



Public Health
England

Protecting and improving the nation's health

English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR)

Report 2018

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Contents

About Public Health England	2
Executive summary	5
1. Introduction	9
2. Antibiotic resistance	11
Introduction	11
Trends in resistance as assessed by the proportions of blood culture isolates resistant to key antibiotics	12
Surveillance of carbapenemase-producing Gram-negative bacteria	20
Surveillance of antimicrobial resistance in <i>Neisseria gonorrhoeae</i>	23
Tuberculosis	24
UK participation in international surveillance of AMR	27
Discussion	29
3. Antibiotic consumption	31
Introduction	31
Antibiotics	31
Prescribing in primary care	37
Quality Premium	39
Prescribing in secondary care	44
CQUIN	49
Independent sector	53
European collaboration	53
Discussion	53
4. Antifungal resistance, prescribing and stewardship	57
5. Antimicrobial stewardship	61
Introduction	61
TARGET toolkit resources development	62
Antimicrobial stewardship in secondary care	68
6. Professional education & training and public engagement	74
Keep Antibiotics Working campaign	74
Antibiotic Guardian campaign	75
Delivery of antimicrobial stewardship workshops and training events for healthcare professionals and students	78
e-Bug stakeholder engagement	86
Health Equity Assessment Tool (HEAT) assessing AMR activities	87
Development of consensus-based national antimicrobial stewardship competencies for UK undergraduate healthcare professional education	88
7: Stakeholder engagement	93
British Dental Association	93
British Society for Antimicrobial Chemotherapy	93
Care Quality Commission	94
The Faculty of General Dental Practice UK	95

National Institute for Health and Care Excellence (NICE)	96
Royal Pharmaceutical Society	97
Acknowledgements	99
Chapter 1: Introduction	99
Chapter 2: Antibiotic resistance	99
Chapter 3: Antimicrobial consumption	99
Chapter 4: Antifungal resistance, prescribing and stewardship	99
Chapter 5: Antimicrobial stewardship	100
Chapter 6: Professional education & training and public engagement	100
Research in antimicrobial stewardship	138
Annex Chapter 2: Antibiotic resistance	151
Methods	151
Annex Chapter 3: Antibiotic consumption	158
Methods	158
Piperacillin-tazobactam supply problems	163

Executive summary

This is the fifth annual report of the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR), which was established in 2013 to support Public Health England (PHE) in the delivery of the UK Five Year Antimicrobial Resistance Strategy 2013 to 2018.

Chapter 2 focusses on the trends in antibiotic resistance for the common causes of bloodstream infection (BSI), gonorrhoea and tuberculosis (TB) from 2013 to 2017.

The proportions of bacterial species causing BSIs that are resistant to key antibiotics have remained stable over the last 5 years. This likely reflects the importance of stewardship activities that have reduced levels of antibiotic prescribing, which in turn reduced selective pressure for spread of resistant strains. However the burden of resistance as measured in terms of total numbers of antibiotic-resistant BSIs has increased by 35% from 2013 to 2017, driven predominantly by the year-on-year increased incidence of BSI.

Referrals of Gram-negative bacteria to PHE for carbapenemase (a group of enzymes that confers resistance to carbapenem antibiotics) testing increased year-on-year, with approximately 3000 isolates confirmed as positive for at least 1 carbapenemase in 2017. The majority of isolates referred were from sites suggesting colonisation rather than clinical infection, with the proportion of isolates from bloodstream infections each year ranging from 11.3% (in 2014) to 7.2% (2017). Although the majority of *E. coli* and *K. pneumoniae* detected from blood (>98%) remain phenotypically susceptible to carbapenems at the present time, there is no room for complacency given the rapid increases in carbapenem resistance reported from a number of other countries.

In 2017, 44,676 diagnoses of gonorrhoea were reported, a 22% increase relative to the previous year. Resistance in *N. gonorrhoeae*, particularly to ceftriaxone and azithromycin which are used in combination as recommended first-line therapy, is monitored through the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP); of the 1,268 gonococcal isolates collected through the sentinel surveillance system in 2017, no isolates were phenotypically resistant to ceftriaxone although the prevalence of azithromycin resistance was 9.2%.

In 2017, 5,102 people were notified with TB in England; 71% were born outside the UK. Resistance predictions from whole genome sequencing for at least isoniazid and rifampicin were available for 98.8% of notified cases of culture-confirmed TB. Among these, 8.5% had resistance to at least 1 first-line antibiotic, of which 5.7% (177/3,115) had resistance to isoniazid without multi-drug resistant TB (MDR-TB) and there were 55

cases of TB where the infecting strain had any resistance to rifampicin, including those with MDR-TB.

Chapter 3 highlights the progress in reducing total antibiotic consumption in England, which fell by 6.1% between 2014 and 2017; this was the inverse of what occurred between 2010 and 2013 when a 6% increase was observed. In 2017, the most commonly used antibiotics in England continued to be penicillins (44.6%), tetracyclines (22.2%) and macrolides (14.7%).

Primary care settings accounted for 81% of all antibiotics prescribed in 2017. However, the number of antibiotic prescriptions dispensed in primary care declined from 754 per 1000 inhabitants in 2013 to 654 per 1000 inhabitants in 2017, equating to a drop of 13.2% in 5 years. Between 2014/15 and 2017/18, there were more than 3.7 million fewer antibiotic prescriptions dispensed from community pharmacies.

In addition, Clinical Commissioning Groups (CCGs), through the national Quality Premium, showed significant progress across 3 antibiotic quality indicators in 2017/18:

- 99% of CCGs delivered a 10% reduction (or greater) in the trimethoprim: nitrofurantoin prescribing ratio
- 95% of CCGs delivered a 10% reduction (or greater) in the number of trimethoprim items prescribed to patients aged 70 years or more
- 85% of CCGs delivered a reduction in total antibiotic prescribing in primary care to levels below the England 2013/14 mean performance value of 1.161 items per STAR-PU (Specific Therapeutic Age-sex weightings Related Prescribing Units; use of STAR-PU allows more meaningful comparisons by taking into account the age and sex distribution of patient populations)

Overall antibiotic consumption in secondary care in England increased by 7.7% between 2013 and 2017. Prescribing for hospital inpatients increased by only 2% but increased by 21% in hospital outpatient settings over the five-year period. This is an improvement compared to the data presented in the first ESPAUR report, where from 2010 to 2013, prescribing to hospital inpatients increased by 11.9%. This potentially reflects improved focus on antibiotic stewardship for hospital inpatients.

In 2017, the increased level of antibiotic prescribing in hospital inpatients also reflects a shortage in the supply of a key broad-spectrum antibiotic, piperacillin/tazobactam. The need to use 2 or more alternative antibiotics to give the same degree of antibacterial coverage resulted in an additional 2.2 million DDDs being dispensed.

In 2017/18, 23%, 75% and 45% of 152 NHS acute Trusts met their objectives to reduce total antibiotic, piperacillin/tazobactam and carbapenem consumption, respectively, as measured through the national Commissioning for Quality and Innovation (CQUIN).

Chapter 4 highlights the ongoing work on fungal resistance and surveillance. It also reports the effective control of *Candida auris* in English hospitals with no sustained outbreaks currently occurring, despite frequent introductions from abroad, as large-scale outbreaks continue to be documented in several continents.

Chapter 5 highlights the ongoing work from PHE and associated professional organisations and research partners on delivering tools, interventions and evaluations related to antimicrobial stewardship. It presents early data from PHE modelling work on inappropriate antibiotic use in secondary care, where through an audit of antibiotic use by NHS antimicrobial stewardship teams, 17.1% of total antibiotic therapy days were estimated to be unnecessary.

PHE produces, develops and maintains key antimicrobial stewardship resources in primary care that are available through the TARGET (Treat Antibiotics Responsibly, Guidance, Education, Tools) toolkit that is held on the Royal College of General Practitioners website. Year-on-year the website receives increased numbers of visits, with almost 7,000 visits in October 2017 and over 8,000 visits in November 2017. A national evaluation of TARGET demonstrated that 99% of CCGs actively promoted the TARGET Antibiotics Toolkit and were using the PHE common infection guidelines, while 94% of CCGs actively promoted TARGET patient leaflets. In addition, in November 2017, 3 of the TARGET 'Treating Your Infection' patient leaflets were endorsed by NICE; 1 for urinary tract infections and text-based and pictorial leaflets for respiratory tract infection.

Chapter 6 highlights the work on public and professional education and awareness. The Keep Antibiotics Working campaign was launched nationally in October 2017. More than 750,000 Keep Antibiotics Working posters and leaflets were distributed to a range of partners including local authorities, health care centres and Housing Associations. Other materials that PHE produces, such as Antibiotic Guardian and TARGET were rebranded in line with this campaign.

The very successful engagement and behaviour change campaign continued to grow, with more than 57,000 Antibiotic Guardian pledges from 129 countries by the end of 2017. The website and pledges are now available in 5 languages, with pledges available for human and animal health professionals, healthcare system leaders and organisations, healthcare students and engaged members of the public.

e-Bug is PHE's international innovative educational resource for children and young people on hygiene, spread of infection and antibiotics. It has effective and highly relevant resources that include an interactive and multi-lingual website (www.e-bug.eu) with a comprehensive collection of teaching packs for use in schools and the community. The e-Bug resources were endorsed by NICE in 2016 and are currently

available in over 30 different languages, being implemented in 26 countries globally; all material present in the e-Bug resources is linked to the English national curriculum. In November 2017, the e-Bug 'Antibiotics Explained' YouTube video received 15,300 views and its World Antibiotic Awareness Week social media campaign gained 62.3k impressions on Twitter.

Finally, Chapter 7 highlights key work from our partner organisations and professional societies. Their input individually to increase awareness and develop tools and also collectively in supporting the ESPAUR oversight group is a key component of the success of this work.

1. Introduction

The English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) was established in 2013 to support Public Health England (PHE) in the delivery of specific aspects of the UK Five Year Antimicrobial Resistance Strategy 2013 to 2018.¹ The aims of the ESPAUR are to:

- develop and maintain robust surveillance systems for monitoring and reporting trends in antimicrobial use and resistance in order to measure the impact of surveillance, antimicrobial stewardship and other interventions on antimicrobial resistance that affect human health
- develop systems and processes to optimise antimicrobial prescribing across healthcare settings

This report highlights that there has been a continued reduction in antibiotic prescribing, driven by reductions in primary care. Antibiotic prescribing has increased in secondary care, in part driven by key antibiotic shortages and replacements of a single broad-spectrum antibiotic with 2 or 3 narrower antibiotics to have the same overall clinical impact.

Despite the improvements in antibiotic prescribing over the last 5 years, we have nonetheless seen a continued rise in the burden of antibiotic-resistant infections, reflecting year-on-year increases in bloodstream infections. It is clear that more work needs to be done to both prevent serious infections and reduce the pressure of antibiotic use for the selection of antibiotic-resistant bacteria.

Without effective antibiotics, cancer treatments and surgical operations may become life-threatening. Cancer diagnoses continue to increase, with more than 350,000 people diagnosed with cancer in 2015, 28% of whom received chemotherapy.² Both cancer and chemotherapy reduce the ability of our immune system to fight infection and antibiotics are critical to both prevent and/or treat infections in these patients. In the national antimicrobial use point prevalence survey (PPS) performed in acute hospitals in 2016, over half of the inpatients under the care of haematology or oncology consultants were receiving an antimicrobial with the indication split between preventative treatment (prophylaxis), treatment of community infections or treatment of

¹Department of Health and Social Care. UK 5 Year Antimicrobial Resistance Strategy 2013 to 2018. Available online from: assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_strategy.pdf

² Cancer Research UK. Cancer diagnosis and treatment statistics. 2015. Available online from: www.cancerresearchuk.org/health-professional/cancer-statistics-for-the-uk#heading-Four

hospital infections. Patients receiving treatment under oncology or haematology specialties were almost 4 times as likely to have a healthcare-associated infection (similar to those in intensive care units) compared to other patients in the hospital and twice as likely to be receiving an antibiotic.

More than 9 million surgical procedures are performed in England each year. Surgical prophylaxis is recommended where the procedure involves the insertion of a prosthesis or implant, in clean-contaminated (incision through respiratory, gastrointestinal or genitourinary tract) or contaminated surgery (breach in sterile technique, gross spillage from the gastrointestinal tract or acute inflammation found at surgery). It is estimated that approximately 1 in 3 surgical procedures require antibiotics to be given prior to or during surgery to prevent infections. The 4 commonest types of surgical procedure requiring antibiotic prophylaxis, with the numbers of procedures performed in the NHS in 2017/18 are outlined in Table 1.1.

Table 1.1: Numbers of common surgical procedures performed in the NHS 2017/18³

Procedure	Number of procedures performed
Hip or Knee replacement	191,635
Caesarean section	174,945
Gastrointestinal tract (oesophagus, stomach and bowel)	87,616
Gall bladder removal	77,126

³ NHS Digital. Hospital Admitted Patient Care Activity 2017/18. Available online from digital.nhs.uk/data-and-information/publications/statistical/hospital-admitted-patient-care-activity/2017-18

2. Antibiotic resistance

Introduction

This chapter focusses on the trends in resistance for the drug/bug combinations recommended for surveillance by the Department of Health and Social Care (DHSC) Expert Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare-Associated Infections (APRHAI) in support of the UK Five Year Antimicrobial Resistance (AMR) Strategy.⁴ It includes the ‘Shadow’ list of drug/bug combinations for which APRHAI recommended a watching brief should be kept (Table 2.1). The data presented cover the period from 2013 (the year of publication of the national AMR strategy) to 2017. The data sources and analytical methods used are described in [Annex - Chapter 2](#) of this report.

Table 2.1 Drug/bug combinations monitored in support of the UK 5-year AMR Strategy, 2013-18

Bacteria	Antibiotics
<i>Escherichia coli</i>	Ciprofloxacin, third-generation cephalosporins, gentamicin, carbapenems, co-amoxiclav, piperacillin/tazobactam*
<i>Klebsiella pneumoniae</i>	Ciprofloxacin, third-generation cephalosporins, gentamicin, carbapenems, co-amoxiclav, piperacillin/tazobactam*
<i>Klebsiella oxytoca</i> *	Ciprofloxacin, third-generation cephalosporins, gentamicin, carbapenems, piperacillin/tazobactam
<i>Pseudomonas</i> spp.	Ceftazidime, carbapenems
<i>Acinetobacter</i> spp.*	Colistin
<i>Streptococcus pneumoniae</i>	Penicillin, erythromycin
<i>Enterococcus</i> spp.*	Glycopeptides
<i>Staphylococcus aureus</i> *	Methicillin
<i>Neisseria gonorrhoeae</i>	Ceftriaxone, azithromycin

* Bacteria or antibiotics in the “Shadow” list

⁴ Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection Annual report 2015. Available online from: assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/707165/ARHAI_annual_report_2014_to_2015.pdf

In 2016, as part of its efforts to tackle the threat to public health posed by AMR, the UK government announced an ambition to reduce the number of healthcare-associated Gram-negative bloodstream infections in England by 50% by March 2021.⁵ To complement this strategic initiative, this chapter reports on initial work aimed at assessing the burden of AMR using estimated numbers of antibiotic-resistant bloodstream infections, based on the drug/bug combinations listed in Table 2.1. The underlying rationale for this work is to develop an improved metric for assessing the impact of interventions aimed at reducing AMR.

This chapter also provides an update on trends in referral and confirmation of carbapenemase-producing bacteria to the national reference laboratory together with an assessment of the use of the Electronic Reporting System for enhanced surveillance of carbapenemase producers. Other topics covered include an update of resistance in *Neisseria gonorrhoeae* and *Mycobacterium tuberculosis* and the UK contribution to the international surveillance of AMR through participation in EARS-Net (European Antimicrobial Resistance Surveillance Network) and GLASS (Global Antimicrobial Resistance Surveillance System) run under the auspices of the European Centre for Disease Prevention and Control (ECDC) and the World Health Organization (WHO), respectively.

Trends in resistance as assessed by the proportions of blood culture isolates resistant to key antibiotics

Gram-negative bacteria

As shown in Figure 2.1, the proportion of isolates of *Escherichia coli*, *Klebsiella pneumoniae*, *Klebsiella oxytoca* and *Pseudomonas* spp. resistant to key antibiotics remained broadly stable between 2013 and 2017. Non-susceptibility to piperacillin/tazobactam and co-amoxiclav in *E. coli* appeared to increase slightly between 2016 and 2017, as did non-susceptibility to piperacillin/tazobactam in *Pseudomonas* spp. However, ongoing work by PHE has raised doubt as to the robustness of this finding, as some data, particularly that reported from laboratories using specific automated antibiotic susceptibility testing devices may be over-estimating resistance levels, particularly intermediate resistance.

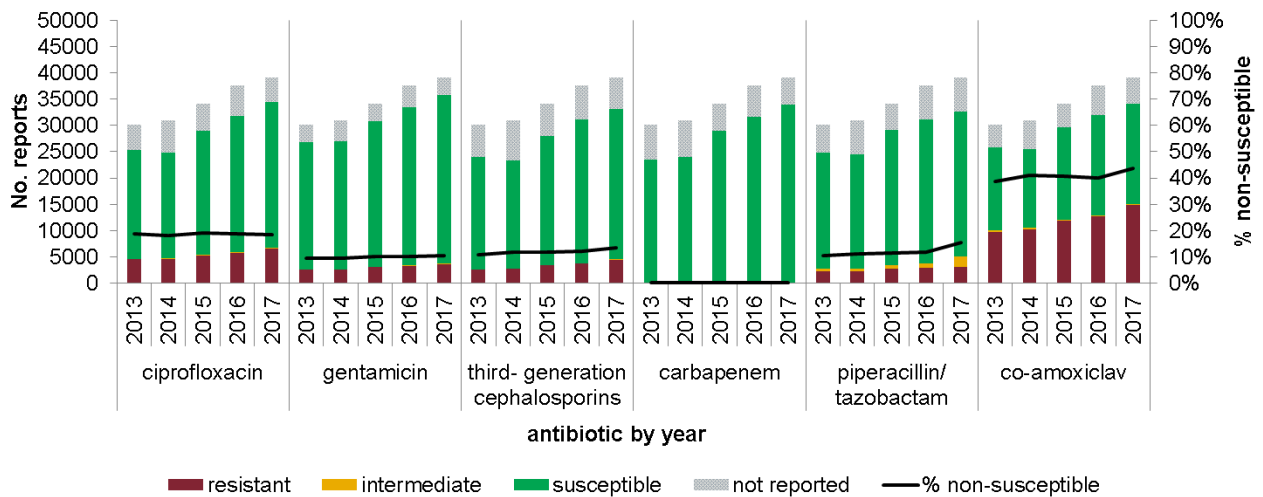
⁵ Department of Health and Social Care. Antimicrobial resistance review: government response. 2016. Available online from: www.gov.uk/government/publications/government-response-the-review-on-antimicrobial-resistance

Gram-positive bacteria

The overall proportion of enterococci reported as non-susceptible to glycopeptides remained stable over time, ranging from 15 to 18%. There was inter-species variation in glycopeptide non-susceptibility with only 2-3% of *Enterococcus faecalis* showing such resistance compared to 23-27% of *Enterococcus faecium* (Figure 2.2).

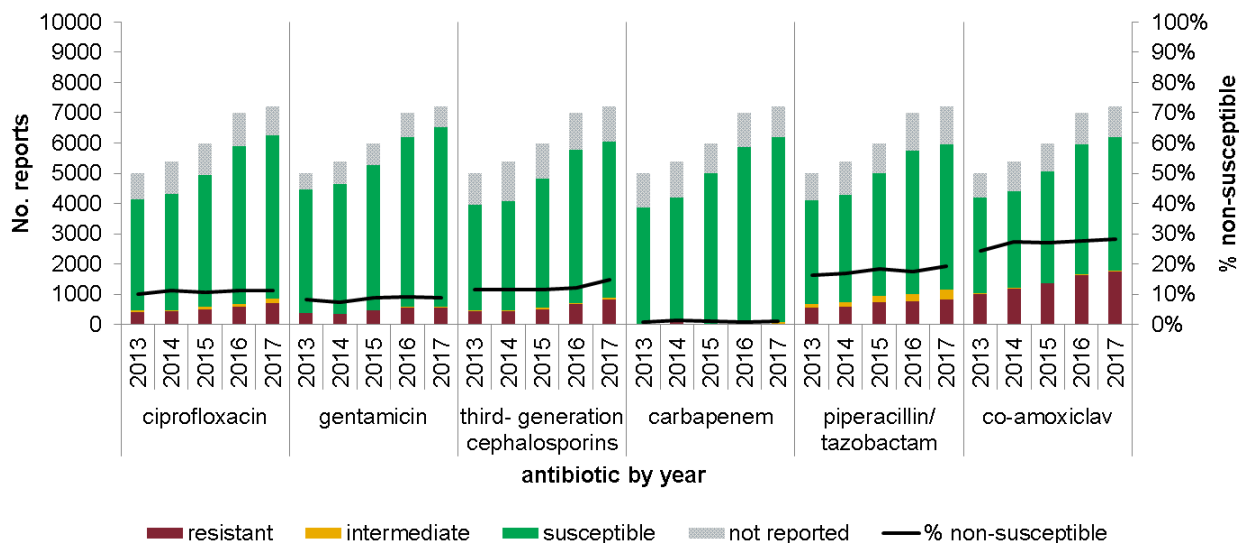
Throughout the 5 year surveillance period, the proportion of bloodstream isolates of *Streptococcus pneumoniae* non-susceptible to penicillin and macrolides remained fairly stable at 3–4% and 5-8%, respectively. Based on reporting to the national mandatory surveillance system, the proportion of *Staphylococcus aureus* that were methicillin-resistant *S. aureus* (MRSA) continued to decline year-on-year from 9.5% in 2012/13 to 6.6% in 2017/18. Detailed trend data for all 3 pathogens are available on-line in the data tables and PowerPoint presentations published alongside this report.⁶

(a) *Escherichia coli*

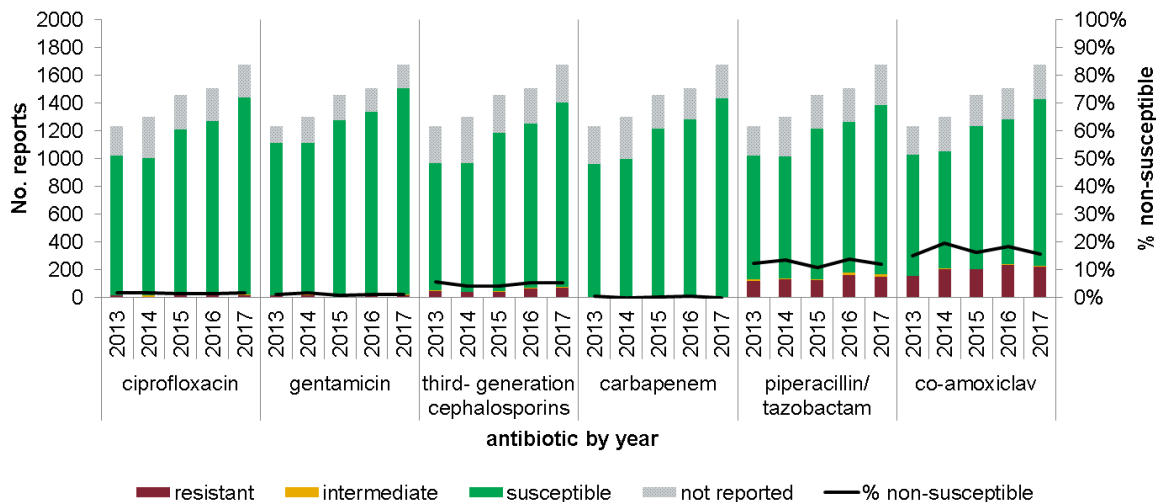


⁶ Public Health England; ESPAUR: report 2018. Available online from: www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report

(b) *Klebsiella pneumoniae*



(c) *Klebsiella oxytoca*



(d) *Pseudomonas* spp.

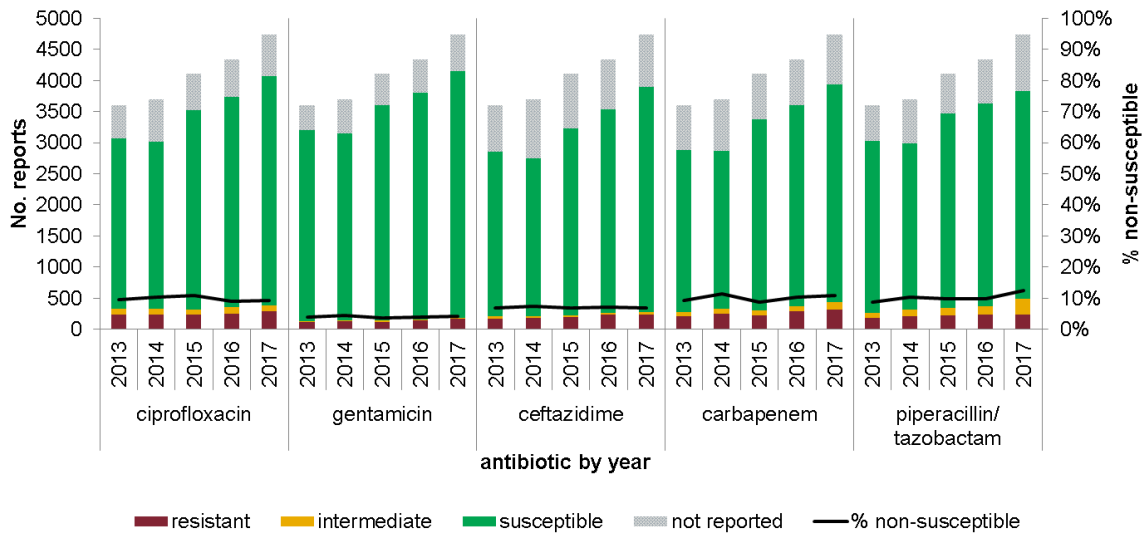
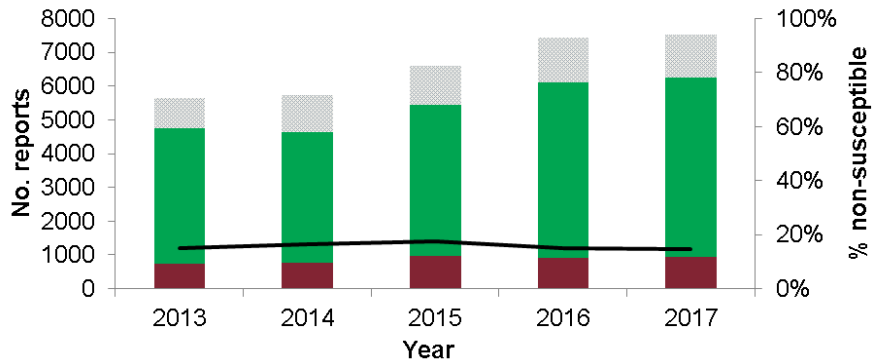
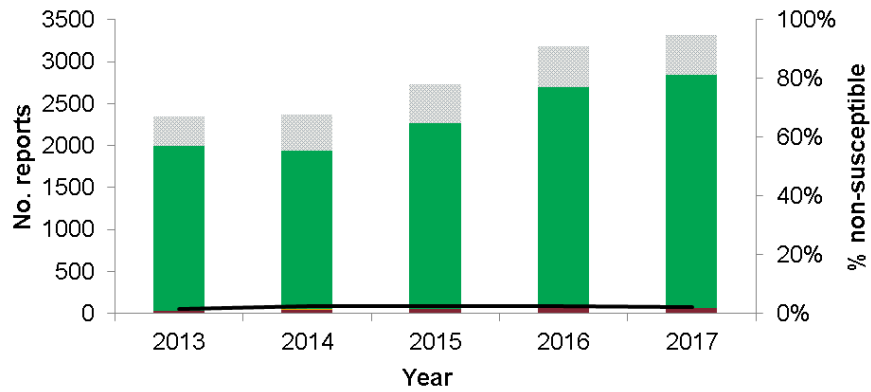


Figure 2.1 Number of bloodstream isolates of (a) *E. coli*, (b) *K. pneumoniae*, (c) *Klebsiella oxytoca* and (d) *Pseudomonas* spp. reported and the proportion non-susceptible to the indicated antibiotics

(a) *Enterococcus* spp.



(b) *Enterococcus faecalis*



(c) *Enterococcus faecium*

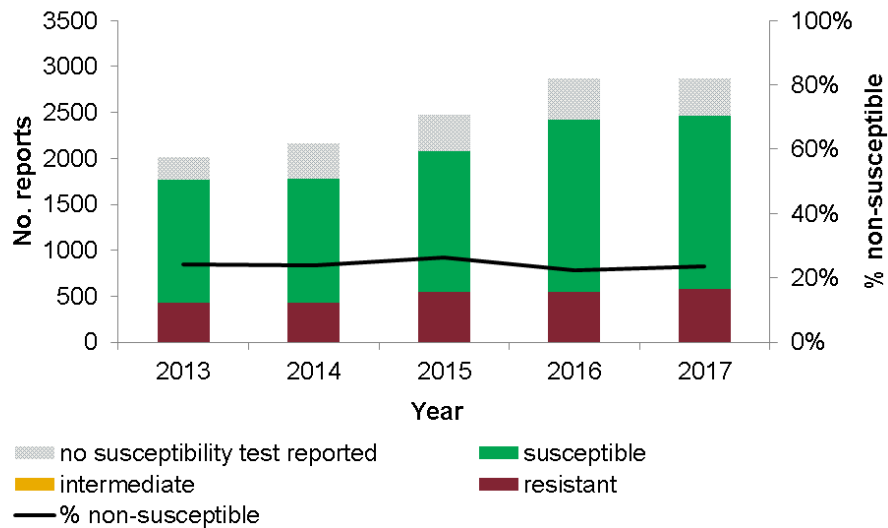


Figure 2.2 Numbers of bloodstream isolates of enterococci and the proportion non-susceptible to glycopeptides

Improvements in surveillance of AMR

Better access to and use of surveillance data was identified as 1 of the 7 key areas for action in the UK Five Year Antimicrobial Resistance Strategy, 2013-2018. Substantial progress has been made towards meeting this action area over the last 5 years.

For many years the mainstay of surveillance in England has been the reporting of routinely generated hospital microbiology laboratory data to a national database maintained by PHE. Up to 2013, microbiology data were primarily stored in a database called LabBase2, with additional antimicrobial susceptibility test data stored in a supplementary database called AmSurv. In 2014 LabBase2 was superseded by the Second Generation Surveillance System (SGSS), with AmSurv being integrated as an AMR module.

In 2013, 82.7% of hospital microbiology laboratories reported data to AmSurv. Since then, there have been substantial improvements in both the representativeness of the data and the timeliness of reporting, with 97% of laboratories providing their antimicrobial resistance data to SGSS in 2017; of these, 92% report on a daily basis and 84% report automatically.

