in 2016, 9.0% in 2019 and 8.4% in 2020; resistance to third-generation cephalosporins was 11.1% in 2016, 16.6% in 2019 and 15.2% in 2020; for carbapenems this was 0.5% in 2016, 1.1% in 2019 and 0.8% in 2020; and for co-amoxiclav the corresponding values were 26.1% in 2016, 31.8% in 2019 and 30.5% in 2020. In contrast, the percentage of isolates resistant to piperacillin/tazobactam increased year-on-year from 13.6% in 2016 to 15.3% in 2019 and again to 16.4% in 2020.

Conversely, between 2016 and 2020, resistance of *K. oxytoca* from blood to most key antibiotics decreased slightly (from 2016 to 2020: ciprofloxacin 2.0% to 1.9%, gentamicin 1.4% to 1.2%, carbapenems 0.4% to 0.1%, respectively). However, a larger decrease was noted for piperacillin/tazobactam from 11.8% in 2016 to 9.0% in 2020 ( $p=0.013$ ) and a slight increase was seen for third-generation cephalosporins from 5.9% in 2016 to 6.2% in 2020 ([Figure 2.2c](#)).

### Box 2.1 Convergence of resistance and virulence in *Klebsiella pneumoniae*

Nosocomial isolates of *K. pneumoniae* have long been associated with antibiotic resistance and often carry carbapenemase genes ([9](#)). *K. pneumoniae* is also responsible for life-threatening, community-acquired infections including liver abscesses and sepsis caused by 'hypervirulent' types, such as K1-ST23 and K2-ST86, that are typically susceptible to antibiotics ([10](#)). Hypervirulent isolates carry non-conjugative virulence plasmids containing genes encoding capsule-upregulation, acquired siderophore systems and heavy metal resistance. Although still rare, reports have increasingly appeared of antibiotic resistance emerging in these isolates, including acquisition of carbapenemase genes ([11](#), [12](#), [13](#)) leading to the prospect of untreatable invasive infections. More worryingly still, the formation of fusion plasmids, from the recombination of a virulence plasmid and a resistance plasmid has generated conjugative hybrid virulence and resistance plasmids that have appeared not only in hypervirulent types, but also in hospital 'high-risk' clones ([14](#), [15](#), [16](#), [17](#), [18](#)).

Since 2016, the Antimicrobial Resistance and Healthcare Associated Infections (AMRHA) Reference Unit has been aware of these, with hybrid virulence or resistance plasmids found in carbapenemase-positive representatives of STs 11, 14, 15, 48, 101, 147, 383 and 834. Nanopore sequencing has revealed examples of these plasmids that contain up to 19 resistance genes, including bla<sub>NDM-5</sub>, all in the same element. All carried rmpA/rmpA2 (capsule-upregulation genes), the aerobactin cluster and tellurite resistance genes, hallmarks of virulence plasmids in hypervirulent strains ([19](#)). These have been found in both carriage isolates and those from invasive disease, and there have been at least 4 examples where these isolates were associated with sepsis and were unfortunately fatal. A fatal outbreak of hypervirulent *K. pneumoniae* ST11 has been described ([20](#)).

Numbers of ‘high-risk’ clones carrying virulence plasmids identified by the reference laboratory remain relatively small (52 non-duplicate representatives to date), but this is an emerging problem of great concern. Many isolates carrying these hybrid virulence or resistance plasmids are resistant to most antibiotics, with some only susceptible to colistin or tigecycline. Surveillance to identify and contain these organisms is urgently required, especially given that the hybrid plasmids that they carry can transfer to other organisms.

## Box 2.2 Update on ESBLs

Extended-spectrum  $\beta$ -lactamases (ESBL) are enzymes produced by bacteria making them resistant to penicillins and cephalosporins. Resistance to third-generation cephalosporins in *E. coli* (and other Enterobacterales) is a broad indicator of the occurrence of ESBLs, with production of an ESBL being associated with increased morbidity and mortality. Accurate and timely detection of ESBL is important to ensure appropriate antimicrobial therapy is given ([21](#), [22](#)).

In England, the guidance for clinical laboratories indicates that ESBL presence should be identified in all clinically relevant isolates of *E. coli* or *Klebsiella* spp ([23](#), [24](#)). The recommendation is to use ceftazidime and cefotaxime, and/or cefpodoxime susceptibility tests results, where resistant results need to be followed by confirmatory tests to confirm ESBL production. Suggested confirmation methods using inhibitor based tests (such as clavulanic acid), molecular tests (such as PCR) or by using Matrix-Assisted Laser Desorption or Ionisation – Time of Flight (MALDI-TOF).

The facility to report the results of a test for presence/absence of an ESBL is included within SGSS, although this is not universally adopted by reporting laboratories, with low proportions of isolates having ESBL test result. Routine surveillance data in 2020 identified that 19% of *E. coli* BSI specimens tested for and resistant to ESBL predictive third-generation cephalosporin combinations were reported with a further test result for ESBL presence (7% of all *E. coli* BSI), and of those assessed, 74% were positive for ESBL (box table 2.1). For *K. pneumoniae*, the presence of ESBL was confirmed slightly more frequently (38% of all tested and 80% of third-generation cephalosporin resistant BSI), although numbers assessed remained low.

### Box table 2.1 Local laboratory ESBL presence test results in *E. coli*, *K. oxytoca* and *K. pneumoniae* BSI, England, 2020

In this table ‘third-generation cephalosporin-resistant BSI’ means resistant to any one of cefotaxime, ceftazidime, and/or cefpodoxime.

	All BSI			Third-generation cephalosporin-resistant BSI		
	Total BSI	Total tested for ESBL presence	Total ESBL present	Total BSI	Total tested for ESBL presence	Total ESBL present
<i>E. coli</i>	30,621	2,226 (7%)	768 (35%)	3,389	687 (19%)	511 (74%)
<i>K. oxytoca</i>	1,586	69 (4%)	10 (15%)	70	10 (15%)	3 (30%)
<i>K. pneumoniae</i>	6,404	457 (7%)	172 (38%)	717	128 (21%)	102 (80%)

Third-generation cephalosporin resistance is not always due to an ESBL, other  $\beta$ -lactamase enzymes (such as AmpC) may be responsible. In some pathogens it is important to distinguish ESBL production and other modes of resistance. These are detected in other ways.

Comparing with British Society of Antimicrobial Chemotherapy (BSAC) bacteraemia resistance surveillance data results (2019 data for the UK) ([25](#)), 5,437 *E. coli* BSI were assessed and 48 (11%; 95% CI: 8.3% - 14.4%) were positive for ESBL. Similarly with the routine surveillance

*K. pneumoniae* ESBL presence was slightly higher, 178 *K. pneumoniae* BSI were assessed and 11% were positive for ESBL (95% CI: 6.7% to 16.4%). The majority of ESBLs identified through the BSAC surveillance were reported as CTX-M type, although this was slightly less dominant in *K. pneumoniae*.

**Figure 2.3 Number of bloodstream isolates of *Pseudomonas* spp. reported and the percentage resistant to key antibiotics, England, 2016 and 2020**

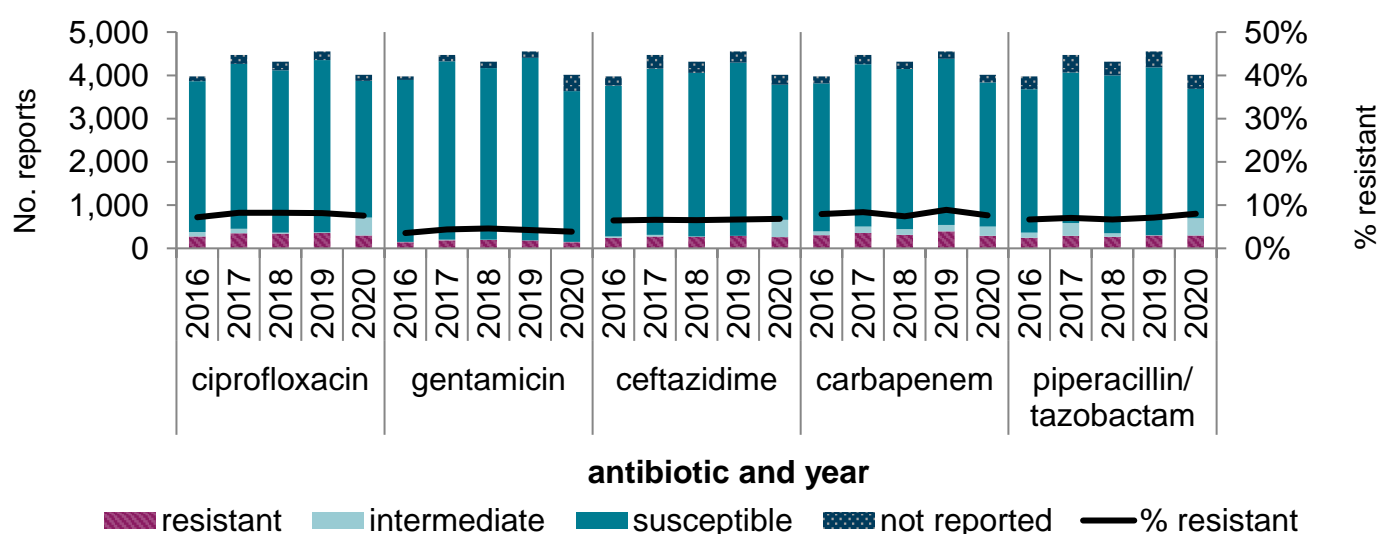


Figure 2.3. shows the percentage resistance to key antibiotics in *Pseudomonas* spp. BSI comparing reports in the period 2016 to 2020. Resistance increased between 2016 and 2020 for all key antibiotics except for carbapenems where there was a slight decrease from 7.9% in

2016 to 7.6% in 2020. It should be noted that carbapenem resistance in 2019 was at the highest level reported over this 5-year period, at 8.9%, with a reduction of 1.3% alone between 2019 and 2020. Similar reductions in resistance between 2019 and 2020 were reported for ciprofloxacin and gentamicin, from 8.2% to 7.6% and 4.2% to 3.9% respectively.

### **Box 2.3 Laboratory surveillance of key Gram-negative pathogens causing hospital BSI**

Laboratory surveillance for BSI caused by key Gram-negative bacteria including *Enterobacter* spp., *Serratia* spp., *Citrobacter* spp., *Proteus* spp., *Morganella* spp. *Providencia* spp. and *Stenotrophomonas* spp. are included in [Chapter 2 online data appendix](#) in this year's report. In particular, trends in incidence, susceptibility testing results to key antibiotics (for the period 2016 to 2020), and in some cases, age and sex breakdowns in BSI in England are available (2020 data only). Details of the data sources are described in the [Methods and caveats annexe for Chapter 2](#), and in the [data appendix](#). Some highlights from the data are presented in this box.

Of note, there has been a steady year-on-year increase in BSI incidence per 100,000 population for *Enterobacter* spp., *Serratia* spp. and *Citrobacter* spp. between 2016 and 2020, including the COVID-19 pandemic; although incidence did level off slightly for *Serratia* spp. between 2019 and 2020.

There was a notable decrease in the percentage of *Enterobacter* spp. BSI isolates resistant to the main antibiotics in 2020 compared to 2019, with the exception of ciprofloxacin and meropenem where resistance to these drugs increased from 4.2% to 4.9% and 0.5% to 0.8% respectively, in this period.

For *Serratia* spp. there was a notable increase in the percentage of isolates resistant to key antibiotics in 2020 compared to 2019. Most notably for cefotaxime and piperacillin/tazobactam, with resistance to these drugs increasing from 11.4% to 12.8% and 6.7% to 8.2%, respectively, in this period. However, due to low episode numbers accounting for greater uncertainty and so should be interpreted with caution.

The overall rates of bacteraemia increased slightly for *Morganella* spp. and *Providencia* spp. in 2020 compared to 2019, from 0.9 to 1.0 and from 0.25 to 0.27 per 100,000 population, respectively. Whereas the rate for *Proteus* spp. bacteraemia decreased slightly in this period, from 6.5 to 6.2 per 100,000 population which is the highest incidence rate of the 3 species. As in previous years, people aged 75 or over had a higher rate of *Proteus* spp., *Morganella* spp., and *Providencia* spp., compared with other age groups. Bacteraemia rates were also higher in males vs. females in this and most other age groups.

The percentage of *Proteus mirabilis* showing resistance to gentamicin has increased in 2020 compared to 2019 (2019:1.3%, 2020: 2.3%).



The rate of *Stenotrophomonas* spp. infection stayed a stable between 2016 and 2020, at around 0.7 per 100,000 population. Consistent with previous years, the majority of *Stenotrophomonas* spp. is caused by *Stenotrophomonas maltophilia*, accounting for 98% in 2020. *S. maltophilia* resistance to co-trimoxazole decreased between 2016 and 2020 from 6.8% to 5.4%, respectively.

The rate of polymicrobial infection increased between 2016 and 2020, and similar with previous years ([26](#)), the most frequently identified organisms involved in polymicrobial infections were *E. coli*, Coagulase-negative *Staphylococcus* (a common skin commensal species) and Coliforms. This align with the most frequently identified monomicrobial infections, where Coagulase-negative *Staphylococcus* (a common skin commensal species), *E. coli* and *S. aureus* were the most frequently identified.

For more information, refer to the [Chapter 2 data and figure appendices](#).

Novel antibiotic combinations, such as ceftazidime/avibactam, are available for treatment of patients with carbapenemase-producing multi-drug resistant pathogens ([Chapter 3](#)), usage of which is increasing ([Chapter 5](#)). Although susceptibility testing for these newer antibiotic combinations is currently selective (susceptibility tests only performed when resistance to first- and second-line treatment antibiotics has been detected), resistance has nonetheless been recorded.

In 2020, 2,009 (7%) *E. coli*, 455 (6%) *K. pneumoniae* and 318 (8%) *Pseudomonas* spp. from blood were tested for ceftazidime/avibactam susceptibility, and 10 (0.5%), 15 (3%) and 21 (7%) were reported as resistant, respectively. Similarly, for ceftolozane/tazobactam, in 2020, 918 (3%), 205 (3%) and 190 (5%) of *E. coli*, *K. pneumoniae* and *Pseudomonas* spp. respectively were tested for susceptibility, and 47 (5%), 24 (12%) and 9 (5%) were resistant.

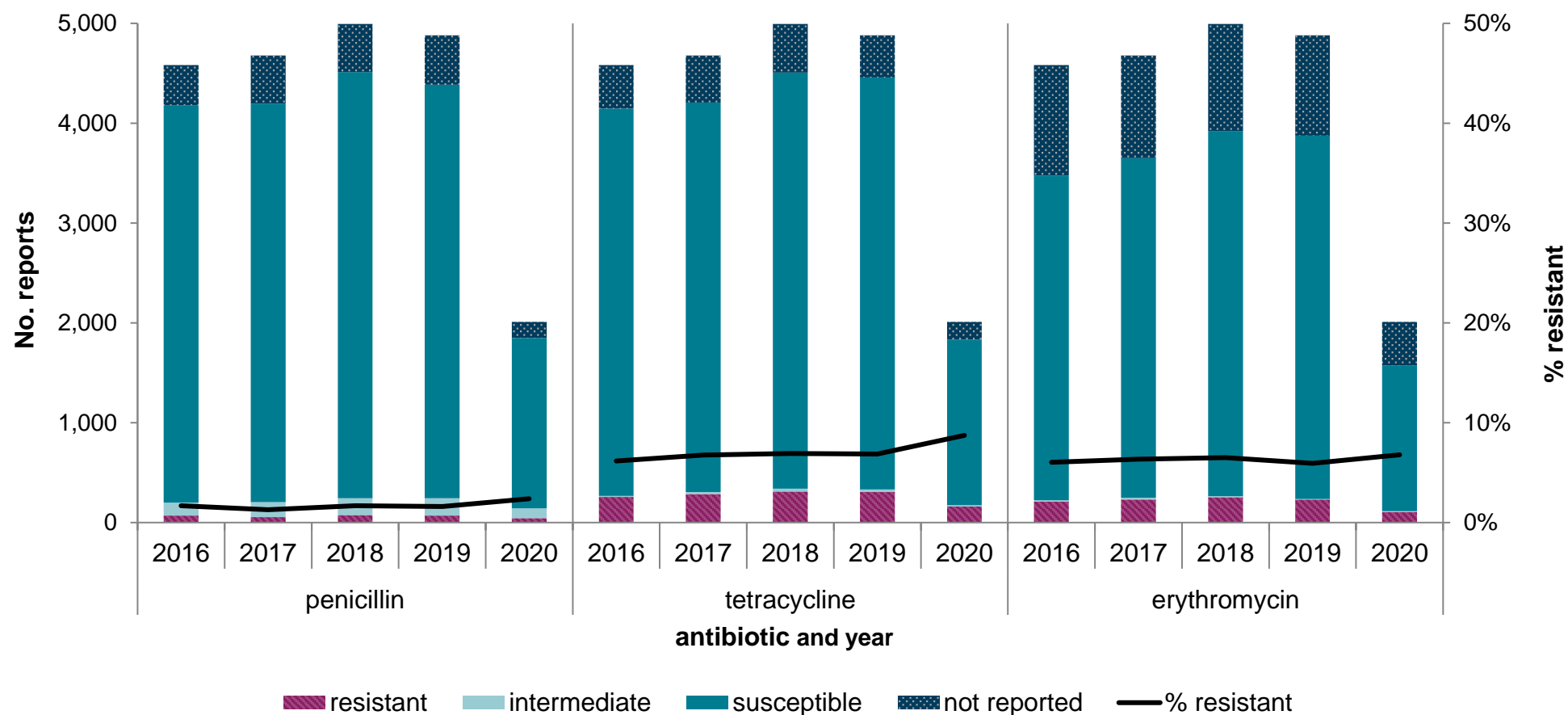
Data tables and graphs for each drug and bug combination are available in the [data and figures appendices](#) accompanying the report.

## Gram-positive bloodstream infections

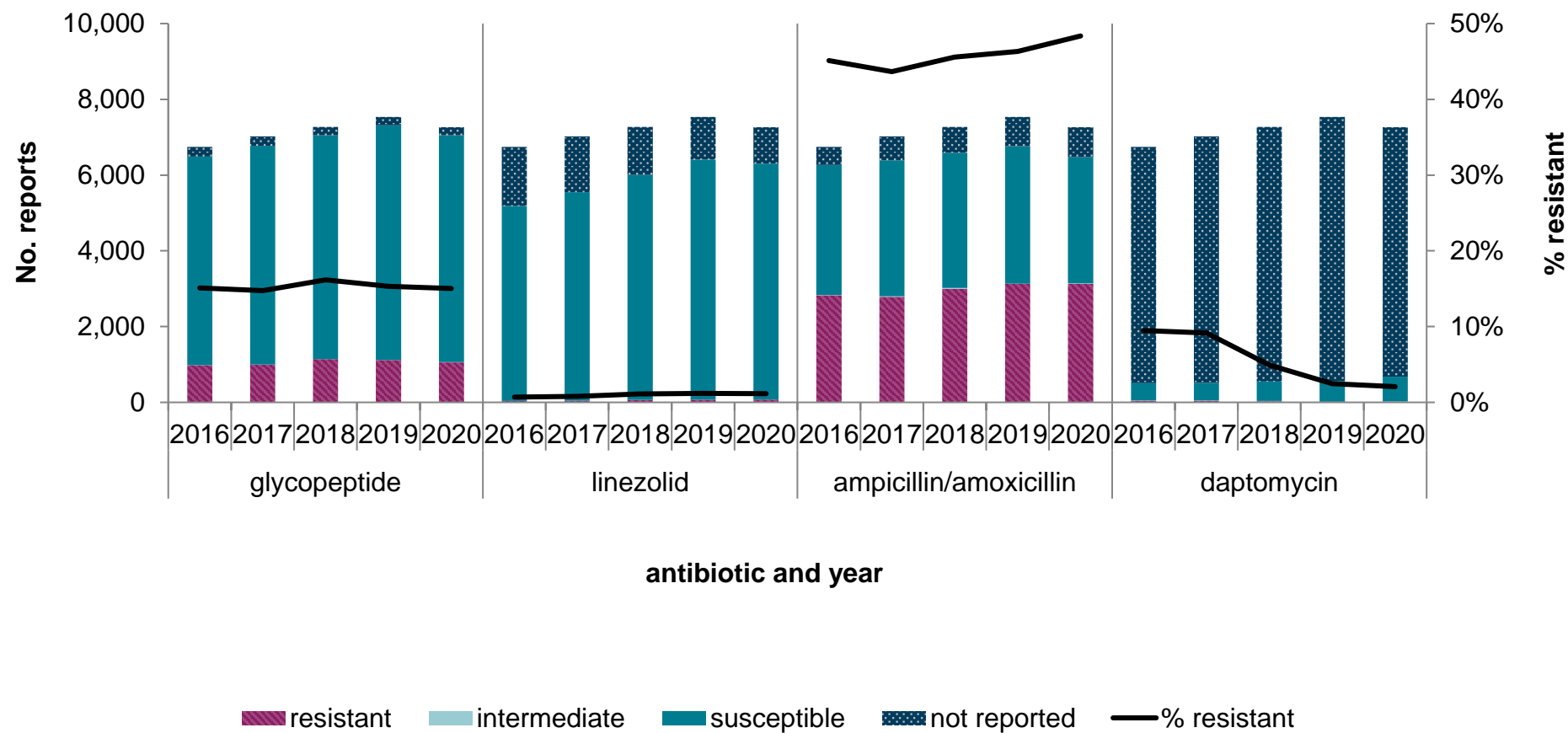
In this section the trend in resistance to key antibiotics in the Gram-positive bacterial pathogens, *S. pneumoniae*, *Enterococcus* spp. and *S. aureus*, between 2016 and 2020 are described (Figure 2.4 a to c).

**Figure 2.4 Number of bloodstream isolates of (a) *S. pneumoniae*, (b) *Enterococcus* spp., and (c) *S. aureus* reported and the percentage resistant to key antibiotics, England, 2016 and 2020**

(a) *S. pneumoniae*

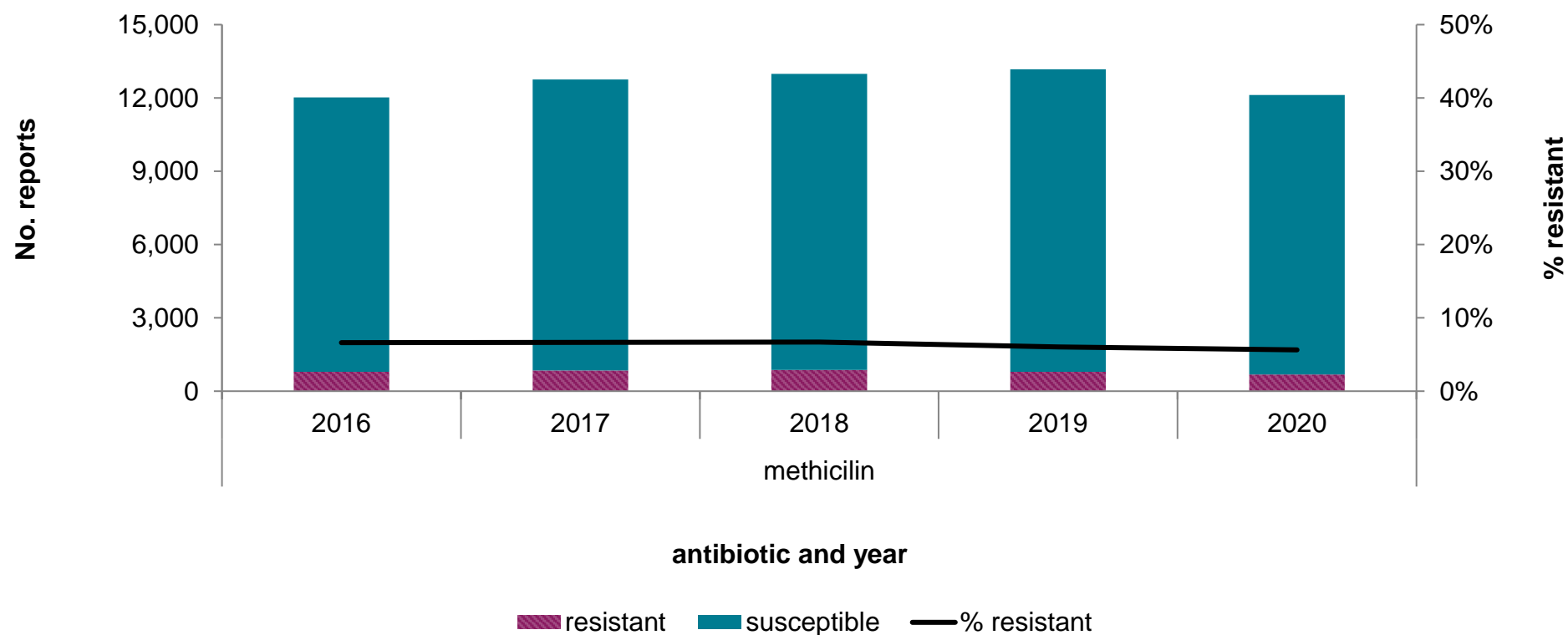


(b) *Enterococcus* spp.



(c) *S. aureus*

Note that *S. aureus* figures are taken from the mandatory surveillance of methicillin-sensitive *S. aureus* and methicillin-resistant *S. aureus* from BSI.



[Figure 2.4a](#) shows the resistance of *S. pneumoniae* to 3 key antibiotics (assessed separately) increased slightly in 2020 compared to 2016, with penicillin resistance increasing from 1.7% to 2.4%, tetracycline resistance increasing from 6.2% to 8.7%, and erythromycin resistance increasing from 6.0% to 6.8%.

Figure 2.4b shows that the resistance to glycopeptides in *Enterococcus* spp. BSI was similar between 2016 (15.1%) and 2020 (15.0%), with only a slight elevation noted across the 5 year time frame in 2018, when resistance peaked at 16.2%. Ampicillin/amoxicillin resistance has been increasing year on year from 2017 onwards, which reflects an increasing percentage of *Enterococcus* spp being *Enterococcus faecium* over the time period ([27](#)). Resistance to linezolid remained relatively stable across the time period, being around 1.1%. Conversely, a decreasing trend in daptomycin resistance has been noted over the past 5 years, reducing from 9.5% to 2.1% between 2016 and 2020, although, susceptibility testing for Daptomycin remains.

While in Figure 2.4c a decrease was seen in the resistance to methicillin amongst *S. aureus* BSIs in 2020 compared with 2016 (6.6% to 5.6%;  $p=0.002$ ). Trends in methicillin-resistant *S. aureus* (MRSA) and methicillin-sensitive *S. aureus* (MSSA) BSI, including a detailed review of the impact of the COVID-19 pandemic, are discussed in depth in the annual epidemiological commentary for the mandatory surveillance ([28](#)).

## The burden of antibiotic resistance

The burden of resistance, measured as the estimated total number of BSIs caused by pathogens resistant to one or more key antibiotics, increased by 4.9% between 2016 (14,829) and 2020 (15,549; [Figure 2.5](#)). (Methodology and pathogen or antibiotic combinations are available in the [Methods and caveats annexe of Chapter 2](#).)

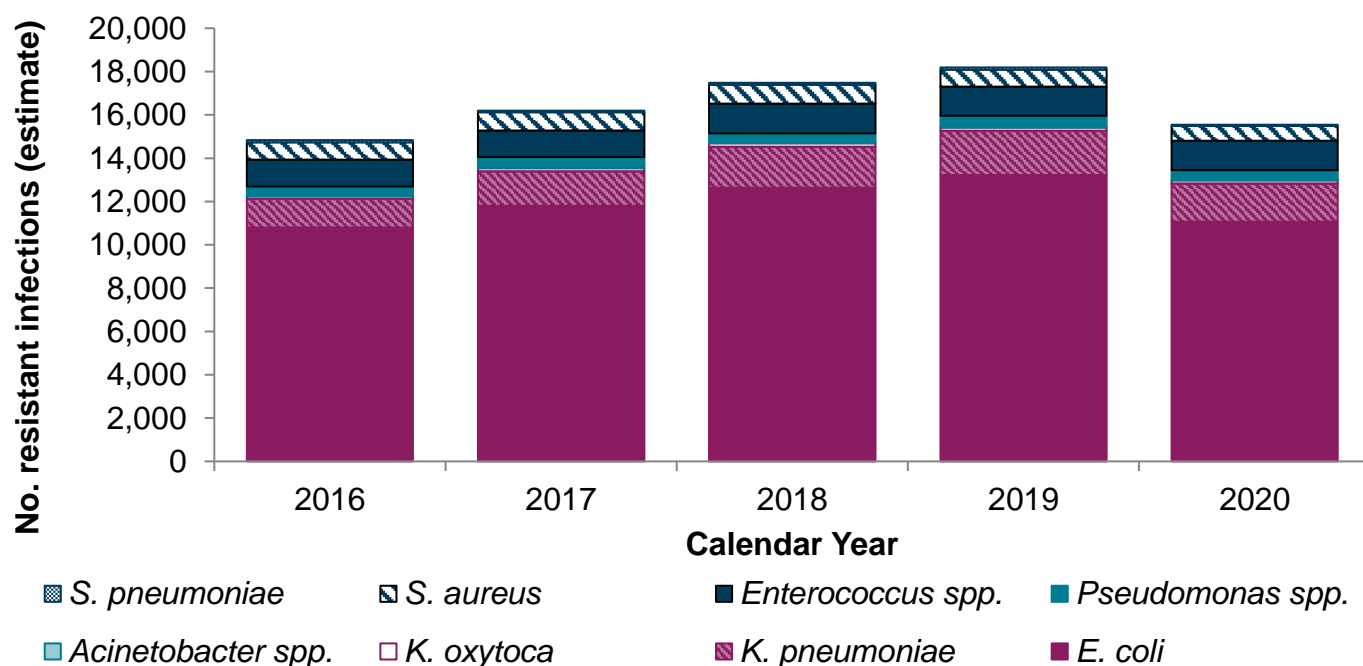
**Figure 2.5 Annual estimated burden of antibiotic resistant bloodstream infections; England 2016 to 2020**

Figure 2.5 shows that while the increase between 2016 and 2020 overall was slight, a year-on-year increase in the estimated number of resistant infections from 2016 to 2019 was evident, peaking at 18,188 in 2019, followed by a subsequent decline in 2020 (14.4%; 15,549). *E. coli* BSIs account for the majority of resistant infections across all years, so the reductions seen in 2020 was the main driver for reductions in the overall burden.

The decrease in the estimated number of resistant BSIs between 2019 and 2020 was largest for Enterobacterales (16% decrease, from 15,413 in 2019 to 12,978 in 2020), and for non-fermenters (14% decrease, from 550 in 2019 to 473 in 2020). The relative decrease in Gram-positive BSIs observed between 2019 and 2020 was smaller (6% decrease, from 2,225 in 2019 to 2,097 BSI in 2020).

In November 2018, the European Centre for Disease Prevention and Control (ECDC) published a methodology for estimating incidence and attributable deaths due to antibiotic-resistant bacteria (29). This method calculated a ratio relating the number of antibiotic-resistant BSIs to the number of antibiotic-resistant surgical site infections (SSIs), antibiotic-resistant urinary tract infections (UTIs) and antibiotic-resistant respiratory infections, using point prevalence survey data alongside BSI incidence data reported through ECDC surveillance schemes. A corresponding estimate of mortality is also calculated. Details on the derivation of the ratios are available in the ECDC publication (29).

The published ratio is applied at drug and bug level to antibiotic-resistant BSI numbers (see [the methods annexe](#) for full list of drug and bug combinations) to generate an estimate of total resistant infections and an estimate of resistant infection related deaths, although it should be noted that the ECDC ratio is at UK level and is being used as a proxy for the ratio in England.

Using this methodology there were an estimated total of 55,384 resistant infections and 2,228 deaths in England in 2020 (down from an estimated 65,583 resistant infections and 2,596 deaths in England in 2019).

The 2020 estimates mark a change from the year-on-year increases that had been noted between 2017 and 2019 (30). Due to the methods used to generate these estimates ([Methods and caveats annexe for Chapter 2](#)), the large drop in *E. coli* bacteraemia reported for 2020 is likely to have had a substantial impact. *E. coli* bacteraemia is often community onset (31) and this, together with a reduction in healthcare interactions and healthcare-seeking behaviour in key risk groups such as the elderly (those advised to shield) and fewer referrals to secondary care during 2020 (32) may have caused this decrease. If so, a return to previously seen incidence would be expected with easing of COVID restrictions.

Detailed antibiotic resistance burden information for infections that occurred in 2018 to 2020 is presented in the [data table web appendix for Chapter 2](#).

## Trends in antibiotic resistance in key pathogens in non-bloodstream infections

### Surveillance of antibiotic resistance in bacterial respiratory tract infections

During 2020, decreases in antibiotic consumption for bacterial respiratory tract infections (RTIs) were noted when compared to previous years, with a few specific antibiotics as exceptions, such as piperacillin/tazobactam and third-generation cephalosporins ([Chapter 5](#)). Some of these prescribing changes are likely attributed to the publication of rapid guidance on prescribing for RTIs in response to COVID 19. Guidance introduced in May 2020 and was regularly updated with the aim to ensure optimal antibiotic management of pneumonia during the COVID-19 pandemic (33, 34).

In an effort to assess the impact of these changes on resistance, monitoring of antibiotic resistance in lower respiratory tract infections (LRTIs) was expanded to look in more detail at a few key causes of bacterial pneumonia between 2018 and 2020. This section of the chapter reports on the occurrence of resistance to key treatment antibiotics in respiratory isolates of *S. pneumoniae* and *Haemophilus influenzae*, which are associated with community-acquired pneumonia (CAP) and *P. aeruginosa* (along with other pathogens not reported here) which may cause hospital-associated pneumonia (HAP).

Lower respiratory tract (LRT) specimens commonly used to diagnose pneumonia (detail on the specimen types used are available in the [Methods and Caveats annexe for Chapter 2](#)) were assessed for several clinically-relevant drug and bug combinations, including:

- *S. pneumoniae* – ampicillin/amoxicillin

- *S. pneumoniae* – macrolides
- *H. influenzae* – co-amoxiclav
- *P. aeruginosa* – ciprofloxacin
- *P. aeruginosa* – piperacillin/tazobactam

Figures 2.6 to 2.8 show trends in antibiotic resistance for each of the drug/bug combinations listed above, for the period 2018 to 2020.

**Figure 2.6 Resistance of *S. pneumoniae* lower respiratory tract isolates to ampicillin/amoxicillin and macrolides; England 2018 to 2020\***

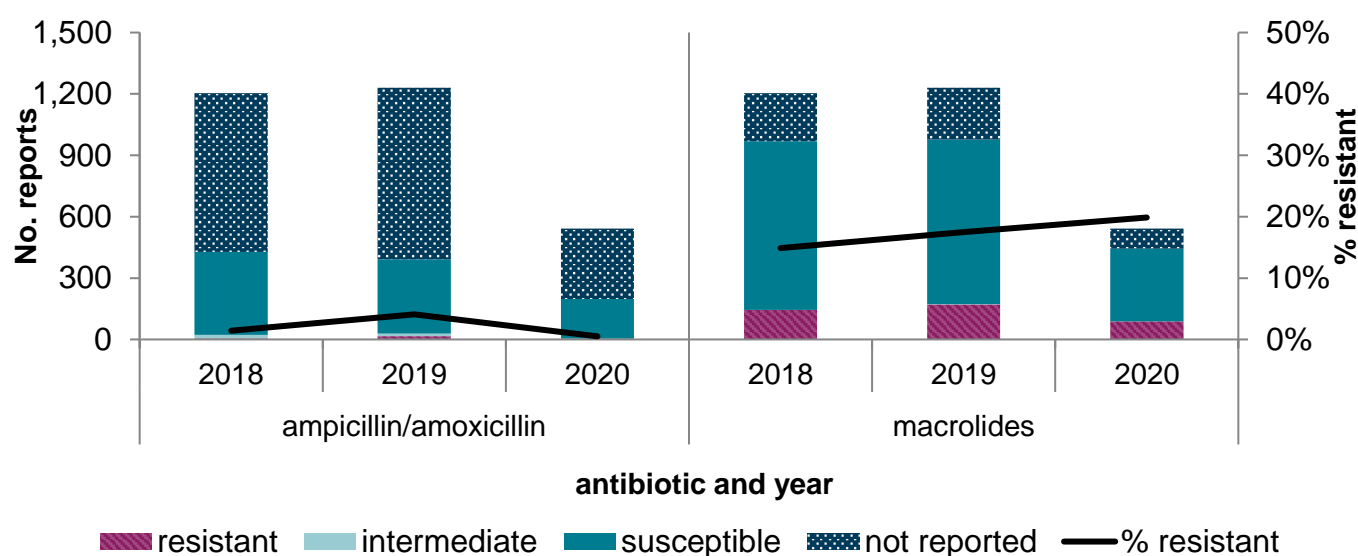


Figure 2.6 shows that the number of *S. pneumoniae* LRT isolates decreased by 56% from 2019 to 2020 (1,230 in 2019 down to 542 in 2020). Macrolide resistance increased year-on-year from 14.9% in 2018 to 19.9% in 2020 while resistance to ampicillin/amoxicillin increased from 1.4% in 2018 to 4.1% in 2019 but then subsequently decreased to 0.5% in 2020, below the resistance observed in 2018.



**Figure 2.7 Resistance of *H. influenzae* lower respiratory tract isolates to co-amoxiclav, England 2018 to 2020**

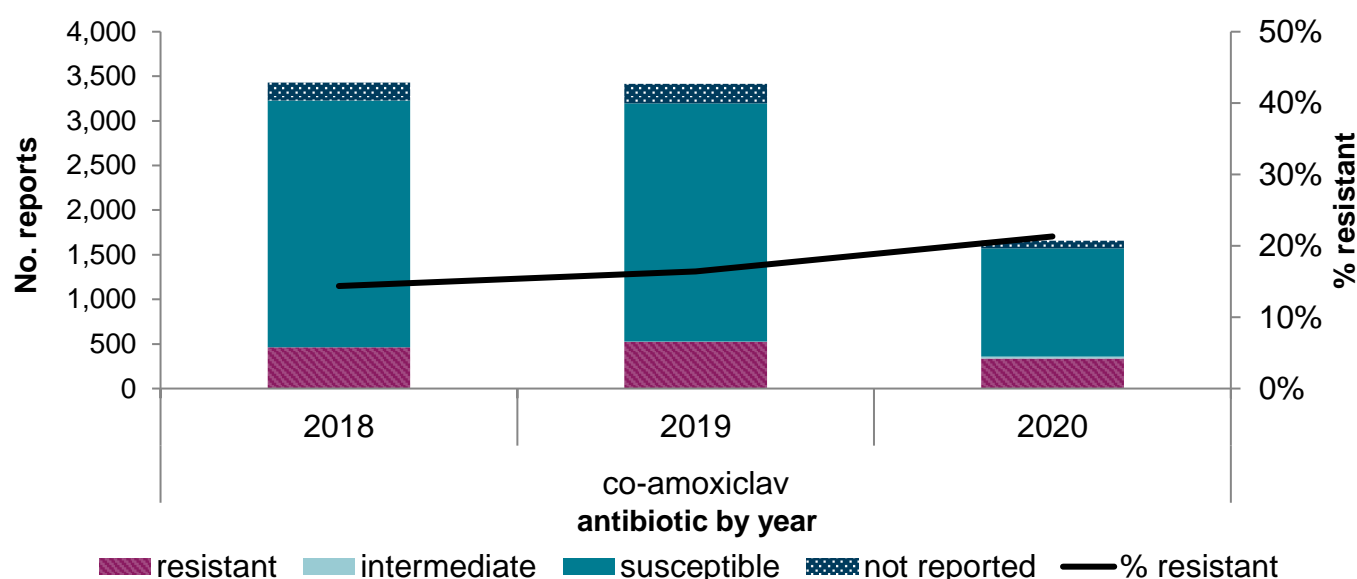
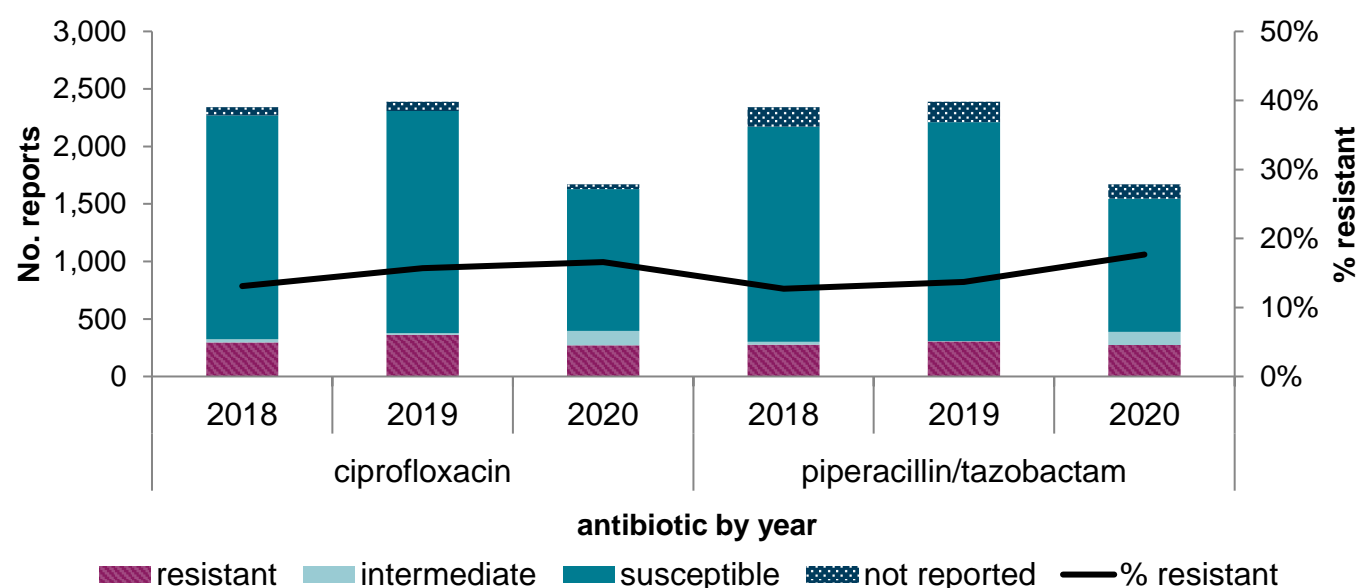


Figure 2.7 shows that the number of *H. influenzae* LRT isolates in 2019 were similar to those in 2018, however, there was a large decline in reports in 2020 (3,416 in 2019 to 1,659 in 2020). A year-on-year increase in the percentage of *H. influenzae* isolates resistant to co-amoxiclav was noted, increasing from 14.4%, 16.4% and 21.3% in 2018, 2019 and 2020 respectively.

**Figure 2.8 Resistance of *P. aeruginosa* respiratory tract isolates to ciprofloxacin and piperacillin/tazobactam, England 2018 to 2020\***



A reduction in reports of LRT specimens positive for growth of *P. aeruginosa*, consistent with reductions seen in the number of BSI isolates, was noted in 2020 compared with the previous 2 years (Figure 2.8). The percentage of *P. aeruginosa* resistant to piperacillin/tazobactam

increased year-on-year between 2018 (12.7%) and 2020 (17.7%; Figure 2.8). Similarly, an increase in the percentage of *P. aeruginosa* resistant to ciprofloxacin was noted, from 15.7% to 16.6% between 2019 and 2020.

Overall, the reduced numbers of isolates of each of the 3 LRT pathogens seen in 2020 compared to previous years. This reduction may be multifactorial with one factor being potentially be reductions in respiratory transmission in both community and the clinical setting. This was especially pertinent early on in the pandemic response, when stringent social distancing measures and other non-pharmaceutical interventions, such as personal protective equipment (PPE), were implemented and where adherence to measures was high (35). As discussed previously, other contributing factors for reduction could be potential reduced healthcare interactions, reduced reporting due to lab capacity constraints as a result of COVID-19 pressures on health systems as well as reduced sampling of bacterial infections.

#### **Box 2.4 Surveillance of AMR in Influenza virus**

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. Whole genome sequencing of influenza virus positive clinical samples allows screening of the neuraminidase for known amino acid substitutions that cause resistance to neuraminidase inhibitors. Viruses with novel neuraminidase amino acid substitutions in enzymatic or structurally significant sites are flagged for phenotypic assessment.

Following whole genome sequencing, a subset of viruses are selected for virus isolation, based on sequence features. Isolates are then tested in a neuraminidase enzyme inhibition assay to determine the phenotypic susceptibility to oseltamivir and zanamivir. Results are reported in the weekly national flu reports during the active influenza season (36) and summarised in the flu annual report for each flu season (37).

Resistance to neuraminidase inhibitors has been very low in the UK in the 2016 to 2020 period.

For A(H3N2) viruses in the last 4 winter seasons for which influenza antiviral susceptibility surveillance was performed, oseltamivir resistance ranged from 0 to 2.9%, (2016 to 2017: 1.6%, 2017 to 2018: 2.9%, 2018 to 2019: 0, 2019 to 2020: 0.06%). The most common resistance mutation identified was the R292K substitution which also causes resistance to zanamivir. A single case of E119V was identified in 2016 to 2017, and in 2017 to 2018 2 cases with a deletion from amino acids 246 to 248 were identified. These viruses were resistant to oseltamivir but retained susceptibility to zanamivir. In all cases with data available, resistance was detected following neuraminidase inhibitor treatment, and most patients had underlying medical conditions.

For A(H1N1) viruses, oseltamivir resistance ranged from 0 to 2.8% (2016 to 2017: 0.02%, 2017 to 2018: 2.8%, 2018 to 2019: 2.3, 2019 to 2020: 0%). No zanamivir resistance was

detected. All resistance detected was caused by the H275Y amino acid substitution and where information was available, most cases identified had received oseltamivir treatment prior to resistance detection. Neuraminidase inhibitor resistance in influenza B viruses remained below 0.05% throughout the period.

### Future work

In 2020, baloxavir marboxil, from a new class of influenza polymerase inhibitors, was licenced for use in the UK. Due to the low circulation of influenza virus in the 2020 to 2021 season, the antiviral was not marketed in UK in the 2020 to 2021 winter season. Baloxavir resistance has been identified during clinical trials, and in clinical use in Japan and the USA, where the drug was licenced in 2018. Amino acids substitution clusters in the Polymerase acidic (PA) catalytic site such as I38X, E23G/K and E199G are known to reduce susceptibility to baloxavir and can arise rapidly during treatment.

In the UK, preparation for baloxavir susceptibility surveillance has been made, and will primarily be achieved through whole genome sequencing of influenza virus positive clinical samples, with analysis of the PA gene for known markers of resistance. Phenotypic testing is under development, to enable characterisation of viruses with novel mutations in the PA as well as other polymerase genes that may function as compensatory mutations.

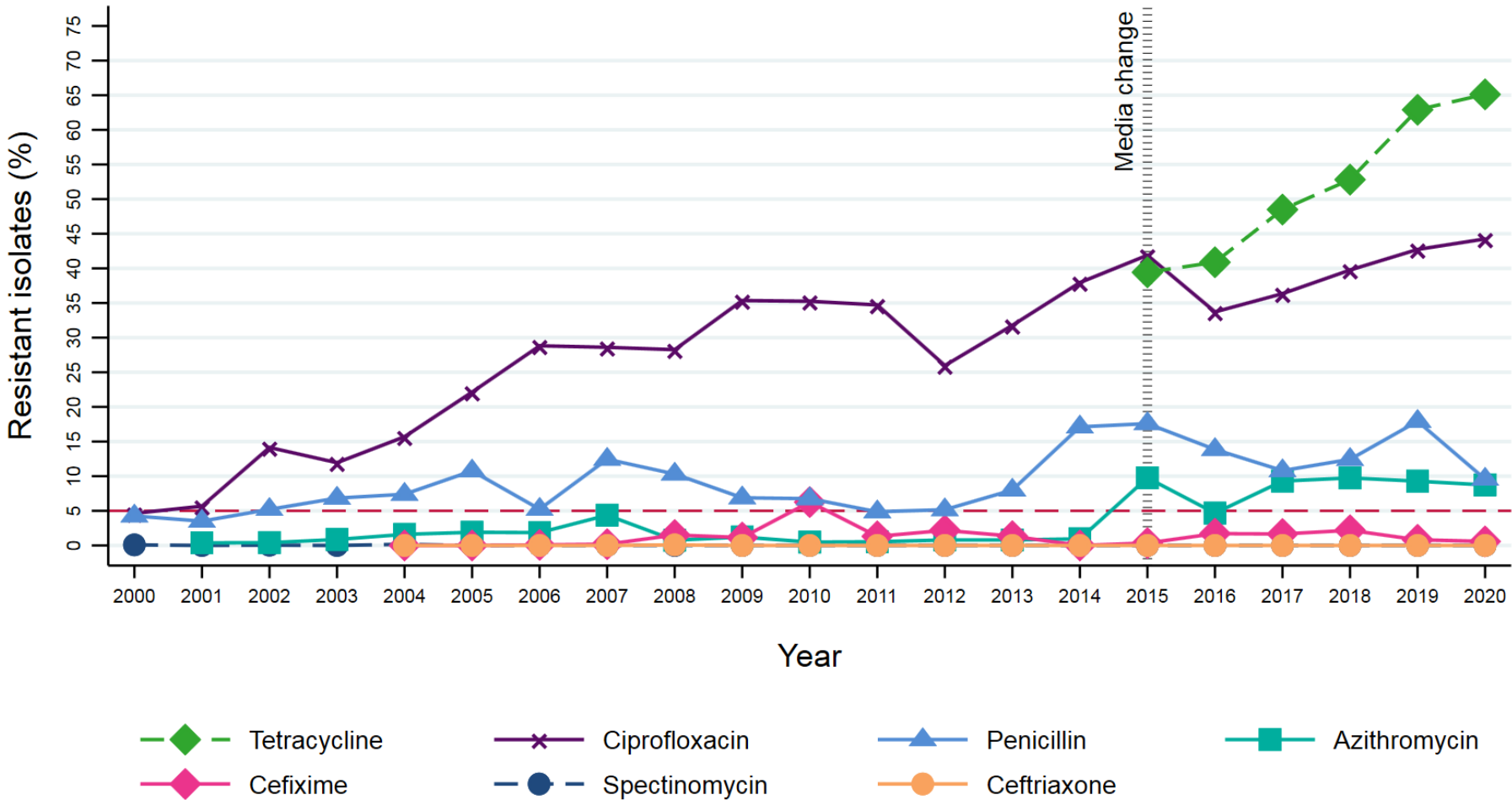
The 2021 to 2022 winter season will also that will provide baseline data in support of future antiviral and vaccine surveillance activities.

## Surveillance of antibiotic resistance in *Neisseria gonorrhoeae*

Surveillance of antibiotic resistance in *Neisseria gonorrhoeae* is monitored through the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP), which comprises a suite of surveillance systems to detect and monitor resistance 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 clinics (SHCs) (25 in England, 2 in Wales) and their 21 associated laboratories over a 2-month period each year. Gonococcal isolates are referred to the PHE Antimicrobial Resistance 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.

Between 2019 and 2020, there was a decrease in reduced susceptibility to ceftriaxone (MIC greater than 0.03 mg/L), the current first-line therapy, from 2.9% to 1.4%, in 2019 and 2020 respectively. This contrast with the steady rise in reduced susceptibility observed from 2013 to 2018 (0.3% to 7.1%). No instances of ceftriaxone resistance (MIC greater than 0.125 mg/L) were observed in the sentinel programme or upon direct referral to the PHE AMRSTI national reference laboratory in 2020 as shown in [Figure 2.9](#).

**Figure 2.9 Percentage of *N. gonorrhoeae* isolates in the GRASP sentinel surveillance system that were resistant to selected antimicrobials, England and Wales, 2000 to 2020**



Due to changes in the diagnostic sensitivity medium used to test antimicrobial susceptibility of sentinel surveillance isolates, MICs for the 2015 to 2020 collections are not directly comparable with those from previous years. Trends from 2000 to 2014 compared to 2015 to 2020 must be interpreted with caution (point of change indicated by vertical dashed black line), particularly for azithromycin and tetracycline (data for tetracycline is only included from 2015 onwards due to this issue). The 5% threshold (equal or greater than 5% of infections resistant to the first-line therapy) at which the WHO recommends that first-line treatment guidelines should be changed is indicated by the horizontal dashed red line.

[Figure 2.9](#) also describes trends in tetracycline, ciprofloxacin, penicillin and spectinomycin resistance from 2000, as well as trends in azithromycin resistance from 2001 and cefixime resistance from 2004. The stabilisation of azithromycin (MIC greater than 0.5 mg/L), cefixime (MIC greater than 0.125 mg/L), ciprofloxacin (MIC greater than 0.06 mg/L) and tetracycline (MIC greater than 1 mg/L) resistance and, most notably, the substantial decline in the proportion of isolates resistant to penicillin (MIC greater than 1 mg/L) in 2020 represents a change in the trend in antimicrobial resistance observed from 2016 to 2019. As was observed across recent years, no spectinomycin resistance (MIC greater than 64 mg/L) was detected in 2020.

Prescribing data demonstrated optimal adherence with the 2019 updated British Association for Sexual Health and HIV (BASHH) UK guideline for managing infection with *N. gonorrhoeae* ([38](#)) with 97.6% of individuals receiving the recommended first-line therapy of ceftriaxone 1g intramuscular monotherapy in 2020.

Further data on antibiotic resistance in *N. gonorrhoeae* is available online in the GRASP report ([39](#)).

## Surveillance of antibiotic resistance in *Mycoplasma genitalium*

Surveillance of antimicrobial resistance in *Mycoplasma genitalium* is monitored through *M. genitalium* Antimicrobial Resistance Surveillance (MARS) which started in 2019. Two pilots of MARS have been conducted to date, with 15 SHCs and 7 associated laboratories in England participating in the most recent pilot (from January to March 2020). Clinics perform *M. genitalium* diagnostic testing for those presenting with non-gonococcal urethritis or pelvic inflammatory disease, and for the current sex partners of those who tested positive for *M. genitalium*. Specimens sent to the PHE AMRSTI national reference laboratory are tested for molecular markers predictive of macrolide and fluoroquinolone resistance in the *M. genitalium* 23S rRNA and parC gene, respectively, and linked to patient demographic, clinical and behavioural data for analysis.

Among 251 individuals included in the second MARS pilot, 190 (76%) were symptomatic. The sample included 131 (52%) heterosexual men, 54 (22%) gay, bisexual or other men who have sex with men (MSM) and 61 (24%) women. Most specimens from women (55%), heterosexual men (69%) and most notably, from MSM (88%) displayed macrolide resistance. Macrolide resistance mutations were more commonly detected among specimens from people of Black or

Black British (80%) ethnicity compared to those who were White (62%), as well as among specimens from individuals who had a previous sexually transmitted infection (STI) in the past year (79%) compared to those who did not (68%). One in 10 specimens were predicted to be resistant to both macrolides and fluoroquinolones.

Further data on antibiotic resistance in *M. genitalium* is available online in the MARS report ([40](#)).

### **Box 2.5 Hepatitis C Virus (HCV) antiviral drug resistance surveillance in the UK**

There are currently 4 classes of direct-acting antiviral (DAA) drugs licensed for the treatment of Hepatitis C virus (HCV) in the UK: NS3 protease inhibitors, NS5A inhibitors, NS5B nucleoside polymerase inhibitors and NS5B non-nucleoside polymerase inhibitors. In most circumstances, an 8 to 12 week course of combination DAA therapy results in cure rates greater than 90%. In many cases, the choice of treatment may be determined by a number of factors, such as the viral strain (genotype and subtype) and the stage of liver disease. Where therapy is unsuccessful, antiviral drug resistance may occur due to the development of mutations in viral genes which encode the protein targeted by the drugs.

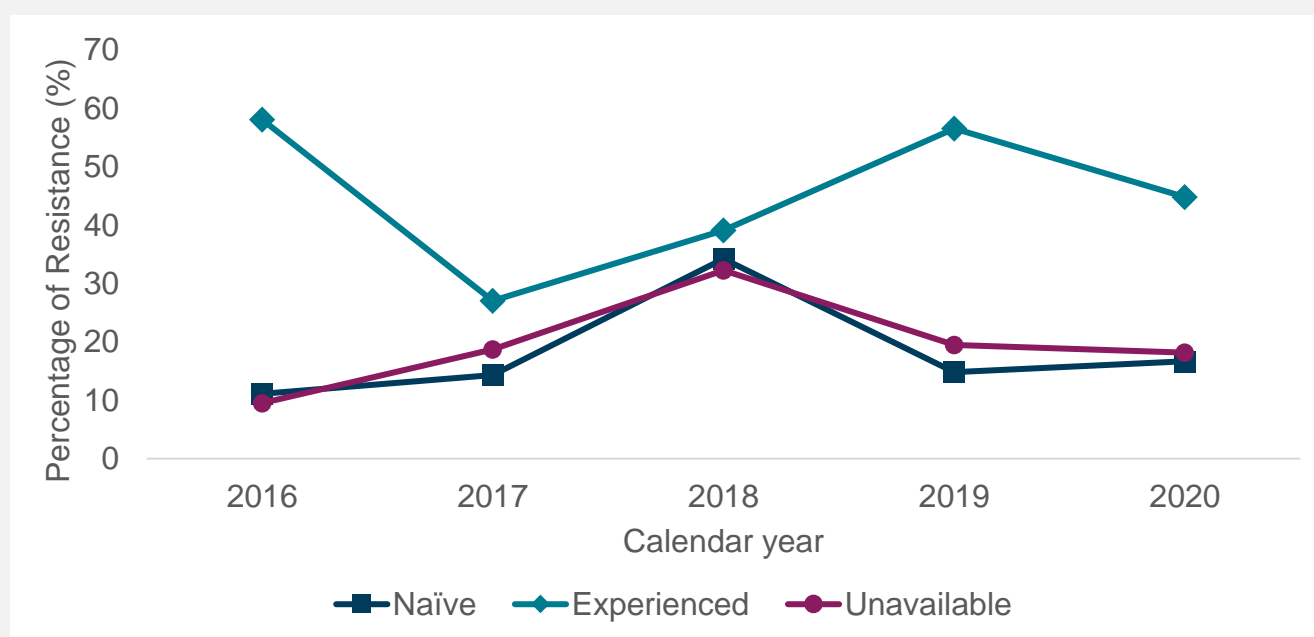
Testing for HCV drug resistance is not universally recommended prior to initiating DAA therapy, as there is no or minimal impact of resistance on cure rates in DAA-naïve individuals in many scenarios. However, in some circumstances, such as prior to starting the regimen elbasvir-grazoprevir in HCV subtype 1a infection, pre-treatment resistance testing of the NS5A gene may be performed to inform the treatment plan. If resistance is detected, this indicates the acquisition of a drug resistant variant.

Where first-line DAA therapy is unsuccessful, re-treatment regimens are also available in many circumstances, which lead to high cure rates, without the need for pre-retreatment resistance testing. Alternatively, sequencing of the NS3, NS5A and NS5B genes may be performed to inform the choice of second-line therapy.

There is no national database of HCV resistance in England. However, the Antiviral Unit within the Virus Reference Department, National Infection Service, UKHSA 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 subtype 1a NS5A 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.

Box figure 2.1 shows the prevalence of resistance to HCV direct-acting antiviral (DAA) drugs where resistance-associated substitutions were detected in the NS5A gene of subtype 1a samples from treatment-naïve and -experienced patients and in patients where treatment information was unavailable from 2016 to 2020 in England, Wales and Northern Ireland (as reported by the PHE's Anti-viral Unit). Percentage of tests where resistance-associated substitutions were detected in NS5A.



**Box figure 2.1**

Most currently available HCV resistance data within PHE/UKHSA is for the NS5A gene of subtype 1a only. Amongst DAA-naïve individuals with subtype 1a infection, NS5A resistance prevalence was 11.1% in 2016, 34.2% in 2018 and 16.6% in 2020, suggesting an increase in transmitted resistance, although the drivers are currently unclear (Figure 2.10). One potential explanation is that resistance has been selected by expansion of elbasvir-grazoprevir since 2016, although this remains to be determined. As shown in Figure 2.13, for DAA-experienced individuals over the same period, the prevalence of NS5A resistance in HCV subtype 1a remained high, indicating the high likelihood of emergent NS5A resistance in this population.

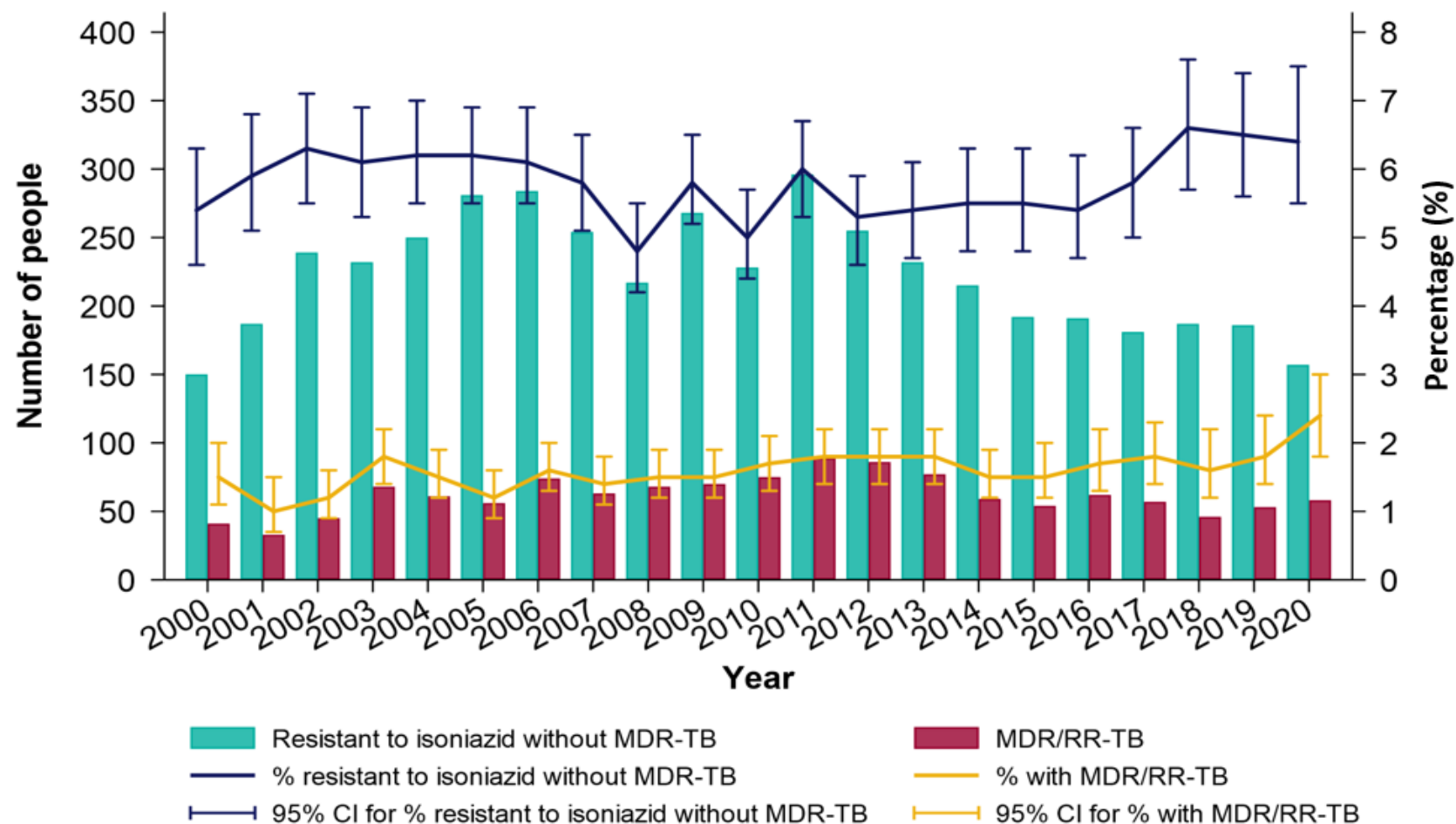
#### Future direction

Genomic surveillance is required to monitor for the prevalence of transmitted drug resistance. Phylogenetic analyses will inform our understanding of whether or not clusters of resistant virus are developing in key populations. In addition, some viral subtypes, which are rare in the UK and other industrialised countries but common in others, are inherently more resistant to many DAA combinations. Genomic surveillance will therefore be important to monitor for the possibility that these 'rare' subtypes become predominant as other strains are eliminated over time.

## Surveillance of antibiotic resistance in tuberculosis

The number of cases of tuberculosis (TB) in England has fallen steadily between 2010 to 2018 but the percentage of drug resistant cases has risen in the last 12 months ([Figure 2.10](#)).

**Figure 2.10. Number and percentage of people notified with TB with initial drug resistance, England, 2000 to 2020 (data extracted from the Enhanced Tuberculosis Surveillance system (ETS))**





Isoniazid (INH) monoresistance is the most frequent resistance pattern in *Mycobacterium tuberculosis* (MTB) isolates in England occurring in around 6% of TB cases ([Figure 2.10](#)). Treatment of INH-resistant TB is longer and more complex than that of fully sensitive TB, also treatment outcomes are worse and more extensive resistance may develop.

Multidrug-resistant TB (MDR) and rifampicin-resistant TB (RR) are defined as MTB resistant to both INH and rifampicin or rifampicin alone. MDR-TB cases now make up over 2% of all TB cases in England; the highest percentage in the past 20 years.

Outcomes for patients with MDR-TB are worse than for drug sensitive disease. In the 2017 cohort of MDR-TB patients 60.9% had completed treatment 24 months after starting compared to 83.6% of patients with drug sensitive TB at 12 months. The drugs used for treatment of MDR-TB are often poorly tolerated and need careful monitoring because of toxicity.

More detail on trends in drug resistance and the impact of social risk factors on outcomes of MDR-TB is presented in the Tuberculosis in England annual report ([41](#)).

## UK participation in international surveillance of AMR

The UK submitted AMR data for 2019 to the European Centre for Disease Prevention and Control (ECDC) for the European Antimicrobial Resistance Surveillance Network (EARS-net) in 2020. Data included resistance to key antibiotics in blood culture and cerebrospinal fluid (CSF) isolates for 8 organisms (*E. coli*, *K. pneumoniae*, *P. aeruginosa*, *Acinetobacter* spp., *S. pneumoniae*, *S. aureus*, *E. faecalis* and *E. faecium*).

The ECDC EARS-net report covering 2019 data, was published on 18 November 2020 ([42](#)).

Replacing the ECDC Ears-Net submission for the UK for 2020 antimicrobial resistance data, was a submission to the World Health Organization (WHO) Central Asian and European Surveillance of Antimicrobial Resistance (CAESAR) network ([43](#)) for inclusion the report in 2021.

The UK submitted AMR data to the WHO Global Antimicrobial Resistance and Usage Surveillance System (GLASS) in October 2021 covering blood and urine isolates from 2020. Information was also provided on the current status of AMR surveillance in the UK. The UK GLASS National Focal Point participated in high-level technical consultation meetings in April 2021 on the future of GLASS surveillance and provided feedback following consultation on GLASS technical documents and protocols.

The WHO GLASS report covering 2019 data, was published in May 2020 ([44](#)).

PHE has been supporting the Oxford GBD (Global Burden of Disease) Group to develop global models of AMR through an agreement with the GBD-Global Research on AntiMicrobial resistance (GRAM) project, enabling data access, data linkage and data analysis of PHE's

unique data sets (for more information see [Chapter 10](#)). This was completed at the end of June 2020 and results are to be summarised in 2021. These results will be discussed in the next ESPAUR report.

## Discussion

There has been an overall decrease in the incidence of BSI of the key pathogens in 2020 compared to 2019, particularly *S. pneumoniae* and *E. coli*. This is consistent with the findings of other reports addressing trends in bacteraemia incidence due to a range of pathogens, including MRSA, MSSA and Gram-negative bacteria BSI mandatory surveillance quarterly reports ([45](#)) and corresponding annual epidemiological commentary ([46](#)); all of which point to trends consistent with those reported here. In addition, intensive care unit (ICU) surveillance indicated a decrease in the number of positive blood cultures and patient bed days in adults over specific periods including January to March 2020 and July to September 2020 periods ([47](#)).

The underlying causes of reductions in BSI incidence have not been established yet and are likely to be multifactorial. What is evident is that the many significant changes in population-level behaviour and healthcare provision (reduced social mixing, reduced healthcare seeking, reduction in secondary care referrals and GP testing) ([48](#)) resulting from the COVID-19 pandemic response are key drivers of the changes observed. More research is required in this area, but in the immediate term it is reasonable to attribute the reported decreases in bacteraemia incidence to multiple factors such as reduction in healthcare interactions, improved infection prevention control (IPC; such as PPE, hand washing and use of hand sanitizer) and behavioural changes such as social distancing, and even possibly diagnostic capacity discussed further below.

Additionally for endogenous pathogens, such as *S. aureus* and *E. coli*, incidence reductions could be due to a change in the patient mix in hospitals and cancellations of elective and non-urgent surgeries with subsequently fewer SSI ([49](#)). *E. coli* contributes substantially to total BSI burden, and the marked reduction in BSI incidence may also be due to changes in healthcare interactions in vulnerable populations and, antibiotic usage ([50](#), [51](#)). The majority of *E. coli* BSI are community-onset so other factors such as improvements in hand hygiene (reducing occurrence of UTI) ([52](#), [53](#)) decreased community transmission (via contamination and food) and even reduced international travel (known as a risk factor for increased colonisation, particularly with more resistant strains) ([54](#)) may also have had a role in the observed reduction. Further work to understand these changes, particularly to understand whether there are disproportionate changes by geographic region or patient demographic, where COVID-19 trends differed or where COVID-19 may have been a competing infection and risk of death are needed. In addition, an increase in patients requiring mechanical ventilation, often associated with VAP, was seen throughout the COVID-19 pandemic. Common VAP pathogens include gram negative bacteria not included in this report, as well as other fungal pathogens ([54](#)). Additionally, trends in incidence of these and other complex and opportunistic infections are not fully captured in this report.

There has been a general increase in the reported percentage resistance for each key drug and bug combination in BSI isolates in over the full 5-year period reviewed (2016 to 2020), although for some drug and bug combinations the percentage resistance is lower in 2020 than in 2019. There were large increases observed between 2016 and 2020 in co-amoxiclav resistance and third-generation cephalosporin resistance in *E. coli* and *K. pneumoniae* as well as both ciprofloxacin and piperacillin/tazobactam resistance in *K. pneumoniae* (Table 2.1). In contrast, the total prescribing of penicillin with inhibitors and fluoroquinolones reduced over the same period, while an increase in the use of third, fourth and fifth-generation cephalosporins has been reported (see [Chapter 5](#)). Also to be considered is that both fluoroquinolone and penicillin with inhibitors consumption increased in secondary care between 2016 and 2020. To investigate the changes in resistance for these and other specific drug and bug combinations in further detail, future ESPAUR reports will include age group breakdowns.

During the COVID-19 pandemic various treatment options for COVID-19 have been reviewed - based on differing clinical severities, including macrolides and doxycycline. The Platform Randomised Trial of Treatments in the Community for Epidemic and Pandemic Illnesses (PRINCIPLE) trial explored the use of doxycycline and clarithromycin for community treatment of suspected COVID-19 in people at increased risk of an adverse clinical course in the UK ([56](#)) and indicated that there is no beneficial effect in those patients aged over 50-years treated at home during the early stages of COVID-19. The Randomised Evaluation of COVID-19 Therapy (RECOVERY) trial indicated no evidence of benefit of azithromycin for clinical outcomes of patients hospitalised with COVID-19 ([57](#)). As well as these, management of COVID-19 included antibiotics for treatment of suspected or confirmed bacterial co-infections ([58](#)). From the review of clinically-relevant drug and bug combinations in respiratory samples, an increase was seen in resistance from 2019 to 2020 in *H. influenzae*, *P. aeruginosa* and *S. pneumoniae*, apart from ampicillin/amoxicillin and *S. pneumoniae*. Potential reasons for these increases could include changes in certain antibiotic being prescribed. While there has been an overall reduction in quinolone usage, increased consumption in the hospital inpatient setting has been seen. Additionally, in secondary care an increase in piperacillin/tazobactam and penicillin with inhibitor consumption has been noted between 2018 and 2020 ([Chapter 5](#)). More information on antibiotic usage of macrolides and other antibiotics used in CAP and HAP can be found in [Chapter 5](#). The full impact of the changes in consumption on AMR may not be seen until 2021 or beyond, and therefore continued monitoring is required. The reduction in respiratory isolates may have occurred due to the reasons outlined above for BSI isolate incidence reduction including reduced transmission and changing case mix in hospital.

This year's report introduces highlights of antiviral susceptibility in key viral pathogens (Boxes 2.4 and 2.5), highlighting the affects that the COVID-19 pandemic have had there. For instance, the seasonal influenza has been affected with low level activity in influenza indicators. However, the importance of influenza prevention measures is key as co-infection with Sars-CoV-2 increases the risk of ICU admission, mechanical ventilation requirement and mortality ([59](#)). The overall antiviral resistance patterns in Influenza A remained low in 2020 with oseltamivir resistance at 0% and 0.06% in A(H1N1) and A(H3N2), respectively. Zanamivir resistance was not seen in any cases of either A(H1N1) or A(H3N2). Further information on cases are reported

in the weekly national flu reports during the active influenza season ([60](#)) and summarised in the flu annual report for each flu season ([61](#)).

In addition to Influenza virus, other virus susceptibility highlights contained in this report include HCV, where an expansion of the DDA agents used for treatment have been seen. In more recent years there has been an increase in resistant HCV in therapy naïve patients. The reason for this is unknown although it is hypothesised that resistance has been selected by expansion of elbasvir-grazoprevir since 2016. In addition, resistance in DAA-experienced individuals has also remained high over this period. Thus, there is a high likelihood of emergent NS5A resistance in this population.

*N. gonorrhoeae* isolates have had a decrease in proportion of reduced susceptibility to first line therapy, ceftriaxone, from 2019 to 2020 which had previously been increasing. The prescribing over this period has been seen to be optimal. Though there has been an increasing trend since 2016 in reduced susceptibility to antibiotics no longer advised in BASHH guidance such as ciprofloxacin and tetracyclines. Further data on antibiotic resistance in *N. gonorrhoeae* is available online in the GRASP report ([62](#)). *M. genitalium* isolates have seen most specimens in different demographic groups become resistant to macrolides. Further data on antibiotic resistance in *M. genitalium* is available online in the MARS report ([63](#)). Over the past few years there have been a reduction in the number of MDR tuberculosis cases however increasing percentage MDR seen. INH monoresistance in tuberculosis has been above 6% since 2018 which remains problematic due to the increased risk of complications and prolonged treatment required. Further data on AMR in tuberculosis is available online in the annual tuberculosis report ([64](#)). Information on HIV resistance in the UK is available online in the UK HIV drug resistance database ([65](#)).

A combination of the above changes in transmission and clinical practice have resulted in an overall antibiotic resistance burden decrease in 2020; a year which saw the lowest estimated burden since 2016. The 5 year AMR NAP has a key ambition to achieve a reduction in the AMR burden. Targeted monitoring of key organisms and resistance trends over the next few years will be important to establish whether this reduction in the estimated incidence of antibiotic resistance will be sustained. While also trying to better understand where the gaps during the COVID-19 pandemic arise, establishing what the drivers were for the reduction in incidence and resistance for some pathogens is essential (for example, laboratory capacity and reduced screening, reduced admissions in key demographic groups). Further investigations into the differences in surveillance data, alongside hospital admission data, will be critical to this. Though these declining trends seen in resistance throughout this report between 2019 and 2020 should consolidate on the reductions noted through increased antimicrobial stewardship and utilising IPC.

More frequent monitoring of AMR was established in 2020 to assess changes to AMR during and after the COVID-19 pandemic and is ongoing in 2021. This data is reviewed each month and over time the inclusion criteria have been expanded to encompass more organism and antibiotics for respiratory and blood culture specimens. Relevant increases are cascaded to

other teams to be acted upon in a timelier manner. This is being conducted alongside surveillance of antimicrobial usage, where changes in usage may have longer term trend impact of AMR ([Chapter 5](#)).

## Future actions

UKHSA will:

- continue to develop a new infrastructure to assess antimicrobial prescribing and resistance at patient level
- investigate antimicrobial usage and antimicrobial resistance in UTIs and new data sources which can be used for this
- investigate usage and resistance of cephalosporin antibiotics, including presence of ESBL
- continue to investigate the impact of the COVID-19 pandemic on antimicrobial resistance, including trends by geography and patient demographic, changes in resistance when co- or secondarily infected with COVID-19 or other respiratory viruses
- investigate further the trends and antibacterial resistance in bacterial LRTI, alongside antibiotic usage against the recommended guidance for HAP, CAP and VAP
- consider and investigate opportunities for intervention measures using IPC and paradigm reframing
- investigate the impact of changing trends in antibiotic resistance specifically reviewing the differences by geographical region, demographic factors and health inequality

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

### Introduction

Increasing levels of antimicrobial resistance (AMR) pose a significant threat to healthcare and economic stability globally. In particular, carbapenems are often referred to as ‘antibiotics of last resort’ due to their activity against multi-resistant bacteria. However, carbapenem resistance due to the emergence of genes encoding acquired carbapenemases (enzymes that can break down carbapenem antibiotics) is most concerning due to their additional ability to transfer between different bacterial species.

In May 2019 PHE received its remit letter outlining its deliverables in support of commitments made in ‘Tackling antimicrobial resistance 2019 to 2024: The UK’s 5-year national action plan’ ([66](#)). The remit directed enhancements and a continuation in the long trend of initiatives (Figure 3.1, and as described in previous years’ reports) ([67](#), [68](#)) aimed at preventing and controlling the spread of Carbapenemase-Producing Enterobacterales (CPE) in England, with a number of key developments occurring during 2020, a few of which are summarised below and discussed in more detail through the chapter.

- In March 2020, there was a recommendation to laboratories from the Royal College of Pathologists (RCPATH) and professional bodies to help mitigate the burden that the COVID-19 pandemic was placing them under ([69](#)). These recommendations included stopping screening for CPE in low-risk settings.
- In October 2020, the Health Protection regulations were updated to include acquired carbapenemase-producing Gram-negative bacteria (CPGNB) isolated from human specimens as notifiable, since which time laboratories in England have been required to report cases to PHE ([70](#)).
- Also during 2020, a national Framework of Actions to contain CPE ([71](#)) were launched to assist NHS Trusts by setting out a range of measures to follow to help reduce spread of CPE (replacing the Acute Trust toolkit for early detection, management and control of CPE) ([72](#)).

This year’s ESPAUR report’s acquired CPGNB (formerly CPE) chapter captures the key updates on an important year for acquired carbapenemase surveillance, and this will provide an update on progress made to contain and control the spread of CPE in England. Included within this chapter is an epidemiological summary of the first quarter of acquired CPGNB notifications, alongside an update on the frequency, or lack, of CPGNB isolates referred to the national Antimicrobial Resistance and Healthcare-Associated Infections (AMRHAI) Reference Unit. In addition to the surveillance updates, the results of a survey of laboratories that was launched in March 2021 are presented, which looked to assess the impact of COVID-19 and



recommendation and guidance changes which were made during 2020. Data tables and graphs for the results presented within this chapter are available in the [data and figures appendices](#) published alongside the report.

## Surveillance of acquired carbapenemase-producing Gram-negative bacteria

Carbapenem resistance encoded by a mobile genetic element was first described in England in 2003 ([73](#)). Since then, several prominent mechanisms conferring carbapenem resistance due to the production of a carbapenemase enzyme have been identified in England, such as KPC, NDM, OXA-48-like, VIM and IMP. These mechanisms have been found in many Gram-negative species including *Escherichia coli*, *Klebsiella pneumoniae* and *Enterobacter cloacae* complex. In some instances, more than one mechanism of resistance has been detected in the same bacterial isolate ([74](#)).

With increasing local laboratory capacity to identify the 'Big 5' carbapenemase families (KPC, OXA-48-like, NDM, VIM and IMP), on 1 January 2019 the AMRHAI Reference Unit amended the referral criteria for carbapenemase testing ([75](#), [76](#)) requesting only locally-confirmed CPE isolated from sterile sites. Although, laboratories were alerted to the imminent change in late 2018 and so there may have been a pre-emptive reduction in referrals for carbapenemase confirmation noted in December 2018.

Data on CPE identified by the PHE AMRHAI Reference Unit, as well as the first quarter (October to December 2020) of CPGNB notifications, is presented in the next few sections of this chapter. Details on the methods and a full timeline of activities relating to CPE can be found in the [methods annexe for Chapter 3](#).

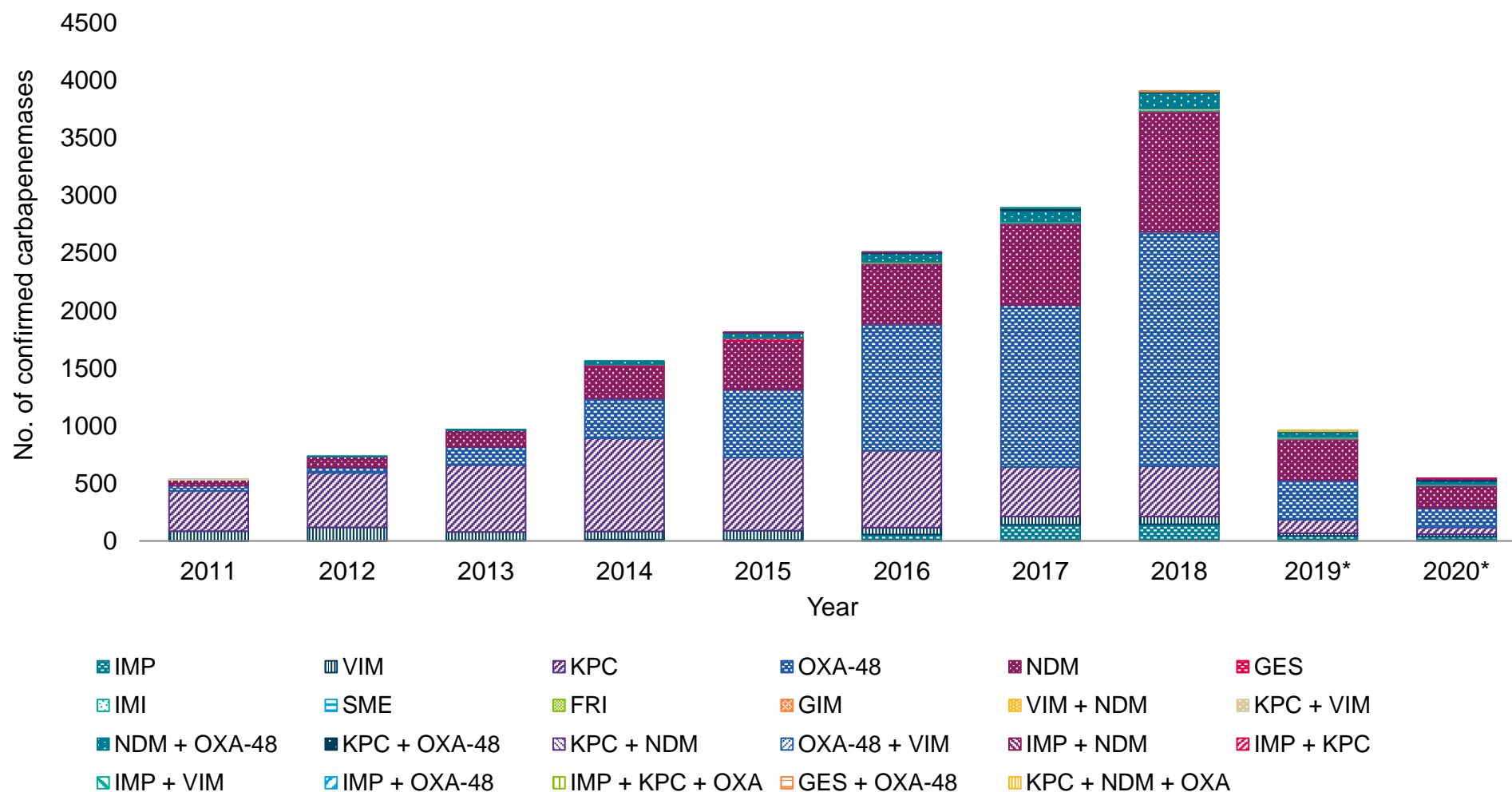
### Carbapenemase producing Gram-negative bacteria referral data

#### AMRHAI Reference Unit

Following the referral criteria change in 2019, a drop in CPE isolates referred to the AMRHAI Reference Unit was noted in 2019. This drop continued into 2020, with only 606 isolates confirmed as positive for at least one carbapenemase by the AMRHAI Reference Unit, or by regional PHE or NHS laboratories from samples referred for other laboratory tests (Figure 3.1).

**Figure 3.1a Number of confirmed CPE isolates referred to PHE's AMRHAI Reference Unit (excluding blood cultures), 2011 to 2020**

Note that following a change to the referral criteria in 2019, only a limited selection of CPE were submitted to the AMRHAI Reference Unit (indicated by an asterisk).





**Figure 3.1b Number of confirmed CPE blood culture isolates referred to PHE's AMRHAI Reference Unit\*, 2011 to 2020**

Note that following a change to the referral criteria in 2019, only a limited selection of CPE were submitted to the AMRHAI Reference Unit (indicated by an asterisk).

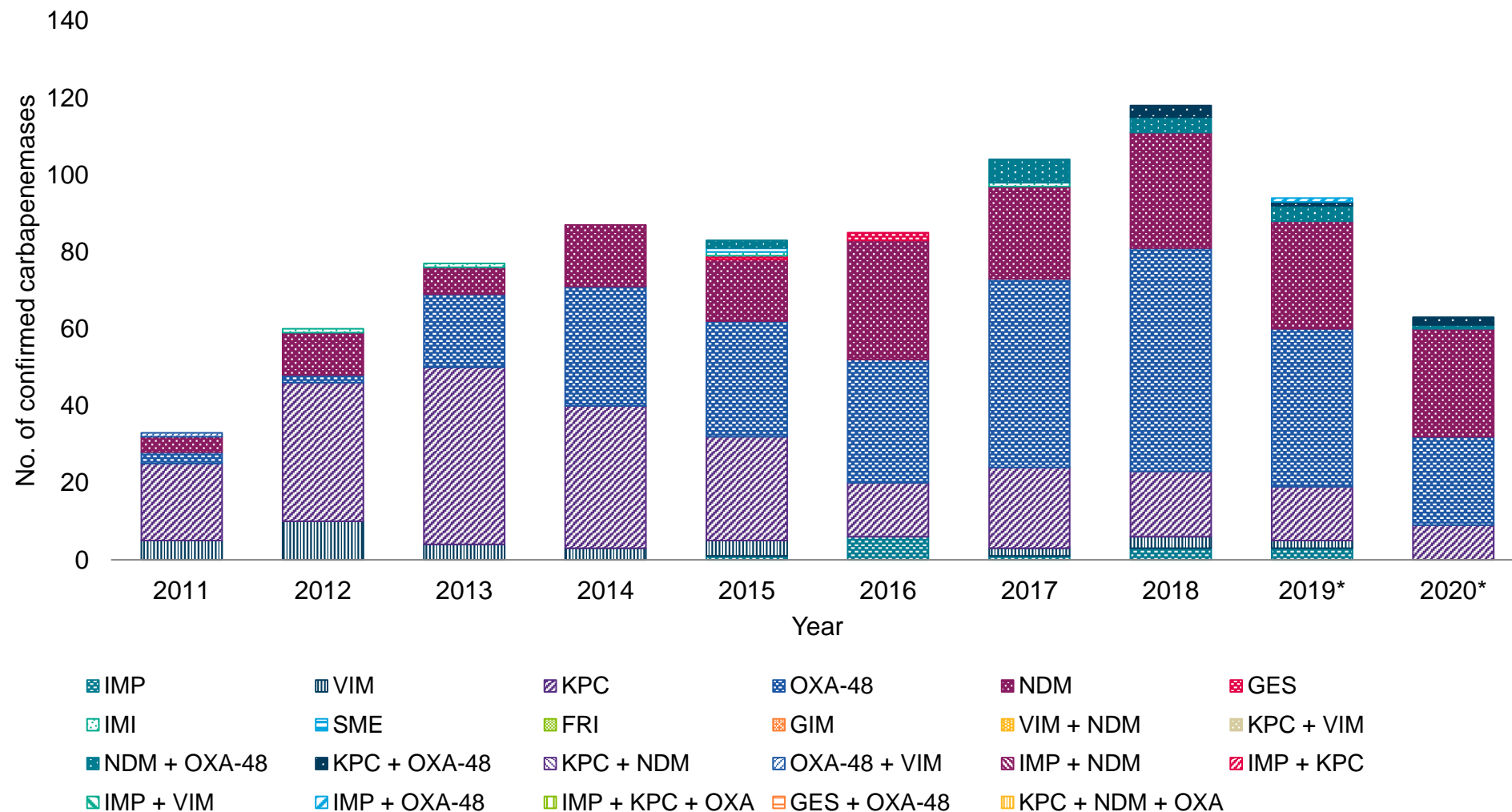


Figure 3.1a demonstrates the impact of the change in referral criteria introduced in January 2019, together with the large reductions in confirmed CPE isolated from non-blood isolates in 2019 and in 2020, compared with the previous years (2011 to 2018). The reductions were less dramatic for blood isolates (Figure 3.1b), reflecting the fact that isolation from normally sterile sites, including blood, remain part of the referral criteria. Beyond the referral criteria change, there are other possible causes for the reduction in recent years, including the introduction of a charge for confirmation of 'Big 5' carbapenemases (introduced in April 2018), alongside increasing local capacity to identify the 'Big 5' mechanisms ([77](#), [78](#)) and, in 2020, changes as a result of the COVID-19 pandemic, which will be picked up through the chapter.

There was a slight increase in the percentage of CPE originating from blood in 2020 compared to 2019 (10.4% vs. 8.9% of confirmed CPE referrals, respectively). The 'Big 5' carbapenemase families (KPC, OXA-48-like, NDM, VIM and IMP) and combinations thereof, continue to dominate and account for over 97% of CPE. NDM carbapenemases accounted for 36% of confirmed CPE in 2020, replacing OXA-48-like (31.7%), as the most common carbapenemase family identified, followed by KPC (11.4%), IMP (5.9%) and VIM (3.8%). The most common host organisms were *Klebsiella* spp. (47%), *E. coli* (25.6%) and *Enterobacter* spp. (20.6%). CPE were referred from all 9 PHE regions, but with foci in London (37.8% of CPE), the East (14%) and South East (11%) of England.

While earlier sections of the chapter reported only on Enterobacterales, the following section focuses on all Gram-negative bacteria.

### Isolates from the Gastrointestinal Bacteria Reference Unit (GBRU)

There were 4,498 *Salmonella* isolates (4,076 human, 251 food, 83 animal, 11 environmental and 77 other sources) from England received at PHE's GBRU. No genetic mutations conferring carbapenem resistance were identified among these isolates.

There were a further 402 *Campylobacter* spp. (314 human, 82 food and 20 other sources), 990 Shiga-toxin producing *E. coli* (STEC) (all human) and 769 *Shigella* spp. (768 human and one from another source) isolates from England received at PHE's GBRU in the same time period and again no genetic mutations conferring carbapenem resistance were identified among these isolates.

## Carbapenemase producing Gram-negative bacteria notification data

### Initiation of mandatory carbapenemase-producing Gram-negative bacteria reporting

From 1 October 2020, all diagnostic laboratories in England have a statutory duty to notify PHE of all Gram-negative bacteria with acquired carbapenemases identified in human samples together with the results of any antimicrobial susceptibility test and any resistance mechanism, for any of the causative agents listed in Schedule 2 of the Health Protection (Notifications) Regulations 2020 ([79](#)). Reporting is via PHE's Second Generation Surveillance System (SGSS). This requirement was launched in conjunction with the new UK Standards for

Microbiology Investigations (SMI) for the detection of bacteria with carbapenem-hydrolysing  $\beta$ -lactamases (carbapenemases), which was published on 30 September 2020 (80).

Following the inclusion of carbapenemase screening in the notification schedule, a mechanism to combine reference laboratory referrals with local laboratory-confirmed carbapenemases was implemented (see [Methods annexe for Chapter 3](#)). Data presented in this section 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 (81) which currently only include local laboratory reports.

October 2020 also marked the introduction of an additional mandatory reporting requirement for acute Trusts to report quarterly totals of rectal swabs and faecal screening specimens taken for CPE through the healthcare-associated infections (HCAI) data capture system (DCS) quarterly mandatory laboratory returns (QMLR) facility.

#### First quarter (October to December 2020) of notification data

Between October and December (Q4) 2020 there were 719 positive carbapenemase specimen reports made through either referral (136; 18.9%) and SGSS (580; 81.1%), from 494 patients, which once de-duplicated for organism, mechanism and specimen type, amounted to 586 notifications (details on notification definition and de-duplication are available in the [Methods annexe for Chapter 3](#)).

**Table 3.1 Number\* and percentage of acquired carbapenemase-producing Gram-negative reports by specimen type in England, Q4 2020**

Specimen type	All reports		From AMRHAI ‡	
	No.	% of all reports¥	No.	% of all reports sent to AMRHAI§
Sterile site samples	35	6.0	20	57.1
Screening samples	417	71.2	61	14.6
Other samples †	134	22.9	41	30.6
All samples	586	100	130	20.8

\* Cases according to the de-duplication method described in the [Chapter 3 methods annexe](#). Results are preferentially selected from the AMRHAI Reference Unit where specimen from both sources have been reported.

† Samples that do not fall into either 'invasive' or 'screening' samples, for example, urine and lower respiratory tract specimens.

‡ The AMRHAI Reference Unit actively encourages submission of sterile site isolates for carbapenemase confirmation; the distribution of specimen type will reflect this.

¥ The percentage of all reports is a column percentage, while the percentage that were sent to AMRHAI is a row percentage.

Table 3.1 shows that the majority were identified in screening samples, accounting for 71.2% of carbapenemase cases, with only 6.0% reported in sterile site specimens. *K. pneumoniae* were the most frequently reported species with a carbapenemase (195; 33.3%), followed by *E. coli*

(143; 24.1%) and *Enterobacter* spp. (116; 19.5%) ([Table 3.2](#)). The most commonly reported carbapenemases in Q4 2020 were OXA-48-like (42.3%), NDM (26.1%) and KPC (21.9%).

The distribution of carbapenemase producers within each Gram-negative species is presented in [Table 3.2](#) (full table available in the web appendix). For *K. pneumoniae*, *E. coli* and *Klebsiella oxytoca*, OXA-48-like carbapenemases were the most frequently identified mechanism, accounting for 52.3%, 49.7% and 47.4% of specimens respectively, followed by NDM and KPC. For *Enterobacter* spp., the most frequently identified mechanism was KPC (34.9%) followed by OXA-48-like (30.2%). Some bacterial species have inherent carbapenemases, and some combinations of species and carbapenemase are considered 'exceptional', a full list of species and mechanisms that are tested for by the AMRHA Reference Unit, and whether they are considered inherent or exceptional are included in [Annexe](#) table 3.1.

**Table 3.2 Acquired carbapenemase-producing Gram-negative reports by species and carbapenemase family for the 'Big 5' (KPC, NDM, OXA-48-like, VIM, IMP) in England, Q4 2020**

Resistance mechanism*	IMP		KPC		NDM		OXA-48-like		VIM		Other‡		Total	
Species	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%	No.	%
<i>Acinetobacter</i> spp.	1	20.0	0‡	0.0	3	60.0	0‡	0.0	0	0.0	1	20.0	5	100
<i>Citrobacter</i> spp.	0	0.0	2	7.1	8	28.6	15	53.6	3	10.7	0	0.0	28	100
<i>Enterobacter</i> spp.	9	7.1	44	34.9	32	25.4	38	30.2	0	0.0	3	2.4	126	100
<i>Escherichia coli</i>	1	0.7	15	10.5	51	35.7	71	49.7	4	2.8	1	0.7	143	100
<i>Klebsiella oxytoca</i>	0	0.0	8	42.1	0	0.0	9	47.4	2	10.5	0	0.0	19	100
<i>Klebsiella pneumoniae</i>	3	1.5	51	26.2	36	18.5	102	52.3	3	1.5	0	0.0	195	100
Other <i>Klebsiella</i> spp.	1	4.2	5	20.8	11	45.8	7	29.2	0	0.0	0	0.0	24	100
<i>Morganella</i> spp.	0	0.0	0	0.0	0	0.0	2	100	0	0.0	0	0.0	2	100
<i>Pseudomonas aeruginosa</i>	7	23.3	2 ‡ <sup>A</sup>	6.7	7	23.3	0	0.0	12	40.0	2	6.7	30	100
Other <i>Pseudomonas</i> spp.	0	0.0	2 ‡ <sup>A</sup>	40.0	1	20.0	0	0.0	2	40.0	0	0.0	5	100
<i>Serratia</i> spp.	0	0.0	0	0.0	1	33.3	2	66.7	0	0.0	0	0.0	3	100
Other Gram-negative bacteria †	1	16.7	0	0.0	2	33.3	3	50.0	0	0.0	0	0.0	6	100
<b>Total</b>	<b>23</b>	<b>3.9</b>	<b>129</b>	<b>22.0</b>	<b>152</b>	<b>25.9</b>	<b>249</b>	<b>42.5</b>	<b>26</b>	<b>4.4</b>	<b>7</b>	<b>1.2</b>	<b>586</b>	<b>100</b>

\* Some resistance mechanisms are not appropriate for every species.

† Includes coliform, other *Escherichia hermannii*, *Hafnia alvei*, and *Raoultella* spp.

‡ Extremely rare in England, more commonly associated with travel.

A *Pseudomonas* spp. contains an AmpC beta-lactamase which is inhibited by boronic acid. Boronic acid also inhibits the class A beta-lactamases (such as KPC), and phenotypic mechanism tests are not capable of discriminating. The phenotypic test is not recommended for use with *Pseudomonas* spp. or *Acinetobacter* spp. but laboratories may do so anyway. Laboratory reporting data received by PHE through SGSS does not include the test used, as a result, these results should be interpreted with caution

¥ Other mechanisms include GES and IMI.

Very few carbapenemase families outside of the 'Big 5' were notified in the first quarter of notifications, and these were reported by the AMRHA Reference Unit only. There were 4 reports of the GES carbapenemase (2 in *Pseudomonas aeruginosa* and one in both *Acinetobacter* spp. and *E. coli* specimens) and there were 3 *Enterobacter* spp. specimen reports positive for the IMI carbapenemase mechanism. None of the rarely identified carbapenemase mechanisms were from invasive specimens.

### Age and sex distribution

The rate per 100,000 population of acquired carbapenemase-producing Gram-negative bacteria generally increased with age (Table 3.3), with the highest rates being noted in the 75 years and over age group (4.8 per 100,000 population; 5.1 and 3.6 per 100,000 in males and females respectively), followed by the 50 to 74 years age group with 4.3 per 100,000 population (4.0 and 3.0 per 100,000 in males and females respectively). Rates were also high among infants under one year old, with 2.4 per 100,000 population (3.0 and 2.0 per 100,000 in males and females respectively). In the majority of age groups, rates of acquired carbapenemase-producing Gram-negative bacteria per 100,000 were higher amongst males compared to females.

**Table 3.3 Acquired carbapenemase-producing Gram-negative reports by age group and sex† per 100,000 population in England, Q4 2020**

Age group	Male			Female			Total		
	No.	%	Rate*	No.	%	Rate*	No.	%	Rate*
under 1	8	2.5	2.4	6	2.4	1.9	15	2.6	2.4
1 to 4	6	1.9	0.4	6	2.4	0.5	14	2.4	0.5
5 to 9	1	0.3	0.1	4	1.6	0.2	6	1.0	0.2
10 to 19	9	2.8	0.5	1	0.4	0.1	11	1.9	0.3
20 to 29	9	2.8	0.1	5	2.0	0.0	14	2.4	0.1
30 to 49	31	9.8	0.4	28	11.2	0.4	64	10.9	0.4
50 to 74	133	42.1	5.0	97	38.8	3.4	236	40.3	4.3
Over 75	119	37.7	6.0	103	41.2	3.9	226	38.6	4.9
Total	316	100.0	1.1	250	100.0	0.9	586	100.0	1.0

\* Rates were calculated using Office for National Statistics' (ONS) Mid-Year Population Estimates (2020) as a denominator.

† Information about patient sex is recorded in 97% of cases.

### Geographical variation

The rate per 100,000 population of acquired CPGNB varied regionally (details of regional mapping are described further in the [Methods and caveats annexe for Chapter 3](#)).

**Figure 3.2a. Rate of acquired carbapenemase-producing Gram-negative reports shown by region in England, Q4 2020**

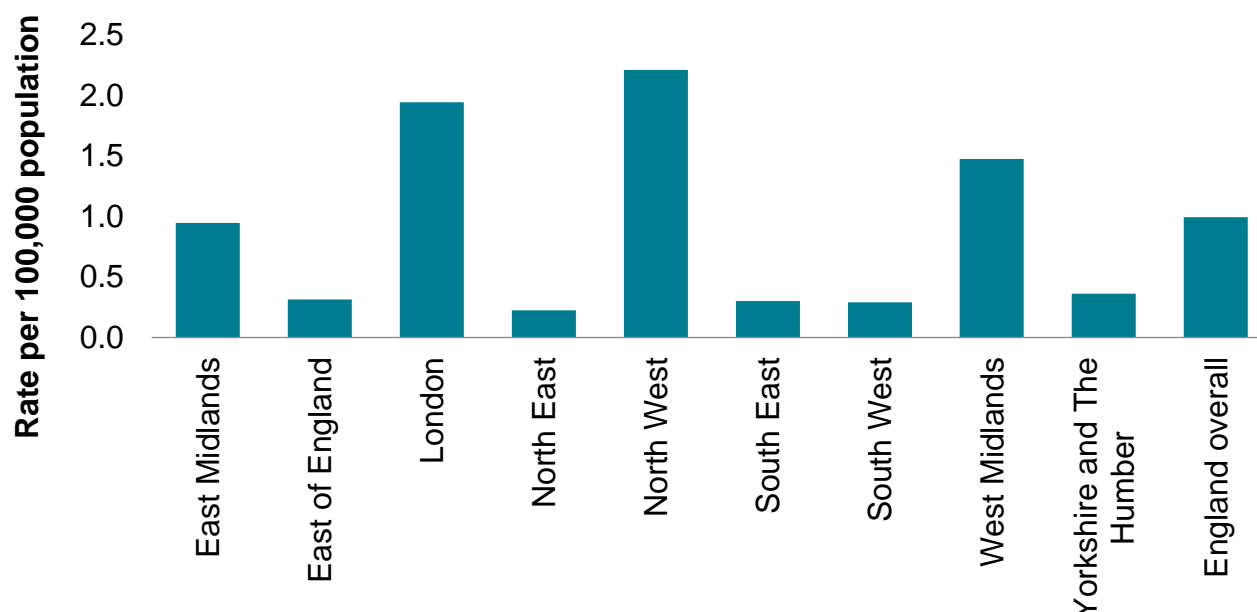


Figure 3.2a shows that the rate of acquired CPGNB ranged from 0.22 per 100,000 population in the North East region to 2.21 per 100,000 population in the North West region. After the North West region, London had the highest rate of confirmed acquired CPGNB isolates, with 1.94 reports per 100,000 population.

**Figure 3.2b. Distribution of acquired carbapenemase-producing Gram-negative reports by resistance mechanism and region in England, Q4 2020**

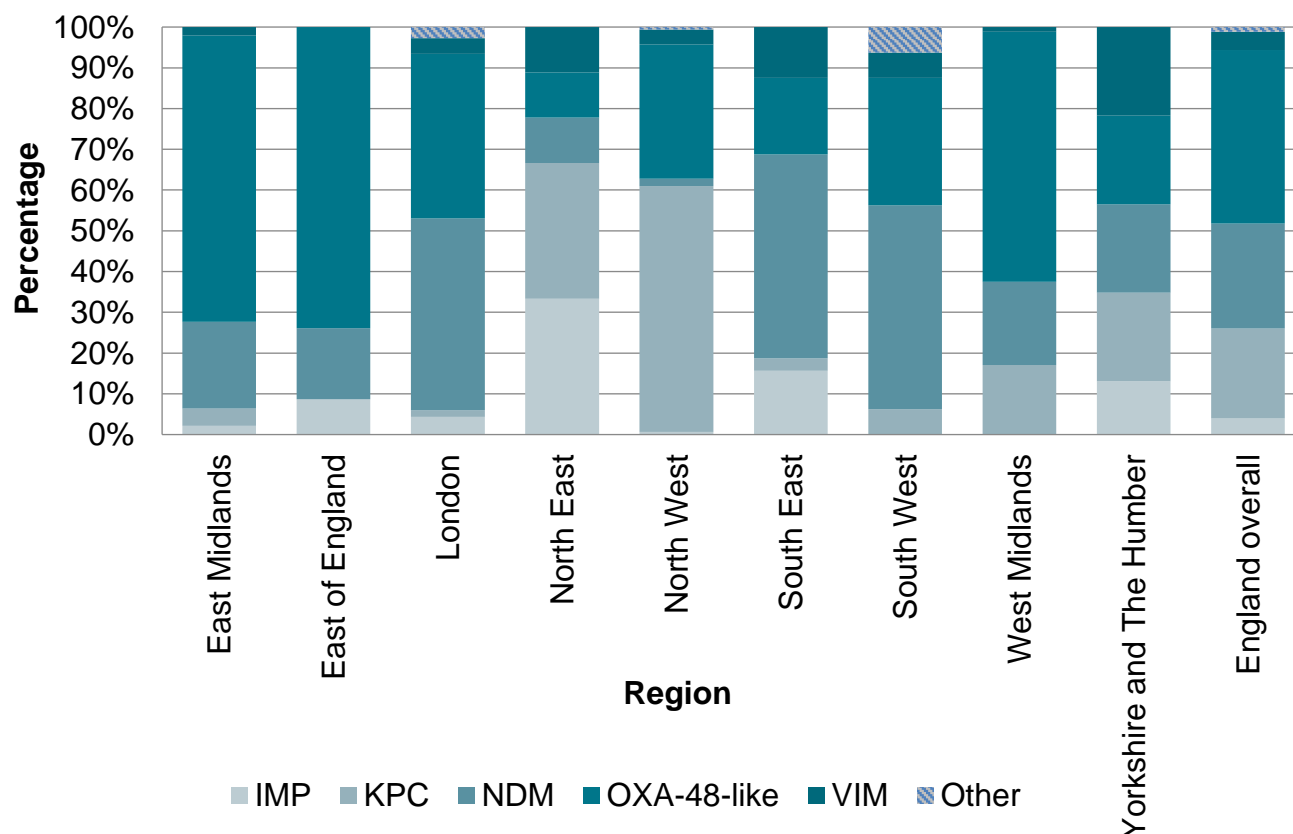


Figure 3.2b shows that the distribution of carbapenemase families also varies by region. The most common carbapenemase families seen in isolates from London were NDM (47.0%) and OXA-48-like (40.4%). In comparison, the most common carbapenemase families in isolates from the North West were KPC (60.4%) and OXA-48-like (32.9%), whilst those seen in isolates from the North East were IMP (33.3%) and KPC (33.3%). In comparison, the most common families seen in isolates from the South West were NDM (50%) and OXA-48-like (31.3%).

### Quarterly Mandatory Laboratory Return (QMLR) reports

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 (82). (This was notified to all acute Trusts through the HCAI DCS information cascade system in October 2020.)

The total number of screens reported for the first mandatory quarter was 101,153, from 105 Trusts (78% of Trusts; Table 3.4). Of the acute Trusts that reported screening data, 5% reported that they conducted zero faecal screens.

**Table 3.4 QMLR returns for the total number of rectal swabs and faecal screening specimens taken for CPE screening by acute Trust type\*, England, October to December 2020**

Trust Type*	Number of Trusts			Total screens reported	
	Submitted screens	Submitted zero screens	Did not submit screens	No.	%
Small	20	1	7	3,654	4
Medium	20	2	4	6,943	7
Large	25	1	2	10,483	10
Multi-service	3	0	1	480	0
Specialist	10	3	3	5,412	5
Teaching	30	0	6	74,181	73
Total	108	7	23	101,153	100

\* Trust type obtained through NHS Digital Estate Return Information Collection (ERIC).

Screening was more predominant in the acute teaching Trusts, accounting for 73% of screening swabs taken in the time period. By reporting acute Trust, the total screens reported for the quarter ranged from 0 to 11,859. The full list of Trust reporting is available in the [data appendix for Chapter 3](#).

There is limited scope for interpreting the screening surveillance data from 2020 given the context of all of the other challenges facing the NHS during 2020. As well as the aforementioned recommendations to reduce CPE screening, there were also widescale changes in healthcare access, patient-mix and infection source noted during 2020. In an



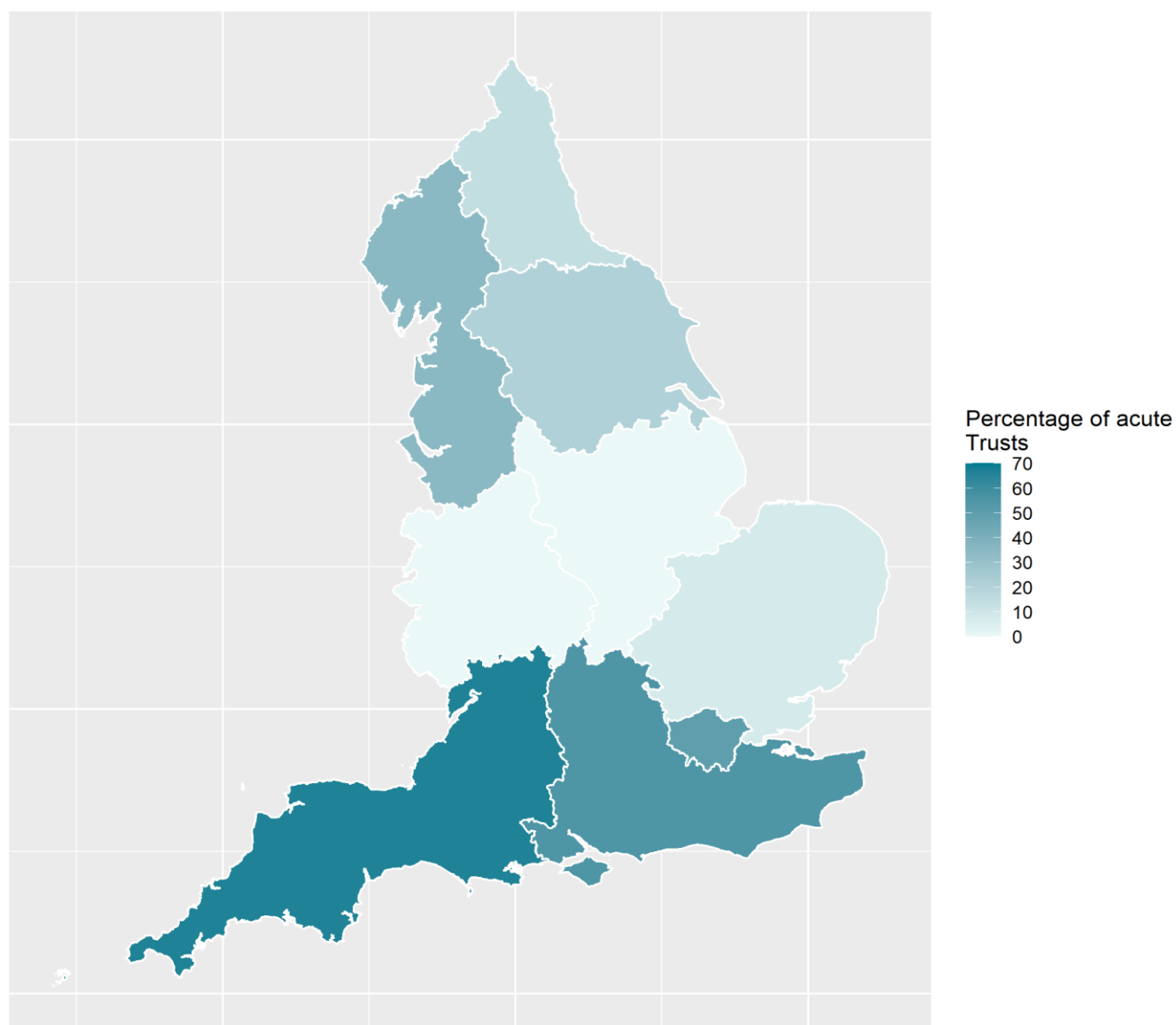
attempt to get a better understanding of changes in screening behaviour, and therefore reporting, PHE launched a survey in March 2021, the results of which are described in the next section.

## Impact survey: Royal College of Pathologists and professional bodies

The Royal College of Pathologists (RCPATH) and professional bodies (Institute of Biomedical Science [IBMS], the Association of Clinical Biochemistry and Laboratory Medicine [ACB] and the Association of Clinical Pathologists [ACP]) released new recommendations in March 2020 with regards to the prioritisation or deferral of pathology laboratory work in light of SARS CoV-2 pandemic. Specifically, for CPE, there was a recommendation ‘for reducing the need for screening of CRE (carbapenem-resistant enterobacteria) and VRE (Vancomycin-Resistant *Enterococcus*) in low risk areas’ ([83](#)) without definition of low risk.

To capture and determine what impact these recommendations may have had on the screening for CPE, an impact survey was distributed to all Trusts in England in March 2021. In total, responders from 47 hospitals across 46 Trusts (33%) completed the survey, representing 5 of the 7 English regions (Figure 3.3). The survey questions can be found in the [Methods and caveats annexe for Chapter 3](#).

**Figure 3.3. Regional distribution of responses to the survey as a percentage of the total acute Trusts in the region (n=47)**



Contains OS data © Crown copyright and database right 2018

The regions with the greatest representation of acute Trusts were the South West (10; 66.7%), South East (12; 55.0%) and London (11; 50.0%; Figure 3.3). There was only one respondent from both the North East and East of England, representing 14.3% and 7.7% of Trusts in the regions respectively. Trusts from the East Midlands and West Midlands were not represented in the survey responses (0.0%).

All of the responding Trusts indicated that they had a CPE screening policy in place. When asked when the CPE screening policy was last updated, the majority of respondents (95%; 40/42) indicated that their policy had been updated recently (since 2015). Of these 40 respondents, 23.8% (10 out of 42) indicated that their Trust had updated their screening policy during 2021, and 21.4% (9 out of 42) had done so in 2020.

Respondents were asked if their Trust had experienced a reduction in screening due to any of a 'natural reduction in the number of patients admitted to hospital who would have previously been screened', following the RCPATH recommendations and/or due to capacity or resource constraints. Of the 41 respondents to the question, 18 (43.8%) indicated a reduction. The question was multi-select, as such, the sum of percentages do not equate to 100%. Of those who reported a reduction, the vast majority of respondents (94.4%) indicated that there had been a 'natural reduction in the number of patients admitted to hospital who would have previously been screened'. In addition, 16.7% indicated that the reduction was due to a change in screening policy following the RCPATH recommendations and 11.1% indicated that the reduction in CPE screening was due to capacity or resourcing constraints.

Respondents were asked about which patients would be screened at their hospital (multiple options were available to select), with 43 responding to the question. Almost all hospitals indicated that they screen patients transferred from healthcare facilities abroad (97.7%; 42/43) and patients previously identified with CPE (39; 90.7%). Furthermore, 79.1% (34) of hospitals reported screening patients that are known contacts of another patient with CPE and 72.1% (31) of hospitals reported screening all patients who have been in any hospital (UK or abroad) in the last 12 months for CPE.

Forty-three responders provided information on their CPE screening regimen as described in their local policy (Table 3.5), multiple options were available for selection. The most common practices for CPE screening were one admission screen (55.8%; 24 out of 43), 3 admission screens 48 hours apart (17; 39.5%) and weekly screening in high risk areas (11; 18.0%). For the majority of hospitals (39; 90.7%), screening policy was the same across the Trust and/or in different areas of the hospital.

**Table 3.5. CPE screening regimen as described by the local CPE screening policy (n=43)**

<b>What is your screening regimen?*</b>	<b>Frequency</b>	<b>%</b>
One admission screen	24	55.8
Three admission screens 48-hours apart	17	39.5
Weekly screening in high risk areas (for example, ITU, NNIC, Oncology units)	11	25.6
Monthly screening in high risk areas	2	4.7
Other	7	16.3

\* Respondents were able to select multiple options for this question.

## CPE Mathematical Models

Research at both within-host and between-host scales has found evidence of CPE presence in English hospitals beyond the situations or places which would previously have been considered most likely – be that bacterial genus or location of patients. Comprehensive vigilance is key to readily discover and contain such outbreaks.

Individual-based, stochastic mathematical modelling was used to investigate transmission of CPE within an English acute Trust and to evaluate admission screening protocols to identify CPE carriers to enable the application of suitable infection prevention and control (IPC) measures. Models were parameterised to represent typical Trusts for all English regions (including those with and without a history of a CPE problem).

Model findings from the evaluation of the screening criteria and testing pathway detailed in the 'Acute Trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae' (2013) [\(84\)](#) informed and supported recommendations to screen all admissions with previous hospital stays in the last year and to simplify the test pathway to confirm carriage in those screened. Broadening prior hospital stays included in the screening criteria (from solely areas with known CPE problems) increases the percentage of colonised patients selected for testing on admission to hospitals in low-prevalence regions from 43% (median, IQR 32% to 55%) to over 80%. Reducing the number of sequential swab tests in the screening test pathway (from 3 to one) increases the overall positive predictive value across all regions, based on the patients selected by the screening criteria, with negligible reduction in negative predictive value and reduces time until a result. Both recommendations combine to reduce colonised patients missed by admission screening and more efficiently uses resources needed for IPC measures.

The magnitude of gains in CPE-carrier pick-up from the switch of screening criteria was found to be affected by whether within-hospital transmission included non-patient sources. Fitting of transmission parameters using observational data from an English hospital indicated that the force of infection in some wards could include such sources. Thus, further research – collection of data and transmission analysis – is in progress examining this issue, specifically considering sink biofilms. It is hoped that the results of this work will assist settings in choosing an appropriate screening and control programme as part of their activities to restrict nosocomial CPE transmission.

A population genetics-based model was developed to describe a plasmid mediated OXA-48 outbreak in a hospital ward. Plasmids often encode the machinery to spread to neighbouring bacteria, with different host bacteria ranges. For this reason, plasmid-mediated outbreaks are challenging to detect as they often involve many different strains, species and even genera. They are often noticed only through appropriate surveillance strategies; therefore, a deeper understanding of the dynamics of specific plasmid outbreaks might help to devise improved surveillance strategies. Complementary roles for both plasmid conjugation and clonal expansion

fuelled the emergence of this outbreak. More specifically the outbreak was fed by a clonal expansion of p-OXA-48 in *E. coli* sequence type (ST) 399, while all the other hosts found in the outbreak likely resulted from independent conjugation events. The association between the plasmid and *E. coli* ST399 is already an interesting result in itself as it is the first time that an *E. coli*, and not a *Klebsiella* species was found to be the main host for this kind of plasmid. Comparative genomics analysis putting both the specific plasmid and the specific strain in the more general genetic landscape of similar plasmids and strains suggest co-evolution between plasmid and strain. The model, which relies on some strong assumptions, allows a phylogenetic analysis-based estimation of a lower bound for the plasmid conjugation rate: 0.23 conjugation events per lineage per year.

## Discussion

For many years there have been increases in the prevalence of CPE globally, and PHE has had the facility to identify the emergence of carbapenemases (85). The increased intensity of CPE related activities had led to the establishment of acquired CPGNB as a notifiable disease (causative agent) (86).

Interpreting the AMRHAI Reference Unit surveillance data from the last 2 years is challenging given the changing guidance around testing for, and the reporting and referring of CPE. Between 2013 and 2018 there was a year-on-year increase in the number of carbapenemase-positive isolates referred to the AMRHAI Reference Unit. Of note, since 2015 there has been increased uptake of commercially-available methods by local diagnostic laboratories (87) prior to 2019 these locally identified carbapenemase-positive isolates would have been referred to the AMRHAI Reference Unit for confirmation, potentially accounting in part for the yearly increases. However, subsequent declines in referrals have been noted in 2019 and 2020. In part the declines can be explained by the charge associated with 'Big 5' carbapenemase confirmation introduced in April 2018 (88) as well as the change to referral criteria, requesting only sterile site specimens be referred as of January 2019 (announced by the AMRHAI Reference Unit in late 2018) (89). It should be noted that locally identified 'exceptional' combinations of species and carbapenemase (annexe table 3.1) are requested for confirmation by AMRHAI Reference Unit, to help identify any emerging issues as well as to ensure that the statutory notification data remains valid.

Referral data alone cannot give a true idea of prevalence, particularly since the change in guidance. The AMRHAI Reference Unit data in 2020 indicated that the top 3 regions referring specimens were London, the East of England and the South East, which contrasts with when looking at the full notification data set (Q4 2020 only), where the North West region featured as prominent reporters of acquired CPGNB specimens. Much of the difference in regional variation between SGSS and the AMRHAI Reference Unit reports can be put down to referral behaviour, where large centres in the North West region have not been referring isolates for CPE confirmation for the last 5 years. Regional variation in CPGNB rates reported in the notification data within this chapter are in line with what has been reported previously; with

higher case rates in the London, North West and West Midlands regions ([90](#), [91](#)). The continued elevation in these regions is likely to be partly as an artefact of testing and screening in Trusts within these regions, with elevated ascertainment due to precautionary measures locally ([92](#), [93](#), [94](#)).

To better understand these differences, further work looking in more detail at the notification data is underway, looking at local capacity versus referral as well as undertaking a review of mechanism testing in specimens identified as carbapenem resistant (more detail on the numbers of bloodstream isolates in key Gram-negative bacteria that are resistant to carbapenems can be found in [Chapter 2](#) and the accompanying materials).

Beyond the data quality, it is hard to truly interpret what is being reported during 2020. The mandatory requirement for CPGNB screening came into effect, however, due to laboratory capacity concerns during the early phase of the COVID-19 pandemic, there were also recommendations to reduce screening for drug-resistant organisms ([95](#)). Although, it was promising that those hospitals which responded to the CPE screening survey did not change their practice as a result, responders did, however, indicate that there was a 'natural' reduction as a result in the reduction in the number of patients who would normally be screened being seen. [Chapter 2](#) of this report also highlights a reduction in *E. coli* bloodstream infection in 2020, as well as a decline in carbapenem resistance in Gram-negative organisms (bloodstream infection only). The reasons for the reductions noted are likely to be multifactorial including changes in patient case-mix, changes in healthcare seeking behaviour, reductions in elective surgeries, limited travel from high-risk areas and reduced person-to-person contact due to social distancing ([96](#), [97](#), [98](#)).

There still remain challenges, particularly due to the mandatory returns included in this report only covering one quarter (October to December 2020), which coincides with escalation towards the second wave peak of the COVID-19 pandemic in England ([99](#)). Careful monitoring going forward is critical to assist in the understanding of the burden of CPGNB, as well as interpreting the potential gaps in surveillance. As part of the continuing improvements in understanding of CPGNB in England, development of an audit feedback mechanism will likely help fill in some of the gaps, particularly where Trusts are not reporting the quarterly mandatory return on screening specimen numbers, or recording resistance mechanism testing results where phenotypic carbapenem resistance is determined. Development of these outputs and improving reporting will help get a much better understanding of the CPGNB testing landscape and allow local units the opportunity to act according to their local situation.

It is also likely that the COVID-19 pandemic had an impact on many of the results presented within the chapter, as well as the implementation of the CPE Framework ([100](#)). As highlighted by the GBRU, there was a large reduction in referral of isolates from patients with food poisoning from the community in 2020, again possibly due to social distancing or lockdowns and improved home IPC practices (such as increased hand hygiene) during the COVID-19 pandemic period ([101](#)). A wider piece of work to evaluate and unravel the variety of possible causes for reduced reporting of CPGNB identified through surveillance is being undertaken to

provide understanding to build from. This includes looking at screening rates, and notification gaps, testing gaps and infections secondary to COVID-19. Those who responded to the survey also provided monthly screening totals for CPE, the full list of which is available in the [Chapter 3 data appendix](#). These responses showed a decline around the peak of the first wave of the COVID-19 pandemic in England, possibly correlating to hospital service redistribution, reduction in patient referrals to secondary care and differences in case-mix (less elective procedure admission with a greater number of admissions more acutely unwell ([102](#), [103](#))).

Effective IPC remains essential and it is crucial that guidelines for CPE remain relevant to the emerging situation. When dealing with outbreaks, a multimodal approach is required to achieve control. Early detection of CPE and rapid implementation of enhanced control measures is crucial to prevent further colonisation, carriage and spread. With this in focus, using the surveillance data to help inform and enable local reaction in a more timely manner is critical. Frequent reporting mechanisms have been developed ([104](#)) with regular more detailed epidemiological analyses planned for 2021. But beyond that, feedback mechanisms to ensure timely, actionable information is supplied to Health Protection Teams and acute Trusts are needed to help identify outbreaks and clusters. With better information and understanding of the nature of CPE outbreaks, improvements to the management and the effectiveness of control could be found ([105](#)). Furthermore, efforts to learn from outbreaks can be effective in early identification and prevention of future outbreaks ([106](#)).

## Future actions

UKHSA will:

- prepare and undertake a point prevalence survey to assess the prevalence of CPE in intensive care units, and investigate data linkage options to further the understanding of clinical risk factors for CPE colonisation and/or infection
- assess the phenotypic susceptibility antibiogram for Gram-negative bacteria confirmed as acquired carbapenemase-producers, and utilise data linkage opportunities to enhance and better understand the epidemiology and spread of CPGNB in English hospitals
- utilise linkage opportunities and phenotypic carbapenem resistance reporting data to provide quality assurance feedback and develop understanding of the notification data
- investigate further the impact of the COVID-19 pandemic on CPE, look at CPE as secondary infection to COVID-19, and assess the possible change in regional mechanism distribution
- seek to better inform the understanding and spread of CPE, investigate whether whole genome sequencing technology can be used to identify missing transmission events
- continue to make the best use of surveillance systems and develop the potential to integrate whole genome sequencing data, to gain insight for public health action

- work with Health Protection Teams and local acute NHS Trusts to develop a feedback mechanism to assist with outbreak and cluster identification

Relevant CPE research summaries are presented in the Research chapter ([Chapter 10](#)).



## 4. Antifungal resistance, prescribing and stewardship

### Introduction

This chapter has been re-introduced into the ESPAUR 2020 to 2021 report to update on ESPAUR fungal sub-group projects and to assess the impact of the COVID-19 pandemic on fungal infection surveillance and antifungal prescribing.

The data presented covers the incidence of resistance against key systemic antifungals utilised in the treatment of candidaemia, between 2016 and 2020, including an update of *Candida auris* in England. Also presented within the chapter are updates from Public Health England's (PHE) Mycology Reference Laboratory (MRL) ([107](#)) in Bristol, and the NHS Mycology Reference Centre Manchester (MRCM) ([108](#)), highlighting some of the infrequently identified fungi, emerging resistance within those species and challenges due to the COVID-19 pandemic. Further details on the 2 reference laboratories and what specimens they would normally receive are included in the [Methods and caveats annexe for Chapter 4](#).

Accompanying the infection data is an update on the prescribing of systemic antifungals in NHS hospitals as well as an update on antifungal stewardship initiatives and activities. While limited in availability, antifungal usage in primary care is also described.

Detailed trend data, including numbers reported as susceptible, intermediate or resistant to key antifungal agents, is available in the [data tables and PowerPoint presentations](#) published alongside this report. The data sources and analytical methods used are described in [annexe for Chapter 4](#) of this report.

### Antifungal resistance in Candidaemia

The incidence of isolation of *Candida* species from blood was 3.5 per 100,000 population (number of blood isolates: 1,971) in 2020 ([Figure 4.1](#)), an overall increase of 3.7% since 2016 (3.4 per 100,000).