Since April 2016, PHE has made data on AMR available through the 'AMR local indicators' profile of Fingertips, a freely accessible web tool that provides access to a wide range of public health data presented as thematic profiles (fingertips.phe.org.uk/profile/amr-localindicators). Fingertips provides local data that can be viewed at the level of National Health Service acute trusts, Clinical Commissioning Groups or General Practitioner practices, all of which can be compared with the corresponding aggregate values for England to allow benchmarking. The data in Fingertips can be viewed in a range of formats including an overview showing counts and rates, interactive maps, spine charts and graphs that show temporal trends over a range of time scales. The aim of the AMR local indicators profile on Fingertips is to support the development of local action plans to reduce AMR and help stakeholders monitor their impact.

Further work to improve surveillance will focus on patient-level linkage of SGSS microbiology data with other complementary datasets such as Hospital Episode Statistics (HES), which provide clinical and co-morbidity data as well as dates of hospital admission and discharge, allowing infections to be categorised as community or hospital-onset. Further work to improve the quality of the data will focus on greater consistency in coding and improved diagnostic standardisation. The development of such linked datasets will provide new insights into the epidemiology of AMR and facilitate the development of new control measures.

Burden of antibiotic resistance

While the proportion of isolates of the above pathogens showing non-susceptibility to key antibiotics generally remained stable over time, the year-on-year increases in the incidence of bacteraemia shown in Figures 2.1 and 2.2 meant that the burden of resistance, as reflected by the numbers of resistant infections, nonetheless increased over time. Using the methodology described in [Annex – Chapter 2](#), the estimated total numbers of bloodstream infections caused by pathogens resistant to 1 or more key antibiotics increased from 12,250 in 2013 to 16,504 in 2017, a rise of 35% (Figure 2.3). As shown in Figure 2.3, and in more detail in Table 2.2 for infections that occurred in 2017, the burden of antibiotic-resistant bloodstream infections is particularly marked for those caused by Enterobacteriaceae, particularly *E. coli*, as they are the infections with the highest incidence, comprising 84.4% of the total. The burden of resistant infections remains unchanged for Gram-positive infections.

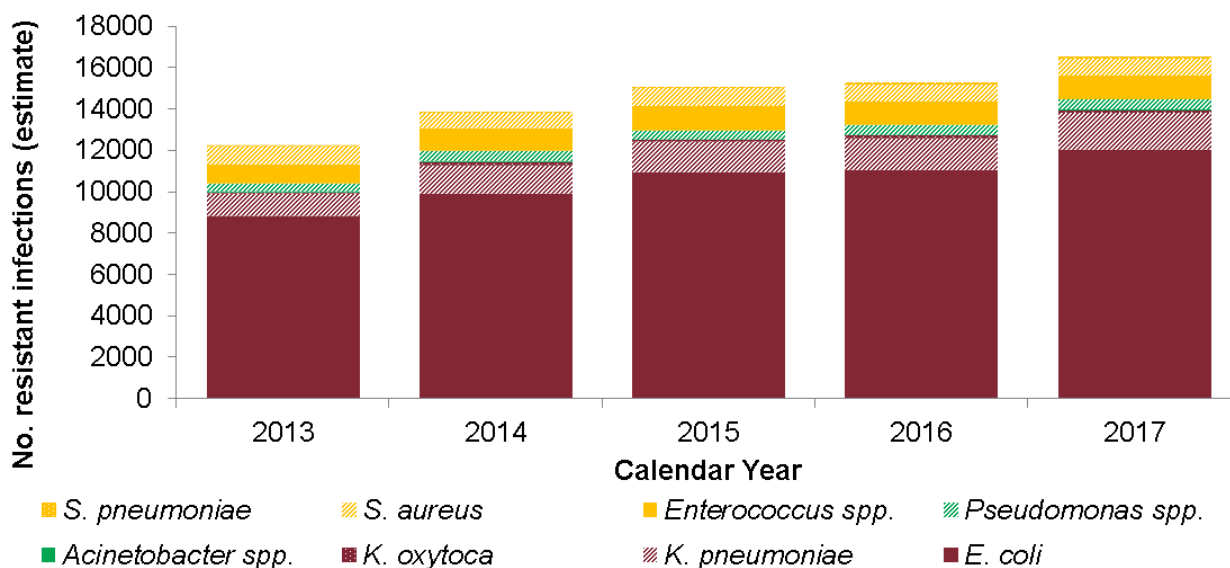


Figure 2.3 Estimated trends in burden of bloodstream infections due to antibiotic-resistant pathogens in England, 2013 to 2017

Table 2.2 Estimated burden of resistant bloodstream infections caused by key drug/bug combinations in England in 2017

Pathogen	Estimated total number of BSI in England [‡]	Proportion resistant (as per SGSS)	Estimated no. of resistant episodes
Enterobacteriaceae	50,727		13,935
<i>Escherichia coli</i> (mandatory reports)	41,287		12,030
Resistant to both carbapenems* and colistin		0.0%	-
Resistant to colistin (but not carbapenems*)		1.1%	439
Resistant to carbapenems* (but not to colistin)		0.1%	22
Resistant to third-generation cephalosporins¥ (but not to colistin or carbapenems*)		13.0%	5,362
Resistant to gentamicin (but not to colistin, carbapenems* or third-generation cephalosporins¥)		6.1%	2,532
Resistant to ciprofloxacin (but not to colistin, carbapenems*, third-generation cephalosporins¥, or gentamicin)		8.9%	3,676
<i>Klebsiella pneumoniae</i>	7,668		1,756
Resistant to both carbapenems* and colistin		0.4%	28
Resistant to colistin (but not carbapenems*)		2.8%	213
Resistant to carbapenems* (but not to colistin)		0.8%	61
Resistant to third-generation cephalosporins¥ (but not to colistin or carbapenems*)		12.6%	967
Resistant to gentamicin (but not to colistin, carbapenems* or third-generation cephalosporins¥)		3.1%	238
Resistant to ciprofloxacin (but not to colistin, carbapenems*, third-generation cephalosporins¥, or gentamicin)		3.2%	247
<i>Klebsiella oxytoca</i>	1,772		149
Resistant to both carbapenems* and colistin		0.0%	-
Resistant to colistin (but not carbapenems*)		1.8%	31
Resistant to carbapenems* (but not to colistin)		0.2%	3
Resistant to third-generation cephalosporins¥ (but not to colistin or carbapenems*)		5.2%	92
Resistant to gentamicin (but not to colistin, carbapenems* or third-generation cephalosporins¥)		0.7%	12
Resistant to ciprofloxacin (but not to colistin, carbapenems*, third-generation cephalosporins¥, or gentamicin)		0.6%	10

‡ except where mandatory reports are available for use as a total - *E. coli* and *S. aureus*; colistin resistance includes those tested for and resistant to polymixins (as reported on SGSS, which may be an overestimate); *meropenem or imipenem and where neither are tested ertapenem; ¥ third-generation cephalosporins include any of ceftazidime, cefotaxime, ceftriaxone or cefpodoxime; ‡ aminoglycosides include gentamicin and amikacin; § resistant to any 3 of ceftazidime, ciprofloxacin, piperacillin/tazobactam or aminoglycosides‡

Pathogen	Estimated total BSI In England Number‡	Proportion resistant (as per SGSS)	Estimated no. of resistant episodes
Non-fermenters Gram-negative	6,134		534
<i>Acinetobacter</i> spp.	1,001		45
Resistant to both carbapenems* and colistin		0.0%	-
Resistant to carbapenems* (but not to colistin)		3.8%	38
Resistant to aminoglycosides‡ and ciprofloxacin (but not to colistin or carbapenems*)		0.6%	6
<i>Pseudomonas</i> spp.	5,133		490
Resistant to colistin		1.2%	63
Resistant to carbapenems* (but not to colistin)		7.9%	403
Resistant to 3 or more antimicrobial groups§ (but not including colistin or carbapenem resistant episodes)		0.5%	24
Gram-positive	26,218		2,035
<i>Enterococcus</i> spp.	7,929		1,116
Resistant to glycopeptides		14.1%	1,116
<i>Staphylococcus aureus</i> (mandatory reports)	12,750		846
Resistant to methicillin (mandatory reports)		7.6%	846
<i>Streptococcus pneumoniae</i>	5,539		73
Resistant to penicillin and macrolides†		0.6%	34
Resistant to penicillin resistant (but not to macrolides†)		0.7%	40
Total	83,079		16,504

‡ except where mandatory reports are available for use as a total - *E. coli* and *S. aureus*; colistin resistance includes those tested for and resistant to polymyxins; *meropenem or imipenem and where neither are tested ertapenem; † third-generation cephalosporins include any of ceftazidime, cefotaxime, ceftriaxone or cefpodoxime; ‡ aminoglycosides include gentamicin and amikacin; § resistant to any 3 of ceftazidime, ciprofloxacin, piperacillin/tazobactam or aminoglycosides‡; † macrolides include erythromycin, azithromycin and clarithromycin

Surveillance of carbapenemase-producing Gram-negative bacteria

Surveillance of carbapenemase-producing bacteria is predicated on the results of molecular tests for the detection of genes that encode carbapenemase enzymes. These tests are performed in the national Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit, but are also increasingly performed in regional PHE and NHS laboratories.

Referrals of Enterobacteriaceae to the AMRHAI Reference Unit increased year-on-year, with approximately 3000 isolates confirmed as positive for at least 1 carbapenemase in 2017 (Figure 2.4). The majority of isolates referred were from sites suggesting colonisation rather than clinical infection, with the proportion of carbapenemase-producing Enterobacteriaceae (CPE) from blood each year varying in the range 11.3% (in 2014) to 7.2% (2017). Detailed information on CPE from blood and the carbapenemases they produced are given in the online annex. The 'big 5' carbapenemase families (KPC, OXA-48-like, NDM, VIM and IMP), and combinations

thereof, accounted for >99% of isolates. Carbapenemases. The OXA-48-like family continue to be the most frequently identified, accounting for 48.5% of confirmed CPE in 2017, followed by NDM (24.4%), KPC (15.1%), IMP (4.7%) and VIM (2.4%). Increased numbers of IMP-positive CPE were identified in 2017 compared with previous years due to an outbreak of IMP-positive *K. pneumoniae* in a London hospital. However, AMRHAI data suggest that IMP-positive CPE may also be becoming more widespread, with 20 laboratories referring 141 isolates in 2017 compared with 14 laboratories referring 63 isolates in 2016. An increase in isolates producing a combination of KPC and OXA-48 enzymes was also observed and was associated with an outbreak of *K. pneumoniae* in a London hospital.

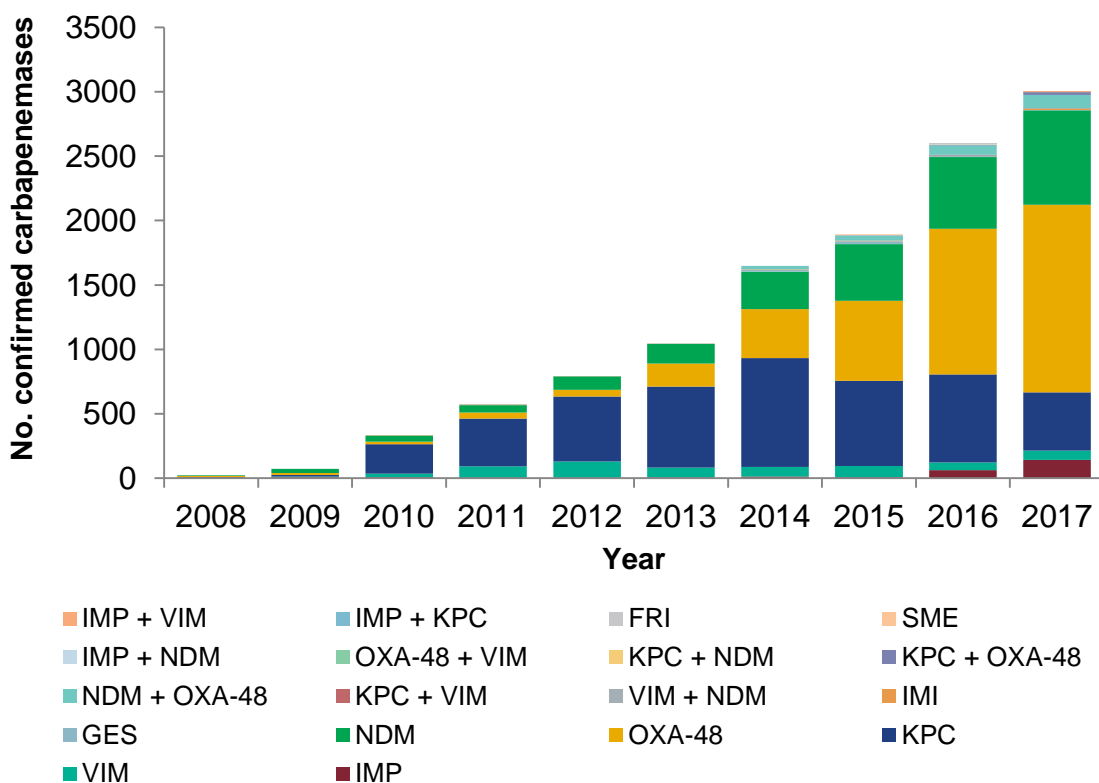


Figure 2.4 Number of confirmed CPE isolates referred to PHE’s AMRHAI Reference Unit, 2008 – 2017

Enhanced surveillance of carbapenemase-producing Gram-negative bacteria via the Electronic Reporting System

To obtain more information on carbapenemase-producing Gram-negative bacteria, an Electronic Reporting System (ERS) was launched in May 2015 to capture enhanced data for isolates submitted to the AMRHAI Reference Unit, with a module to capture local molecular testing added in July 2016. By December 2017, a total of 8,870 de-duplicated organisms (by patient and bacterial species) had been submitted via the ERS. In 2017, approximately 70% of organisms referred to the AMRHAI Reference Unit were received via the ERS.

In the ERS, completion of the data fields for patient demographics and specimen details is mandatory at the time isolates are referred for testing. In contrast, the enhanced data fields for collection of risk factor information are filled in retrospectively on a voluntary basis, following confirmation of carbapenemase production. To date these fields have been poorly completed; for example, in 2017, only 26% of records included information on foreign travel and 14% reported the clinical specialty. An evaluation of the ERS undertaken by the National Institute for Health Research (NIHR) Health Protection Research Unit in Evaluation of Interventions at the University of Bristol confirmed that substantial improvements in the level of reporting of these data are required if sufficient information is to be gathered to allow a better understanding of important risk factors for transmission of carbapenem-resistant bacteria and subsequent infection and/or colonisation of patients.

Due to the poor reporting of enhanced surveillance data and the increase in local laboratories testing for carbapenemase production, PHE is working on integrating data on carbapenemase-producing bacteria derived from local testing into the second generation surveillance system (SGSS). This would result in both phenotypic and genotypic data on carbapenem resistance being available in the same dataset. A survey to ascertain the methods used by local laboratories and investigate how data are stored in local laboratory information management systems was launched in July 2018, and the findings from this survey will inform the development of SGSS to accommodate local carbapenemase test results. Further developments will focus on the linkage of the integrated data in SGSS with complementary data sets such as Hospital Episode Statistics that will provide additional clinical and co-morbidity data, to reduce the data burden on the NHS.

Currently, screening of *Pseudomonas* spp. for carbapenemase genes is only carried out if either AMRHAI or a local laboratory identifies significant imipenem/EDTA synergy and/or a high-level ceftolozane/tazobactam MIC, which are putative markers for the presence of a metallo-enzyme. Although the incidence of *Pseudomonas* spp. producing metallo-enzymes has been increasing, this has not been to the same extent as observed among Enterobacteriaceae. The majority of carbapenemase-positive *Pseudomonas* spp. confirmed by AMRHAI are *P. aeruginosa*, however, metallo-

enzymes have also been identified in *P. putida* group isolates. Most (>80%) harbour a VIM metallo-enzyme, but isolates producing NDM, IMP, DIM and SPM⁷ metallo-enzymes have been identified. The majority of these isolates belong to globally successful 'high risk' clones.⁸ In recent years AMRHAI has also identified small numbers of *Pseudomonas* spp. harbouring non-metallo-enzymes belonging to the GES⁹ and OXA-48-like¹⁰ families.

Most carbapenem-resistant *Acinetobacter* spp. have intrinsic or acquired OXA-type carbapenemases, which are rarely seen outside of the genus. As with *Pseudomonas* spp., screening for other carbapenemase families is dictated by detection of significant imipenem/EDTA synergy either by AMRHAI or the referring laboratory. Whilst numbers of *Acinetobacter* spp. producing metallo-enzymes are low, there has been a steady year-on-year increase in numbers, with NDM and IMP metallo-enzymes the most frequently detected.

Surveillance of antimicrobial resistance in *Neisseria gonorrhoeae*

44,676 diagnoses of gonorrhoea were reported in 2017, a 22% increase relative to the previous year.¹¹ Resistance in *N. gonorrhoeae* is monitored through the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP), which comprises a suite of initiatives to detect and monitor resistance and potential treatment failures.¹² Trend data are derived from the national sentinel surveillance system which collects gonococcal isolates from consecutive patients attending a network of 26 participating genitourinary medicine (GUM) clinics (24 in England, 2 in Wales) over a 3-month period each year. The isolates are referred to PHE's 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. In addition, primary diagnostic laboratories may report the results of their routine susceptibility testing to SGSS. PHE's national reference laboratory also undertakes *ad hoc* testing of gonococcal isolates referred from primary diagnostic laboratories for investigation of suspected resistance to ceftriaxone and/or azithromycin, which are the current recommended first-line therapies.

⁷ Hopkins KL *et al.* J Med Microbiol 2016; 65:696-7.

⁸ Wright *et al.* J Antimicrobial Chemother 2015; 70:103-10.

⁹ Hopkins KL *et al.* GES carbapenemases in Enterobacteriaceae and *Pseudomonas aeruginosa* in the United Kingdom. ASM Microbe 2016; Boston, Mass.

¹⁰ Meunier D *et al.* J Antimicrob Chemother 2016; 71:2056-7.

¹¹ PHE STI report:

assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/713944/hpr2018_AA-STIs_v5.pdf

¹²PHE GRASP report: www.gov.uk/government/publications/gonococcal-resistance-to-antimicrobials-surveillance-programme-grasp-report

Resistance to recommended first-line treatment for gonorrhoea

None of the 1,268 gonococcal isolates collected through the sentinel surveillance system in 2017 were phenotypically resistant to ceftriaxone, defined as a minimum inhibitory concentration (MIC) of >0.125 mg/L, although 7 isolates had MICs on the breakpoint. The modal MIC increased from 0.008 mg/L in 2016 to 0.015 mg/L in 2017, with this increase being seen in isolates from all patient gender and sexual orientation subgroups. Between 2016 and 2017, the prevalence of azithromycin resistance increased from 4.7% to 9.2%, a similar level to the prevalence in 2015.

Among the isolates referred by primary diagnostic laboratories, there were 637 cases of azithromycin resistance confirmed between January 2015 and May 2018, of which 130 exhibited high-level resistance (HLAziR; MIC \geq 256 mg/L). Further epidemiological analyses of 118 of these cases have been previously reported.¹³ Cases emerged among heterosexuals in Leeds but spread across England and into sexual networks of MSM as the outbreak progressed. Molecular studies using whole genome sequencing found evidence of sustained transmission of *N. gonorrhoeae* with the HL-AziR phenotype on a national scale.^{14,15} Further data on antimicrobial resistance in *N. gonorrhoeae* are reported in the GRASP report available on-line.¹⁶

Tuberculosis

In 2017, 5,102 people were notified with tuberculosis (TB) in England, a rate of 9.2 notifications per 100,000 population (95% confidence interval (CI) 8.9-9.4); 71% (3,556/5,010) were born outside the UK.

Drug resistance in TB

Initial resistance (identified within 3 months) to first-line drugs

In 2017, drug susceptibility test (DST) results or whole genome sequencing (WGS) resistance predictions for at least isoniazid and rifampicin were available for 98.8% (3,115/3,153) of notified cases of culture-confirmed TB. Among these, 8.5% (265/3,115) had resistance to at least 1 first-line antibiotic, of which 5.7% (177/3,115)

¹³ Smolarchuk C *et al.* Persistence of an outbreak of gonorrhoea with high-level resistance to azithromycin in England, November 2014–May 2018. *Eurosurveillance* 2018;23(23):1-7.

www.eurosurveillance.org/content/10.2807/1560-7917.ES.2018.23.23.1800287

¹⁴ Fifer H *et al.* Sustained transmission of high-level azithromycin-resistant *Neisseria gonorrhoeae* in England: an observational study. *Lancet Infect Dis* 2018; 18: 573-581.

¹⁵ Chisholm SA *et al.* An outbreak of high-level azithromycin resistant *Neisseria gonorrhoeae* in England. *Sex Trans Infect* 2016; 92: 365-367.

¹⁶ PHE GRASP report: www.gov.uk/government/publications/gonococcal-resistance-to-antimicrobials-surveillance-programme-grasp-report

had resistance to isoniazid without multi-drug resistant TB (MDR-TB) (Figure 2.5, Table 2.3).

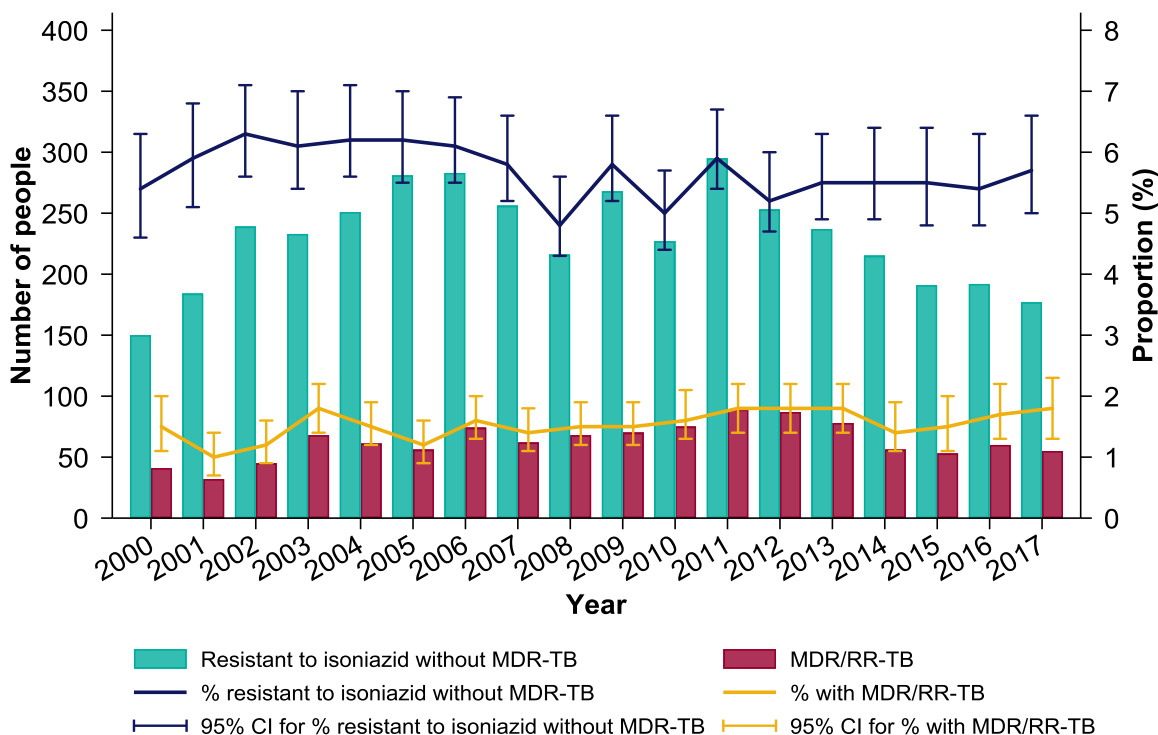


Figure 2.5 Number and proportion of people with TB with initial drug resistance, England, 2000-2017

Cases of TB where the infecting strain had any resistance to rifampicin, including those with MDR-TB, are hereafter referred to as multi-drug-resistant/rifampicin-resistant (MDR/RR) TB. The number of people with MDR/RR-TB in 2017 (55) was lower than in 2016 (60), while the proportion increased slightly from 1.7% to 1.8% (Figure 2.5; Table 2.3). In 2017, 42.6% (23/54) of cases with MDR/RR-TB with results for all 4 first-line drugs (isoniazid, rifampicin, ethambutol and pyrazinamide) were resistant to all 4. The majority of people with MDR/RR-TB notified in 2017 were born outside the UK (74.5%, 41/55), and for those where year of entry to the UK was known, 56.4% (22/39) had entered the UK within the past 6 years. The most frequent countries of birth of people with MDR/RR-TB were the UK (14), India (12) and Lithuania (9). People with TB born in Lithuania had the highest proportion of MDR/RR-TB (23.7%, 9/38). A high proportion of people with MDR/RR-TB notified in 2017 had at least 1 social risk factor (23.4%, 11/47).

Table 2.3 Number and proportion of people notified with TB^a with initial drug resistance, England, 2000-2017

Year	Isoniazid resistance without MDR-TB		Rifampicin resistance without MDR-TB		MDR-TB (including XDR)		MDR/RR-TB (including XDR)		XDR-TB	
	n	%	n	%	n	%	n	%	n	%
2000	150	5.4	13	0.5	28	1.0	41	1.5	0	0.0
2001	184	5.9	10	0.3	22	0.7	32	1.0	0	0.0
2002	239	6.3	10	0.3	35	0.9	45	1.2	0	0.0
2003	233	6.1	19	0.5	49	1.3	68	1.8	1	0.03
2004	251	6.2	16	0.4	45	1.1	61	1.5	0	0.0
2005	281	6.2	15	0.3	41	0.9	56	1.2	0	0.0
2006	283	6.1	20	0.4	54	1.2	74	1.6	0	0.0
2007	256	5.8	13	0.3	49	1.1	62	1.4	0	0.0
2008	216	4.8	18	0.4	50	1.1	68	1.5	2	0.04
2009	268	5.8	11	0.2	59	1.3	70	1.5	2	0.04
2010	227	5.0	10	0.2	65	1.4	75	1.6	2	0.04
2011	295	5.9	8	0.2	81	1.6	89	1.8	6	0.12
2012	253	5.2	10	0.2	77	1.6	87	1.8	2	0.04
2013	237	5.5	10	0.2	68	1.6	78	1.8	3	0.07
2014	215	5.5	4	0.1	52	1.3	56	1.4	3	0.08
2015	191	5.5	8	0.2	45	1.3	53	1.5	10	0.29
2016	192	5.4	7	0.2	53	1.5	60	1.7	7	0.20
2017	177	5.7	10	0.3	45	1.4	55	1.8	3	0.10

^a People with culture confirmed TB with a result (DST or WGS) for isoniazid and rifampicin

Second line drug resistance and extensively drug-resistant (XDR) TB

Extensively drug-resistant TB (XDR-TB) is defined as resistance to isoniazid and rifampicin (MDR-TB), plus resistance to at least 1 injectable agent (capreomycin, kanamycin or amikacin) and at least 1 fluoroquinolone (ofloxacin, moxifloxacin or ciprofloxacin). Among people with MDR/RR-TB, 7 had infections that were resistant to at least 1 injectable agent (amikacin, capreomycin or kanamycin) and 18 were resistant to a fluoroquinolone (ofloxacin, moxifloxacin or ciprofloxacin).

There were 3 cases with initial XDR-TB notified in 2017, compared to 7 in 2016 and 10 in 2015. Between 2013 and 2017, the number of cases of XDR-TB born in Lithuania, the UK and India were 10, 6 and 3, respectively.

UK participation in international surveillance of AMR

EARS-Net (European Antimicrobial Resistance Surveillance Network)

The European Centre for Disease Prevention and Control (ECDC) EARS-Net programme collects data on resistance to key antibiotics in blood culture and cerebrospinal fluid (CSF) isolates for 8 pathogens (*E. coli*, *K. pneumoniae*, *P. aeruginosa*, *Acinetobacter* spp., *S. pneumoniae*, *S. aureus*, *E. faecalis* and *E. faecium*). Results are published as annual reports¹⁷ and also made publically available via the ECDC Surveillance Atlas of Infectious Diseases.¹⁸

In England, data are obtained from participating laboratories through an annual extraction of routinely submitted AMR data from SGSS. In June 2018, antimicrobial susceptibility testing data from 71 laboratories in England covering the year 2017 were submitted to ECDC along with data from Northern Ireland, Scotland and Wales. The collated results were published on the ECDC Surveillance Atlas in mid-October and the ECDC annual EARS-Net report will be published on European Antibiotic Awareness Day in November 2018.

GLASS (Global Antimicrobial Resistance Surveillance System)

The aim of the World Health Organisation's (WHO) GLASS is to strengthen the evidence base on AMR through enhanced global surveillance and research, focusing initially on human priority bacterial pathogens considered the greatest threat globally. The UK enrolled in the GLASS programme in July 2017 and data describing the status of the UK AMR surveillance programme was provided to GLASS in April 2018 and is published on the online country profile visualisation tool (Figure 2.6).

ECDC and WHO (Europe) aim to avoid double reporting of AMR data by assisting the countries that have enrolled in GLASS by submitting the national AMR data provided to EARS-Net to the GLASS platform on their behalf. Therefore, UK AMR data isolated from blood will be shared by ECDC with WHO/Europe via ECDC's TESSy platform in October 2018 for inclusion in the forthcoming GLASS report for the following priority pathogens: *S. pneumoniae*, *S. aureus*, *E. coli*, *K. pneumoniae* and *Acinetobacter* spp. In addition, the UK has provided urine specimen AMR data for the year 2017 directly to GLASS for *E. coli* and *K. pneumoniae* since EARS-Net data are currently exclusively based on isolates from blood or cerebrospinal fluid.

¹⁷ European Centre for Disease Prevention and Control. Annual surveillance reports on antimicrobial resistance. Available online from: ecdc.europa.eu/en/antimicrobial-resistance/surveillance-and-disease-data/report

¹⁸ European Centre for Disease Prevention and Control. Data from the ECDC Surveillance Atlas – AMR 2018. Available online from: ecdc.europa.eu/en/antimicrobial-resistance/surveillance-and-disease-data/data-ecdc

Data from the European Gonococcal Antimicrobial Surveillance Programme (ECDC Euro-GASP) and European Food and Waterborne Diseases and Zoonoses Network (FWD-Net) covering specimens of *N. gonorrhoeae* from urethral and cervical swabs, *Salmonella* spp. from blood and faeces and *Shigella* spp. from faeces will also be provided to GLASS via ECDC’s TESSy in early 2019 along with available historical ECDC AMR data for GLASS priority pathogens.