**Figure 4.1. Rate per 100,000 population of *Candida* species sterile site patient specimen reports in England, 2016 to 2020 (note that data from 2020 is likely to be impacted by the COVID-19 pandemic and should be interpreted with care)**

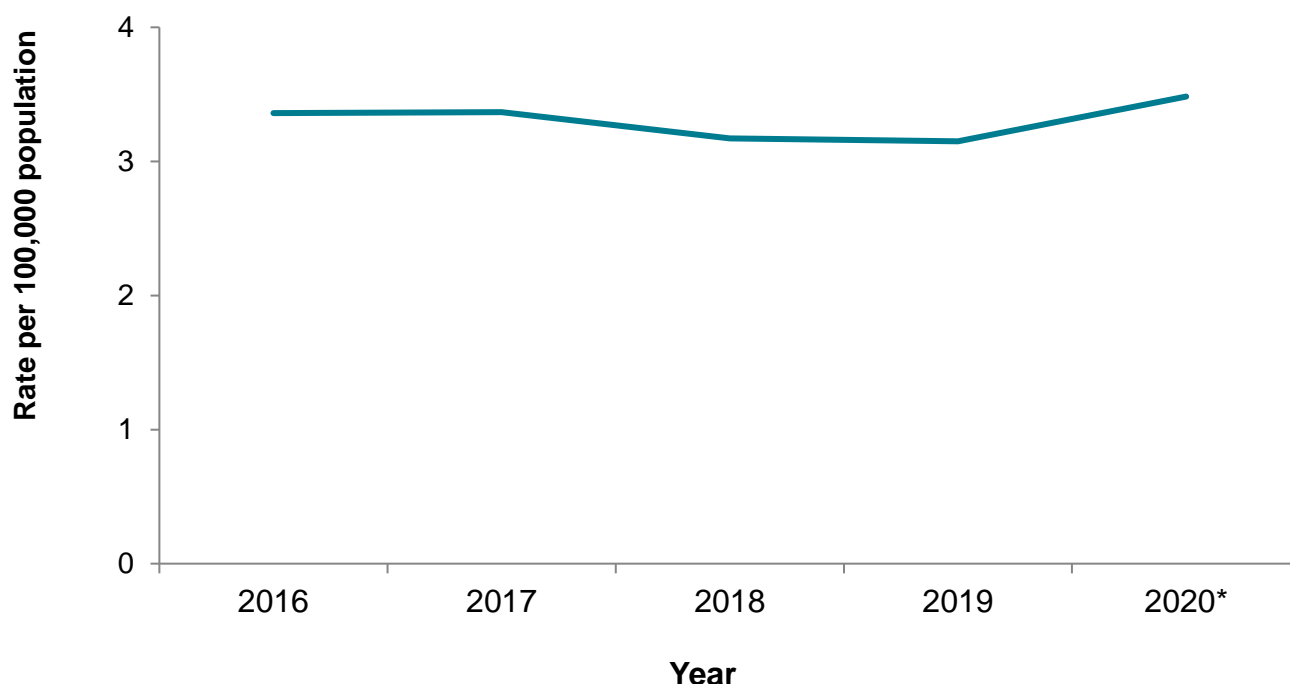


Figure 4.1 shows that prior to 2020 the incidence of *Candida* species isolated from blood specimens had been decreasing, with a 6.3% decrease between 2016 and 2019 (3.2 per 100,000 population in 2019; number of blood isolates: 1,775). However, between 2019 and 2020 the incidence increased by 10.6%, which may have been influenced by the large number of intensive care unit (ICU) patients experiencing candidaemia during the first wave of the COVID-19 pandemic.

Further information on candidaemia in 2020 can be found in the [Chapter 2 appendix](#), which contains a table summarising polymicrobial episodes for bacteraemias and fungaemias, including those caused by *Candida* species. The table contains a summary of polymicrobial patient episode numbers, the percentage of total polymicrobial episodes, and organism polymicrobial rank in 2020.

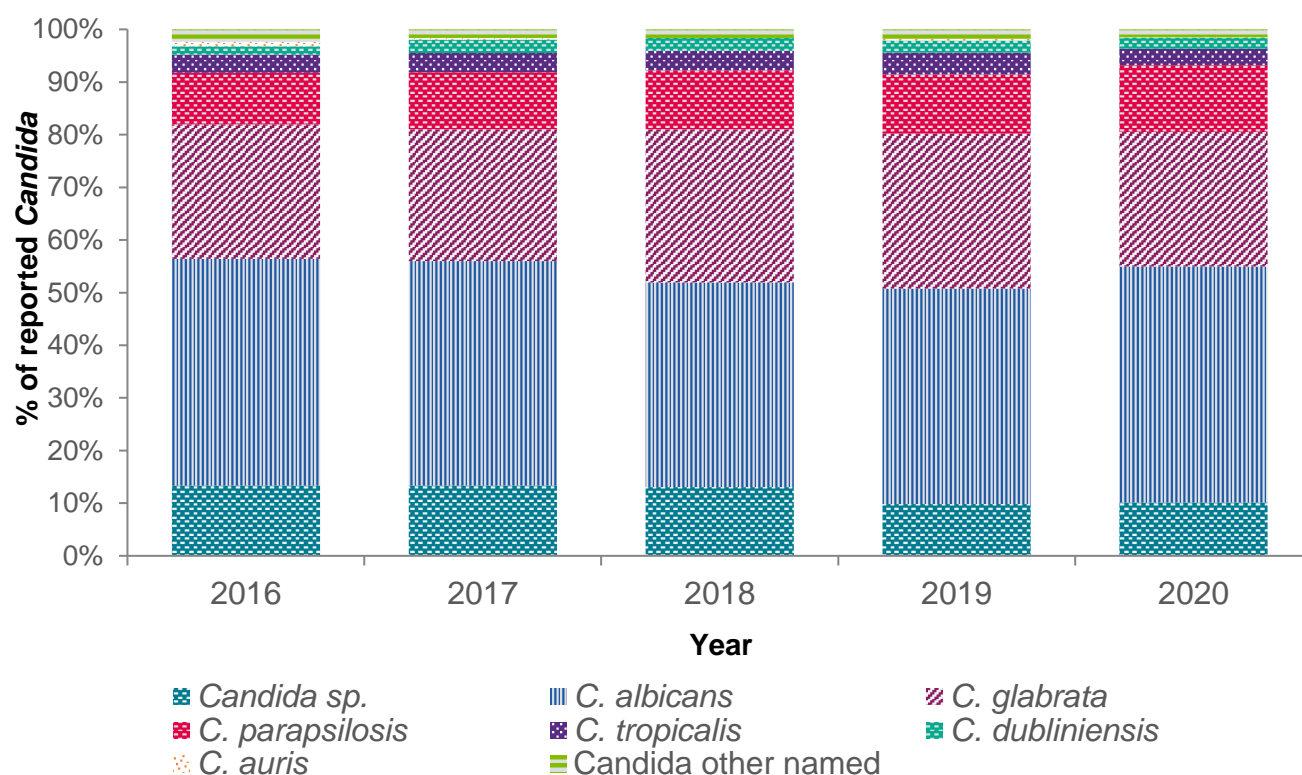
**Figure 4.2 Reports of sterile site isolates of *Candida* by species, 2016 to 2020**

Figure 4.2 shows *Candida albicans* was the most frequently isolated *Candida* species across the 5-year time period, accounting for 44.8% of candidaemia in 2020. In common with many other surveillance studies the second most frequently reported species was *Candida glabrata*, which was identified in 29.4% and 25.5% of candidaemia episodes in 2019 and 2020 respectively.

Routine laboratory surveillance reports submitted to PHE's Second Generation Surveillance System (SGSS) showed that in 2020, 77.4% (1,526 out of 1,971) of *Candida* isolated from blood were subjected to susceptibility testing. This section will focus on susceptibility test results for 3 key antifungals (amphotericin B, caspofungin and fluconazole). Details on case definitions and episode grouping are described in the [chapter annexe](#). More detailed trend data, including numbers reported as susceptible, intermediate or resistant is available in the appendix (available on-line).

Overall, resistance to the key antifungals appears to have been decreasing in all *Candida* species. Fluconazole resistance decreased from 8.2% of *Candida* blood isolates tested in 2016 to 3.2% in 2020 (Table 4.1). Resistance to amphotericin B and caspofungin fluctuated slightly, but overall changed little, with resistance only slightly decreasing from 2016 to 2020, by 1.3% to 1.1%, and 3.4% to 3.3% respectively.

For the 2 key species, amphotericin B resistance remained low in 2020 (1.5% in *C. albicans* and 0.8% in *C. glabrata* blood isolates; Table 4.1). Caspofungin and fluconazole resistance were also low in *C. albicans* in 2020 (1.3% and 1.0% respectively), whereas resistance was higher in

*C. glabrata* candidaemia isolates, as expected with its natural lower susceptibility to certain drugs and ability to acquire resistance ([110](#)) with 9.0% and 9.1% resistant to caspofungin and fluconazole, respectively. However, it has been recognised for a while that in vitro susceptibility testing with caspofungin can be problematic and in general anidulafungin is preferred as the sentinel echinocandin for in vitro testing purposes. The percentage of samples with resistance to fluconazole halved from 2016 to 2020 (20.6% to 9.1%). However, there was a marked decrease in the numbers of samples tested during this time, and the European Committee on Antimicrobial Susceptibility Testing (EUCAST) and the Clinical and Laboratory Standards Institute (CLSI) breakpoints for fluconazole differ in their interpretation ([111](#)), perhaps accounting for the large decrease and complicating analysis of any trend.

**Table 4.1 Number of all *Candida* species combined, and *C. albicans* and *C. glabrata* isolates assessed separately, displaying resistance to key antifungals in England, 2016 to 2020**

		<i>All Candida</i> species			<i>Candida albicans</i>			<i>Candida glabrata</i>		
Drug	Year	Number tested	Number (%) resistant		Number tested	Number (%) resistant		Number tested	Number (%) resistant	
Amphotericin B	2016	1,177	15	(1.3)	540	2	(0.4)	353	4	(1.1)
	2017	1,161	11	(0.9)	508	1	(0.2)	374	6	(1.6)
	2018	1,171	6	(0.5)	497	3	(0.6)	419	3	(0.7)
	2019	1,237	11	(0.9)	525	6	(1.1)	407	1	(0.2)
	2020	1,238	14	(1.1)	583	9	(1.5)	372	3	(0.8)
Caspofungin	2016	922	31	(3.4)	422	12	(2.8)	289	9	(3.1)
	2017	926	38	(4.1)	426	19	(4.5)	276	7	(2.5)
	2018	917	26	(2.8)	415	7	(1.7)	285	11	(3.9)
	2019	870	28	(3.2)	405	4	(1.0)	251	16	(6.4)
	2020	932	31	(3.3)	478	6	(1.3)	245	22	(9.0)
Fluconazole	2016	1,310	108	(8.2)	611	7	(1.1)	378	78	(20.6)
	2017	1,235	61	(4.9)	579	5	(0.9)	356	42	(11.8)
	2018	1,198	49	(4.1)	557	4	(0.7)	346	30	(8.7)
	2019	1,229	57	(4.6)	629	9	(1.4)	288	32	(11.1)
	2020	1,267	40	(3.2)	707	7	(1.0)	263	24	(9.1)

#### Box 4.1 Antifungal drug resistance in other fungal pathogens with intrinsic, emerging and multidrug resistance encountered during 2020: perspective from National Mycology Reference Laboratory

During 2020, PHE's National MRL, Bristol, received a large number of isolates (over 200) of *Aspergillus fumigatus* from respiratory samples of patients on ICUs suffering from COVID-19 infection. At least a quarter of these patients had supporting biomarker evidence of invasive disease suggesting co-infection and would be classified as having COVID-associated pulmonary aspergillosis (CAPA). Five of the isolates displayed *in vitro* resistance to voriconazole, the first line agent for invasive aspergillosis, and on molecular analysis were found to display the relevant mutations suggesting this resistance was due to environmental exposure to triazole agents (112).

There were also 2 cases of secondary mucormycosis in patients with COVID-19 in the UK identified through PHE's routine reporting in 2020 (a further 2 were identified up to March 2021). This was a much smaller number than reported from India where this has been a significant public health issue, due in part to the high prevalence of diabetes and the extensive use of steroids, which are known risk factors (113). Minimum inhibitory concentrations (MICs) from susceptibility testing of mucoraceous mould isolates to antifungals in England have been collated by the National MRL and presented in Box Table 4.1. These isolates are almost always susceptible to amphotericin B so high dose lipid forms of this drug are first-line treatments. Different genera and species, and even different isolates within those species, display varying degrees of susceptibility to isavuconazole and posaconazole which can be used as adjunctive or follow-on agents as indicated by specific susceptibility testing (Box Table 4.1.). All isolates are innately resistant *in vitro* to voriconazole and the echinocandin class of agents so data on these drugs is not included.

**Box Table 4.1 Susceptibility testing for fungal species known to cause mucormycosis compiled from PHE Mycology Reference Laboratory data 2006 to 2020**

Species	Antifungal	(Number Tested)	MIC (mg/mL)		
			Range	MIC50	MIC90
<i>Lichtheimia corymbifera</i>	Amphotericin B	(112)	0.03 to 1	0.25	0.5
	Posaconazole	(99)	0.06 to 2	0.25	1
	Isavuconazole	(28)	0.125 to over 16	4	over 16
<i>Mucor</i> sp.	Amphotericin B	(99)	0.03 to 8	0.25	0.5
	Posaconazole	(98)	0.03 to over 16	1	over 16
	Isavuconazole	(21)	4 to over 16	over 16	over 16
<i>Rhizopus arrhizus</i>	Amphotericin B	(26)	0.06 to 2	0.25	0.5
	Posaconazole	(28)	0.125 to over 16	0.5	8
	Isavuconazole	(12)	1 to over 16	2	over 16

<i>Rhizopus microsporus</i>	Amphotericin B	(96)	0.06 to 2	0.5	1
	Posaconazole	(82)	0.06 to over 16	0.5	4
	Isavuconazole	(23)	1 to more than 16	2	8
<i>Rhizomucor pusillus</i>	Amphotericin B	(37)	0.03 to 0.5	0.25	0.5
	Posaconazole	(35)	0.06 to 4	0.5	1
	Isavuconazole	(5)	4 to 8	N/A	N/A

Another public health issue in India has been the emergence and spread of a terbinafine-resistant strain of the dermatophyte *Trichophyton mentagrophytes*, genotype VIII, now being mooted as a new species in its own right. Having evolved the ability to pass from human-to-human and being a cause of aggressive and recalcitrant tinea cruris ('jock itch') infections, it is likely that this will spread globally and has already been reported from several other countries; we have encountered it in the UK in a small number of individuals recently returned from India.

## Antifungal prescribing

### Total consumption of antifungals

The total consumption of systemic antifungals prescribed in the community and NHS hospitals in England has been decreasing year on year.

**Figure 4.3 Consumption of total systemic antifungals in community and NHS hospital setting, expressed as DDD per 1,000 inhabitants per day, England, 2016 to 2020 (data from 2020 is likely to be impacted by the COVID-19 pandemic and should be interpreted with care)**

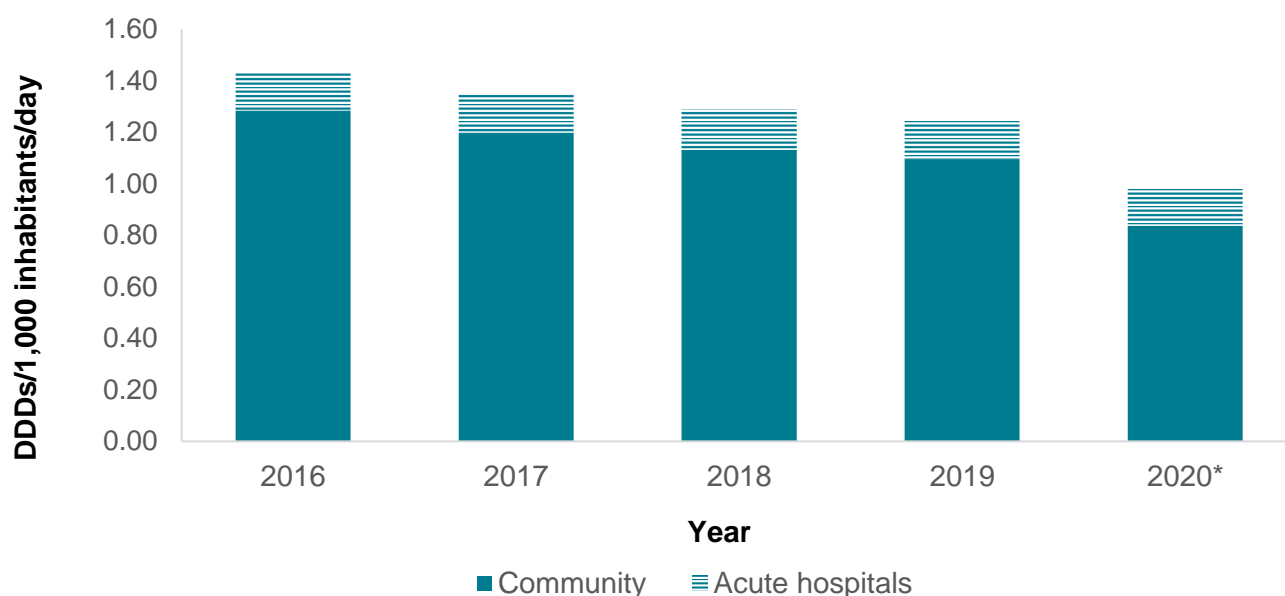


Figure 4.3 shows that from 2016 to 2019 prescribing rate decreased by 12.8% from 1.4 to 1.25 defined daily doses (DDDs) per 1,000 inhabitants per day. There was then a 21% decrease in systemic antifungal consumption between 2019 and 2020 from 1.25 to 0.99 DDDs per 1,000 inhabitants per day. The decrease was predominantly driven by reduced use in the community; from 2019 to 2020 there was only a 6.2% decrease in hospital usage from 0.16 to 0.15 DDDs per 1,000 inhabitants per day.

This is likely a reflection of the COVID-19 pandemic (see [Prescribing in NHS Hospitals](#) later in the chapter for a more in-depth look at the effect this had on prescribing in secondary care). In 2020, 85% of systemic antifungal prescribing took place in the community setting. It is difficult to know if this is a true representation as several antifungal agents can be supplied as over the counter (OTC) medicines, which are not captured in this data set.

## Prescribing in the community

The total prescribing of systemic antifungals in the community decreased by 34.8%, from 1.3 to 0.8 DDDs per 1,000 inhabitants per day, between 2016 and 2020 (Figure 4.4).

**Figure 4.4 Total systemic antifungal prescribing in the community, expressed as DDD per 1,000 inhabitants per day, England, 2016 to 2020 (data from 2020 is likely to be impacted by the COVID-19 pandemic and should be interpreted with care)**

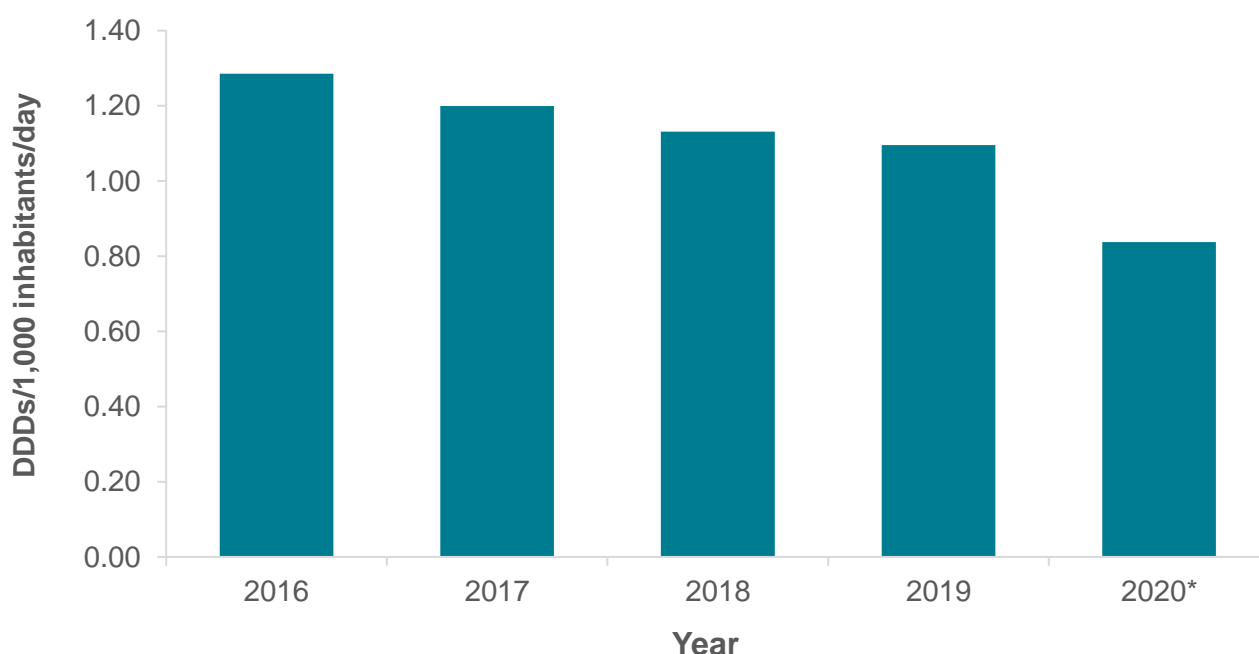
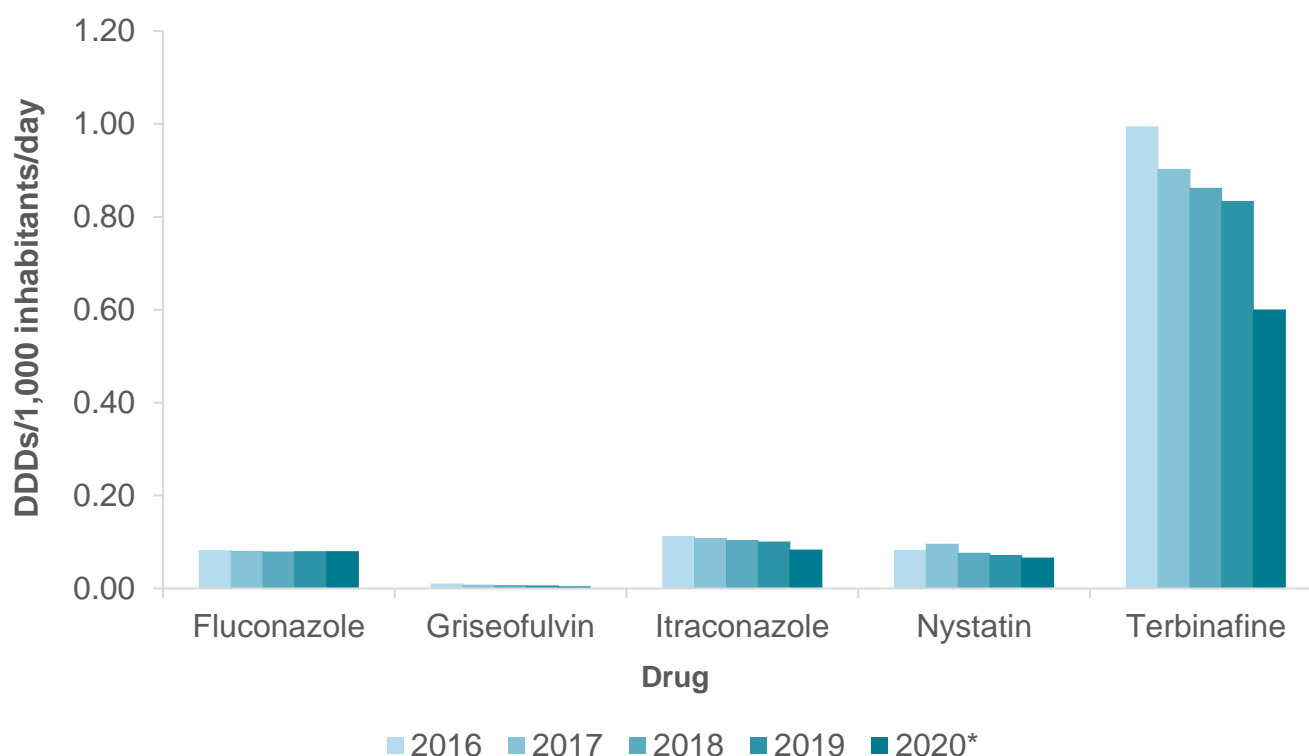


Figure 4.4 shows that the greatest decrease in total systemic antifungal prescribed in the community was recorded between 2019 and 2020 (23.5%), with annual reductions previously at less than 10% (2016 to 2017: 6.7%, 2017 to 2018: 5.6% and 2018 to 2019: 3.2%).



**Figure 4.5 Antifungal prescribing in the community by antifungal group, expressed as DDD per 1,000 inhabitants per day, England, 2016 to 2020 (data from 2020 is likely to be impacted by the COVID-19 pandemic and should be interpreted with care)**

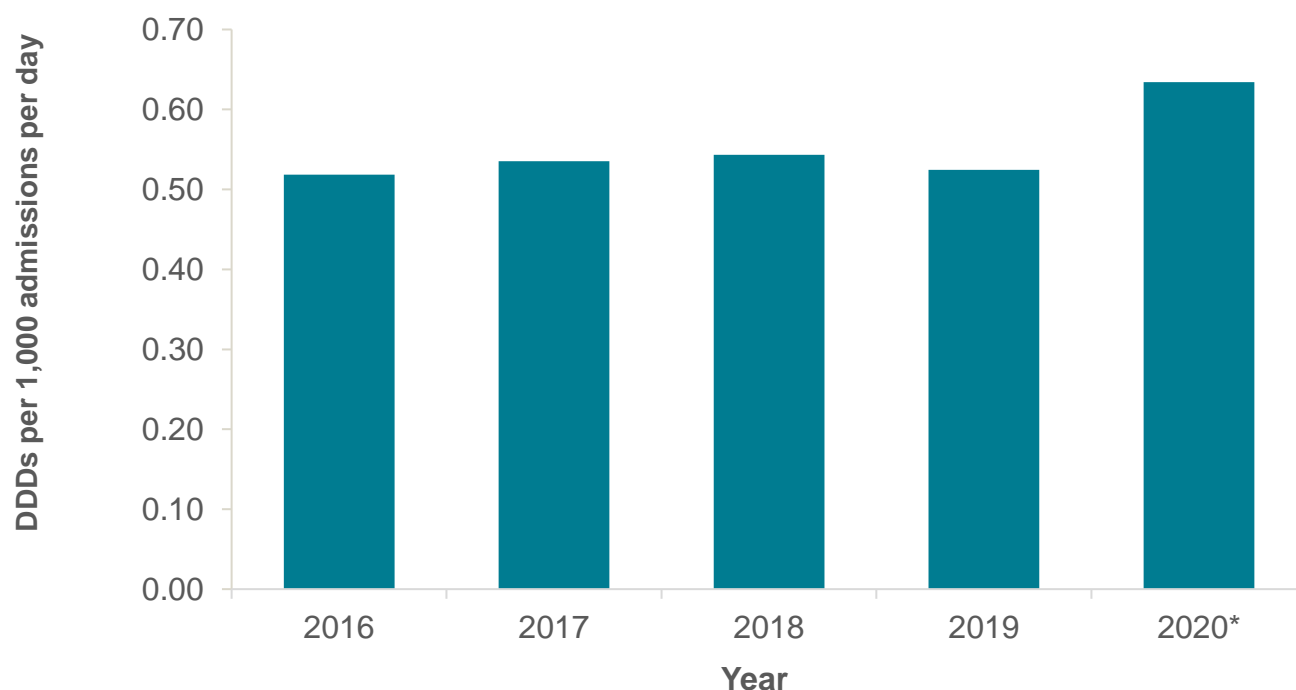


As Figure 4.5 shows, the most frequently prescribed drug in the community was terbinafine (0.6 DDDs per 1,000 inhabitants per day in 2020), an oral agent active against dermatophyte infections of the skin, hair and nails, which are amongst the most frequent infections in the global population. There are a limited number of drugs shown in Figure 4.5, as there are limited types of antifungal prescribed for systemic use in the community setting; more variety is seen in the hospital setting. Oral fluconazole, most often used for cutaneous and mucosal yeast infections, is available OTC and so the numbers presented may not reflect the true use. Dispensing of all antifungal agents in the community appears to have decreased from 2016 to 2020, with terbinafine showing a 39.6% decrease. As dermatophyte infections readily pass from person to person in communal changing areas such as those at swimming pools and sports centres there may well have been a decrease in transmission during lockdown conditions imposed for the control of COVID-19 infection. Moreover, many individuals may have reserved GP (general practice) or other health facility access during this time for serious or life-threatening health concerns.

## Prescribing in NHS hospitals

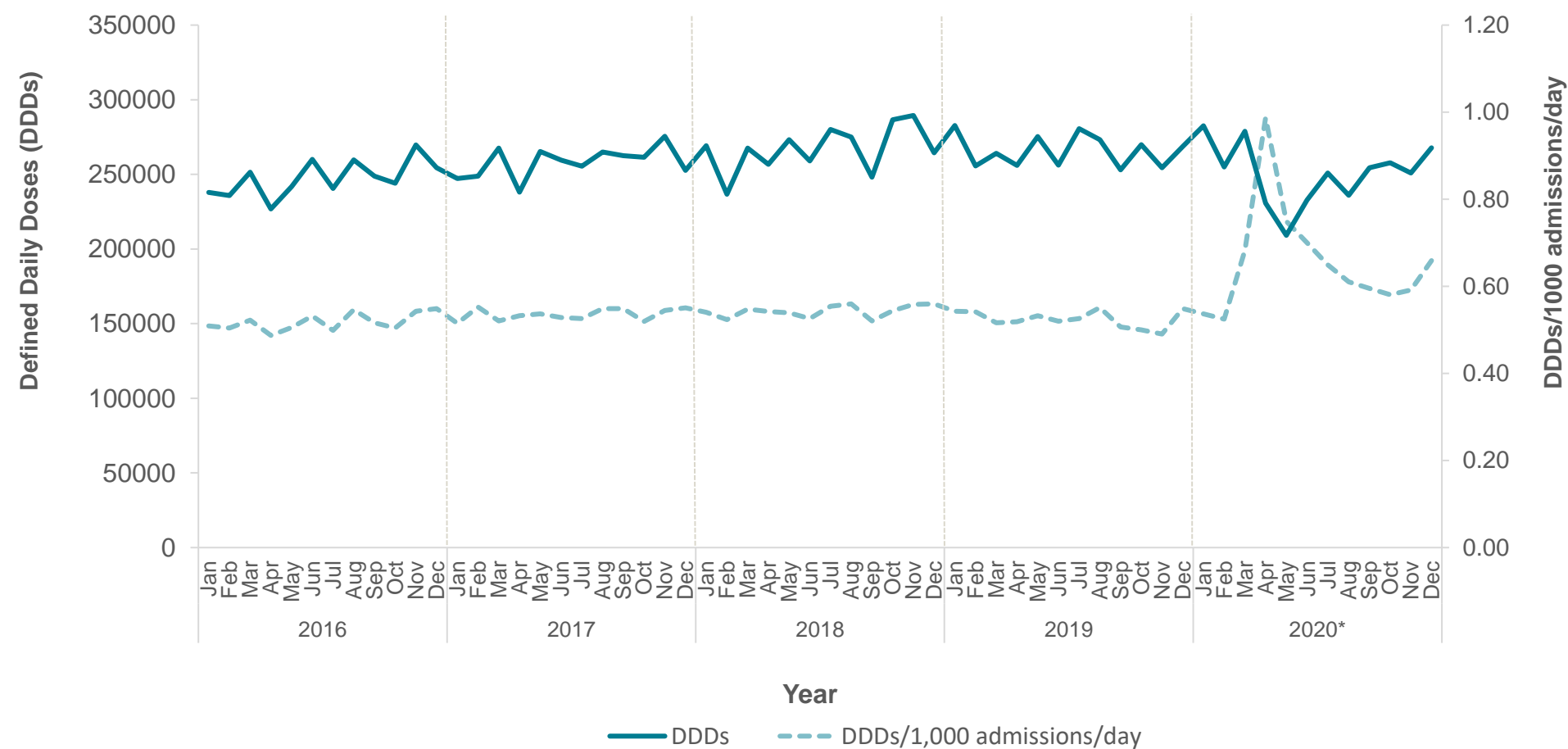
The total systemic antifungal prescribing in NHS acute Trusts for 2016 to 2020 are presented as DDD's per 1,000 admissions per day in Figure 4.6.

**Figure 4.6. Total systemic antifungal prescribing in NHS hospital Trusts captured by Rx-Info, expressed as DDD per 1,000 admissions per day, England, 2016 to 2020 (data from 2020 is likely to be impacted by the COVID-19 pandemic and should be interpreted with care)**



As can be seen in Figure 4.6 total consumption of antifungals in NHS acute Trusts in 2020 was 0.6 DDDs per 1,000 admissions per day, which represents a 21.0% increase in the rate of prescribing from 2019 (0.52 DDDs per 1,000 admissions per day). From 2016 to 2019 the prescribing rate of antifungals in hospitals was stable (range: 0.52 to 0.54 DDDs per 1,000 admissions per day).

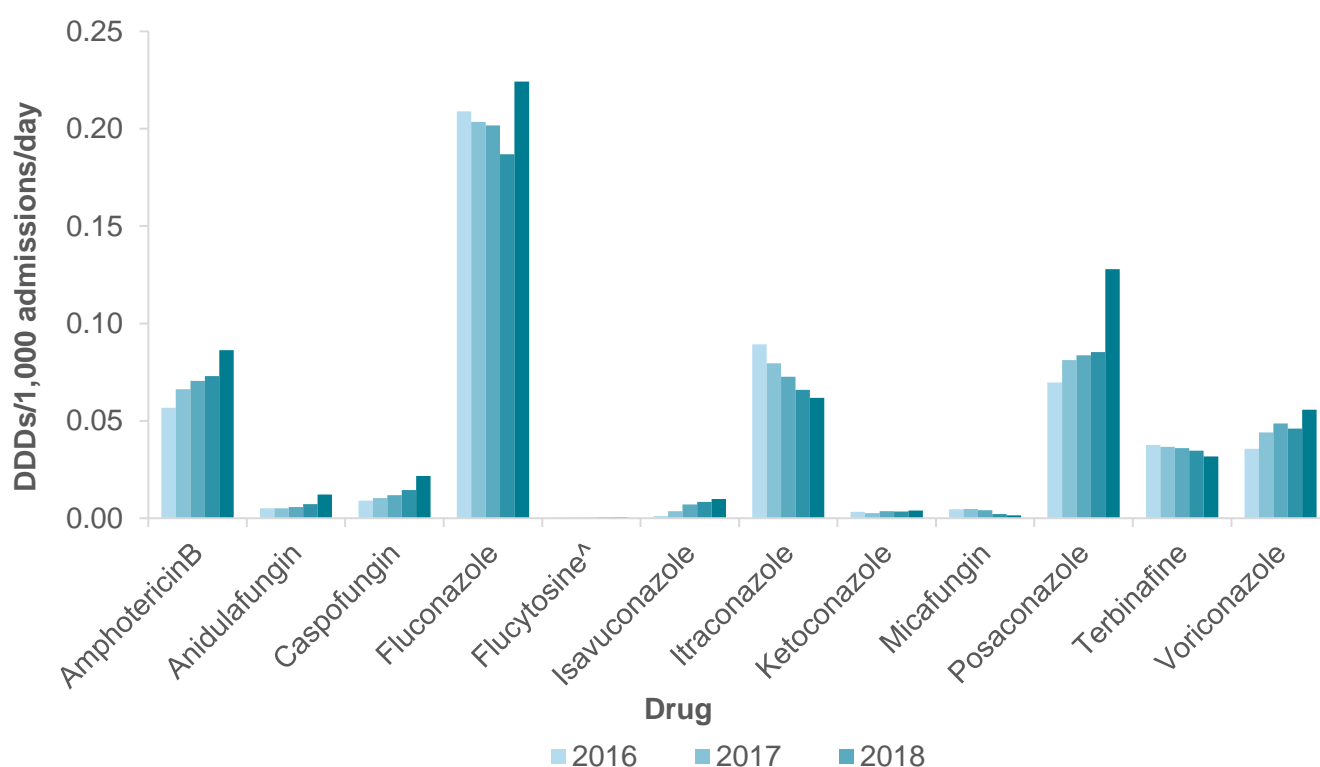
**Figure 4.7 Total systemic antifungal prescribing in NHS hospital Trusts, expressed as DDD per 1,000 admissions per day, in England, viewed by month for 2016 to 2020 (data from 2020 is likely to be impacted by the COVID-19 pandemic and should be interpreted with care)**



The monthly changes in antifungal prescribing in secondary care have been monitored to assess the effect the COVID-19 pandemic had on prescribing practices. Figure 4.7 shows that from March 2020, when national lockdown was announced in response to the pandemic, there was a clear decrease in the total DDDs up to May 2020, with the DDDs 25.0% lower in May than March (March 2020: 278,824 DDDs vs. May 2020: 209,142 DDDs). The number of antifungal DDDs consumed in May 2020 was also 24.0% lower than in May 2019. Over the rest of 2020 the DDDs gradually increased, with the usage at the end of 2020 similar to 2019 (December 2020: 267,854 DDDs versus December 2019: 268,725 DDDs).

Conversely the rate of prescribing, measured as DDDs per 1,000 hospital admissions per day, increased sharply. In March 2020 the rate had already begun to increase, with the rate 30.1% higher than February 2020, and continued to increase by 44.6% to a peak in April 2020 (0.99 DDDs per 1,000 admissions per day). Overall, between February and April 2020 there was an 88.1% increase in prescribing rate, corresponding with peak numbers of COVID-19 patients in the ICU during the first wave of the pandemic ([114](#)) and a 90.3% increase from April 2019 to April 2020. Thereafter, the rate rapidly decreased, although it was still raised compared to pre-pandemic levels. Furthermore, the rate of DDDs per 1,000 admissions per day started to increase again from December 2020, with the rate 20.1% higher than December 2019 (December 2020: 0.66 versus December 2019: 0.55 DDDs per 1,000 admissions per day). More detail on which group of systemic antifungal agent were prescribed in NHS acute Trusts between 2016 and 2020 are presented in Figure 4.8.

**Figure 4.8 Systemic antifungal prescribing in NHS hospitals by antifungal group, expressed as DDD per 1,000 admissions per day, England, 2016 to 2020 (data from 2020 is likely to be impacted by the COVID-19 pandemic and should be interpreted with care)**

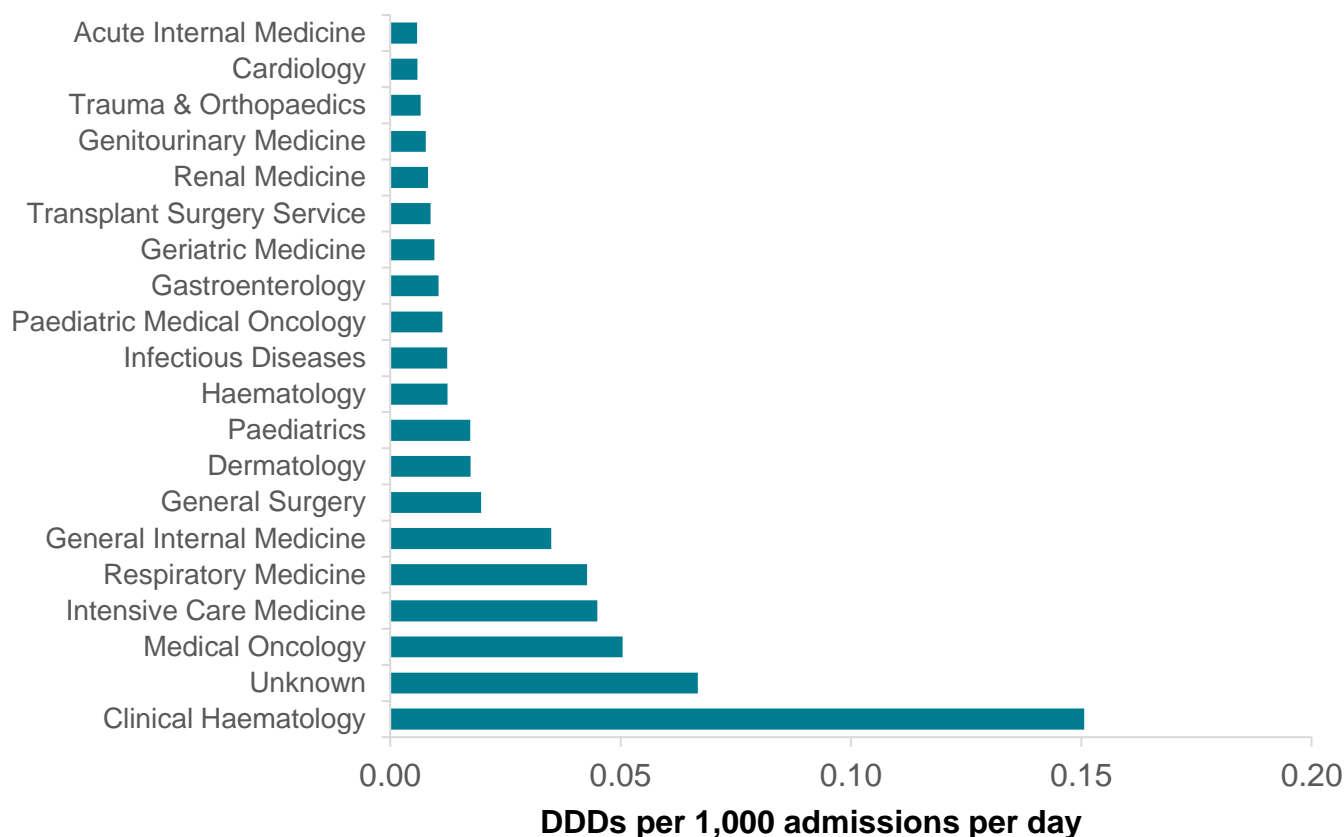


Due to the comparatively low levels of flucytosine prescribing, the flucytosine data is not registering on the graph. The numbers for flucytosine usage are available in the [appendix](#).

Fluconazole was the most prescribed systemic antifungal in NHS acute Trusts in 2020, with 0.22 DDDs per 1,000 admissions per day. This is a first-line agent for mucosal and deep yeast infections and possibly reflects the increase in candidaemia seen in ICU patients with COVID-19. This was followed by posaconazole, which is often used as a prophylactic agent in patients at serious risk of invasive mould infection (0.13 DDD per 1,000 admissions per day) and may have been used more widely in the haematology setting to keep patients safe in hospital or at home during the COVID-19 pandemic. Amphotericin B, a broad-spectrum agent suitable for most invasive yeast and mould infections, was also widely prescribed (0.09 DDD per 1,000 admissions per day) (Figure 4.8). This potentially reflects the number of coinfections seen in COVID-19 patients with yeasts and moulds, particularly *A. fumigatus*. Voriconazole is a first-line agent for invasive aspergillosis but anecdotal reports from clinicians around autumn 2020 suggest its use was often hampered by lack of availability of the IV formulation, potentially leading to increased prescribing of amphotericin B in these patients.

Between 2019 and 2020, there was an increase in DDDs per 1,000 admissions per day for most of the antifungal medicines in use in secondary care, following the overall trend for total antifungal use (Figure 4.6). However, micafungin, terbinafine and itraconazole showed a decrease in DDDs per 1,000 admissions per day between 2019 and 2020; 30.4%, 8.3% and 6.3%, respectively. The greatest increase between 2019 and 2020 in DDDs per 1,000 admissions per day was observed for anidulafungin (68.3%), although this was from quite a low starting point (0.007 DDDs per 1,000 admissions per day in 2019 to 0.012 DDDs per 1,000 admissions per day in 2020). Whilst this drug is used almost exclusively to treat yeast infection, it is particularly useful in patients with underlying liver function disorders which were often encountered in COVID-19 patients ([115](#)). Posaconazole, employed most often as a prophylactic agent, had the second highest increase (49.8%; from 0.09 in 2019 to 0.13 DDDs per 1,000 admissions per day in 2020).

**Figure 4.9 Total systemic antifungal prescribing in NHS hospitals for the 20 highest prescribing clinical specialties, expressed as DDD per 1,000 admissions per day, England, 2020 (data from 2020 is likely to be impacted by the COVID-19 pandemic and should be interpreted with care)**



When comparing systemic antifungal prescribing for patients by specialty level, Figure 4.9 shows that 'Clinical Haematology' had the highest usage per 1,000 admissions per day (0.15 DDDs per 1,000 admissions per day) in 2020, followed by 'Medical Oncology' (0.05 DDDs per 1,000 admissions per day) and 'Intensive Care Medicine' (0.04 DDDs per 1,000 admissions per day).

#### **Box 4.2 Fungal infection and antifungal resistance in 2020: perspective from the Mycology Reference Centre Manchester**

In 2020, the MRCM saw a significant increase in laboratory requests for Galactomannan (GM) and Beta-D-glucan on serum and respiratory samples. Testing more than doubled during the COVID-19 pandemic; in the first 3 months of 2020 (pre-/early-pandemic), a total of 723 GM and 705 Beta-D-glucan tests were requested, whilst for the same period in 2021 (height of COVID-19 wave 2 peak) these numbers were respectively 1,826 and 1,900. Biomarker test requests have since remained high, even though the critically ill COVID-19 patient numbers have decreased. Also, to assist the COVID-19 testing effort, the Manchester Royal Infirmary transferred all testing from superficial specimens (specimens of skin, hair, and nails) to MCRM during 2020. Despite the pandemic, the superficial workload increased by 275% between January to February 2020 and January to February 2021. These changes are

hypothesized to be due to increased awareness regarding invasive fungal infections, local testing availability, effective turn-around time, and paucity of diagnostic stewardship resources during the pandemic.

An audit on fungal co-infections in critically ill COVID-19 patients took place at Wythenshawe Hospital (part of the Manchester University Foundation NHS Trust) between 15 March and 3 June 2020. The aim was to:

- (i) evaluate the rate of invasive fungal infection in patients hospitalised in ICU with respiratory failure secondary to COVID-19
- (ii) to assess adherence to local (Trust) guideline regarding diagnosis of fungal infections

Seventy patients were admitted to the ICU during the audit period, of which 20 (29%) patients were diagnosed with possible, probable or proven invasive fungal infection: 14 (20%) with *Candida* species candidaemia and 6 (9%) with CAPA. Of the 70 patients, 24 (34%) had sputum tested for GM, of which 19 (79%) had 2 or more specimens taken as per Trust guideline. Four patients (out of the 24 tested for GM; 16.7%) had one or more positive sputum GM results and 3 of these patients underwent further examination with Thoracic computed tomography scanning. However, none of these 4 patients had *Aspergillus* PCR tested on respiratory samples, as recommended per Trust guideline. In addition, 31 patients had a serum GM tested, 16 with more than one specimen, with no positive results. An additional outcome from this audit was the need to increase awareness on how correct diagnostic testing will impact antifungal stewardship practices; diagnostic tests need to be used in line with Trust guidelines, more than as found in the audit, so that the appropriate interpretation of mycological investigations can be drawn and subsequently the best antifungal prescribing can occur.

Antifungal sensitivities in *Aspergillus* species strains tested at MRCM did not change in 2019 and 2020 compared to data from previous years. MRCM continued to see a spectrum of cryptic species of *A. fumigatus* isolated from patients with chronic and allergic aspergillosis, as previously reported in 2018 ([118](#)). However, it was noted that there may have been a slight exceedance in cases of invasive infections caused by non-fumigatus *Aspergillus*. While only small numbers, an audit has been initiated to confirm and shed light on the subject.

A novel glucan synthase inhibitor antifungal agent Ibrexafungerp ([119](#)) has been developed for the treatment and prevention of fungal infections, including serious and life-threatening infections due to *Candida* species, *Aspergillus* species, and *Pneumocystis jirovecii* ([118](#)). While no patient at the National Aspergillosis Centre is currently receiving Ibrexafungerp to treat a mould infection, investigations to assess susceptibilities were undertaken (recruitment for clinical trial delayed due to the pandemic, due to start later this year). Ibrexafungerp MICs were performed on 115 mould isolates obtained from 57 patients during 2020. Of these, 107 (93%) isolates were identified as *A. fumigatus*, 7 (6%) as non-fumigatus *Aspergillus*, and 1 (0.9%) as *Scedosporium apiospermum*. Furthermore, 108 (93.9%) of these isolates had a

lower MIC than what modelling had deemed as an achievable tissue concentration for Ibrexafungerp, suggesting susceptibility to the drug. The 7 (6%) isolates with a higher MIC were *A. fumigatus*, of which 4 were pan-azole resistant. Azoles are typically the treatment of choice for *Aspergillus* ([119](#)) so it would be ideal for new antifungals to work against azole resistant isolates.

Although there have been no yeast antifungal sensitivity audits in the last year, the situation appears stable, and no radical changes were observed. The aim is to audit antifungal resistance in yeasts in the near future.

## Antifungal stewardship

In February 2017, NHS England and NHS Improvement (NHSE/I) started a project related to Antifungal Stewardship. The project group included all Clinical Reference Groups likely to be involved in antifungal stewardship and representatives of PHE, the UK Clinical Mycologists Network, and the British Society for Medical Mycology, alongside pharmacy support from NHSE/I.

Initially, the group developed a consensus of key targets. An audit of guidelines for 10 providers revealed that there was a lack of consistency in the application of guidelines.

The project therefore focussed on 3 key areas:

- clinical guidelines
- prophylactic use of antifungal agents
- auditing the use of antifungal agents

An implementation pack was developed and shared with Providers. A Commissioning for Quality and Innovation (CQUIN) payment was developed to help improve antifungal stewardship across the NHS in England.

The CQUIN was shared if a provider met the following criteria:

- an antifungal stewardship team was established
- guidelines were developed
- a diagnostic gap analysis was carried out and an additional diagnostic analysis was carried out and the key findings highlighted the extended turnaround times

The CQUIN was first implemented for the 2019 to 2020 financial year, and in the first year 85 providers opted to take part, identified by the development of an antifungal stewardship team. When applying Trust mergers, this led to 79 NHS acute Trusts out of 141 (56.0%) signed up by the end of January 2020. The data collection, through auditing, for the 2019 to 2020 antifungal



CQUIN was due to start in April 2020 but was prevented due to COVID-19. As such both the 2019 to 2020 and 2020 to 2021 CQUINs were halted because of COVID-19 on 23 March 2020 and are not going to be re-instated. While an antifungal CQUIN might not be re-instated, other antifungal stewardship work will continue.

**Figure 4.10 Total systemic antifungal prescribing in NHS hospitals that did and did not opt to take part in the 2019 to 2020 antifungal CQUIN, expressed as DDDs per 1,000 admissions per day, England 2016/2017 to 2020/2021 (data from 2020 to 2021 is likely to be impacted by the COVID-19 pandemic and should be interpreted with care)**

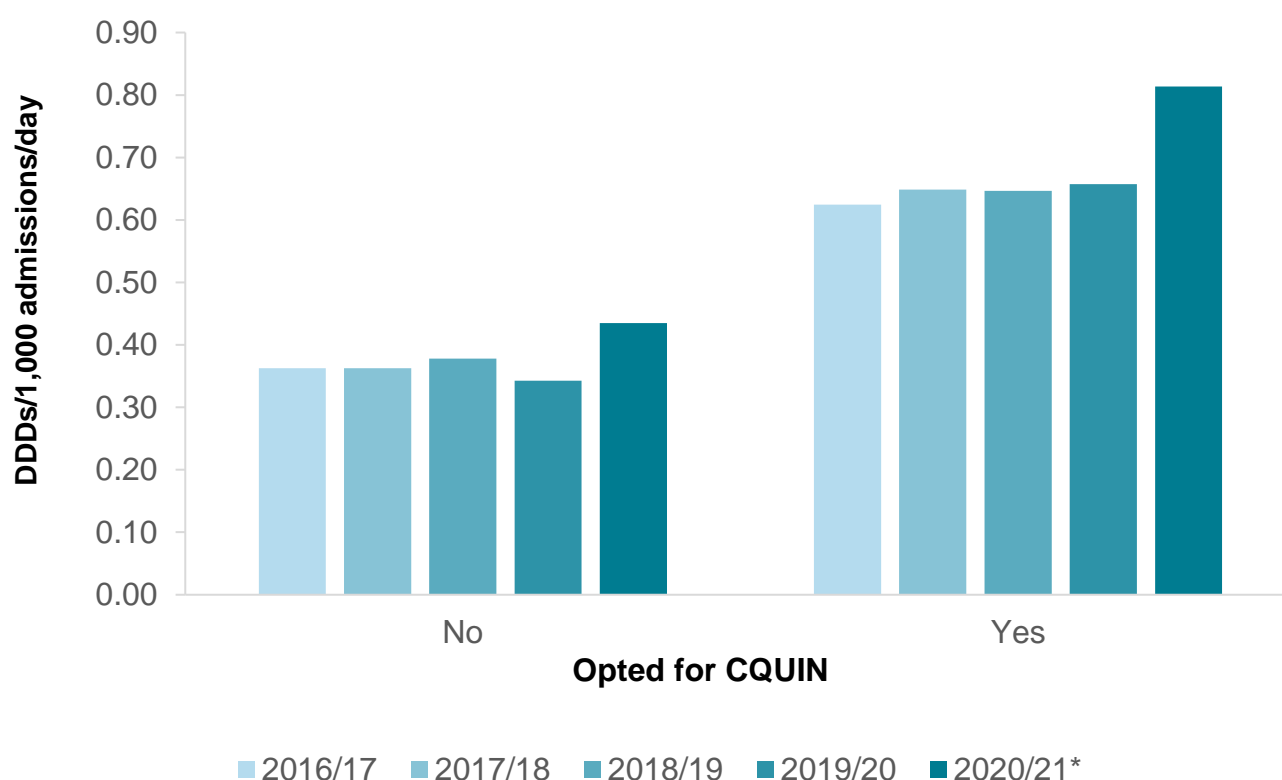


Figure 4.10 shows that antifungal usage was higher in the Trusts engaged in the CQUIN than in those not signed up. Between financial years 2016 to 2017 and 2018 to 2019 the DDDs per 1,000 admissions per day have increased very slightly in the Trusts enrolled in the CQUIN (0.62 DDDs per 1,000 admissions per day versus 0.65 DDDs per admissions per day, respectively). In 2019 to 2020, when the CQUIN was initiated, the DDDs per 1,000 admissions per day remained stable compared to the previous financial year (0.66) before increasing again in the 2020 to 2021 year (0.81) by 23.8%.

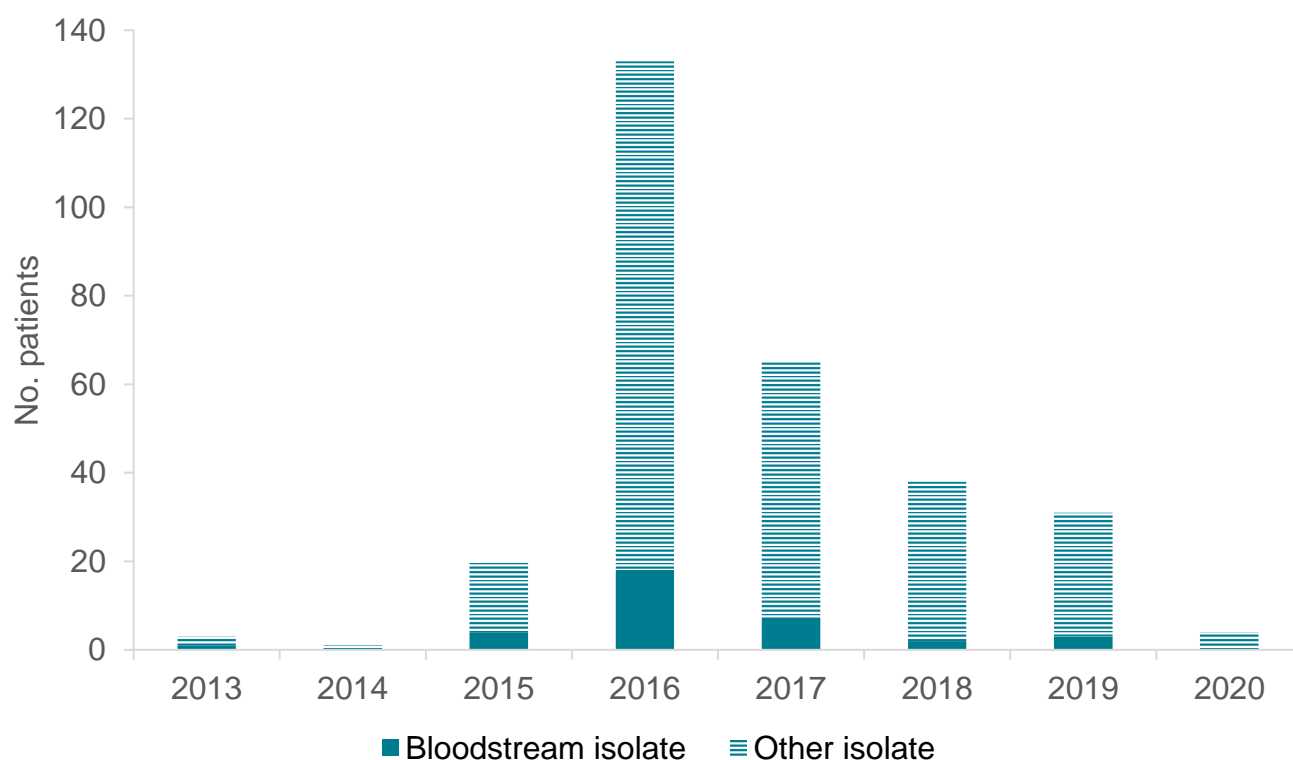
Conversely the antifungal usage in the Trusts not signed up to the CQUIN (62/141; 44.0%) decreased very slightly between financial years 2016 to 2017 and 2019 to 2020 (2016 to 2017: 0.36 DDDs per 1,000 admissions per day versus 2019 per 2020: 0.34 DDDs per 1,000 admissions per day). However, the rate of DDDs did increase in 2020/21 in these Trusts, to 0.43 DDDs per 1,000 admissions per day (increase of 26.9%).

The higher prescribing rate in Trusts opting to take part in the CQUIN might be due to the case mix of patients in each hospital Trust, with those wishing to participate more likely to be handling greater numbers of patients at risk of fungal infection. The increases in 2020 to 2021 are again likely to be due to the COVID-19 pandemic, with more patients present in ICUs. During the pandemic antifungal stewardship teams have been redeployed to other areas. As services are restored there will be a need to redevelop these antifungal stewardship teams.

## *Candida auris* update

*Candida auris*, the fluconazole-resistant and sometimes multi-drug-resistant yeast that has been responsible for multiple ICU outbreaks globally including several in the UK, has proved to be a problem in COVID-19 patients in countries where *C. auris* is endemic. Fortunately, the concern that this yeast could cause similar problems in ICUs in England treating COVID-19 patients or in the large Nightingale hospital wards set up for COVID-19 patients have not been observed in 2020.

**Figure 4.11 Number of persons with confirmed *Candida auris* by year, England 2013 to 2020**



Overall in England, there were a total of 295 cases of *C. auris* reported between 2013 and 2020 (Figure 4.11), with a total of 35 isolates from blood specimens, accounting for 12% of detections overall. As shown in Figure 4.11, the peak incidence of *C. auris* identified from both colonisations and bloodstream isolates in England was in 2016 (133 detections). It has since declined year-on-year to 2020 where fewer than 5 detections were recorded.

In 2020, there were no on-going outbreaks in England, just sporadic introductions representing infections and cases of colonisation with no onward transmission. In 2019 there were 31 isolations including 7 infections and 24 cases of colonisation. In 2020 there were just 4 cases of colonisation, probably reflecting the lack of new introductions from endemic areas due to extreme travel restrictions associated with COVID-19 regulations. Although currently the MRL receives most isolates, *C. auris* will be added to the list of organisms actively looked at by them through routine monitoring. In addition, a weekly exceedance alert system based on local laboratory reporting (through SGSS) has been developed, to notify regional teams and supply guidance to reduce the possibility of onward transmission.

The 2017 ESPAUR report highlighted that a prevalence study was being undertaken, with the aim to get an assessment of background prevalence of colonisation. Close to 1,000 patients were screened on admission to ICUs during this study and no positive cases were identified.

## Discussion

This report provides an update on antifungal resistance, prescribing and stewardship, which has not been looked at in detail since the ESPAUR report in 2017. In this time there have been improvements in the reporting of susceptibility testing of *Candida* isolates; 77% of specimens were tested in 2020 compared to a reported 59% in 2016 ([121](#)). There remain challenges in interpreting the susceptibility reports in full; without knowledge of the method employed or the breakpoints applied we cannot assess whether the trends being reported are genuine ([122](#), [123](#)). For caspofungin susceptibility testing, only the Etest method is reliable, which requires expertise to read; many laboratories are moving to anidulafungin as a sentinel echinocandin instead, as resistance mutations in *Candida* isolates confer resistance to both drugs ([124](#)). With this in mind, it may be helpful to develop a surveillance mechanism for echinocandin resistance in *Candida* isolates to establish which tests and antifungal breakpoints laboratories are applying.

COVID-19 has had an impact on fungal infections and subsequent prescribing. With increased numbers of patients being admitted to ICUs for longer stays as a result of COVID-19 infection ([125](#)), this could explain the increase in candidaemia incidence reported in 2020. Patients on ICU's are often at higher risk for candidaemia as the setting allows the opportunistic pathogen to become invasive, with many risk factors for candidaemia, such as central venous catheter, overlapping with characteristics of patients on ICUs ([126](#)).

It quickly became apparent that patients with COVID-19 were also susceptible to pulmonary infection with *A. fumigatus*, and a new disease term COVID-associated pulmonary aspergillosis (CAPA) was coined. This is a diagnosis that is complicated by the not infrequent isolation of *A. fumigatus* from respiratory secretions of ventilated patients on ICUs. Therefore, in order to confirm the diagnosis it was important to have a microscopic analysis of tissue or respiratory secretions and/or the associated finding of positive fungal biomarkers such as *Aspergillus*-specific polymerase chain reaction (PCR), galactomannan positivity in bronchoalveolar lavage

(BAL) or serum and/or beta-glucan positivity in serum. In this way a diagnosis could be classified as proven, probable or possible ([127](#)). Data on such infections was fed into a PHE working group on COVID-19 coinfections and a sub-group looked at the increased length of hospital stay and mortality associated with such infections. Voriconazole is the first-line agent for such infections leading to an increase in prescribing of this agent but anecdotal reports of a lack of availability of IV voriconazole in the lead up to the peak of the second wave of the pandemic, and in some cases anxiety over possible resistance, probably led to an increase in amphotericin B prescribing in some of these patients.

There have been some improvements in the surveillance of antifungal prescribing over the last few years, with Rx-Info now capturing data from 100% of NHS acute Trusts (reported as 86% in 2016). The antifungal prescribing rate in NHS acute hospitals increased during 2020, particularly on ICUs, where there was a 43.6% increase from 2019 in DDDs prescribed per 1,000 admissions; most other specialty increases were less than 20%. There was a decrease in antifungal DDDs prescribed in 2020 compared to 2019, possibly explained by both an overall reduction in admitted patients, as well as a reduction in patients admitted for elective procedures, particularly during the first lockdown period (March to June 2020). It has been well reported that the general case-mix of patients in 2020 changed compared to previous years, creating challenges in assessing trends; however, this may help to explain the rise in antifungal DDDs per 1,000 hospital admissions. In addition to this, an increased proportion of admissions were being sent to the ICU where antifungals are used more readily (often as pre-emptive treatment to avoid infections such as candidaemia which are associated with long stays on ICU wards) ([129](#), [130](#)).

Unfortunately, the collection of the NHS England Antifungal CQUIN data was interrupted by COVID-19. Preliminary data from those hospitals that engaged with the CQUIN, even without the formal call for data, tended towards the higher range of DDDs per 1,000 admissions than those that did not sign up. This difference could reflect local awareness of increased antifungal usage, and active engagement with stewardship tools available, or be to do with hospital type.

Data presented in this chapter on systemic antifungal usage in the community shows a steadily decreasing trend between 2016 and 2019, with a much larger drop in 2020. This drop is again likely to be as result of the COVID-19 pandemic, with fewer patients acquiring anthropophilic fungal infections or attending healthcare facilities throughout the lockdown periods leading to fewer antifungals being prescribed overall (see also [Chapter 5](#)). Another challenge in interpreting the trend is whether there was a move to OTC antifungals as a result of limited GP access. OTC availability of antifungals is an ongoing challenge for antifungal stewardship and surveillance, limiting the ability to truly estimate the level of antifungal use in the population and to interpret trends in resistance. It is possible that this could be improved by working with pharmaceutical companies to assess sales of such drugs, or alternatively to develop a mechanism to estimate usage via mathematical modelling; an area to investigate development opportunities.

## Future actions

UKHSA will:

- investigate the antifungal susceptibility tests employed by routine laboratories to further understand the antifungal resistance data being reported to SGSS in England
- WHO has introduced a protocol to include *Candida* species in its Global Antimicrobial Resistance and Use Surveillance System (GLASS) data gathering initiative so UKHSA will provide data panels on *Candida* species susceptibility profiles from SGSS and the MRL.
- work with NHS England to promote the development of the antifungal stewardship toolkit
- continue to explore the impact of COVID-19 on fungal infection rates and antifungal prescribing
- investigate options for including laboratory fungal biomarker diagnostic results with routine laboratory surveillance reports, and enhance surveillance data through linkage to hospital episode statistics (HES) ([131](#)) to investigate improving invasive infection identification
- link microbiology data in SGSS with patient-level clinical, epidemiological and risk factor data in HES

## 5. Antibiotic consumption

### Introduction

The UK's 5-year National Action Plan (NAP) 2019 to 2024 ([132](#)) recognised the achievements, and the challenges still faced, following the previous 5-year antimicrobial resistance (AMR) strategy 2013 to 2018 ([133](#)). The current strategy presents a set of ambitions for the next 5 years, whilst acknowledging the significant challenge that AMR poses, which is unlikely to be addressed in a single 5-year plan. The strategy has therefore been developed to provide support and is in alignment with the UK 20-year vision for AMR ([134](#)).