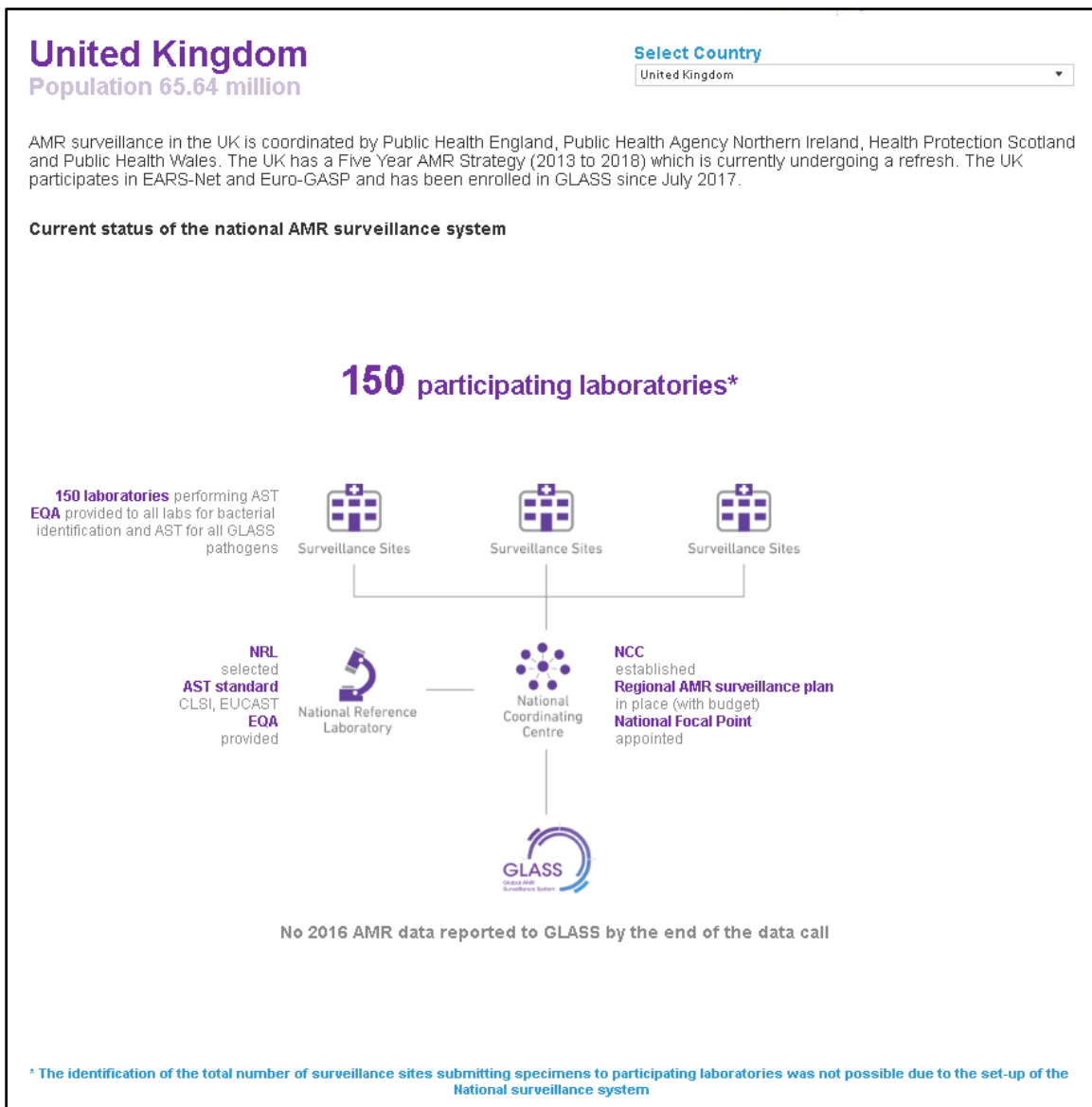


Figure 2.6 GLASS infographic describing the status of the UK national AMR surveillance system in 2017¹⁹

¹⁹ World Health Organisation. GLASS country profiles. 2018. Available online from: apps.who.int/gho/tableau-public/tpc-frame.jsp?id=2004

Discussion

As in previous ESPAUR reports, the surveillance data show a mixed picture. On the one hand, the proportion of isolates of the pathogens under surveillance that are resistant to key antibiotics remained relatively stable, arguably reflecting antimicrobial stewardship activities that reduced levels of antibiotic prescribing, which in turn reduced the selective pressure for the spread of antibiotic-resistant strains of bacteria. However, the year-on-year increase in the incidence of bacteraemia caused by these pathogens has meant that the numbers of bloodstream infections caused by strains resistant to key antibiotics has nonetheless continued to rise. Thus, future work to reduce the burden of AMR will require a renewed focus on infection prevention and control. Such an approach, if successful, would both reduce the numbers of antibiotic resistant infections, and, by reducing the overall burden of infection, also reduce the numbers of patients requiring antibiotics.

This report also presents a new methodological approach to estimating the burden of AMR in terms of the numbers of resistant infections. The data are likely to become increasingly robust, as 2017 saw the implementation of mandatory surveillance of bloodstream infections caused by *Klebsiella* spp. and *P. aeruginosa* in response to the UK government's ambition to halve healthcare-associated Gram-negative bacteraemias by 2021. Mandatory surveillance increases the level of case ascertainment and hence yields a more accurate measure of disease incidence. In addition, the last 5 years have seen improvements in the routine reporting of antibiotic susceptibility test results to SGSS, the national AMR database, which serves to further enhance the quality of national surveillance of AMR. In addition to monitoring the numbers of antibiotic-resistant infections, as outlined in the Research Annex, work is also ongoing to develop methods to estimate the clinical burden in terms of excess morbidity (resulting in increased length of hospital stay) and mortality.

Surveillance does not just involve the collection and analysis of data but includes as an essential component, the feedback of information to stakeholders. The implementation of the AMR local indicators profile on the PHE Fingertips web portal in 2016 was a major advance in that local data on AMR, healthcare-associated infections (HCAI), antibiotic prescribing and antimicrobial stewardship (AMS) activities are now freely accessible in a range of formats that allow all stakeholders such as hospitals, CCGs, other healthcare providers, policy makers and the public to benchmark themselves against both the national picture and comparable healthcare providers.

The last 5 years have seen the UK increasingly involved in international collaborative efforts to tackle AMR, the most recent development being the enrolment of the UK in the WHO GLASS programme. The UK is widely recognised as a world leader in the fight against AMR, and as outlined here, development of surveillance and other activities continue apace.

Future actions

ESPAUR will continue to:

- emphasise the importance of infection prevention and control with the objective of reducing the numbers of antibiotic-resistant infections
- develop methods to estimate the clinical burden in terms of resistant infections in terms of excess morbidity (resulting in increased length of hospital stay) and mortality
- integrate phenotypic and genotypic data on carbapenemase-producing bacteria derived from local testing into SGSS
- link microbiology data in SGSS with patient-level clinical, epidemiological and risk factor data in HES
- improve the quality of the data collected through improved coding and diagnostic standardisation
- collaborate with veterinary and international colleagues to promote a global one-health approach to surveillance of AMR

3. Antibiotic consumption

Introduction

In England, antibiotics are prescribed by medical professionals and non-medical prescribers in a number of settings: general practices (GP), dental practices, hospitals, out-of-hours services and walk-in centres. Tracking the use of antibiotics continuously over time is essential to determine the effectiveness of antimicrobial stewardship (AMS) programmes in different prescriber populations.

In this chapter, data on antibiotic consumption and surveillance for primary and secondary care are presented, with methods in the chapter annex. Outcomes from the quality improvement initiatives for antibiotic consumption, namely the Quality Premium (QP) for primary care and Commissioning for Quality and Innovation (CQUIN) for secondary care are also presented. The objectives of ESPAUR on delivering the UK Five Year Antimicrobial Resistance Strategy 2013 to 2018 were set out in the ESPAUR 2014 report²⁰; the progress and updates on the prescribing objectives are set out in the chapter. Figures presented in the chapter are available in the online annex.

Antibiotics

Total antibiotic consumption

In England, the total consumption of antibiotics in primary and secondary care declined by 4.5%, from 22.2 Daily Defined Doses (DDDs) per 1,000 inhabitants per day in 2013 to 21.1 DDDs per 1,000 inhabitants per day in 2017, with a 1.9% reduction from 2016 to 2017. The peak of antibiotic consumption over the last 20 years occurred in 2014; a 6.1% reduction in total consumption occurred between 2014 and 2018.

The most commonly used antibiotics in England remained stable between 2013 and 2017 and were: penicillins (44.6% in 2017), tetracyclines (22.2% in 2017) and macrolides (14.7% in 2017). Over the 5-year period, significant declining trends of consumption were observed for penicillins (inhibitor combinations only), first and second-generation cephalosporins, sulfonamides and trimethoprim, and anti-*Clostridium difficile* agents (Table 3.1). In contrast, consumption trends for third, fourth and fifth-generation cephalosporins and other antibacterials (definition for other antibacterials are included in the methods in [Annex – Chapter 3](#)) have significantly

²⁰ Public Health England; ESPAUR: report 2014. Available online from: assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/362374/ESPAUR_Report_2014__3_.pdf

increased, with the rise of nitrofurantoin use particularly of note (discussed in more detail later on the chapter).

Table 3.1 Total antibiotic consumption by antibiotic groups, expressed as DDDs per 1,000 inhabitants per day, 2013-2017

Antibiotic Group	2013	2014	2015	2016	2017	Trend	p-value
Penicillins (excluding inhibitors)	8.183	8.302	7.987	8.073	7.875		0.101
Penicillins (inhibitor combinations only)	1.797	1.815	1.708	1.614	1.561		0.010 ⁺
First and second-generation cephalosporins	0.367	0.347	0.301	0.268	0.257		0.003 ⁺
Third, fourth and fifth-generation cephalosporins	0.053	0.057	0.057	0.063	0.074		0.027 ⁺
Carbapenems	0.076	0.081	0.082	0.079	0.079		0.549
Tetracyclines	4.829	4.946	4.841	4.749	4.697		0.133
Macrolides, lincosamides and streptogramins	3.286	3.360	3.221	3.196	3.111		0.058
Sulfonamides and trimethoprim	1.430	1.438	1.354	1.265	1.055		0.025 ⁺
Quinolone antibacterials	0.533	0.537	0.519	0.515	0.522		0.161
Anti- <i>Clostridium difficile</i> agents	0.377	0.381	0.359	0.336	0.332		0.015 ⁺
Other antibacterials	1.094	1.135	1.197	1.272	1.445		0.010 ⁺

*p-value for trend from 2013 to 2017

Antimicrobial usage in prescriber settings has remained constant between 2013 and 2017. The majority of antibiotics were prescribed in the GP setting (72.7%), followed by hospital inpatients (11.5%), hospital outpatients (7.1%), dental practices (5.2%) and other community settings (3.5%) in 2017 (Table 3.2).

Table 3.2 Total antibiotic consumption by antibiotic groups and prescriber settings, expressed as DDDs per 1,000 inhabitants per day, 2017

Antibiotic Group	General Practice	Hospital Inpatient	Hospital Outpatient	Dentist	Other Community	Total
Penicillins (excluding inhibitors)	5.552	0.727	0.334	0.872	0.390	7.875
Penicillins (inhibitor combinations only)	0.669	0.527	0.305	0.005	0.055	1.561
Tetracyclines	4.181	0.209	0.233	0.005	0.070	4.697
Macrolides, lincosamides and streptogramins	2.411	0.283	0.224	0.084	0.108	3.111
Sulfonamides and trimethoprim	0.818	0.087	0.109	0.000	0.040	1.055
First and second-generations cephalosporins	0.173	0.054	0.022	0.002	0.007	0.257
Third, fourth and fifth-generations cephalosporins	0.001	0.058	0.014	0.000	0.000	0.074
Carbapenems	0.000	0.068	0.011	0.000	0.000	0.079
Quinolone antibacterials	0.290	0.097	0.121	0.000	0.013	0.522
Anti- <i>Clostridium difficile</i> agents	0.109	0.000	0.000	0.123	0.004	0.236
Other antibacterials	1.089	0.213	0.090	0.000	0.052	1.445
Aminoglycosides	0.007	0.089	0.030	0.000	0.000	0.126
Amphenicols	0.000	0.002	0.000	0.000	0.000	0.002
Total	15.301	2.414	1.494	1.090	0.741	21.039

Penicillins

Penicillins were the most commonly prescribed group of antibiotics in 2017, accounting for 44.6% of total antibiotic use in England. The overall rate of consumption of penicillins decreased by 5.5% between 2013 and 2017 from 10.0 to 9.4 DDDs per 1,000 inhabitants per day; there was a 1.9% decrease in consumption from 2016 to 2017 (from 9.6 to 9.4 DDDs per 1,000 inhabitants per day).

In the 5-year period from 2013 to 2017, the consumption of penicillins in the GP setting declined by 10.9%, whilst prescribing of penicillins in the dental setting remained largely the same. Prescribing of penicillins in the other community settings has been steadily rising, from 0.338 to 0.445 DDDs per 1,000 inhabitants per day, in the same

period (31.6%). In the hospital setting, prescribing of penicillins was higher in 2017 for both inpatients (2.4%) and outpatients (14.7%) compared to 2013.

Prescribing of co-amoxiclav and amoxicillin between 2013 and 2017 decreased by 11.3% and 7.4% respectively, whereas flucloxacillin consumption remained broadly stable.

Between 2016 and 2017, the usage of pivmecillinam increased from 0.041 to 0.053 DDDs per 1,000 inhabitants per day (29.3%). This rising trend was likely to be related to changes in PHE guidance for urinary tract infection (UTI) prescribing.²¹

Piperacillin/tazobactam usage decreased by 30.2% overall between 2013 and 2017. However, from 2013 to 2015 consumption increased by 15% and declined in 2016 and 2017 by 39%; the largest reduction was observed between 2016 and 2017 from 0.093 to 0.065 DDDs per 1,000 inhabitants per day (37.7%) related to an international supply shortage in 2017,²² with alternative antibiotics recommended for treatment (see [Annex – Chapter 3](#)). The impact on other antibiotics is outlined within the hospital section of this chapter.

Cephalosporins

The usage of cephalosporins decreased from 0.420 to 0.331 DDDs per 1,000 inhabitants per day (-21.4%), mainly due to reductions within primary care. This was also largely reflecting the decreased use of cefalexin, although the rate observed between 2016 and 2017 remained unchanged for cephalosporins overall. Whilst the trends for the use of cefalexin and cefradine declined from 2013 to 2017, both ceftazidime and ceftriaxone increased by 45.0% and 67.9% ,respectively, in the same period, reflecting the use as an alternative antibiotics to piperacillin/tazobactam. Cefotaxime use was unchanged. Ceftazidime/avibactam, a new cephalosporin with a novel beta-lactamase inhibitor was used at very low volumes in secondary care.

Tetracyclines

Tetracyclines were predominantly prescribed in General Practice (89.0% in 2017). Overall consumption was unchanged between 2013 and 2017. Doxycycline (49.7% in 2017) and lymecycline (36.3% in 2017) were the most predominantly prescribed tetracyclines since 2013. Consumption of minocycline (-59.7%), oxytetracycline (-

²¹ Public Health England; Management and treatment of common infections: guidance for consultation and adaptation 2017. Available online from: www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care

²² BSAC; DH advises on Piperacillin-Tazobactam infection supply problems 2017. Available online from: www.bsac.org.uk/dh-advises-on-piperacillin-tazobactam-injection-supply-problems/

36.7%) and tetracycline (-33.2%) fell between 2013 and 2017; possibly due to alternatives to antibiotics now being prescribed for acne.

Quinolones

Quinolone consumption remained broadly stable (0.522 DDDs per 1,000 inhabitants per day in 2017) from 2013 to 2017, although there was a 14.5% decline in the trend of quinolones consumption in General Practices for the same period, from 0.339 to 0.290 DDDs per 1,000 inhabitants per day. Ciprofloxacin was the main quinolone prescribed, accounting for 78.1% of total quinolone use in 2017. Ciprofloxacin, norfloxacin and ofloxacin prescriptions have all declined from 2013 to 2017, whereas the trend of rising levofloxacin consumption continued in 2017 with a 98.0% rise from 0.031 to 0.061 DDDs per 1,000 inhabitants per day over the 5-year period.

Macrolides

Macrolide use declined, from 3.2 to 3.0 DDDs per 1,000 inhabitants per day, from 2013 to 2017 (-5.8%). Azithromycin usage continued to increase in 2017 and the overall consumption has risen 31.3% since 2013; this may relate to the new NICE evidence review²³ and randomised controlled trials showing that it reduced exacerbations in non-cystic fibrosis related bronchiectasis. In contrast, erythromycin consumption has declined over the same period (-40.7%) and is the main reason for the observed decline use of the macrolides class. The change in macrolides consumption is most likely due to a change in antibiotics usage from erythromycin to other macrolides according to clinical guidelines.

Sulfonamides and trimethoprim

Consumption of sulfonamides and trimethoprim showed a decline over the 5 year period since 2013 (-26.3%) with a 16.7% decrease from 2016 to 2017. The decrease of consumption was driven by the decline in usage of trimethoprim in GP and hospital inpatient prescribing; as recommended in PHE common infection guidance²⁴ and in line with the Quality Premium in primary care. The trend for prescribing in hospital outpatients and in other community settings remained broadly stable.

²³ Non-cystic fibrosis bronchiectasis: long-term azithromycin. November 2014. Available online from www.nice.org.uk/advice/esuom38/chapter/Key-points-from-the-evidence

²⁴ Public Health England; Management and treatment of common infections: guidance for consultation and adaptation 2017. Available online from: www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care

Nitrofurantoin and trimethoprim

The trend in nitrofurantoin consumption continued to increase, with a 28.8% increase from 2013 to 2017, increasing to 1.091 DDDs per 1,000 inhabitants per day in 2017. This increasing trend of nitrofurantoin prescribing was observed in all settings, with the rise in General Practice (13.5% from 2016 to 2017) especially of note. This was most likely due to nitrofurantoin being recommended as first-line treatment, instead of trimethoprim, for lower uncomplicated UTIs in adults since 2014 and the inclusion of a target for reduction in the trimethoprim:nitrofurantoin prescribing ratio in the 2016/17 Quality Premium (see [QP](#)).

Aminoglycosides

Aminoglycoside consumption has remained largely stable between 2013 and 2017. There was a 5.6% rise in consumption from 2016 to 2017, from 0.119 to 0.126 DDDs per 1,000 inhabitants per day, due to an increase in consumption in the hospital setting. Prescribing in General Practice decreased 58.8% from 2013 to 2017, which may be related to a reduction in inhaled aminoglycoside prescriptions for bronchiectasis in line with specialised commissioning guidelines.

Parenteral glycopeptides and daptomycin

The use of parenteral glycopeptides (vancomycin and teicoplanin) and daptomycin occurred almost exclusively in hospitals (99.7% in 2017). More specifically, use occurred most commonly in hospital inpatients, with the level of prescribing in this group increasing by 40.1% over the 5-year period.

Between 2013 and 2017, the increase in usage of teicoplanin from 0.053 to 0.078 DDDs per 1,000 inhabitants per day (47.0%) was the main reason for the overall rising trend of parenteral glycopeptides and daptomycin from 0.078 to 0.106 DDDs per 1,000 inhabitants per day (34.8%).

Colistin

Total colistin consumption has remained low and largely the same for the past 5 years, as colistin is a last resort antibiotic used frequently to treat multidrug-resistant infections. Consumption of colistin was 0.078 DDDs per 1,000 inhabitants per day in 2017. The trend of colistin prescription continued to decrease in General Practice, however an increasing trend was observed for the secondary care outpatient setting; most likely reflecting a switch from GP to specialised centres prescribing for nebulised colistin. Moreover, colistin usage remained stable for hospital inpatients and other community settings between 2013 and 2017.

Collection, analysis and reporting of antimicrobial usage data from primary and secondary care

Antimicrobial usage data across primary and secondary care in England were presented for the first time in the 2014 ESPAUR Report. The programme's first report focussed on NHS geographical boundaries to encourage a complete healthcare economy approach to antibiotic prescribing and to highlight key differences in prescribing across the country; the geographical data was only available from 2009.

PHE launched a data warehouse in January 2017. The warehouse acts as a single repository for antimicrobial usage data, translating primary care data collated by NHS BSA and secondary care data provided by the human health data science company IQVIA, as well as by NHS Trusts as part of the Commissioning for Quality and Innovation (CQUIN) payments framework. Implementation of the data warehouse has allowed PHE to monitor trends in antibiotic prescribing and publish them at increasing levels of granularity in successive annual ESPAUR Reports.

The data warehouse developed by ESPAUR has also made it possible for PHE to: monitor usage of specific antibiotics (for example following the launch of a newly licensed drug or restriction/shortage of existing treatments); in combination with microbiological isolate data, to detect emerging patterns and alert laboratory and clinical colleagues to these and therefore support the NHS staff in their effort to improve patient safety and outcomes.

Prescribing in primary care

Primary care settings accounted for 81.0% of all antibiotics prescribed in 2017. This section describes the antibiotic use in terms of antibiotic items, where each item is an individual antibiotic prescription, and more than 1 antibiotic item could be prescribed at a single consultation.

Antibiotic prescribing in primary care settings, measured in terms of antibiotic items, declined from 2.067 items per 1,000 inhabitants per day (or 754 prescriptions per 1000 inhabitants per year) in 2013 to 1.794 items per 1,000 inhabitants per day (654 per 1000 inhabitants per year) in 2017, equating to a drop of 13.2% in 5 years. In 2017, there was a 4.5% reduction in prescribing compared to 2016. The decline in items prescribed in primary care is predominantly driven by reductions in General Practice antibiotic prescribing (-13.4% from 2013 to 2017), which accounts for 86.3% of total community prescribing. An increasing trend in prescribing (16.4%) was observed in other community settings since 2013 which accounted for (5.5%) of total prescribing in primary care in 2017. A decreasing trend (-23.9%) in prescribing has been observed in

dental practices from 2013 to 2017, this sector contributed to 8.2% of antibiotic prescription items primary care in 2017.

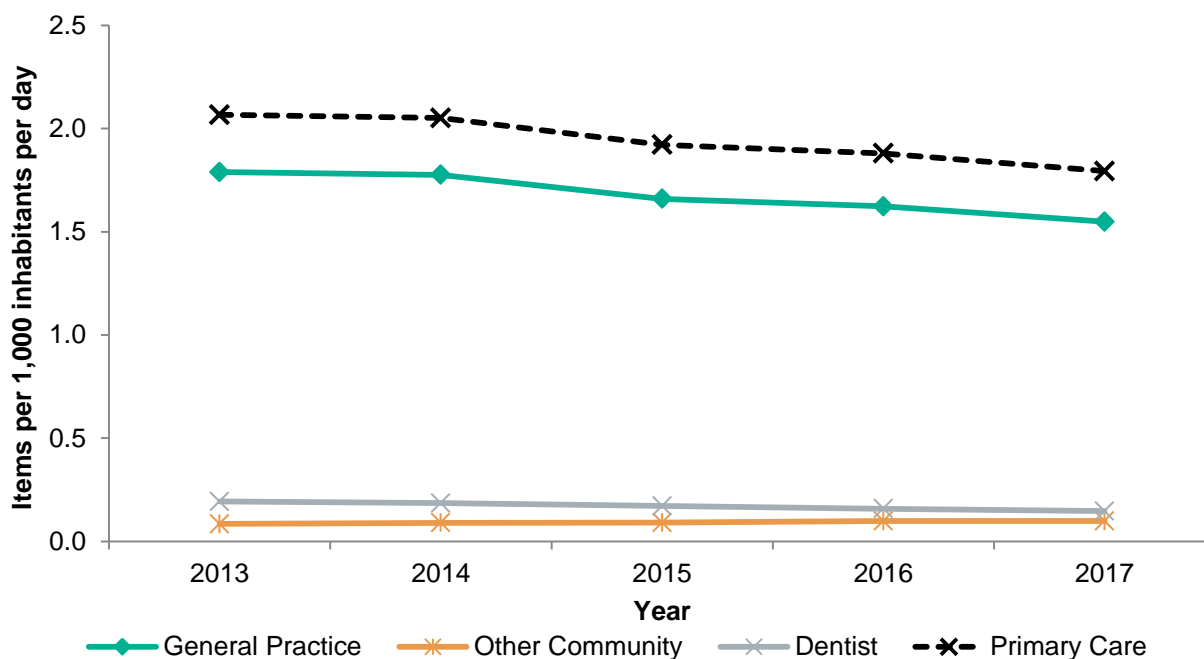


Figure 3.1 Antibiotic items in primary care by prescriber group, expressed as items per 1,000 inhabitants per day, 2013-2017

General practice

Although prescribing of penicillins decreased by 18.4% between 2013 and 2017, they remained the most commonly prescribed antibiotic group in the General Practice setting, accounting for 46.5% of all antibacterial prescriptions. The second most highly prescribed antibiotic group in the GP setting was tetracyclines (13%), followed by macrolides (11.7%) by items prescribed per 1,000 inhabitants per day.

The reduction of usage of penicillins was the main contributor to the decreased rate of total antimicrobial prescribing in the GP setting. Utilisation of other antimicrobials in the GP setting also decreased, including sulfonamides and trimethoprim (-29.5%), other β -lactam antibacterials (-35.1%), anti-*C. difficile* agents (-21.1%) and macrolides (-16.9%). Other antibacterials (description in [Annex – Chapter 3](#)) was the only group with an increasing trend (54.8%) over the 5-year period, due to the increase in the use of nitrofurantoin in the GP setting with a rise of 24.7% from 2016 to 2017, from 0.124 to 0.154 items per 1,000 inhabitants per day.

Quality Premium

NHS England has published a national QP to improve antibiotic prescribing in primary care each financial year since 2015/16. Over 2.7 million fewer antibiotics were dispensed in 2016/17 in comparison to 2014/15, following the introduction of the AMR QP.²⁵ There have been significant and sustained declines in both antibiotic items per 1000 population and antibiotic items per Specific Therapeutic group Age-sex Related Prescribing Unit (STAR-PU), which is a weighted value used to adjust data to reflect the age and sex of distribution of patients in each practice or Clinical Commissioning Group (CCG). The median CCG value for antibiotic items per STAR-PU reduced from 1.188 to 1.086 over this 2-year period. The mean proportion of broad-spectrum antibiotics (co-amoxiclav, cephalosporins and quinolones) as a proportion of all antibiotic items reduced from 10.7% to 8.9%.

Quality Premium 2017/18

The 2017/18 QP is focused on reducing Gram-negative bloodstream infections (GNBSIs) and inappropriate antibiotic prescribing in at-risk groups. This national QP seeks to sustain the successful reductions in antibiotic prescribing enabled by previous QPs and to respond to ambitions set by Government following the O'Neill Review of AMR.²⁶ These ambitions include:

- 50% reduction of GNBSIs by 2021
- 50% reduction of the number of inappropriate antibiotic prescriptions by 2021

There were 2 parts focussing on antibiotic use:

Part b) reduction of inappropriate antibiotic prescribing for UTIs in primary care.

- 10% reduction (or greater) in the trimethoprim: nitrofurantoin prescribing ratio based on CCG baseline data (June15 - May16) for 2017/18
- a 10% reduction (or greater) in the number of trimethoprim items prescribed to patients aged 70 years or greater on baseline data (June15 - May16) for 2017/18

²⁵ Beech E *et al.* Does a national NHS England incentive scheme to reduce inappropriate antibiotic prescribing in primary care deliver improvement? Presented at PHE Conference 2018

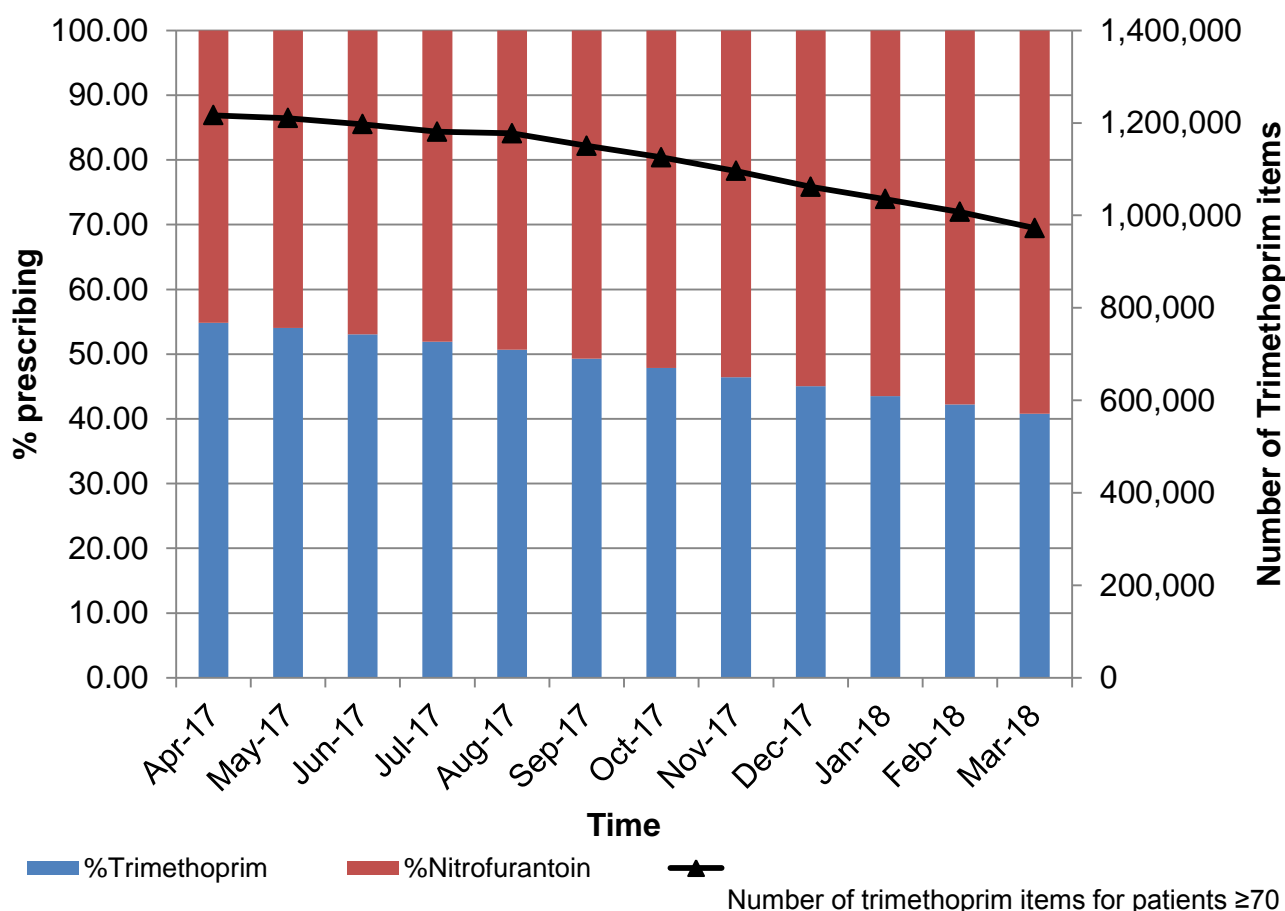
²⁶ Department of Health and Social Care. Government response to the Review on Antimicrobial Resistance. 2016. Available online from: www.gov.uk/government/publications/government-response-the-review-on-antimicrobial-resistance

Part c) sustained reduction of inappropriate prescribing in primary care:

- per STAR-PU must be equal to or below England 2013/14 mean performance value of 1.161 items per STAR-PU

The NHS Business Services Authority (NHS BSA) provided quarterly data on antibiotic prescribing in the community, while PHE openly published QP indicator data on the Fingertips AMR local indicators portal and PrescQIPP published data on their AMS hub. NHS England and NHS BSA also published a monthly antibiotic QP dashboard that was freely accessible on the NHS England website. It provided CCG QP performance data and was intended to be used by CCGs, Commissioning Support Units (CSUs) and NHS England assurance teams to monitor performance against the primary care prescribing elements of the QP. NHS England informed CCGs through their assurance team networks by email and webinars, professional networks by email and twitter, and targeted communication to healthcare staff.

Almost all CCGs (99%: 205/207) met or exceeded the ambition to reduce the ratio of trimethoprim to nitrofurantoin prescribing by 10%; 95% (197/207) of CCGs met this target in the 70 year old or greater population (Figure 3.2).



*each month depicts 12 months' worth of data up to and including the month stated

Figure 3.2 Proportion of nitrofurantoin to trimethoprim prescribing and the number of trimethoprim items prescribed to patients aged 70 years or greater in primary care

Over 1 million fewer antibiotics were dispensed in 2017/18 compared to 2016/17 with a continued decline in both antibiotic items per 1,000 population and per STAR-PU (Table 3.3). There was a progressive improvement over 2017/18 with 175 of 207 (85%) CCGs meeting their objective to reduce antibiotic items/STAR-PU by the end of the financial year. The median CCG value for antibiotic items per STAR-PU reduced from 1.179 to 1.043 from 2013/14 to 2017/18.

Table 3.3 Impact of Quality Premium on antibiotic prescribing in CCGs between 2014/15 and 2017/18

Financial year	Antibiotic items	Antibiotic items per STAR-PU*	Items per 1000 population/day
2014/15	37,352,851	1.17	1.87
2015/16	34,680,427	1.08	1.71
2016/17	34,662,834	1.07	1.71
2017/18	33,645,553	1.02	1.65

Although no longer part of the QP, appropriate prescribing of broad-spectrum antibiotics is an indicator within the NHS England AMR CCG Improvement and Assessment Framework. By March 2018, 156 of 207 (75%) CCGs had met or exceeded the expected threshold to reduce prescribing of broad-spectrum antibiotics (co-amoxiclav, cephalosporins and quinolones) as a proportion of total antibiotic prescribing to 10% or below. The median CCG value for the number of broad-spectrum antibiotics items as a proportion of total antibiotic items reduced from 10.6% to 8.7% between 2013/14 and 2017/18.

However, significant variation continues to exist across CCGs with two- and three-fold differences, respectively, in items per STAR-PU and proportion of broad spectrum antibiotics, respectively, remaining between high and low-prescribing CCGs.

Development of antimicrobial prescribing quality measures to improve prescribing in primary and secondary care and implementation of systems to measure their impact

In 2014, ESPAUR supplied data and expertise to the Department of Health and Social Care advisory committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection (APRHAI) to aid in the development of Antibiotic Prescribing Quality Measures to curb unnecessary use of antibiotics in England. These measures were implemented from April 2015 in the form of a Quality Premium (QP) awarded to CCGs for reducing antibiotic prescribing in primary care and from April 2016 within a CQUIN for reducing antibiotic consumption in NHS acute Trusts. Antibiotic consumption indicators supporting the QP and CQUIN have been included within the AMR local indicators profile of Fingertips since 2016 to support organisations in tracking progress toward their quality improvement goals.

Other community prescribing

Other community prescribing includes antibiotic prescribing in a number of community services (see [Annex – Chapter 3](#)), which has increased 16.4% since 2013, although the level of prescribing in 2017 remained similar to 2016, at 0.099 items per 1,000 inhabitants per day.

Antibiotic prescribing in out-of-hours services contributed to 56.6% of all antibiotic prescribing in the other community settings in 2017. Prescribing from hospitals but dispensed in community pharmacies on FP10(HP) continued to rise, from 0.002 to 0.005 items per 1,000 inhabitants per day, during the 5 years from 2013, although the level of items prescribed remained low. (Figure 3.3)

The increase in prescribing seen in urgent care (5.4% of total other community prescribing) is possibly an artefact with changes in classification from walk-in centres reported to NHSBSA since the 2013 NHS reorganisation.²⁷

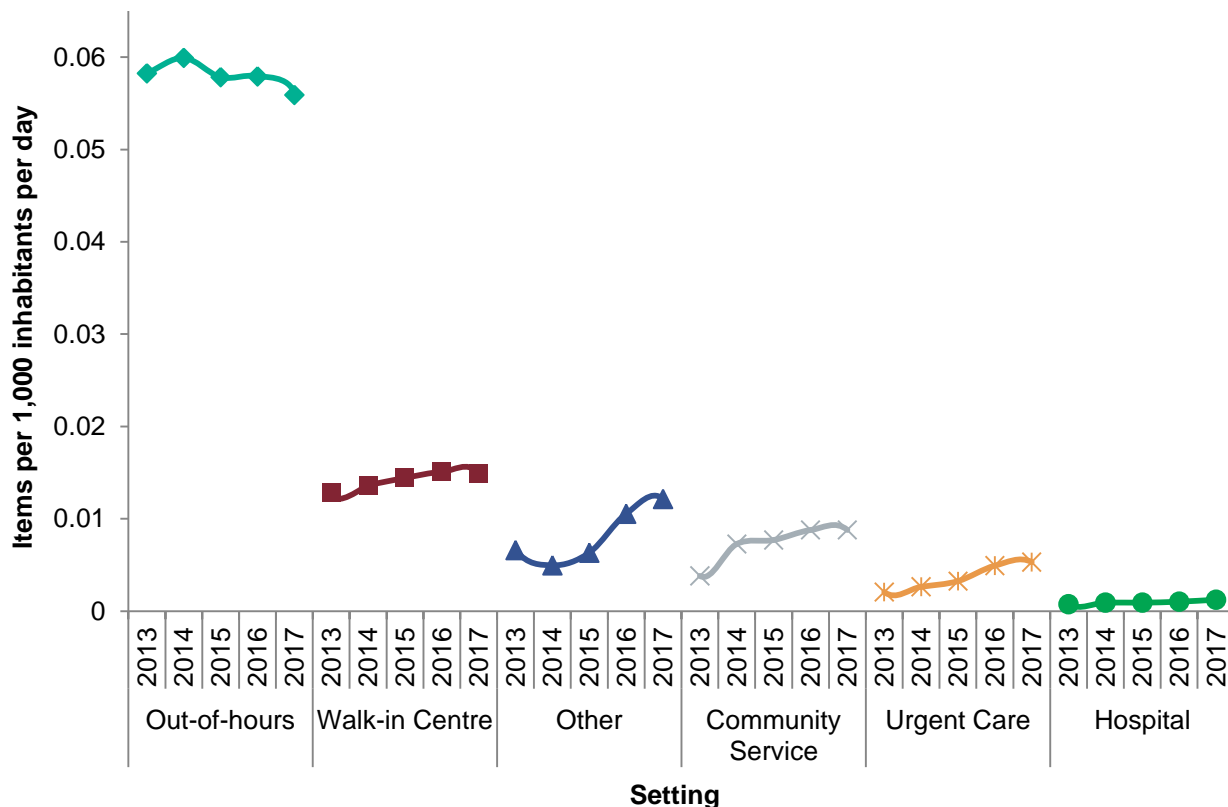


Figure 3.3 Other community antimicrobial consumption, expressed as items per 1,000 inhabitants per day, England, 2013-2017

Dental practice

Dental practice prescribing is only available for NHS practices and consultations. From 2013 to 2017, the trend of antimicrobial prescriptions continued to decrease (-24.8%); with an 8.3% decrease from 2016 to 2017. The decline was largely attributed to less amoxicillin being prescribed between 2013 and 2017, from 0.125 to 0.096 items per 1,000 inhabitants per day. The most commonly prescribed antibiotics in 2017 were amoxicillin (66.6%), metronidazole (28.8%) and erythromycin (3.6%). (Figure 3.4)

A Dental Prescribing Dashboard was developed by NHSBSA and PHE, including data for NHS Local Area Teams.²⁸ Besides items prescribed, the dashboard also includes

²⁷ NHS England. NHS structure explained. 2016. Available online from: www.nhs.uk/using-the-nhs/about-the-nhs/nhs-structure-explained

²⁸ Public Health England; Dental Health: 2016 Dental Prescribing Dashboard 2016. Available online from: www.nwph.net/dentalhealth/Prescribing.aspx

net ingredient cost. It demonstrates that an antibiotic prescription was dispensed after 8.2% of dental treatments.

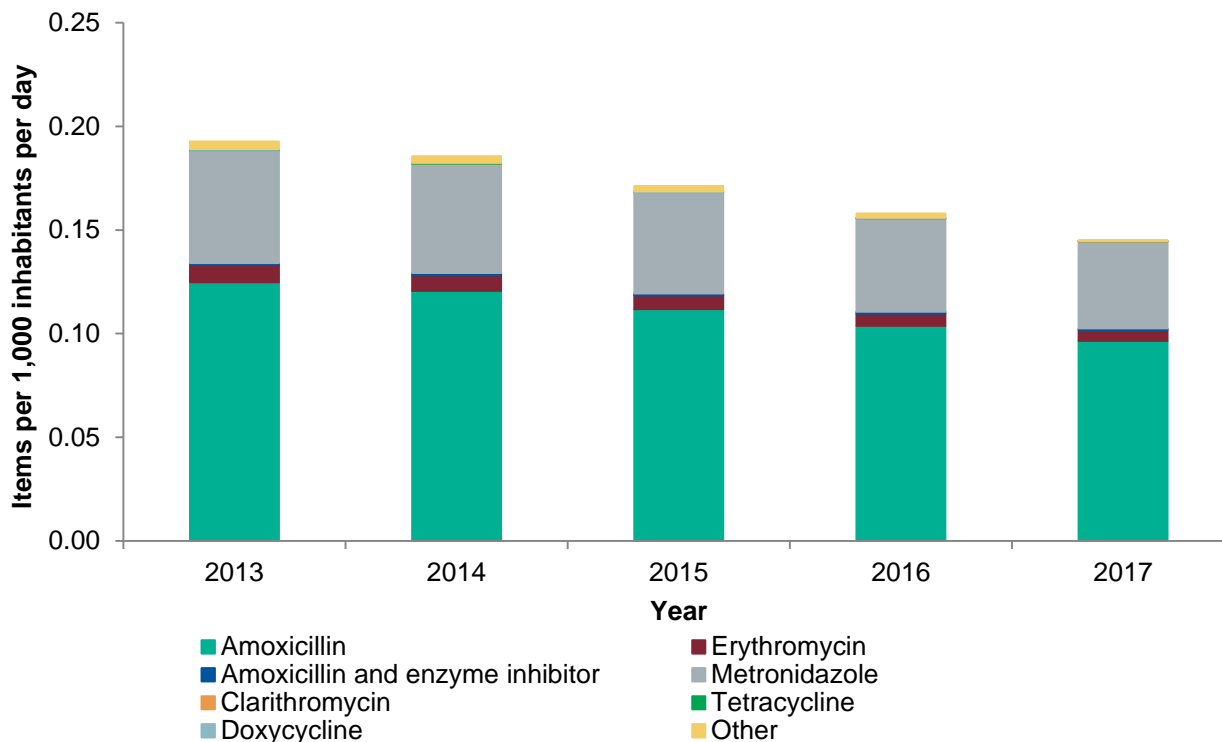


Figure 3.4 Antibiotic items prescribed in dental practices, expressed as items per 1,000 inhabitants per day, England, 2013-2017

* Note: Other includes oxytetracycline, ampicillin, phenoxymethylpenicillin, cefalexin, cefradine, azithromycin and clindamycin.

Prescribing in secondary care

Antibiotic consumption in secondary care in England increased (7.7%) between 2013 and 2017, from 3.631 to 3.865 DDDs per 1,000 inhabitants per day. Prescribing for hospital inpatients increased only 2% from 2.354 to 2.403 DDDs per 1,000 inhabitants per day over the 5-year period but increased 21% in hospital outpatient settings (from 1.276 to 1.545 DDDs per 1,000 inhabitants per day).

In acute Trusts in England, despite a reduction in antibiotic prescribing in 2015, the level of antimicrobial prescribing is generally on the rise from 2013 to 2017, with 5,150 DDDs per 1,000 admissions in 2017.

Data by Trust type should be interpreted with caution, as data on the Trust level is only comparable from 2014 onwards; merging and demerging of Trusts were not taken into account in 2013. Consumption of antimicrobials differs in different Trust types (See

Annex – Chapter 3 for Trust definitions); increasing trends of antibiotic consumption were observed in acute large and specialist Trusts, whereas a decreasing trend was observed in teaching Trusts from 2014 to 2017. Other Trust types have remained broadly stable with some fluctuations.

Antibiotic prescribing in secondary care by key antibiotic group in 2017 has broadly remained similar to 2016: the increase of antibiotic use was observed in the groups of other antibacterials (10.2%), β -lactam antibacterials (8.3%) and tetracyclines (5.6%). The largest increases in the other antibacterials group were seen in nitrofurantoin (9.9%), parenteral metronidazole (9.1%) and teicoplanin (6.5%), which are likely to reflect the usage of alternative antibiotics due to the piperacillin/tazobactam shortage. In contrast, sulfonamides and trimethoprim (-6.9%), macrolides (-1.8%) and anti-*C. difficile* agents (-1.3%) have declined over the same period.

Broad-spectrum prescribing

This section discusses 3 broad-spectrum antibiotics: colistin, piperacillin/tazobactam and carbapenems, which are of particular concern in hospitals in England.

Colistin

Colistin consumption in secondary care continued to increase in 2017 to 39.6 DDDs per 1,000 admissions. Both parenteral and inhalation administration routes continued to increase from 2013 to 2017, with inhalation in particular showing a dramatic increase from 1.8 to 11.7 DDDs per 1,000 admissions during this period.

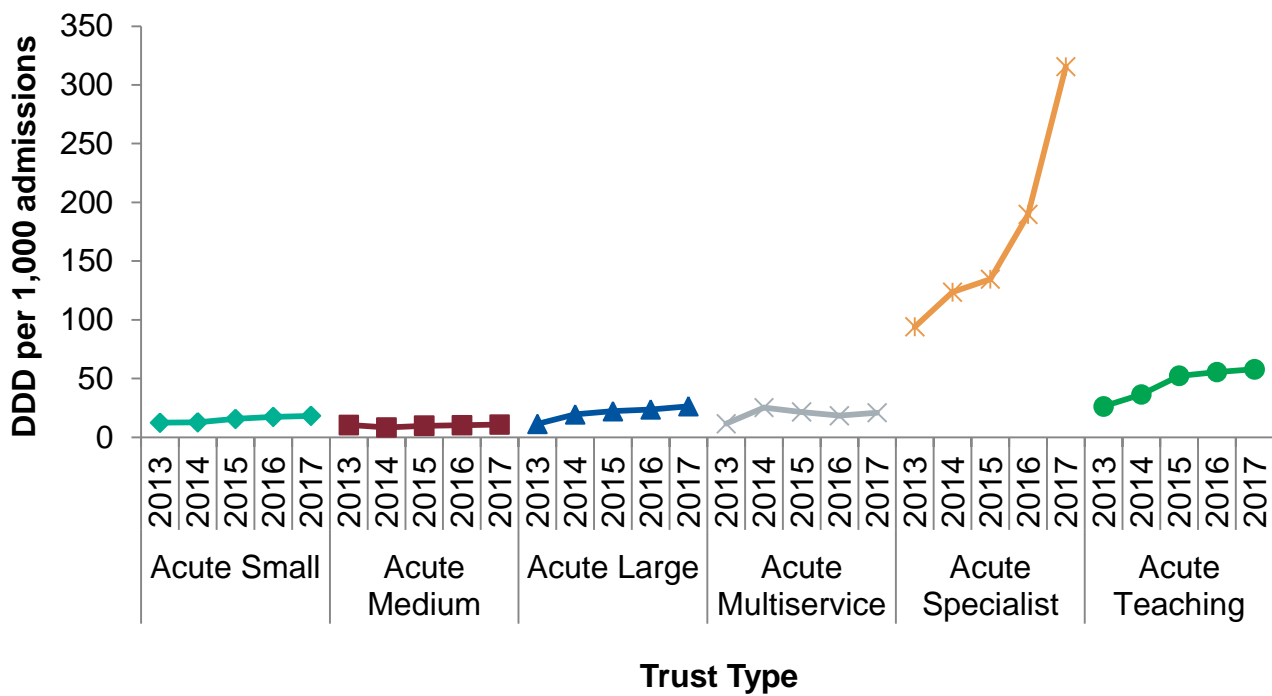


Figure 3.5 Consumption of colistin in NHS acute Trusts by Trust type, expressed as DDDs per 1,000 admissions, England, 2013-2017

There was an increase in the trend of consumption during the 5-year period for specialist, teaching, large and small Trust types; particularly, specialist Trusts have increased even further to 315.6 DDDs per 1,000 admissions in 2017, a 66.3% increase from the previous year. This may relate to changes in colistin prescribing for bronchiectasis and cystic fibrosis, associated with new specialised commissioning guidelines. Colistin usage in medium and multi-service Trusts remained broadly stable between 2013 and 2017. (Figure 3.5)

Piperacillin/tazobactam

From 2016 to 2017, piperacillin/tazobactam consumption decreased by 786,813 DDDs (37.3%), from 2,108,290 to 1,321,478 DDDs. The total alternative recommended antibiotics increased by 2,185,334 DDDs (4.5%), from 48,178,899 to 50,364,233 DDDs. The largest percentage increase in consumption of the substitute antimicrobials were observed in temocillin (89.7%), ceftazidime (35.2%) and levofloxacin (34.7%).

Although the reduction in piperacillin/tazobactam usage is favourable and is in line with current policy (discussed in the **CQUIN** section of this chapter), an additional 1,398,521 DDDs were used in the antibiotics recommended for switching (Table 3.4).

Combination therapy of the antibiotic substitutes (eg treating severe sepsis with ceftriaxone, metronidazole and amikacin, instead of using piperacillin/tazobactam) is likely to have contributed to this increase of DDDs but the extent could not be measured on the chemical level.

Table 3.4: Piperacillin/tazobactam shortage in 2017 and related changes in antibiotic use in secondary care, expressed as DDDs

Antibiotic	2016	2017	% Change
Piperacillin/Tazobactam	2,108,290	1,321,478	-37.3
Total alternative antibiotics	48,178,899	50,364,233	4.5
Temocillin	75,973	144,107	89.7
Ceftazidime	222,684	300,970	35.2
Levofloxacin	718,671	967,996	34.7
Aztreonam	113,432	148,557	31.0
Fosfomycin (Parenteral)	183,927	230,724	25.4
Cefuroxime	550,308	669,807	21.7
Ceftriaxone	659,725	797,729	20.9
Linezolid	193,831	229,004	18.1
Metronidazole (Parenteral)	961,331	1,113,583	15.8
Gentamicin	1,648,219	1,783,730	8.2
Amikacin	109,360	118,260	8.1
Teicoplanin	1,458,493	1,574,254	7.9
Vancomycin (Oral)	35,262	37,186	5.5
Cefotaxime	336,182	353,448	5.1
Co-amoxiclav	14,941,962	15,578,598	4.3
Flucloxacillin	10,210,913	10,491,096	2.7
Meropenem	1,415,538	1,436,611	1.5
Amoxicillin	8,798,518	8,859,845	0.7
Ciprofloxacin	3,047,740	3,055,162	0.2
Metronidazole (Oral)	1,890,460	1,878,129	-0.7
Vancomycin (Parenteral)	435,790	431,938	-0.9
Ertapenem	170,577	163,501	-4.1

Prior to the decrease in usage, the trends for the use of piperacillin/tazobactam were generally increasing in all Trust types besides multi-service and medium Trusts. (Figure 3.6)

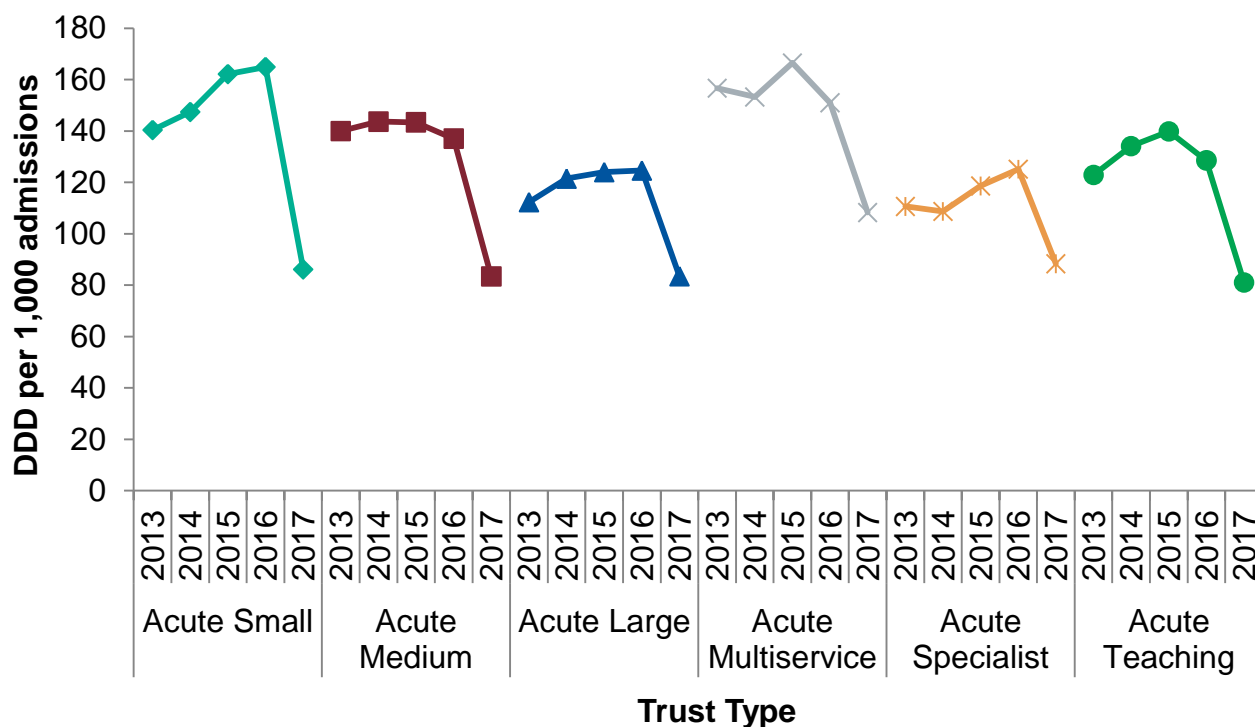


Figure 3.6 Consumption of piperacillin/tazobactam in NHS acute Trusts by Trust type, expressed as DDDs per 1,000 admissions, England, 2013-2017

Carbapenems

Carbapenems consumption in secondary care has remained stable from 2013 to 2017, with 101.6 DDDs per 1,000 admissions in 2017. Meropenem is still the main carbapenem prescribed in secondary care (89.4%), with a slight increase in consumption compared to 2016 (0.6%).

Among acute Trusts, specialist and teaching Trusts prescribed the most carbapenems and both trust types increased their usage of this drug class by 24.0% and 3.6%, respectively, between 2016 and 2017. A decline in usage was observed in multiservice, small, medium and large Trusts.

Speciality prescribing

Secondary care antimicrobial consumption was analysed and is reported by speciality grouping in this chapter. Specialities within each group are defined in [Annex – Chapter 3](#).

In terms of speciality, antibiotic consumption was highest within intensive care units (ICUs) comprising 71.6 DDDs per ICU admission in 2017. This may be related to the unavailability of piperacillin/tazobactam, discussed earlier in the chapter, as the effect of the switch of a single antibiotic to a combination of 2 to 3 antibiotics for treating the same condition. On the other hand, a decrease in the trend of prescribing was

observed within specialist medicine, from 4.2 to 3.8 DDD per specialist medicine admission from 2013 to 2017. Consumption in other speciality groups remained largely stable with some fluctuations.

CQUIN

NHS England has published a national Commissioning for Quality and Innovation (CQUIN) to improve antibiotic prescribing and stewardship in secondary care each financial year since 2016/17. For the first time NHS England has published a 2 year scheme (covering 2017/19) with the aim of providing greater certainty and stability regarding CQUIN goals, thereby giving health communities more time to focus on implementing the initiatives. The 'reducing the impact of serious infection' 2017/19 CQUIN focused on antimicrobial resistance and sepsis.²⁹ The AMR component encompassed reductions in antibiotic consumption and a focus on ensuring prescriptions for sepsis were reviewed within 72 hours of commencing an antibiotic.

AMR CQUIN 2017/18

The AMR CQUIN required that a specific percentage of antibiotic prescriptions were reviewed by a senior staff member within 72 hours per 30 antibiotic prescriptions taken from a representative sample of sepsis patients each quarter. The standard required that senior clinicians:

- perform an empiric review for at least 25% of cases in the sample in Q1
- perform an empiric review for at least 50% of cases in the sample in Q2
- perform an empiric review for at least 75% of cases in the sample in Q3
- perform an empiric review for at least 90% of cases in the sample in Q4

Reductions in total, carbapenem and piperacillin/tazobactam consumption measured in DDDs per 1000 admissions were required as follows:

- 1% reduction for those Trusts with 2016 consumption indicators below 2013/14 median value per Trust type, or
- 2% reduction for those Trusts with 2016 consumption indicators above 2013/14 median value per Trust type

The number of NHS acute hospitals submitting antibiotic review data to PHE in quarters 1 to 4 of 2017/18 was 117 (77%), 122 (80%), 116 (76%) and 115 (76%) respectively. The proportion of antibiotic prescriptions reviewed within 72 hours remained stable but

²⁹ NHS England Technical guidance for refreshing NHS Plans 2018/19 annex A: Commissioning for Quality and Innovation (CQUIN) indicator specification 2017-2019. Available online from: www.england.nhs.uk/publication/cquin-indicator-specification

high in 2017/18 (Table 3.5). Although the proportion of acute hospitals meeting the CQUIN target remained high, there was a slight decrease from quarter 3 possibly related to the target proportion of prescriptions reviewed increasing incrementally each quarter.

Table 3.5: Review of antibiotic prescriptions from sepsis patients within 72 hours in accordance with the 2017/18 AMR CQUIN

Financial quarter	Proportion of antibiotic prescriptions reviewed within 72 hours	CQUIN target milestones (% prescriptions reviewed according to CQUIN criteria)	Proportion of Trusts meeting the antibiotic review AMS CQUIN (n=152)
Q1 2017/18	91.3%	25%	77.0%
Q2 2017/18	93.8%	50%	78.9%
Q3 2017/18	91.5%	75%	72.4%
Q4 2017/18	92.2%	90%	65.1%

Additional data collected on the outcome of the prescribing decision related to Start Smart Then Focus (SSTF) is outlined in Table 3.6 and approximately 85% of prescriptions reviewed at 24-72 hours were continued. From June 2017 the proportion of prescriptions with stop and stop/switch/IV-oral switch decisions were openly published to encourage greater discussion around acceptability of stopping or switching antibiotic treatment following review at 72 hours.

Table 3.6: Prescribing decision outcomes for audited antibiotic prescriptions, expressed as percentage of prescriptions reviewed

Prescriptions with documented decision following review	Q1 2017/18 (n=4660)	Q2 2017/18 (n=5520)	Q3 2017/18* (n=5354)	Q4 2017/18* (n=5841)
Stopped	13.6	16.1	17.0	16.6
Continued	41.7	43.7	44.9	47.4
Switch	23.5	18.9	18.9	17.8
IV to oral switch	18.0	20.3	20.4	21.7
Outpatient Parenteral Antimicrobial Therapy (OPAT)	0.3	0.9	0.3	0.3

Note: Percentages for quarter 3 and 4 were over 100% in total as Trusts could choose more than 1 option of decision outcomes (ie IV to PO switch and switch to another antibiotic).

The number of NHS acute Trusts submitting antibiotic consumption CQUIN data to PHE in quarters 1 to 4 of 2017/18 was 140 (92%), 140 (92%), 138 (91%) and 131 (86%), respectively.

In 2017/18, 35 (23.0%), 114 (75.0%) and 74 (48.7%) of 152 NHS acute Trusts met their objectives to reduce total antibiotic, piperacillin/tazobactam and carbapenem consumption, respectively (Figure 3.7 highlights progress).

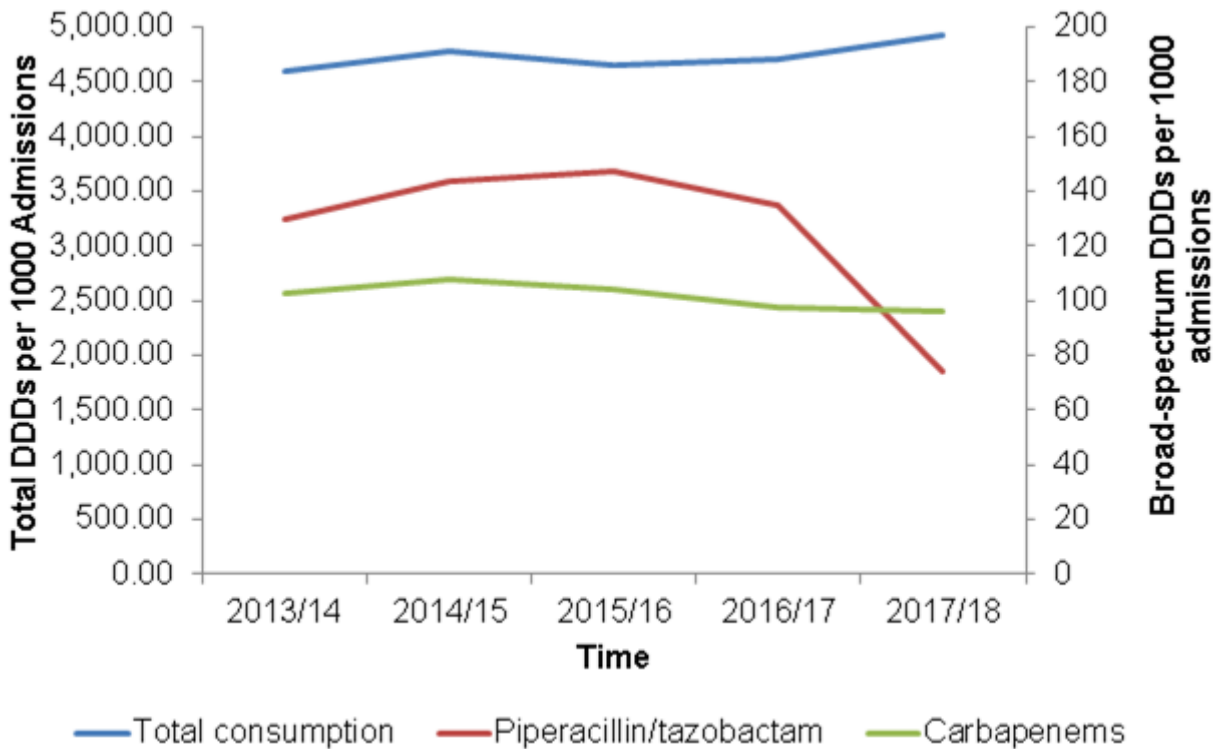


Figure 3.7 Total and broad spectrum antibiotic consumption in NHS acute

Development and implementation of methods to monitor the clinical outcomes including any unintended consequences following reductions in antibiotic prescribing

Researchers at the Imperial College HPRU are investigating the impact of national antimicrobial stewardship programmes on clinical outcomes. An abstract of their work to develop a baseline from which the impact of quality improvement programmes can be determined is included in the [research annex](#).