The NAP outlines an overall target to reduce total UK antimicrobial use in humans by 15% by 2024, from the 2014 baseline. Changes have been observed in antibiotic consumption during the COVID-19 pandemic and have been described within the sections of this chapter. The ability to monitor antimicrobial usage highlights the importance and utility of our current surveillance systems, in assessing trends in antimicrobial usage across different prescribing settings and over time, including the COVID-19 pandemic duration. Improving data access and linkage, and maintaining surveillance systems is of importance to identify current and future capacity and effectiveness in the changing environment of antimicrobial stewardship.

Antibacterial consumption in England between 2016 and 2020 in primary and secondary care is presented in this chapter. Prescribing settings include general practice (GP), dental practice, out-of-hours services, inpatient and outpatient services in hospitals. Methods and research activities can be found in the [annexe for Chapter 5](#). Data and figures presented in the chapter are available in the [chapter data tables and figures appendix](#).

### Total antibiotic consumption

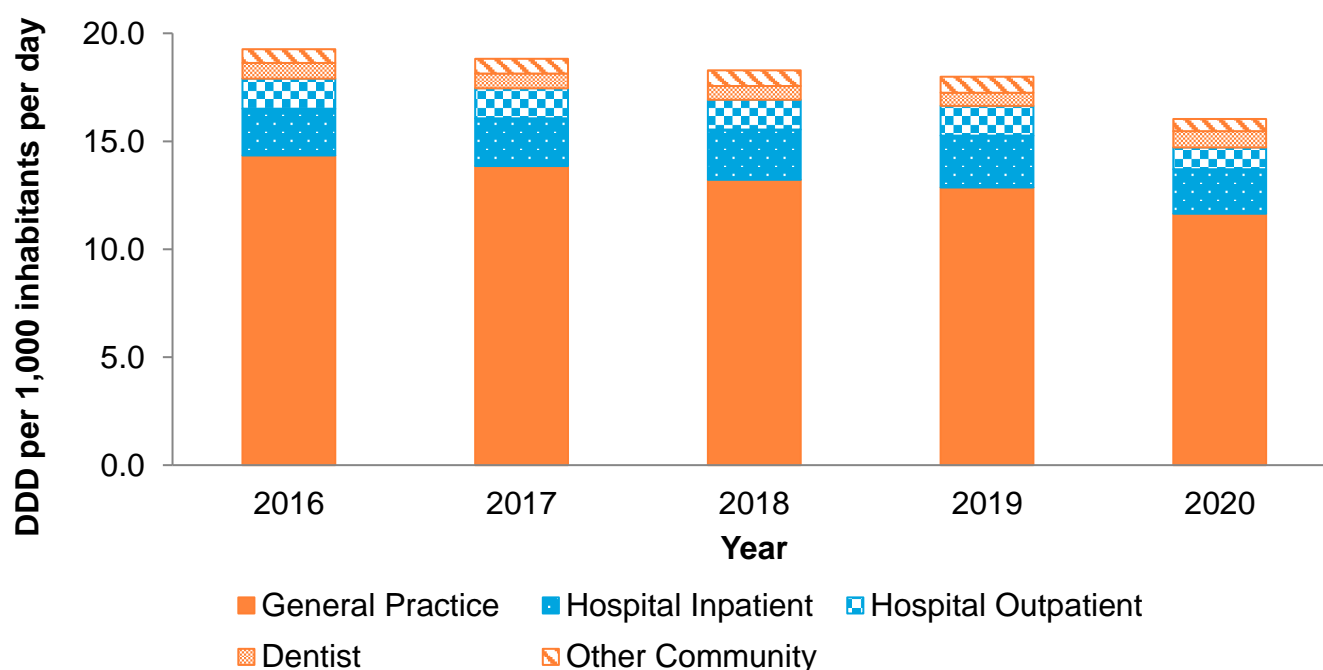
Total antibiotic consumption in England has been decreasing since 2014, with an evident COVID-19 impact on the level of total antibiotic consumption in terms of Defined Daily Doses (DDD) per 1,000 inhabitants per day (DID) (Figure 5.1). Over the 4 years that span 2016 to 2019, antibiotic consumption reduced by 6.6%, with a further decrease of 10.9% between 2019 to 2020. Similar declines between 2019 to 2020 have been noted in the incidence of key BSIs (Chapter 2: [Figure 2.5](#)).

The majority of antibiotics prescribed in 2020 were within the GP setting (72.7%; 11.65 DID), followed by hospital inpatients (12.8%; 2.05 DID), hospital outpatients (6.3%; 1.01 DID), dental practice (4.7%; 0.75 DID) and other community settings (3.5%; 0.57 DID). Prescribing in the GP setting has seen continuous year-on-year decreases, including 2020 (reduction of 10.4% between 2016 and 2019 and a further 9.4% reduction between 2019 to 2020). The absolute reduction in antibiotic consumption was greatest within the GP setting. Notably, the absolute

total reduction seen from 2016 to 2019 (-1.27 DID) was similar to the reduction in prescribing seen between 2019 to 2020 (-1.96 DID).

Similarly, prescribing in the dental setting has seen year-on-year reductions over the previous 4 years (2016 to 2019). However, this altered in 2020 with antibiotic consumption increasing by 22.1% compared to the previous year. This was the only setting to have seen an increase between 2019 to 2020, following a decreasing trend of 15.3% between 2016 and 2019.



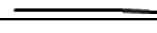
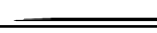

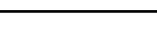

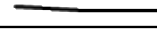
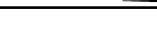


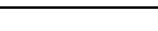
**Figure 5.1 Total antibiotic consumption by setting, expressed as DDDs per 1,000 inhabitants per day, England, 2016 to 2020**



In 2020 the highest total consumption by key antibiotic groups expressed as DDD per 1,000 inhabitants per day in England was attributed to penicillins (35.8%, 4.74 DID), followed by tetracyclines (27.2%, 4.35 DID) and 'macrolides, lincosamides and streptogramins' (14.6%, 2.35 DID) (Table 5.1). Previous declining prescribing trends for penicillins (excluding inhibitors), 'macrolides, lincosamides and streptogramins' and carbapenems were evident. However, the rate of prescribing notably further decreased for these antibiotics between 2019 and 2020 (-17.0%, -14.0% and -12.8% respectively,  $p$  less than 0.05). Third, fourth and fifth-generation cephalosporin prescribing exhibited a previous increasing trend between 2016 to 2019, one of the few antibiotic groups to be showing a positive trend over this time period; however, there was a reversal to the slope with a reduction in the trend between 2019 to 2020 (-10.8,  $p$  greater than 0.05). Between 2016 to 2020 the use of 'other antibacterials' saw the highest increase of 31.7% ( $p$  less than 0.05).



**Table 5.1 Total antibiotic consumption by antibiotic groups, expressed as DDDs per 1,000 inhabitants per day, 2016 to 2020**

Antibiotic Group	2016	2017	2018	2019	2020	Trend	p-value
Penicillins (excluding inhibitors)	6.292	6.091	5.890	5.711	4.740		0.030 <sup>+</sup>
Penicillins (inhibitor combinations only)	1.145	1.102	1.118	1.106	0.997		0.090
First and second-generation cephalosporins	0.268	0.257	0.243	0.238	0.237		0.012 <sup>+</sup>
Third, fourth and fifth-generation cephalosporins	0.063	0.074	0.079	0.078	0.070		0.474
Carbapenems	0.056	0.056	0.052	0.052	0.045		0.021 <sup>+</sup>
Tetracyclines	4.754	4.703	4.618	4.752	4.350		0.179
Macrolides, lincosamides and streptogramins	3.204	3.083	2.872	2.730	2.348		0.004 <sup>+</sup>
Sulfonamides and trimethoprim	1.267	1.056	0.851	0.777	0.749		0.013 <sup>+</sup>
Quinolone antibacterials	0.522	0.531	0.558	0.509	0.459		0.241
Anti- <i>Clostridioides difficile</i> agents <sup>^</sup>	0.004	0.004	0.004	0.004	0.004		0.001 <sup>+</sup>
Oral metronidazole	0.337	0.323	0.306	0.298	0.304		0.035 <sup>+</sup>
Other antibacterials*	1.227	1.398	1.550	1.603	1.616		0.017 <sup>+</sup>

+ Statistically significant *p*-value for trend from 2016 to 2020.

<sup>^</sup> Anti-*Clostridioides difficile* agents: oral vancomycin and fidaxomicin.

\* Other antibacterials (ATC 3rd level pharmacological subgroup 'J01X') include: glycopeptide antibacterials, polymyxin, steroid antibacterials, imidazole derivatives, nitrofurantoin derivatives, other antibacterials (full list in [chapter annexe](#)).

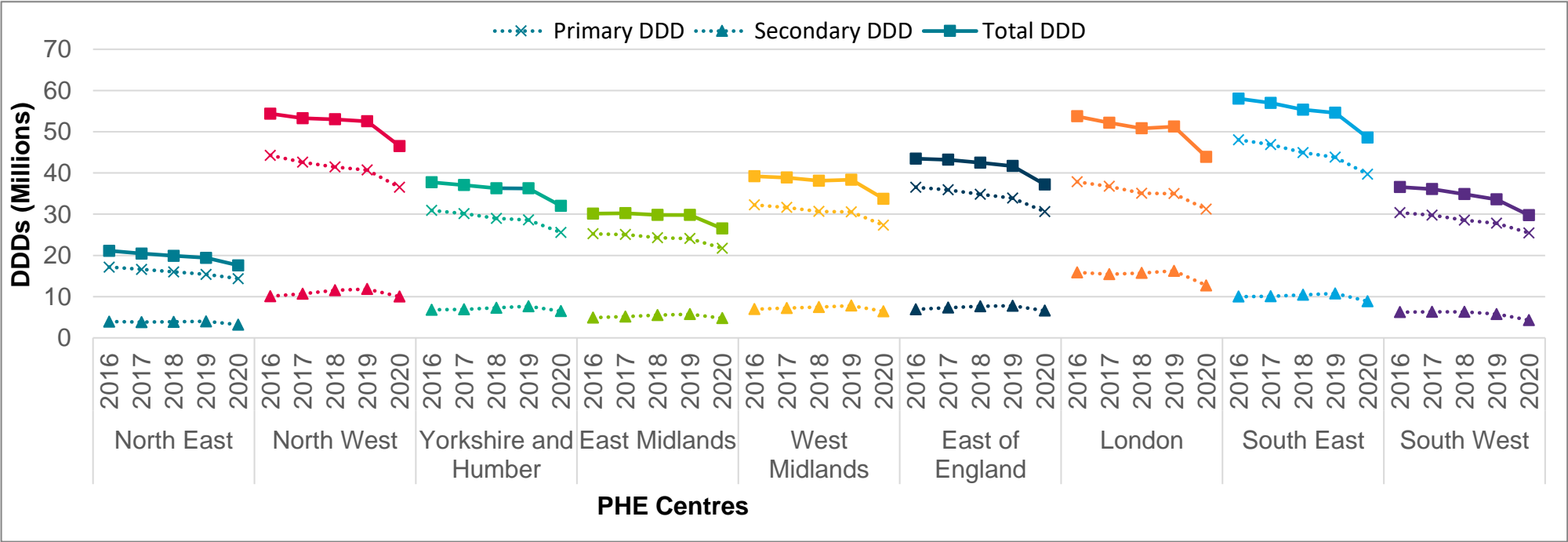


**Box 5.1 Regional variation in antibiotic consumption in England**

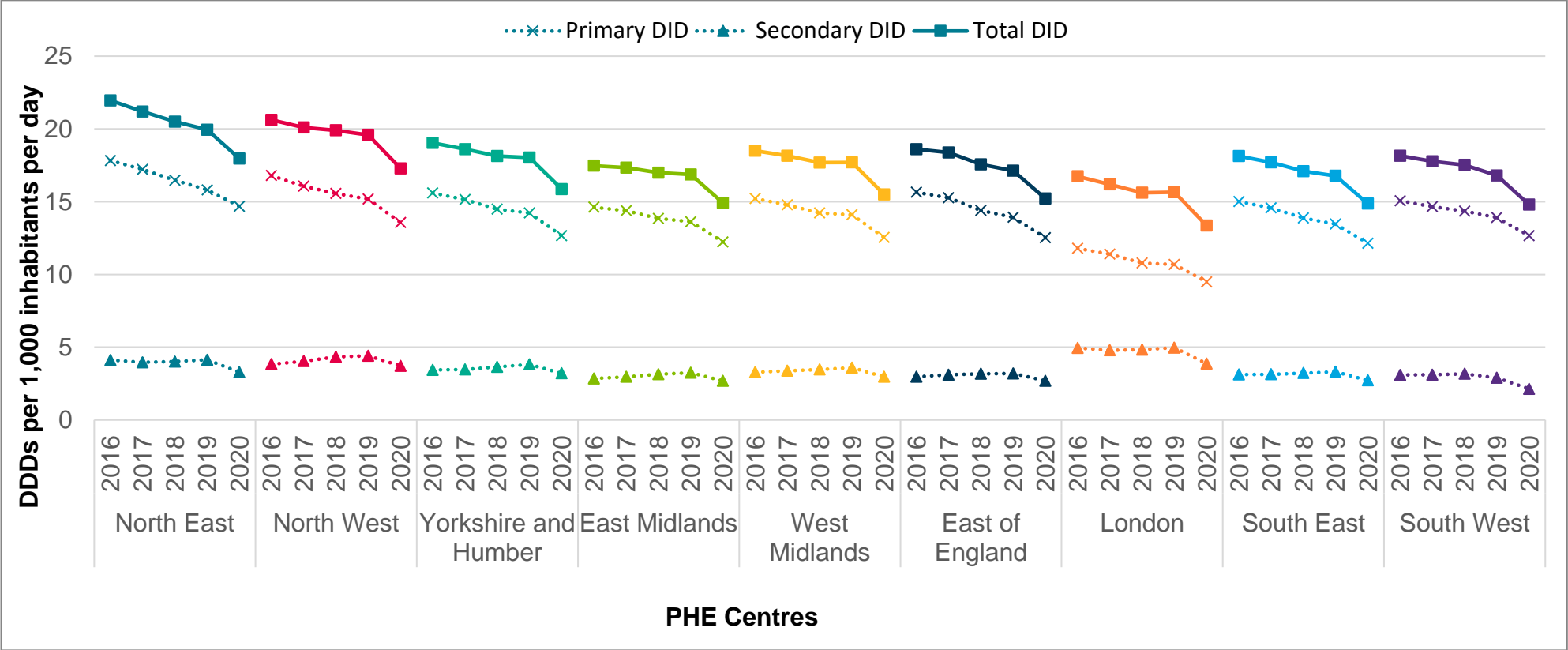
In England, antibiotic stewardship measures are set at a national level, with the focus of this chapter also looking at national-level consumption. This section assesses the regional context of antibiotic prescribing and the differences seen during the COVID-19 pandemic regionally (by PHE centre) and by setting across these centres.

The South East, North West and London PHE centres have the greatest antibiotic consumption levels in England based on DDDs; that is, in total use, as well as within both primary and secondary care (Box Figure 5.1.1). When the underlying population was taken into account, regional differences were evident in the trends, with DDDs per 1,000 inhabitants per day being greatest within the North East and North West of England (Box Figure 5.1.2).

**Box Figure 5.1.1. Total, primary and secondary care antibiotic consumption by PHE centres, expressed as DDDs, 2016 to 2020 (excludes dental practice data)**



**Box Figure 5.1.2. Total, primary and secondary care antibiotic consumption by PHE centres, expressed as DDDs per 1,000 inhabitants per day, 2016 to 2020 (excludes dental practice data)**



Prior to 2020, primary care prescribing rate has consistently been the highest within the North East of England and lowest in London. Conversely, secondary care consumption rate has been the highest within London, and lowest in the South West and East Midlands (Box Figure 5.1.2).

From 2016, total antibiotic prescribing trends have seen year-on-year decreases across all the PHE centres in England (Box Figure 5.1.2). This reduction in total antibiotic use from 2016 to 2019, for all PHE centres, were predominantly related to reductions in the primary care setting (Primary care data does not include dental care prescribing in this analysis as dental data at the PHE centre-level was not available).

Secondary care prescribing for all PHE centres, apart from the South West PHE centre (which had decreased by 6.4%, and as mentioned above had the lowest secondary care prescribing levels), exhibited increasing trends from 2016 to 2019.

The COVID-19 pandemic saw regional reductions in the rate of total antibiotic consumption (DDDs per 1,000 inhabitants per day, DID) as well as across settings (primary and secondary care DIDs). London, West Midlands and Yorkshire and Humberside showed the greatest decline in total and primary antibiotic consumption between 2019 to 2020 (primary care DID: -11% for each PHEC; total DID: -14.7, -12.5 and -12.0% respectively) (Box Figure 5.1.2). The greatest reductions in secondary care prescribing were seen during this period within the South West PHE centre (-26.1% in DID) (Box Figure 5.1.2). It should be noted that the secondary care data included in this Box is by DID and not antibiotic consumption by hospital admissions; it is presented as such for ease of comparison across settings. Later analysis within this chapter suggests a national increase between 2019 and 2020 in secondary care antibiotic consumption by hospital admission, thought to be related to a greater decrease in the hospital admission denominator than in DDDs. Hence, the analysis here has not taken into consideration the change in the number of patients and hospital episodes of care, as well as the change in case-mix over this time period (with elective surgeries and so on being postponed during the early parts of the COVID-19 pandemic).

Although total antibiotic consumption has reduced over time nationally and across PHE centres, there remains unexplained variation in prescribing across the country. Antibiotic prescribing has been associated with deprivation, with higher prescribing occurring in more deprived communities and areas ([135](#)). Research which accounted for patient demographics (that is, age, gender), chronic conditions, comorbidities or smoking status found that disparate consumption rates prevail, with the most deprived areas having the higher prescribing rates ([136](#)). Patient healthcare seeking behaviours may in part explain the differences seen across regions and PHE centres in England. However, there is a need to better understand why such variation persists. There is also future scope and work being completed to assess the variation in the prescribing of broad-spectrum antibiotics regionally in England.

## Penicillins

Penicillins are the most frequently prescribed antibiotics in England, and account for 35.8% of total antibiotic prescribing in 2020 (29.6% accounted for by penicillins excluding inhibitors, and 6.2% by penicillin inhibitor combinations only).

Consumption of penicillins have steadily decreased by 8.3% between 2016 and 2019 (from 7.44 to 6.82 DID), with a further 15.8% decline (5.74 DID) between 2019 and 2020 (Table 5.1). While there was a reduction in utilisation across most of the antibiotics in the penicillin class between 2016 and 2020, a larger decrease between 2019 and 2020 than between previous years was observed. Amoxicillin use decreased by 22.9% between 2019 and 2020 compared to less than a 10% year-on-year reduction across the 4 previous years (2016 to 2019). Even with the large annual reduction between 2019 and 2020, amoxicillin (2.30 DID) continues to be the most commonly prescribed penicillin in 2020, followed by flucloxacillin (1.65 DID).

A 9.9% decrease was observed in co-amoxiclav and an 18.2% reduction in phenoxymethylpenicillin prescribing between 2019 and 2020 compared to less than or equal to 1% and less than or equal to 6% in prior yearly reductions, respectively.

Of note, pivmecillinam prescribing continued to increase with a 90.5% rise between 2016 and 2019 (0.041 to 0.079 DID respectively), and a further 12.2% increase between 2019 and 2020 (0.079 DID to 0.088 DID respectively). This is most likely related to a continued increased usage for lower urinary tract infections (UTIs), as recommended by NICE guidance ([137](#)).

Prescribing for piperacillin/tazobactam is still lower when compared to 2016 with an overall decrease of 30.2% from 2016 to 2020 (0.105 to 0.073 DID respectively). Piperacillin/tazobactam use has been steadily increasing since the 2017 supply shortage (12.2%) ([138](#)). However, a reduction was observed in 2020 (-5.7%, from 0.78 in 2019 to 0.73 DID respectively).

The overall reduction in penicillins consumption was seen across most settings and notably the GP setting decreased 27.4% between 2016 and 2020, from 5.02 DID to 3.64 DID.

## Cephalosporins

There has been a decline in the overall consumption of cephalosporins from 0.33 to 0.31 DID (-7.4%) between 2016 to 2020. First and second-generation cephalosporins usage decreased by 11.7% during the same period while third, fourth and fifth-generation cephalosporin prescribing increased between 2016 and 2020 by 10.7% (Table 5.1). However, as first and second-generation cephalosporins account for the majority of the cephalosporin class, the overall reduction in cephalosporins is related to the reductions in first and second-generation cephalosporins. The reductions are mainly attributable to decreases seen in the GP setting.

## Tetracyclines

Tetracyclines are still prescribed predominantly in the GP setting (87.7%). The overall consumption has remained relatively stable with a slight decrease of 8.5% over the past 5 years from 4.75 DID in 2016 to 4.35 DID in 2020 (Table 5.1). Doxycycline and lymecycline remain the most prescribed tetracyclines, with an increase observed in doxycycline (12.6%) but a decrease in lymecycline (-1.4%) between 2016 and 2019, followed by a decrease in both (-8.4% and -6.7%, respectively) between 2019 and 2020. Minocycline prescribing showed the largest percentage decrease (55.7%) from 0.052 DID in 2016 to 0.023 DID in 2020.

## Quinolones

The use of quinolones accounted for 2.9% of total antibiotic usage in 2020. Since 2018 there has been a general decline in quinolone consumption, with a 17.7% reduction between 2018 and 2020 and an overall decrease of 12.1% over the past 5 years. The predominant antibiotic used was ciprofloxacin which accounted for 73.2% of quinolone use in 2020 though its use has decreased steadily since 2016 (-20%; 2016: 0.42 DID vs. 2020: 0.34 DID). Quinolones are mainly prescribed at general practices (2020: 54.2%) though prescribing in this setting has reduced by 14.9% from 0.29 DID in 2016 to 0.25 DID in 2020. Conversely, quinolone prescribing to hospital inpatients has increased by 19.0% over the past 5 years (from 0.094 DID in 2016 to 0.11 DID in 2020; Table 5.1).

## Macrolides

Usage of macrolides has steadily declined since 2016, with a 26.7% reduction from 3.20 DID in 2016 to 2.35 DID in 2020. Erythromycin experienced the highest percentage reduction (48.4%), from 0.73 to 0.38 DID between 2016 and 2020. In contrast, azithromycin has increased year-on-year over the past 5 years, with a total increase of 15.9% from 0.48 to 0.56 DID. General practices account for 79.0% of prescribing for macrolides, where there was a 26.4% reduction in macrolide prescribing between 2016 to 2020 (from 2.52 to 1.86 DID respectively).

## Sulphonamides, nitrofurantoin and trimethoprim

The overall consumption for this group of antibiotics has declined by 40.9% between 2016 to 2020 (1.27 to 0.75 DID; Table 5.1). This decrease is driven by the decline observed in general practice and in the other community setting (-45.5% and -60.4%, equivalent of -0.46 and -.03 DID, respectively). Despite a reduction of 12.7% between 2016 and 2019 in prescribing of sulphonamides, nitrofurantoin and trimethoprim in the hospital inpatient setting, there has been very little change over the past year (-0.4% between 2019 and 2020, from 0.086 to 0.085 DID).

Overall nitrofurantoin consumption has increased by 40.8% between 2016 and 2020 (26.3% increase from 2016 to 2019), and continued to show an annual increase (11.5%) from 1.09 in 2019 to 1.22 in 2020. While the rise in consumption of nitrofurantoin has been observed across all settings, the greatest absolute difference in DID was observed in the GP setting (0.77 DID in 2016 to 1.06 in 2020). However, the highest percentage increase was seen in 'other community'

settings (135.9% increase from 0.028 DID in 2016 to 0.067 DID in 2020). The increase in nitrofurantoin consumption is likely related to initial changes in 2014 to PHE primary care guidelines recommending nitrofurantoin as first-line treatment for lower urinary tract infections in adults ([139](#)). This shift away from prescribing of trimethoprim to nitrofurantoin was further encouraged with the implementation of the 2017 to 2019 Quality Premium ([140](#)).

## Aminoglycosides

Aminoglycosides make up a small amount of overall prescribing (0.7%). Consumption of this antibiotic class has also decreased by 11.7% over the past 5 years from 0.12 DID to 0.11 DID (Table 5.1). Prescribing decreased between 2016 and 2020 across all settings; however, there were previous annual increases in hospital inpatient consumption between years 2016 to 2019 and hospital outpatient consumption between 2016 to 2018. The greatest absolute change in DID was observed in the hospital inpatient setting from 0.084 DID in 2016 to 0.073 DID in 2020, a 13.9% decrease. Greater percentage reductions were observed in both other community settings (-77.3%, 2016:0.00004 to 2020:0.00001 DID) and the GP setting (-48.5%, 2016: 0.008 DID to 2020: 0.004 DID).

## Parenteral glycopeptides and daptomycin

Parenteral glycopeptides (vancomycin and teicoplanin) and daptomycin consumption have all decreased from 0.102 DID to 0.095 DID between 2016 to 2020, a decrease of 7.2%. This is mainly driven by the reduction in prescriptions from the hospital inpatient (-3.6%, -0.003 DID) and hospital outpatient settings (-23.4%, -0.004 DID) over the past 5 years. Prescription of parenteral glycopeptides and daptomycin occurred almost exclusively within the hospital inpatient setting (87.2%) and hospital outpatient (12.5%).

## Colistin

Consumption of colistin, a last resort antibiotic used to treat multidrug-resistant infections, has experienced a marginal increase from 0.037 to 0.040 DID (7.8%) over the past 5 years, (6.0% increase from 2016 to 2019, and a further 1.6% increase between 2019 and 2020). Despite reduced usage across all other settings (including hospital inpatients), the use of colistin in the hospital outpatient setting has increased from 0.012 DID in 2016 to 0.018 DID in 2020 (58.3%).

## Oral metronidazole

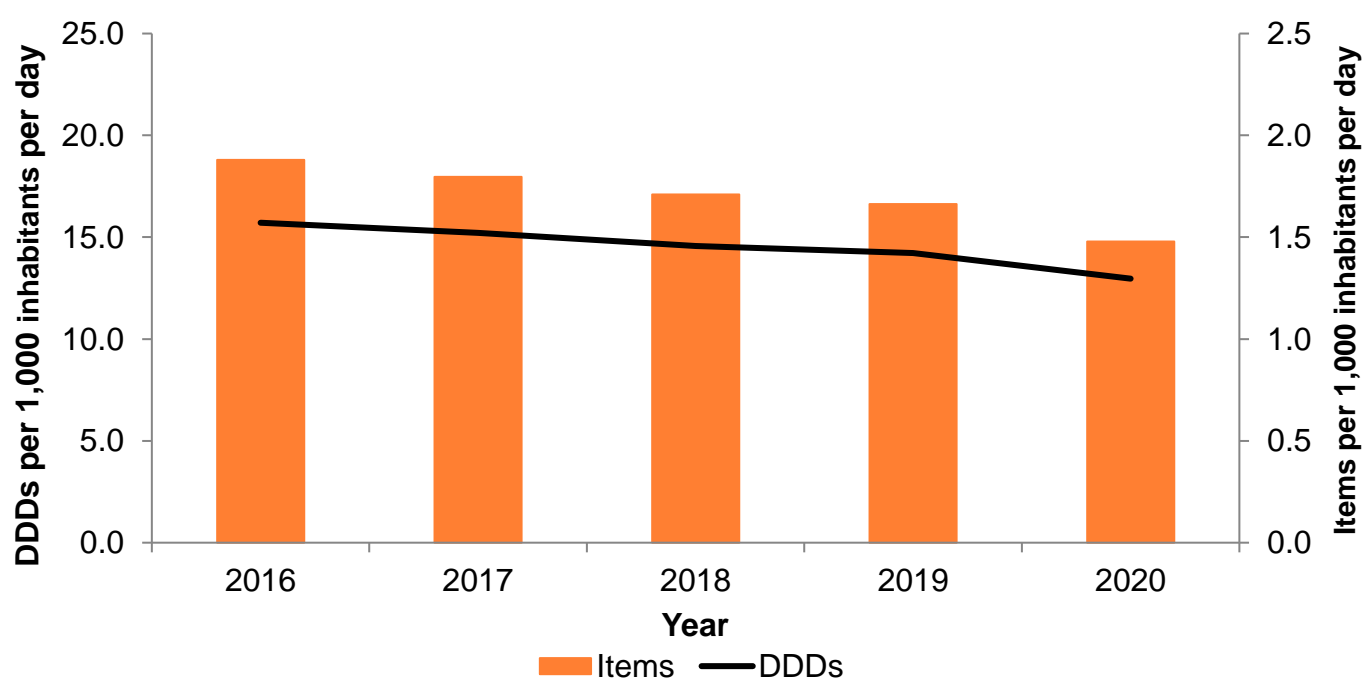
Consumption of oral metronidazole decreased by 9.8% between 2016 and 2020, from 0.34 to 0.30 DID. The use of oral metronidazole increased solely in the dental setting from 0.12 DID to 0.14 DID between 2016 and 2020. Despite a steady reduction in prescribing since 2016 in the dental practice, there was an increase of 28.3% between 2019 (0.11 DID) and 2020.

## Prescribing in primary care (in items)

Total antibiotic prescribing in primary care settings, measured by antibiotic items, decreased from 1.88 to 1.66 Items per 1,000 inhabitants per day, equating to an 11.6% drop between 2016 and 2019. There was a further reduction of 11.1% between 2019 and 2020 alone, which accounted for 45.8% of the overall 5-year decrease. After year-on-year decreases in primary care prescribing (Figure 5.2), the change between 2019 and 2020 was greater than in previous years, likely due to the impact of COVID-19 on primary care prescribing.

General practice accounts for 84.2% of prescribing for items per 1,000 inhabitants per day. This was followed by the dental (10.3%) and other community settings (5.5%). The decline in items prescribed in primary care was predominantly driven by reduced prescribing in the GP setting (-23.2% in items from 2016 to 2020, from 1.62 to 1.25 items per 1,000 inhabitants per day). Dental prescribing, following a previously decreasing trend, saw a 17.6% increase between 2019 and 2020, from 0.13 to 0.15 items per 1,000 inhabitants per day.

**Figure 5.2 Total antibiotic consumption in primary care, expressed as DDDs and Items per 1,000 inhabitants per day, England, 2016 to 2020**



### General practice

For the GP setting, penicillins continue to remain the most commonly prescribed antibiotic item, accounting for 43.5% of all prescriptions. However, penicillin use has declined by 32.5% over the past 5 years (0.80 to 0.54 items per 1,000 inhabitants per day) and 20.2% between 2019 and 2020 alone (Table 5.2). The overall reduction in penicillin use has been a contributing factor for the observed decline in total GP prescribing over the last 5 years, and across the COVID-19 period. After penicillin, the next most prescribed antibiotic within the GP setting are other antibacterials 16.0% (see [Chapter Annexe](#) for definition) and tetracyclines 15.7%.



The greatest percentage change over the past 5 years was in the prescribing of amphenicols, which decreased by 56.6%, followed by other antibacterials which increased by 55.7%. All key antibiotic groups (apart from anti-*Clostridioides difficile* agents and other antibacterials) have shown reductions between 2016 and 2020 within the GP setting, including the prescribing of broad-spectrum antibiotics (cephalosporins, quinolones and co-amoxiclav), encouraged by the previous quality improvement schemes ([141](#), [142](#)). However, following year-on-year decreases in cephalosporins, there was a slight increase of 4.4% from 2019 to 2020 (from 0.035 to 0.037 items per 1,000 inhabitants per day. Table 5.2).

As shown in [Figure 5.3](#), between 2016 and 2020 all age groups have seen a reduction in items prescribed per 1,000 inhabitants per day in the GP setting (see [Chapter Annexes](#) for age information). Prescribing changed mostly for children aged 0 to 4 years with a reduction of 51.6% in antibiotic items prescribed between 2016 to 2020 (p less than 0.05). Furthermore, while all age groups have seen year-on-year declines in prescribing, the change between 2019 and 2020 was greater than the annual changes in the preceding 4 years. The greatest percentage change in items prescribed between 2019 and 2020 was amongst children aged 0 to 4 years, with a 39.9% reduction from 0.57 to 0.34 items per 1,000 inhabitants. Children aged 5 to 14 had the next greatest percentage decrease (-25.9%) from 0.28 to 0.21 items per 1,000 inhabitants. This might be due to reduction in amoxicillin prescribed to children aged 0 to 9 years.



**Table 5.2 Antibiotic items prescribed by GP, expressed as Items per 1,000 inhabitants per day, England, 2016 to 2020**

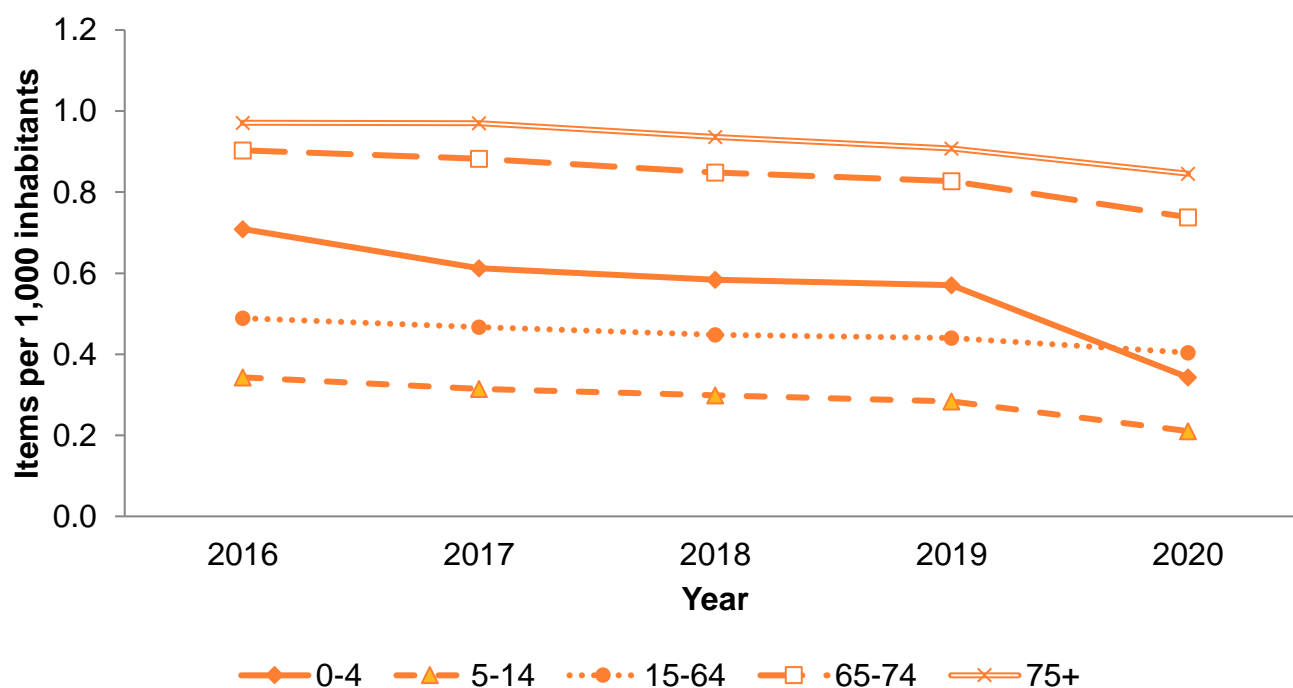
Antibiotic Group	2016	2017	2018	2019	2020	Trend	p-value
Penicillins (excluding inhibitors)	0.732	0.687	0.649	0.623	0.487		0.015 <sup>+</sup>
Penicillins (inhibitor combinations only)	0.071	0.066	0.061	0.056	0.055		0.003 <sup>+</sup>
First and second-generation cephalosporins	0.043	0.040	0.037	0.035	0.037		0.055
Third, fourth and fifth-generation cephalosporins	0.000	0.000	0.000	0.000	0.000		0.010 <sup>+</sup>
Carbapenems	0.000	0.000	0.000	0.000	0.000		0.034 <sup>+</sup>
Tetracyclines	0.212	0.210	0.205	0.212	0.195		0.180
Macrolides, lincosamides and streptogramins	0.203	0.190	0.174	0.165	0.141		<0.001 <sup>+</sup>
Sulfonamides and trimethoprim	0.170	0.134	0.097	0.084	0.081		0.015 <sup>+</sup>
Quinolone antibacterials	0.031	0.030	0.030	0.025	0.024		0.017 <sup>+</sup>
Anti-Clostridioides difficile agents <sup>^</sup>	0.000	0.000	0.000	0.000	0.000		0.176
Oral metronidazole	0.032	0.029	0.027	0.026	0.025		<0.001 <sup>+</sup>
Other antibacterials <sup>*</sup>	0.128	0.159	0.187	0.194	0.200		0.016 <sup>+</sup>

+ Statistically significant p-value for trend from 2016 to 2020.

<sup>^</sup> Anti-*Clostridioides difficile* agents include: oral vancomycin and fidaxomicin.

<sup>\*</sup> Other antibacterials (ATC 3rd level pharmacological subgroup 'J01X') include: glycopeptide antibacterials, polymyxin, steroid antibacterials, imidazole derivatives, nitrofurantoin derivatives, other antibacterials.

**Figure 5.3 Total consumption in items in general practices by age group, expressed as Items per 1,000 inhabitants, England, 2016 to 2020**



### **Box 5.2 Antibiotic consumption and appointments in general practices, in England, during the COVID-19 pandemic period**

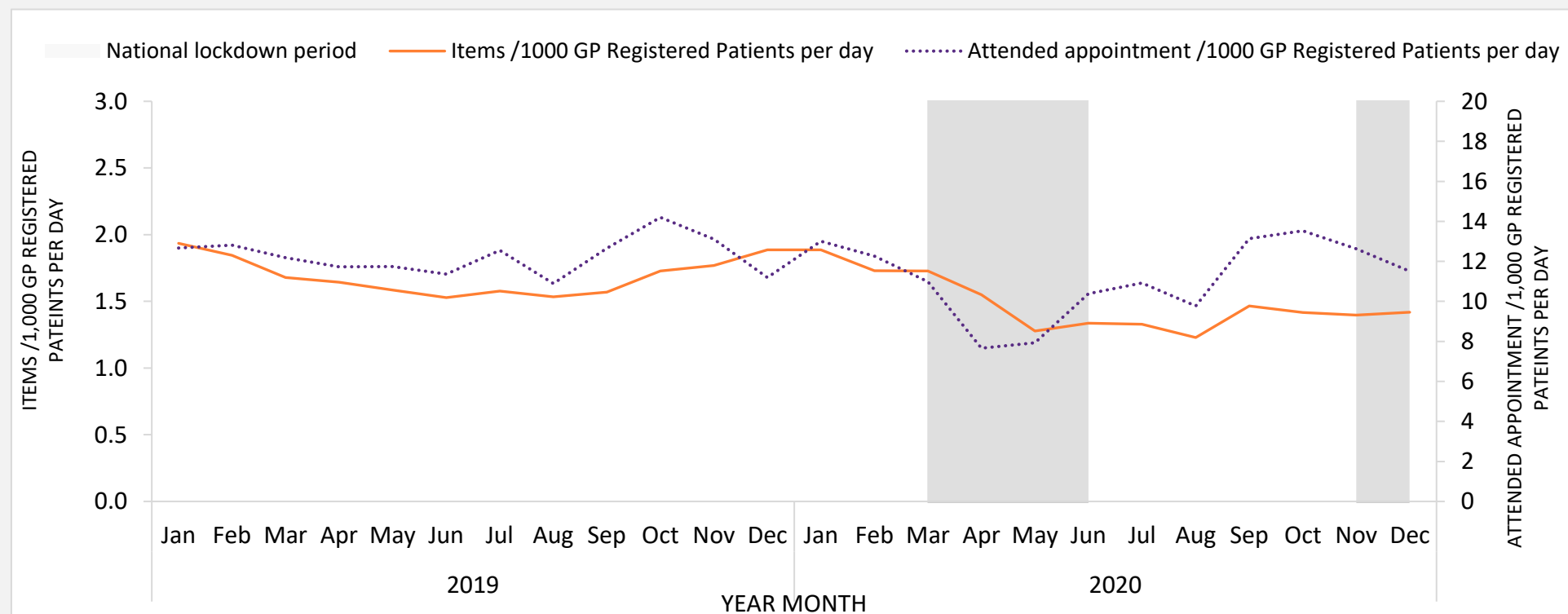
International assessment of antibiotic consumption in primary care settings, predominantly general practices, is often calculated as items or DDDs per 1,000 inhabitants per day. This permits the comparison of rates between settings (with DDDs per 1,000 inhabitants per day [DID] used for comparisons between primary and secondary care) and across different populations.

As described in the section above and in recent literature, the COVID-19 pandemic has coincided with decreases in antibiotic consumption in general practices ([143](#), [144](#), [145](#)). However, changes have also been apparent in the population demographics of patients seeking health care and healthcare seeking behaviour, perhaps related to increases in knowledge and practice of infection control measures (for example, improved hand hygiene) as well as reduced travel and social contact (with national 'lockdown' measures encouraging 'social isolation') and, therefore, assumed reductions in subsequent spread of infections and demand of healthcare and antibiotic therapy. A growth in patient concern about accessing health care services, potential reductions in general practice capacity and the introduction of the NHS 111 service may have also contributed to the changes seen in attended appointments. The introduction of the NHS 111 service introduced an alteration in health provision, with patients triaged and diverted from Emergency Departments and general practices to other settings such as walk-in centres, urgent treatment centres and community pharmacies. Shifts in the provision of care and settings have not been captured within the figures presented here but may have had an effect on reducing the numerator of antibiotics prescribed in the general practice setting, as well as the appointments held in this setting.

Box Figure 5.2.1 displays the trends in attended appointments (both face-to-face and remote. Please see [Annexe](#) for further information on definitions and data used.) in general practices across a 2-year period in England and the implications the COVID-19 pandemic may have had on these appointments and subsequent antibiotic prescribing in this setting. It is evident that the expected seasonal peaks (often seen between November to January) in attended general practice appointments (per 1,000 inhabitants per day) began to decline in December 2019, with a further drop in the trend during the first national 'lockdown' period (from March 2020; approximately a 10% decline in appointments when compared to March 2019). However, this reduction in attended appointments was not sustained once restrictions were eased and began to increase to similar levels seen previously. The second 'lockdown' period did not seem to have the same level decrease in appointments attended (face-to-face and remote), although there was a reduction in the trend compared to previous months and to what may have been expected with seasonal November and December months.

Antibiotic prescribing trends similarly seemed to be on an increasing trend during the winter months prior to the pandemic, peaking in January 2020, with a seasonal decline thereon (Box Figure 5.2.1). The drop in antibiotic prescribing during the first 'lockdown' period was not as steep as that seen in the trend of attended appointments, suggesting that a reduction in prescribing was indicative of a decline in appointments, and that a greater proportion of appointments were being prescribed antibiotics during the first national 'lockdown'. The decline in antibiotic prescribing items seems to have been sustained since the start of the COVID-19 first lock-down period, with no substantial increases but rather a steady rate seen in the following winter season (November to December 2020).

**Box Figure 5.2.1 Trends in attended GP appointments and antibiotic items by registered patients**



Not only was there a decline in attended general practice appointments within the first lockdown period, described above (Box Figure 5.2.1), but a concurrent shift towards telehealth and remote consultations was observed (Box Figure 5.2.1). Prior to March 2020, the mode of appointments every month had more than 80% held as face-to-face and less than 15% as remote appointments (see [chapter](#)

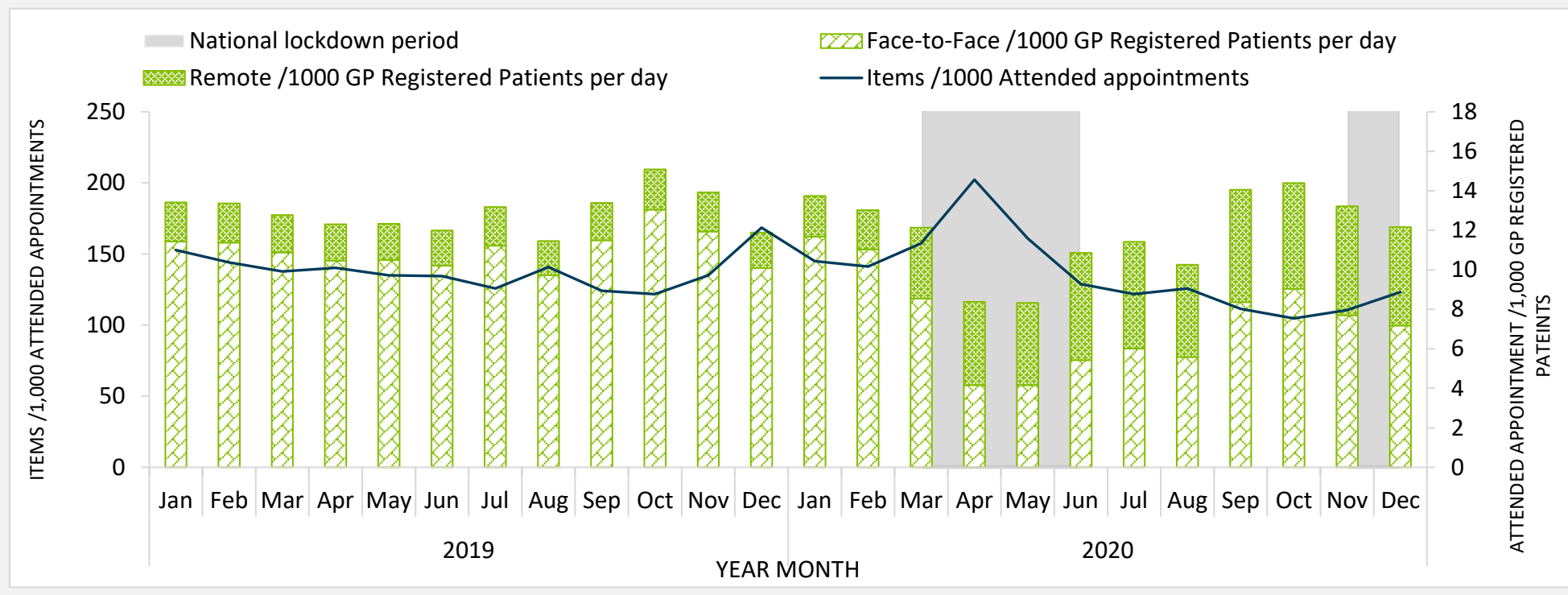
[annexe](#) for details of appointment type definitions). In order to prevent and reduce COVID-19 transmission risk, the modes of appointments changed during the pandemic to 47% and 48% in April 2020, respectively for face-to-face and remote appointments.

Box Figure 5.2.2 also presents the rate of antibiotic items per 1,000 attended appointments (face-to-face and remote). This trend displays a peak (202 per 1,000 attended appointments) in April 2020, mid 'lockdown' and where the decline in the attended appointment level was most evident (Box Figure 5.2.2). Box Figure 5.2.1 shows that from March 2020, the slope of the decline in attended appointments was not concurrent to the decline seen in antibiotic consumption during the same time period, hence the peak seen in March to April 2020 when looking at items per 1,000 attended appointments (Box Figure 5.2.2). This could be suggestive of an increase in inappropriate and over prescribing of antibiotics, with prescribers being more cautious during this period (particularly as telehealth appointments may not have permitted certain examinations which may otherwise have been conducted, for example, dipstick for urinary tract infections), and attempting to maintain continuity of access to therapy, particularly for pre-existing conditions or infections which may otherwise result in an unintended severe infection.

However, an alternative and perhaps more plausible hypothesis given the overall antibiotic prescribing reductions seen, is that the increase in prescribing rate per attended appointment could be suggestive of an increase in severity of infections or patients who have presented with more severe indications, perhaps due to delayed consultations and treatment (where patients with initial milder symptoms did not access healthcare) and; therefore, appropriate antibiotic prescribing given illness severity. It is also likely that with a reduction in routine work (for example, hypertension, diabetes) within general practices during the COVID-19 period, the proportion of consultations related to acute infections may have increased, hence antibiotic prescribing for consultations may have been elevated compared with pre-COVID-19 rates. However, at present there is insufficient evidence to determine which, or whether both, factors are at play.

Further research to inform on appropriateness of antibiotic prescribing during the COVID-19 pandemic would be valuable, albeit possibly difficult to obtain and assess. Similarly, further work into the changes in composition of patients consulting and case-mix would be beneficial, as well as assessment of any associated negative consequences and risk to patient safety.

**Box Figure 5.2.2. Trends in antibiotic items prescribed by attended general practice appointments and changes in mode of consultations**



## Other community

'Other community' prescribing covers antibiotic prescribing within several community services (see [chapter annexe](#) for full list), and as a whole this has declined by 18.9% (0.10 to 0.08 antibiotic items per 1,000 inhabitants per day) between 2016 to 2020. However, this marks a reverse in the trend seen previously; as from 2016 the level of items prescribed slowly increased from 0.10 in 2016 to 0.11 in 2019. Conversely, 2020 saw a reduction in the items prescribed to 0.08 items per 1,000 inhabitants per day; an annual reduction of 26.3%, causing the overall decline in the 5-year period.

The majority of antibiotic item prescribing took place in out-of-hours services which contributed to 55.5% of all antibiotic prescribing in 'other community' settings in 2020. Prescribing increased by 33.5% from 0.011 to 0.015 items per 1,000 inhabitants per day in 'other' within the 'other community' setting group, while a 15.4% increase was observed in urgent care settings from 0.007 to 0.008 items per 1,000 inhabitants per day. These, however, represent a decrease from 2019 rates, and there were no increases in prescribing seen across all categories between 2019 and 2020.

## Dental

Data for prescribing in the dental practice setting is only available for NHS practices and consultations. Antibiotic prescribing in the dental setting steadily decreased from 2016 to 2019 (0.16 and 0.13 items per 1,000 inhabitants per day respectively, -18.4%). This decline was interrupted in 2020 with an increase of 17.6% reported (from 0.13 to 0.15 items per 1,000 inhabitants per day). Dental pain and infection are usually amenable to procedures rather than prescriptions. During the pandemic, access to dental procedures (including aerosol generating procedures) were restricted and therefore it is highly likely that this was associated with the increased prescribing of antibiotics and analgesics.

The predominant antibiotic prescription in 2020 was amoxicillin (66.1%), followed by metronidazole (29.2%) and erythromycin (2.6%).

Prescribing of the most common antimicrobials in the dental practice setting have decreased over the last 5 years, however, between 2019 to 2020 there were substantial increases in antibiotics prescribed in the dental practice setting (Table 5.3). The most evident inclines observed were in clarithromycin (+109.9%, however, this only accounts for 0.4% of all dental prescribing), amoxicillin (+17.3%, accounts for the majority of antibiotic prescribing in this setting, as stated above), and metronidazole (+19.5%) usage.

**Table 5.3 Dental antibiotic consumption for the most commonly used antibiotics, expressed as DDDs and items per 1,000 inhabitants per day, 2016 to 2020**

Antibiotic		2016	2017	2018	2019	2020	Trend	p-value
Amoxicillin	Items	0.104	0.096	0.090	0.085	0.100		0.526
	DDD	0.541	0.512	0.480	0.460	0.558		0.916
Co-amoxiclav	Items	0.001	0.001	0.001	0.001	0.001		0.070
	DDD	0.003	0.002	0.002	0.002	0.002		0.058
Clarithromycin	Items	0.000	0.000	0.000	0.000	0.001		0.068
	DDD	0.003	0.004	0.004	0.004	0.006		0.076
Clindamycin	Items	0.001	0.001	0.001	0.001	0.001		0.759
	DDD	0.003	0.002	0.002	0.002	0.003		0.727
Erythromycin	Items	0.006	0.005	0.004	0.004	0.004		0.016+
	DDD	0.045	0.041	0.036	0.031	0.034		0.036+
Oral Metronidazole	Items	0.045	0.042	0.039	0.037	0.044		0.679
	DDD	0.118	0.114	0.109	0.106	0.136		0.511

## Prescribing in secondary care (by admission)

### Box 5.3 Antibiotic consumption and COVID-19

A manuscript on the descriptive trends of antibacterial use in both primary and secondary care in England at the beginning of the pandemic in 2020 has been published (148). In summary, overall volumes of antibacterial use as measured by DDDs decreased in hospital settings, although the rate of usage per admission in hospitals increased steeply in April 2020 due to changes in hospital populations (that is, variation in case-mix of patients) and a decrease in hospital admissions within the first wave. These changes are likely due to cancellation of elective procedures and patients who were admitted to hospital were likely to be more acutely and seriously ill.

Use of antibacterials prescribed for respiratory infections and broad-spectrum antibacterials (predominantly 'Watch' antibiotics under the AWaRe categories from the WHO Essential Medicine List adopted in England for hospital settings) increased. Moreover, the use of antibiotics ('last-resort' or new) in the 'Reserve' category has also increased in hospitals during the beginning of the pandemic. Further analyses are underway to investigate the impact of COVID-19 on antimicrobial prescribing in subsequent waves of the pandemic and at a regional level (also see AWaRe - access, watch and reserve subsection below).

## Total antibiotic use

Antibiotic use in secondary care, measured using hospital admissions as the denominator, showed prescribing increased by 1.9% (from 4,586 to 4,674 DDDs per 1,000 admissions) between 2016 and 2019. This increase was driven by a rise in prescribing for hospital inpatients (+6.3%), in contrast to hospital outpatient prescribing which decreased by 4.9%, over the same



period. Similar trends were also seen between 2019 and 2020, with inpatient antibiotic consumption further increasing by 10.6% and outpatient antibiotic consumption decreasing by 5.2%. The increase in inpatient prescribing may be related to changes in prescribing behaviours with a shift away from broad-spectrum to narrow-spectrum antibiotic use, that is, an increase in more than one antibiotic (2 or more narrow-spectrum antibiotics) being used in replacement of single broad-spectrum antibiotics for the same clinical indication.

The COVID-19 pandemic has had a marked effect on antibiotic prescribing in secondary care in 2020. There was a 4.8% increase in total antibiotic prescribing (4,674 to 4,899 DDDs per 1,000 admissions) between 2019 and 2020. This increase in prescribing rate masks a reduction in total DDDs prescribed, and an even greater decrease in hospital admissions between 2019 and 2020 (-18.4% and -22.1% respectively). This reflects the changes in hospital populations since the start of the pandemic; more acutely ill patients were admitted while elective procedures were cancelled.

The rate of total antibiotic prescribing increased in all acute Trust types over the past 5 years (data in [annexe](#)). Acute specialist had the highest increase between 2016 and 2020 from 4,975 to 6,524 DDD per 1,000 admission (31.2%). Definitions of acute Trust types can be found in the [chapter annexe](#).

As [Table 5.4](#) shows, statistically significant increases in the last 5 years have been observed for third, fourth and fifth-generation cephalosporins, tetracyclines, anti-*Clostridioides difficile* agents, and 'other antibacterials' (see [chapter annexe](#) for definition). Between 2016 and 2020, significant decreases in usage were observed for penicillins (excluding inhibitors), oral metronidazole, and macrolides, lincosamides and streptogramins ([Table 5.4](#)).

Despite the decreasing year-on-year trend in prescribing of 'macrolides, lincosamides and streptogramins' and oral metronidazole the rate of prescribing increased for these antibiotics between 2019 and 2020 by 0.4% and 1.6%, respectively. Other notable increases in use between 2019 and 2020 include the anti-*C. difficile* agents (23.8%) and sulphonamides and trimethoprim (19.6%). This is likely due to the inclusion of vancomycin and co-trimoxazole respectively within the 'National Institute for Health and Care Excellence (NICE) COVID-19 rapid guideline: antibiotics for pneumonia in adults in hospital' (May 2020) ([149](#)). Prescribing of all antibiotic groups increased in rate between 2019 and 2020 with the exception of penicillins (excluding inhibitors). Furthermore, the annual increase between 2016 and 2018 observed in third, fourth and fifth-generation cephalosporin use (79.3 to 98.8 DDD per 1,000 admissions) reversed in 2019 with a slight reduction (95.9 DDD per 1,000 admissions); however, in 2020 their usage increased once again (110.3 DDD per 1,000 admission).

**Table 5.4 Antibiotic consumption in Trusts by antibiotic group, expressed as DDDs per 1,000 admissions, England, 2016 to 2020**

Antibiotic Group	2016	2017	2018	2019	2020	Trend	p-value
Penicillins (excluding inhibitors)	1149.1	1139.5	1135.2	1108.9	1083.2		0.011+
Penicillins (inhibitor combinations only)	810.9	787.4	829.7	829.9	907.9		0.085
First and second-generation cephalosporins	90.8	97.1	96.8	93.6	102.6		0.172
Third, fourth and fifth-generation cephalosporins	79.3	93.6	98.8	95.9	110.4		0.031+
Carbapenems	72.2	71.8	65.9	63.7	71.5		0.534
Tetracyclines	544.6	571.8	619.3	703.5	718.1		0.004+
Macrolides, lincosamides and streptogramins	674.4	658.1	630.8	573.7	576.2		0.010+
Sulfonamides and trimethoprim	273.5	251.9	245.4	241.9	289.3		0.786
Quinolone antibacterials	279.4	291.5	315.7	294.0	316.3		0.146
Anti-Clostridioides difficile agents^	3.8	4.0	4.1	4.4	5.4		0.039+
Oral metronidazole	125.1	122.5	117.1	113.8	115.7		0.030+
Other antibacterials*	330.1	361.5	381.5	387.2	425.8		0.004+

+ Statistically significant p-value for trend from 2016 to 2020.

^ Anti-Clostridioides difficile agents include oral vancomycin and fidaxomicin.

\* Other antibacterials (ATC third level pharmacological subgroup 'J01X') include: glycopeptide antibacterials, polymyxin, steroid antibacterials, imidazole derivatives, nitrofurantoin derivatives, other antibacterials.

## AWaRe – Access, Watch and Reserve

The World Health Organization (WHO) updated the Essential Medicine List (EML) in 2017 and classified key antibiotics into 3 categories (AWaRe): to improve access (Access), to monitor important antibiotics (Watch) and preserve 'last resort' antibiotics (Reserve). The list was adopted for use in antimicrobial stewardship policies across the UK. The target to increase the proportion of antibiotic usage in the 'Access' category featured in the 'Reducing the impact of serious infections (antimicrobial resistance and sepsis) of Commissioning for Quality and Innovation (CQUIN) scheme 2017 to 2019' for NHS acute Trusts ([150](#)). To preserve the most important antibiotics, a target of 10% reduction in the use of drugs in the 'Reserve' and 'Watch' categories was set out in the UK 5-year National Action Plan (NAP) ([151](#)). The full AWaRe index of each antibiotic with ATC code is available in the paper describing the adaptation of WHO's EML in England ([152](#)). Fingertips indicators for monitoring the progress at NHS acute Trust level are available for 'Access', 'Watch' and 'Reserve' antibiotics ([153](#)).

Out of all antibiotic prescriptions in NHS acute Trusts, antibiotics in the 'Access' and 'Watch' categories were prescribed the most in 2020, with 50.8% of DDDs per 1,000 admissions classified as 'Access' antibiotics (2,487 DDDs per 1,000 admissions), 45.8% as 'Watch' antibiotics (2,248 DDDs per 1,000 admissions), and only 3.1% as 'Reserve' antibiotics (154 DDDs per 1,000 admissions). A small number of antibiotics are not classified in any of the AWaRe categories, with prescriptions of these 'Other' antibiotics making up 0.2% of DDDs per 1,000 admissions. These percentages are broadly like previous years.

Between 2017 (the NAP baseline year) and 2019, a decrease of 1.8% and 0.5% was observed in the 'Watch' and 'Reserve' antibiotic prescriptions respectively (from 2,136 to 2,097 DDDs per 1,000 admissions, and 133 to 132 DDDs per 1,000 admissions, respectively), and an increase of 4.1% in 'Access' antibiotics (from 2,340 to 2,436 DDDs per 1,000 admissions).

When comparing 2017 to 2020, an increase was observed of 5.2% in 'Watch' antibiotics (2020: 2,284 DDDs per 1,000 admissions), 16.0% in 'Reserve' antibiotics (154 DDDs per 1,000 admissions), and 6.3% in 'Access' antibiotics (2,487 DDDs per 1,000 admissions).

The changes seen in the AWaRe antibiotic consumption rates described above have been calculated as DDD per 1,000 admissions (that is, using a hospital admissions denominator), this is in-line with the rest of the secondary care consumption section. However, it should be noted that hospital admissions during the COVID-19 pandemic period have decreased, along with changes in the case-mix of hospitalised patients, and therefore changes in the rate of AWaRe consumption may in part be reflective of this. [Consumption of 'Access', 'Watch' and 'Reserve' antibiotics calculated as DDD per 1,000 inhabitants per day (DID), showed a decline across all AWaRe groups between 2019 and 2020, following an incline in consumption for all categories between 2016 to 2019.]

The increase in DDD per 1,000 admissions in Watch and Reserve antibiotics in 2020 have been reflected in the reductions seen in the percentage of total antibiotics accounted for by the

'Access' category and an increase in percentage of antibiotics from the Watch and Reserve categories (reduction between 2019 to 2020 from 52.1% to 50.8% in 'Access', and an increase from 47.7% to 49.0% in 'Watch' and 'Reserve' antibiotics). It is not yet clear whether these are sustained differences in the use of AWARe antibiotics and, as mentioned above, may be related to changes in case-mix of patients admitted into hospital during the COVID-19 pandemic.

## Colistin

Usage of colistin in secondary care although low, continued to increase in the last 5 years (from 17.59 to 31.96 DDDs per 1,000 admissions, an 81.7% increase), with a 28.6% increase alone between 2019 and 2020. The increase was observed in usage for both administration routes (inhalation and parenteral) between 2016 and 2020, with a 102.5% increase for colistin administered by inhalation and a 59.4% increase for parenteral medication. Over the same period, there was a decrease of colistin usage in acute multiservice Trusts (-33.6%).

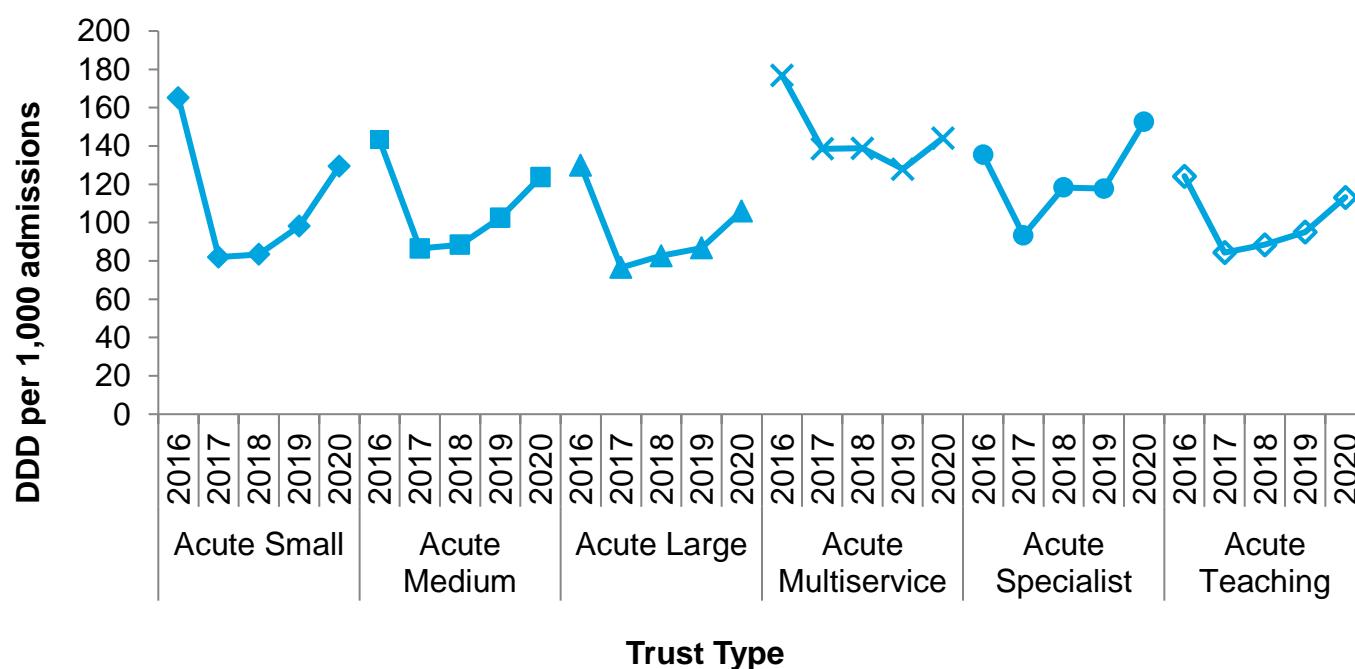
Consumption figures for all other acute Trust types have increased, particularly within specialist Trusts where usage reached 291.63 DDDs per 1,000 admissions in 2020.

## Carbapenems

There was a small decrease in carbapenem consumption in the past 5 years (-0.9%, Table 5.4). However, there has been a sharp increase in use between 2019 and 2020 (12.3%). This has been driven by an increase of 7.83 DDD per 1,000 admissions (14.7%) of meropenem, likely due to use during the COVID-19 pandemic due to its inclusion within NICE hospital-acquired pneumonia (HAP) guidelines ([154](#)). Carbapenem consumption has fallen for medium and large acute Trusts in the last 5 years. However, all acute Trust types saw increases in carbapenem use between 2019 and 2020.

## Piperacillin/tazobactam

Following the large reduction in piperacillin/tazobactam use (-38.1%) due to an international shortage from 135.42 DDDs per 1,000 admissions in 2016 to 83.86 DDDs per 1,000 admissions in 2017, overall consumption subsequently increased from 2018 to 2020 by 32.8% to 116.97 DDDs per 1,000 admissions in 2020. This increase was most marked between 2019 and 2020 (21.7%, from 96.06 to 116.97 DDDs per 1,000 admissions), and increases were seen across all Trust types within this time period (Figure 5.4). This is likely because piperacillin/tazobactam is included within both NICE HAP guideline (NG139, Sep 2019) and COVID-19 rapid guideline: antibiotics for pneumonia in adults in hospital (NG173, May 2020) ([156](#)).






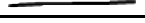


**Figure 5.4 Piperacillin/tazobactam consumption in Trusts by Trust type, expressed as DDDs per 1,000 admissions, England, 2016 to 2020**

## Quinolones, cephalosporins and inhibitor combinations

As a result of the piperacillin/tazobactam shortage and stewardship schemes, which aimed to reduce the use of broad-spectrum antibiotics, there was an increase in usage of antibiotics that can be used as alternatives. Increases in cephalosporins and quinolones were observed from 2017 onwards. Ciprofloxacin usage, for example, increased in 2018 but returned to pre-shortage levels in 2019. Usage levels of cephalosporins and quinolones remained similar in 2020, compared to 2019.

Although the recently launched cephalosporin/ $\beta$ -lactamase inhibitor combinations ceftolozane/tazobactam and ceftazidime/avibactam, are used in small amounts in secondary care, both have shown a steady increase since they were licenced for use in 2016 and 2017 respectively (Table 5.5).

**Table 5.5 Quinolone antibacterials and cephalosporins consumption in Trusts, expressed as DDDs per 1,000 admissions, England, 2016 to 2020**

Antibiotic	2016	2017	2018	2019	2020	Trend	p-value
Ciprofloxacin	203.1	203.5	213.8	197.3	209.2		0.804
Levofloxacin	46.1	61.4	74.2	75.9	82.1		0.012+
Cefuroxime	35.4	42.6	43.4	42.4	44.3		0.114+
Cefotaxime	21.5	22.4	23.6	21.9	26.1		0.150
Ceftazidime	14.5	19.4	18.2	17.5	15.4		0.998
Ceftriaxone	42.3	50.7	55.7	54.8	66.7		0.014+
Ceftazidime/avibactam	-	0.1	0.3	0.5	0.8		0.001+
Ceftolozane/tazobactam	0.1	0.2	0.4	0.5	0.7		0.001+

- not authorised for use in the UK

## Speciality prescribing

Prescribing in secondary care by speciality groups is reported here. See [chapter annexe](#) for specialities grouping within each group. In terms of speciality within secondary care, intensive care units (ICUs) had the highest antibiotic usage, with 54.96 DDDs per ICU admission in 2020 (Table 5.6). Prescribing decreased in all speciality groups between 2019 and 2020, with the exception of the 'Other' specialty. This is unsurprising as many elective procedures were cancelled during the COVID-19 pandemic.

ICUs accounted for the highest usage of piperacillin/tazobactam and carbapenems in 2020 (6.6% and 5.7% of total DDDs per admission respectively). For colistin, paediatrics had the highest proportion of prescribing (5.3%, [Table 5.6](#)). These specialist groups remain unchanged as the highest users of these antibiotic classes.

**Table 5.6 Percentage of all antibiotic prescribing attributed to piperacillin/tazobactam, carbapenems and colistin in secondary care by speciality, expressed as DDDs per admissions, England, 2020**

Specialist Group	DDDs per admission	Piperacillin/tazobactam	Carbapenems	Colistin
Intensive Care Unit	54.96	6.6%	5.7%	0.1%
AE/Non-specific Out-Patient Department	6.95	1.4%	0.6%	0.2%
Geriatrics	2.71	4.6%	1.8%	0.0%
General Medicine	1.44	4.4%	2.0%	0.2%
General Surgery	2.34	3.2%	1.5%	0.0%
Specialist Medicine	2.44	4.6%	3.6%	3.5%
Other	3.09	2.9%	1.8%	0.0%
Orthopaedics	1.94	3.0%	1.7%	0.0%
Obstetrics and Gynaecology	1.44	1.0%	0.5%	0.0%
Paediatrics	1.10	2.4%	2.5%	5.3%
Specialist Surgery	0.66	3.4%	2.9%	1.5%

## Discussion

The year-on-year decreases in total antibiotic consumption has continued, with a decline from 19.27 DDDs per 1,000 inhabitants per day (DID) in 2016 to 16.03 DID in 2020. A substantial decline in antibiotic consumption was particularly evident during the COVID-19 pandemic, with a 10.9% reduction from 2019 to 2020. The findings demonstrate the continued progress made towards the NAP targets to reduce antibiotic prescribing ([156](#)) and highlights the significant impact that the COVID-19 pandemic and subsequent change in healthcare delivery has had on antibiotic usage.

The GP setting continues to account for the greatest quantity of total antibiotic prescribing (72.7% in 2020). Across the different settings, GP antibiotic prescribing exemplified the largest reductions seen, hence declines in total consumption has been largely driven by reductions in the GP setting, particularly of penicillin items which markedly declined between 2019 and 2020 (-15.8%). Similarly, between 2016 and 2020 reductions were seen in broad-spectrum antibiotics (cephalosporins, quinolones and co-amoxiclav) within the general practice setting, these reductions in prescribing have been encouraged by previous quality improvement schemes ([157](#), [158](#)). To note, there was a slight increase of cephalosporin prescribing of 4.4% from 2019 to 2020 (from 0.035 to 0.037 items per 1,000 inhabitants per day), following a previously decreasing trend.

Assessment of changes in the burden and mode of consultations in general practices during the COVID-19 pandemic (Box 5.2) revealed that declines in antibiotic prescribing within this setting may be in relation to reductions in attended appointments. Interestingly, where consultation



rates are now somewhat returning to expected levels, the same level increase in antibiotic prescribing has not yet been observed, with a sustained reduction during winter months of 2020. This is suggestive of improved knowledge of infection prevention and control within patients themselves, reductions of severe bacterial infections and transmission (related to national 'lockdown' periods where social isolation has been encouraged, and travel reduced) and perhaps an increase in patient concern of accessing health care services ([159](#), [160](#)). The greatest reduction in items prescribed in general practices was amongst children aged 0 to 9 years. Early years settings remained open and available during the second COVID-19 pandemic 'lockdown' in England. However, as mentioned above, COVID-19 restrictions or reduced social interactions, improved knowledge of infection control (by the centres and parents, and improved hand hygiene) are likely to have impacted the spread of self-limiting and more severe communicable infections and altered healthcare seeking behaviours. Alongside a reduction in the incidence and burden of infections which is likely to have reduced antibiotic consumption between 2019 to 2020, there has also been a decrease in the count of isolates reported (Chapter 2, [Figure 2.4a](#)).

Although the NHS 111 service impacted health provision during the COVID-19 pandemic period (with patients triaged to hospital emergency departments, urgent treatment centres, walk-in centres and community pharmacy), there has not been an indication of a shift in antibiotic prescribing or service provision from general practices to other settings, as 'other community' settings and hospital (both inpatient and outpatient, including emergency department) prescribing have also decreased during the same time period.

All settings demonstrated decreases in total prescribing between 2019 to 2020, except antibiotic consumption within dental practices which saw an increase of 22.1% DID. The incline in antibiotic prescribing by dental practices, following an otherwise downward trend, has been associated with restricted, often remote, access to dental care since the start of the COVID-19 pandemic. Dental services were advised to suspend routine and non-urgent care, with emergency dental care, analgesics and antibiotics thereon provided via remote consultations ([161](#)). This change in service delivery seems to have impacted the overall level of antibiotics prescribed in 2020 in this setting.

Increases in secondary care antibiotic prescribing between 2016 and 2019 were evident, based on rates calculated using hospital admission (1.9%, from 4,586 to 4,674 DDDs per 1,000 admissions). The COVID-19 pandemic did have a further marked effect on secondary care antibiotic prescribing rates. There was a 4.8% increase in total secondary care antibiotic prescribing (4,674 to 4,899 DDDs per 1,000 admissions) between 2019 and 2020. This is reflective of the changes seen in hospital case-mix and populations since the start of the pandemic, with cancellations of elective procedures, more acutely ill patients admitted, along with a decrease in hospital admissions (the denominator used) between 2019 and 2020.

The decreasing year-on-year trend of 'macrolides, lincosamides and streptogramins' and oral metronidazole prescribing in secondary care, reversed between 2019 and 2020 to an increase of 0.4% and 1.6% respectively. Other notable increases in usage between 2019 and 2020 in



secondary care include the anti-*Clostridioides difficile* agents (23.9%), sulphonamides and trimethoprim (19.6%) and third, fourth and fifth generation cephalosporin (15.1%). Following an international shortage of piperacillin/tazobactam in 2016, overall consumption has been increasing from 2018 to 2020 and a marked increase was evident between 2019 to 2020 (21.7%). At the same time, the proportion of piperacillin/tazobactam resistance in blood stream infections for multiple organisms (*K. pneumonia*, *P. aeruginosa* and *E. coli*) has increased, with increased consumption a possible contributing factor ([Chapter 2](#) provides further evidence as to the changes in the incidence and burden of resistance). Finally, carbapenem consumption has increased (12.3%; driven by an increase in meropenem use, where previous carbapenem trends were on the decline). The incline in piperacillin/tazobactam and carbapenems are likely due to increased use following the inclusion of these antibiotics within NICE HAP guidelines (NG139, Sep 2019) and COVID-19 rapid guideline: antibiotics for pneumonia in adults in hospital (NG173, May 2020) ([162](#), [163](#)).

PHE have worked closely with key stakeholders, particularly during the COVID-19 pandemic. This chapter highlights the relevance and importance of monitoring trends over time, in so doing providing insight to the impact of external forces on antibiotic prescribing, on progress towards national targets and utilising information for action to improve national surveillance systems, inform clinical treatment guidelines and research. Where progress in prudent antibiotic prescribing has been made, particularly during the COVID-19 pandemic, it is important to maintain reductions in consumption and continue promotion of national stewardship awareness programmes, otherwise it is likely that the gains that have been made in preventing antibiotic misuse will be lost.

## Antibiotic consumption surveillance

### COVID-19 and antimicrobial consumption

Changes in antimicrobial prescribing during the COVID-19 pandemic were anticipated, given clinical features of severe respiratory infection syndrome caused by SARS-CoV-2 mirroring bacterial respiratory tract infections, and a proportion of co- and secondary infections were likely; albeit now known to be rare ([164](#)). Concerns were raised that the COVID-19 pandemic would challenge the recent gains in prudent antibacterial use intended to protect patients from harm and combat AMR.

Enhanced surveillance of antimicrobial use and documentation of national antimicrobial stewardship interventions during the pandemic started with protocol development, including the selection of antimicrobials and rationales. The protocol was then refined with feedback from key groups, including the antimicrobial usage (AMU) COVID-19 Stakeholder and ESPAUR Oversight Groups. An update on AMU surveillance data was presented in late 2020 and the Stakeholder Group was invited to discuss use of this surveillance as information for action and next steps, led by PHE's Primary Interventions Unit (PCIU) ([Chapter 8](#)) and PHE's Behavioural Insights Team.

A manuscript on descriptive trends of antibacterial use in both primary and secondary care in England at the beginning of the pandemic has been published (further details can be seen in [Box 5.3](#)) ([165](#)).

### Unintended consequences

To improve the understanding of antibiotic prescribing changes and potential subsequent unintended consequences, PHE undertook an options appraisal for monitoring and analysing the use of antibiotics with potential consequences, such as AMR. Options were presented to the ESPAUR Oversight Group and included analyses at the ecological and individual level.

Ecological analysis was completed using national aggregate-level data to monitor the changes in AMU and impact of the COVID-19 pandemic (see COVID-19 and AMU section and [Box 5.3](#)). AMR trends are also being monitored on a monthly basis, with future work planned to combine AMU and AMR trends for selected drug/bug combinations (see [Chapter 2: Antimicrobial Resistance](#)).

### Unified Infections Data Set

Having previously been awarded a bid for AMR Research Capital Funding by the National Institute for Health Research (AMR Call 2018), PHE have invested this into developing a system which will provide linked data on infections, AMR, antimicrobial prescribing and clinical outcomes. The system, termed the Unified Infection Data Set (UID), is being designed to perform routine and on-demand linkage of data from 4 core data sets currently held by PHE/UKHSA. Data linkage and increased granularity of available data will improve PHE/UKHSA's health protection functions, including surveillance, epidemiological analyses, generation of public health intelligence and scientific research. Please see [Chapter 10](#) for further details.

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

Antimicrobial consumption data has continued to be collated from England and the devolved administrations (Northern Ireland, Scotland and Wales), providing an overarching UK-wide view on the progress made towards the antimicrobial reduction targets set within the UK AMR 5-year National Action Plan ([166](#)).

England, as part of the UK, has continued to submit data to the European Centre for Disease Prevention and Control (ECDC) via the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) in 2020 (2019 data) ([167](#)). Due to the UK's exit from the European Union (EU), data has not been provided to ECDC for 2020. Data will be submitted to WHO GLASS on AMC for 2020, with data submission in Autumn 2021.

PHE research collaborations were undertaken with the production of ESAC-Net led publications in the Journal of Antimicrobial Chemotherapy. Ten articles were published in a supplementary focused on community antibiotic consumption from 30 EU and European Economic Area countries over 2 decades (1997 to 2017). The articles analysed trend over time, seasonal variations, changes in change-points and composition of antibiotic groups ([168](#)).

## Future actions

As mentioned in the section above ([‘COVID-19 and antimicrobial consumption’](#)), enhanced surveillance of antibiotic consumption was established in 2020 to monitor changes during the COVID-19 pandemic, and is ongoing in 2021 to support the incident response in England and inform antimicrobial stewardship activities at a local and national level. This is being conducted alongside surveillance of AMR (see [Chapter 2: Antibiotic Resistance](#)).

To continue developing access to patient-level antimicrobial prescribing data and contribute to ongoing work with the UID project.

To continue work on assessing potential unintended consequences following changes in antibiotic use in England. This will build on previous collaborative work between PHE and the Health Protection Research Unit in Healthcare Associated Infections and Antimicrobial Resistance (HPRU HCAI and AMR) at Imperial College London, which assessed reductions in antibiotic prescribing associated with the introduction of the Quality Premiums and unintended consequences ([169](#), [170](#)) and will provide further insight in this growing research domain.

To continue exploring avenues of research for the impact of COVID-19 and PHE/UKHSA's antimicrobial stewardship campaigns on dentistry and other community services, particularly given the increases seen in primary care consumption.

In line with what has been initiated in [Chapter 2 Antibiotic Resistance](#) future analysis will assess trends in antiviral consumption, and the potential impact of COVID-19.

An ESPAUR subgroup was formed in April 2021 to review the appropriateness of UK metrics and denominators currently in use for surveillance of antimicrobial consumption. The group has commenced discussions on potential alternative metrics for any future UK NAP for AMR, and any national policy and improvement incentive schemes in the devolved nations. The NHS England and NHS Improvement (NHSE&I), AMR Programme Board and the Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection (APRHAI) will be consulted for endorsement of the optimal metrics to meet requirements for surveillance and quality improvement.

## 6. Antimicrobial Stewardship

### Introduction

Tackling antimicrobial resistance (AMR) requires a multifaceted approach to optimize antimicrobial use and reduce the emergence and transmission of resistance. A crucial element of this approach is the implementation of antimicrobial stewardship (AMS) interventions. AMS enables healthcare workers to choose the most appropriate drug, dosage and duration of treatment, whilst limiting the microbe's ability to develop or acquire resistance. Optimising prescribing in this way is a key focus of the UK's 5-year National Action Plan on tackling AMR ([171](#)), which includes a target to reduce UK antimicrobial use in humans by 15% by 2024.

This chapter summarises the principal antimicrobial stewardship (AMS) activities implemented during 2020 to 2021:

1. Primary care, including:

- TARGET (Treat Antibiotics Responsibly, Guidance Education and Tools)
- newly developed TARGET UTI audits
- PHE/NICE quick reference tools update
- implementation of the antibiotic checklist in community pharmacies
- supporting the implementation of NICE/PHE antibiotic guidelines during COVID-19

2. Assessing the impact of COVID-19 on secondary care AMS

### Primary care

#### TARGET resource updates around COVID-19

The TARGET antibiotics toolkit ([172](#)) is a suite of AMS resources to support prescribers and is designed to be used by the whole primary care team within a GP practice or out of hours setting. The toolkit, designed and developed by PHE, is hosted on the Royal College of General Practitioners (RCGP) website and remains the most accessed toolkit of their website.

#### TARGET use 2020 to 2021

Overall TARGET website views dropped considerably in the summer months immediately following the first wave of the COVID-19 pandemic. Website visits started to return to normal in October 2020, potentially driven by the World Antimicrobial Awareness Week (WAAW) campaign and the launch of 2 new webinars focusing on remote consultations (see the [Professional Education and Training chapter](#)). There were 98,315 web views over the year (Figure 6.1).

**Figure 6.1 TARGET Toolkit: monthly total views between April 2020 and March 2021**

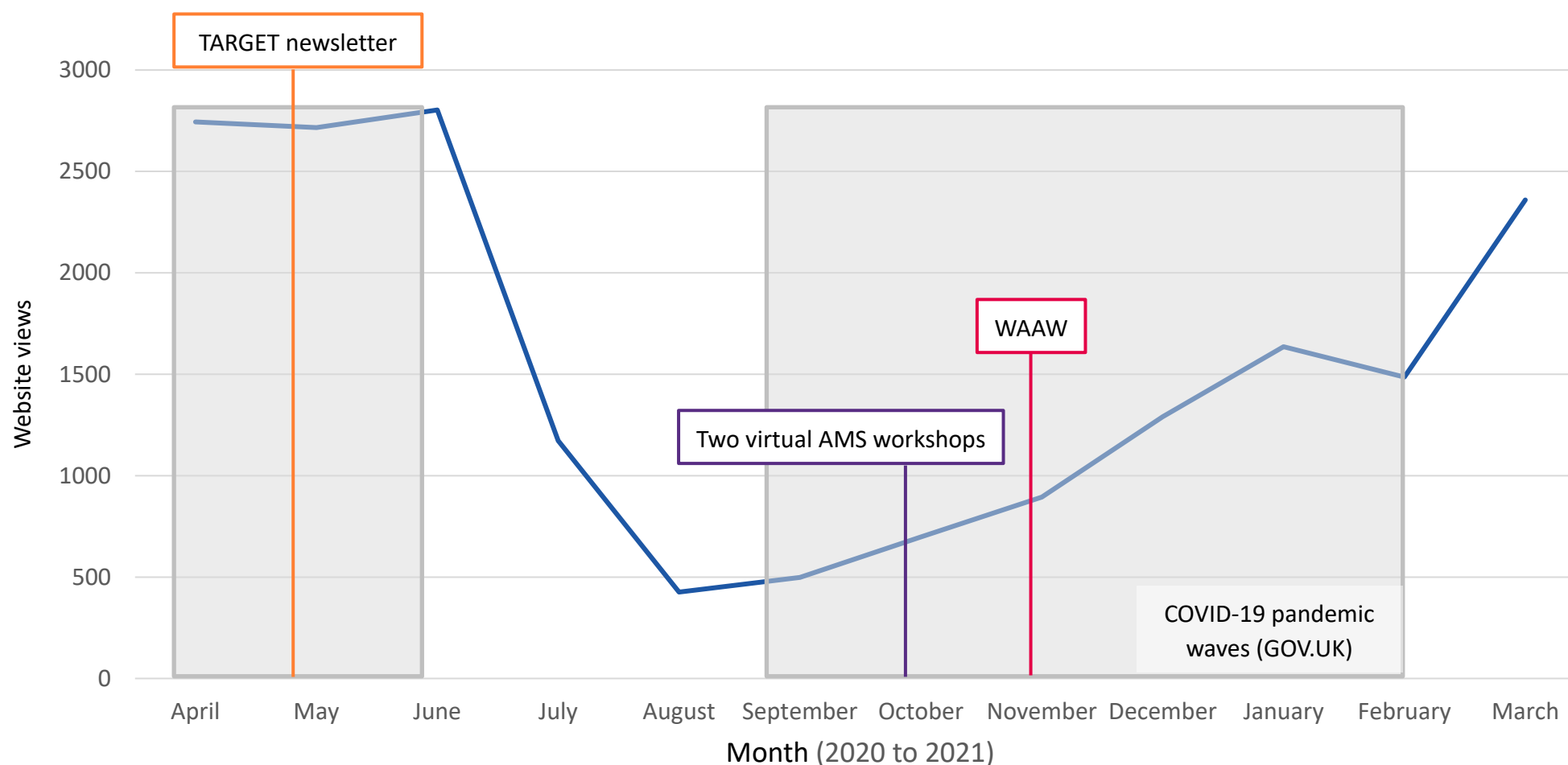


Figure 6.1 shows monthly views of the TARGET website ([173](#)) from April 2020 to March 2021; data points represent total numbers of visits to the website per month. Promotional activities and release of new resources are indicated by coloured lines, grey shaded area indicates COVID-19 pandemic waves during this period.

**Figure 6.2 TARGET toolkit: clicks per page, for sections of the website between April 2020 and March 2021**

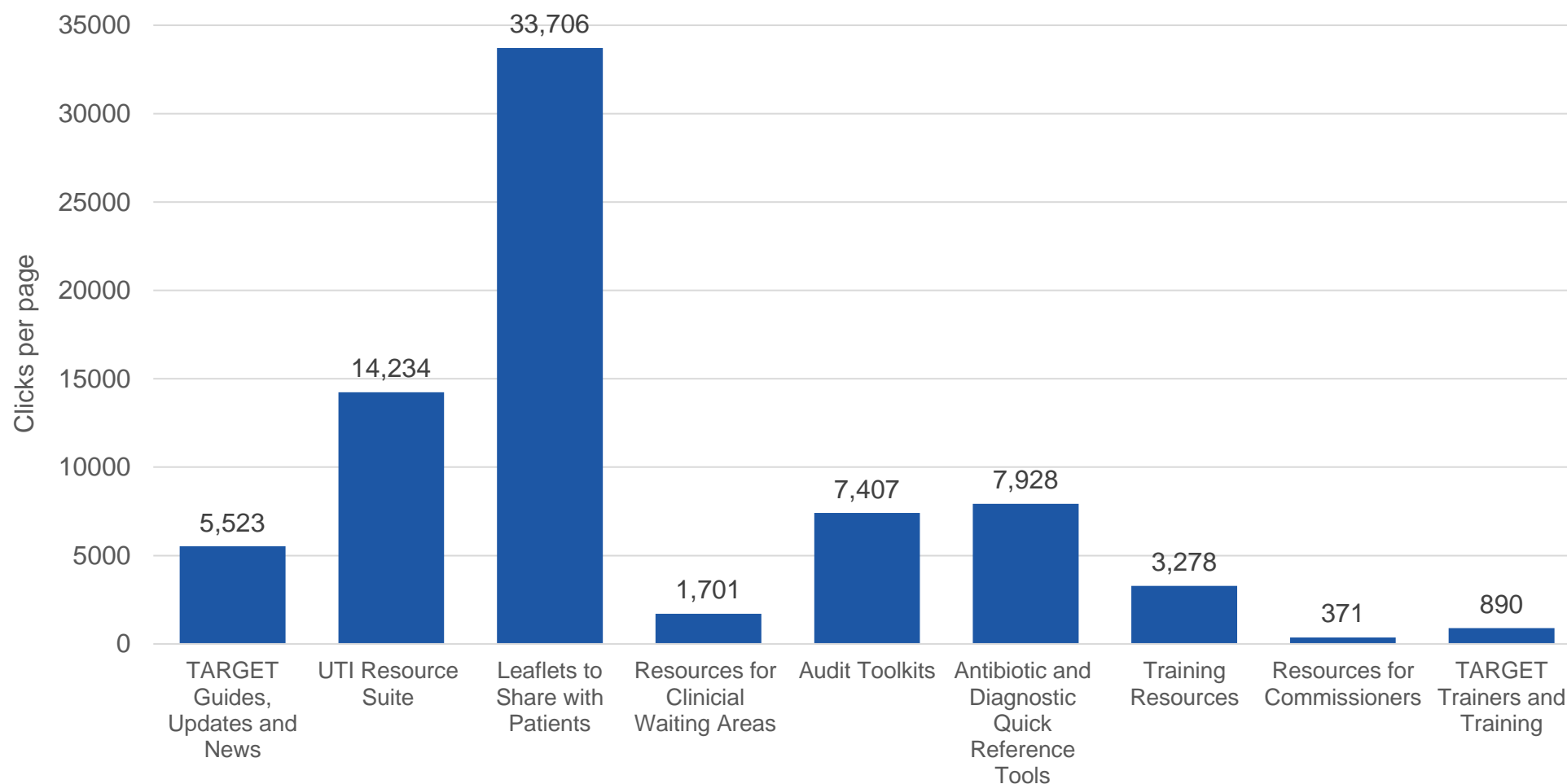


Figure 6.2 [shows total clicks per page for the 9 sections of the TARGET Toolkit website](#). The 'Urinary Tract Infection (UTI) Resource Suite' and 'Leaflets to Share with Patients' were the most visited website sections).

**Figure 6.3 TARGET Toolkit: top resource downloads between April 2020 and March 2021**

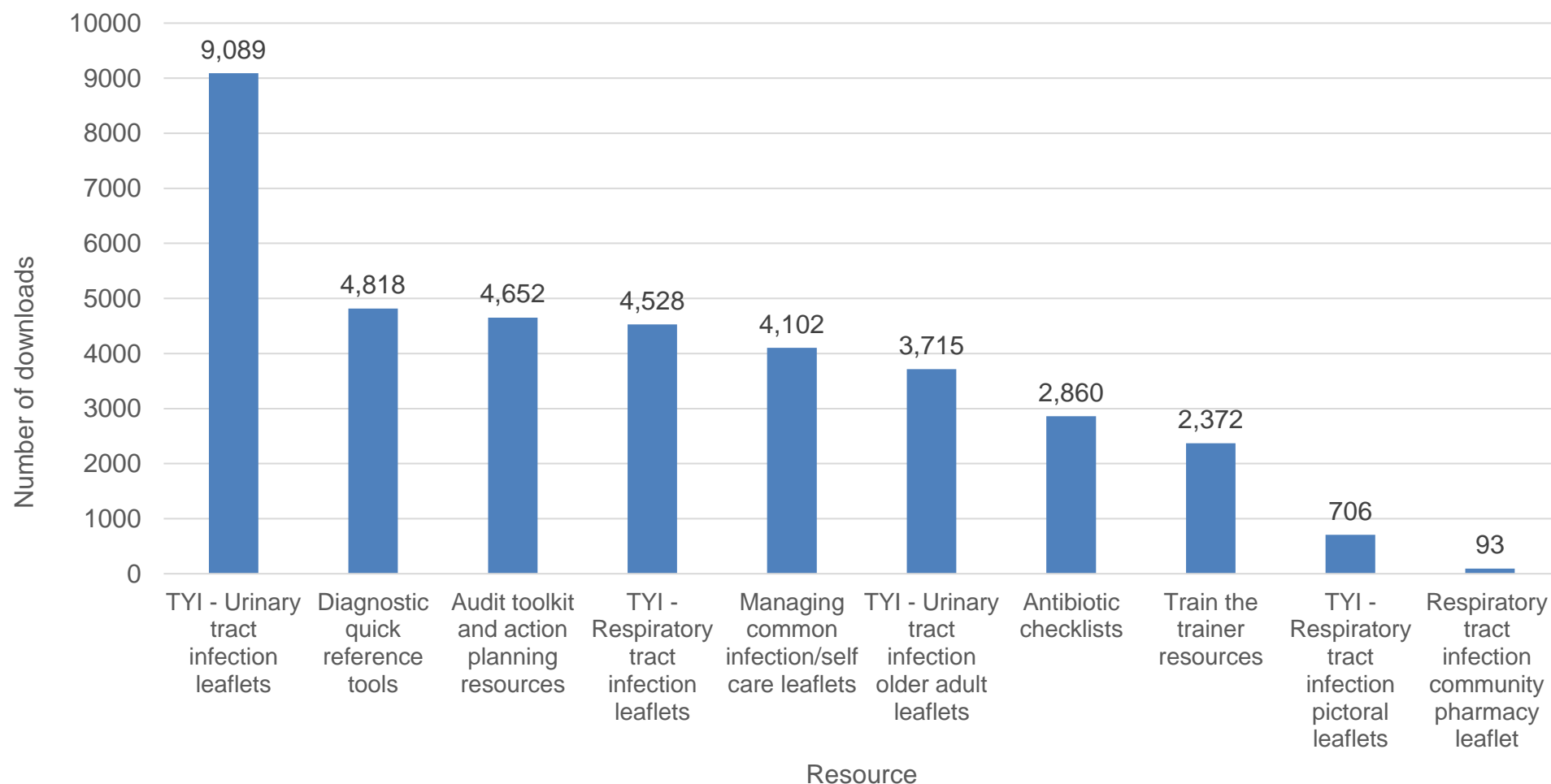


Figure 6.3 shows the number of downloads for resources on the TARGET toolkit website, between April 2020 and March 2021. The Treating Your Infection-UTI (TYI-UTI) leaflet for under 65 year olds was the most downloaded item throughout the year. The patient information leaflets were originally designed to be used during face-to-face consultations, and are still being used despite the move to remote consultations during the COVID-19 pandemic.

All patient-facing resources were updated to include considerations for COVID-19 guidance in November 2020, paying particular attention to patient Safety Netting sections. COVID-19 played a factor in some of the changes in how TARGET resources were used this year, for example, less people requesting or accessing AMS training pages during the first wave of the pandemic.

## Updates to the TARGET toolkit

Based on user feedback the TARGET antibiotics toolkit has had the following updates.

### TARGET Managing Your Common Infection (self-care) leaflet


The new TARGET Managing Your Common Infection (self-care) leaflet ([174](#)) aims to empower patients and carers to be able to self-care when suffering from a common infection such as colds, flu and winter vomiting bugs. Development of the leaflet was rigorous and user-based, involving qualitative patient and healthcare professional discussions informed by behavioural theory and online questionnaires ([175](#)). This qualitative work identified leaflet usefulness, information priorities for a common infection leaflet, leaflet design and suggestions for its implementation. The leaflet, shown in figure 6.4, is designed to be printed or provided online, and used by healthcare professionals to support discussions with patients around self-care and safety netting for common infections. Information, in line with NICE guidance (NG63) ([176](#)), includes:

- what are the symptoms of a common infection?
- what if I think I have coronavirus (Covid-19)?
- how can I treat a common infection?
- how long could my infection last?
- will my infection need antibiotics to get better?
- how can I stop my infection from spreading?
- what symptoms of serious illness should I look out for?
- what if I suspect signs of sepsis?

The leaflet was launched and promoted during WAAW 2020 and has been downloaded 4,102 times between November 2020 and 31 March 2021.



Figure 6.4 TARGET Managing Your Common Infection (self-care) leaflet



## How can I manage my common infection?

A leaflet for adults aged 16 years and over

### 1. What are the symptoms of a common infection?

**A Eyes**

- Sticky eyes

**B Ears, nose and throat**

- Pain or soreness
- Runny nose
- Swollen tonsils

**C Chest**

- Cough
- Shortness of breath
- Green or yellow mucus

**D Gut**

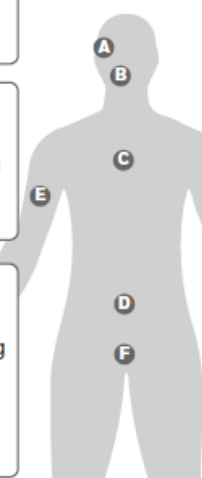
- Vomiting
- Diarrhoea

**E Skin**

- Infected blisters
- Redness or swelling around a wound
- Athlete's foot (an itchy rash between the toes)

**F Genital and urinary**

- Pain on passing urine
- Passing urine more often at night
- Cloudy urine
- Discharge
- Pain in lower tummy




### 2. What if I think I have coronavirus (Covid-19)?

If you think you may have COVID-19 then please visit <http://www.gov.uk/coronavirus> or <http://www.nhs.uk> for the latest guidance and information.


TARGET is operated by the UK Health Security Agency.  
Developed in collaboration with professional medical bodies.

Version 1.1: Nov 2020  
Revision: Nov 2023


### 3. How can I treat a common infection?




**Get plenty of rest** until you feel better.




**Take pain relief** if you need to (make sure you follow the instructions).




**Drink plenty of fluids** (6 to 8 drinks, or 2 litres) so that you pass pale-coloured urine regularly.






For **coughs**, try honey and cough medicines.  
For **sore throats**, try medicated lozenges and pain relief.








Soothe **eye infections** with a clean warm or cold damp flannel.



For an **outer ear infection**, apply local heat (such as a warm flannel).









### 4. How long could my infection last?

Cough	Sore throat or earache	Common cold	Norovirus (winter vomiting)	Sinus infection
				
21 days	7 to 8 days	14 days	2 to 3 days	14 to 21 days





**Contact your GP** if your symptoms are getting worse or if you are not better by the times above.

Visit [www.nhs.uk](http://www.nhs.uk) for **self-care advice** on common infections

### 7. What symptoms of serious illness should I look out for?

 <b>Severe</b> headache and vomiting	 Ongoing <b>fever or chills</b> (temperature above 38°C or less than 36°C)
 Problems <b>swallowing</b> <b>Turning blue</b> around the mouth	 Coughing <b>blood</b>
 <b>Breathing</b> faster or slower than usual	 <b>Kidney pain</b> in your back just under your ribs
 <b>Chest pain</b> or tightness New <b>very fast or slow pulse</b>	 Visible <b>blood</b> in urine <b>Severe pain</b> on passing urine, or passing more urine at night <b>Cloudy urine</b> not improving in 1 to 2 days with fluids


**If you have the symptoms above, contact your GP urgently or use the following services for your region.**

<b>NHS England</b>  When it's less urgent than 999 <a href="http://www.111.nhs.uk">www.111.nhs.uk</a>	<b>NHS Direct Wales</b>  <a href="http://www.111.wales.nhs.uk">www.111.wales.nhs.uk</a>	<b>NHS Scotland</b>  <a href="http://www.nhs24.scot">www.nhs24.scot</a>	<b>Northern Ireland</b>  Contact your GP practice
---	--	--	---

These services can provide a confidential interpreter if you need one.




### 5. Will my infection need antibiotics to get better?

- Your **body can normally fight off** common infections on its own.
- You do not usually need antibiotics, unless symptoms of a **bacterial** infection (such as a urine infection) are severe – a healthcare professional can advise you on this.
- Taking antibiotics when you do not need to puts you and your family at risk.
- Follow your **healthcare professional's advice on antibiotics**.





 Find out more about antibiotics at [www.antibioticguardian.com](http://www.antibioticguardian.com)


### 6. How can I stop my infection from spreading?


**If you need to cough or sneeze:**


<b>Catch it</b>  with a tissue (or your inner elbow)	<b>Bin it</b>  throw away used tissues	<b>Kill it</b>  by cleaning your hands
--	--	--

**Clean hands** for at least 20 seconds with soap and water or hand sanitiser:

-  before preparing and eating food
-  after touching pets or animals
-  after using the toilet
-  when leaving and arriving home

 **Avoid touching** your eyes, nose or mouth with unclean hands.  
If possible, **keep your distance from others** (2 meters or 6 feet), especially vulnerable people in your household.

 **Do not share items** that come into contact with your mouth, such as eating utensils and toothbrushes.

 **Keep yourself and your family up to date with vaccinations.**  
**Always get winter vaccines** (such as flu) if you are eligible.

**Visit or call a pharmacy for further advice on common infections**

### 8. What if I suspect signs of sepsis?

Sepsis is a life-threatening reaction to an infection. Possible signs are:

- S**lurred speech, confusion or drowsiness
- E**xtrême shivering
- P**assing no urine in a day
- S**evere breathlessness
- I**t feels like you're going to die, and
- S**kin blotchy or discoloured.

**Call 999 immediately if you or others have signs of sepsis**

## Newly developed TARGET UTI audits

Three UTI primary care audits have been developed with input from GPs:

- uncomplicated UTI
- catheter-associated UTI
- UTI in over 65 year olds

Each audit assesses prescriber compliance against PHE diagnostic guidelines ([177](#)) and NICE/PHE antibiotic treatment guidelines ([178](#)). They are available in both MS Word and MS Excel formats to download from the TARGET Toolkit, carry out in practice and support users to develop action plans based on the audit results. The audits were developed with stakeholders, piloted amongst 5 TARGET trainers and modified based on feedback prior to publication. Those who piloted the audits found them either 'very useful' or 'useful'. The latest version of the UTI audits were published in July 2021 and subsequently promoted to users via TARGET and Royal College of General Practitioners (RCGP) social media channels as part of their joint UTI campaign. TARGET Toolkit users are encouraged to provide feedback on the audits, and future resource download analytics will help to gain an understanding of audit use.

## NICE/PHE quick reference tools update

### NICE/PHE management of common infections guidelines and associated quick reference tools ([179](#))

NICE, supported by PHE, continued to develop antimicrobial prescribing guidelines (APGs) for managing common infections although some of this work was delayed because of a need to focus on COVID-19. The guidelines offer evidence-based guidance for primary and secondary care and provide recommendations for appropriate antimicrobial use in the context of tackling AMR. In 2020 to 2021 there were 3 APGs published covering:

- secondary bacterial infection of eczema and other common skin infections
- human and animal bites
- insect bites and stings

PHE and NICE also produce a joint summary of antimicrobial prescribing guidance which is updated when new APGs are published or based on user feedback.

The UTI diagnostic flowcharts quick reference tools ([181](#)) published in 2018 continue to be widely used in primary care. Between April 2020 and March 2021, the tools had 10,541 unique page views and were downloaded over 9,000 times. The flowcharts were updated in October 2020 to align further with NICE and other national guidance for UTI management.

## Implementation of the antibiotic checklist in community pharmacies

The TARGET Antibiotics Toolkit includes a pharmacy Antimicrobial Stewardship Intervention (PAMSI), developed to support community pharmacy staff in their role ensuring the safety of patients and educating the public about appropriate antibiotic use and managing common infections. During the COVID-19 pandemic patients have accessed their community pharmacy more for information and advice on infections.

As a follow-on to the 2020 to 2021 AMS criterion of the Pharmacy Quality Scheme (Annexe 1), NHS England and Improvement published a roll out to include online training on AMS and the Antibiotic Checklist developed by PHE and Health Education England (among others) across all community pharmacies in England.

To embed learning from 2020 to 2021, the HCAI and AMR division (Primary Care and Interventions Unit [PCIU] and Lead Pharmacist):

1. Held a webinar for community pharmacy staff, delivered by pharmacists on how to use the Antibiotic Checklist. This webinar was recorded and is available on the AG website. Details of the webinar are provided in [Chapter 6 'Professional Education, Training and Public Engagement \(PPET\)'](#).
2. Set up a secure data collection tool for community pharmacy staff to pilot input of data.
3. Printed and delivered 2 laminated copies of the Antibiotic Checklist to all community pharmacies (11,370) in England, along with a cover letter ([annexe 2](#)) informing them of their purpose. These hard copies could be used as an aide in community pharmacies to support implementation of the AMS criterion of the 2020 to 2021 Pharmacy Quality Scheme. A sticker (Figure 6.6) was also developed to accompany the envelopes. These were dispatched to community pharmacies on 28, 29 and 30 March 2021. The posters detail the steps in the antibiotic checklist to be displayed in community pharmacies and assist in delivery of the intervention.

The Pharmaceutical Services Negotiating Committee (PSNC) also supported the promotion of both the webinar and the poster. The support from PSNC increased the attendance at the webinars as there were over 500 professionals who signed up and more than 200 who attended the webinars. This also demonstrates that PSNC are supportive of AMS and recognise the value of AMS interventions in pharmacies. The Antibiotic Checklist has now been embedded as part of the 2021 to 2022 Pharmacy Quality Scheme.

The following screenshots ([Figure 6.5](#)) show the Antibiotic Checklist, which was delivered to community pharmacies in England. The first page includes a checklist for the pharmacy team to complete with questions around the appropriateness of the antibiotic prescribed. The second page is to be completed by the patient attending the pharmacy with an antibiotic prescription. A

sticker was developed to accompany the resources sent to community pharmacies on 28, 29 and 30 March 2021 (Figure 6.6).

**Figure 6.5 Hard copy of the Antibiotic Checklist to be used as an aide in community pharmacies**

for Pharmacy team

## Checklist points

Date this checklist was completed:

Assessing the antibiotic prescription. Please tick as appropriate.

I have checked	n/a	yes	no
... for allergies, risk factors, other medication interactions.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
... treatment with the same antibiotic in the previous 3 months.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
This information is collected from page 1.			
... the antibiotic against the local guidance.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
... the antibiotic is appropriate for the infection indicated.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
... the dose is correct for the indication and patient.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
... the duration is correct for the indication.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

I have contacted the prescriber about this antibiotic prescription. Please write the reason and outcome below.
 

	n/a	yes	no
<input type="radio"/>	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

The following antibiotics have been dispensed

<input type="radio"/> None	<input type="radio"/> Amoxicillin	<input type="radio"/> Flucloxacillin	<input type="radio"/> Nitrofurantoin
<input type="radio"/> Doxycycline	<input type="radio"/> Clarithromycin	<input type="radio"/> Phenoxymethylpenicillin (Penicillin V)	
<input type="radio"/> Metronidazole	<input type="radio"/> Trimethoprim	<input type="radio"/> Co-Amoxiclav	
<input type="radio"/> other Please specify the antibiotic in the space below.			

Giving advice on antibiotics. Please tick as appropriate.

	n/a	yes	no
I have discussed antibiotic resistance with the patient/carer as the patient has had the same antibiotic in the last three months.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>
I have checked the Patient responses to the statements overleaf and given advice as required.	<input type="radio"/>	<input type="radio"/>	<input type="radio"/>

Tick the circles ☒ next to the statements opposite when the advice has been given.

Staff complete on preparation and hand out of prescriptions. Retain for audit.

**TARGET**  
Keep Antibiotics Working

**ANTIBIOTIC GUARDIAN**  
Keep Antibiotics Working

Antibiotic Checklist (Laminated) Version 2 March 2021.

I have given the following patient information leaflet:  
☐ UTI    ☐ UTI for older adults    ☐ dental  
☐ RTI    ☐ RTI pictorial    ☐ other  
☐ managing common infections (self-care)

Visit the TARGET Antibiotics website to download.  
 Scan the QR code or visit:  
[www.RCGP.org.uk/TARGET-patient-leaflets](http://www.RCGP.org.uk/TARGET-patient-leaflets)

Administering the flu vaccine. Please tick as appropriate.  
☐ I have discussed flu vaccine eligibility with the patient  
☐ I have given the flu vaccine on site

The Antibiotic Checklist has not been fully completed because:  
☐ the patient's representative did not know the information  
☐ the antibiotics are supplied by delivery service. Consider including a patient information leaflet with the prescription.  
☐ the antibiotics are already dispensed  
☐ the patient declined  
☐ other reason. Please write the reason in the space below.

for Patients

## Antibiotic Checklist

Help us to Keep Antibiotics Working. Please tick

Are the antibiotics for you? yes ☐ no ☐

If they are not for you, please fill in the rest of this form for the person named on the prescription

Are you taking any other medicines? yes ☐ no ☐ don't know ☐


Have you taken the same antibiotics in the last 3 months? yes ☐ no ☐ don't know ☐


Are you allergic to any antibiotics? yes ☐ no ☐ don't know ☐


If yes, please provide the following information about your allergy:


Antibiotic name  Type of allergy


Do you have one of these common infections? Tick ☒ if yes.


chest ☐  


throat ☐  


ear ☐  



urine ☐  



tooth ☐  



skin ☐  



Or something else?   
Please indicate here.


Does this describe you? Tick ☒ if yes.

problem with kidney function ☐  


problem with liver function ☐  


breast feeding ☐  


pregnant ☐  


over 65 ☐  











Have you had a flu vaccine this year? yes ☐ no ☐ don't know ☐

Your pharmacist can tell you about the things that you can do to help you get better, and give you a leaflet with more information.

Please let your pharmacist know if you need this information in a different language.

Patients complete on hand in of prescription. Staff retain for audit.

Help us to help you by ticking yes ☒ or no ☒ by the following statements:

 I know what to do if I miss a dose of my antibiotics. yes <input type="radio"/> no <input type="radio"/>	 I know whether my antibiotics should be taken with or without food. yes <input type="radio"/> no <input type="radio"/>	 I know why I must take my antibiotics as advised by my doctor, nurse or pharmacist. yes <input type="radio"/> no <input type="radio"/>
 I know about the side effects that I might get from my antibiotics. yes <input type="radio"/> no <input type="radio"/>	 I know whether I need to avoid alcohol whilst I am taking my antibiotics. yes <input type="radio"/> no <input type="radio"/>	 I know why I must never share my antibiotics or keep for later use. yes <input type="radio"/> no <input type="radio"/>
 I know how long my symptoms are likely to last. yes <input type="radio"/> no <input type="radio"/>	 I know when I should seek further help with my infection. yes <input type="radio"/> no <input type="radio"/>	 I know why I must return any unused antibiotics to the pharmacy. yes <input type="radio"/> no <input type="radio"/>

I am happy for someone on behalf of Public Health or TARGET Antibiotics to contact me about my visit today.

I would like to be contacted ☐ by mobile ☐ by email. Tick where appropriate.

Please write your email or mobile number below, using one letter or number per box.

**Figure 6.6 Envelope sticker sent with the Antibiotic Checklist to community pharmacies in England**





## Assessing the impact of COVID-19 on secondary care AMS

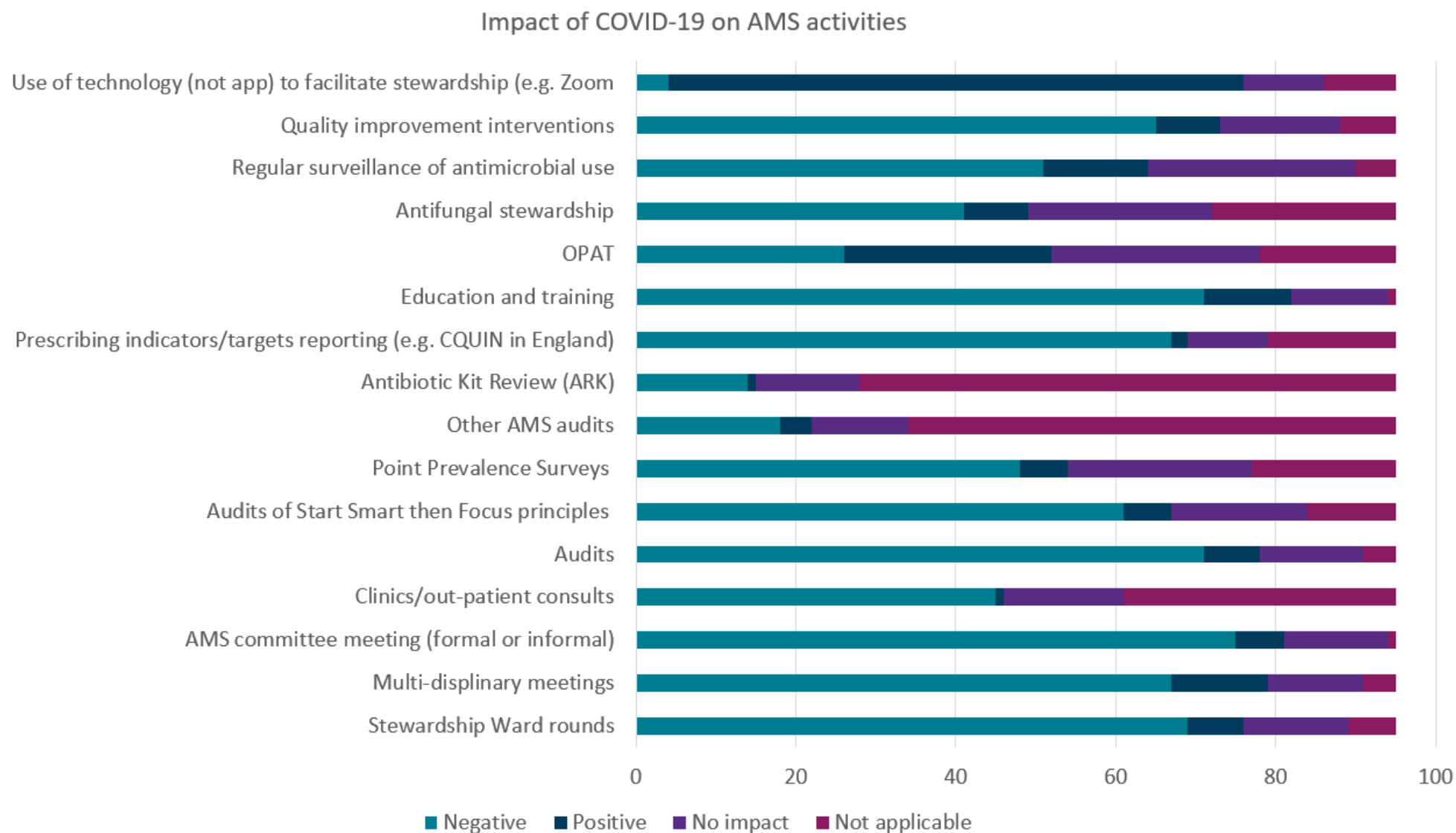
Since first identified in late 2019, SARS-CoV-2 and the resulting COVID-19 pandemic have overwhelmed healthcare systems worldwide, often diverting key resources in a bid to meet unprecedented challenges. A study by Ashiru-Oredope and others ([185](#)) investigated the impact of COVID-19 on national AMS activities, using a quantitative survey-based approach. A 20-item questionnaire was disseminated to 169 AMS leads in the UK and 95 responded. [Full methodology \(including the survey questions\) and results](#) are available online.

The findings of this survey provides, for the first time, quantitative and qualitative data on the impact of the COVID-19 pandemic on AMS activities undertaken across the UK. The survey found that the COVID-19 pandemic has had a significant impact on the AMS activities undertaken across the UK. Most respondents reported a reduction in AMS activity with 64% (61 out of 95) reporting that COVID-19 had a negative impact on routine AMS activities (Table 6.2). A quarter of respondents thought that overall there were both positive and negative effects on AMS due to the COVID-19 pandemic. Negatively impacted activities included audit, quality improvement initiatives, education, AMS meetings, and multidisciplinary working including ward rounds ([Figure 6.7](#)). However, positive outcomes were also identified, with technology being increasingly used as a tool to facilitate stewardship for example, virtual meetings and ward rounds and increased acceptance of using procalcitonin tests to distinguish between viral and bacterial infections. The long-term impact of reduced AMS activities on incidence of AMR are not yet known.

**Table 6.2 UK AMS leads responses to ‘In your opinion, how much impact would you say COVID-19 has had on your routine AMS activities?’**

Impact on AMS	n	%
No impact	1	1.1
Very negative impact	29	30.5
Some negative impact	32	33.7
Neither negative or positive	1	1.1
Positive impact	7	7.4
Very positive impact	0	0.0
A mix of positive and negative impact	24	25.3
Unsure or unable to assess	1	1.1
Total	95	100.0

**Figure 6.7 Impact of coronavirus 2019 (COVID-19) on antimicrobial stewardship (AMS) activities (n = 95 survey respondents)**





While the impact of the COVID-19 pandemic on AMS activity has been quantified, the psychological impact of additional roles, secondment to other specialties, and additional responsibilities that antimicrobial pharmacists have undertaken has yet to be evaluated and may form the basis of further studies. It is important that those who lead on AMS continue to have protected time to focus on AMS during current or future pandemics.

The legacy of innovation, use of technology, and increased collaboration or links with non-infection specialists, which the pandemic made necessary, could in fact strengthen AMS in the post-pandemic era and presents further opportunities for development of AMS roles. In addition, the networking and support network that has been developed will continue to support pharmacists in this role in future.

## Future actions

Research has shown that patient demand for antibiotics has increased however patient acceptance of delayed or backup antibiotics prescriptions for RTIs and UTIs has also increased. As such the TARGET toolkit will be updated to provide more information on having difficult discussions with the patient and incorporate how and when to offer delayed or backup antibiotics prescriptions.

With the increase in remote consultation there is a need to ensure patient facing resources are accessible and can be used on multiple forms of digital technology. TARGET will publish all patient facing leaflets in html format and work with providers to integrate these and diagnostic tools into digital technology being used by health care providers for remote consultations.

To support AMS in the care home setting TARGET aim to develop a simplified diagnostic flowchart for UTI.

Further research into how users would prefer to access training and learning resources on the TARGET website, and how we promote resources like audits will be carried out in the coming months.

To help refresh and implement appropriate prescribing in primary care TARGET and the RCGP rolled out 2 campaigns this year:

- July to August 2021: UTI campaign
- November 2021: AMS campaign to coincide with WAAW

Findings will be reported in the 2021 to 2022 ESPAUR report.

TARGET are developing and aim to launch a suite of tools to help support and embed the NICE/PHE skin infection guidance in the spring of 2022.

Finally, and importantly, future actions will include the consideration of secondary care AMS interventions in the context of COVID-19.

## 7. NHS England and NHS Improvement: improvement and assurance schemes

### Reducing antibiotic consumption by NHS Trust providers of acute care

During the financial years 2017 to 2018 and 2018 to 2019, NHS hospital Trusts providing acute care services participated in the NHS Commissioning for Quality and Innovation (CQUIN) scheme to reduce their antibiotic consumption, and this requirement moved into the NHS Standard Contract 2019 to 2020. Within this contract, all NHS Trusts providing acute care were required to reduce their antibiotic consumption by 1% from their own 2018 calendar year baseline value. Performance was measured as the total number of antibiotics as Defined Daily Dose (DDD) per 1,000 hospital admissions and reported in the ESPAUR Report 2019 to 2020. However, since that publication, we refreshed the data due to updates made to admissions data, DDDs on RxInfo and acute Trust mergers, and the 2019 to 2020 NHS Standard Contract performance has been re-published in the [Chapter 7 data tables](#) that accompany this report. As a result total consumption of antibiotics for 2019 to 2020 reduced from 4,669 DDD per 1,000 admissions as reported in the 2019 to 2020 ESPAUR Report ([187](#)) to 4,612 DDD per 1,000 admissions. However, the number of Trusts meeting the requirement to reduce total consumption by 1% did not change.

The NHS Standard Contract 2020 to 2021 ([188](#)) continued this focus to reduce antibiotic consumption with a requirement for all NHS Trusts providing acute care to reduce antibiotic consumption by 2% from the same 2018 calendar year baseline value. However, this contract, which included the requirement to reduce antibiotic consumption, was suspended in March 2020 ([189](#)) in response to the COVID-19 pandemic. Consequently, the NHS Standard Contract 2021 to 2022 ([190](#)) now includes the requirement to reduce antibiotic consumption by 2% from the 2018 calendar year baseline by 31 March 2022. The effect of the COVID-19 pandemic on antibiotic consumption in NHS acute Trust has been reported in [Chapter 5](#).

### NHS Commissioning for Quality and Innovation (CQUIN) scheme 2020 to 2021

The NHS standard contract 2020 to 2021 ([191](#)) included an AMR CQUIN scheme 'CCG1: Appropriate antibiotic prescribing for urinary tract infections (UTI) in adults aged 16 years and over' ([192](#)). Improving the diagnosis, antibiotic prescribing and management of UTI, including review of urinary catheter use, will reduce treatment failure, risk of healthcare associated bacteraemia, and reduce associated length of stay. This CQUIN scheme also supports continued improvement delivered in the NHS England 2019 to 2020 CQUIN scheme 'CCG1a: Improving the management of lower urinary tract infections in older people'. However, the 2020 to 2021 CQUIN scheme was suspended in March 2020 in response to the COVID-19 pandemic, and the NHS standard contract 2021 to 2022 does not include any CQUIN schemes.

## Improving the management of lower urinary tract infection in older people in primary care

NHS England and NHS Improvement released the RightCare UTI data packs to enable local health systems to identify opportunities for further improvement in the safe and effective management of UTI in primary care, in particular in older people, and builds on the improvement delivered by the NHS 2019 to 2020 CQUIN scheme 'Improving the management of lower urinary tract infections in older people' ([193](#)). The packs are available from the Urology site in the Outpatient Transformation Platform Empowering Patients ([194](#)) site on the FutureNHS ([195](#)) collaborative platform. In addition the antibiotic prescribing metrics used in the data packs are reported by the NHS Business Services Authority in a new ePACT2 ([196](#)) Antimicrobial Stewardship RightCare UTI dashboard, and the 9 antibiotic prescribing metrics are published by NHS BSA ([197](#)).

These metrics report at a variety of NHS organisational levels, and are updated monthly, supporting local health care system improvement of appropriate antibiotic prescribing for lower UTI in adults aged 70 years and over.

NICE guidance Urinary tract infection (lower): antimicrobial prescribing ([198](#)) advises that a lower risk of resistance may be more likely if trimethoprim has not been used in the past 3 months. The ePACT2 Antimicrobial Stewardship RightCare UTI dashboard reports 153,097 people had been prescribed trimethoprim more than once in any 3 consecutive months in the last 12 months to March 2021. The dashboard facilitates NHS primary care clinician review of this patient group.

In 2021 to 2022 the RightCare UTI data will be also be published in the NHS Model Health System supporting system level assurance activity.

## Reducing antibiotic prescribing in primary care

The NHS Oversight Framework ([200](#)) is intended as a focal point for joint work, support and dialogue between NHS England and NHS Improvement, clinical commissioners, providers and sustainability and transformation partnerships and integrated care systems. The NHS Oversight Framework contains the 2 antimicrobial resistance (AMR) related indicators with set targets that have been used in NHS improvement and assurance schemes for CCGs since 2015. The indicators are:

- 107a: reduction in the number of antibiotics prescribed in primary care to be equal to or below value of 0.965 antibacterial items per Specific Therapeutic Group Age-sex Weightings-Related Prescribing Units (STAR-PU) (12 months)
- 107b: number of co-amoxiclav, cephalosporins and quinolones as a percentage of the total number of selected antibacterials prescribed in primary care to be 10% or below

## NHS Oversight Framework data sources

NHS England and NHS Improvement, in collaboration with the NHS Business Services Authority, report CCG performance for these 2 AMR indicators in order to monitor antibiotic prescribing in primary care and report CCG progress towards the national targets within the NHS Oversight Framework. The NHS Business Services Authority report CCG performance monthly in the [NHS England and NHS Improvement Antimicrobial Resistance NHS Oversight Framework 2020 to 2021 dashboard](#).

## Antimicrobial prescribing in primary care and NHS clinical commissioning group performance

NHS CCGs have participated in NHS England improvement and assurance schemes since 2015 and have delivered sustained reductions in primary care antibiotic prescribing during this time frame. In financial year (FY) 2020 to 2021 133 out of 135 (99%) CCGs met or exceeded the national target to reduce antibacterial items per STAR-PU to the national target of 'at or below 0.965'. This is an improvement on FY 2019 to 2020 when 96 out of 191 (50%) CCGs met or exceeded this target. However this is a far larger reduction than expected, due to reduced primary care antibiotic use during the COVID-19 pandemic, and delivered an England value of 0.744 antibacterial items per STAR-PU. This is a lower value than that reported in the previous FY 2019 to 2020, and is a 36% reduction compared to the 2013 to 2014 baseline.

At the same time, 59 out of 135 (44%) CCGs met or exceeded the national targets to reduce the proportion of co-amoxiclav, cephalosporins and quinolones to less than or equal to 10%; a reduction on the financial year 2019 to 2020 where 171 out of 191 (90%) CCGs met or exceeded this target. However, this prescribing metric has been impacted by the large reduction in the denominator value, resulting in an increase in England value to 10.2%, despite a small reduction in the number of prescription items for broad spectrum antibiotics in primary care from 2,552,634 in financial year 2019 to 2020 to 2,510,802 prescription items in financial year 2020 to 2021. The NHS Business Services Authority report CCG performance monthly in the [NHS England and NHS Improvement Antimicrobial Resistance NHS Oversight Framework 2020 to 2021 dashboard](#).

## NHS System Oversight Framework 2021 to 2022

The 2 AMR indicators remain in use to monitor primary care antibiotic prescribing in the new NHS System Oversight Framework ([201](#)) in 2021 to 2022, but now with the introduction of a new lower target: Antibacterial Items per STAR-PU 'at or below 0.871'. The NHS Business Services Authority continue to report CCG and STP performance monthly in the [NHS England and NHS Improvement Antimicrobial Resistance NHS System Oversight Framework 2021 to 2022 dashboard](#).

## NHS Pharmacy Quality Scheme 2020 to 2021

The Pharmacy Quality Scheme (PQS) ([202](#)) forms part of the Community Pharmacy

Contractual Framework (CPCF). It supports delivery of the NHS Long Term Plan and rewards community pharmacy contractors that deliver quality criteria in 3 quality dimensions: clinical effectiveness, patient safety and patient experience. Details of the PQS for 2020 to 2021 have been provided in Part VIIA ([203](#)) of the Drug Tariff and include an Infection Prevention and Control and Antimicrobial Stewardship Domain. This aims to reduce the potential harm caused by antimicrobial resistance (AMR) through the promotion of Antimicrobial Stewardship (AMS) activity in community pharmacy, and specifies quality criteria aligned to this aim.

### Quality criteria

On the day of the declaration, all patient-facing pharmacy staff that provide advice on medicines or health care must have satisfactorily completed the PHE Antimicrobial Stewardship for Community Pharmacy e-learning and e-assessment ([204](#)) on the Health Education England e-Learning for Healthcare website.

In addition, contractors must have available, at premises level, an antimicrobial stewardship action plan for the pharmacy, which details how they will promote AMS. The action plan must demonstrably include details of how all pharmacy staff involved in the provision of self-care advice will incorporate the principles of AMS into self-care advice, including reinforcing the messages around appropriate use of antibiotics, and the uptake of vaccinations, including the influenza vaccination. All patient-facing staff that provide health advice, should also become antibiotic guardians, if they have not already done so, and have an awareness of the local antibiotic formulary.

Details of the Pharmacy Quality Scheme 2021 to 2022 ([205](#)) have been published. The scheme includes a requirement to enhance antimicrobial stewardship using the PHE TARGET Antibiotic Checklist ([206](#)).

## 8. Professional education, training and public engagement

In its first year, the COVID-19 pandemic has had an immense impact on the healthcare profession. Healthcare professionals were required to divert attention to the pandemic response and adapt to the necessary restrictions it imposed. Unsurprisingly, this has resulted in disruptions to antimicrobial stewardship (AMS) programme implementation, including professional education, training and public engagement ([207](#)). Research highlights overprescribing of antibiotics in general practice and concerns around an increase in antimicrobial resistance (AMR) ([208](#)).

Training, education and public engagement are a crucial component of AMS and have been highlighted in both the UK 20-year vision for AMR ([209](#)) and the UK 5-year National Action Plan (NAP) for AMR 2019 to 2024 ([210](#)) to minimise infection, provide safe and effective care to patients and engage with the public.

Whilst the delivery of, and engagement with, AMS training reduced initially, there has been a renewed demand following the first wave of the pandemic, particularly around refresher training, antibiotic prescribing guidance implementation and remote consultations. This chapter provides an outline of, and shows engagement with, a number of initiatives from professional education and training, and community engagement carried out in England during 2020 to 2021 to help meet these needs.

### PHE professional education and training: e-learning

#### TARGET Future Learn eModule

The TARGET Antibiotics: Prescribing in Primary Care e-learning course, developed in collaboration with the British Society for Antimicrobial Chemotherapy (BSAC), is a free course hosted on the Future Learn platform ([211](#)). The course, contains 6 weekly, one-hour modules aimed at primary care healthcare professionals involved in the treatment of common infections. Each weekly module comprises varying numbers of steps.

Week 1: Introduction to AMR in primary care

Week 2: Prescribing in urinary tract infections

Week 3: Assessing the need for antibiotics

Week 4: Managing patient expectations and back up or delayed prescribing

Week 5: Antibiotics for children

Week 6: Common practice approach



The course ran a total of 4 times from May 2020 to March 2021. Whilst 1,437 individuals enrolled in the course, 645 actively participated. The proportion of learners who actively participated dropped over the 4 runs. The course was generally very well-received as indicated by end of course survey results, with 94 (92.1%) out of 102 respondents stated that the course met or exceeded their expectations. Participants found it informative and appreciated the resources. The course will continue throughout 2021 to 2022 with rolling registration, however it may need adapting to include more information around remote consultations.