Integration of antimicrobial usage data with data on AMR and rates of *Clostridium difficile* infection

Projects are underway using business intelligence applications to link antimicrobial prescribing data from both primary and secondary care with other PHE and/or NHS datasets, including AMR data collated by the PHE Second Generation System (SGSS) and Hospital Episode Statistics (HES) data maintained by NHS Digital. Data models will be created enabling on-line reports to be produced that visualise these combined data sources. Antimicrobial use is recognised as a major driver of AMR, hence a key aim of ESPAUR is to investigate the impact of antimicrobial usage patterns in primary and secondary care on antibiotic resistance in England. Correlation of antimicrobial usage data with microbiology surveillance data including antibiotic susceptibility test results allows increasing insight into the epidemiology and interdependency of antibiotic prescribing and AMR. These insights will be critical for developing new interventions, including behavioural change approaches, aimed at reducing rates of infection and AMR and improving clinical outcomes of patients treated for infection. A pilot project conducted to assess the data linkage capabilities between national, patient-level antimicrobial usage data successfully linked data provided by the NHS Business Service Authority (NHSBSA) and obtained from PHE's laboratory surveillance data.

Work is ongoing linking patient-level GP prescribing data to PHE's laboratory surveillance (SGSS) and HES data to provide baseline data informing the national ambition to halve healthcare-associated Gram-negative blood stream infection rates across the NHS by March 2021. This project will be used to build a working version of the production process to be run on a regular basis for linking and analysis of the linked data set.

Reducing the consumption of critically important broad-spectrum antibiotics, specifically carbapenems and piperacillin/tazobactam, has been the subject of NHS England quality improvement measures since 2016/17. ESPAUR analysts have also worked with the Department of Health and Social Care advisory committee on antibiotic prescribing, resistance and healthcare associated infections (APRHAI) to amend the World Health Organisation 'AWaRe' index for use in stewardship in England. The 'AWaRe' index groups antibiotic use into 3 surveillance categories to improve access (Access), monitor important antibiotics (Watch) and to preserve new and 'last resort' antibiotics (Reserve). NHS England introduced a new CQUIN indicator in 2018/19 for acute Trusts to increase the proportion of total antibiotic prescribing within the 'Access' category of the AWaRe (England) index. Indicators supporting CQUIN measures around antibiotic consumption are made openly available at acute Trust level on PHE Fingertips on a quarterly basis.

Independent sector

Due to resource issues affecting PHE's AMR surveillance team, the Association of Independent Healthcare Organisations (AIHO) Independent Sector Prescribing Data project was suspended in September 2017. Independent sector healthcare providers that had participated in the pilot project to collate antimicrobial usage data were informed and no further data were submitted.

Since June 2018, ESPAUR's collaborating partner AIHO has ceased operation and NHS Partners Network have begun to represent the interests of the independent healthcare sector service delivery including both NHS-funded and privately-funded services. The approach to future data collection from the sector will be reviewed in due course.

European collaboration

The United Kingdom submits antibiotic consumption data to the European Centre for Disease Prevention and Control via the European Surveillance of Antimicrobial Consumption Network (ESAC-Net).³⁰ PHE submits the national data for England and the devolved administrations (Northern Ireland, Scotland, and Wales) submit their national data individually. Data for 2017 has been submitted and will be published during European Antibiotic Awareness Day³¹ in November 2018.

In 2016, of the countries submitting data, the UK ranked 14th lowest for community antibiotic consumption (out of 29 countries) and the third highest for hospital antibiotic consumption (out of 23 countries). While it is useful to compare the consumption data and trends within countries, the reliability of comparisons across countries is less robust and limited by the variation in antibiotics used and the in-country ability to collect prescribing data.

Discussion

Prescribing

Total consumption of antibiotics in England continues its downward trend with a 1.9% reduction between 2016 and 2017. The 5-year trend of consumption has shown a decline of -4.5% from 22.1 to 21.1 DDD per 1000 inhabitants per day. While most antibiotic prescribing occurs in the GP setting, consumption measured in both DDD (-

³⁰ European Centre for Disease Prevention and Control. Antimicrobial consumption database (ESAC-Net). 2018. Available online from: ecdc.europa.eu/en/antimicrobial-consumption/surveillance-and-disease-data/database

³¹ European Centre for Disease Prevention and Control. European Antibiotic Awareness Day. 2018. Available online from: antibiotic.ecdc.europa.eu/en

9.2%) and items (-13.4%) has nonetheless declined. Although prescribing in other community settings continues to increase (27.5% between 2013 and 2017), the sector remains a relatively small contributor to overall antimicrobial prescribing (3.5% of total prescribing in 2017). However, we still have much to do to achieve the best in class status. The Swedish equivalent programme, STRAMA,³² has been in place for more than 25 years. Between 1992 and 2016, the number of prescriptions per 1000 in outpatient and primary care decreased by 43%, from 560 to 318 prescription items per 1000 of the population. In the last 5 years we have decreased the same metric in primary care from 754 to 654 antibiotic prescriptions per 1000 of the population, a 13% decline.

Antibiotic consumption has increased within secondary care, specifically to inpatients over the last 5 years, from 2.35 to 2.47 DDD since 2013 (4.8%), when measured by inhabitants per day. However, the change between 2013 and 2017 when using hospital admissions as a measure of hospital activity prescribing increased 7.7%.

Penicillins (44.6 %), tetracyclines (22.2%) and macrolides (14.7%) remain the most common drug classes prescribed in 2017. Over the period 2013 to 2017, a significant decreasing trend of consumption was observed for penicillin/inhibitor combinations, first and second-generation cephalosporins, anti-*C. difficile* agents, sulfonamides and trimethoprim. A significant increased trend was observed for third, fourth and fifth-generation cephalosporins and other antimicrobials.

Much of the significant changes in antibiotic consumption observed between 2016 and 2017 come as a consequence of the national shortage in piperacillin/tazobactam and the resulting choices made when switching to piperacillin/tazobactam alternatives alongside the continuing influence of national prescribing quality improvement schemes in primary and secondary care settings.

In secondary care, this is the first year (and retrospectively to 2014) in which the data are available for download at Trust level, enabling processing of data according to merged and demerged Trusts and their respective Trust types. Further work on the Trust data is required to understand reasons behind why teaching and multiservice Trusts had lower antimicrobial consumption than other Trust types in 2017.

Variation in prescribing levels within primary and secondary care settings continues; the data demonstrating the variation in practice can be reviewed on Fingertips.³³

³² Strama – Collaboration against antibiotic resistance 2018. Available online from: strama.se/about-strama/?lang=en

³³ Public Health Profiles AMR local indicators 2018. Available online from: fingertips.phe.org.uk/profile/amr-local-indicators/data#page/0/gid/1938132909/pat/158/par/SP_trust/ati/118/are/RBS

Quality Premium

The reductions achieved through previous QPs have been sustained and further reductions were made in 2017/18. However, considerable variation in prescribing reductions and QP attainment remains geographically. An evaluation is required to understand the levers and barriers to quality improvement in high and low performing regions.

There is a wealth of support available to help GP practices achieve the AMR QP from resources such as the TARGET toolkit³⁴ to data portals such as PrescQIPP,³⁵ NHS England QP monitoring dashboard and PHE Fingertips. The NHSBSA are launching a new reporting platform for primary care prescribing data which will include an AMS dashboard to support CCGs and GP stewardship activity by reporting antibiotic prescribing data by age bands. TARGET will be producing UTI diagnostic and management flow charts for health professionals to support the QP. ESPAUR will continue to work with partners to facilitate better understanding and use of these resources, in addition to displaying the data openly and transparently.

AMR metrics used within the 2015/16 and 2016/17 NHS England Antibiotic QP are reported in the NHS England CCG Improvement Assessment Framework (IAF). This and the extension of the QP to a 2-year scheme ensure CCGs will continue to remain focussed on reducing inappropriate antibacterial prescribing.

CQUIN

The proportion of empiric antibiotic prescriptions reviewed within 72 hours remained high in 2017 to 2018 suggesting that the indicator was easy to achieve and that this aspect of stewardship no longer required a quality improvement focus. This indicator was slightly amended to include an IV rationale and duration/review dates for all relevant decisions.

Uncertainties around antibiotic supply are apparent in consumption data and CQUIN attainment for 2017/18. The impact of antibiotic shortages was clearly seen in the striking reduction of piperacillin/tazobactam use in 2017/18. Carbapenems were among the potential candidates to switch to from piperacillin/tazobactam; however, a modest reduction in carbapenem consumption was recorded in 2017/18. It is therefore likely that shortages prompted a switch to multiple narrow-spectrum agents and this is supported by the fact that acute Trusts struggled to maintain the decrease in total antibiotic consumption seen in the 2016/17 CQUIN.

³⁴ Royal College of General Practitioners. TARGET Antibiotic Toolkit. 2018. Available online from: www.rcgp.org.uk/clinical-and-research/resources/toolkits/target-antibiotic-toolkit.aspx

³⁵ PrescQIPP. PrescQIPP in brief. 2018. Available online from: www.prescqipp.info

Future actions

ESPAUR will continue to:

- support the 2017-19 CQUINs and future CQUIN proposals
- develop CQUIN resources and tools for hospital implementation
- measure and evaluate the impact of NHS incentives on primary and secondary care antibiotic prescribing
- work with research partners to assess the impact and mediators of the QP and CQUIN
- assess the impact on the prescribing of antibiotic solutions, as a surrogate for prescribing in children; an abstract from these data is presented in the research annex
- explore changes in antibiotic prescribing in acute Trusts, in relation to those organisations which have/have not participated in and those who have not participated in the CQUIN
- extend quality improvement to develop indicators on antibiotic susceptibility testing to improve laboratory practice
- review the resources required to collect data from the independent sector

4. Antifungal resistance, prescribing and stewardship

Introduction

In recent years there have been increasing reports of invasive fungal disease and the emergence of more intrinsically resistant species of pathogenic fungi, such as *Candida auris*.³⁶ In 2015 the ESPAUR group formed a subgroup on antifungal consumption and resistance surveillance with national experts to identify gaps in current surveillance and to explore and implement improvements to the national surveillance on fungal infections as well as antifungal consumption.

Subsequently, national antifungal resistance, consumption and stewardship data were presented for the first time in the ESPAUR report 2016. It showed routinely reported resistance to key antifungals in the most frequently reported species of moulds (*Aspergillus* and *Fusarium*) and yeasts (*Candida albicans* and *C. glabrata*) from clinical isolates and consumption of systemic antifungals prescribed in general practice and NHS hospitals in England.

In 2017, ESPAUR published additional antifungal resistance data provided by PHE's National Mycology Reference Laboratory (MRL), Bristol, and the Mycology Reference Centre (MRCM), Manchester. Antifungal prescribing data were presented at specialty-level.

The ESPAUR subgroup also conducted and published a survey on antifungal stewardship and was subsequently invited to join the NHS Improvement Antifungal Stewardship project group. In addition, a joint PHE, UK Clinical Mycology Network (UKCMN) and British Society for Medical Mycology (BSMM) national survey on laboratory mycology testing capacity was launched by the subgroup in 2017. A summary of the results was published in last year's ESPAUR report.³⁷

To ensure that the survey findings were shared with a wide audience, members of the subgroup presented the results to clinicians and mycologists at the 28th European Congress of Clinical Microbiology & Infectious Diseases (ECCMID) in Madrid and to the

³⁶ Jeffery-Smith A *et al.* *Candida auris*: a Review of the Literature. [Review]. *Clinical Microbiology Reviews*. 2018;31(1):01

³⁷ PHE. ESPAUR Report 2017; Chapter 6. www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report

UKCMN Steering group at the 13th Annual Fungal Update Meeting in London,. The findings have also been written up and will be submitted for publication.

NHS England Improving Value Antifungal Stewardship Project

The NHS Improving Value AMS Project group was formed in February 2017 with the overall aim to achieve improved value from NHS England's spend on antifungal medicines – this includes preserving the future effectiveness of antifungals and improving patient outcomes.

Antimicrobial stewardship has so far mostly focused on antibiotic use but safe and effective use of antifungals is now just as crucial. The ESPAUR subgroup's survey on AMS showed that only 11% of responding NHS Trusts had AMS programmes in place compared with 100% of responding Trusts actively promoting antimicrobial stewardship.³⁸ With the support of ESPAUR's antifungal and antibiotic stewardship subgroups the NHS Improvement project group audited 8 NHS Trusts' antifungal guidelines during 2017 and found significant variation in practice.

Based on these findings and an evidence review, the NHS Improving Value Antifungal Stewardship Project group developed improvement principles with the following specific key objectives:

- improved antifungal stewardship across the NHS in England
- greater standardisation in the use of antifungals across the NHS in England
- optimised use of generic products wherever clinically appropriate to ensure best value

ESPAUR contributed to the development of the Antifungal Stewardship Implementation Pack which provides information and guidance to support the local implementation of this NHS Improving Value initiative. The pack is currently being finalised and options for presenting antifungal stewardship indicators on PHE's web portal Fingertips are being discussed.

Update on *Candida auris* : the current picture in England

Through to the end of September 2018, England has seen fewer numbers of cases of colonisation and infection with *C. auris* compared to 2017. This is not the situation

³⁸ Micallef C *et al.* An investigation of antifungal stewardship programmes in England. J Med Microbiol. 2017 Nov;66(11):1581-1589.

internationally, with increasing numbers of countries reporting case detections for the first time, and large-scale ongoing outbreaks documented in several continents.^{39,40}

A review of the incident responses to date from England has identified both specific and structural areas for improving the response to novel, emerging pathogens. Sporadic cases continue to be introduced into English hospitals, with 4 new Trusts reporting single introductions in 2018, primarily involving patients repatriated from overseas. A small number of hospitals that have had previous cases have reported sporadic new case detections. These have been recognised early, and through case isolation, enhanced infection prevention and control measures, and wider screening, have been contained. Only 1 hospital has seen limited transmissions, which have also been controlled. Of note, another hospital has documented introductions of 2 distinct clades of *C. auris*, suggesting that this pathogen is being frequently introduced into the UK, thus highlighting the need for continued vigilance. There have been approximately 250 reported case detections in England, with 1 quarter of those reflecting clinical infections, including 31 candidaemias. To date no reported mortality has been attributable to *C. auris*.

PHE's *C. auris* incident management team and affected hospitals and other scientific institutions continue to add to the international literature through collaborative projects, including a wide-ranging evaluation of the epidemiology, transmission dynamics, and control methods.⁴¹ PHE Porton continues to test different disinfectants and cleansing agents, to determine which have greatest efficacy against *C. auris*.⁴² Tests have included attempting to establish whether *C. auris* can remain in an aerosolised state for any period of time. Whole genome sequencing has shown that within lineages, it is difficult to distinguish new cases from transmission events, though further work is ongoing to better characterize this within England.⁴³ Collaborations with academic institutions on genomic studies and outbreak response have proved fruitful.⁴⁴ The first national point prevalence study has helped evaluate diagnostic capacity using conventional techniques, and its findings will be disseminated at international conferences and via journal publications.⁴⁵ Analysis of the national diagnostic capacity

³⁹ Adams E *et al.* *Candida auris* in Healthcare Facilities, New York, USA, 2013-2017. *Emerg Infect Dis.* 2018;24(10):1816-1824

⁴⁰ Ruiz-Gaitan A *et al.* An outbreak due to *Candida auris* with prolonged colonisation and candidaemia in a tertiary care European hospital. *Mycoses.* 2018;61(7):498-505

⁴¹ Jeffery-Smith A *et al.* *Candida auris*: a Review of the Literature. [Review]. *Clinical Microbiology Reviews.* 2018;31(1):01

⁴² Moore G *et al.* Yeastocidal activity of chemical disinfectants and antiseptics against *Candida auris*. *Journal of Hospital Infection.* 2017;97(4) 371-375

⁴³ Rhodes J *et al.* Genomic epidemiology of the UK outbreak of the emerging fungal pathogen *Candida auris*. *Emerging Microbes Infect.* 2018;7(1):43

⁴⁴ Eyre DW *et al.* A *Candida auris* outbreak and its control in an intensive care setting. *N Engl J Med.* 2018;379(14):1322-1331

⁴⁵ Sharp A *et al.* Assessing routine diagnostic methods for detecting *Candida auris* in England. *J Infect.* 2018. doi.org/10.1016/j.jinf.2018.07.012

for *C. auris* detection has been undertaken. PHE's National Mycology Reference Laboratory remains committed to collaborating with local hospitals, industry, and international bodies to further diagnostic and novel antifungal testing.

A review of European preparedness highlighted that the UK has met the key recommendations for *C. auris* monitoring and control.^{46,47} It remains clear that *C. auris* continues to be an ongoing threat internationally. Work is continuing to ensure guidance documents are updated, hospitals are given assistance in managing new introductions, surveillance systems are in place to ensure new cases are documented and acted upon, and longitudinal trends are monitored.

Various members of the incident management group have participated in national and international events and site reviews to help define an ongoing action plan to address the many unanswered questions about transmission dynamics, outbreak prevention, individual case management, and drug resistance.

Future actions

The ESPAUR subgroup on antifungal consumption and resistance surveillance will work co-operatively to wind down the subgroup without jeopardising stakeholder relationships. Antifungal surveillance will continue encompassing activities including:

- exploring options for presenting antifungal resistance and/or prescribing data on PHE's Fingertips web portal, including for example, antifungal stewardship indicators and routine surveillance data quality indicators such as species level identification and reporting of antifungal susceptibility test results for *Candida* isolates from blood
- strengthening quality of antifungal surveillance data by improving species-level reporting from NHS laboratories to SGSS
- continuing to scope harmonisation of breakpoints and access to diagnostic testing in collaboration with relevant networks given that reporting of AMR data for *Candida* and *Aspergillus* will be considered by WHO GLASS in the next the evaluation phase

⁴⁶ European Centre for Disease Prevention and Control. *Candida auris* in healthcare settings – Europe [Rapid Risk Assessment] April 2018. Available online from: ecdc.europa.eu/en/publications-data/rapid-risk-assessment-candida-auris-healthcare-settings-europe

⁴⁷ Kohlenberg A, Struelens MJ, Monnet DL, Plachouras D *et al.* *Candida auris*: epidemiological situation, laboratory capacity and preparedness in European Union and European Economic Area countries, 2013 to 2017. *Eurosurveillance*. 2018;23(13)

5. Antimicrobial stewardship

Introduction

Optimising prescribing, through the development and implementation of antimicrobial stewardship (AMS) programmes and toolkits is 1 of the 7 key areas for action in the UK 5-year Antimicrobial Resistance (AMR) Strategy 2013 to 2018.⁴⁸

This chapter outlines the results from key projects during 2017/18 including:

- further development of Treat Antibiotics Responsibly, Guidance, Education, Tools (TARGET) for primary care
- management of self-limiting infections in community pharmacies: implementation of the TARGET Antibiotics Community pharmacy leaflet
- assessment of inappropriate prescribing in secondary care

Antimicrobial stewardship in primary care

The TARGET antibiotics toolkit⁴⁹ optimises prescribing practice through supporting AMS in primary care. It aims to help primary care clinicians and commissioners in England reduce inappropriate antibiotic prescribing. The TARGET toolkit is an evidence-based AMS initiative that aims to help influence prescribers' and patients' personal attitudes, social norms and perceived barriers to optimal antimicrobial prescribing. The toolkit resources (including patient leaflets) educate patients and the public about appropriate antimicrobial use and AMR during consultations. Hosted on the Royal College of General Practitioners (RCGP) website, the TARGET toolkit is freely available to all primary care health professionals.

Both the TARGET randomised controlled trial⁵⁰ and qualitative mixed methods evaluation confirmed that the TARGET workshop (promoting the tools and feedback on antimicrobial use) significantly reduced antimicrobial use in non-research general practices and was valued by GP staff.⁵¹ However, the work showed that Clinical

⁴⁸ Department of Health and Social Care. UK 5 Year Antimicrobial Resistance Strategy 2013 to 2018. Available online from: www.gov.uk/government/publications/uk-5-year-antimicrobial-resistance-strategy-2013-to-2018

⁴⁹ Royal College of General Practitioners. TARGET Antibiotic Toolkit. 2018. Available online from: www.rcgp.org.uk/clinical-and-research/resources/toolkits/target-antibiotic-toolkit.aspx

⁵⁰ Jones LF *et al.* An evaluation of the TARGET (Treat Antibiotics Responsibly; Guidance, Education, Tools) Antibiotics Toolkit to improve antimicrobial stewardship in primary care—is it fit for purpose? *Family Practice* 2018; 35(4):461–467. doi: [10.1093/fampra/cmz131]

⁵¹ McNulty CAM *et al.* Effects of primary care antimicrobial stewardship outreach on antibiotic use by general practice staff: Pragmatic Randomised Controlled Trial of the TARGET Antibiotics workshop. *J Antimicrob Chemotherapy* 2017.

Commissioning Groups (CCGs) need to promote the resources more and undertake more action planning within the workshops.

TARGET Toolkit process evaluation

Ninety-nine percent of CCGs promote TARGET to their general practices. A process evaluation of the TARGET toolkit website has been undertaken to assess number of visitors to the site over the course of the year (particularly looking at times of peak use) and the resources that most used. Google Analytics was used to collect participant interaction with the TARGET website. TARGET is the most accessed page on the RCGP website by primary care clinicians, with over 69,000 visits between July 2017 and June 2018. Website visits in 2018 have increased further from 2017 and 2016. An increase in visits to the website is seen over the winter months every year, in particular in the build up to World Antibiotic Awareness Week (WAAW); October 2017 had nearly 7,000 visits and November 2017 had over 8,000 visits (Figure 5.1).

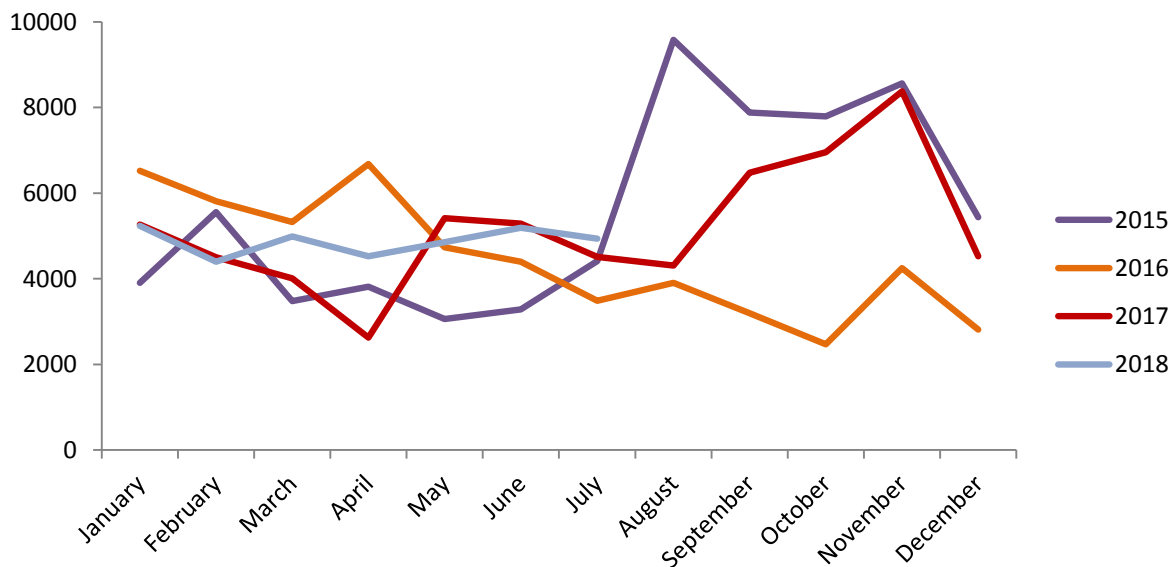


Figure 5.1 Total TARGET website visits January 2015 - July 2018

TARGET toolkit resources development

TARGET and the Quality Premium

TARGET has developed a suite of urinary tract infection (UTI) resources that can assist CCGs and primary care providers achieve a reduction in Gram-negative bloodstream infections (GNBSIs) and inappropriate antibiotic prescribing in higher risk groups. These resources support the 2017-18 QP measure for a reduction in GNBSIs as they were designed to sustainably reduce inappropriate antibiotic prescribing for UTIs in primary care and improve the diagnosis and management of UTIs in vulnerable groups

as well as flag issues such as sepsis and pyelonephritis. All tools were developed using behaviour change models to target key areas of the care pathway specific to UTI prevention, diagnosis, management, and safety netting.

Key resources include:

The TARGET treating your infection leaflets which address management, safety netting and self-care for key groups at risk of UTIs. This includes a leaflet for women under 65 years with uncomplicated UTI and a newly published leaflet that targets older adults who are at risk of a UTI. They can be downloaded free of charge from the TARGET website and have been translated into multiple languages (women <65 years).

Clinicians can use these leaflets when consulting with patients. The older adult leaflet is also designed for carers of those who are at risk of a UTI and can be given as a resource to improve prevention, care seeking, management and safety netting. The audit template for common infections including UTI allows clinicians to determine how their management of urinary symptoms compares to national guidance. It includes common Read codes and formulae to calculate an individual's compliance with the management and antibiotic guidance for UTIs.

The e-learning modules for UTIs provide training scenarios that can be used by staff to improve their case management and earn accredited CPD.

The TARGET website⁵² now has a dedicated section for all the UTI resources so primary care clinicians and commissioners can find all the UTI resources in 1 place.

A urinary tract infection (UTI) leaflet for older adults and carers

Previously developed TARGET resources included a patient information leaflet for uncomplicated UTIs in women less than 65 years. However, as the majority of GNBSIs occur in patients over 65 years of age with UTI as the commonest source, the TARGET team developed a specific leaflet for older adults. The 'Treating Your Infection – UTI leaflet for older adults' is for healthcare professionals to share with older adults, their relatives and carers when they present with urinary symptoms, or with other health care staff/patient contacts to help prevent future UTIs.

The leaflet was developed by undertaking an extensive needs assessment with input from general practitioners, care home staff and residents, elderly patients and their relatives, and professional organisations including Public Health Wales, Scottish UTI Network and HSC Public Health Agency Northern Ireland. The leaflet underwent

⁵² Royal College of General Practitioners. TARGET Antibiotic Toolkit. 2018. Available online from: www.rcgp.org.uk/clinical-and-research/resources/toolkits/target-antibiotic-toolkit.aspx

iterative modifications after each interview or focus group. Data collection and leaflet development was informed by the Theoretical Domains Framework (TDF). As a result of the findings from the study the older adult leaflet was developed to provide information on prevention and self-care for UTIs, to improve understanding of dipsticks and asymptomatic bacteriuria, to highlight other causes of confusion, to highlight the signs and symptoms of sepsis, and to provide information on antibiotics and AMR.

The leaflet can be used in different ways including: to provide information on UTIs to those at- risk, carers and care-home staff may wish to share this leaflet with older adults in their care and/or their relatives; and during primary care consultations to facilitate the conversation between a patient and their GP on specific topics such as treatment choice or safety netting advice. The 'what signs and symptoms should I look out for' section of the leaflet is an important source of reassurance for patients and their carers. The leaflet is designed to be used as a tool to interact with patients, rather than as a 'parting gift' to give the patient/carer the confidence and knowledge to manage the patients UTI appropriately.

TARGET leaflets endorsed by NICE

Three of the TARGET Treating Your Infection (TYI) leaflets were endorsed by NICE in November 2017; Urinary Tract Infection (UTI) leaflet, Respiratory Tract Infection (RTI) leaflet and the pictorial RTI leaflet. The TYI-UTI leaflet has been designed to be used with women who are experiencing urinary symptoms suggesting non-complicated UTIs, supporting implementation of recommendations in the NICE guidelines on processes for antimicrobial stewardship and behaviour change for antimicrobial stewardship. The RTI leaflet and pictorial RTI leaflet has been designed to be used with patients who are experiencing self-limiting upper RTIs and supports implementation of recommendations in the NICE guidelines on processes for antimicrobial stewardship, behaviour change for antimicrobial stewardship and antibiotic prescribing for respiratory tract infections.

TARGET leaflets available on GP systems

The TARGET Treating Your Infection RTI and UTI leaflets are now available available for inclusion on GP clinical record software systems, EMIS and future work will aim to develop methods to integrate it within SystmOne. This means that health professionals can access the TARGET leaflets directly from their GP system when consulting with a patient, personalise and print off the leaflet to facilitate communication around the patient's infection. There are user guides on the TARGET website with instructions on how to upload the leaflets to the respective GP system.

TARGET audit review, redesign and implementation

There are 5 antibiotic prescribing audits in the TARGET toolkit; Acute sore throat, acute sinusitis, UTI, acute otitis media, and acute cough. In 2017, each of the audit tools were

reviewed and updated to be in line with NICE and PHE guidelines and have also been redesigned to make them more user friendly. The Excel audit tool allows users to input their consultation records for a particular condition to evaluate their antibiotic prescribing against current local and/or national guidelines and support identification of areas for quality improvement.

TARGET stakeholder engagement

TARGET publish 4 newsletters a year to engage with stakeholder and highlight: resource updates, new resource developments, research publications and any planned future work that medicines management teams and primary care practitioners may wish to be involved in. To sign up to the mailing list complete the link [online](#).

TARGET have launched a twitter account @TARGETabx to reach out to health professionals, CCGs and stakeholders to share our research and resources. In the 8 months since the twitter launch, it receives regular tweet impressions of over 3000 (the number of times the users saw the tweet). At conferences, meetings and events, work is showcased via posters, presentations and exhibition stands and feedback on other antimicrobial stewardship work.