## Dental massive open online course (MOOC)

The 'Tackling antibiotic resistance: What should dental teams do?' MOOC, developed by BSAC and the World Dental Federation (FDI), is a free 3-week course available via the Future learn platform ([212](#)). The MOOC has been designed for the international audience and recognises the breadth of experience in dental antibiotic stewardship, differences in local contexts and the rapid pace of new developments. The course covers:

Week 1: Antibiotic resistance: the problem

Week 2: Keeping patients safe from antibiotics and infections

Week 3: How can you be part of the global solution to tackle AMR?

On the subject of completion, the course aims to provide a tailored action plan to help dental teams tackle antibiotic resistance.

Since its launch during WAAW 2020, the dental AMS MOOC has been completed by more than 1,800 learners in 104 countries across Europe, Asia, Africa, Australia and North and South America. Feedback has been excellent with over 90% of learners reporting that they learned something new from the course. The course is still live and new learners are regularly signing.

## Pharmacy AMS Intervention (PAMSI)

PHE in partnership with Health Education England (HEE), BSAC, the Royal Pharmaceutical Society (RPS), University of Leeds, and University of Nottingham developed a freely available e-learning session on the AMS role of community pharmacy staff ([213](#)). The e-Learning also highlights the Antibiotic Checklist ([214](#)) as a tool to personalise patient advice when dispensing antibiotics. Since its launch at the start of 2020 to March 2021, the e-Learning had over 120,000 visits.

The e-Learning was included as a requirement of the 2020 to 2021 Pharmacy Quality Scheme (PQS) ([215](#)) under the AMS criterion. Following learning, community pharmacies were required to pledge to be an Antibiotic Guardian (AG) ([216](#)) and develop a practice-level AMS action plan.

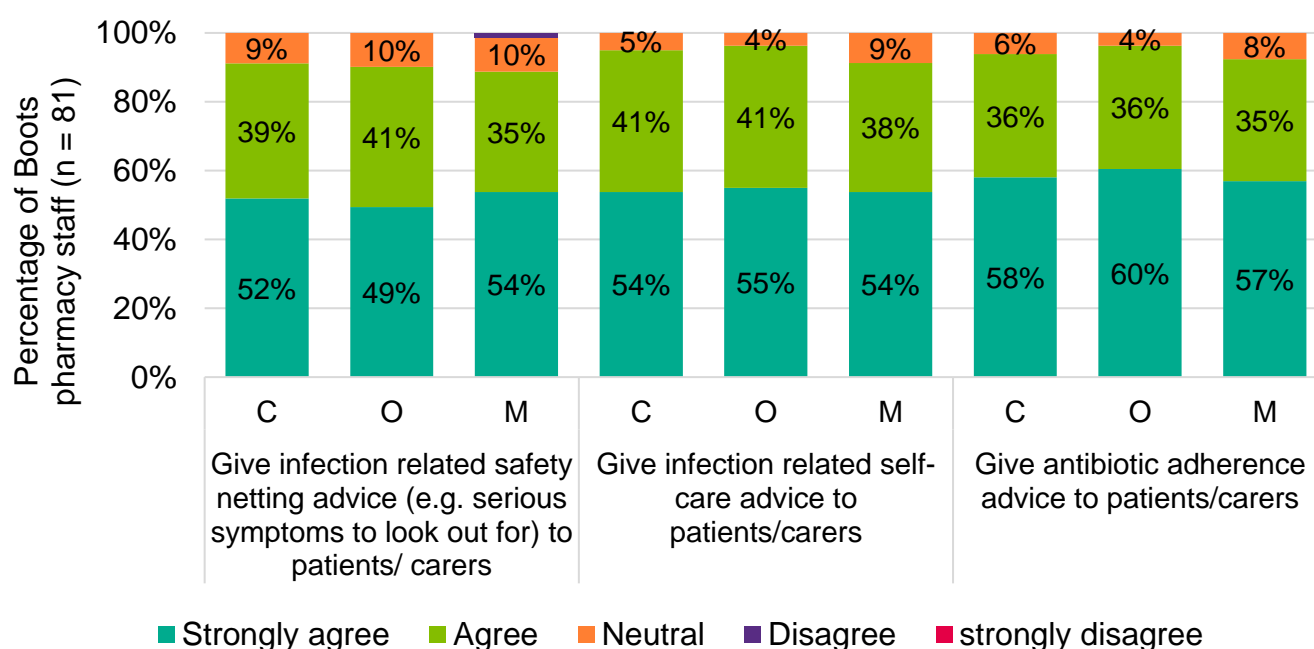
### PAMSI evaluation

PHE in collaboration with Boots UK carried out a mixed method evaluation of the PAMSI in Winter 2020 to explore intervention impact on staff and patients' AMS behaviours. English Boots UK pharmacies were invited to use PAMSI for 4 to 6 weeks.

## Staff findings

101 staff from 66 pharmacies participated in pre- and post-intervention questionnaires and 6 in post-intervention qualitative interviews. Preliminary analyses suggested that at post-intervention, more staff self-reported checking antibiotic appropriateness and gave patients more advice on antibiotic adherence, antibiotic resistance and self-care. Figure 8.1 shows staff's self-reported improvement to their capability, opportunity and motivation in AMS behaviours (strongly agree – strongly disagree) after using PAMSI. Staff also reported improved confidence and better communication with patients. Barriers included patients not attending the pharmacy in person due to COVID-19 and in some cases, staffing and time pressures affected implementation of the Antibiotic Checklist with patients.

**Figure 8.1 Boots UK pharmacy staffs' self-reflection on their capability (C), opportunity (O) and motivation (M), to provide infection and antibiotic advice to patients, following use of the PAMSI**

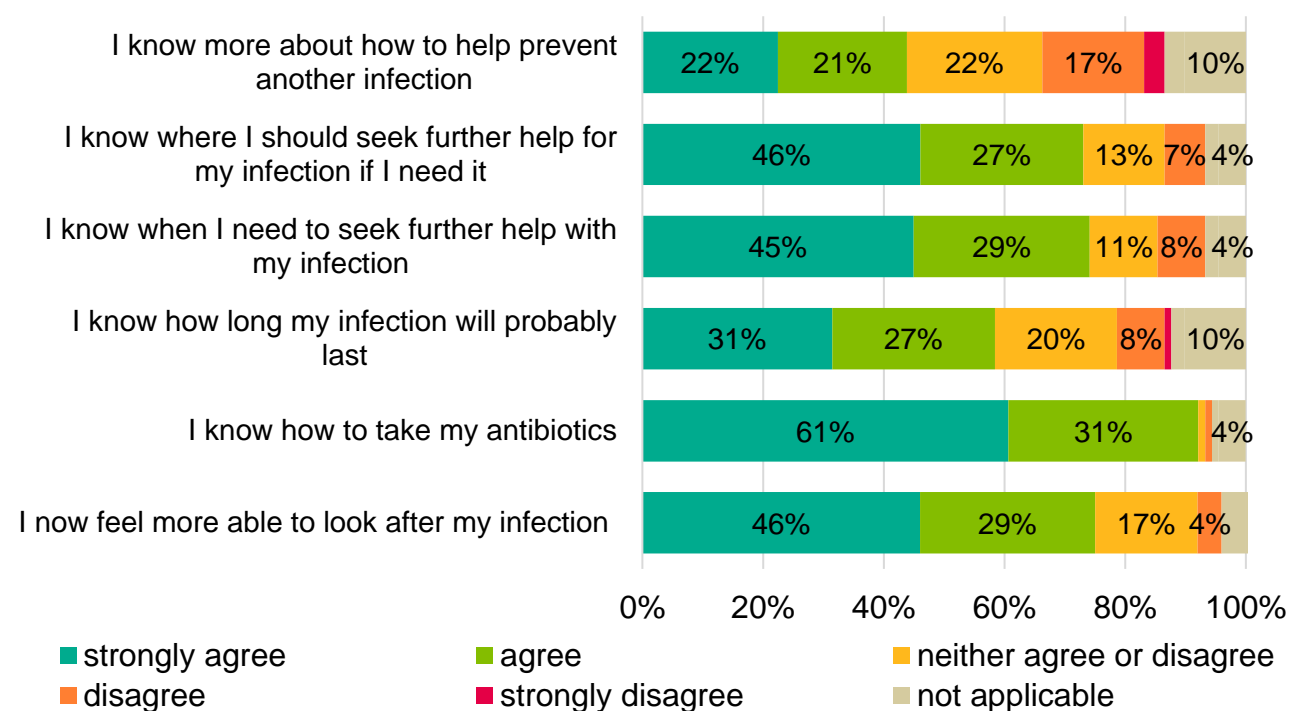


## Findings from patients

Of 91 patients responding to a follow up questionnaire about their visit to the pharmacy, 21% did not know the name of the antibiotic they had been prescribed. Patients most often reported receiving information from pharmacy staff on, how long to take antibiotics (75%), information regarding food consumption (72%), alcohol consumption (44%), and side effects (44%). Less reported how long it would take to feel better (30%), self-care actions they could take to feel better (30%) and information on AMR (32%). 2% reported receiving no information at all from the pharmacy team and 3% did not remember advice. Figure 8.2 shows patients' self-reported knowledge after receiving advice from their community pharmacy, highest knowledge was reported around how to take their antibiotics and when and where to seek further help; less for how long their infection may last and knowing how to prevent future infections.



**Figure 8.2 Patients' self-reported knowledge of antibiotic and infection management, after receiving advice at their community pharmacy (n=91)**



### Implications

PAMSI is an effective, feasible and acceptable intervention to support community pharmacy staff in their key AMS roles. Pharmacy staff reported difficulties in communicating advice to patients not attending the pharmacy in person (due to isolation for COVID-19 or otherwise). To overcome this barrier, an online information tool will be developed to complement the current resource, which can be signposted by pharmacy staff in deliveries of antibiotics along with information leaflets.

## TARGET remote prescribing webinars

In response to the increase in remote consultations the TARGET Antibiotics Toolkit published 2 freely available remote consultation webinars ([217](#)) in March 2021:

- Common infections in extraordinary times – decision points for remote management
- Using national antibiotic resources to help improve antibiotic prescribing

These webinars focus on remote consultation during COVID-19 with the aim of helping prescribers identify important decision points for remote management of common infections including:

- ear, nose or throat infections
- UTIs
- cough
- COVID-19
- insect bites

They include downloadable slide decks so that the training can be cascaded in general practice if desired. High engagement in the first month of publication highlighted the need for such tools. The webinars were viewed over 500 times, received 10,903 impressions across social media, 140 social engagements (likes, shares and link clicks) and 288 clicks from emails.

## Continuing AMS Interventions in secondary care during COVID-19 webinar

A webinar entitled 'Continuing AMS Interventions in Secondary Care During COVID-19' was held on 30 March 2021 via Microsoft teams. One-hundred-and-sixty-six healthcare professionals registered and 78 attended the live event. Of those who registered, 73.5 % were pharmacists, 4.2% were pharmacy technicians, 3.6% were microbiologist, 3% were public health practitioners and the remaining 15.7% included a range of other roles. Speakers attended from across the UK and covered:

- the impact of COVID-19 on antimicrobial use in England and AMS activities and programs in the United Kingdom
- antibiotic and antifungal prescribing in patients with suspected and confirmed COVID-19 in Scottish hospitals – survey findings
- shared learning on hospital AMS interventions carried out during COVID-19

The event was recorded and is hosted on the [Antibiotic Guardian website](#). No feedback was gathered for this event.

## AMS in community pharmacy shared learning webinar

A webinar entitled 'AMS in Community Pharmacy' was held on 30 March 2021 via MS Teams - 424 community pharmacy staff registered and 150 attended the live event. Of those who registered, 81% were pharmacists, 9.7% were pharmacy technicians or dispensers and the remaining 9.3% included a range of other roles. Topics covered included:

- AMS in community pharmacy and tools available
- AMS and the role of community pharmacy
- Implementation of the TARGET ([218](#)) antibiotic checklist in community pharmacy

The event also featured a panel discussion of 5 community pharmacists who shared their experience of using the Antibiotic Checklist and practicalities of developing and implementing their AMS plan and other interventions utilised in their pharmacies. The event was recorded and is hosted on the [Antibiotic Guardian website](#).

Those who completed the evaluation stated that the webinar equipped them with the knowledge and confidence to lead or support the AMS plan in their pharmacy using the tools provided. Respondents also stated that the webinar made them feel more confident to implement AMS

interventions with 56% of 68 respondents stating that they either have, or plan to put up the poster and leaflets within the next week. Other actions included:

- make use of the TARGET leaflets and checklist, starting with UTIs and adding on other conditions each month
- actively engage with patients who have been prescribed antibiotics and provide more self-care and safety netting with patients
- be more familiar with local antibiotics formulary and work together with local GPs to encourage them to adhere to guidelines
- engage with patients who have been on long term antibiotics and those who have been prescribed the same antibiotic every 6 to 8 weeks for a UTI
- discuss with the whole pharmacy team how to take forward AMS in the pharmacy

Evaluation findings highlight the benefit of using webinars as a tool for education and communication.

## e-Bug Future Learn training for educators

The e-Bug 'Health Educator Training' e-Learning course ([219](#)) is hosted on the FutureLearn platform and was developed by PHE and BSAC for teachers and educators and others who work with children or young people. The free course, which is accredited by the Royal College of Pathologists, contains 3 weekly 2-hour modules aimed to improve knowledge and confidence to deliver health education on microbes, preventing the spread of infection, and antibiotic use in an engaging and age-appropriate manner.

Each weekly module has been designed to last 2 hours and covers the following topics:

Week 1: Introduction to microbes, hand hygiene, and respiratory hygiene

Week 2: Food hygiene and oral hygiene

Week 3: Antimicrobial resistance

The course ran a total of 6 times from January 2020 to February 2021. Given the virtual nature of the course, there was a significant increase in user uptake in run 2 after the first COVID-19 lockdown was announced. Whilst 3,257 individuals enrolled in the course, 1,932 (59.3%) actively participated. Most users were between 26 to 35 years old. The course was generally very well-received as indicated by the end of course survey results; a total of 98% stated that the course exceeded or met their expectations, with participants finding it informative and appreciating the resources. The course will continue to run throughout 2021 to 2022 with rolling registration.

## Preventing and managing infections in childcare and pre-school e-learning

At the beginning of the COVID-19 pandemic in England, schools and childcare settings closed to all but a few key workers' children. Fear grew around interaction between members outside of your household; this caused significant concern about schools and day care settings reopening, with parents and staff wanting answers to questions. This 'Preventing and managing infections in childcare and pre-school' e-learning course ([220](#)) was specifically developed to support Early Years setting staff to improve understanding of how infections spread and how to protect children from infections, within a nursery setting. The rationale for the course was to support nursery nurses, day care staff, childminders, and carers, with information when implementing COVID-19 guidelines, with a view to life post pandemic.

The e-learning, hosted on the FutureLearn platform, was split into a 2-week course, taking 2 hours per week. The course cost £10,000 to develop, using existing e-Bug material and some additional filming.

Four-thousand-seven-hundred-and-sixty-three participants enrolled in the e-learning during the first 4 runs (August 2020 and March 2021). Fifty-five per cent were active learners (completed at least one step at any time in any course week). In total, participants signed up from 149 countries, with the top 5 countries being UK (48%), India (5%), Nigeria (3%) and USA or Australia (2%). The majority of learners were aged 18 to 35 years old (49%). This course received a very high number of comments and was very positively received, scoring 4.8 out of 5 stars from 123 reviewers. The learners consistently mentioned that they had learned something new, or how useful they found the content.

To conclude, the e-learning successfully supported Early Years setting staff to understand how infections spread and how to protect children from infections, within a nursery setting. The FutureLearn platform is an effective mechanism to connect with the early years workforce; a demographic that, traditionally, has been hard to reach and could be used to develop further educational resources.

## PHE professional education and training: workshops

### TARGET train the trainer remote workshops

Necessary social distancing restrictions established in response to the COVID-19 pandemic have resulted in the need to deliver all training remotely. TARGET delivered 2 virtual workshops, via Microsoft Teams, to 19 attendees in October 2020 who cascaded delivery to at least 33 attendees between October 2020 and March 2021. According to attendees, barriers to delivering cascaded AMS workshops included:

- time constraints
- remote delivery and technology

- COVID-19
- lack of healthcare professional engagement

Ninety-eight per cent (43 out of 44) of post-workshop survey respondents stated that the workshop content and presenter knowledge were either 'very good' or 'good'. Since March 2021 there has been renewed interest in the uptake of AMS workshops.

## Planning your own WAAW/EAAD during a COVID-19 pandemic Workshop

A workshop entitled 'Planning your WAAW/EAAD 2020 activities in the context of COVID-19' took place virtually on 30 September 2020. This workshop was designed to share ideas for how AMS messaging could be promoted in spite of the challenges of the COVID-19 pandemic. Over 105 delegates attended the workshop, representing more than 100 organisations.

The workshop comprised presentations from PHE (now UKHSA), TARGET, e-Bug and Antibiotic Guardian Award Winning projects. The presentations were followed by a breakout session. This was an opportunity for attendees to discuss their WAAW projects and gain helpful advice and tips. The workshop was recorded and is available on the [Antibiotic Guardian website](#).

Post-workshop questionnaire responses from attendees highlighted that they were inspired to engage with e-Bug and TARGET materials, take part in the AG Ambassadors programme, record AMS pledge videos and share on social media, use QR codes to share WAAW resources and register organisational activities on the AG webpage, promote NICE guidance, audit team antibiotic prescribing and plan publicity campaigns in collaboration with organisational communications teams.

## PHE professional education and training: conferences and programmes

### Healthcare students AMR conference

The fourth National Student AMR Conference ([221](#)) was held on 21 November 2020 as a virtual event, and encouraged students to 'Be part of the change – Help Keep Antibiotics Working'. The conference included lectures and workshops covering a 'One Health' approach and a focus on tackling AMR, including presentations on clinical trials and vaccine development in the context of COVID-19. Speakers came from medicine, pharmacy, veterinary and other healthcare sciences disciplines, as well as from clinical trials or research backgrounds. Five-hundred-and-fifty-eight students and early career healthcare professionals registered to attend, and 159 students from across the specialities attended on the day. Delegates engaged in breakout sessions throughout the conference, for discussion, sharing and consolidation of learning.

## Antibiotic Guardian shared learning event and awards

The fifth AG shared learning and awards event took place virtually on 26 November 2020 to acknowledge, celebrate and share learning around the work of healthcare professionals across the UK and abroad in tackling AMR. A keynote speech was delivered by honorary guests Dr Keith Ridge (Chief Pharmaceutical Officer for the UK) and Dr Haileyesus Getahun (Director of Antimicrobial Resistance, Global Coordination and Partnership, WHO). A congratulatory message was also sent by Ruth May (Chief Nursing Officer).

The event was attended by 128 delegates from organisations across England, Scotland, Wales, Europe, Africa, the Americas, India and Asia. Poster presentations for the winners, and those highly commended for each category, from this and previous years are available on the [Antibiotic Guardian website](#).

Due to the pandemic, the event itself was postponed from June until November 2020, and project submissions were reopened from 25 June until 13 July. These shared learning events provide PHE (now UKHSA) and other national organisations with a robust selection of case studies of work ongoing to tackle AMR that have been peer reviewed through the judging process. Several projects which started locally and have won or been highly commended at the AG awards have gone on to become national projects and/or feature in the UK AMR national action and implementation plan. A full list of shortlisted entries across all years can be viewed on the [Antibiotic Guardian website](#).

With the highest number of entries since the inception of the awards event in 2016, 105 projects and case studies were submitted in the categories of Animal Health, Agriculture and Food Supply, Children and Family, Community Communications, Diagnostics, Infection Prevention and Control, Innovation, Prescribing and Stewardship, Research, Student of the Year and the Das Pillay Memorial AMS Award. The 'Multi-country collaborations and activities to tackle AMR' category was also introduced in 2020, for partnerships between more than one country in any area of AMR, performed by organisations. This category received 13 entries in 2020. Thirty entries from across the categories were received from international organisations. Table 8.1 presents the number of entries per category in 2020.

**Table 8.1 A summary of the number of entries received per category for the Antibiotic Guardian shared learning and awards event 2020**

Category	Number of entries
Student of the Year	6
Research	6
Public Engagement	12
Prescribing and Stewardship	20
Multi-Country Collaboration	15
Innovation and Technology	11



Category	Number of entries
Infection Prevention and Control	3
Diagnostic Stewardship	4
Animal Health, Agriculture and Food Supply	4
Children and Family	11
Community Communications	8
Das Pillay Memorial AMS Award	5
<b>Total</b>	<b>105</b>

## Royal Pharmaceutical Society AMS Programme 2020 to 2021

In 2020 to 2021 Health Education England (HEE) provided further funding for the Royal Pharmaceutical Society (RPS) to enrol learners into their AMS programme, following on from the 2019 cohort in London and the South East. This was split into 2 intake rounds in February and November 2020.

The training is a blended programme for pharmacists with at least 2 years post-registration practice experience in patient-facing roles. It aims to develop the knowledge, skills and attributes to enable learners to be able to lead AMS improvement initiatives in their workplace that test and implement behaviour change techniques to improve antimicrobial prescribing. Throughout the training, learners are supported to apply their learning in their workplace and are required to have established an AMS improvement initiative by the end of the training.

### Programme delivery in 2020

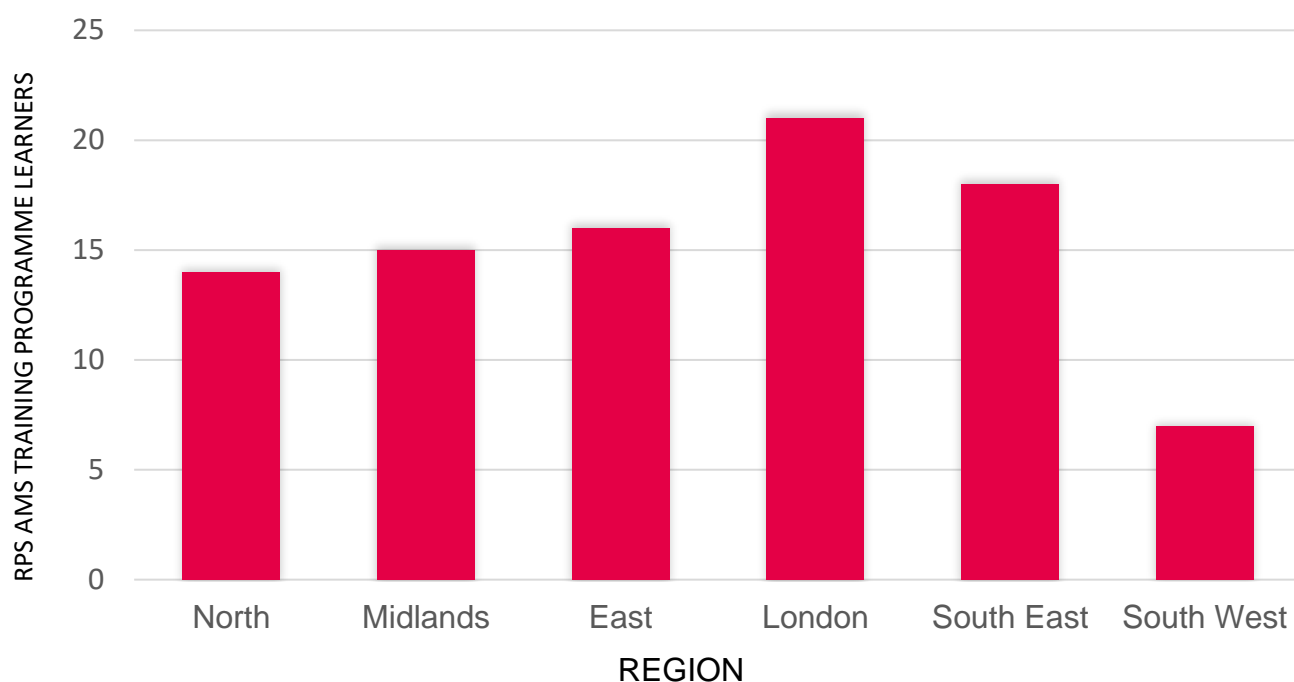
An overview of the 2020 cohorts are provided in Table 8.2 below. Unfortunately, the February intake was closed early due to the first wave of the COVID-19 pandemic.

**Table 8.2 Overview of 2020 intakes to the RPS AMS Programme 2020 to 2021**

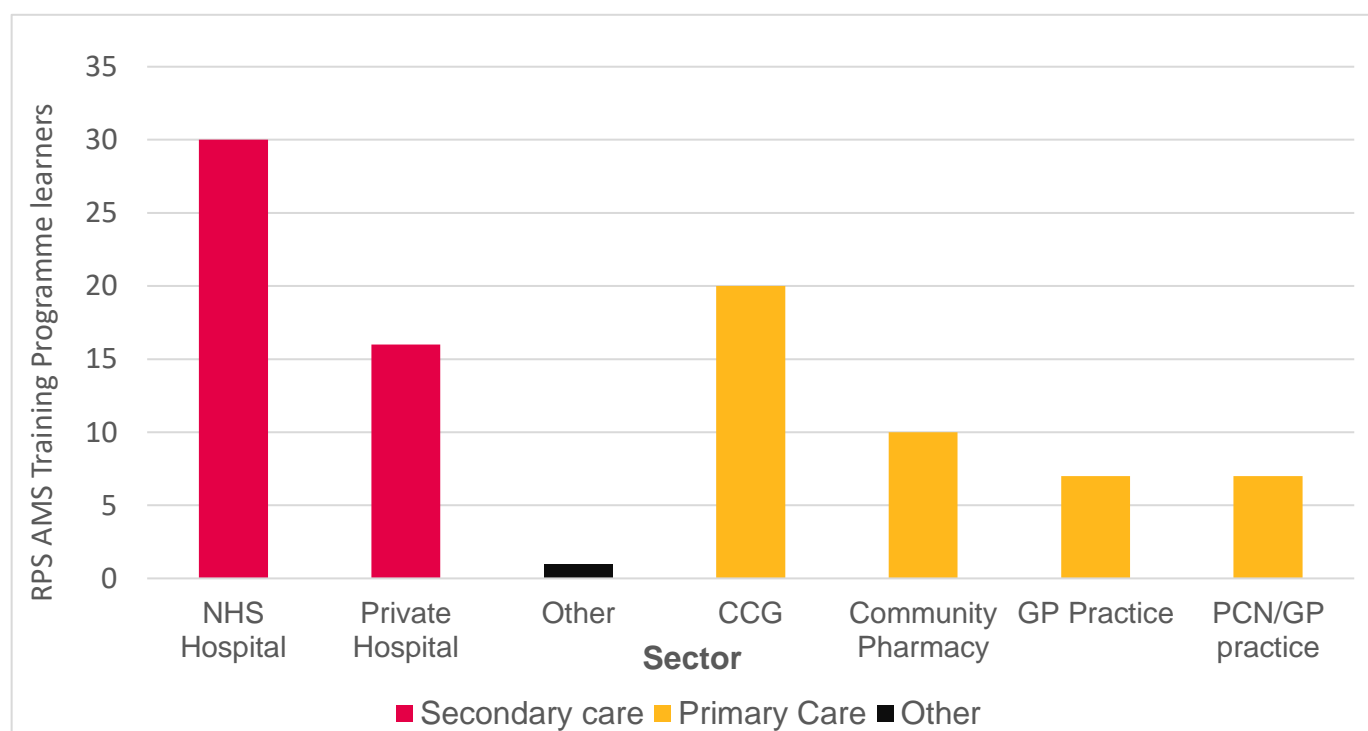
Intake	Training day	Group discussion presentations	Portfolio and assessment
February to April 2020 (Closed early due to COVID-19)	61 attended	45 presentations (11 groups)	N/A
November 2020 to March 2021	Session 1: 30 attended Session 2: 29 attended	31 presentations (5 groups)	14 completed, 6 delayed

Figures 8.3 and 8.4 detail the learner breakdown by sector and region.

**Figure 8.3 Breakdown of RPS AMS Training programme learners in 2020 by region**



**Figure 8.4 Breakdown of RPS AMS training programme learners in 2020 by sector**



Despite the significant challenges posed by the pandemic for all learners this year, positive engagement was maintained in both intakes. A total of 91 learners attended the training day programme that included sessions on AMS essentials, behaviour change, and quality improvement. This was delivered face to face for the February intake in Bristol and Leicester, and online as a series of 2 webinars for the November intake. The RPS collaborated with the Manchester Implementation Science Collaboration to deliver the behaviour change session.



Two rounds of small group discussion sessions were scheduled for each intake with a total of 76 learners taking part to share and discuss work on workplace improvement projects. Only one round of sessions was able to be delivered for the February cohort.

#### Key evaluation outcomes in 2020

Ongoing evaluation of the training has taken place through analysis of learner projects, quizzes and surveys. A summary of workplace AMS improvement activity is provided in Table 8.3 below. This was evaluated through analysis of learner portfolio evidence by RPS staff. These achievements are commendable considering the challenges posed by COVID-19 to learners and workplaces.

**Table 8.3 Summary of workplace AMS improvement activity by RPS learners in 2020**

	Workplace improvement outcomes during training					
<b>Intake</b>	<b>Identified improvement topic in workplace</b>	<b>Secured workplace support for QI project</b>	<b>Improved understanding of problem through data collection</b>	<b>Conducted test of change</b>	<b>Promoted improvement initiative</b>	<b>Provided education to colleagues</b>
February 2020	45	25	4	0	9	1
November 2020	19	13	15	4	11	8
Total	64	38	18	4	20	9

A small number of learners from the February intake (13 of 61) also responded to a follow up survey 10 months post training. It was encouraging to see that 4 learners had reported that their improvement projects had continued despite the pandemic, with 2 reporting that there had been achievement of improved outcomes.

## e-Bug

e-Bug, operated by PHE (now UKHSA), is a free educational resource for classroom and home use and makes learning about micro-organisms, the spread, prevention and treatment of infection, fun and accessible for all teachers and students. All activities and lesson plans support national infectious disease strategies and action plans for AMR, as well as supporting implementation of the National Curriculum for example, RSHE, Science. The website and resources are available in over 20 languages.

### e-Bug engagement summary stats

Between April 2020 and March 2021, the e-Bug website received almost 2.8 million visits, the highest annual figure on record by over 1 million hits. Table 8.4 shows the most accessed pages on the e-Bug website 2020 to 2021, the COVID-19 page and hand and respiratory hygiene lesson plans were the most viewed.

**Table 8.4 Top English e-Bug pages accessed 1 April 2020 to 31 March 2021**

In this table [n] denotes new to the top 10 in 2020 to 2021 so no figures available for 2019 to 2020.

Page	Page views 2019 to 2020	Page views 2020 to 2021
e-Bug Homepage	99,887	156,670
Covid-19 Page	[n]	82,693
KS1 Horrid Hands	75,277	78,154
Junior Student Homepage	32,073	63,070
KS2 e-bug Lessons Homepage	25,391	54,820
Junior Games Homepage	37,371	49,727
KS2 Hand Hygiene	42,431	42,978
KS1 Super Sneezes	29,900	38,518
KS2 Respiratory Hygiene	21,151	23,249
Junior Quiz Page	[n]	16564

Table 8.5 shows top 10 countries visiting the e-Bug website. UK users made up over 43% of total users worldwide. Users from France had increased by nearly 6 times, compared to the same period the previous year.

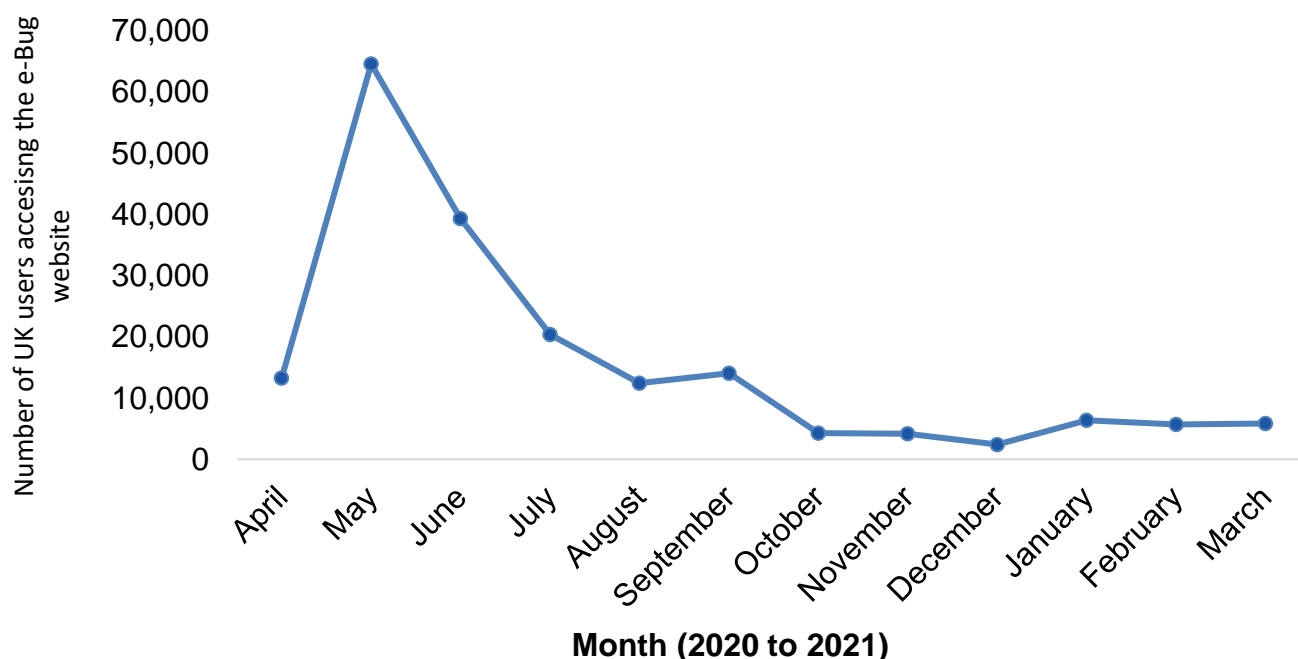
**Table 8.5 Top countries accessing the e-Bug website 1 April 2020 to 31 March 2021 compared with 1 April 2019 to 31 March 2020**

In this table [n] denotes new to the top 10 in 2020 to 2021 so no figures available for 2019 to 2020.

Country	Users 2019 to 2020	Users 2020 to 2021	% users 2020 to 2021
United Kingdom	130,328	183,172	43.41%
France	18,981	126,477	29.97%
United States	9,863	11,627	2.76%
Spain	8,784	10,141	2.40%
Italy	4,066	7,181	1.70%
Kosovo	[n]	6,007	1.42%
Greece	4,172	4,749	1.13%
Denmark	3,236	3,431	0.81%
Germany	[n]	3,154	0.75%
Mexico	[n]	3,010	0.71%

Figure 8.5 shows the number of UK visitors to the e-Bug website, monthly. The greatest number of visitors was observed in May 2021, coinciding with the announcement of schools re-opening following the first lockdown. During this time, e-Bug also published 2 new posters and a storybook to support primary aged children returning to school, which have been some of the most downloaded resources this year (Table 8.6).

**Figure 8.5 Number of UK users accessing the e-Bug website each month between 1 April 2020 and 31 March 2021**



**Table 8.6 Top English e-Bug resources downloaded 1 April 2020 to 31 March 2021**

Resource	Downloads 2020 to 2021
'My Back to School Bubble' e-storybook	12,027
Hand Hygiene Poster	10,774
KS1 Giant Sneeze Poster	10,112
Cover Coughs And Sneezes Poster	9,067
KS1 Full Lesson Pack	3,654

## Development of 'My Back to School Bubble' e-storybook to reinforce key public health messages for primary aged children

In June 2020, schools were preparing to return following the first period of closure caused by the COVID-19 pandemic. At this time, a gap in age appropriate resources to support the transition of children back to educational settings was identified. A rapid scoping exercise was launched to identify topics to cover within a children's online storybook '[My Back to School Bubble](#)'.

A total of 71 known contacts within networks across Public Health England, local authorities, health protection teams and Department for Education were invited to input topics and feedback for a proposed 'return to school' storybook. Responses were thematically analysed and findings used to inform the development of 'My Back To School Bubble' in collaboration with [NABU](#). Following online publication, users were asked to provide informal feedback via an online survey to assess their impressions of the story.

Findings from 31 respondents highlighted that children are likely to hold differing feelings regarding COVID-19, depending on their own temperament and lockdown experiences, including changes in relationships with family and friends. Following the launch of 'My Back to School Bubble' e-storybook, it has been downloaded over 12,000 times and 21 users provided feedback via survey. Fourteen respondents (67%) indicated that the storybook was a useful tool for providing support to children, and 12 (57%) reported that the resource helped children understand their own feelings.

Clear, accurate information about the new school environment should be provided in the context of COVID-19. It is especially important to support children with special educational needs and disabilities, including those with autism. Encouraging children to take ownership of their health and hygiene behaviour, such as handwashing, will help to normalise this and prevent the spread of infection. Lessons learnt from the development of '[My Back to School Bubble](#)' online storybook suggest the clarity of imagery could be improved to better support children with autism.

## Antibiotic Guardian (AG)

PHE launched the pledge-based AG campaign in 2014, with the aim of transitioning from raising awareness to increasing engagement. The campaign uses an online pledge-based approach among human and animal health professionals, scientists and educators and the public.

From initiation in 2014 to the end of 2020, there have been 112,021 pledges on the main AG webpage. During 2020, the campaign website was visited 86,581 times, this resulted in 36,733 pledges (the highest number of pledges since the campaign began and over double any other annual figure) from 118 countries. See Table 8.7 for annual page visits to the AG website since 2017, and annual pledge figures since inception, respectively. AGs from more than 60% of countries made a pledge in 2020. Pledge translations are available in Dutch, French, German, Russian and Turkish.

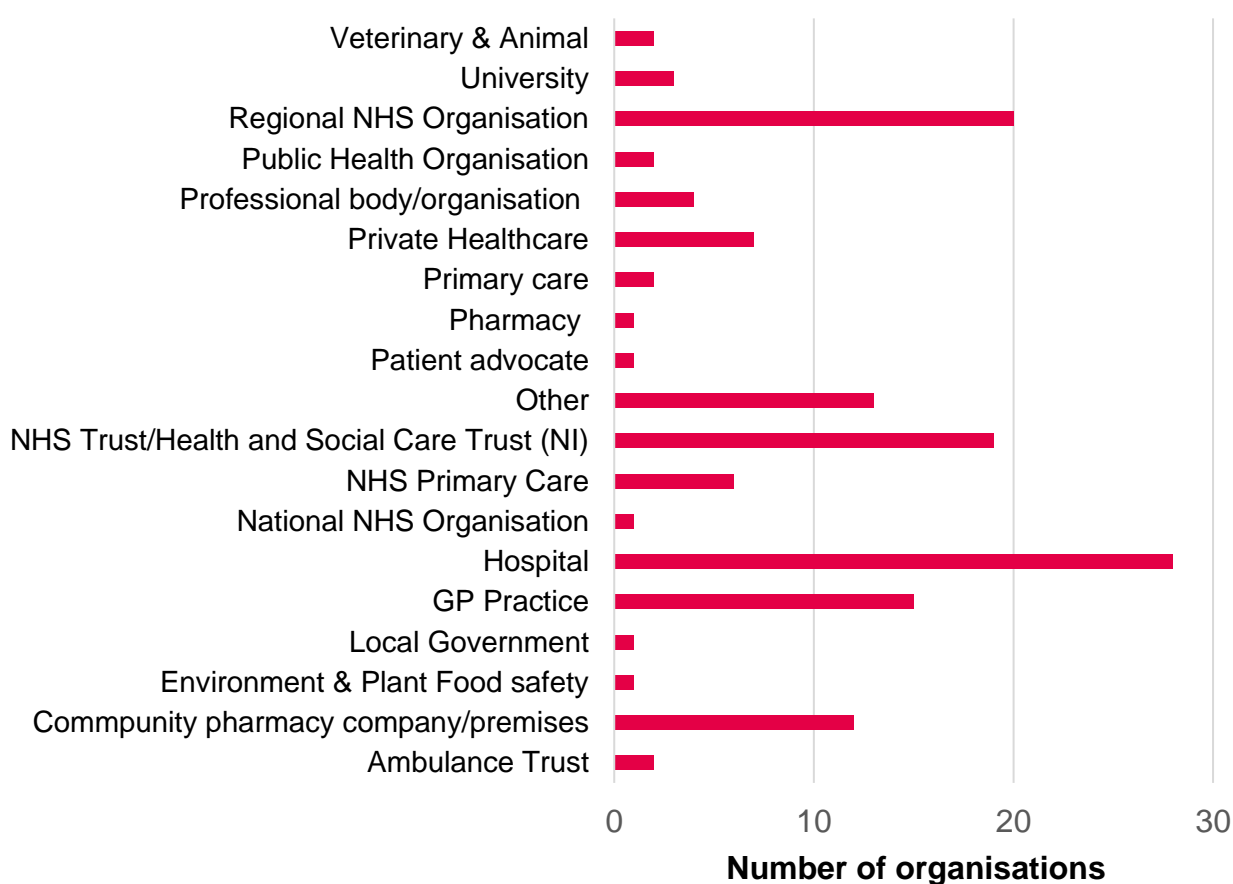
**Table 8.7 Antibiotic Guardian pledges 2014 to 2020**

	2014	2015	2016	2017	2018	2019	2020
<b>Number of pledges</b>	12,315	15,002	15,140	15,170	8,373	9,289	36,733
<b>Number of AG site visits</b>	-	-	-	53,111	54,178	64,971	86,581

In November 2019, in collaboration with Africa CDC, the Africa AG page was launched including tailored pledges for Africa content. It is available for all African Union member states to use in their national campaigns. The total number of AG pledges on the African site is 541 (7 November 2019 to 31 December 2020), with representation from 35 countries. Of these, 41% are healthcare professionals, 9% members of the public and 50% students and educators.

#### Registration of organisations on AG website

Figure 8.6 shows the 106 organisations across the UK that registered their AMS activities on the AG website in 2020. This included 13 from the UK generally and 93 from England specifically. Thirty-five non-UK organisations registered activity (18 from the Africa page and an additional 17 from the main page), including 7 from Nigeria, 3 from India, 3 from Kenya, 3 from South Africa, 2 from Cameroon, 2 from Tanzania, 2 from the USA and one from Bermuda, Canada, Channel Islands, Côte d'Ivoire, Ghana, Iran, Isle of Man, Malawi, Pakistan, Rwanda, Sudan, United Arab Emirates and Zimbabwe, respectively.

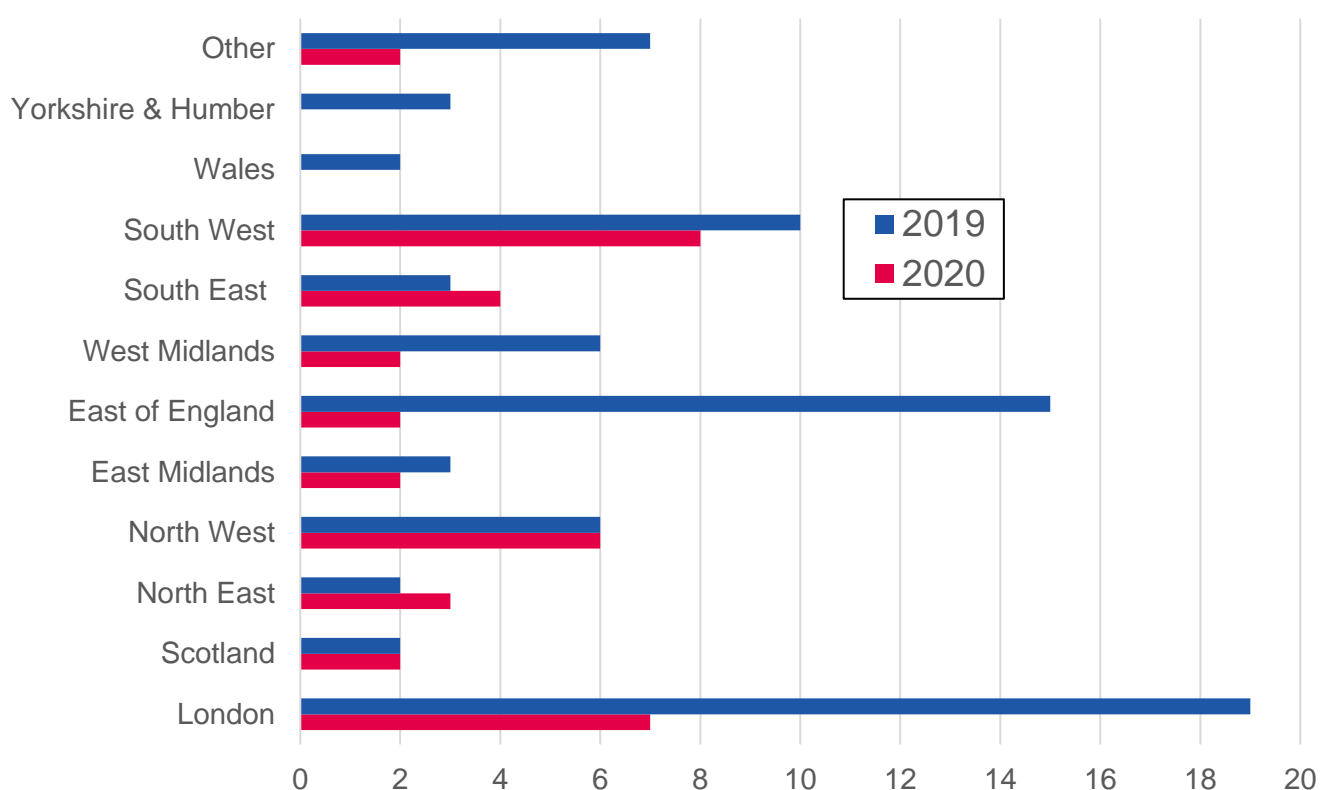
**Figure 8.6 A summary of the number of organisations that registered their AMR activity on the Antibiotic Guardian website during 2020, broken down by organisation type**

## Antibiotic Guardian: school ambassadors programme

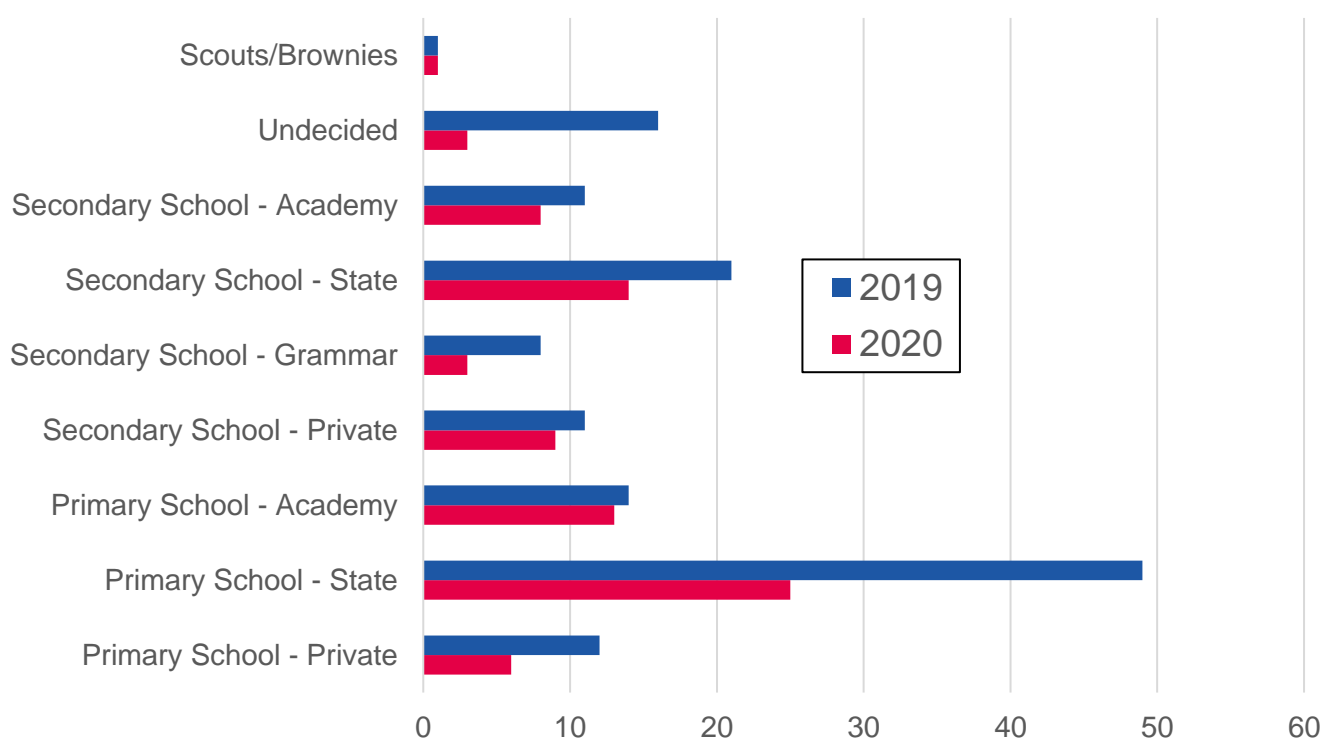
A pilot programme to develop AG school ambassadors was developed during 2019 ahead of WAAW. This scheme aimed to connect Healthcare professionals (HCPs) with local schools and community groups, in order to share information about AMR. Due to the COVID-19 pandemic, the second ambassadors pilot was significantly adapted in order to minimise risk to ambassadors and school staff or students in 2020. The 2020 pilot focussed only on ambassadors circulating a newsletter piece, rather than providing teaching sessions in person. This newsletter item was adapted to include information on COVID-19 and self-care, hand hygiene and links to updated e-Bug materials. An updated Ambassadors toolkit was also produced for 2020, including changes in the light of COVID-19 and government guidance on schools and distancing. Links to updated e-Bug resources and distancing-friendly games were included in place of those that would not comply with government guidelines.

Thirty-two individuals signed up to be an AG Schools Ambassador in 2020. Of these 78.9% were pharmacists, 10.6% scientists, 5.3% public health specialist/consultant colleagues, 2.6% nursing colleagues and 2.6% technician colleagues (47.4% of signups were from within PHE). Volunteer geographical and targeted establishment demographics can be seen in Figures 8.7 and 8.8.

**Figure 8.7 Geographical demographics of Antibiotic Guardian Schools Ambassador volunteers during 2019 and 2020**



**Figure 8.8 Educational establishment types that Antibiotic Guardian Schools ambassadors intended to target**



Ambassadors were asked to encourage schools and community groups to register that they had promoted the newsletter item. Three schools registered their activity (2 from the South East and one from the West Midlands, 2 were primary state schools and one was a secondary school academy). Collectively, these respondents estimated that the newsletter items had reached over 1,500 students during WAAW 2020.

## World Antibiotic Awareness Week (WAAW) and European Antibiotic Awareness Day (EAAD) 2020

Despite barriers introduced by the COVID-19 pandemic in 2020, WAAW and EAAD continued to provide an excellent opportunity to engage with healthcare workers and the public on tackling AMR. Although there were challenges in producing the annual letter – usually co-signed by England's chief professional officers and senior PHE colleagues and sent to colleagues in CCGs and NHS Trusts asking for their support in promoting WAAW – senior NHS and health system leaders instead promoted this messaging through more focussed bulletins during WAAW.

### WAAW healthcare professional toolkit

A new WAAW and EAAD toolkit ([223](#)) was developed and uploaded to the .GOV website on 22 October 2020. The toolkit provided guidance to support the NHS, local authorities and others to



actively lead WAAW and EAAD activities and to encourage responsible use of antibiotics. For 2020, the toolkit was updated in an accessible format for users of assistive technology. In the context of the COVID-19 pandemic, the focus of the updated toolkit was digital activities for WAAW and key actions for those with limited time. Between publication and the end of 2020, the webpage holding the toolkit was visited 1,847 times, with the toolkit being downloaded 704 times.

## WAAW Twitter activity

An international Twitter storm on 18 November 2020 was organised by the US Centers for Disease Control and Prevention (CDC), the World Health Organization (WHO) and the European Centre for Disease Prevention and Control (ECDC). PHE adapted resources and hashtags for use in England. The Twitter storm encouraged users to use the hashtags #AntibioticGuardian, #KeepAntibioticsWorking, #WorldAntimicrobialAwarenessWeek and #EAAD. During the period 17 to 25 November 2020 25,874 Twitter users collectively sent 52,442 tweets. #WAAW2020 was the most used hashtag during WAAW 2020, tweeted 13,825 times.

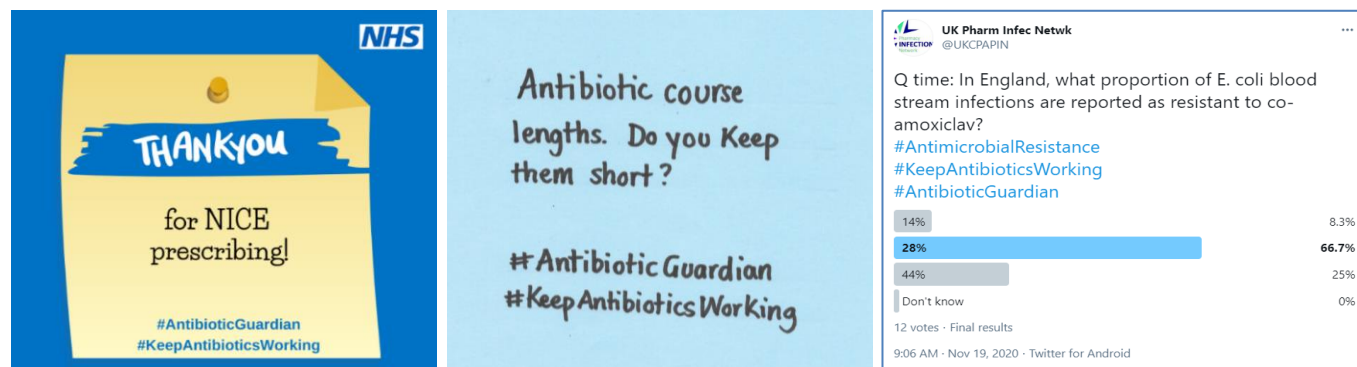
The [Antibiotic Guardian](#) website was featured in 521 tweets during this period and was the second most tweeted URL in Twitter storm tweets. Recommended hashtags #AntibioticGuardian, #KeepAntibioticsWorking, #WorldAntimicrobialAwarenessWeek and #EAAD combined, were used 14,685 times during this period.

## WAAW online resources and sticky note campaign

A subgroup of the national WAAW and EAAD planning group was established to develop a range of digital resources for WAAW 2020 for health care workers. These resources included a daily Twitter poll during WAAW, hosted on the UK Clinical Pharmacy Association (UKCPA) pharmacy infection network Twitter account, as well as 'sticky note' and 'Thank you note' campaigns. The work of the subgroup was designed to standardise efforts in disseminating AMR messages in 2020, when there was already a lot of public and professional communications around COVID-19. They were also developed considering the difficulty in running local WAAW events during the pandemic and the results of the UK Healthcare Workers Survey and actions for the UK.

The resources aimed to increase awareness of WAAW/EAAD among healthcare workers, improve availability of resources, promote existing materials and utilise social media. [Thank You notes](#) were created using NHS and AG branding and were also available in an adaptable format for local messages. [Sticky notes](#) were produced in yellow and blue formats in a variety of writing styles, local teams were also encouraged to create their own messages. The [Twitter polls](#) were released each day, between 17 and 20 November, with the answer shared the next day and used to promote messages on AMS, IPC and available resources. Examples of each can be seen in [Figure 8.9](#).

**Figure 8.9 ‘Thank you’ notes, sticky notes and Twitter poll examples produced for WAAW 2020**



Across the 4 days of Twitter polls, the average number of votes was 37, with the highest engagement on 17 November (n =66) and the lowest on 19 November (n =12) the average % of correct responses was 81.4%, with the highest percentage (92%) correctly answering that antibiotic resistant bacteria can spread from person to person. The lowest proportion of correct answers was seen for the question: ‘In England, what proportion of *E. coli* blood stream infections are reported as resistant to co-amoxiclav?’ – 66.7% correctly answered ‘28%’, whilst a quarter of respondents responded ‘44%’ and 8.3% selected ‘14%’ (n=12).

## Future actions

TARGET will develop a digital version of PAMSI to support shielded and other patients who cannot visit the pharmacy in person.

In a recent GP survey (224) leg ulcers, and cellulitis were ranked in the top 6 most highly rated illness/conditions where respondents felt they required more evidence to support their daily practice. To support health care professionals integrate updated NICE antibiotic prescribing guidance on skin infections into their daily practice, TARGET will develop and launch a series of educational tools for these conditions.

The e-Bug programme will review and renew all school resources to cover Early years and Key Stages 1 to 4 and aim to roll out to schools in September 2021.

A recent systematic review (225) highlighted the distinct lack of consideration of the developmental aspects of children and their knowledge of and understanding of IPC in acute paediatric settings, stating that greater education interventions are needed to strengthen the involvement of children and parents in AMS and IPC roles. As such e-Bug, in collaboration with Southampton Children's Hospital, will develop and evaluate educational resources on IPC and AMS, for children and their parents in this setting.

In 2021, another WAAW/EAAD workshop will be run in a ‘Knowledge Café’ format – based on the success of the 2020 workshop, as well as the ‘Antibiotic Café’ event, which was hosted by

Northumbria Healthcare NHS Foundation Trust in 2020. The Knowledge Café format seeks to help surface the group's collective knowledge; learn from each other; share ideas and insights.

The AG Schools Ambassadors scheme will enter its third year, with a focus on public health and healthcare staff promoting a toolkit of teaching resources around AMS and hygiene to local schools. Ambassadors will also be encouraged to record a short introductory video to the lessons, based around their unique perspectives on why tackling AMR is important.

The sixth AG Shared Learning and Awards event will be held in June 2022, with the call for entries opening during WAAW 2021. A new category will be added to include 'learning and insights from the COVID-19 pandemic'.

In 2021 an online, module-based experience – hosted on the Antibiotic Guardian webpage – will be piloted, based on the recorded sessions provided during the first 4 years of the Healthcare students AMR conference. Students will be able to choose a module of previous presentations and will be able to view the content in their own time, at their own pace. The modules available in this pilot will be 'Human health', 'Animal Health', 'Dental', 'Vaccines', 'Innovation', 'Behaviour Change and Quality Improvement', and 'Multidisciplinary', and each module will contain between one and 3 videos from previous student conferences.

## 9. Keep Antibiotics Working evaluation

### Introduction

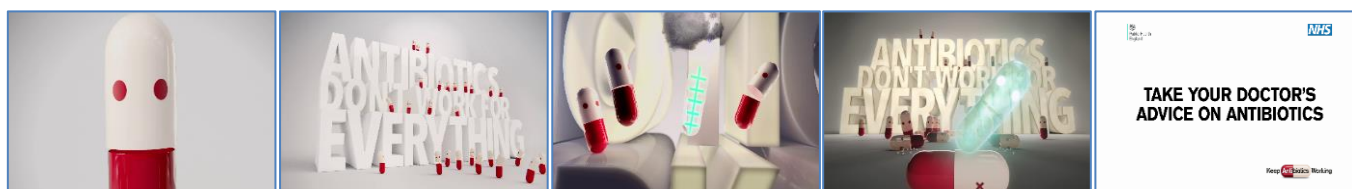
Keep Antibiotics Working is a social marketing campaign that ran from 2017 to 2019. It was England's first attempt to use marketing and communications as part of an integrated strategy to combat antibiotic overprescribing. The campaign was piloted in the North West region in 2017, to assess impact, before being rolled out nationally.

The campaign targeted the general public, with a particular focus on groups most likely to use antibiotics (women aged 20 to 45 who have primary responsibility for family health and men and women aged over 50), and healthcare professionals.

This was a sophisticated multi-channel campaign, involving broadcast advertising (a television commercial, video on demand, radio, newspaper advertising and posters) plus highly targeted and contextually relevant advertising in social media, engagement with the news media, stakeholders and other partners. People who were searching online for information on cold and flu were served with an advert encouraging them to go to the pharmacy instead of the GP. The direct-to-public communications were supplemented with resources that prescribers could download and customise for their surgeries. Marketing materials were supplied to all GP practices, and healthcare professionals ordered over 270,000 additional leaflets and posters for their surgeries and 19,000 self-care prescription pads (Source: PHE Campaign Resources Centre). Key visuals from some of the creative materials are shown below.

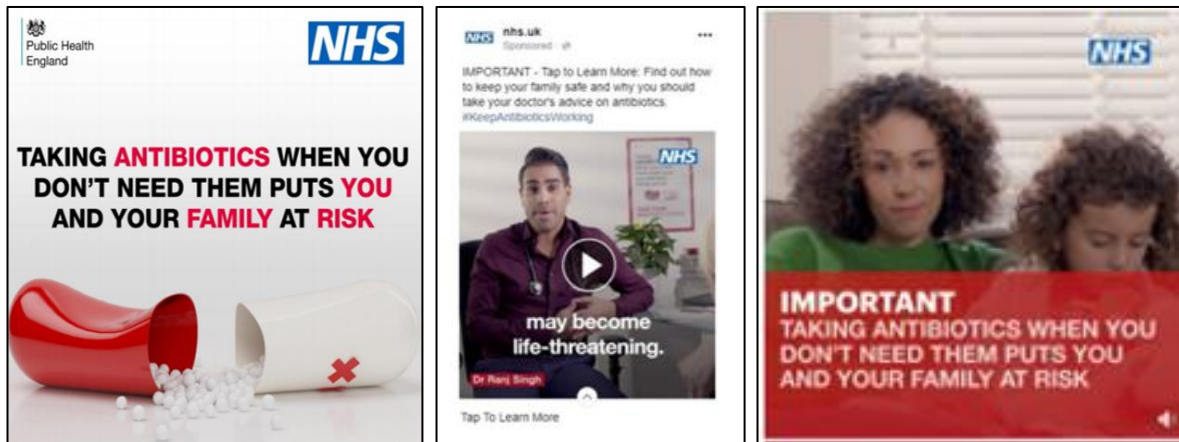
#### Figure 9.1 Key frames from the television commercial

Five still frames from the Keep Antibiotics Working television advertisement including: an animated antibiotic tablet, the words 'Antibiotics don't work for everything' and 'Take your doctor's advice on antibiotics'.



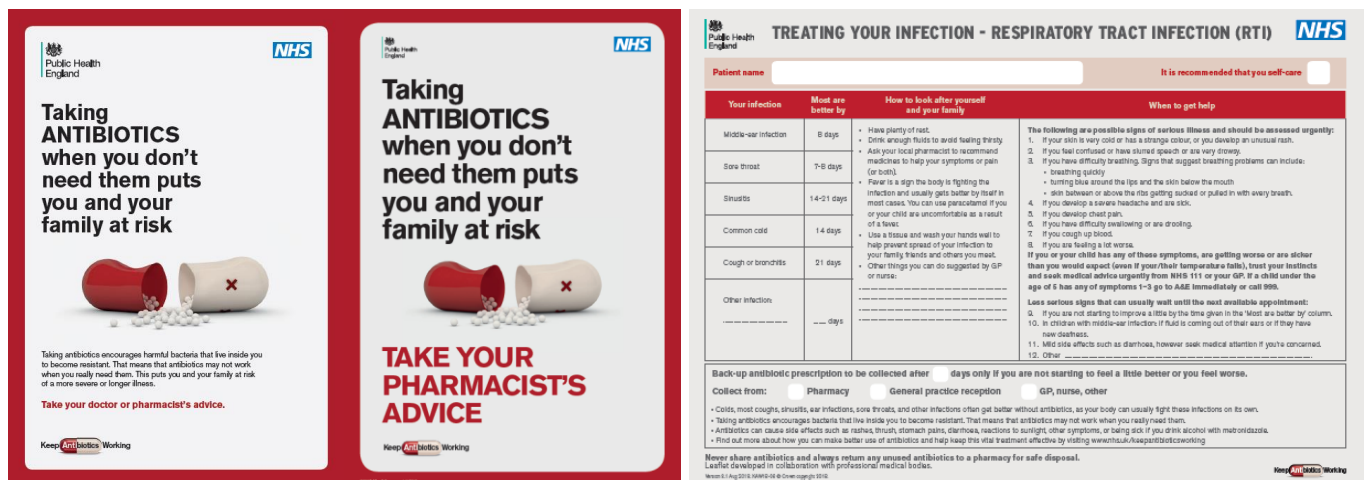
## Figure 9.2 Advertising in other channels

Adverts that appear in digital spaces, featuring a media medic and a parent and her child, with the text 'Taking antibiotics when you don't need them puts you and your family at risk'.



## Figure 9.3 Materials for healthcare professionals

Posters that healthcare professionals can display in their surgeries, showing the animated antibiotic and the text 'Taking antibiotics when you don't need them puts you and your family at risk' and a prescription pad, with the words 'Treating your infection'.



These and other resources are available [online](#).

## Development of the campaign

In common with all PHE marketing and communications campaigns, Keep Antibiotics Working was grounded in the best available evidence, including original research (qualitative and quantitative) commissioned for the project, analysis of prescribing data, and extensive clinical and stakeholder engagement. Development of the campaign followed the Government Communication Service's OASIS (Objectives, Audience Insight, Strategy, Implementation and Scoring) model and, additionally, conforms to the Wellcome Trust's key principles for communicating AMR effectively ([226](#)).

Research with prescribers and the public ([227](#), [228](#)) uncovered a number of pertinent insights that guided the development of the campaign, including that:

- patients had limited understanding of AMR, with many misconceptions (for example, that antibiotics are effective against colds and flu)
- when patients did recognise AMR as an issue, for most, this did not have personal relevance (that is, it is a massive, global issue, to be solved by the scientific community developing more and better antibiotics, against which their personal actions are insignificant)
- among those who did recognise that they should not always expect antibiotics, there was a difference between ‘cold state’ thinking (rational, prosocial thinking that people readily engage in when they are well) and ‘hot state’ thinking (a more anxious and needy state, which people find themselves in when they are, or someone they love is, unwell)
- there is a social gradient in awareness of AMR, with people in socioeconomic groups ABC1 tending to be better informed than those in groups C2DE. Other inequalities persist, for example, males know less about AMR than females. Some ethnic minorities are also more likely to expect to receive antibiotics, particularly if they grew up in countries where these were available over the counter

At the heart of antibiotic overprescribing is a transaction between patient and doctor, which could be described as follows: The patient expects antibiotics, which the GP, who has limited time for the appointment, can feel under pressure to prescribe. If antibiotics are prescribed, the patient credits them for their recovery, even though they might have got better anyway. This reinforces the behaviour, so asking for antibiotics becomes normal.

Neither patient nor GP gets a ‘reward’ for best practice in this cycle, which can be hard to disrupt ([228](#)).

Using insights from behavioural science, the campaign sought to influence this transaction by:

1. Reducing patient expectation of or demand for antibiotics when these are not needed, by making the issue of AMR personally relevant. This was communicated via messaging that explained that overuse of antibiotics by any individual increased the likelihood that they would not work for that individual when really needed.
2. Increasing prescribers' confidence in resisting pressure to prescribe antibiotics when not needed. This included ‘priming’ patients not to expect antibiotics (for example providing GPs with campaign materials to display in waiting areas) and investing in ‘self-care prescribing pads’ which offered GPs something physical to give to patients to counter the loss aversion of leaving the practice without antibiotics.

To reinforce both of the above (and to counter other risky behaviours, such as hoarding or sharing antibiotics), all materials reinforced the importance of taking your doctor's advice.



**Figure 9.4 Healthcare professionals demonstrating examples of AMR prescribing pads and other customisable assets**



## Evaluation methods

A rigorous evaluation programme was put in place, to quantify the impact of the campaign, allow for year-on-year optimisation of creative and channel mix and so that learnings could potentially be shared with other countries.

The evaluation involved:

- 6 waves of quantitative research with the public (one pre and one post each burst of advertising for each of the 3 years in which the campaign ran) carried out on PHE's behalf by leading independent market research company, Kantar – each wave involved a minimum of 1,000 respondents, with the sample boosted among key sub-groups, such as mothers of children aged 0 to 16
- 3 waves of quantitative research with general practitioners (one post each burst of advertising), also carried out by Kantar – each wave of research had approximately 300 participants
- analysis of prescribing data
- further in-depth qualitative analysis, to allow for annual refinement of the core creative assets

Additionally, response levels and cost per click for the digital components of the campaign were monitored in real-time, so that resources could be focused on the best-performing adverts.

A holistic evaluation, which brought all these data sources together, was provided by our evaluation partner, Wavemaker. We are currently working on submission of the evaluation findings to a peer reviewed journal.

## Key performance indicators

Before launch, the team set primary and secondary key performance indicators for the campaign, working with their agency partners, and taking account of what had been achieved by campaigns on other subjects, but with comparable spends.

Primary indicators are:

- at least 53% of the public to report they are very unlikely to ask GP for antibiotics for self
- at least 38% of the public to report they are very unlikely to ask GP for antibiotics for child

Secondary indicators are:

- campaign recognition: at least 56% of the public to recognise the campaign
- understanding of core messages: at least 29% to agree it is definitely true that 'antibiotics will stop working for you if taken for the wrong things'
- demand reduction or personal risk: at least 36% of the public to agree that 'taking antibiotics when you don't need them puts you and your family at risk of antibiotic resistant infections'
- demand reduction or increased concern: at least 37 to 39% of the public choosing 5 to 7 (on a scale of 1 to 7), for their level of concern about antibiotic resistance for themselves personally and 46 to 49% of the public choosing 5 to 7 for their level of concern about antibiotic resistance for their children
- supporting healthcare professionals: at least 70% of GPs to agree that 'the advertising makes me more confident to say no to patients asking for antibiotics when they aren't needed'

## Summary of findings

The campaign was successful in its ambition to alert the public to AMR. The campaign creative is well-liked, although fatigue was beginning to set in by the end of 2019.

A particular strength was the way the campaign supported the patient-doctor interaction, with GPs very positive towards the campaign and increasingly confident to refuse antibiotics when not needed.

The attempt to personalise the issue of AMR has been more challenging, although some progress has been made.

The campaign supported a range of actions across the healthcare system, which collectively resulted in a decline in antibiotic consumption of 7.5% between 2015 and 2019 (Source: ESPAUR report 2018 to 2019).



Since the start of the COVID-19 pandemic, the news landscape has changed. AMR is no longer at the top of the health agenda (or of people's health-related concerns). This will make AMR much harder to communicate in future.

## Performance against key metrics

The campaign saw many year-on-year increases over the 3 years of activity.

**Table 9.1 Key metrics over the KAW campaign period**

Key metrics over the campaign period	2017	2018	2019
Campaign recognition	56%	65%	71%
Percentage of GPs to agree that 'the advertising makes me more confident to say no to patients asking for antibiotics'	70%	77%	79%
Campaign message: 'antibiotics will stop working for you if taken for the wrong things' (def true)	29%	33%	35%
Personal risk: 'Taking antibiotics when you don't need them puts you and your family at risk of antibiotic resistant infections' (def true)	36%	45%	48%
Concern: level of concern about antibiotic resistance for self, (percentage choosing 5 to 7 on a scale of 1 to 7)	37 to 39%	41 to 34%	47 to 49%
Concern: level of concern about antibiotic resistance for child, (percentage choosing 5 to 7 on a scale of 1 to 7)	49 to 46%	53 to 54%	56 to 55%
% very unlikely to ask GP for antibiotics for self	53%	53%	48%
% very unlikely to ask GP for antibiotics for child	38%	34%	33%

Source: Wavemaker (2020) PHE AMR holistic evaluation 2017 to 2020

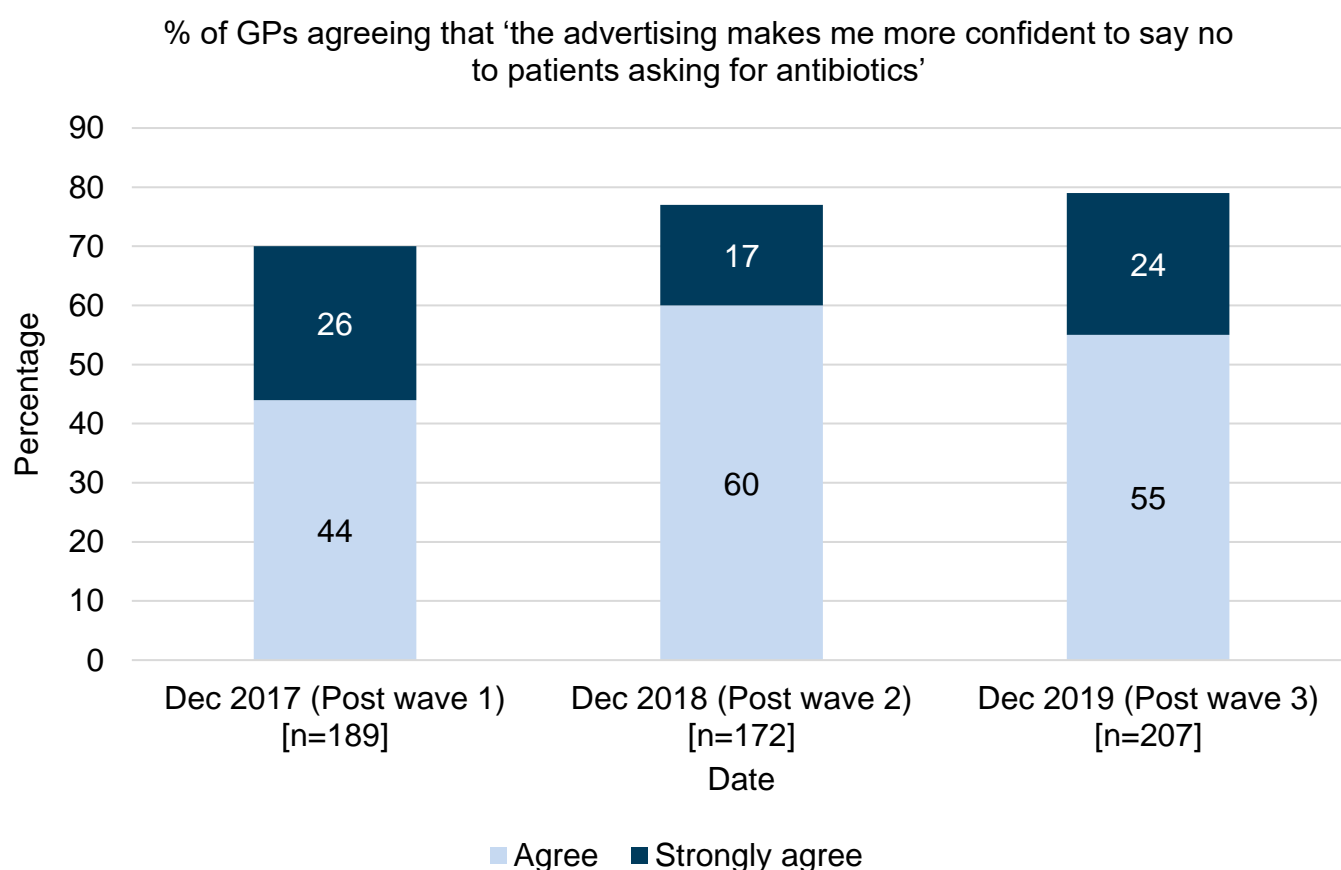
Sample sizes:

- Public: December 2017 (1,201), December 2018 (1,352), December 2019 (1,350)
- GPs (base = all aware of campaign): December 2017 (189), December 2018 (172), December 2019 (207)

## Impact of the campaign on prescribers

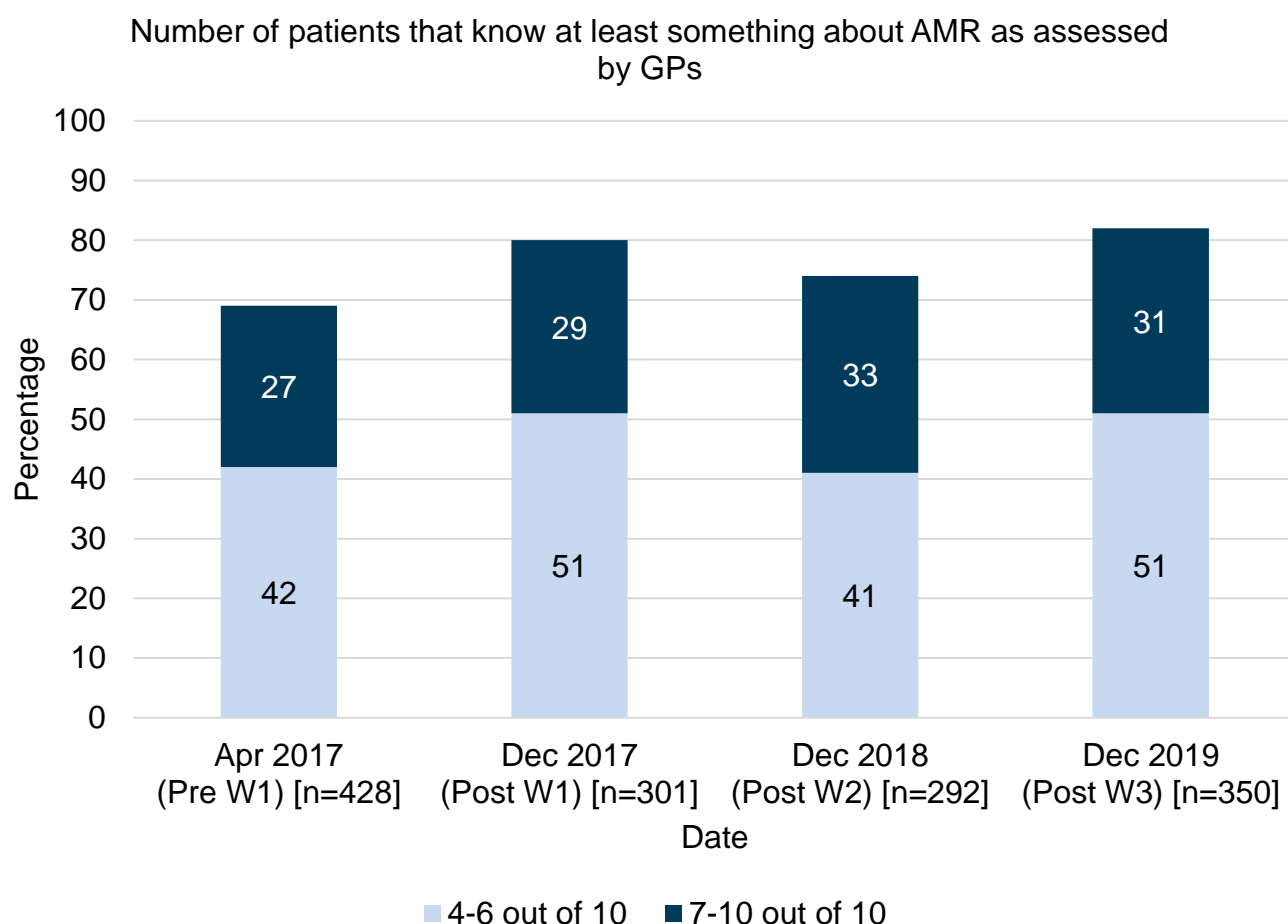
The campaign was received particularly well by GPs. The percentage of GPs reporting that ‘the advertising makes me more confident to say no to patients asking for antibiotics’ was high at launch and has been maintained over the 3 years. The percentage of GPs stating that their patients know at least something about AMR has also increased significantly.

**Figure 9.5 Impact of the KAW campaign on GPs**



The total percentage of GPs who agreed that the advertising campaign made them more confident to say no to patients asking for antibiotics rose from 70% in 2017 to 77% in 2018 and 79% in 2019.

**Figure 9.6 Number of patients that know at least something about antimicrobial resistance as assessed by GPs**

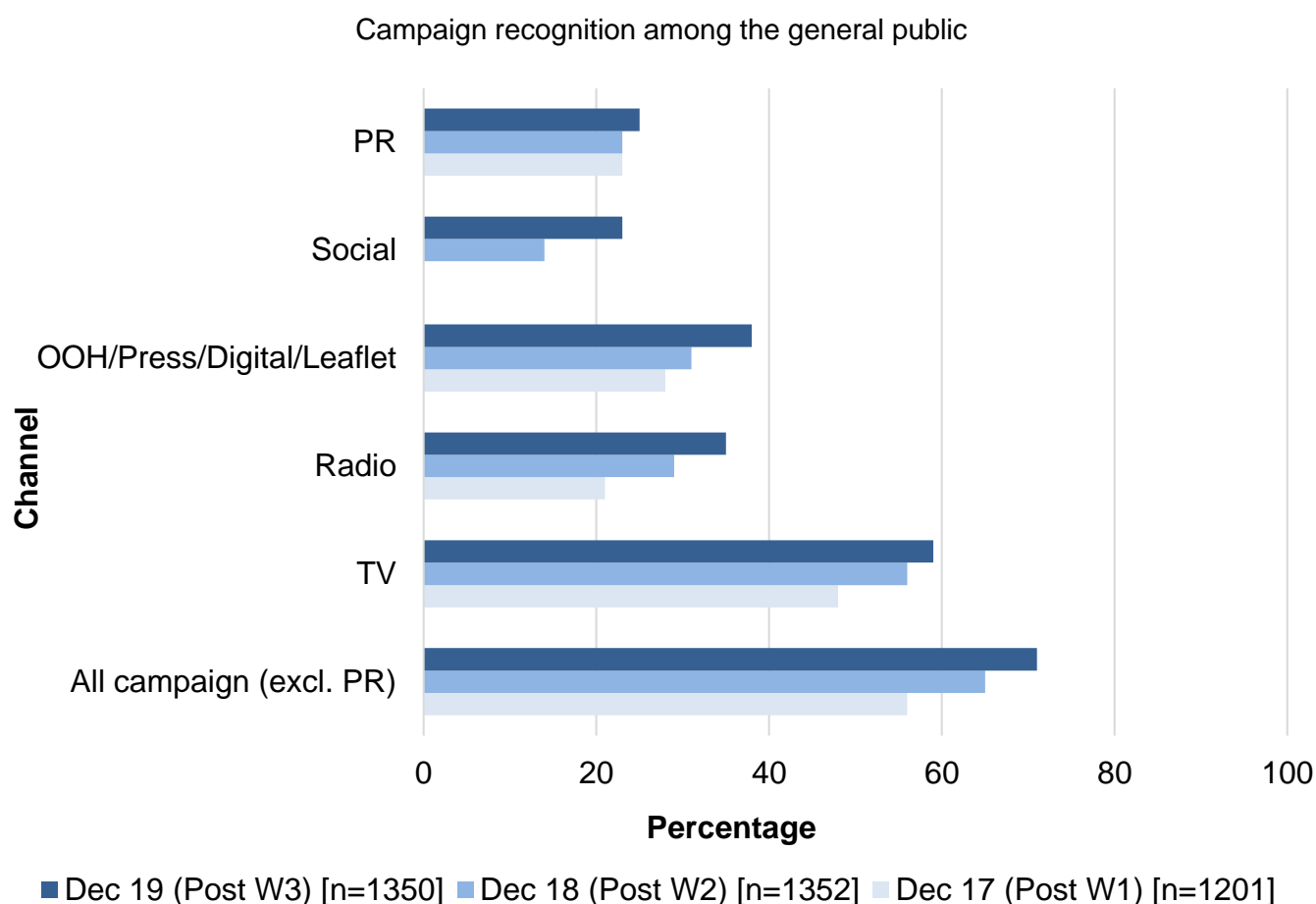


The total percentage of GPs agreeing that their patients know at least something about antimicrobial resistance rose from 69% before the campaign to 80% after the first wave of advertising. It dropped to 74% in 2018 but rose again to 82% after the campaign finished in 2019.

However, the issue remains, with 44% of GPs surveyed in 2019 reporting they are still frequently asked to prescribe antibiotics when they are not needed and they feel pressure to do so.

## Impact of the campaign on the public

Campaign recognition targets have been met every year, with the choice of broadcast channels successfully cutting through and achieving incremental reach. There was also substantial high-profile news coverage in support of the launch.

**Figure 9.7 Campaign recognition among the general public**

Campaign recognition increased from 56% in 2017 to 65% in 2018 and 71% in 2019. The most recognised element of the campaign was the television advert, which was recognised by 48% of the public in 2017, 56% in 2018 and 59% in 2019. Awareness of other channels – radio adverts, posters, leaflets, digital advertising, social media and PR – were lower, but also increased.

The campaign messages cut through, particularly in the first year with the campaign (Table 9.2).

**Table 9.2 Percentage of the general public agreeing they always take their doctor's advice b. Percentage of the general public that agree 'Antibiotics will stop working for you if taken for the wrong things'**

a.

Date	Don't know	Strongly disagree	Tend to disagree	Tend to agree	Strongly agree	Net agree
Apr 2017 (Pre W1) [n=1,000]	3	1	4	45	46	91
Dec 2017 (Post W1) [n=1,201]	4	1	4	40	51	91

Date	Don't know	Strongly disagree	Tend to disagree	Tend to agree	Strongly agree	Net agree
Oct 2018 (Pre W2) [n=1,350]	2	1	6	39	52	91
Dec 2018 (Post W2) [n=1,352]	3	2	4	36	55	91
Oct 2019 (Pre W3) [n=1,572]	3	2	6	32	56	88
Dec 2019 (Post W3) [n=1,350]	2	2	5	38	53	91

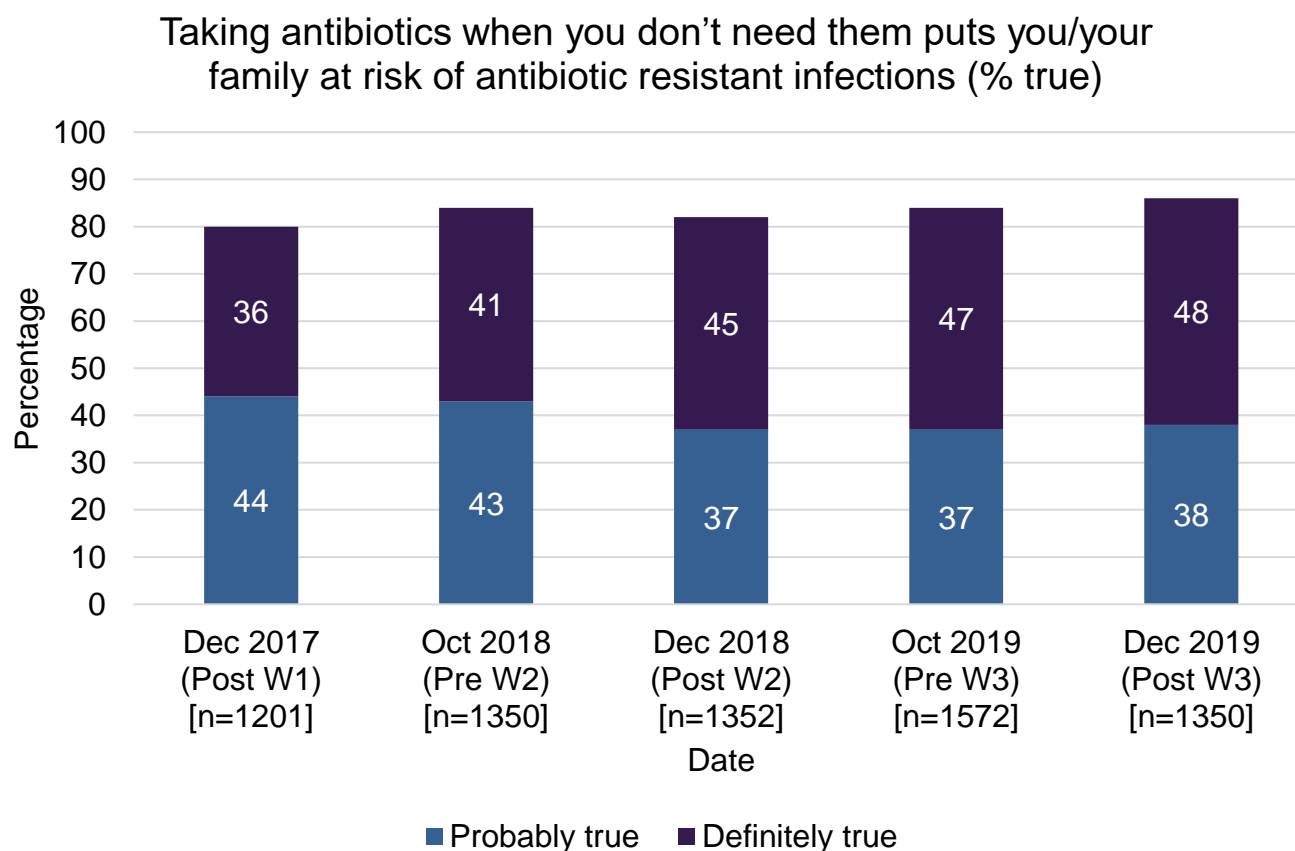
**b.**

Date	Don't know	Definitely false	Probably false	Probably true	Definitely true	Net true
Apr 17 (Pre W1) [n=1,000]	15	2	14	47	23	69
Dec 17 (Post W1) [n=1,201]	13	2	9	47	29	76
Oct 18 (Pre W2) [n=1,350]	11	1	10	47	30	77
Dec 18 (Post W2) [n=1,352]	13	2	8	45	33	77
Oct 19 (Pre W3) [n=1,572]	9	2	10	45	34	79
Dec 19 (Post W3) [n=1,350]	9	2	12	43	35	78

Overall, attitudes towards the creative remain positive: in 2019, 85% agreed the adverts were clear and easy to understand, 70% agreed the adverts are attention grabbing and 71% thought the adverts stood out. However, 18% of respondents said they were fed up with seeing the advertising, a significant increase on the previous year, suggesting that the campaign may require a creative refresh for future years.

The campaign has also resulted in a significant increase in people believing that taking antibiotics when not needed increases personal risk (Figure 9.8) and improvements in 'hot state' actions (Figure 9.9).

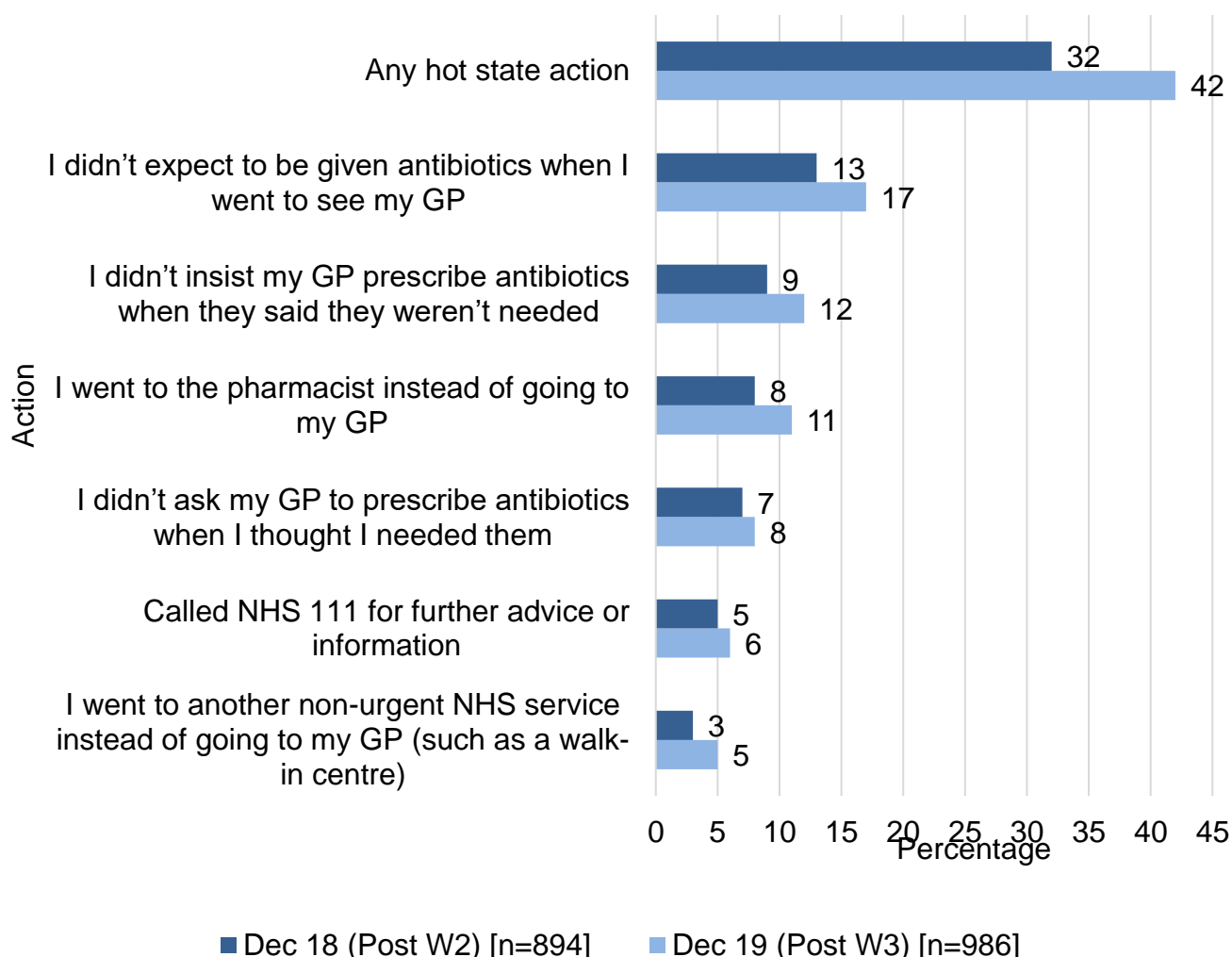
**Figure 9.8 Percentage of people believing that taking antibiotics when not needed increases personal risk**



Among members of the public who were aware of the campaign, agreement that the statement 'taking antibiotics when you don't need them puts you/your family at risk of antibiotic infections' is probably or definitely true rose from 81% in 2017 to 86% in 2019. Those saying that the statement was definitely true rose from 36% in 2017 to 48% in 2019.

**Figure 9.9 Improvements in ‘hot state’ actions**

Hot state actions taken as a result of seeing the campaign  
(based on those who recognised any element of the campaign)



Among those aware of any element of the campaign, desirable ‘hot state’ actions (such as not insisting on antibiotics) improved following the campaign. All desirable actions increased from 32% in 2018 to 42% in 2019. The most common actions were: ‘I didn’t expect to be given antibiotics when I went to see my GP’ (increased from 13% to 17%); ‘I didn’t insist my GP prescribe antibiotics when they said they weren’t needed’ (increased from 9% to 12%) and ‘I went to the pharmacist instead of going to my GP’ (increased from 8% to 11%).

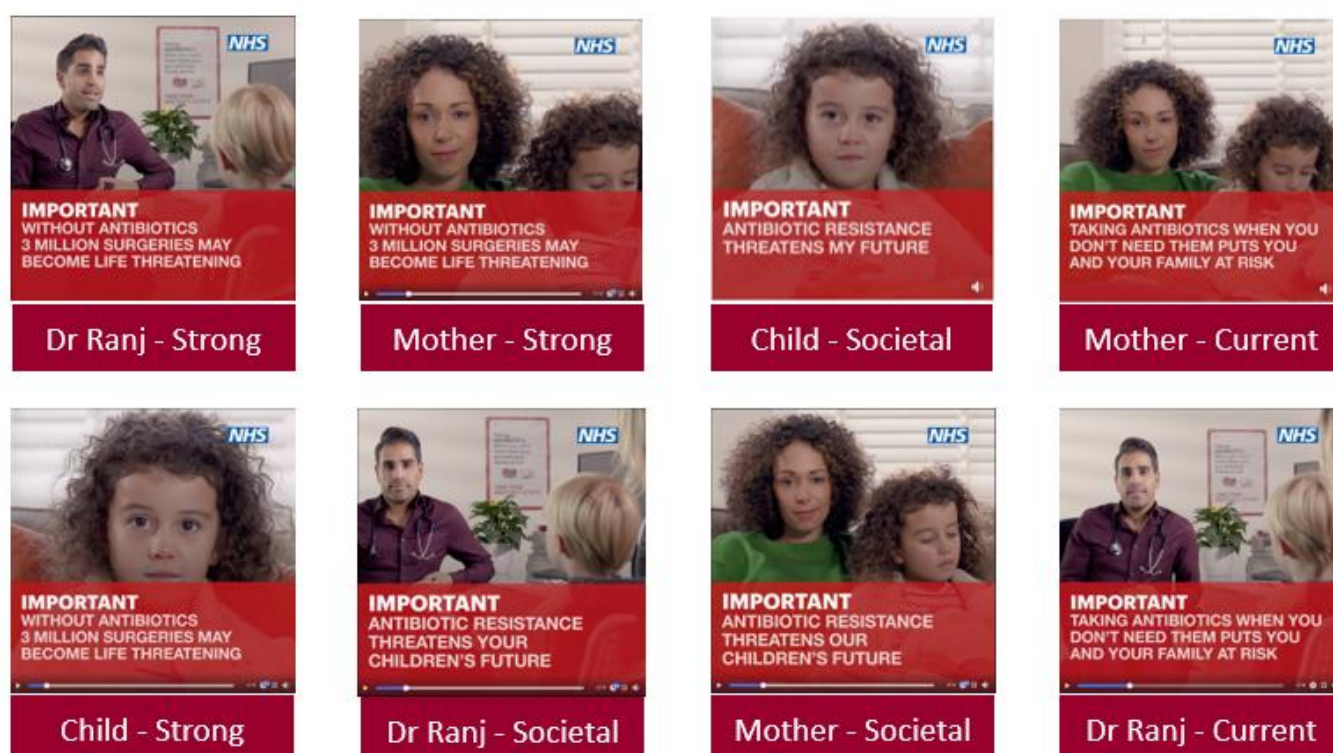
## How the campaign has evolved in response to the evidence

Over the 3 years the campaign has been running, social and digital display channels have become increasingly focused on tackling personal relevance, with the creative adapted from the main campaign to better resonate with specific audiences, such as parents. Facebook,

Instagram and Twitter have performed especially well, using a mix of creative treatments, featuring a prominent media medic and, for personal relevance, different treatments of parents and their children.

### Figure 10 Creative content for the KAW campaign

A variety of adverts for digital spaces, comparing different visuals (a media medic, a mother and her child, and the child in isolation) with different headlines (including 'Important: without antibiotics 3 million surgeries may become life threatening'; 'Important: antibiotic resistance threatens my future' and 'Important: taking antibiotics when you don't need them puts you and your family at risk').



A/B testing of different creative executions showed that Doctors, Nurses and Pharmacists can give you advice on antibiotics' outperformed 2 alternatives: 'There are on average 65 new antibiotic resistant infections per day in the UK' and 'Without antibiotics, more than 3 million surgical operations and cancer treatments a year may become life-threatening'.

## Impact of COVID-19

Since 2017, interest from the news media in AMR has declined, with COVID-19 taking priority from the end of 2019 to the present day. It is likely that maintaining personal relevance for AMR will be challenging, given the immediate and real threat of coronavirus to many of our key audiences.



## Conclusion

The evaluation of the Keep Antibiotics Working campaign proves the concept that marketing and communications can contribute to a reduction in antibiotic prescribing, as part of a range of actions across the healthcare system.

Specifically, the campaign has been successful in changing the climate around antibiotic prescribing, supporting patients to self-care and giving confidence to GPs to prescribe antibiotics appropriately.

As Professor Dame Sally Davies, chief medical officer when the campaign was commissioned, said:

“PHE used deep insight into the relationship between healthcare professional and patient and behavioural science to remodel that relationship, in a way that is better for the patient and more sustainable for the healthcare system – and indeed humanity – in the long term... I would add that many healthcare professionals have personally told me how useful this campaign is to them, in their fight to conserve our precious stocks of antibiotics.”

Given the ongoing impact of the pandemic, communicating about antimicrobial resistance may be increasingly challenging. Much has changed since the most recent quantitative research into the campaign (December 2019). Further research would therefore be recommended to assess attitudes to antibiotics and usage in the pandemic era to help refine any future campaign activity.

## 10. Research

### Introduction

A variety of research, spanning disciplines, has been undertaken in the field of healthcare-associated infections (HCAI) and antimicrobial resistance (AMR), from improving understanding of the mechanisms of antibiotic resistance, to designing and evaluating intervention strategies. This research has improved the evidence base for public health, with many studies having a clear focus on translation for public health action. A list of 2020 to 2021 publications is provided in the annexe.

The HCAI and AMR research and development priorities, encompass 4 main areas:

1. Data science – including enhanced data collection and linkage, as well as maximised use of such data to gain insight.
2. Transmission – increasing understanding of the burden and risk factors for carriage, infection and serious clinical outcomes and to understand and quantify mechanisms and dynamics of transmission.
3. Translational science – catalysing the development pathway for new rapid diagnostics, antibiotics, antimicrobials and vaccines for humans.
4. Interventions and evaluation – enhancing the evidence base for the design and evaluation of existing and novel control strategies, including infection prevention and control, antimicrobial stewardship (AMS), diagnostics, antimicrobials and novel alternatives, such as vaccines and host-directed therapies.

### Key research projects 2020 to 2021

#### Health protection research units

The National Institute for Health Research (NIHR) has funded 14 health protection research units (HPRUs) to run from April 2020 to March 2025 to address public health threats. The HPRUs are partnerships between universities and the United Kingdom Health Security Agency (UKHSA), forming multi-disciplinary centres of excellence across topic areas, with a focus on collaboration, training and knowledge sharing.

Two HPRUs were funded in the topic area of HCAI and AMR, led by Imperial College London and Oxford University, both in partnership with PHE/UKHSA.

Within the Oxford-led HCAI and AMR HPRU the 4 main research themes are:

1. Populations – which aims to exploit large-scale, rich, linked electronic healthcare record data from multiple sources to optimally automate routine surveillance and identify ‘at-risk’ populations.
2. Interventions – which will combine multi-disciplinary approaches to complex interventions, including behaviour change techniques, mathematical modelling and whole genome sequencing (WGS), to develop, improve, pilot and test approaches to, and tools for, AMS and management of key HCAI and AMR threats, and target interventions to those most at-risk.
3. Contexts – which will increase our understanding of the contexts within which HCAI and AMR proliferate and disseminate, identifying those that are the most important drivers for HCAI and AMR, and how we can manage and/or reduce their influence. This theme has a ‘One Health’ emphasis, considering humans, farms and livestock, external water and wastewater environments, and hospital ward and wastewater environments.
4. Sequencing – which will deliver public health WGS services to industry standards incorporating the newest components.

Within the Imperial-led HCAI and AMR HPRU the 4 main themes are:

1. Priority pathogens – which aims to understand how and why microbes become resistant, why we see this more in some species or groups than others, how to detect which infections are drug resistant and why some patient groups are more at risk than others.
2. Precision prescribing – which will work to optimise antimicrobial prescribing, preserving their effectiveness and minimising AMR by tailoring prescribing to the individual and the infection.
3. Practice, design and engineering – which will explore ways of reducing HCAI/AMR through the use of intelligent design. It will consider redesigning the ways in which information is captured or presented to improve practice and behaviour, physical environments and patient pathways to reduce risk.
4. Population health and policy – which will link large health data sets available locally and nationally. Develop methods and tools for understanding risk at a population level and where to target action. It will also allow us to evaluate the impact of policies and interventions, including any unintended consequences.

Both HPRUs have a focus on utilising a range of health-systems data such as: antimicrobial usage data, patient demographics, infection episodes, surveillance and microbiology data in a range of investigations from theoretical and modelling approaches through to basic science investigations, all with the purpose of informing and helping to combat AMR and HCAs.

Both build on the research, infrastructures and collaborations established in the previous HCAI and AMR HPRUs, which ran for 5 years, ending in March 2020. These previous HCAI and AMR HPRUs conducted an impressive array of research which in itself impacted patient and public

health, but importantly also established the foundations for ongoing research with even greater emphasis on translation. The main outputs and impacts of the first HCAI and AMR HPRUs are provided in the annexe.

## Open innovation for AMR

NIHR AMR Capital funding was awarded for an initiative to generate an 'open access' virtual centre for AMR-innovation and research, comprising 3 areas, namely a data model, an intervention model, and a healthcare environment model.

### Data model: unified infection data set

There is currently no single national data set that gathers data on all clinically significant infections with their corresponding antimicrobial susceptibility results, healthcare pre-exposure and clinical correlates. Through NIHR AMR Capital funding, the Unified Infection Data Set (UID) will provide linked patient-level data on infection episodes, hospital admissions and, in the near future, primary care prescribing and weekly mortality data. The UID will perform routine and on-demand linkage of data from core data sets held by PHE/UKHSA and will be scalable to accommodate other data sets in future. UID users are also able to upload their own custom data in the form of line lists for onwards linkage. The UID will assist PHE/UKHSA in executing its health protection functions, including surveillance, epidemiological analyses and generation of public health intelligence. UID gives scientists access to data sets of de-duplicated and linked data for reproducible investigation into infection and AMR. A Beta version of the UID has been developed, has passed data validation testing and is being extended to incorporate COVID-19 case data. The UID is scheduled to go live to UKHSA scientists in October 2021.

### Intervention and healthcare environment models

The 5-year AMR National Action Plan and 20-year vision documents, published by Department of Health and Social Care (DHSC) in 2019 ([229](#)) highlighted the need to broaden the pipeline of therapeutics, with novel approaches from a wider scientific community, to ensure that new therapies are available in the future. With this infrastructure funding, new capabilities allow non-traditional antimicrobial agents to be evaluated against clinically relevant, multidrug resistant pathogens, working in partnership between academia, industry and PHE/UKHSA. This Open Innovation programme builds on previous work at PHE, which has developed a detailed screening cascade for drug evaluation, resulting in a number of publications ([230](#), [231](#), [232](#), [233](#), [234](#), [235](#)) and supporting the ongoing evaluation of potential therapies. Innovative approaches are also being developed for assessing antibiotic susceptibility to support evaluation of antimicrobial agents and as a possible basis for new susceptibility tests to support evidence-based prescribing.

Within the 5-year AMR National Action Plan ([236](#)) for how the UK will contribute to containing and controlling AMR, there is acknowledgement that more research on how the built environment contributes to the spread of AMR and how it can be designed to limit such spread is required. Assessing the impact of design modifications in a real-life clinical setting is difficult, especially if, although potentially transformative, it would disrupt clinical practice. To address

this, a simulated full-scale hospital ward has been designed to study the built environment and its impact on AMR. This unique research facility will be used to help ‘design out’ HCAs and generate evidence to inform strategies and investment to deliver better infection prevention and control.

## AMR in sexually transmitted infections

Research and development in PHE/UKHSA relating to AMR in sexually transmitted infections (STIs) is focused on 2 main pathogens where the burden of AMR is greatest, *Neisseria gonorrhoeae* and *Mycoplasma genitalium*. In collaboration with University College London, 3 STI Health Protection Research Unit (HPRU) projects with an AMR focus are underway.

### *Neisseria gonorrhoeae*

A project is underway to look at the feasibility and acceptability of using real-time WGS data from *N. gonorrhoeae* diagnosed in sexual health clinic attendees to guide clinical decision making and individualised patient interventions for STIs, HIV and blood-borne viruses, including the detection of genotypic antimicrobial susceptibility.

The second project is the development and roll-out of a molecular test that detects ceftriaxone resistance in *N. gonorrhoeae* directly from clinical specimens without the need for a cultured isolate. As only approximately 50% of gonorrhoea cases have associated successful cultures, this means that ceftriaxone (current first-line treatment option) resistance detection is not possible for nearly half of all UK gonorrhoea cases. The assay will be used in a pilot ceftriaxone resistance molecular surveillance programme as well as within reference microbiology to identify treatment failures and subsequently interrupt transmission.

In collaboration with the European Centre for Disease Prevention and Control (ECDC) and Örebro University Hospital, UKHSA will perform WGS on gonococcal isolates collected in 2020. The WGS data will be used in conjunction with the phenotypic and epidemiological data to examine resistance determinants, monitor AMR trends over time, identify AMR clones and transmission networks across Europe. To provide guidance to UK laboratories, in collaboration with Public Health Wales, UKHSA is evaluating a number of different agar media and gradients strips for susceptibility testing of *N. gonorrhoeae* to ensure laboratories produce reliable AMR results.

Other gonococcal work includes investigating the increase of tetracycline resistance in *N. gonorrhoeae* and the association with men who have sex with men (MSM) following reports of self-sourced doxycycline use to prevent sexually-transmitted infections, as well as updating England’s response plan to control and manage the threat of multi- and extensively-drug resistant *N. gonorrhoeae*. This will include updates on:

1. Strengthening and raising awareness of treatment failure reporting.
2. Enriching surveillance data with WGS information.
3. Disseminating data on antimicrobial resistance in *N. gonorrhoeae* in real-time to relevant stakeholders.

### *Mycoplasma genitalium*

For *M. genitalium*, a feasibility study on culturing isolates from urine specimens to establish antimicrobial susceptibility testing assays to provide phenotypic susceptibility profiles of cultured isolates to allow correlation of minimal inhibitory concentrations (MICs) with clinical treatment outcome is on-going as part of the STI HPRU. Other PHE activities for *M. genitalium* include determining mutations in the *gyrA* gene in strains harbouring non-wild-type *parC* sequences to investigate the presence of mutations associated with fluoroquinolone treatment failure. Assessing risk factors associated with macrolide and fluoroquinolone resistance in *M. genitalium* will be determined within the pilot for *M. genitalium* AMR surveillance.

## Behavioural research insights on antibiotic prescribing: prescriber and public perspectives

Exploratory evaluation of the impact of COVID-19 on the patient consultation pathway  
The COVID-19 pandemic has had an unprecedented impact on the primary care patient consultation pathway. A qualitative study among health care professionals (HCPs), including general practitioners (GPs), nurses and community pharmacists during the first year of the COVID-19 pandemic, explored their experiences and views on the future of primary care patient pathways.

Semi-structured interviews explored how COVID-19 has impacted the following core areas of patient care:

1. The organisation of the physical space where the patients are seen.
2. Organisation and prioritisation of face-to-face consultations.
3. Organisation of remote consultations.
4. Remote prescribing.
5. Impact of changes on HCPs.
6. Impact of changes on patients and patient care.
7. Impact of changes on the future of primary care patient pathways.

Research findings pointed to the diversity and polarisation of experiences of HCPs with a variety of positive and negative impacts (Table 10.1), as well as changes to the patient profile (for example, fewer respiratory and urinary tract infection consultations).

**Table 10.1 Identified advantages and disadvantages to organised structure changes during the first 12 months of the coronavirus pandemic**

Workload and efficiency	Benefits	Flexible working.
		More time to see patients.
		More efficient follow ups.
	Disadvantages	Urgent need to upskill.
		Increased workload for some staff.

		Initial triaging not sufficient especially for complex issues.
		Poorly set up online registration systems.
		Concern about managing backlog.
Remote triage and consultation	Benefits	Improved patient care.
		Faster more efficient service.
		Relaxed patients.
	Disadvantages	Difficulties in diagnosing some patients due to lack of physical examination.
Communication	Benefits	Increase in communication and collaboration between local surgeries and local specialist services at primary care level.
	Disadvantages	Deterioration in in-person communication.
		Increase in online message exchange leading to staff being overwhelmed.

HCPs expressed varying views regarding antibiotic prescribing depending on the condition and patient situation. However, overall the majority felt that their prescribing thresholds were lower than before the pandemic. Reasons included:

- increased prescribing out of caution due to lack of physical examination
- increased patient expectation for antibiotics
- increased dispensing of rescue packs
- increased patient interest in their own health that is, patients who previously were not taking their long term antibiotic therapy now requesting their treatment

Findings such as these are valuable to help facilitate the delivery of appropriate consultations and for informing future intervention development.

#### Motivations for antibiotic prescribing audit use within the primary care setting: a scoping review

Research suggests that antibiotic prescribing audits can be an effective AMS tool if used appropriately. However, outside of revalidation requirements little is known on how often audits take place or what motivates prescribers to audit. A scoping review of literature aimed to provide an overview of audit implementation in general practice and highlight key research gaps. Findings suggested that although much research has gone into developing audits, with evaluation demonstrating favourable outcomes under research conditions, little is known about whether prescribers continue to audit after the initial researcher implementation, or on the long-term effect of audit and feedback. No identified research examined prescriber motivation to carry out audits. Although audit use can bring positive changes in antibiotic prescribing behaviours, further research is required into prescriber motivation factors to ensure audit use continues over time.

### Incidence, healthcare-seeking behaviours and antibiotic use for respiratory tract infections (RTIs) during the COVID-19 pandemic: a population-based survey

To better understand the impact of COVID-19 on people's behaviour and attitudes towards and use of antibiotics, Ipsos MORI surveyed 1,676 adults in England between 26 February and 2 March 2021 and data was compared to that gathered in 2020.

Actions, either of self-management such as self-medicating or taking extra rest, or consulting a healthcare professional, all increased, suggesting individuals were more proactive and conscious of looking after themselves than in 2020. The expectations and realities of patients' engagement with healthcare services for their RTIs (for example, expectations of antibiotics or seeking advice), in 2021 versus 2020 are shown in [Figure 10.1](#). The proportion of people saying that they had completed their course of antibiotics increased significantly since 2020 (from 81% to 90%).

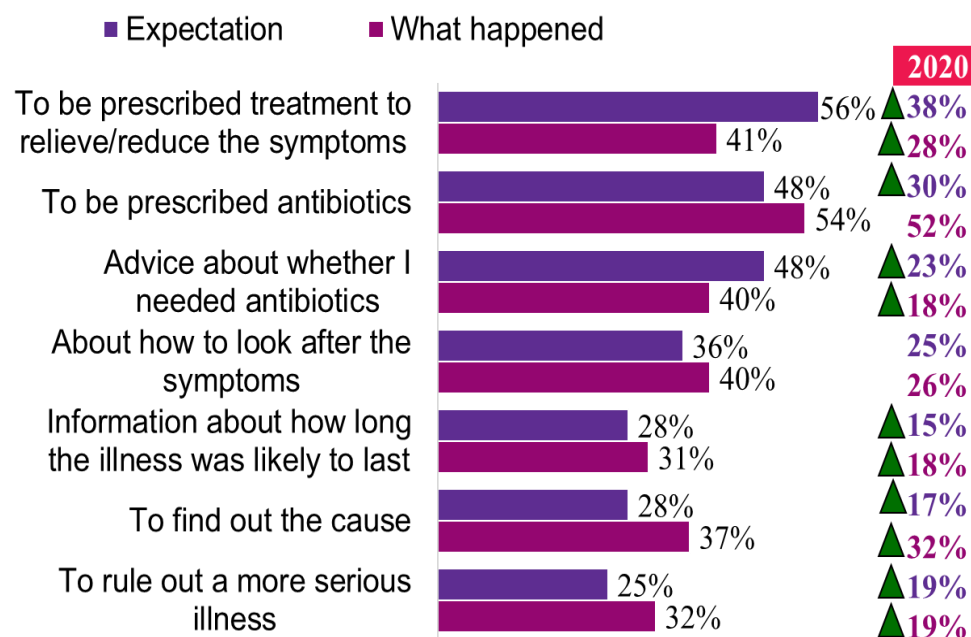


### Figure 10.1 What did the public expect compared to what happened when they visited a) GPs, out-of-hours or NHS walk-in; b) pharmacy for their most recent RTI

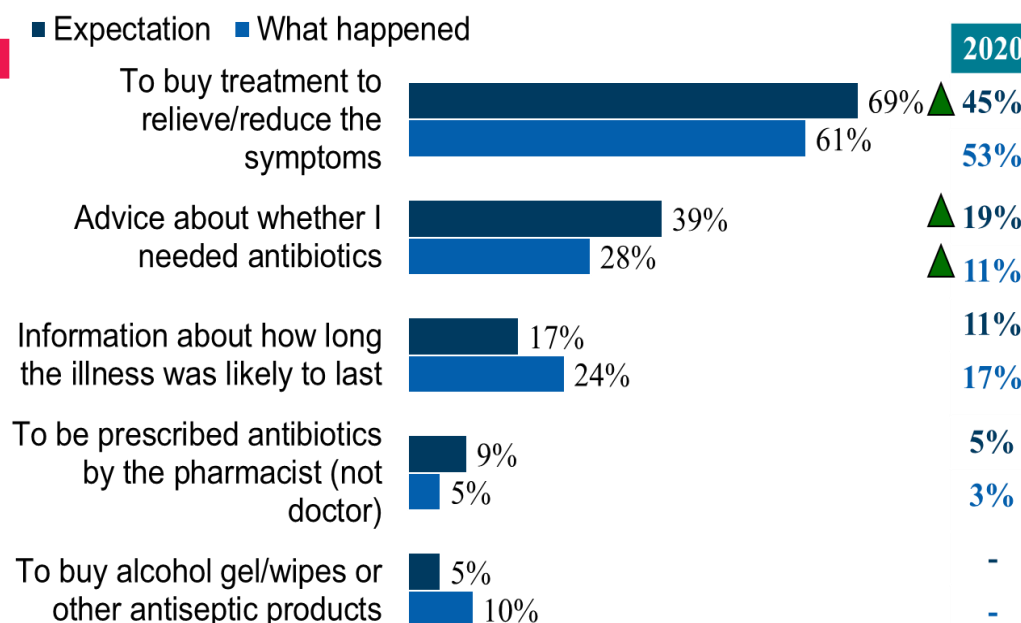
In addition, findings indicated that public support for delayed antibiotic prescribing for urinary, ear or throat infections increased significantly. Compared to if they fell ill pre-COVID-19, more individuals would accept delayed or back-up antibiotic prescriptions and fewer would take leftover antibiotics or those prescribed to another person. There was greater evidence of parents managing their child's illness independently of a healthcare professional, by either giving a non-prescription treatment, continuing with usual activities or encouraging extra rest.

### What did you expect and what happened when you consulted with: A) GP; B) Pharmacy for your most recent RTI?

#### A) GP/ Out-of-Hour/ NHS Walk-In



#### B) Pharmacy



Base: All adults aged 18+ in England who visited a GP/ walk-in centre (n=149; 2020 n=253); or pharmacy (n=65; 2020 n=78) for their most recent illness. Fieldwork dates: 26 February to 2 March 2021

▲ ▼ = significantly higher/lower than 2020

Knowledge of antibiotic resistance was mixed: 37% believed antibiotics are a fail-safe treatment and should be used if in doubt (consistent with 2020). However, fewer believed that there was nothing they or society could do to avoid antibiotics becoming ineffective.

### [Incidence, severity, help seeking, and management of uncomplicated urinary tract infection during the COVID-19 pandemic: a population-based survey](#)

Another online population-based survey, facilitated by Ipsos MORI was undertaken between 31 March and 13 April 2021 into the prevalence of Urinary Tract Infections (UTIs) and antibiotic use among 4,153 adult women in England with the objectives of determining patients' consultation pathways and whether tests and antibiotics were given.

Study results showed 43% of women who have ever had a UTI had an episode in the last year, with incidence highest among 16 to 34 year olds and women from an ethnic minority background. One quarter stated that their episode had been severe and nearly three-quarters that it affected their daily life. Of those with a UTI in the last year, 79% made contact with a HCP, 50% with their local GP, 21% with a pharmacist. Among those who did not seek advice, the reason was predominantly because their symptoms were not severe enough, although COVID-19 was a barrier to accessing healthcare services.

Of women who presented with a UTI: 43% provided a urine sample (67% of these confirmed); 63% were prescribed an antibiotic (9% delayed/back-up). Individuals who had one episode in the last year were more likely than others to be advised to take their antibiotics as soon as possible (93% vs. 89% overall), whereas 21% of those who had experienced between 3 and 4 episodes were prescribed delayed or back-up antibiotics versus 9% overall.

### [Reducing antibiotic prescribing in children: a systematic review of parent and child education interventions](#)

Antibiotic overuse remains a significant contributor to AMR worldwide. Children are frequent users of antibiotics, and by educating parents, caregivers and children about appropriate antibiotic use, there is the potential to reduce antibiotic demand. A systematic review, undertaken with the University of Bristol, aimed to identify and appraise the most effective methods and components of reducing demand through family education programmes.

Interventions to improve knowledge and understanding of appropriate antibiotic use delivered to parents, children or caregivers at a national, community or household level, and those which measured antibiotic prescribing rates or knowledge were reviewed.

## [Modelling and health economics](#)

Modelling and health economics research ranges from quantifying the health and economic burden of resistant infections, through to evaluation of interventions. Example research projects are described below:

### Quantifying the potential health and cost impact of antimicrobial resistance on surgical procedures

As well as increasing the difficulty of treating primary infections (such as respiratory or urinary tract infections), AMR poses an unknown risk to the safety of life-saving treatments that rely on antibiotic prophylaxis to reduce the risk of infection, as attempts to quantify this burden have been limited. These procedures include chemotherapy, common surgical procedures, emergency surgeries, as well as elective surgeries such as hip and knee replacements.

Work has been undertaken to develop a framework for quantifying the health and cost implications of AMR in the context of surgical procedures. Three pathways through which AMR impacts on the cost and health outcomes of surgery were identified: i) reduction in the efficacy of prophylaxis, potentially leading to an increase in the number of surgical site infections (SSIs); ii) reduction in efficacy of antibiotics used to treat SSIs, resulting in more severe outcomes; iii) withdrawal of non-essential procedures for patients where the risk-benefit profile is considered unfavourable.

A model structure has been developed allowing each of these effects of AMR to be quantified and 2 case studies have been explored; i) emergency hip fracture operation and ii) elective bowel resection for cancer patients. Evidence was sought from the literature to parameterise the model. Where evidence was sparse key parameters were prioritised for a structured expert elicitation exercise.

The framework developed in this project provides an important contribution to understanding the mechanisms by which AMR impacts on surgery, how these impacts can be quantified, the type of evidence required, and where evidence gaps could be addressed by further research. The framework provides the starting point for further analyses on the overall burden of AMR on SSIs that will be subsequently addressed in future research projects.

### Cost–benefit analysis of surveillance for surgical site infection following caesarean section

Surgical site infection surveillance enables hospitals to monitor rates of surgical site infection (SSI), compare their results to a benchmark and feedback the results to surgical teams to inform action to improve practice through infection reduction interventions and thus reduce infection rates. This in turn will reduce antibiotic prescribing.

Data linkage and modelling was used to estimate the economic burden of surgical site infection (SSI) following caesarean section and potential savings achievable through surveillance and feedback of data. Data from the caesarean section SSI surveillance cohort study ([237](#)) was linked to Hospital Episode Statistics Admitted Patient Care (HES APC), National Schedule Reference Costs and other sources in the model. The burden of infection was estimated for both community (28%) and hospital costs (72%), providing a more representative estimate of the overall economic burden of SSI to the health service.

Through assessment of costs, and modelling the impact of various surveillance strategies, the study demonstrated that the benefits of a surveillance strategy can outweigh the costs through reductions in incidence of SSI ([238](#)).

### Impact of AMR on health-related quality of life

In order to undertake economic evaluations of past and potential interventions that tackle AMR, an understanding of both the costs of AMR to the NHS and the impact of AMR on population health-related quality of life are necessary. As part of this work, in collaboration with the NIHR HPRU in HCAI and AMR at Imperial College London, a systematic literature review was conducted ([239](#)). This review highlights the lack of evidence in understanding the Quality-adjusted Life Year (QALY) impact of AMR on infections, such as bloodstream and surgical site infections. In light of this, research on how best to adapt established QALY methods and online burden calculators to estimate the QALY impact of AMR in England is being undertaken. This will be a key parameter in future cost-effectiveness evaluations of AMR-related interventions.

### Global research on AntiMicrobial resistance (GRAM) project

PHE is collaborating with the Global Research on AntiMicrobial resistance (GRAM) Project, the flagship project of the Oxford Global Burden of Disease (GBD) Group. GRAM is a collaboration between the University of Oxford Big Data Institute (BDI) and the Institute for Health Metrics and Evaluation (IHME) at the University of Washington and is funded by the UK Department of Health's Fleming Fund, the Wellcome Trust and the Bill and Melinda Gates Foundation.

The GRAM project aims to quantify the morbidity and mortality due to AMR and make this quantification comparable across diseases, locations and years included in the Global Burden of Disease study. This will inform both specialised audiences and the public on changes on AMR within and between countries, across time and comparatively to other aspects of global health.

### Model-based evaluation of CPE transmission and control

Mathematical and statistical modelling, utilising a range of surveillance and microbiological data, has been used to investigate transmission of carbapenemase-producing enterobacteriales (CPE) in English hospitals at both patient and within-host scales. Individual-based, stochastic mathematical models have been developed to simulate CPE transmission in hospitals of varying CPE prevalence across regions in England. In collaboration with Nottingham University, transmission parameters were estimated including both human and non-human sources of transmission. These models have been applied to evaluate the impact of admission screening protocols on CPE infection in patients and work is ongoing to further quantify the contribution of biofilms to the total nosocomial CPE transmission. At a within-host scale, whole genome sequencing data from a hospital outbreak of CPE, detected by routine surveillance, was investigated using a Markov model of plasmid transmission between bacterial hosts' lineages to estimate the plasmid's conjugation rate. This modelling highlighted complementary roles for both plasmid conjugation and clonal expansion in the emergence of this outbreak, which should be taken into account when devising effective surveillance strategies for CPEs.

### COMBACTE-CDI: Impacts of Testing and Antimicrobial Usage on *Clostridioides Difficile* Infection (CDI)

The true prevalence of *Clostridioides difficile* infection (CDI) has proven challenging to determine and without systematic testing in hospitals, the unchecked transmission of CDI can lead to outbreaks in more susceptible cohorts. As part of the COMBACTE-CDI project (within the Innovative Medicines Initiative, New Drugs 4 Bad Bugs programme), a stochastic, dynamic transmission model of CDI in hospitalised patients was developed, with the aim of examining the impact of testing rates and antimicrobial stewardship on the incidence of CDI nationally. The model estimates the true incidence of colonised and infected cases in the hospital setting from national sampling and testing rates. The model also predicts the effect of increasing or decreasing testing rates, as well as the effect of changes in the defined daily dose (DDD) of antimicrobials on the incidence of CDI. The model considers both the optimistic scenario of increased testing and decreased antimicrobial consumption as well as the potential scenarios of decreased testing and increased antimicrobial consumption as may be seen in some settings in response to the COVID-19 pandemic.

### Reducing Gram-negative Bloodstream Infections (GNBSIs)

The ambitions within the AMR National Action Plan ([240](#)) outline a reduction in healthcare associated Gram-negative bloodstream infections (GNBSIs) by 2024. With the aim of quantifying the most effective strategies and interventions for reducing GNBSIs, work is ongoing to investigate patient pathways that lead to GNBSIs, with a focus on urinary tract infection (UTI) (catheter and non-catheter related) or hepatobiliary pathways, considering hospital, community and long-term care facility (LTCF) acquired infections. An individual based mathematical model of patients and their pathways to GNBSIs has been developed to investigate and quantify (in terms of reduced incidence and resistance as well as costs) the potential benefits of different intervention strategies.

## 11. Stakeholder engagement

The ESPAUR Oversight Group comprises a wide range of stakeholders including the devolved administrations, professional and educational bodies, healthcare providers and regulators. Stakeholders have continued to contribute to tackling antimicrobial resistance (AMR) and promote good antimicrobial stewardship (AMS) whilst also supporting the COVID-19 response.

### British Infection Association (BIA)

The [British Infection Association](#) is the professional body representing NHS Infection Specialists and trainees in Microbiology, Virology and Infectious Diseases. The Association also has a growing Associate Membership made up of allied healthcare professionals working broadly in the field of infection medicine. It publishes the prestigious [Journal of Infection](#) and [Clinical Infection in Practice](#), a new open-access journal focused on the advancement of knowledge and discussion of clinical infection in practice.

During 2020 to 2021 the Association has developed new Best Practice Standards for the delivery of NHS Infection Services which include specific recommendations for the delivery of minimum antimicrobial stewardship activity in acute NHS Hospitals. These standards have been developed in close liaison with the Royal College of Physicians and the Royal College of Pathologists and are currently 'in press' with Clinical Infection in Practice.

The Association has begun working with the [Public Health England Standards for Microbiology Investigations](#) (SMI) to develop a series of Quick Reference Guides to support front-line clinicians select and interpret diagnostic tests to support appropriate antibiotic prescribing in secondary care. These will be published later in 2021.

### British National Formulary (BNF)

The BNF continues to update content in line with NICE's management of common infections guidance and any relevant national guidance on the use of antimicrobials in the management of COVID-19. These updates are highlighted to BNF users by the inclusion in the BNF changes record which is published monthly.

### British Society for Antimicrobial Chemotherapy (BSAC)

The [British Society for Antimicrobial Chemotherapy \(BSAC\)](#) represents one of the world's most influential networks of infection specialists (including, but not limited to, infectious disease physicians, microbiologists, pharmacists, and researchers).



It provides high-quality open access support which takes many forms: free membership, workshops, conferences, and research publications via its [Journal of Antimicrobial Chemotherapy](#), and the online open access education and research journal, [JAC-Antimicrobial Resistance](#).

It also provides:

- the longest-running resistance surveillance programme in Europe, offering more than 60,000 isolates to the UK's research community
- a national susceptibility testing programme, supporting harmonisation of methodologies with EUCAST
- the Outpatient Parenteral Antimicrobial Therapy (OPAT) programme, bringing care closer to home
- an [open access virtual learning platform](#), which itself includes:
  - massive open online courses on antimicrobial stewardship (AMS), accessed by tens of thousands of learners from 135 countries, with translations in Mandarin, Russian, Spanish, Brazilian Portuguese – and a bespoke course for the African continent
  - e-learning courses on Gram-negative infections, rapid diagnostics, wound management, and vaccines – among others
  - AMS fora for: Middle East and North Africa; nurses; pharmacy technicians; Commonwealth pharmacists
  - an e-Book on AMS
- publication of evidence-based guidelines and good practice recommendations
- the secretariat for the [All-Party Parliamentary Group on Antibiotics](#); meetings with UK Government representatives and the NHS; public engagement through [The Mould that Changed the World](#), and campaign partnerships through [Stop Superbugs](#)

It responded to COVID-19 by reinventing its grants programme, establishing an info hub, and commissioning articles from scientists and healthcare professionals.