Management of self-limiting infections in community pharmacies: implementation of the TARGET antibiotics community pharmacy leaflet

Community pharmacy teams have a key role in contributing to tackling AMR. The TARGET TYI-RTI leaflet was already in use and implemented for General Practice. The same leaflet was adapted and published for community pharmacy in 2015 as a self-care guide to treating infections, but was not widely implemented. It was proposed that pharmacists use the TARGET community pharmacy leaflet with patients seeking advice for managing common infections.

The study involved a national and local partnership team working together to assess the impact of i) provision of an AMS educational webinar to pharmacy teams and ii) implementation of the TARGET self-care leaflet on:

- consultation outcomes, including referrals to doctors or provision of self-care advice, over-the-counter (OTC) medicines, or written information
- pharmacy team members' behaviour in managing self-limiting infections, assessed using the COM-B (capability, opportunity, motivation and behaviour) model

The study was conducted as a 2-armed non-blinded, cluster randomised controlled trial (RCT), with individual pharmacy premises as the unit of randomisation.

All pharmacies within 6 Local Pharmaceutical Committee areas (LPCs, representing community pharmacies locally) in the South West, Lambeth, Southwark and Lewisham

LPC were invited to take part by seeking expressions of interest through the LPCs. Pharmacies were stratified according to rural or urban and independent or chain (multiples) categories and randomly allocated to either the intervention or control arm. The trial was conducted early in 2018; a flow-chart of activities for the study period is shown in Figure 5.2. Ethics approval was granted by PHE Research Ethics and Governance Group.

Pharmacies in each arm recorded consultations between pharmacy staff and patients presenting with common self-limiting Respiratory Tract Infections (RTIs). Consultations with patients attending the pharmacy with prescriptions for antibiotics and patients attending for specific OTC medicines were excluded.

Consultation data were submitted via the PharmOutcomes® portal.

A random effects statistical model was applied to inferential analysis of the effect of the intervention on each outcome, taking into account clustering by pharmacies.

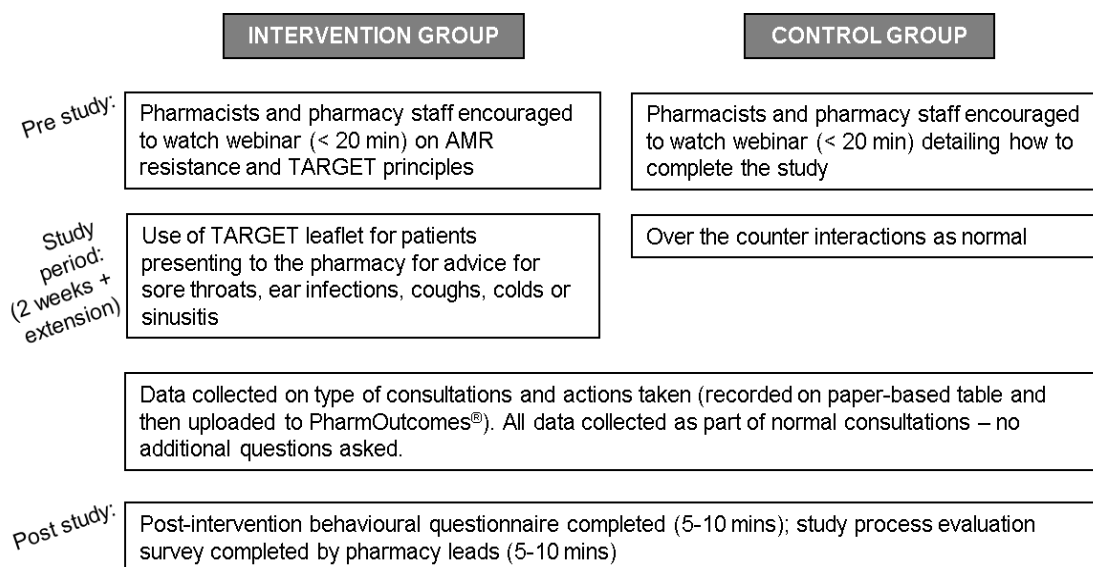


Figure 5.2 Simple flowchart of activities for the TARGET RCT

One hundred and eighty two out of 272 possible pharmacies submitted consultation data (participation rate of 66.1%). The number of independent and chain pharmacies were similar between the 2 arms. The median number of individual patient consultation data forms submitted per pharmacy was 13.5 and 15.5 for the intervention and control arms, respectively.

Data were analysed from 3649 individual patient consultations overall. Consultations were similar between study arms in terms of patient age, gender and type of RTI. Overall, 59.8% patients were adult, 23.5% were classed as elderly, and 11.6% and 5.0% were children or teenagers, respectively; 54% of patients were female. The most

commonly reported RTI types were cough (44.5% consultations), common cold (34.5%) and sore throat (26.1%). Patients frequently presented with more than 1 type of RTI.

The analysis provided evidence to suggest that the use of the TARGET leaflet was associated with a decrease in GP referrals for certain RTI types: middle ear infection OR = 0.18 (95% CI 0.06-0.49), sinusitis OR = 0.20 (95% CI 0.07-0.56) and possibly cough OR = 0.54 (95% CI 0.25-1.19). The intervention was also associated with increased provision of self-care although only early on in the study period. Patients in the intervention arm were more likely to receive written information if also provided with self-care advice. Furthermore, patients having an over-the-counter product recommended were less likely to receive GP referrals but more likely to receive self-care advice in the intervention group.

A total of 296 COM-B based questionnaires were submitted from 157 unique pharmacies, of which:

- greater than 90% agreed or strongly agreed that they knew how long common infections last, what self-care advice to provide and what is meant by the term antibiotic resistance
- 25% found it difficult to explain to patients why antibiotics were not needed
- 41% of respondents agreed that they did not get the opportunity to provide all the self-care advice they wanted due to time pressures
- 74% believed they have a key role in helping control antibiotic use and 95% believed it is important they give self-care advice for common infections
- 54% reported that on a typical day they would often or very often have self-care conversations. 33% would often or very often give out self-care resources, information and advice; 24% reported that they would have liked to give self-care resources, information or advice but were unable to

A process evaluation questionnaire was made available for participating pharmacies. This was completed by 156 individual pharmacies (response rate of 57.4%). Major findings are outlined:

- over 70% of respondents felt their pharmacy teams were well-informed on the project and project resources were easy to identify
- 56% reported that consultation data was usually completed after each relevant consultation. Nearly one-third of respondents felt that only 25-50% of relevant consultations were captured and around 40% respondents put this estimate at 75%. The main reasons reported for inability to complete the data submission were staff being too busy (63% respondents) or forgetting (55%)
- over half of the respondents stated that they would appreciate extra online training on managing infections. 41% requested easier access to local antibiotic guidance and 36% requested resources to support patient information around compliance

This study is the first large-scale AMR-focused RCT intervention in community pharmacy and adds to the body of evidence for AMS activities. The results suggest that the community pharmacy-adapted TARGET leaflet may aid pharmacy staff in the delivery of self-care advice, also helping to reduce the demand for unnecessary antibiotics through reducing GP referrals. Support from the LPCs during the initial design of the study and gaining engagement from pharmacies was an important aspect that contributed to the success of the research.

The leaflet, which is intended to improve and enhance pharmacy practice, was demonstrated to:

- empower pharmacy staff to have infection-related self-care conversations with patients
- support appropriate use of NHS resources and potentially reduce pressure on GPs
- support awareness of the appropriate use of antibiotics using available resources and signposting to sources of advice. This is an important aspect of Healthy Living Pharmacy champions as part of Making Every Contact Count (MECC).⁵³ Materials such as the TARGET leaflet provide clear, consistent messages, reinforcing discussions with patients

With the results of this study, PHE have confirmed that the TARGET community pharmacy leaflet will be made available through the Stay Well this Winter and Keep Antibiotics Working campaigns.

Antimicrobial stewardship in secondary care

Assessment of inappropriate prescribing in secondary care

Antibiotic consumption reduction targets have previously been set through CQUINs. However, the proportion of consumption that is unnecessary and can be safely reduced is unknown. In 2016, the UK Government set an ambition to reduce inappropriate antibiotic prescribing by 50% by 2020. Estimates for primary care have been defined.⁵⁴ However, estimates specific to secondary care are also required to inform future inappropriate prescribing reduction targets.

Having determined that accurate data was lacking on which to base antibiotic prescribing reduction targets, the Department of Health and Social Care (DHSC) Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare

⁵³ Making Every Contact Count Available online from: www.gov.uk/government/publications/making-every-contact-count-mecc-practical-resources

⁵⁴ Smieszek T *et al.* Potential for reducing inappropriate antibiotic prescribing in English primary care. *The Journal of antimicrobial chemotherapy.* 2018;73(suppl_2):ii36-ii43

Associated Infection (APRHAI) was tasked to consider the scientific evidence and deliver recommendations for measures by which to reduce inappropriate prescribing. Defining appropriateness is a prerequisite to accurately estimating the proportion of prescribing that is inappropriate and deriving safe reduction targets. Infection experts convened at an APRHAI led-workshop in February 2017, to define appropriate prescribing.

Three priority aspects were subsequently agreed upon to define inappropriate prescribing in a UK hospital setting:

- prescribing an antibiotic for a patient in the absence of (documented) evidence of bacterial infection
- prescribing a critical broad-spectrum antibiotic to patients in the absence of a (documented) rationale
- continuing an antibiotic prescription beyond the course length recommended in local or national guidelines, in the absence of a (documented) rationale

The workshop consensus, APRHAI then recommended to the DHSC, was that the following work be undertaken to improve the evidence base:

- perform an analysis of the 2016 national PPS to assess levels of inappropriate prescribing
- develop, pilot and validate an audit tool to capture total and inappropriate days of antibiotic therapy

In this chapter we present the interim findings. Further findings are presented in the [research annex](#) and are being prepared for peer-review.

An analysis of the 2016 national PPS data, combined with the development, pilot and validation of an audit tool to estimate inappropriate antibiotic prescribing in secondary care in England was conducted by PHE. The 2 approaches were utilised together to inform the development of target prescribing reduction measures in terms of total antibiotic prescribing, broad-spectrum antibiotics and specific antibiotics which will contribute to the Government's ambition to reduce inappropriate prescribing by 50% by 2020.

The workflow and relationship between the 2 projects are outlined in Figure 5.3.

The audit tool was developed through a 2 round Rand-modified Delphi process involving an expert panel of 19 multidisciplinary infection and public health experts. Validated data items that contributed to the development of defining and assessing inappropriate prescribing within secondary care were included in the final audit tool. The validated audit tool was then piloted in 12 acute Trusts over a 2 week period in

December 2017. Collected data were analysed to assess the percentage of inappropriate antibiotic prescribing (expressed as non-essential therapy days against appropriate days), from each participating Trust and overall. Participating Trusts were provided with individual feedback that included a benchmarking opportunity from the overall pilot result.

Collated national evidence-based treatment guidelines and expert consultation/review were used to develop definitions of prescribing appropriateness for community-acquired pneumonia, bronchitis, cystitis and pyelonephritis. The PPS data were coded to produce descriptive measures of prescribing and prescribing appropriateness for each indication, according to choice of specific antibiotics and therapy duration. Ongoing modelling and sensitivity analysis will inform summary proportional measures and recommendations for reductions in inappropriate prescribing. Where possible, the modelling work will incorporate findings from the audit tool data. Further analysis is ongoing to assess the appropriateness of antibiotic use for surgical prophylaxis. There were challenges related to the inherent complexity of data coding, and limitations with the availability of robust evidence-based clinical guidance and clinical data in the PPS. Extensive discussion and expert review helped address these issues.

From the Delphi; 8 of the 19 original panel members (42%) agreed that the audit tool was fit-for-purpose, with 26% (5/19) disagreeing. The remaining 6 panel members expressed a neutral view (5/19) with 1 panel member stating they were unable to assess this question. The participants were asked if the time taken to complete the audit tool is a worthwhile investment of NHS resources for the benefit of patient safety and public health, with 43% (8/19) agreeing that it is, 26% (5/19) disagreeing, 21% (4/19) having a neutral view and 10% (2/19) being unable to assess this.

Audit data on 397 patients were submitted by 12 individual trusts, representing 717 individual antibiotic prescriptions and over 3800 therapy days; 17.1% of total therapy days were estimated to be non-essential by auditors, with 9.2% therapy days not-indicated from the start of therapy.

Feedback from the process evaluation indicated that the diverse time taken to complete audits depended on the availability of information within electronic prescribing systems, paper drug charts and patient notes. In addition, it identified a need for a specific paediatric audit tool. It was also recommended that future iterations would need to incorporate the tool into electronic-prescribing systems to reduce data collection burden. The majority (92%, 11/12) of pilot sites would be prepared to do the audit again with over half (58%, 7/12) of participating sites willing to complete it twice yearly or more frequently. The audit tool is currently being updated based on feedback from the pilot.

During the process evaluation, certain pilot sites fed back that they are using the audit tool locally within areas of high antibiotic prescribing. Trust specific results had also been presented internally with prescribers in order to highlight areas of improvement and potential training needs. There has been interest from the CDC in the USA and colleagues in Australia on the outcomes from the pilot process with initial discussion on mutual sharing and learning of a range of methods to assess inappropriate prescribing.

The PPS contained data on 6796 antibiotic prescriptions, from 5238 patients (median age: 77; 51.8% patients were female) for the 4 common community onset conditions studied. These conditions, accounting for 26.6% of antibiotic prescribing in the PPS, were pneumonia (59.5% of the 6796), complicated cystitis (14.8%), bronchitis (14.7%), pyelonephritis (7.8%) and uncomplicated cystitis (3.3%). Across all 4 conditions 65.6% (95% CI: 64.4-66.7%) of antibiotics prescribed were in agreement with national guidelines while 12.4% (95% CI: 11.6-13.2%) of prescriptions exceeded the maximum duration recommended in national guidelines.

These results estimate levels of inappropriate prescribing in secondary care using data from both the PPS and pilot audit, which will be used to inform future national policy and reduction targets for secondary care.

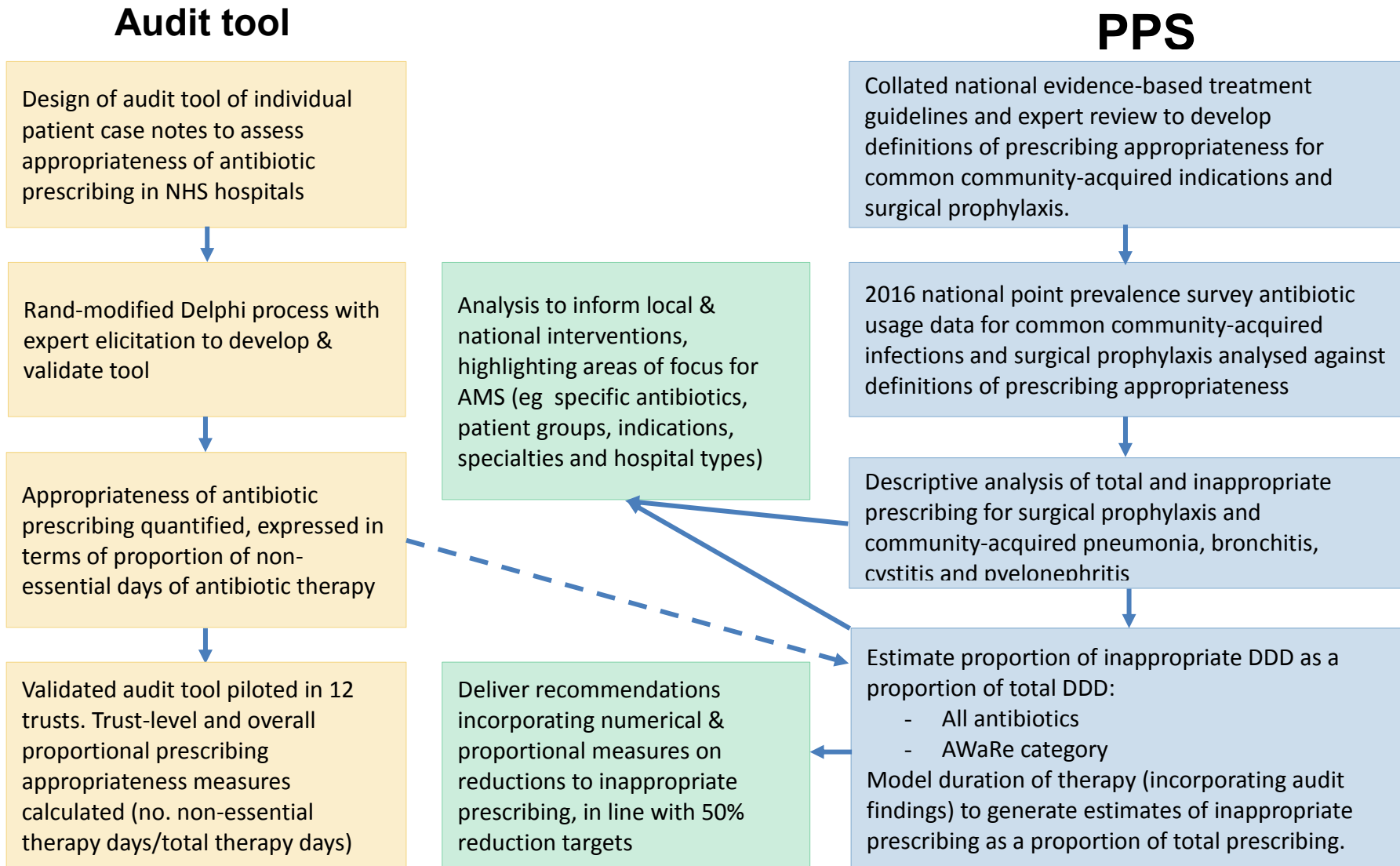


Figure 5.3. Workflow of the project to assess inappropriate prescribing in secondary care

Future actions

The TARGET logo and resources are being rebranded in line with the PHE's Keep Antibiotics Working campaign. The resources will keep their TARGET content but have a new look in line with the colour schemes of Keep Antibiotics Working to ensure there is greater brand recognition and continuity nationally. As part of the Keep Antibiotics Working campaign the TARGET resources will be promoted nationally and locally across England.

The TARGET Treating Your Infection leaflets on RTI and URI are being updated on the GP systems EMIS and SystmOne. TARGET plan to launch this achievement in the run up to WAAW so that health professionals are aware they can access the TARGET leaflets directly from their GP system when consulting with a patient and can personalise and print the leaflet to facilitate communication around the patient's infection. A UTI diagnostic flowchart will also be developed.

Three of the TARGET Treating Your Infection leaflets (UTI, RTI and the pictorial RTI leaflet) have been endorsed by NICE. The latest Treating Your Infection leaflet for UTIs in older adults is currently seeking NICE endorsement and supports implementation of recommendations in the NICE guidelines on processes and behaviour change for AMS. The TARGET training resources will also seek NICE endorsement to be promoted in the run up to WAAW.

The community pharmacy study supports the use of the TARGET community pharmacy leaflet on the management of RTIs (including provision of self-care advice) within the community pharmacy. During 2018/19 we will work with organisations to consider how the findings from the study could potentially be integrated into routine pharmacy delivery of health advice. The TARGET community pharmacy leaflet will also be made available through the Stay Well This Winter and Keep Antibiotics Working campaigns.

Further work is planned with the audit tool related to unnecessary prescribing.

The next steps are to:

- incorporate changes, for example inclusion of additional data fields (antibiotic route of administration, start/stop dates) and the application of definitions to allow consistent categorisation of infection diagnosis prior to making it available for local use
- revise the audit tool and make it available for local use
- once changes have been revised and retested, seek NICE endorsement for the tool

6. Professional education & training and public engagement

Introduction

This chapter outlines key interventions delivered as part of implementing key area 3 of the UK Antimicrobial Resistance (AMR) Strategy (Professional education and training and public engagement) during 2017/18 and includes:

- mass media 'Keep Antibiotics Working' campaign which reduces public expectation for antibiotics
- pledge-based 'Antibiotic Guardian' campaign, for healthcare professionals and members of the public
- summary of key activities from World Antibiotic Awareness Week (WAAW) and European Antibiotic Awareness Day (EAAD)
- delivery of antimicrobial stewardship workshops and training events for healthcare professionals and students
- e-Bug activities, which focus on bacteria, AMR and hygiene education of children and teenagers
- TARGET antibiotics toolkit for primary care prescribers
- assessment of PHE's public facing AMR activities using the PHE's Health Equities tool (HEAT)
- AMR Training Resources coordinated by Health Education England (HEE)
- development of consensus-based national antimicrobial stewardship competencies for UK undergraduate healthcare professional education

Keep Antibiotics Working campaign

Following a successful pilot in the North West in February 2017, PHE launched a national campaign in October 2017 to alert the public to the issue of AMR, with the aim of reducing patient's expectation for antibiotics, which supports GPs in their efforts to reduce prescribing. The campaign contributes to the government's ambition to halve inappropriate prescribing of antibiotics by 2021.

A successful PR launch on 23 October made use of hard-hitting statistics to show the imminent danger of antibiotic resistance. In total the campaign has had 769 pieces of coverage and appeared on most of the major national news programmes.

Consumer-friendly advertising ran across TV, radio, billboards, press, social media and digital and featured animated pills and a catchy song to get people's attention and

highlight that taking antibiotics unnecessarily puts people at risk. The videos on social media have been viewed over 10 million times.

PHE worked in close partnership with the NHS, and engaged with 92% of GP practices in England. During the campaign period, over 766,000 posters and leaflets were distributed to a range of partners including local authorities, health care centres and Housing Associations. In addition over 21,000 specially designed self-care prescription pads were sent to health care professionals, providing a tangible evidence-based intervention to satisfy patient concerns and help alleviate pressure to prescribe on clinicians.

The campaign has started to change the narrative on AMR from the future risk to humanity, towards the immediate risk to the individual. The campaign achieved a good level of awareness and the key message resonated well, with 81% of the public acknowledging that taking antibiotics unnecessarily puts them and their family at risk. Significantly, there was a positive impact on intended behaviour, with 78% of the public stating that they would be unlikely to ask their GP for antibiotics. Additionally, GPs have welcomed the campaign, with 93% saying they felt it supports them to say 'no' to antibiotics when they are not needed.

In 2018, the campaign will continue to improve public awareness of AMR to help reduce patient expectation for antibiotics. This will continue support GPs in their conversations with patients. Resources to support Keep Antibiotics Working will be sent automatically to all GP Practices and community pharmacies in England. Additional free resources for a variety of settings can be ordered or downloaded from the PHE Campaign Resource Centre.⁵⁵

Antibiotic Guardian campaign

PHE launched the pledge-based 'Antibiotic Guardian' 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.⁵⁶ An impact evaluation carried out after the first year of the campaign highlighted that those who chose pledges on the website and became Antibiotic Guardians (AGs) had increased knowledge and behaviour change (self-reported), as well as increased commitment to tackling AMR.

⁵⁵ Keep Antibiotics Working 2018. Available online from: campaignresources.phe.gov.uk/resources/campaigns/58-keep-antibiotics-working

⁵⁶ Ashiru-Oredope D *et al.* Antimicrobial resistance: moving from professional engagement to public action. *Journal of Antimicrobial Chemotherapy*. 2015;70(11):2927-2930

Since the start of the campaign (2014) up to 31/12/2017, the website has been visited 470,968 times. This translated into 57,627 pledges from 129 countries. Antibiotic Guardians were therefore present in 50% of countries worldwide. The number of pledges has increased each year from 12,315 in 2014, 15,002 in 2015, 15,140 in 2016 and 15,170 in 2017. There have been year-on-year increases in the number of pledges received during WAAW/EAAD, with notably higher numbers of pledges in 2016 and 2017 compared to previous years. Translations of the AG programme are now available in Dutch, French, Russian and Turkish supporting the AMR recommendation related to a worldwide awareness campaign.

In both 2016 and 2017, the most common group making pledges comprised healthcare professionals (60.6%) with 18.5% being pharmacy students. In addition to the 2 previously published peer-review publications, a qualitative evaluation of the AG campaign was peer-reviewed and published in BMC Public Health Journal.⁵⁷ In February 2018, the peer-reviewed manuscript: Expansion of the 'Antibiotic Guardian' one health behavioural campaign across Europe to tackle antibiotic resistance: pilot phase and analysis of AMR knowledge was published in European Journal of Public Health.⁵⁸

Junior/Family Antibiotic Guardian

Junior and Family Antibiotic Guardian consist of tasks being completed based on e-Bug; a free educational resource which aims to reduce antibiotic resistance by helping children and young people understand infections and antibiotic use. Scouts continued to work towards achieving their AG badges, raising awareness in children and families. A Scouting AG badge was expanded in 2017 across Leicestershire⁵⁹ following initial development by West Lancashire Scouts and PHE.⁶⁰

Summary of activities from World Antibiotic Awareness Week (WAAW) and European Antibiotic Awareness Day (EAAD) 2017

The key goals for 2017/18 were to:

⁵⁷ Kesten JM *et al.* The Antibiotic Guardian campaign: a qualitative evaluation of an online pledge-based system focused on making better use of antibiotics. BMC Public Health 2017 doi: 10.1186/s12889-017-4552-9

⁵⁸ Newitt S *et al.* Expansion of the 'Antibiotic Guardian' one health behavioural campaign across Europe to tackle antibiotic resistance: pilot phase and analysis of AMR knowledge. European Journal of Public Health 2018; 28(3):437-439. academic.oup.com/eurpub/article/28/3/437/4833566?guestAccessKey=7f699118-934a-480c-9d45-63af024a93d5

⁵⁹ Leicestershire Scouts Antibiotic Guardian Scheme – Leader training 2017. Available online from: www.leicestershirescouts.org.uk/2017/11/antibiotic-guardian-scheme-leader-training

⁶⁰ West Lancashire Scouts Antibiotic Guardian Scheme 2017. Available online from: www.westlancscouts.org.uk/antibiotic-guardians

- bring together the purpose and credibility of the Antibiotic Guardian Programme with the scale and recognition of the nationwide Keep Antibiotics Working and develop a single unifying brand for AMR public campaigns
- increase the proportion of AGs who are members of the public and increase the number of healthcare student pledges
- increase the number of organisations registering planned activities by 10%

WAAW, led by the World Health Organisation, and EAAD, led by the European Centre for Disease Prevention and Control, promote the coordination of antibiotic awareness campaigns internationally. PHE coordinates the activities for England. For the fourth consecutive year, PHE continued to develop and lead the UK-wide AG campaign as a move from raising awareness to stimulating behaviour change and increase engagement to tackle AMR by healthcare professionals and engaged members of the public.

All resources for WAAW/EAAD 2017 were updated with the new Antibiotic Guardian branding, including:

- resources toolkits (for healthcare professionals and students)
- Antibiotic Guardian badges
- Junior and Family Antibiotic Guardian resources
- resources including crossword puzzles and quizzes for healthcare professionals and the public
- Antibiotic Awareness Key Messages
- Start Smart Then Focus leaflets and secondary prescribers' checklists

During WAAW 2017, www.antibioticguardian.com was visited 11,363 times, 4,682 pledges were received and 2,333 individuals participated in Twitter's social media with 5,737 tweets posted using the #AntibioticGuardian hashtag. Table 6.1 shows the number of visits the [Antibiotic awareness resources webpage](#) has had over the last 4 years.

Table 6.1: Antibiotic awareness resources webpage - Number of visits, 2014-2017

Year	Number of visits
2014	16, 347
2015	25, 933
2016	21, 832
2017	20, 761

A key activity for WAAW 2017 was to increase the number of organisations that registered planned activities by 10%. A new organisation page was developed and

launched on AG website.⁶¹ In 2016, 90 organisations and 239 community pharmacies registered planned activities for WAAW with PHE. In 2017, 149 organisations registered planned activities, leading to a 166% increase in registrations over the prior year. There was no focus on Community pharmacy in 2017 since this was taken forward via the Royal Pharmaceutical Society. In addition to the registered organisations - internet searches on social media highlighted an additional 98 organisations participated in WAAW. Furthermore, letters (signed by PHE and England's Chief Professional Officers) were sent to encourage organisations to register to promote Antibiotic awareness during WAAW.

Delivery of antimicrobial stewardship workshops and training events for healthcare professionals and students

TARGET workshops

TARGET delivered 2 workshops to nurse prescribers in Gloucestershire CCG in spring 2018. The first workshop was the TARGET antimicrobial stewardship (AMS) workshop; primary care clinicians can disseminate and deliver this workshop to their practices. The second workshop was the TARGET train the trainer workshop which aimed to provide nurses with local CCG and practice specific prescribing data to increase their knowledge, confidence and skills to facilitate their own TARGET AMS workshop in their general practice. Overall the evaluation feedback was very positive and from this pilot training TARGET have developed a training package which can be rolled out to other CCG's and is available on the TARGET website. The TARGET toolkit is promoted by 99% of CCGs and all TARGET training resources are freely available on the website.⁶²

Online training sessions, shared learning and case studies

Five online training sessions were delivered during 2017/18 and have been made available through the Antibiotic Guardian (AG) website⁶³ which included the following:

- AMR CQUIN 2018/19
- AMS and self-care advice for community pharmacy
- AMR indicators on PHE Fingertips
- appropriateness of antibiotic therapy
- tackling AMR Community Pharmacy

⁶¹ Antibiotic Guardian Organisations 2018. Available online from: www.antibioticguardian.com/organisations/

⁶² Royal College of General Practitioners. TARGET Antibiotic Toolkit. 2018. Available online from: www.rcgp.org.uk/clinical-and-research/resources/toolkits/target-antibiotic-toolkit.aspx

⁶³ Antibiotic Guardian Resources – Webinars. 2018. Available online from: www.antibioticguardian.com/webinars

In addition, a shared learning portal is now available on the AG website which includes projects shortlisted for the Antibiotic Guardian awards following peer review.⁶⁴

Healthcare students national AMR conference

The UK's first multidisciplinary conference for students on AMR: *Antimicrobial Resistance Conference: Advocating a Behaviour Change* was held on 18th November 2017 (EAAD). The Conference promoted collaboration amongst all health-related fields through a One Health approach, providing students and young professionals an opportunity to participate in AMR-related talks and workshops. Over 200 students attended the conference. The presentations from the conference are available online.⁶⁵ A questionnaire was distributed to delegates before and after the conference. The results were analysed to identify any gains in knowledge towards AMR. We are currently analysing this data in preparation to submit for peer review publication. An abstract is presented in the research chapter. In addition, this data will be used to tailor the conference next year to cover the areas where students demonstrated a lack of knowledge both pre- and post- conference.

e-Bug activities

e-Bug is an innovative educational resource for children and young people (4-18) on hygiene, spread of infection and antibiotics. Established in 2006, e-Bug utilises a multidisciplinary strategy for effective and synchronous education of young people across England and Europe. A key component of this strategy is the development of effective and highly relevant resources that include an interactive and multi-lingual website (www.e-bug.eu) and a comprehensive collection of teaching packs for use in schools and the community. The e-Bug resources were endorsed by NICE in 2016 and are currently available in over 30 different languages, being implemented in 26 countries globally; all material present in the e-Bug resources is linked to the national curriculum.