The last 12 months have also seen the society plan for the:

- transfer of the resistance surveillance programme to St Andrews University and the University of Dundee
- launch of an antimicrobial drug registry
- launch of a global accreditation scheme for AMS

Website: [www.bsac.org.uk](http://www.bsac.org.uk)

Twitter: [@BSACandJAC](https://twitter.com/BSACandJAC)

## Care Quality Commission (CQC)

The Care Quality Commission makes sure health and social care services provide people with safe, effective, compassionate, high-quality care and encourages care services to improve. We regulate against the Health and Social Care Act 2008.

This year CQC carried out Infection Prevention and Control (IPC) inspections of adult social care homes and published a [report](#) in November 2020. In secondary care we have monitored how hospitals ensured robust infection prevention and control and carried out focused IPC inspections where we had concerns about a provider's oversight of infection risk. We have also published a [COVID-19 insight report](#) into the safe and effective use of medicines in NHS Trusts.

As part of our strategy to deliver an intelligence-driven approach to regulation, we are working with partner organisations, including NHS England and NHS Improvement (NHSEI) and PHE to improve the data available to inspection teams relating to the prescribing and use of antibiotics in services.

## Faculty of General Dental Practice UK (FGDP)

Over the year, the Faculty of General Dental Practice UK (FGDP) continued to emphasise the importance of appropriate antimicrobial prescribing in dentistry, and to raise awareness of AMR and of the need for AMS to reduce drug-resistant infections.

The third edition of the [Antimicrobial Prescribing in Dentistry](#) guidelines was co-published in December by the FGDP and the Faculty of Dental Surgery of the Royal College of Surgeons of England (FDS). Developed by an intercollegiate working group led by Dr Nick Palmer Dip. FFGDP(UK) FDSRCS FCGDent, it updates FGDP's Antimicrobial Prescribing for General Dental Practitioners guidance to reflect changes in the evidence base since the previous edition, and covers a much wider range of conditions. Its scope has been extended to include management of oral and dental infections by all prescribers, not only general dental practitioners but those working in secondary dental care (including trainees), specialists (including oral and maxillofacial surgeons), and those involved in dental education and research. Its recommendations are also now appropriate for all dental patients, including adults, children, the elderly and those with special needs treated in the primary and secondary care setting. The new guidance is available free of charge in PDF format on the [College of General Dentistry](#) and [FDS](#) websites. Print copies were distributed to the FGDP's 4,000 members.

The faculty's online advice for dentists on appropriate antimicrobial prescribing during the COVID-19 pandemic continued to be highlighted in NHS England's Standard Operating Procedure for dental practices.



FGDP(UK) organised a press and social media campaign around World Antibiotic Awareness Week and European Antibiotics Awareness Day 2020, which promoted the message to patients that ‘antibiotics do not cure toothache’, highlighted the increase in antimicrobial prescribing in dentistry during the coronavirus pandemic, and reminded dental teams that antibiotics should only be used as an adjunct to definitive clinical management of the cause, and only where indicated. The eighth annual collaboration of its kind, it was supported by the Association of Clinical Oral Microbiologists, the College of General Dentistry, the British Dental Association, the British Association of Oral Surgeons, the Association of Dental Hospitals and the dental sub-group of the Scottish Antimicrobial Prescribing Group.

The Faculty also collaborated with these organisations to urge dentists to participate in a [national survey of antibiotic prescribing](#).

FGDP continued to promote use of the dental AMS toolkit by its members and the wider profession, in particular the [Antimicrobial Prescribing Self-Audit Tool](#). It also continued to raise awareness of AMR and dental AMS through its dedicated Antimicrobial Prescribing webpage, which co-hosted the toolkit, articulated the scale, nature and relevance of the problem of AMR to dentistry, provided links to the Faculty’s guidelines on antibiotic prescribing in dentistry, and encouraged take-up of the British Association of Oral Surgeons’ [Antimicrobial Stewardship e-Learning Modules](#).

Dr Nick Palmer represented the Faculty at meetings of the ESPAUR Dental Sub-group and ESPAUR Oversight group.

## Health Education England (HEE)

### AMR innovation fund update

1. Action on AMR – Case studies: Triled in the North-West in the Action on AMR focussed on equipping teams with QI skills to deliver their improvement work and share successful initiatives on demonstrating a significant reduction in Gram-negative bloodstream infections (GNBSI) rates in the region. It is hoped that infection rates will be reduced in future as the teams progress their improvement work using the skills and knowledge gained.

2. Antimicrobial Stewardship (AMS) change – Case studies: The University of Manchester – AMS change project developed a cohort of ‘AMS CHANGERS’: experts in behaviour change related to AMS, with the capability, opportunity and motivation to drive change in health professional practices related to AMS. The report ‘AMS Change: Practical training to apply behavioural science to antimicrobial stewardship’, outlines the development and training that has been created. It can support the development of AMS Change projects in local areas.

We aim to encourage all regions to engage and implement the outcomes from both these projects; further details can be found on the [About the antimicrobial resistance and infections programme](#) webpage.

## Education on an optimal blood culture pathway

Education on the blood culture pathway has been identified as a key priority by the NHS. Working with the NHSEI AMR Diagnostics Team and Clinical Lead we developed 2 animations to raise awareness and develop understanding of an optimal blood culture pathway as set out by PHE.

The [main animation](#) can be utilised throughout the NHS to improve the collection of blood cultures. It is aimed at all staff and provides a general overview on the issues faced and importance of an optimal blood culture pathway in supporting antimicrobial and diagnostic stewardship and sepsis management that will enhance patient care and outcomes.

The [second film](#) covers the process of obtaining a blood culture that is aimed at clinical staff. It provides a step-by-step guide to good practice for the appropriate collection of blood cultures during the pre-analytical phase.

## Pharmacist IPC and AMS Training

1. Inclusion of HEE Infection Prevention and Control - [Level 1](#) and [Level 2](#) training and 'Antimicrobial Stewardship for Community Pharmacy' [training](#) as part of the quality criteria within the '[Community Pharmacy Quality Scheme 2019 to 2020](#)'.
2. Following the success of the 'RPS Antimicrobial stewardship training for pharmacists' AMR 2018 to 2019 innovation fund pilot project in London and the South-East, this was rolled out nationally in 2019 to 2020 with 60 funded places on offer. The blended learning approach aimed to upskill pharmacists from all settings to apply Plan, Do, Study, Act (PDSA) cycles and behaviour change interventions to improve AMS in their workplace.

Further details on [HEE's AMR activities](#) can be found online.

## National Health Service England (NHSE)

The COVID-19 pandemic has had a considerable impact on the AMR Programme in England across 2020 to 2021:

- the pandemic has impacted on prescribing patterns, cohorts of patients presenting to primary and secondary care and trends in prevalence of infections
- redeployment of staff to support the COVID response has also impacted on progress in a number of workstreams
- we have stress tested and strengthened national IPC practice or structures

- the increased focus on infection management and treatment and the demand for improved access to data have given the opportunity to accelerate change
- progress has been made in the development of an initial version of an AMR dashboard and trusted research environment to support understanding of key factors influencing the use of antibiotics in different localities and settings
- a patient pathway approach to quality improvement in infection management is exemplified by the launch of the RightCare UTI Data Pack in collaboration with NHS BSA
- processes have been agreed with NICE to pilot alternative approaches to funding and incentivising the development of new antibiotics
- arrangements have been developed for co-ordinating priorities between the AMR and the National Patient Safety Team's Managing Deterioration Programme for patients at risk of acute deterioration, who can be significant users of antibiotics

## Specialist Pharmacy Service (SPS)

The NHS Specialist Pharmacy Service (SPS) has worked on several workstreams involving antimicrobials.

As part of their wider [Medicines Governance Do Once programme](#) SPS, with the support of ESPAUR and specialist stakeholders (NICE, RCGP, ARPHAI, PHE, NHSE), have published the first national [PGD template for the immediate administration of a single dose of benzylpenicillin injection](#) for use prior to transfer to secondary care in suspected bacterial meningitis or meningococcal septicaemia. During 2020 to 2021 SPS sought support from ARPHAI to develop a wider national PGD programme for antimicrobial therapies in the out-of-hospital setting and will develop this workstream during 2021 to 2022.

In response to the COVID-19 pandemic, SPS arranged and delivered a webinar entitled '[Antimicrobial Use and Stewardship in the context of COVID-19](#)'. The expert speaker was Dr Diane Ashiru-Oredope, Lead Pharmacist, HCAI and AMR Division, PHE. The focus of the session was the impact of the pandemic on AMR and AMS.

SPS continues to support local antimicrobial networks by hosting the [antimicrobial resistance networks in England](#) on its website.

## Public Health Wales (PHW)

The Healthcare Associated Infection, Antimicrobial Resistance and Prescribing Programme (HARP), Public Health Wales, provide professional support to the NHS in Wales to reduce the burden of healthcare associated infections and antibiotic resistance across Wales. This is delivered through feedback of surveillance data for antimicrobial usage, resistance and HCAI to the NHS and Welsh Government as well as providing technical expertise in microbiology, antimicrobial stewardship and infection prevention and control. The HARP team supports and advises the Wales AMR and HCAI Steering Group, chaired by the deputy CMO Wales as well as the AMR and HCAI Delivery Boards set up to deliver the UK AMR strategy in Wales.

A number of reports are published annually by the HARP team, including antimicrobial prescribing in primary and secondary care, resistance in both primary and secondary care, and the annual Welsh antimicrobial point prevalence study. Due to the national COVID-19 response in PHW, this year we have published fewer reports, including focusing the annual antimicrobial point prevalence study on respiratory patients in secondary care. For HCAI surveillance, the HARP team provide a monthly dashboard of HCAI. Wales data is also provided to the UK AMR delivery board and WHO GLASS.

PHW provides a comprehensive, integrated microbiology service for Wales including a network of diagnostic laboratories, reference laboratories and an active genomics programme. The genomics programme has been particularly active this year in the tracing of Covid-19 variants. Wales has a dedicated antimicrobial resistance reference laboratory (Specialist Antimicrobial Chemotherapy Unit), which provides molecular confirmation of antimicrobial resistance, including carbapenemase producing Gram-negative bacteria. The unit analyse and report targeted surveillance on the mechanisms of resistance to third-generation cephalosporins in Gram-negatives, and drivers of carbapenem use. Each year the Welsh HBs participate in the European Antibiotic Awareness Day, supported by materials and communications from PHW and WG, and again, public engagement activity in AMR was reduced this year due to Covid-19 activity.

More information, including all our published reports, can be found on the [Healthcare associated infection and antimicrobial resistance programme](#) webpage.

## Public Health Agency (Northern Ireland)

The Public Health Agency (Northern Ireland) continues to support efforts to decrease Methicillin-resistant staphylococcus aureus (MRSA) bloodstream infections, CDI, Gram-negative bacteraemias and antibiotic consumption through the work of the Regional Healthcare associated Infections and Antimicrobial Stewardship Improvement Board and the Health Protection department. We have led and supported a number of activities that were focused on public engagement including continuation of a social and mass media campaign and attending

an agricultural event to distribute information on overuse of antibiotics. Much of the social media campaign focused on World Antimicrobial Awareness Week, and aimed to highlight the role of AGs. We have continued to monitor and process antimicrobial usage data, as well as health care acquired infection data. Since February 2020 the team began to focus on the SARS-CoV-2 pandemic, including monitoring and reporting on healthcare associated SARS-CoV-2 infections. We aim to fully elucidate the effect of the pandemic on antimicrobial usage, and antimicrobial resistance.

## Scottish One Health Antimicrobial Use and Antimicrobial Resistance (SONAAR)

In recognition of the importance of the 'One Health' ethos to the sustainable control of AMR, the SONAAR programme within ARHAI Scotland produces an annual report containing information on use of antibiotics in humans in primary care and acute hospitals along with small animal veterinary practices, and the levels of antibiotic resistance found in a range of important human and animal infections.

This data is used by organisations such as the Scottish Antimicrobial Prescribing Group (SAPG) to inform antimicrobial prescribing policy and develop initiatives for antimicrobial stewardship and the Scottish Microbiology and Virology Network (SMVN) to support the development of testing strategies for NHS diagnostic laboratories in Scotland.

The SONAAR 2021 report will be published in November 2021 and will be available online.

## Royal College of Nursing (RCN)

The RCN continued to deliver its Education programme on Infection Prevention and Control (IPC) which is shaped around the antimicrobial stewardship competencies developed by the University of Cardiff (Courtenay and others). Specimen collection and the practical application of IPC in all care settings are the key themes of the programme. 5 cohorts were delivered 2020 to 2021. Additionally the RCN continues to support antimicrobial stewardship programmes impacting on nursing practice and in 2020 supported development and distribution of a survey on nurses engagement in AMS. The RCN actively supports self-care week annually and promotes this via the Public Health Forum and IPC network.

## Royal Pharmaceutical Society (RPS)

As the professional membership body for pharmacy, we are committed to continue supporting the UK National Action Plan and 20-year vision, and the global strategy for AMR. Our Chief Executive, President, Executive Team, National Boards and Expert Groups support this vital

work by highlighting the important contribution that pharmacy and pharmaceutical sciences can make to AMR.

During 2020, we continued delivering our expert-led AMS Training Programme for pharmacists practising in patient-facing roles. Commissioned by HEE, this programme is the first of its kind in England and was delivered in collaboration with PHE and the UK Clinical Pharmacy Association Pharmacy Infection Network (UKCPA PIN). Following on from our 2019 cohort in London and the South East, HEE provided further funding to enrol pharmacists across England into 2 intake rounds, in February and November 2020. Despite the significant challenges posed by the COVID-19 pandemic, a total of 91 pharmacists attended the training day and positive engagement was maintained throughout both intakes. Small group discussions enabled learners to share and discuss their projects on workplace improvement covering topics such as antibiotic prescribing and dosing, surgical prophylaxis, as well as documentation of antibiotic indication and allergy status. This initiative was shortlisted for an AG Award in the Prescribing and Stewardship category and received a 'Highly commended' award.

We continued delivering [webinars](#) and [podcasts](#) covering topics linked to current practice and as part of WAAW 2020, we worked with UKCPA PIN and our AMR Expert Advisory Group (AmEAG) to deliver webinars focusing on COVID-19 and management of infection. Our Boards, Committees and AmEAG continue working closely together to respond to consultations on AMS and management of infections and contribute to national and global AMR campaigns. Our AmEAG has continued to meet monthly to share intelligence to support AMS and, through 2 longer meetings, has been able to share and discuss trends in antibiotic use during the pandemic across the 4 UK nations. We continue working alongside other national groups to support engagement and confidence in optimising the use of antimicrobials and encourage all pharmacists to become AGs.

## Veterinary Medicines Directorate (VMD) and Department for Environment, Food and Rural Affairs (DEFRA)

The Veterinary Medicines Directorate (VMD) is an executive agency of DEFRA. The VMD is the policy lead for government on antibiotic resistance in animal health and is responsible for the surveillance of antibiotic usage and resistance in animals in the UK. The VMD publishes the annual UK Veterinary Antimicrobial Resistance and Sales Surveillance (UK-VARSS) Report, including data on resistance, sales and use. The latest data available (from 2019) reveals an overall reduction of 50% in antibiotic sales for farmed animals since 2014, and a fall of 74% since 2015 in sales of antibiotics most critical for human health. We are the lowest user of antibiotics in Europe amongst countries with significant livestock farming, and the fifth lowest user overall (only Norway, Iceland, Sweden and Finland are lower). Monitoring of resistance in bacteria from animals is undertaken both in healthy animals at slaughter and in veterinary and zoonotic pathogens sampled from clinical investigations. Overall, the UK has seen decreasing



trends of resistance in healthy pigs at slaughter since 2015, and levels of AMR in veterinary and zoonotic pathogens have remained stable over the reporting period (2017 to 2019).

## The National Institute for Health and Care Excellence (NICE)

### NICE work on AMS during 2020 to 2021

Strong progress has been made on the project to develop and test innovative models for the evaluation and purchase of antimicrobials, which NICE is co-leading with NHS England and NHS Improvement. Key objectives are to demonstrate the feasibility of an approach to evaluation that recognises the full public health value of antimicrobials together with payment models that support good stewardship. The model tests paying companies for antimicrobials based on an evaluation of the overall benefit to the NHS, as opposed to the volumes used. Such models, if widely adopted internationally, have the potential to provide the 'market pull' incentive to stimulate increased investment in the development of new antimicrobials.

The project launched in July 2019 and following engagement with companies and other stakeholders, the project team developed contract documents and an evaluation framework. A competitive tender was launched in June 2020 where the NHS offered 2 contracts to pharmaceutical companies through which we are testing the new approach. The 2 selected antimicrobial products, cefiderocol and ceftazidime with avibactam were announced in December 2020. These products are now undergoing an evaluation by NICE to estimate their value to the NHS using adapted methods for antimicrobials. Where possible, value will be measured in quality adjusted life years (QALYs). A special NICE Committee has been established for the 2 antimicrobial product evaluations which are due to be completed in December 2021. The outcomes of the NICE evaluation will inform final discussions between NHS England and NHS Improvement and the companies on payment levels under the contracts. The final contracts are expected to be in place by April 2022 and run for an initial 3-year period with the option to extend for up to 10 years.

There has been a high level of international interest in the project and the project team is working with the DHSC Global and Public Health Group to collaborate with international partners in promoting similar models.

NICE continues to work with PHE to develop antimicrobial prescribing guidelines (APGs) for managing common infections. The guidelines offer evidence-based guidance for primary and secondary care and provide recommendations for appropriate antimicrobial use in the context of tackling AMR. A NICE Committee is producing these guidelines which are jointly badged by both NICE and PHE. In 2020 to 2021 there were 3 APGs published on insect bites and stings, human and animal bites, secondary bacterial infection of eczema and other common skin conditions, with more topics in development.



The format of APG content comprises a visual summary of the recommendations, the guideline, the associated evidence review and a summary document that includes content from all APGs alongside PHE's guidance for primary care. Some guidelines also include decision aids to inform shared decision making, such as cystitis – taking an antibiotic. NICE will continue to engage both at a national and regional level with key external stakeholders including PHE, NHS England/Improvement, Health Education England and the CQC to support the wider implementation of the APGs.

To support the appropriate use and stewardship of new antimicrobials at the point of launch, NICE is also developing evidence summaries for antimicrobial prescribing. Topics published in 2020 to 2021 were on imipenem with cilastatin and relebactam, [cefiderocol](#) and also on [delafloxacin for acute bacterial skin and skin structure infections](#).

In January 2017, NICE published a guideline Antimicrobial stewardship (AMS): changing risk-related behaviours in the general population (NG63) aiming to change people's behaviour to reduce AMR. It also includes measures to prevent and control infection. This guidance is complementary to the 'NICE guideline on Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use (NG15)' which provides recommendations about how to correctly use antimicrobial medicines and the hazards associated with their overuse and misuse. The NICE guideline on Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use (NG15); was reviewed for update in January 2018. Based on a review of current policy and evidence since publication, and the views of topic experts and stakeholders the guideline was considered current and accurate.

NICE also produce Medtech Innovation Briefings (MIBs) on new medical devices and diagnostics. These briefings help to avoid the need for organisations to produce similar information locally, saving staff time and resources. MIBs can be quickly developed (in around 15 weeks) on most technologies, and provide factual information for organisations to consider. MIBs published in 2020 of relevance to infections (including wound care) include:

- MIB234 [ClearGuard HD Antimicrobial Barrier Cap for preventing haemodialysis catheter-related bloodstream infections](#)
- MIB230 [3C Patch System for treating diabetic foot ulcers](#)
- MIB224 [FebriDx for C-reactive protein and myxovirus resistance protein A testing](#)
- MIB31 [Tegaderm CHG securement dressing for vascular access sites](#)
- MIB212 [MolecuLight i:X for wound imaging](#)
- MIB220 [Prontosan for acute and chronic wounds](#)
- MIB204 [Plus Sutures for preventing surgical site infection](#)
- MIB208 [NATROX oxygen wound therapy for managing diabetic foot ulcers and complex or chronic non-healing wounds](#)

The Diagnostics Assessment Programme also represents NICE on the UK AMR Diagnostics Collaborative which brings together key partners across the NHS, industry and academia to deliver the UK's diagnostic ambitions for AMR.

## NICE work on COVID-19

Since March 2020, NICE has produced 24 COVID-19 rapid guidelines on a variety of topics related to COVID-19. These include guidelines on managing COVID-19, guidelines on service delivery during the pandemic and guidance on conditions which require the use of drugs that affect the immune response.

In March 2021, the 7 of these 24 original individual guidelines on different aspects of the management of COVID-19 were integrated into one guideline: managing COVID-19 (NG191). The COVID-19 team has also developed guidance on the management of the long-term effects of COVID-19 and is responsible for maintaining and updating the NHSE&I specialty guides relating to COVID-19.

The following workstreams in the COVID-19 team link into antimicrobial stewardship (AMS) activities.

### Development and publication of the initial cohort of COVID-19 rapid guidelines (March 2020)

In the initial response to the pandemic NICE developed 24 guidelines on a variety of topics. Included in these were guidelines on managing suspected or confirmed pneumonia in adults in the community and antibiotics for pneumonia in adults in hospital. Both of these guidelines contained information on diagnosing bacterial pneumonia (to direct appropriate use of antibiotics) and also outlined antibiotic choices for both community and hospital acquired pneumonia. They also contained information on when not to prescribe antibiotics. These guidelines aimed to ensure that antibiotics were being used appropriately, that is not for viral infection. They also aimed to ensure that where antibiotics are needed the most appropriate antibiotics were used, taking into account the spectrum of antibiotic activity and any supply issues.

### Living guideline approach to the COVID\_19 rapid guidelines

The suite of COVID-19 rapid guidelines is under continuous review for emerging evidence that may warrant a change to recommendations. If any evidence becomes available about novel therapeutics or repurposing of existing drugs (for example, azithromycin and tocilizumab), then evidence is reviewed, the recommendations are updated by the COVID-19 expert panel, then the recommendations are published typically within a 4 week timescale of the evidence becoming available.

### Managing COVID-19

In March 2021, the 7 guidelines on the diagnosis and treatment of COVID-19 were integrated into 1 guideline to provide clearer advice to people using the guideline, whilst also reducing duplication and updating the guidance to the current clinical context. This included a review of

the guidance for antibiotics that were originally within the COVID-19 rapid guidelines managing suspected or confirmed pneumonia in adults in the community and antibiotics for pneumonia in adults in hospital. As part of this update, the panel decided that it was appropriate to refer to the existing NICE antimicrobial guidelines for the management of hospital and community acquired pneumonia (NG138 and NG139). The panel also decided that if a person being treated for COVID-19 has a secondary bacterial pneumonia, then the antibiotic choices in the existing NICE antimicrobial guidelines for the management of hospital and community acquired pneumonia should be followed, therefore providing clear and consistent guidance on choice of antibiotics and aiming to improve AMS.

### Therapeutics process and links with rapid C-19 initiative

In March 2021, as part of the integration of the COVID-19 rapid guidelines into the managing COVID-19 guideline, the COVID-19 team set up a process so that emerging evidence could be reviewed quickly and recommendations made in a timely manner so that best practice could be disseminated as efficiently as possible. We have developed a process that links with the Rapid C-19 initiative so that we can develop guidance that links with the priorities of Rapid C-19. In addition, through this process our evidence reviews are used to help inform NHSE&I's commissioning policy. To date, through this process we have made a negative recommendation on azithromycin which will limit inappropriate use in the treatment of COVID-19. A review of doxycycline will be published soon. Recommendations have also been made on use of remdesivir, corticosteroids, tocilizumab and sarilumab in the treatment of COVID-19; by recommending effective therapeutics for the management of COVID-19 we are contributing the effective treatment of COVID-19 and reducing the inappropriate use of antibiotics for the treatment of COVID-19.

# References

1. DHSC. '[Tackling antimicrobial resistance 2019 to 2024: the UK's 5-year national action plan](#)' January 2019
2. DHSC. '[Contained and controlled: the UK's 20-year vision for antimicrobial resistance](#)' January 2019
3. PHE. [Laboratory Reporting Guidelines](#) July 2016
4. PHE. '[English Surveillance Programme for Antimicrobial Utilisation and Resistance \(ESPAUR\) Report 2019 to 2020](#)'
5. Amin-Chowdhury, Z and others (2021). 'Impact of the coronavirus disease 2019 (COVID-19) pandemic on invasive pneumococcal disease and risk of pneumococcal coinfection with severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2): Prospective national cohort study, England'. *Clinical Infectious Diseases* 2021 March 1: volume 72, issue 5, pages e65 to e75 doi: 10.1093/cid/ciaa1728
6. PHE. '[Annual epidemiological commentary: Gram-negative, MRSA and MSSA bacteraemia and C. difficile infection data, up to and including financial year April 2020 to March 2021](#).' November 2021
7. Denny S, Rawson TM, Hart P and others. '[Bacteraemia variation during the COVID-19 pandemic; a multi-centre UK secondary care ecological analysis](#).' *BMC Infectious Diseases* volume 21, issue 556 (2021)
8. PHE. '[Annual epidemiological commentary: Gram-negative, MRSA and MSSA bacteraemia and C. difficile infection data, up to and including financial year April 2020 to March 2021](#).' November 2021
9. Brolund A, Lagerqvist N, Byfors S and others. 'Worsening epidemiological situation of carbapenemase-producing Enterobacteriaceae in Europe, assessment by national experts from 37 countries July 2018.' *Eurosurveillance* 2019 volume 24, page 1,900,123
10. Shon A, Bajwa RPS, Russo TA. 'Hypervirulent (hypermucoviscous) *Klebsiella pneumoniae*: a new and dangerous breed.' *Virulence* 2013: volume 4, pages 107-118
11. Roulston KJ, Bharucha T, Turton JF and others. 'A case of NDM-carbapenemase-producing hypervirulent *Klebsiella pneumoniae* sequence type 23 from the UK.' *JMM Case Reports* 2018 volume 5, page e005130
12. Turton JF, Payne Z, Coward A and others. 'Virulence genes in isolates of *Klebsiella pneumoniae* from the UK during 2016, including among carbapenemase gene-positive hypervirulent K1-ST23 and 'non-hypervirulent' types ST147, ST15 and ST383.' *Journal of Medical Microbiology* 2018: volume 67 pages 118-128
13. Dong N, Lin D, Zhang R and others. 'Carriage of blaKPC-2 by a virulence plasmid in hypervirulent *Klebsiella pneumoniae*'. *Journal of Antimicrobiological Chemotherapy* 2018: volume 73 pages 3,317-3,321
14. Turton JF, Payne Z, Coward A and others. 'Virulence genes in isolates of *Klebsiella pneumoniae* from the UK during 2016, including among carbapenemase gene-positive hypervirulent K1-ST23 and 'non-hypervirulent' types ST147, ST15 and ST383.' *Journal of Medical Microbiology* 2018: volume 67 pages 118-128

15. Dong N, Lin D, Zhang R and others. 'Carriage of blaKPC-2 by a virulence plasmid in hypervirulent *Klebsiella pneumoniae*.' Journal of Antimicrobial Chemotherapy 2018: volume 73 pages 3,317-3,321
16. Xie M, Dong N, Chen K and others. 'A hybrid plasmid formed by recombination of a virulence plasmid and a resistance plasmid in *Klebsiella pneumoniae*.' Journal of Global Antimicrobial Resistance 2020: volume 23 pages 466-470
17. Xie M, Chen K, Ye L and others. 'Conjugation of virulence plasmid in clinical *Klebsiella pneumoniae* strains through formation of a fusion plasmid.' Advanced Biosystems 2020: volume 4 page e1900239
18. Lam MMC, Wyres KL, Wick RR and others. 'Convergence of virulence and MDR in a single plasmid vector in MDR *Klebsiella pneumoniae* ST15.' Journal of Antimicrobial Chemotherapy 2019: volume 74 pages 1,218-1,222
19. Turton J, Davies F, Turton J and others. 'Hybrid resistance and virulence plasmids in 'high-risk' clones of *Klebsiella pneumoniae*, including those carrying blaNDM-5.' Microorganisms 2019: volume 7 page 326
20. Gu D, Dong N, Zheng Z and others. 'A fatal outbreak of ST11 carbapenem-resistant hypervirulent *Klebsiella pneumoniae* in a Chinese hospital: A molecular epidemiological study.' Lancet Infectious Diseases 2018: volume 18 pages 37–46
21. ECDC. '[European Antimicrobial Resistance Surveillance Network annual report.](#)'
22. Rottier WC, Ammerlaan HS, Bonten MJ. 'Effects of confounders and intermediates on the association of bacteraemia caused by extended-spectrum beta-lactamase-producing Enterobacteriaceae and patient outcome: a meta-analysis.' Journal of Antimicrobial Chemotherapy 2012: volume 67 pages 1,311-1,320 B, III
23. BSAC. '[Detection of extended-spectrum  \$\beta\$ -lactamases \(ESBLs\) in \*E. coli\* and \*Klebsiella\* species.](#)'
24. Public Health England 2016. '[Detection of Enterobacteriaceae producing extended spectrum  \$\beta\$ -Lactamases.](#)' UK Standards for Microbiology Investigations. B 59 Issue 4.1
25. BSAC. '[BSAC Bacteraemia Resistance Surveillance Programme.](#)'
26. Public Health England. '[Polymicrobial bacteraemia and fungaemia in England, Wales and NI; annual bacteraemia reports.](#)'
27. Public Health England. '[Voluntary surveillance of \*Enterococcus\* spp. bacteraemia in England: 2020.](#)' October 2021
28. Public Health England. '[Annual epidemiological commentary: Gram-negative, MRSA and MSSA bacteraemia and \*C. difficile\* infection data, up to and including financial year April 2020 to March 2021.](#)' November 2021
29. Cassini and others. 'Attributable deaths and disability-adjusted life-years caused by infections with antibiotic-resistant bacteria in the EU and the European Economic Area in 2015: a population-level modelling analysis.' Lancet Infectious Diseases 2019: volume 19 pages 56-66
30. Public Health England. '[English Surveillance Programme for Antimicrobial Utilisation and Resistance \(ESPAUR\) Report 2019 to 2020.](#)' November 2020



31. Public Health England. '[Annual epidemiological commentary: Gram-negative, MRSA and MSSA bacteraemia and \*C. difficile\* infection data, up to and including financial year April 2020 to March 2021.](#)' November 2021
32. The Health Foundation (2020). '[Use of primary care during the COVID-19 pandemic.](#)' (Accessed on 16 July 2021)
33. National Institute for Health and Care Excellence. '[COVID-19 rapid guideline: managing suspected or confirmed pneumonia in adults in the community.](#)'
34. NICE guideline [NG173]. '[COVID-19 rapid guideline: antibiotics for pneumonia in adults in hospital.](#)' 1 May 2020, last updated 9 October 2020
35. Brueggemann AB, Jansen van Rensburg MJ, Shaw D and others. 'Changes in the incidence of invasive disease due to *Streptococcus pneumoniae*, *Haemophilus influenzae*, and *Neisseria meningitidis* during the COVID-19 pandemic in 26 countries and territories in the Invasive Respiratory Infection Surveillance Initiative: a prospective analysis of surveillance data.' *Lancet Digital Health* 2021: volume 3 issue 6 page :e360-e370 [published correction appears in *Lancet Digital Health* 2021 May 26 doi:10.1016/S2589-7500 21: 00077-7]
36. Public Health England. '[Weekly national flu reports](#)'
37. Public Health England. '[Annual flu reports](#)'
38. '[British Association for Sexual Health and HIV \(BASHH\) guidelines](#)'
39. Public Health England. '[Surveillance of antimicrobial resistance in \*Neisseria gonorrhoeae\* in England and Wales. Key findings from the Gonococcal Resistance to Antimicrobials Surveillance Programme \(GRASP\).](#)' Report 2020, published November 2021
40. Public Health England. '[Mycoplasma genitalium Antimicrobial Resistance Surveillance \(MARS\). Pilot report 2020](#)' published August 2021
41. Public Health England. '[Tuberculosis in England: 2020.](#)' November 2020
42. European Centre for Disease Prevention and Control. 'Antimicrobial resistance in the EU/EEA (EARS-Net) Annual Epidemiological Report 2019.' Stockholm: ECDC 2020
43. WHO. '[Central Asian and European Surveillance of antimicrobial resistance network.](#)'
44. WHO. 'Global antimicrobial resistance surveillance system (GLASS) report: early implementation 2020.' Geneva: World Health Organization 2020. Licence: CC BY-NC-SA 3.0 IGO
45. Public Health England (2021). '[MRSA, MSSA, Gram-negative bacteraemia and Clostridioides difficile \(CDI\) quarterly reports](#)'
46. Public Health England (2021). '[Annual epidemiological commentary: Gram-negative, MRSA and MSSA bacteraemia and \*C. difficile\* infection data, up to and including financial year April 2020 to March 2021.](#)'
47. '[ICU Data Capture System](#)' (2021) (accessed 16 July 2021)
48. The Health Foundation (2020). '[Use of primary care during the COVID-19 pandemic.](#)' (accessed 16 July 2021)
49. Denny S, Rawson TM, Hart P and others. '[Bacteraemia variation during the COVID-19 pandemic; a multi-centre UK secondary care ecological analysis.](#)' *BMC Infectious Diseases* 2021 volume 21 issue, 556

50. Hammond A. [‘Plummeting number of UTI diagnoses since the advent of COVID brings huge uncertainty to the management of serious infections in vulnerable patients.’](#) (accessed 25 August 2021)
51. Lishman H, Costelloe C, Hopkins S and others. ‘Exploring the relationship between primary care antibiotic prescribing for urinary tract infections, *Escherichia coli* bacteraemia incidence and antimicrobial resistance: an ecological study.’ International Journal of Antimicrobial Agents December 2018: volume 52, issue 6, pages 790-798
52. Bou-Antoun S, Davies J and others. (2016) ‘Descriptive epidemiology of *Escherichia coli* bacteraemia in England, April 2012 to March 2014.’ Eurosurveillance volume 21 page 30,329
53. Public Health England (2021). [Fingertips AMR local indicators](#)
54. Collignon P and Beggs JJ (2020). ‘CON: COVID-19 will not result in increased antimicrobial resistance prevalence.’ JAC-Antimicrobial Resistance volume 2 dlaa051
55. Maes, Mailis and others. ‘Ventilator-associated pneumonia in critically ill patients with COVID-19.’ Critical Care: volume 25, 11 January 2021. doi:10.1186/s13054-021-03460-5
56. PRINCIPLE. [‘Azithromycin and doxycycline are not generally effective against COVID-19 in patients treated at home, shows PRINCIPLE trial.’](#) January 2021
57. [‘RECOVERY trial finds no benefit from azithromycin in patients hospitalised with COVID-19.’](#) December 2020
58. National Institute for Health and Care Excellence. [‘COVID-19 rapid guideline: managing suspected or confirmed pneumonia in adults in the community.’](#)
59. Stowe J, Tessier E, Zhao H, Guy R and others. [‘Interactions between SARS-CoV-2 and influenza, and the impact of coinfection on disease severity: a test-negative design.’](#) International Journal of Epidemiology 2021: pages 1,124–1,133
60. PHE. [Weekly national flu reports](#)
61. PHE. [Annual flu reports](#)
62. PHE. [‘Surveillance of antimicrobial resistance in \*Neisseria gonorrhoeae\* in England and Wales. Key findings from the Gonococcal Resistance to Antimicrobials Surveillance Programme \(GRASP\). Report 2020.’](#) Published November 2021
63. PHE. [‘Mycoplasma genitalium Antimicrobial Resistance Surveillance \(MARS\). Pilot report 2020.’](#) Published August 2021
64. PHE. [‘Tuberculosis in England: 2021 report.’](#) Published October 2021
65. UK HIV Drug Resistance Database. [‘HIV drug resistance in the UK.’](#)
66. DHSC. [‘Tackling antimicrobial resistance 2019 to 2024: the UK’s 5-year national action plan.’](#) January 2019
67. PHE (2019). [‘English surveillance programme for antimicrobial utilisation and resistance \(ESPAUR\) report 2018 to 2019.’](#)
68. PHE (2020). [‘English surveillance programme for antimicrobial utilisation and resistance \(ESPAUR\) report 2019 to 2020.’](#)
69. RCPATH. [‘Prioritisation or deferral of Pathology Laboratory Work \(in light of SARS-CoV-2 \(COVID19\) epidemic\).’](#)



70. PHE (2020). '[New statutory duty on reporting results of antimicrobials susceptibility testing.](#)' Health Protection Report (News): volume 14 issue 17
71. PHE (2020). '[Actions to contain carbapenemase-producing Enterobacterales \(CPE\): Framework of actions to contain carbapenemase-producing Enterobacterales.](#)'
72. PHE (2013). '[Acute Trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae \(withdrawn\).](#)'
73. Trepanier P and others. 'Carbapenemase-producing Enterobacteriaceae in the UK: a national study (EuSCAPE-UK) on prevalence, incidence, laboratory detection methods and infection control measures.' Journal of Antimicrobial Chemotherapy: volume 72, issue 2 February 2017, pages 596–603
74. PHE (2019). '[English surveillance programme for antimicrobial utilisation and resistance \(ESPAUR\) report 2018 to 2019.](#)'
75. PHE-AMRHAI (2019). '[Antimicrobial Resistance and Healthcare Associated Infections Reference Unit \(AMRHAI\) guidance.](#)' AMRHAI reference unit: reference and diagnostic services.
76. PHE (2020) '[English surveillance programme for antimicrobial utilisation and resistance \(ESPAUR\) report 2019 to 2020.](#)'
77. PHE (2020). '[UK SMI B 60: detection of bacteria with carbapenem hydrolysing  \$\beta\$  lactamases \(carbapenemases\).](#)'
78. PHE (2021). '[Commercial assays for the detection of acquired carbapenemases.](#)'
79. PHE (2020). '[New statutory duty on reporting results of antimicrobials susceptibility testing.](#)' Health Protection Report (News): volume 14 issue 17
80. PHE (2020). '[UK standards for microbiology investigations B 60: detection of bacteria with carbapenem hydrolysing  \$\beta\$  lactamases \(carbapenemases\).](#)'
81. PHE (2021). '[Notifiable diseases: causative agents report for 2021.](#)'
82. PHE (2020). '[New statutory duty on reporting results of antimicrobials susceptibility testing.](#)' Health Protection Report (News): volume 14 issue 17
83. RCPATH. '[Prioritisation or deferral of Pathology Laboratory Work \(in light of SARS-CoV-2 \(COVID19\) epidemic\)](#)'
84. PHE (2013). '[Acute trust toolkit for the early detection, management and control of carbapenemase-producing Enterobacteriaceae.](#)' December 2013 (withdrawn).
85. PHE (2020). '[English surveillance programme for antimicrobial utilisation and resistance \(ESPAUR\) report 2018 to 2020.](#)'
86. PHE (2020). '[New statutory duty on reporting results of antimicrobials susceptibility testing.](#)' Health Protection Report (News): volume 14 issue 17
87. PHE (2019). '[Detection of acquired carbapenemases: commercial assays.](#)'
88. PHE (2020). '[English surveillance programme for antimicrobial utilisation and resistance \(ESPAUR\) report 2019 to 2020.](#)'
89. PHE (2020). '[English surveillance programme for antimicrobial utilisation and resistance \(ESPAUR\) report 2019 to 2020.](#)'
90. PHE (2019). '[English surveillance programme for antimicrobial utilisation and resistance \(ESPAUR\) report 2018 to 2019.](#)'
91. PHE (2017) [ESPAUR Report 2017](#)

92. Patel B and others (2020). 'A 10-year review of carbapenemase producing Enterobacterales (CPE) in London, United Kingdom.' Infection Control and Hospital Epidemiology volume 41 issue S1: The Sixth Decennial International Conference on Healthcare-Associated Infections Abstracts, March 2020: Global Solutions to Antibiotic Resistance in Healthcare October 2020: pages s6 to s7
93. Donker T, Henderson KL, Hopkins KL and others. 'The relative importance of large problems far away versus small problems closer to home: insights into limiting the spread of antimicrobial resistance in England.' BMC Medicine 2017: volume 15 issue 1, page 86 published April 2017. doi:10.1186/s12916-017-0844-2
94. Descraene V and others. '[A large, refractory nosocomial outbreak of \*Klebsiella pneumoniae\* carbapenemase-producing \*Escherichia coli\* demonstrates carbapenemase gene outbreaks involving sink sites require novel approaches to infection control.](#)' Antimicrobial Agents and Chemotherapy 62:e01689-18
95. RCPATH. '[Prioritisation or deferral of pathology laboratory work \(in light of SARS-CoV-2 \(COVID19\) epidemic\).](#)'
96. Denny S, Rawson TM, Hart P and others. '[Bacteraemia variation during the COVID-19 pandemic; a multi-centre UK secondary care ecological analysis.](#)' BMC Infectious Diseases volume 21: issue 556 (2021)
97. PHE (2021). '[Annual epidemiological commentary: Gram-negative, MRSA and MSSA bacteraemia and \*C. difficile\* infection data, up to and including financial year April 2020 to March 2021.](#)'
98. The Health Foundation (2020). '[Use of primary care during the COVID-19 pandemic.](#)' (accessed 16 July 2021)
99. PHE (2021). '[National flu and COVID-19 surveillance reports: 2021 to 2022 season.](#)'
100. PHE (2020). '[Actions to contain carbapenemase-producing Enterobacterales \(CPE\): Framework of actions to contain carbapenemase-producing Enterobacterales.](#)'
101. Knight GM, Glover RE and others. (2021) '[Antimicrobial resistance and COVID-19: Intersections and implications.](#)' eLife 2021;10:e64139
102. Gardner T, Fraser C (2021). '[Longer waits, missing patients and catching up.](#)' The Health Foundation. 13 April 2021
103. Lyall MJ, Lone NI (2021). 'Higher clinical acuity and 7-day hospital mortality in non-COVID-19 acute medical admissions: prospective observational study.' Emergency Medicine Journal 2021: volume 38 pages 366-370
104. PHE (2021). '[Notifiable diseases: causative agents report for 2021.](#)'
105. PHE (2020). '[Actions to contain carbapenemase-producing Enterobacterales \(CPE\): Framework of actions to contain carbapenemase-producing Enterobacterales.](#)'
106. Gharbi M, Moore LS, Gilchrist M and others. 'Forecasting carbapenem resistance from antimicrobial consumption surveillance: lessons learnt from an OXA-48-producing *Klebsiella pneumoniae* outbreak in a West London renal unit.' International Journal of Antimicrobial Agents 2015: volume 46 pages 150-156
107. [Mycology reference laboratory](#)
108. [Mycology Reference Centre Manchester](#)

109. Fraser M and others. 'Resistance to echinocandin antifungal agents in the United Kingdom in clinical isolates of *Candida glabrata*: 15 years of interpretation and assessment.' Medical Mycology 2020: volume 58 issue 2
110. Arendrup, C. and Patterson, T. 'Multidrug-Resistant Candida: Epidemiology, Molecular Mechanisms, and Treatment.' The Journal of Infectious Diseases 2017: volume 216 issue 3
111. PHE (2019) '[Laboratory surveillance of candidaemia in England, Wales and Northern Ireland 2018](#)'
112. Buil JB and others. 'The fading boundaries between patient and environmental routes of triazole resistance selection in *Aspergillus fumigatus*.' PLoS Pathogens 2019: volume 15, issue 8
113. Raut and Huy. 'Rising incidence of mucormycosis in patients with COVID-19: another challenge for India amidst the second wave?' The Lancet Respiratory Medicine 2021
114. Doidge J and others. 'Trends in intensive care for patients with COVID-19 in England, Wales and Northern Ireland.' American Journal of Respiratory and Critical Care Medicine 2021: volume 203, issue 5
115. Jothimani D and others. 'COVID-19 and the liver.' Journal of Hepatology 2020 volume 73
116. Bongomin F, Moore CB, Masania R, Rowbotham E, Alastruey-Izquierdo A, Novak-Frazer L, Richardson MD. 'Sequence analysis of isolates of *Aspergillus* from patients with chronic and allergic aspergillosis reveals a spectrum of cryptic species.' Future Microbiology 2018
117. Davis MR, Donnelley MA and Thompson GR (2020). 'Ibrexafungerp: A novel oral glucan synthase inhibitor.' Medical Mycology: volume 58, issue 5, July 2020, pages 579–592
118. Ghannoum M and others. 'Ibrexafungerp: A novel oral triterpenoid antifungal in development for the treatment of *Candida auris* Infections.' Antibiotics 2020: volume 9, issue 9, page 539
119. Joint Formulary Committee. [British National Formulary](#)
120. Sharp A and others. 'Screening for *Candida auris* in patients admitted to 8 intensive care units in England, 2017 to 2018.' Eurosurveillance 26, 2021
121. PHE (2018) [English Surveillance Programme for Antimicrobial Utilisation and Resistance \(ESPAUR\) report 2017](#)
122. Mroczynska M and Brillowska-Dabrowska A (2020). 'Review on status of echinocandins use.' Antibiotics 2020: volume 9, issue 5, page 277
123. Montagna M and others (2015). 'Susceptibility to echinocandins of *Candida* spp. strains isolated in Italy assessed by European Committee for Antimicrobial Susceptibility Testing and Clinical Laboratory Standards Institute broth microdilution methods.' BMC Microbiology: volume 15, issue 106 (2015)
124. Johnson EM and Arendrup MC. 'Susceptibility test methods: yeast and filamentous fungi (2019)' In Manual of Clinical Microbiology 12th edition, volume 2, edited by Carroll KC, Pfaller MA, Landry ML, McAdam AJ, Patel R. Richter SS and Warnock DW. ASM Press pages 2,351 to 2,375
125. Borman AM, Fraser M, Patterson Z, McLachlan S, Palmer MD, Mann C, Oliver D, Brown P, Linton CJ, Dzietych A, Hedley M, Gouch M and Johnson EM. 'The considerable impact

- of the SARS-CoV-2 pandemic and COVID-19 on the UK National Mycology Reference Laboratory activities and workload.' (2021). Medical Mycology doi:10.1093/mmy/myab038
126. Shoham, S. and Marwaha, S. (2009). 'Invasive fungal infections in the ICU.' Journal of Intensive Care Medicine: volume 25, issue 2, pages 78-92
  127. Borman AM, Palmer MD, Fraser M, Patterson Z, Mann C, Oliver D, Linton CJ, Gouch M, Brown P, Dzietczyk A, Hedley M, McLachlan S, King J and Johnson EM. 'COVID-19-associated invasive aspergillosis: data from the UK national Mycology Reference Laboratory.' (2020). Journal of Clinical Microbiology doi:10.1128/JCM.02136-20
  128. Burn S and others. 'What happened to English NHS hospital activity during the COVID-19 pandemic?' Institute for Fiscal Studies Briefing Note (2021) doi: 10.1920/BN.IFS.2021.BN0328
  129. Tagliaferri E and Menichetti F (2015). 'Treatment of invasive candidiasis: between guidelines and daily clinical practice. Expert Review of Anti-infective Therapy, 13:6, 685-689
  130. Zhang and others (2020) 'Risk of invasive candidiasis with prolonged duration of ICU stay: a systematic review and meta-analysis.' BMJ Open 2020; 10:e036452
  131. NHS Digital. [Hospital Episode Statistics \(HES\)](#)
  132. Department of Health and Social Care. '[UK 5-year action plan for antimicrobial resistance 2019 to 2024.](#)' 2019
  133. Department of Health and Social Care. '[UK 5-year antimicrobial resistance strategy 2013 to 2018.](#)' 2013
  134. Department of Health and Social Care. '[UK 20-year vision for antimicrobial resistance.](#)' 2019
  135. Thomson and others. '[An examination of trends in antibiotic prescribing in primary care and the association with area-level deprivation in England.](#)' BMC Public Health 20 1,148 (2020)
  136. Adekanmbi and others. '[Antibiotic use and deprivation: an analysis of Welsh primary care antibiotic prescribing data by socioeconomic status.](#)' JAC. 2020
  137. '[Urinary tract infection \(lower\): antimicrobial prescribing.](#)' NICE NG109
  138. BSAC. '[DH advises on Piperacillin-Tazobactam infection supply problems 2017.](#)'
  139. '[Management of infection guidance for primary care for consultation and local adaptation.](#)'
  140. [Quality Premium guidance 2017 to 2019 on reducing gram negative blood stream infections \(BSI\) across the whole health economy – Parts A and B](#)
  141. NHS England. [Quality Premium guidance 2017 to 2019 \(2018\)](#)
  142. NHS England. [Quality Premium guidance 2015 to 2016 \(2015\)](#)
  143. Rezel-Potts and others. '[Antimicrobial stewardship in the UK during the COVID-19 pandemic: a population-based cohort study and interrupted time-series analysis.](#)' British Journal of General Practice 2021: volume 71
  144. Zhu and others. '[Investigating the impact of COVID-19 on primary care antibiotic prescribing in North West London across 2 epidemic waves.](#)' Clinical Microbiology and Infection. CMI 2021
  145. Malcolm and others. 'Impact of the COVID-19 pandemic on community antibiotic prescribing in Scotland.' JAC 2020. doi: 10.1093/jacamr/dlaa105

146. Rezel-Potts and others. '[Antimicrobial stewardship in the UK during the COVID-19 pandemic: a population-based cohort study and interrupted time-series analysis.](#)' British Journal of General Practice 2021: volume 71
147. Bou-Antoun and others. 'Age-related decline in antibiotic prescribing for uncomplicated RTIs in primary care in England following the introduction of a national financial incentive (the Quality Premium) for health commissioners to reduce use of antibiotics in the community: an interrupted time series analysis.' Journal of Antimicrobial Chemotherapy 2018 doi: 10.1093/jac/dky237
148. Andrews A and others. '[Surveillance of Antibacterial Usage during the COVID-19 Pandemic in England, 2020.](#)' Antibiotics 2021 volume 10 issue 841
149. NICE guideline NG173. '[COVID-19 rapid guideline: antibiotics for pneumonia in adults in hospital](#)'. 1 May 2020, last updated 9 October 2020
150. [NHS England CQUIN 2017/2019](#)
151. Department of Health and Social Care. '[UK 5-year action plan for antimicrobial resistance 2019 to 2024.](#)' 2019
152. Budd E and others. 'Adaptation of the WHO Essential Medicines List for national antibiotic stewardship policy in England: being AWARe.' Journal of Antimicrobial Chemotherapy 2019: volume 74, pages 3,384-3,389
153. PHE. [Public Health Profiles – AMR local indicators](#)
154. [NICE Pneumonia \(hospital-acquired\): antimicrobial prescribing NG139](#)
155. [NICE Pneumonia \(hospital-acquired\): antimicrobial prescribing NG173](#)
156. Department of Health and Social Care. '[UK 5-year action plan for antimicrobial resistance 2019 to 2024.](#)' 2019
157. NHS England. '[Quality Premium guidance 2017 to 2019.](#)' 2018
158. NHS England. '[Quality Premium guidance 2015 to 2016.](#)' 2015
159. Rezel-Potts and others. '[Antimicrobial stewardship in the UK during the COVID-19 pandemic: a population-based cohort study and interrupted time-series analysis.](#)' British Journal of General Practice 2021 volume 71
160. Zhu and others. '[Investigating the impact of COVID-19 on primary care antibiotic prescribing in North West London across 2 epidemic waves.](#)' Clinical Microbiology and Infection CMI 2021
161. Shah S, Wordley and Thompson W. 'How did COVID-19 impact on dental antibiotic prescribing across England?' British Dental Journal 2020: volume 229 pages 601–604
162. NICE '[Pneumonia \(hospital-acquired\): antimicrobial prescribing NG139](#)'
163. NICE '[COVID-19 rapid guideline: antibiotics for pneumonia in adults in hospital NG173](#)'
164. Gerver Sarah M and others. 'National surveillance of bacterial and fungal co- and secondary infection in COVID-19 patients in England – Lessons from the first wave.' Clinical Microbiology and Infection 2021 doi:10.1016/j.cmi.2021.05.040
165. Andrews A and others. '[Surveillance of antibacterial usage during the COVID-19 pandemic in England, 2020.](#)' Antibiotics 2021 volume 10 page 841
166. Department of Health and Social Care. '[UK 5-year action plan for antimicrobial resistance 2019 to 2024.](#)' 2019



167. European Centre for Disease Prevention and Control. '[Antimicrobial consumption database \(ESAC-Net\)](#).' 2019
168. '[European surveillance of antimicrobial consumption: antibiotic consumption in the community 1997 to 2017](#).' Journal of Antimicrobial Chemotherapy 2021: volume 76, issue Supplement 2
169. Bou-Antoun and others. 'Age-related decline in antibiotic prescribing for uncomplicated RTIs in primary care in England following the introduction of a national financial incentive (the Quality Premium) for health commissioners to reduce use of antibiotics in the community: an interrupted time series analysis.' Journal of Antimicrobial Chemotherapy 2018. doi: 10.1093/jac/dky237
170. Balinskaite and others. 'An Assessment of Potential Unintended Consequences Following a National Antimicrobial Stewardship Program in England: An Interrupted Time Series Analysis.' Clinical Infectious Diseases 2018. doi: 10.1093/cid/ciy904
171. '[UK 5 -year national action plan](#).' January 2019
172. PHE. [TARGET antibiotic toolkit](#).
173. [TARGET antibiotics website](#)
174. [TARGET antibiotics toolkit patient information leaflets](#)
175. Hayes CV, Mahon B, Sides E, Allison R, Lecky, DM, McNulty CAM. '[Empowering patients to self-manage common infections: qualitative study informing the development of an evidence-based patient information leaflet](#).' Antibiotics 2021 volume 10 page 1,113
176. '[Antimicrobial stewardship: changing risk-related behaviours in the general population](#).' January 2017
177. [TARGET antibiotics toolkit quick reference tools](#)
178. [NICE antimicrobial stewardship prescribing guidance summary tables](#)
179. [TARGET antibiotics toolkit quick reference tools](#)
180. [NICE antimicrobial stewardship prescribing guidance summary tables](#)
181. [Guidance: Urinary tract infection: diagnostic tools for primary care](#)
182. PSNC. [AMS virtual event now on-demand. 21 April 2021](#)
183. [COVID-19 rapid guideline: managing COVID-19. Update September 2021](#)
184. [PrescQIPP anti-microbial stewardship](#)
185. Ashiru-Oredope D, Kerr F, Hughes S, Urch J, Lanzman M, Yau T, Cockburn A, Patel R, Sheikh A, Gormley C, Chavda A, Vaghela T, Phillips C, Reid N, Brady A. 'Assessing the impact of COVID-19 on antimicrobial stewardship activities and programs in the United Kingdom.' Antibiotics 2020: volume 10, issue 110. doi:10.3390/antibiotics10020110
186. NHS. [2019 to 2020 NHS standard contract](#)
187. PHE. '[ESPAUR Report 2019 to 2020](#).' November 2020
188. NHS. [Full-length NHS standard contract 2020 to 2021](#). March 2020
189. NHS. [NHS operational planning and contracting guidance](#)
190. NHS. [Full-length NHS standard contract 2020 to 2021](#). March 2020
191. NHS. [Full-length NHS standard contract 2020 to 2021](#). March 2020
192. NHS. [Commissioning for Quality and Innovation \(CQUIN\)](#). February 2020
193. NHS. [Antimicrobial resistance CQUIN 2019 to 2020](#)
194. NHS. [Outpatient transformation platform empowering patients](#)

195. NHS. [Future NHS](#)
196. [ePACT2](#)
197. [Antimicrobial Stewardship - RightCare UTI focus pack dashboard](#)
198. NICE. [NICE guidance: urinary tract infection \(lower\) antimicrobial prescribing](#). October 2018
199. [NHS Model Health System](#)
200. [NHS Oversight Framework](#)
201. [NHS System Oversight Framework](#) June 2021
202. [Pharmacy Quality Scheme 2021 to 2022](#)
203. [Drug Tariff Part VIIA Pharmacy Quality Scheme](#) NHSBSA
204. [PHE Antimicrobial Stewardship for Community Pharmacy e-learning and e-assessment](#). February 2020
205. [Pharmacy Quality Scheme 2021 to 2022](#) NHSBSA
206. [PHE Target Antibiotic Checklist](#) April 2021
207. Ashiru-Oredope D, Kerr F, Hughes S, Urch J, Lanzman M, Yau T, Cockburn A, Patel R, Sheikh A, Gormley C and others. '[Assessing the Impact of COVID-19 on antimicrobial stewardship activities and programs in the United Kingdom](#).' Antibiotics 2021: volume 10 page 110
208. Armitage R and Nukkums LB. '[Antibiotic prescribing in general practice during COVID-19](#).'
209. '[UK 20-year vision for antimicrobial resistance](#).' January 2019
210. '[UK 5-year national action plan for antimicrobial resistance 2019 to 2024](#).' January 2019
211. [TARGET Antibiotics – Prescribing in Primary Care](#). January 2019
212. '[Tackling antibiotic resistance: what should dental teams do? Future learn MOOC](#).' 2020
213. [Antimicrobial stewardship for community pharmacy staff](#). Updated August 2021
214. [TARGET antibiotic checklist](#). Updated July 2021
215. [LPC members' area](#)
216. [Antibiotic Guardian](#)
217. [TARGET antibiotics toolkit - training resources](#)
218. [TARGET antibiotics toolkit](#)
219. [e-Bug Health Educator Training](#) 2019
220. '[Preventing and managing infections in childcare and pre-school](#).' 2020
221. [National Student AMR Conference website](#) November 2020
222. [Antibiotic Guardian Awards shortlist](#) 2020
223. [Antibiotic awareness: toolkit for healthcare professionals in England](#) updated October 2020
224. Lecky DM, Granier S, Allison R, Verlander NQ, Collin SM, McNulty CAM. '[Infectious disease and primary care research—what English general practitioners say they need](#).' Antibiotics 2020: volume 9 issue 265
225. Kilpatrick M, Hutchinson A, Manias E and others. '[Paediatric nurses', children's and parents' adherence to infection prevention and control and knowledge of antimicrobial stewardship: A systematic review](#).' American Journal of Infection Control
226. Wellcome Trust. 'Reframing resistance: How to communicate about antimicrobial resistance effectively.'
227. Ipsos MORI (2014) 'Use, knowledge and attitude survey about antibiotics.'



228. Solutions Research (2015) 'Antimicrobial resistance: Qualitative communications research'
229. HM Government (2019) '[Tackling antimicrobial resistance 2019 to 2024: the UK's 5-year national action plan](#)'
230. Garratt I and others. 'Long-term exposure to octenidine in a simulated sink-trap environment results in selection of *Pseudomonas aeruginosa*, *Citrobacter* and *Enterobacter* isolates with mutations in efflux pump regulators.' *Applied and Environmental Microbiology* 2021
231. Toscani A and others. 'Development of photoactivable phenanthroline-based manganese(I) CO-Releasing molecules (PhotoCORMs) active against ESKAPE bacteria and bacterial biofilms.' *European Journal of Medicinal Chemistry* 2021
232. Wand ME and others. 'Mutations in the 2 component regulator systems PmrAB and PhoPQ give rise to increased colistin resistance in *Citrobacter* and *Enterobacter* spp.' *Journal of Medical Microbiology* 2020
233. Manzo G and others. 'A pleurocidin analogue with greater conformational flexibility, enhanced antimicrobial potency and in vivo therapeutic efficacy.' *Communications Biology* 2020
234. Spencer DC and others. 'A fast impedance-based antimicrobial susceptibility test.' *Nature Communications* 2020
235. Impey RE and others. 'Overcoming intrinsic and acquired resistance mechanisms associated with the cell wall of Gram-negative bacteria.' *Antibiotics (Basel)* 2020
236. HM Government (2019). '[Tackling antimicrobial resistance 2019 to 2024: the UK's 5-year national action plan](#).'
237. Wloch C, Wilson J, Lamagni T and others. 'Risk factors for surgical site infection following caesarean section in England: results from a multicentre cohort study.' *BJOG* 2012: volume 119 pages 1,324–1,333
238. Wloch C, Van Hoek AJ, Green N, Conneely, J, Harrington P, Sheridan E, Wilson J, Lamagni T. 'Cost–benefit analysis of surveillance for surgical site infection following caesarean section.' *British Medical Journal Open* July 2020: 10:e036919
239. Protocol on [The health-related quality of life impact of antibiotic resistance: a systematic review](#)
240. HM Government (2019). '[Tackling antimicrobial resistance 2019 to 2024: the UK's 5-year national action plan](#)' (accessed 30 April 2021)

# Acknowledgements

## Infographics

Jon White

## Chapter 1. Introduction

Susan Hopkins

## Chapter 2. Antibiotic resistance

Emma Carter, Jamie Rudman, Daniel Bradshaw, David Canitrot, Martin Dedicoat, Rosanne DeJong, GRASP team, Angie Lackenby, Tamyo Mbisa, Rachel Merrick, Respiratory Virus Unit, Tuberculosis Unit, Kate Wilson, Sarah Gerver, Rebecca Guy.

## Chapter 3. Acquired carbapenemase-producing Gram-negative bacteria

Kirsty Bennet, Colin Brown, Sarah Gerver, Gauri Godbole, Katie Hopkins, Alice Ledda, Diane Pople, Rebecca Guy.

## Chapter 4. Antifungal resistance, prescribing and stewardship

Holly Fountain, Andy Borman, Colin Brown, Elizabeth Johnson, Mark Leach, Malcolm Qualie, Riina Rautema-Richardson, Sarah Gerver, Rebecca Guy.

## Chapter 5. Antibiotic consumption

Sabine Bou-Antoun, Emma Budd, Colin Brown, Angela Falola, Holly Fountain, Susan Hopkins, Hanna Squire, Sarah Gerver.

## Chapter 6. Antimicrobial stewardship

Donna Lecky, Elizabeth Beech, Ella Casale, Emily Cooper, Shawon Gonzales, Catherine Hayes, Eirwen Sides, Amy Thomas, Diane Ashiru-Oredope.

## Chapter 7. NHS improvement and assurance schemes

Elizabeth Beech, Emma Budd, Audrey Opoku, Hanna Squire.

## Chapter 8. Professional education and training and public engagement

Donna Lecky, Rosie Allison, Catherine Hayes, Wendy Thompson, Mohamad Sadak, Magda Hann, Gina Chen, Emily Cooper, Kirn Chakraborty, Angela Baker, Jordan Charlesworth, Aoife

Hendrick, Shawon Gonzales, Elizabeth Ward, Vincent Ng, Graham McKenzie, Diane Ashiru-Oredope.

## Chapter 9. Keep antibiotics working evaluation

Alison A Hardy.

## Chapter 10. Research

Emily Agnew, Gisela Robles Aguilar, Haroon Ahmed, Juliet Allibone, Rosie Allison, Michelle Cole, Simon Collin, Emily Cooper, Stephanie Evans, Natalie Gold, Aleksandra Herbec, Alison Holmes, Donna Lecky, Alice Ledda, Monsey McLeod, Cliodna McNulty, Ginny Moore, Nichola Naylor, Diane Pople, Brieze Read, Leigh Sanyaolu, Eirwen Sides, Mark Sutton, Amy Thomas, Sarah Tonkin-Crine, Sarah A Walker, Catherine Wloch, Julie Robotham.

## Chapter 11. Stakeholder engagement

Diane Ashiru-Oredope, Christian Binns, Naomi Bull, Ella Casale, Michael Corley, Mary Collier, Tamsin Dewe, Jeff Featherstone, Rose Gallagher, Shawon Gonzales, Kieran Hand, Kitty Healey, Martin Llewelyn, William Malcolm, Sannah Malik, Angela McFarlane, Nicholas Reid, Tracy Rogers, Helena Rosado, Mohamed Sadak, Muhammad Sartaj, Jonathan Underhill, Jamie Woodward.

## Further acknowledgements

With very many thanks to the ESPAUR Oversight Group for their help in reviewing this report.

The authors would also like to express their utmost thanks to Professor Alan Johnson, who although retired in March 2019 has helped edit this report and all the previous ESPAUR reports.

This report has been project managed by Diane Ashiru-Oredope, Ella Casale and Shawon Gonzales.

# About the UK Health Security Agency

The [UK Health Security Agency](#) is an executive agency, sponsored by the [Department of Health and Social Care](#).

© Crown copyright 2021

Published: November 2021

Publishing reference: GOV-9892



You may re-use this information (excluding logos) free of charge in any format or medium, under the terms of the Open Government Licence v3.0. To view this licence, visit [OGL](#). Where we have identified any third party copyright information you will need to obtain permission from the copyright holders concerned.



UKHSA supports the UN  
Sustainable Development Goals