Website and digital media

The e-Bug website is an interactive educational resource that provides lesson plans, activities, games and digital media on hygiene, infections and antibiotics. Established in 2009, the website has undergone several developments and has been translated into 26 different languages. From September 2017 to July 2018, the top 5 country users

⁶⁴ Antibiotic Guardian Shared Learning resources 2018. Available online from: www.antibioticguardian.com/sharedlearning

⁶⁵ Antibiotic Guardian First National Students AMR Conference 2017. Available online from: antibioticguardian.com/Meetings/students-amr-conference-2017/

were: UK (27% of users); France (10.5%); Spain (9.3%); United States (7.3%); and Greece (4.5%) (Table 6.2).

Table 6.2: Top countries accessing e-Bug website (September 2017 – July 2018)

Country	Users	% Users
United Kingdom	18,989	27.0
France	7,410	10.5
Spain	6,556	9.3
United States	5,111	7.2
Greece	3,099	4.4
Belgium	2,130	3.0
Denmark	1,952	2.8
India	1,666	2.4
Australia	1,330	1.9
Italy	1,282	1.8
Germany	1,103	1.6
Hungary	1,020	1.4
Other countries		26.7

In this period, the website gained 98,041 sessions and 763,048 page views. In addition, 84.1% of users (69,953) were new visitors to the website. Details on individual page view each Autumn are outlined in Table 6.3.

Table 6.3: e-Bug website analytics (2016-2018)

Resource	Page views 2016		Page views 2017		Goals for 2018	
	1 Sep 2016 - 31 Dec 2016	Nov 2016	1 Sep 2017 - 31 Dec 2017	Nov 2017	1 Sep 2018 - 31 Dec 2018	Nov 2018
e-Bug website (all pages)	331,436	100,721	348,602	92,703	370,000	110,000
e-Bug student games (all pages with 'games' in url)	79,409	24,509	81,692	22,152	90,000	25,000
e-Bug antibiotic animation (you tube video views)	46,282	12,743	55,800	15,300	60,000	20,000
Beat the Bugs homepage (webpage)	1,066	493	962	324	1500	500
Antibiotic peer education lesson (webpage)	267	101	258	79	300	120

e-Bug website discovery

To align with modern technologies such as mobile devices and touchscreens, the e-Bug website will undergo re-development. The re-development will be informed by a discovery phase, starting September 2018. For the Discovery Phase, user research will be performed with students, educators, AMR researchers and stakeholders, public health professionals and healthcare workers. e-Bug envisage that the new website application will align with the PHE and UK AMR Five Year Strategy.

The key aims of the discovery phase include:

- to understand if there is a user need for educational activities to teach young people in schools and community settings, and the general public, in an age appropriate manner about microbes, hygiene, antibiotics and vaccinations
- to understand what educational materials or tools are needed for schools and the home setting, to teach young people in an age appropriate manner about microbes, hygiene, antibiotics and vaccinations
- to understand how educational activities can be successfully presented and delivered to young people and educators in the school and community setting
- to determine the different educator tools, websites and other resources that are currently available to successfully improve knowledge and behaviour around microbes, hygiene, antibiotics and vaccination

Beat the Bugs

Beat the Bugs is a community resource developed by e-Bug that educates on hygiene, infection prevention and control and self-care. The resource was piloted with adults with learning disabilities and young mothers in 2016/17 with results indicating effective learning and behavioural change. e-Bug have now collaborated with the Open University and have recruited a PhD student to formally evaluate Beat the Bugs in community settings, namely with adults with learning disabilities. The PhD project begins in October 2018 and will be completed by October 2021. The expected outcomes of the project are development of a novel method to evaluate community educational resources on infection prevention and control and AMR, and data demonstrating the effectiveness of Beat the Bugs in this specific community setting.

Peer education

e-Bug have developed a new peer education antibiotics lesson to promote antimicrobial stewardship in teenagers and young adults (ages 16-18) in collaboration with Manchester University and Cardiff University. A multi-level peer education approach was investigated involving university students and high school students. Effectiveness of the lesson was assessed through measurement of knowledge, gain on prudent

antibiotic use and measurement of antibiotic consumption. Data analysis is currently on-going.

Train the Trainer

A key component of the e-Bug project is the organisation of Train the Trainer workshops that train educators and public health professionals on the e-Bug resources and materials. The e-Bug Train the Trainer initiative was launched in 2016 and is comprised of 2 key models: 1) Training of educators and professionals in-house and; 2) Collaboration with local authorities for widespread dissemination of e-Bug in regional schools and educational settings. Progress and results from the 2 models will now be discussed.

In-house training

Since its launch in 2016/17, e-Bug has trained 123 individuals as either e-Bug approved educators (school) or Beat the Bugs (community) trainers (Table 6.4). In addition, in 2018 e-Bug piloted use of YouTube training videos to deliver online training for Liverpool Council and for knowledge exchange with European and international partners.

Table 6.4 Professional status of individuals who received in-house e-Bug training 2016-2018

Profession	Total trained
Public Health Nurse	10
Health and Wellbeing Assistant	15
Public Health Community Health Trainer	7
Healthy Schools Lead	30
Teacher or Teaching Assistant	11
School Nurse	4
Family Practitioner	7
Dental care professional	1
Public Health Practitioner	3
Other or undisclosed	35

Local authority collaborations

A new model being investigated is collaboration with local authorities for widespread implementation of e-Bug in different regions. This model was piloted with South Gloucestershire council in 2017 where 4 primary schools were trained on e-Bug activities before implementing them in classrooms. Public health practitioners and

health school leads from South Gloucestershire effectively engaged schools and aligned the project to the Healthy Schools Silver Award. To assess effectiveness of e-Bug activities, pre- and post-knowledge questionnaires were completed by students; educators also completed a feedback survey and commented on the real-time application of the resources. Data are currently being analysed by South Gloucestershire council alongside evaluation of absenteeism rates in intervention schools.

In 2017 e-Bug also collaborated with Public Health Wales (PHW) to coordinate and disseminate e-Bug in 22 local authority regions. In Wales, e-Bug was disseminated via the Welsh Network of Healthy Schools Schemes (WNHSS) during the period 1st April 2017 to 31st March 2018. This involved training 25 healthy school leads and science coordinators. The total fund from Welsh Government under the AMR project delivery line in 2017-18 was £37,000. During the financial year, £1500 was allocated to each WNHSS on demonstrating evidence that they had plans to deliver education sessions in line with the training they had received from the PHW e-Bug team in December 2016. This included purchasing e-Bug resources and delivering training via a variety of self-reported methods at certain points throughout the year. No formal evaluation was completed by PHW, however e-Bug was implemented in 91% local authority areas. e-Bug are currently working with Public Health Agency, Northern Ireland to implement e-Bug in schools across regions. The e-Bug Train the Trainer video is available online.⁶⁶

Public engagement events

In 2017/18 e-Bug carried out a wide range of public engagement activities to engage young people on AMR and infection prevention and control.

In March 2018, e-Bug attended the Big Bang Fair in Birmingham during British Science Week (March 12-19) and delivered 3 educational activities on microbes, respiratory hygiene and a new activity on the gut microbiome. At the event, approximately 1000 school students participated in the activities. To further engage students attending the event, an e-Bug Snapchat Geofilter was designed in collaboration with NICE and mapped to the event location. All attendees visiting the event could use the filter on their own mobile devices via Snapchat. The geofilter gained 9.1k views and was used 133 times in 3 days (Figure 6.1).

In collaboration with AG and Girlguiding Gloucestershire, e-Bug is currently developing an educational pack for Brownies and Guides. The Brownie pack is based on the Scouts educational pack developed and tested in Leicester and Lancashire.

⁶⁶ e-Bug Science Outreach Video 2018 Available online from: www.youtube.com/watch?v=4QRDZ5uQoBI

e-Bug activities for WAAW

For WAAW 2017, e-Bug employed a multidisciplinary strategy that involved a social media campaign and public engagement event. The social media campaign was targeted at educators and science communicators and included informative graphics on antibiotic resistance (Figure 6.1).

The use of social media around e-Bug led to 62,000 Twitter impressions and 120 new followers during WAAW. Working closely with NICE, a general packet radio service (GPRS)-targeted Snapchat filter was also organised, increasing staying value.

An interactive exhibition was also installed at 'We the Curious' museum in Bristol. The drop-in exhibit included a new activity that educates young people on the effect of antibiotic treatment on the gut microbiome. 590 visitors to the museum participated in the activity and exhibition. In addition, in collaboration with NICE, an AMR-themed GPRS-targeted Snapchat filter was used on EAAD at We the Curious science museum. Visitors attending the museum that date could use the filter on their own devices via the Snapchat application. The Snapchat filter was used 24 times and achieved 368 swipes and 563 views.



Figure 6.1: e-Bug social media tools

- A) Snapchat Geofilter designed for Big Bang Fair, Birmingham (9.1k views);
- B) Snapchat Geofilter designed for EAAD event at We the Curious (563 views);
- C) Social media graphic utilised on Facebook and Twitter during WAAW.

e-Bug stakeholder engagement

NICE

In 2017/18, e-Bug formed an effective collaboration with NICE for the development of digital content for social media platform, Snapchat. NICE use Snapchat as a promotional tool at events and during campaigns. The NICE Snapchat account was used by e-Bug to publish Snapchat geofilters during WAAW (We the Curious museum event) and during British Science Week 2018 (e-Bug exhibition at Big Bang Fair Birmingham), as reported in the previous section.

Institute for Research in Schools

The Institute for Research in Schools (IRIS) work with universities to operate research projects in schools across England. Swab and Send is a citizen science research project, operated by Dr Adam Roberts, Liverpool School of Tropical Medicine that aims to identify and discover new antimicrobials from environmental isolates. IRIS and Dr Adam Roberts are currently piloting Swab and Send as a school-led research project involving both primary and secondary students. e-Bug collaborated with this group and provided educational materials on antibiotics and microbes to support the pilot project in Sheffield in 2018. 12 primary schools participated in the pilot project.

Nesta

e-Bug have partnered with e-Bug for the 10 year anniversary event in 2019. The event is being held at the Wellcome Collection in January to celebrate the achievements of e-Bug and highlight current research on AMR education.

Safeconsume

e-Bug is currently involved in a EU Horizon 2020 multi-consortium project, Safeconsume¹. The project aims to reduce the health burden associated with foodborne illness through education, communication and food safety policy. In addition, the project also aims to communicate risks associated with foodborne illness such as increased transmission of antibiotic resistant bacteria. The project involves 13 countries and is comprised of 9 work packages. e-Bug is leading work package 6 (WP6) that aims to develop new educational materials on food hygiene and food safety for teenagers (11-18 year olds). In 2017/18, e-Bug led a needs assessment in collaboration with research groups in France, Portugal and Hungary, to inform the development of educational materials. Student and educator interviews were performed to assess knowledge, attitudes and beliefs around food hygiene and food safety education. Initial findings in England have demonstrated that students are not concerned about foodborne illness and do not recognise the home as a risky environment for food poisoning.

Health Equity Assessment Tool (HEAT) assessing AMR activities

A review was conducted to assess health inequalities relating to public facing AMR activities. An internal PHE HEAT assessment tool was used, that shared similar characteristics to the WHO version; it included the 5 stages of the assessment (Prepare, Assess, Refine, Apply and Review). A focus on using the protected characteristics of the Equality Act 2010 during the assessments was adopted. The AMR activities assessed are in Table 6.5; a focus on using the protected characteristics of the Equality Act 2010 during the assessments was adopted therefore, the protected characteristics are listed beneath the table.

Table 6.5: Description of AMR activities

Campaign	Description
eBug	Web based platform used to improve the management of infection in the community and primary care via research guidance, resources and education. This is done by increasing understanding of infections, how they spread, self-care and safety netting. The aim is to reduce infections in the hard-to-reach, less educated groups.
TARGET antibiotics toolkit	Paper based platform used to improve the management of infection in the community and primary care via research guidance, resources and education.
Antibiotic Guardian	Web based platform used to increase knowledge and engagement on antimicrobial stewardship (AMS) along with changing behaviour for healthcare professionals and members of the public.
Keep Antibiotics Working	Mass media campaign which reduces the general public's expectation for antibiotics and raises awareness of the risks of antibiotic resistance. The campaign also supports healthcare professionals' to reduce prescribing.

* These protected characteristics are: age; sex; race; religion or belief; disability; sexual orientation; gender reassignment; pregnancy and maternity; marriage and civil partnership.

The assessment showed some notable highlights that demonstrate equality and/or diversity within individual activities:

- e-Bug website translated into over 30 languages and used worldwide
- beat the Bugs e-Bug community hygiene course with wide range of resources to suit all abilities including hard to reach groups such as those with learning difficulties
- ‘Keep Antibiotics Working’ materials were distributed to a wide range of partners such as GPs and prisons aiming to reach those from lower socio-economic backgrounds
- ‘Keep Antibiotics Working’ advertising features red and white pills that have no gender or racial bias
- AG pledges from 129 countries across the world and translated into 5 languages

There are opportunities to improve equity and diversity within specific groups across AMR campaigns for example by tailoring promotion materials to hearing and visually impaired individuals and continued use of a paper based system in order to capture a wider audience (eg the elderly). Awareness campaigns, such as WAAW and EAAD, continue to be important opportunities to respond to any recommendations and increase overall reach. It was found that there is currently a lack of data to support which population groups use most antibiotics inappropriately. Further research would help support a more targeted approach to each activity. The findings from this project will be presented at the 2018 Antibiotic Guardian conference and submitted for peer review.

Development of consensus-based national antimicrobial stewardship competencies for UK undergraduate healthcare professional education

Current undergraduate healthcare professional students in the UK receive limited knowledge about antibiotics during their training, and perhaps more importantly, they do not receive any training in communication and teamwork surrounding the management of antibiotics^{67,68}. For such reasons, a collaboration of researchers and healthcare workers from several universities and health centres across the UK led by Professor Molly Courtenay, Cardiff University developed a competency framework for use by UK undergraduate healthcare professional students, which supports the optimal use of antibiotics.

⁶⁷ Castro-Sánchez, E *et al.* Mapping Antimicrobial Stewardship in Undergraduate Medical, Dental, Pharmacy, Nursing and Veterinary Education in the United Kingdom. *PLoS ONE* 2016,11(2): e0150056. doi:10.1371/journal.pone.0150056

⁶⁸ Dyar O.J *et al.* Assessing the knowledge, attitudes and behaviors of human and animal health students towards antibiotic use and resistance: A pilot cross-sectional study in the UK. *Antibiotics*. 2018;7:10 doi: 10.3390/antibiotics7010010

The project, which was conducted between October and December 2017, involved selecting a group of expert lecturers, researchers, practitioners and policy-makers from across the UK, and inviting them to participate in several rounds of a voting process ('Delphi'), where an initial list of competencies identified from previous research was gradually refined until a definite set was agreed upon by all participants.

The competency framework was published in the *Journal of Hospital Infection*⁶⁹ in July 2018 and has been endorsed by scientific and professional societies.⁷⁰ It supports the National Institute for Health and Care Excellence (NICE) guidance and recommendations⁷¹ and quality statements⁷² and is aligned to the UK national antimicrobial prescribing and stewardship competences developed by PHE in 2013.⁷³ It is aimed primarily at students to identify gaps in their knowledge, and secondarily at educators involved in undergraduate healthcare professional education to ensure AMS competencies are covered in curricula.

The framework comprises of 6 domains including:

- domain 1: Infection prevention and control
- domain 2: Antimicrobials and antimicrobial resistance
- domain 3: The diagnosis of infection and the use of antibiotics
- domain 4: Antimicrobial prescribing Practice
- domain 5: Person centred care
- domain 6: Interprofessional collaborative practice

Each Domain has an overarching competency statement (each statement represents the knowledge, skills, attitudes, and values that shape the judgements essential for AMS), and 51 individual descriptors, designed to reflect the level of experience of the learner and type of practice setting, therefore enabling educators to easily incorporate the competencies onto any existing curricula or develop suitable resources for learners.

Future research will investigate whether experts and students around the world identify a similar set of competencies and explore any differences. Additionally, the impact of the competencies and resources developed on prescribing practice will be evaluated.

⁶⁹ Courtenay M. *et al.* Development of consensus-based national antimicrobial stewardship competencies for UK undergraduate healthcare professional education. *Journal of Hosp Infection*. 2018; 245:256
doi.org/10.1016/j.jhin.2018.06.022

⁷⁰ Cardiff University School of Healthcare Sciences Research. Being antibiotic aware 2018. Available online from: www.cardiff.ac.uk/healthcare-sciences/research/publications/being-antibiotic-aware

⁷¹ NICE (2015). Antimicrobial stewardship: systems and processes for effective antimicrobial medicines use. Available online from: www.nice.org.uk/guidance/ng15/chapter/2-Implementation-getting-started

⁷² NICE (2016) Antimicrobial stewardship. Available online from: www.nice.org.uk/guidance/qs121

⁷³ Department of Health and Social Care. Antimicrobial prescribing and stewardship competencies. 2013. Available online from: www.gov.uk/government/publications/antimicrobial-prescribing-and-stewardship-competencies

AMR Training Resources

During 2017/18, Health Education England (HEE) launched a guide on AMR training resources⁷⁴ to promote available learning on the management of infective states, infection prevention and control, antimicrobial resistance and antimicrobial stewardship by:

- signposting educational materials available to health workers and students
- providing a centralised resource portal to educators on supporting learners
- supporting commissioning, regulatory and quality improvement teams (including infection prevention and control and antimicrobial management teams) by highlighting available educational resources to improve practice
- encouraging learners to access available learning sessions to support their learning needs
- highlighting learning sessions that can be embedded within clinical training pathways

HEE also committed to work with stakeholders to explore the factors that help or hinder education about antimicrobial resistance and to identify good practice materials for promotion. Those that train healthcare workers were asked on what works well in an educational environment, what the challenges are and how HEE might support the education of prudent, responsible use of antimicrobials. Stakeholders were also consulted on the feasibility of developing a system wide formative assessment. The themes from these reports will inform the future direction of HEE's antimicrobial resistance programme.^{75,76}

Future action

e-Bug is currently working with Fun Kids Learn children's radio station to develop an audio and video series on infections, antibiotics and hygiene. The series will deliver important messages around AMR, infection prevention and control (IPC) and hygiene. The series is estimated to launch during WAAW 2018. In January 2019, e-Bug will organise a 2 day international conference focused on effective strategies and methodologies for educating young people on AMR and IPC.

⁷⁴ Health Education England. Antimicrobial resistance: A training resources guide. 2017. Available online from: www.hee.nhs.uk/sites/default/files/documents/Antimicrobial%20resistance%20-%20A%20training%20resources%20guide.pdf

⁷⁵ Health Education England. Tackling antimicrobial resistance: educational priorities. 2018. Available online from: www.hee.nhs.uk/sites/default/files/documents/Tackling%20antimicrobial%20resistance%20-%20educational%20priorities%20report.pdf

⁷⁶ Health Education England. Tackling antimicrobial resistance: the role of formative assessments. 2018. www.hee.nhs.uk/sites/default/files/documents/Tackling%20antimicrobial%20resistance%20the%20role%20of%20formative%20assessments.pdf

e-Bug will perform a needs assessment with students in Gloucestershire to inform development of new resources on the microbiome for secondary school students. e-Bug will launch an AMR Z Card © for teenagers in November 2018 in collaboration with Antibiotic Guardian.

WAAW 2018 will focus on further embedding of resources developed during 2017 including Keep Antibiotics Working, Antibiotic Guardian, e-Bug and TARGET resources.

Plans for 2018 WAAW will include letters from Chief Professional Officers and promotion of organisational registration and AG, social media activities including blogs and social media messages, webinars with case studies from those that have led impactful local campaigns.

All new activities will consider recommendations from assessment of PHE AMR public facing activities using the Health Equities Assessment Tool (HEAT).

e-Bug will run an activity day on AMR and hygiene for Brownies across Gloucestershire. The activity day will be comprised of e-Bug educational games and activities on AMR.

e-Bug will also organise another social media campaign comprised of engaging graphics targeted at educators and public health professionals the outputs (including presentations as well as shared learning) 2018 Antibiotic Guardian Conference and Awards will be published on the Antibiotic Guardian website by November 2018.

The TARGET logo and resources will be rebranded to in line with the Keep Antibiotics Working campaign. The resources will keep their TARGET content but have a new look in line with the colour schemes of Keep Antibiotics Working to ensure there is greater brand recognition and continuity nationally. As part of the Keep Antibiotics Working campaign the TARGET resources will be promoted nationally and locally across England.

TARGET aim to raise awareness of TARGET training to CCGs. The TARGET toolkit is promoted by 99% of CCG's; therefore during WAAW we will be communicating with CCG's to promote the TARGET AMS workshops and TARGET train the trainer workshops to actively encourage CCG's and general practices to run their own TARGET workshops. All TARGET training resources are freely available on the website www.rcgp.org.uk/TARGETantibiotics The TARGET training pilot with nurse prescribers conducted in Gloucestershire CCG in 2018 was very successful.

TARGET webinars will be developed into e-Learning on the Virtual Learning Environment. TARGET is collaborating with BSAC to launch TARGET webinars on the Virtual Learning environment to be accessible in an e-Learning format. TARGET will be promoting the e-Learning modules during WAAW at conferences, exhibitions and events as well as through the TARGET stakeholder newsletters and twitter channels.

Publish findings from the evaluation of AMS initiatives across Medicines Management teams. The 'Local implementation of national AMS initiatives across Medicines Management teams study' findings aim to be published around WAAW and raise further awareness of national AMS initiatives and increase awareness of the TARGET Toolkit to primary care clinicians and commissioners.

TARGET future research includes the development of a UTI leaflet in the pharmacy setting. The TARGET Treating Your Infection leaflets on UTI for use in general practice and for older adults in general practice and in care homes have been available on the TARGET website since November 2016 and June 2018, respectively. Our future research will include a service evaluation of the Treating Your Infection UTI leaflets in a pharmacy setting to understand how pharmacists might use the leaflets, how they currently communicate with patients suffering with UTI symptoms and what modifications may be required to the leaflets to be able to implement their use in the pharmacy setting.

Other TARGET research includes a feasibility study of the use of Resources, Education and Enhanced Feedback (REEF) to reduce *E. coli* UTIs and bacteraemia in the elderly. The TARGET team will be evaluating the effect of the UTI resources with a TARGET UTI workshop quantitatively and qualitatively.

7: Stakeholder engagement

British Dental Association

The British Dental Association (BDA) has continued its national and international work to lead antimicrobial stewardship efforts in dentistry, working with a range of high-level partners to support the One Health agenda. Within the UK, the BDA has been represented on the Department of Health and Social Care's Human Health Antimicrobial Resistance (AMR) Stakeholder Group, which is developing the new UK 5 year strategy and an underpinning 20 year vision to address AMR, and at a Parliamentary round table discussion on diagnostics. BDA representatives also act as advisers to the NICE committee developing guidelines on the management of common infections. The BDA has continued to lobby for reform of the dental contract to provide adequately funded time for the treatment of dental emergencies without inappropriate recourse to antibiotics.

The BDA works through the Council of European Dentists to influence European policy on AMR, and is also active on a global level via the International Dental Federation (FDI).

British Society for Antimicrobial Chemotherapy

BSAC is British by name and global by action, supporting healthcare communities internationally through a range of activities including:

- UK Resistance Surveillance Programme, longest running sentinel surveillance scheme (respiratory and bacteraemia) in Europe offering a biobank of over 60,000 isolates to the research community
- hosting a national susceptibility testing centre at Cardiff and is actively supporting harmonisation of testing methodologies with the EUCAST method
- virtual learning platform offering open access education across the globe including:
- massive Open Online Course on AMS, accessed by almost 50,000 learners from 131 countries, with translations in Mandarin, Russian, Spanish and Brazilian Portuguese
- e-Learning courses on Point Prevalence Surveys, Gram-negative infections, TARGET prescribing for GPs, and courses on outpatient parenteral antimicrobial therapy (OPAT), facilitating uptake of rapid diagnostics and IV to oral switch are under development

- e-Book – Antimicrobial Stewardship: From Principles to Practice⁷⁷
- public education through high profile activities such as The Mould that Changed the World musical,⁷⁸ educating school age children through a high school musical
- publication of evidence-based guidance and guidelines.
- collaborative working with UK and international organisations working strategically and politically by acting as Secretariat to the All Party Parliamentary Group on Antibiotics, continuing to work on the Antibiotic Guardian Campaign which the Society originally co-developed and underwrote, maintaining active membership of the Learned Society Partnership on AMR, active founder member of the Conscience for Antimicrobial Resistance Alliance, established to monitor implementation of the United Nations Declaration on AMR and as partner on the EU Innovative Medicines Initiative DRIVE-AB Project

In summary BSAC is committed to supporting ESPAUR and implementation of the UK and international strategies on antimicrobial resistance.

Care Quality Commission

The Care Quality Commission (CQC) 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 the CQC have updated the information and training available to our inspectors across all health and social care services about antimicrobial stewardship. This has included additional prompts and questions on inspection visits about the recording of the indication for antimicrobials, the timing of dose administration, treatment of sepsis and identification of the deteriorating patient. The next phase of NHS Trust inspections is well underway, underpinned by the strengthened approach to antimicrobial stewardship in the annual inspection of the 'Well Led' key question: [The five key questions we ask | Care Quality Commission](#).

Following inspections of on-line primary care providers, the CQC published a report which highlighted concerns about the prescribing of antibiotics in this sector.⁷⁹ The CQC continues to support PHE and NICE with the development of guidance that can be applied across all service types.

⁷⁷ bsac.org.uk/antimicrobial-stewardship-from-principles-to-practice-e-book/

⁷⁸ antibiotic-action.com/the-mould-that-changed-the-world-musical-education-through-innovation/

⁷⁹ www.cqc.org.uk/publications/major-report/state-care-independent-online-primary-health-services

The Faculty of General Dental Practice UK

The Faculty of General Dental Practice UK (FGDP(UK)) has continued to emphasise the importance of appropriate antimicrobial prescribing in dentistry, and to raise awareness of AMR and of the need for antimicrobial stewardship (AMS) to reduce drug-resistant infections.

Over the last year, FGDP(UK) has continued to promote use of the dental AMS toolkit by its members and the wider profession - **in particular the Antimicrobial Prescribing Self-Audit Tool** – as well as the **National Institute for Health and Care Excellence (NICE) Quality Standard on Antimicrobial Stewardship**. It has also continued to raise awareness of AMR and dental AMS through its dedicated **Antimicrobial Prescribing webpage**, which co-hosts the toolkit, articulates the scale, nature and relevance of the problem of AMR to dentistry, and provides links to the leading text on antibiotic prescribing in dentistry, FGDP(UK)'s **Antimicrobial Prescribing for General Dental Practitioners**.

'Antimicrobial Prescribing for General Dental Practitioners' continues to be made available to dentists in hard copy, as an e-book and freely on the FGDP(UK) website, where it has been viewed over 100,000 times since 2015. Work continues with the Faculty of Dental Surgery (FDS) to extend the scope of the guidance to include secondary care prescribing.

Together with the Association of Clinical Oral Microbiologists, FGDP(UK) organised a social media **Thunderclap** for EAAD 2017, which asked dental professionals to take the pledge: "to reduce dental infections and the need for antibiotics in children, I will promote prevention to families". The fifth annual dental collaboration of its kind, it was again supported by Public Health England, the BDA, the British Society for Antimicrobial Chemotherapy, and Antibiotic Action, and new support was gained from Health Protection Scotland and the Welsh Government. The initiative was widely covered in dental media and reached 89,000 people.

FGDP(UK)'s AMR Lead, Dr Nick Palmer - a leading authority on dental antibiotic prescribing and author of the Faculty's guidelines – represented the Faculty at meetings of the ESPAUR Dental Sub-group and ESPAUR Oversight group, and has been **appointed dental adviser** to NICE for its development of a suite of antimicrobial prescribing guidelines for the management of common infections. Dr Palmer has also contributed to the development by the British Association of Oral Surgeons of new **Antimicrobial Stewardship e-Learning Modules**, which are relevant for all general dental practitioners, available free of charge, provide 3 hours' verified CPD, and which the Faculty is promoting to its members and on its website.

FGDP(UK) gave **detailed feedback** to the Scottish Dental Clinical Effectiveness Programme for its development of advice for dentists on implementing the **NICE guideline on antimicrobial prophylaxis against infective endocarditis** in their practice. FGDP(UK) is a formal supporter of the finalised guidance, which it is promoting to its members and on its website.

The Faculty Dean also participated in a roundtable meeting on AMR convened by the Chief Medical and Veterinary Officers for Northern Ireland, and FGDP(UK) contributed to a Health Education England **survey of educational materials on antimicrobial resistance**.

National Institute for Health and Care Excellence (NICE)

NICE continues to work with PHE to develop a series of antimicrobial prescribing guidelines (APGs) on managing common infections to encourage the responsible use of antibiotics, building on the existing PHE guidance for primary care. The guidelines offer evidence-based guidance for primary and secondary care and provide recommendations for appropriate antimicrobial use in the context of tackling antimicrobial resistance. A Public Health Advisory Committee is producing these guidelines and they are jointly badged by both NICE and PHE and the first 3 topics on acute sinusitis, acute sore throat and acute otitis media published in 2017/18 with work on further topics underway. Presentation of the APG content includes a visual summary of the recommendations, a guideline, an evidence review and a summary document that includes content from all APGs alongside PHE's guidance for primary care. The British National Formulary (BNF) will incorporate these new guidelines into their treatment summaries on antimicrobials as they are produced and subsequently updated.

To support the appropriate use and stewardship of new antimicrobials at the point of launch, NICE is also developing evidence summaries for antimicrobial prescribing. The first advice on Ceftazidime-avibactam (Zavicefta) was published in November 2017.

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 antimicrobial resistance. 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.

NICE is also collaborating with DH colleagues on a research project exploring the concept of undertaking Technology Appraisals on new antimicrobials offering high potential to address unmet need. Within this exploration, the value, if any, that

Technology Appraisals can contribute to the appropriate use and stewardship of new antimicrobials will be considered. The research is being delivered by the DH Economic Evaluation Policy Research Unit (EEPRU) at the University of York. The DH is exploring new payment methods that delink payments to companies from the volumes of new antimicrobials used. The EEPRU project also explores how NICE Technology Appraisal could inform such delinked payment models, if such a scheme were implemented.

NICE also produce Medtech Innovation Briefings (MIBs) on new medical devices and diagnostics. The briefings will help 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, particularly those that offer incremental benefits compared to existing technologies, which is likely to be the majority of new diagnostic technologies that relate to AMS. Other NICE outputs (such as NICE guidelines, Diagnostics guidance, or Technology Appraisal) can be reserved for the few technologies that are transformative, have a high potential to address an unmet need, or for medicines that have a new mode of action that is less susceptible to development of resistance.

NICE's Diagnostics Assessment Programme produces guidance on the use of innovative diagnostic technologies, including those that are relevant to the AMR strategy.

Guidance has been published on:

- procalcitonin testing for diagnosing and monitoring sepsis
- tests for rapidly identifying bloodstream bacteria and fungi
- integrated multiplex PCR tests for identifying gastrointestinal pathogens in people with suspected gastroenteritis
- diagnostics guidance is also being developed on 'rapid tests for Group A streptococcal infections in people with a sore throat'

The NICE Key Therapeutic Topics work includes Antimicrobial Stewardship as a topic. Prescribing data from the comparators developed by NHS Digital are also included to allow organisations to benchmark and assess the degree of variation in key areas of antimicrobial prescribing.

Royal Pharmaceutical Society

The Royal Pharmaceutical Society (RPS) is committed to continue supporting ESPAUR as part of the UK cross-government AMR Strategy. Their Chief Executive, President, Executive Team and National Boards for England, Scotland and Wales support this vital work by highlighting the important contribution that pharmacy can make to AMS.

Members and the wider workforce continue to be supported by RPS ensuring that AMS is included in all relevant RPS standards, guidance and other resources to support practice. In 2017, the RPS hosted a GB-wide campaign with messaging to all healthcare professionals and the general public, about the important role of pharmacy in AMS. New AMS and handwashing guides, and a policy document - The Pharmacy Contribution to Antimicrobial Stewardship⁸⁰ are also available.

Following a successful AMS campaign, RPS continues to develop resources and support regional and local events to help pharmacists make a valuable contribution to AMS in all settings of practice. In 2019 RPS will be hosting the Science and Research Summit, with Dame Sally Davies opening the day and with a session of invited speakers dedicated to AMS.

The Science and Research Board and Antimicrobial Expert Advisory Group are working more closely together to take forward issues around AMS - as highlighted in the recommendations in the New Medicines, Better Medicines, Better Use of Medicines document. Both continue to provide comment and input across a wide range of work streams relating to antimicrobial utilisation and resistance, including responses to consultations on AMS and management of infection.

⁸⁰ www.rpharms.com/Portals/0/RPS%20document%20library/Open%20access/Policy/AMS%20policy.pdf

Acknowledgements

Chapter 1: Introduction

Susan Hopkins, Alan Johnson

Chapter 2: Antibiotic resistance

Alan Johnson, Rebecca Guy, Katie Hopkins, Rachel Freeman, Berit Muller-Pebody, Dean Ironmonger, Richard Puleston, Angela Kearns, Susan Hopkins.

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Chapter 3: Antimicrobial consumption

Amelia Au-Yeung, Emma Budd, Berit Muller-Pebody, Susan Hopkins, Elizabeth Beech, Emma Cramp, Diane Ashiru-Oredope, Cliodna McNulty, Dean Ironmonger.

Chapter 4: Antifungal resistance, prescribing and stewardship

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Chapter 5: Antimicrobial stewardship

Diane Ashiru-Oredope, Charlotte Eley, Carla Brown, Anne Doble, Graeme Hood, Rachel Freeman, Kieran Hand, Natalie Gold, Tracey Thornley, Anna Sallis, Ayoub Saei, Eno Umoh, Donna Lecky, Chaamala Klinger, Jasmin Islam, Emily Cooper, Leah Jones and Rosie Allison, Clodna McNulty, Susan Hopkins.

Chapter 6: Professional education & training and public engagement

Diane Ashiru-Oredope, Carla Brown, Charlotte Eley, Eleanor Walsh, Malcolm Fawcett, Graeme Hood, Eno Umoh, Molly Courtenay, Mohammed Sadak, Susan Hopkins.

Annex: Research

Research in antibiotic resistance

Epidemiology of carbapenemase-producing bacteria in England, 2016–2018: results from the national enhanced surveillance system

Rachel Freeman, Dean Ironmonger, Katie L. Hopkins, Richard Puleston, Berit Muller-Pebody, Russell Hope, Susan Hopkins, Alan Johnson, Neil Woodford, Isabel Oliver

Background: In May 2015, following an increase in reported cases, Public Health England launched an enhanced surveillance system to electronically capture data on patients infected/colonised with carbapenemase-producing Gram-negative bacteria. Our study aimed to identify high risk groups to inform infection prevention and control interventions.

Methods: Cases were defined as patients with a carbapenemase-producing organism isolated from a screening or clinical specimen in England between April 2016–March 2018. Cases were de-duplicated by patient, bacterial species, specimen site and resistance mechanism for each year of surveillance.

Results: There were 3953 cases reported via the system. 1786 (45.2%) patients were female and 2163 (54.7%) were male. The median age of patients was 69.5 years. Most cases were hospital inpatients (3436, 86.9%). Enhanced fields including foreign travel and clinical specialty were poorly completed (14% and 21%, respectively). The majority of organisms reported were from screening specimens (3151, 79.7%), with 798 clinical cases recorded (20.2%). Of the clinical specimens, the most common specimen types were urine (330, 41.4%), blood (102, 12.8%) and sputum (57, 7.1%). Carbapenemase enzymes were identified in 15 different genera. The most common species were *Klebsiella pneumoniae* (1424, 36.0%) and *Escherichia coli* (1119, 28.3%). Nine resistance mechanisms were identified; OXA-48-like enzymes were the most frequently identified (2076, 52.5%), followed by NDM (904, 22.9%) and KPC (890, 22.5%).

Conclusions: The enhanced surveillance system is voluntary and poor completion of enhanced data fields is limiting our ability to identify high risk patient groups to inform public health action. However, the system does capture comprehensive patient demographic data and functions as an electronic referral system. Future work will involve data linkage to allow us to identify groups at greater risk and focus control and prevention efforts.

Multidrug resistance (MDR), ie, resistance to 3 or more antimicrobial classes: Genomic Insights into National Surveillance Of Methicillin-Resistant *Staphylococcus Aureus* Bacteraemia In England

Kearns A, Bubba L, Nsonwu O, Davies J, Doumith M, Thelwall S, Johnson A, Woodford N, Pichon B, Hope R

Aim: Set against a background of declining MRSA bacteraemia rates in England and advances in whole-genome sequencing (WGS), we sought to combine patient-level and genomic data to provide epidemiological insights into these cases at a national level.

Methods: We reviewed the national reference service database (Public Health England, London); WGS results for cases of MRSA bacteraemia were matched with enhanced mandatory surveillance data using patient identifiers. Cases identified ≥ 3 days after admission were defined as hospital-onset (HO-MRSA); the remainder as community-onset (CO-MRSA). For each isolate, the MLST, SCC*mec* type, toxome and resistome were derived. MRSA were considered multi-drug resistant (MDR) when genotypically resistant to β -lactams and ≥ 2 other classes of antibiotic.

Results: A total of 602 MRSA bacteraemia cases were reported nationally between April and December 2017. Of these, 77% (n=464) were deterministically linked with WGS data. Most (295; 64%) were CO-MRSA. The median age was 69 years (range 0-102); cases among males were more common (68%). MRSA were genotypically diverse: 18 different MLST-clonal complexes and 6 SCC*mec* (sub)types were identified; 39 (8.4%) were PVL-positive. CC22-IVh (EMRSA-15) predominated (209; 45%) with 118 (56.4%) being CO-MRSA. CC5-IV was the second most common lineage (58; 12.5%) and frequently defined as CO-MRSA (44; 75.9%). Genotypically, 71.6% (332) were MDR; decreased susceptibility to decolonization agents was less common (*mupA* 3.7%, *qacA/C* 16%).

Conclusions: The integration of genomic and patient-level data has provided unprecedented insights into the complex epidemiology of MRSA bacteraemia in England which should support the development of interventions to reduce the incidence.

Up to 4 keywords: Bacteraemia, whole-genome sequencing, molecular epidemiology, multi-drug resistance

Excess Mortality and Length of Stay Associated with *Escherichia coli* Bacteraemia Inpatients in England, estimated using National Surveillance Data

Nichola Naylor, Russell Hope, Nathan Green, Katherine Henderson, Julie Robotham, Sarah Deeny

Background: Bacteraemias due to *Escherichia coli* create a considerable population health burden globally. Infections due to *E. coli* which are non-susceptible to ciprofloxacin, third generation cephalosporins (3GC) and sometimes even carbapenems – leaving few therapeutic options – are occurring in increasing numbers. Here we estimate, for the first time nationally, excess in-hospital mortality and excess length of stay (LoS) for *E. coli* bacteraemia in-patients in England. Such estimates are necessary to determine burden of these infections and evaluate interventions.

Materials/methods: All *E. coli* bacteraemia cases in adults, reported to the English national mandatory surveillance database from 1 July 2011 to 30 June 2012 were linked to complete microbiological (including resistance testing), clinical and hospital information (from English national hospital administrative inpatient dataset – HES). Controls were all inpatients 18 years and over, without an *E. coli* bacteraemia, admitted to all English hospitals during the same time period, taken from HES. The datasets enabled classification of non-healthcare associated community onset, healthcare associated community onset and hospital onset cases. Time-dependent Cox proportional hazards models were fit to the data to determine differences in hazard of death and discharge, controlling for patient characteristics (such as age, sex and underlying comorbidities) and infection characteristics (such as community/hospital onset and suspected focus of infection). Multistate models were constructed to estimate excess LoS, accounting for time dependency bias and competing hazards.

Results: 19,325 *E. coli* bacteraemia cases were included, of which 2,469 were resistant to ciprofloxacin, 1,223 were resistant to 3GC and 11 were resistant to carbapenems. From the Cox model we estimated *E. coli* bacteraemia cases incurred a higher hazard of in-hospital mortality [HR=2.00 (95% CI; 1.92 - 2.08)] and a lower hazard of discharge [HR= 0.43 (95% CI; 0.43 - 0.44)] compared to non-infected controls, and thus a longer excess LoS. Neither ciprofloxacin resistant nor 3GC resistant cases had significantly different hazards of in-hospital mortality when compared to their susceptible controls, however they did have a lower hazard of being discharged, implying a longer LoS. Excess LoS, estimated using the multistate model, suggested a mean excess LoS of 2.17 days for ciprofloxacin resistance and 5.04 days for 3GC resistance.

Conclusion: This research suggests *E. coli* bacteraemia creates a substantial burden on the patient and the hospital due to excess LoS, though further work is needed to quantify uncertainty around these estimates. This work also implies antibiotic resistant, versus susceptible, *E. coli* bacteraemia infections have a marked effect on excess LoS but interestingly little effect on in-hospital mortality. However, further work is needed to

further adjust for the impact of patient characteristics. Estimates produced in this analysis can be utilised in future health economic models, evaluating interventions for the control of antibiotic resistance.

Selection and co-selection of antibiotic resistances by antibiotic use in primary care: an ecological study

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Objectives: To evaluate which antibiotic groups prescribed in primary care may select for resistance against amoxicillin, cephalexin, ciprofloxacin, co-amoxiclav and nitrofurantoin among *Escherichia coli* isolated from urinary samples in England.

Participants: Monthly national primary care prescribing data aggregated at the clinical commissioning group (CCG) level were obtained from NHS digital. Monthly positive *Escherichia coli* records from urine samples from patients between April 2014 and January 2016 in England were extracted from the national Second Generation Surveillance System (SGSS), and were aggregated at the CCG level.

Main outcome measures: Associations between levels of antibiotic prescribing of different antibiotic groups and amoxicillin, ciprofloxacin, nitrofurantoin, co-amoxiclav, and cephalexin resistance among urinary *E. coli* samples.

Results: Amoxicillin prescribing was positively associated with amoxicillin (RR 1.03, 95%CI 1.01 to 1.04) and ciprofloxacin resistance (RR 1.09 95%CI 1.04 to 1.17) among urinary *E. coli* samples. Nitrofurantoin prescribing had a positive association with nitrofurantoin resistance (RR 1.52, 95%CI 1.00 to 2.24), however prevalence of resistance was low (median 2%, 25th -75th percentile 1% to 4%). In contrast, nitrofurantoin prescribing was associated with lower levels of resistance to amoxicillin (RR 0.92, 95%CI 0.84 to 0.97). CCGs with higher levels of trimethoprim prescribing also had higher levels of ciprofloxacin resistance (RR RR 1.34 95%CI 1.10 to 1.59).

Conclusions: Amoxicillin is the most frequently used antibiotic in England and is frequently used for respiratory conditions, which are responsible for the largest share in inappropriate antibiotic prescribing in English primary care. Amoxicillin prescribing is associated with higher levels of amoxicillin, ciprofloxacin and trimethoprim resistance in *E. coli* urine isolates, suggesting that there is a substantial potential to reduce selective pressure via (co-)selection with unnecessary treatment with amoxicillin. When modelling the potential impact of interventions on antibiotic resistance it is important to account for co-selection by antibiotics.

Useful discordance: economic justification for whole genome sequencing of resistant bacteria in institutional outbreak management

Desmond Hsu, Anna Jeffery-Smith, Kanchan Dhamija, Michel Doumith, Bruno Pichon, Angela Kearns, Benny Cherian, Rohini Manuel, Martina Cummins

Background: Meticillin-resistant *Staphylococcus aureus* (MRSA) is an important cause of nosocomial infections contributing to significant patient morbidity and mortality. Conventional reference laboratory typing methods for MRSA can lack discrimination when compared with newer techniques such as whole-genome sequencing (WGS). Inconclusive or falsely indicative results can impede effective infection prevention and control. WGS offers the promise of differentiation down to a single nucleotide difference, allowing for accurate mapping of transmission events. The technique can also provide important information pertaining to antimicrobial susceptibility, virulence and identification of high risk clones. However, routine utilisation of WGS is limited by affordability and availability. We describe the investigation and management of a cluster of the USA300 clone of community acquired-MRSA by WGS.

Material/methods: Over a period of 11 days, Panton-Valentine Leukocidin-MRSA colonisation was identified in 7 babies across 2 neonatal units (NNUs) within different hospitals in neighboring districts. Phenotypic susceptibility patterns and conventional typing data (spa and PFGE) indicated that the MRSA recovered from both NNUs were indistinguishable and belonged to a lineage seen relatively rarely in England (USA300 clone), thus prompting a cross-site outbreak investigation. When no link was identified, WGS was employed.

Results: Phylogenetic analyses clearly indicated 2 different strains were involved and, despite chronological association, there was no cross-site spread. An evaluation of the absolute costs associated with the investigation and management of presumed cross-site spread was undertaken. In addition to the routine involvement of infection prevention and control, microbiology, NNU and maternity personnel; the presumed cross-site nature of the outbreak necessitated the further participation of reference laboratory scientists, Occupational health and Public health teams. Additional processes undertaken included: parent interviews, equipment screening, environmental screening, site visits, hand hygiene audits, healthcare worker (HCW) training and screening. Four HCWs were potential common links between the 2 units. All 4 HCWs were temporarily excluded from clinical duties pending screening results. Total staffing costs attributed to unnecessary processes that resulted from the management of the presumed cross-site outbreak totaled in excess of £16,000. This consisted of expenditure in temporary staffing, and 'opportunity cost' in staff time. Further absolute costs include additional cleaning, carrier eradication and screening expenses. Non-quantifiable costs include reputational damage, emotional costs to parents and HCWs involved.

Conclusions: There has been much work demonstrating the use of WGS for epidemiological mapping during suspected outbreaks. Here we demonstrate its utility in

discriminating between cases initially thought to be linked. While the value of routine WGS is debatable, we have highlighted a specific situation where a discordant result provides a strong economic justification for its utilisation. Timely employment of WGS can be justified in presumed outbreak scenarios where discordant results could mitigate resources being unnecessarily spent on non-routine infection prevention and control measures.

Multiple independent acquisitions of the putative pathogenicity island (ACME) by ST22-MRSA in the UK

Kearns AM, McTavish S, Doumith M, Harwin L, Kulishev C, Ganner M, Pichon B

Background: The putative pathogenicity island, Arginine Catabolic Mobile Element (ACME), is believed to have contributed to the success of the so-called USA300 clone of Community-Associated MRSA (CA-MRSA). Aside from strain fitness, ACME is also thought to enhance the ability of staphylococci to colonise the host. ACME has been reported sporadically in other lineages including ST239, CC97 and CC1. In 2011, it was reported for the first time in 2 strains of ST22-IV in Ireland. In this study, we report the first identification in England and Northern Ireland (NI) of ACME in ST22-MRSA, which includes EMRSA-15, the dominant Healthcare-Associated MRSA (HA-MRSA) lineage in the UK.

Material/methods: A total of 494 MRSA strains belonging to ST22 subjected to whole-genome sequencing (WGS) at Public Health England from 2014-2016 were screened by mapping methodology against reference sequences for ACME (*arcA-D* and *opp3A-C*), PVL phage (*lukS/F_PV*), Immune evasion cluster (IEC: *chp*, *sak*, *scn*) and a range of acquired and chromosomal markers of resistance to antibiotics, biocides and heavy metals. SCCmec types were deduced by Blast analysis of *ccr* genes and *mec* element sequences on de novo assemblies. Phylogeny based on single nucleotide polymorphisms was inferred by the Maximum Likelihood method. Spa typing was performed on WGS DNA extracts.

Results: Overall, 43 (8.7%) ST22-MRSA harboured an ACME II element, including 13 (30%) from cases of bacteraemia. Almost half (21/43; 48.8%) originated from NI, the remainder were from 5 different centres in England. Four exhibited a truncated *arc* gene cluster with excision of *arcB* and *arcC* genes. Nine spa types were identified, t032 predominated (26/43; 60%). Three different SCCmec types were identified: 35 harboured SCCmecIV (2B), 5 exhibited a composite cassette containing *ccr* types 2 and 4 (2B&4) and 3 encoded *ccrC* together with *ccrA2/B2* (2B&5). All were PVL-negative, harboured IEC type I and were genotypically resistant to β -lactams (*blaZ*, *mecA*) and quinolones (*griA_SA3(80:S-F)*; *gyrA_SA3(84:S-L)*). Genes associated with resistance to macrolides (*erm(C)*), trimethoprim (*dfrA*), aminoglycosides (*aacA-aphD*), tetracycline (*tet(K)*), heavy metals (*arsB*, *cadA*, *cadX* and *czrC*) and decreased susceptibility to biocides (*qacA*) were less common (4.6 to 65%). Phylogenetic analysis

suggested the existence of an NI clade distant from England cases, with ACME being acquired by isolates from England on multiple independent occasions. Truncated ACME II was detected in a cluster of cases in London plus an unrelated case suggesting possible expansion of this clone.

Conclusions: Retrospective analysis of WGS data showed 8.7% ST22-MRSA examined were ACME-positive. Whilst this was not a systematic structured study, the results show ACME has been acquired by ST22-MRSA including EMRSA-15 (ST22-IV) on independent occasions and has been associated with outbreaks in some settings. Prospective surveillance for ACME-positive isolates will further our understanding of the public health burden, fitness and virulence of such strains.

National MRSA Bacteraemia Surveillance in the Genomic Era – Opportunities and Challenges

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Introduction: Reporting of methicillin-resistant *Staphylococcus aureus* (MRSA) bloodstream infections (BSI) has been mandatory in England since 2001, and enhanced epidemiological surveillance has been in place since 2005. Academic sequencing studies of MRSA isolates have been used to confirm/refute outbreaks, and to reveal the emergence and spread of epidemic clones in the UK and globally. The aim of this study was to explore the feasibility of conducting combined epidemiological and genomic surveillance for MRSA BSI within a national public health surveillance programme.

Methods: Epidemiological surveillance of MRSA BSI was conducted by Public Health England. Data were collected from infection control teams in acute National Health Service (NHS) Trusts via the mandatory enhanced surveillance system. All NHS diagnostic microbiology laboratories in England were invited to submit MRSA bloodstream isolates to the Staphylococcal Reference Service, PHE Colindale. Whole-genome sequencing was performed at the Wellcome Trust Sanger Institute. Phylogenetic analyses, based on comparison of single nucleotide polymorphisms in the core genome compared to reference genomes for each clonal complex, were performed.

Results: Preliminary analysis shows that a total 977 MRSA BSI were reported between October 2012 and September 2013. 60% of cases were male and the median age was 71 years (range 0 – 103 years). 382 (39.1%) cases were apportioned to acute NHS Trusts, and 46% (417) were classified as hospital-acquired. 347 (35.5%) cases had the focus of infection recorded. Mortality data were available for 516 (52.8%) patients, 275 of whom died within 30 days of the BSI. A total of 559 bloodstream isolates from 433 patients were sequenced using a HiSeq instrument. Sequence analysis showed that isolates could be assigned to 11 MLST clonal complexes (CCs). CC22 predominated (>65%), and was present in all NHS regions, followed by CC5 (9%), CC30 (7%) and CC8 (6%). Seven of the 29 CC8 isolates belonged to the USA300 clone. Nine isolates were CC59, a dominant community-associated clone in Asia. Isolates belonging to different CCs were widely distributed, and regional clustering of specific lineages was apparent. The South West region had the most diverse range of defined CCs, and included CCs that were not found elsewhere. We included isolates from 2 Cambridgeshire outbreaks, which were genomically distinct, demonstrating the potential to detect local outbreaks and / or emerging pathogenic clones

Conclusions: We demonstrate that combined epidemiological and genomic surveillance in England is feasible, and could provide benefits such as early detection of emerging pathogenic clones and spread between different hospitals. Current logistical challenges include mandatory submission of epidemiological data and bacterial isolates, timely sequencing of bacterial isolates, and linkage of clinical, microbiological and sequence data within the national surveillance system. This would provide an invaluable resource for public health, in the UK and beyond.

Useful discordance: economic justification for whole genome sequencing of resistant bacteria in institutional outbreak management

Desmond Hsu, Anna Jeffery-Smith, Kanchan Dhamija, Michel Doumith, Bruno Pichon, Angela Kearns, Benny Cherian, Rohini Manuel, Martina Cummins

Background: Meticillin-resistant *Staphylococcus aureus* (MRSA) is an important cause of nosocomial infections contributing to significant patient morbidity and mortality. Conventional reference laboratory typing methods for MRSA can lack discrimination when compared with newer techniques such as whole-genome sequencing (WGS). Inconclusive or falsely indicative results can impede effective infection prevention and control. WGS offers the promise of differentiation down to a single nucleotide difference, allowing for accurate mapping of transmission events. The technique can also provide important information pertaining to antimicrobial susceptibility, virulence and identification of high risk clones. However, routine utilisation of WGS is limited by affordability and availability. We describe the investigation and management of a cluster of the USA300 clone of community acquired-MRSA by WGS.

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Conclusions: There has been much work demonstrating the use of WGS for epidemiological mapping during suspected outbreaks. Here we demonstrate its utility in discriminating between cases initially thought to be linked. While the value of routine WGS is debatable, we have highlighted a specific situation where a discordant result provides a strong economic justification for its utilisation. Timely employment of WGS can be justified in presumed outbreak scenarios where discordant results could mitigate resources being unnecessarily spent on non-routine infection prevention and control measures.

Defining Reservoirs of ESBL-Producing *Escherichia coli* and the Threat Posed to Personal, Animal and Public Health in the UK

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Background: ESBL-producing *E. coli* (ESBL-Ec) cause increased morbidity or mortality in a variety of infections, including bacteraemias; they frequently are co-resistant to other antibiotic classes besides cephalosporins. ESBL-Ec are also gut colonists of healthy humans and are found in the food chain and the environment. We investigated: (i) the frequency of ESBL-Ec human gut colonisation in 5 UK regions; and (ii) the contribution of non-human sources to the burden of human colonisation/infections in the UK, by comparison of ESBL-Ec from human faeces, sewage, farm slurry, animals and foodstuffs with those from bacteraemias.

Methods: Isolation of ESBL-Ec from human faeces undergoing routine microbiological testing ($n=20,243$ samples), bacteraemias, sewage ($n=325$), farm slurry ($n=97$), animals undergoing veterinary investigation, retail meat ($n=397$), and fruit and vegetables ($n=400$) obtained in 3 regions of England, and in Scotland and Wales was performed using 2 agars (CHROMagars ESBL and CTX). Identification of presumptive ESBL-Ec was by MALDI-ToF; MICs were determined by agar dilution. Whole genome sequencing was performed and data analysed to determine MLST and antimicrobial resistance genes.

Results: A total of 938 ESBL-Ec ($n=938$) were obtained, from human faeces ($n=360$), sewage ($n=67$), farm slurry ($n=24$), retail meat ($n=111$), animals ($n=83$), and bacteraemias ($n=293$). Overall, 11% of humans were colonised by ESBL-Ec, but the London carriage rate (17%) was almost twice that in other UK regions (8-10%). *E. coli* ST131 dominated in ESBL-Ec from human faeces (36%), blood (64%) and sewage (22%). ESBL-Ec were also isolated from 28% of slurry samples and, after enrichment, from 65% retail chicken, 3% pork and 2% beef samples, though never from fruit and vegetable samples. Amongst ESBL-Ec from non-human sources STs 602 and 23 dominated (12% and 11%, respectively); only 2 ST131 ESBL-Ec were isolated, both from chicken and carrying CTX-M-1. CTX-M-15 was the most common ESBL in ESBL-Ec of human origin accounting for 78% of ESBLs in blood isolates, 71% in human faeces and 54% in sewage isolates vs. 7% in meat and slurry isolates. Conversely, CTX-M-1 was found in 56% ESBL-Ec from non-human sources, but in only 5% ESBL-Ec from blood or human faeces and in 10% from sewage.

Conclusion: Most human colonisations/infections are caused by a few successful STs, particularly ST131, which presumably spread person-to-person through poor hygiene. Currently, non-human reservoirs of ESBL-Ec have a limited contribution to the major burden of human disease in the UK.

Acknowledgments/ References:

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Evaluation of the AusDiagnostics Easy-Plex™ assay for detection of carbapenemases and colistin resistance genes *mcr-1/-2* in multidrug-resistant Gram - negative bacteria

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Background: The dissemination of KPC, OXA-48-like, NDM, VIM and IMP carbapenemase genes is of public health concern. As such these genes are the focus of most commercial detection assays meaning that the rapid detection of rarer carbapenemases is challenging. We evaluated a commercial assay (AusDiagnostics Easy-Plex™ assay) for the detection of carbapenemases and acquired colistin resistance genes *mcr-1/-2*.

Material/methods: The 16-plex tandem PCR assay allows detection of *bla*_{KPC}, *bla*_{OXA-48-like}, *bla*_{NDM}, *bla*_{VIM}, *bla*_{IMP}, *bla*_{SIM}, *bla*_{GIM}, *bla*_{SPM}, *bla*_{FRI-1-like}, *bla*_{IMI}, *bla*_{GES} (differentiating ESBL and carbapenemase GES variants), *bla*_{SME} and *mcr-1/-2*. It was evaluated against Enterobacteriaceae, *Pseudomonas* and *Acinetobacter* isolates, tested retrospectively (n=211 with previously characterised resistance mechanisms) and prospectively (n=182 sent for investigation of carbapenem or colistin resistance mechanisms). Two isolates coproduced a carbapenemase and a GES ESBL. The assay was performed on 2-3 colonies from overnight growth. The AusDiagnostics Easy-Plex™ assay was performed on an Easy-Plex 384 (High Plex) System according to the AusDiagnostics Easy-Plex™ assay protocol. Results were automatically interpreted using the Easy-Plex™ software and compared with in-house PCR results and whole-genome sequencing data.

Results: The AusDiagnostics Easy-Plex™ was easy to use and was performed in less than 4h from colony to result output. When combining the data from the first runs of both retrospective and prospective evaluations, the AusDiagnostics Easy-Plex™ detected 268/270 carbapenemase genes, including *bla*_{KPC} (n=48), *bla*_{OXA-48-like} (n=79), *bla*_{NDM} (n=62), *bla*_{VIM} (n=26), *bla*_{IMP} (n=24), *bla*_{SPM} (n=1), *bla*_{FRI-1-like} (n=1), *bla*_{IMI} (n=7), *bla*_{GES} (n=18) and *bla*_{SME} (n=2). One *bla*_{GES-5} and one *bla*_{OXA-48-like} were not initially detected. The detection of *bla*_{SIM} and *bla*_{GIM} by the assay was assessed by testing in each run a positive control combining the 13 targeted genes. Seventeen out of 21 *mcr-1*-producing isolates were correctly identified, as were 2 GES ESBL producers. The

overall sensitivity and specificity of the assay were initially 97.9% and 99.6%, respectively. Repeat testing of the false-positive and false-negative results resulted in detection of all carbapenemase producers and reduced the number of false-positive results from 26 to zero. The overall specificity of the assay was 100% and the sensitivity was 98.6% as 4/21 *mcr-1* producers were still negative due to the instability of the *mcr-1* plasmid in these isolates. The positive and negative predictive values for this isolate panel were 91.7% and 99.9%, respectively and were improved to 100% and 99.9%, respectively upon repeat testing.

Conclusions: The AusDiagnostics Easy-Plex™ assay allowed detection of the carbapenemase families and carbapenemase gene variants detected in the UK in Enterobacteriaceae, *Pseudomonas* and *Acinetobacter* spp. Its coverage is greater than other products marketed for detecting carbapenemases, thereby offering increased confidence that isolates negative in the assay are unlikely to be carbapenemase producers. It also allowed the concomitant detection of *mcr-1/-2* genes in colistin-resistant isolates.

Multicenter evaluation of the BYG Carba test v2.0, a simplified electrochemical assay for the rapid laboratory detection of carbapenemase-producing Enterobacteriaceae

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Background: Accurate, timely detection of carbapenemase-producing *Enterobacteriaceae* (CPE) is a major challenge for microbiology laboratories. The BYG Carba test v2.0 is an electrochemical carbapenemase detection technique based on an electro-active polymer biosensor. It detects CPE in less than 30 minutes from a direct deposit of 1 to 3 single bacterial colonies on the electrodes without preliminary suspension in any buffer. BYG v2.0 was assessed in a multicentre study in 4 European reference laboratories (Centres A to D).

Material/methods: Firstly, in centre A the BYG Carba test v2.0 was compared with the BYG v1.0 against a collection of 57 isolates for which β -lactam resistance mechanisms

had been previously characterized. The test was then evaluated in the 4 reference centres against a collective total of 1181 isolates (408, 198, 376, and 199 tested in centres A, B, C and D, respectively gathering 511 retrospective isolates and 670 prospective isolates referred in 2015 on suspicion of CPE). These comprised CPE [n=704] with OXA-48-like [n=359], KPC [n=114], NDM [n=107], VIM [n=78], IMP [n=17], NDM + OXA-48-like [n=14] and other less common carbapenemases [n=15] as well as non- CPE [n=477]. Results obtained by the BYG v2.0 were compared with those of in house PCR/sequencing assays, which were taken as the gold standard.

Results: For the initial 57 isolates, the BYG v2.0 showed a significant improvement in the positivity signal strength (in arbitrary units, AU) compared with BYG v1.0 (Mean value 97.8 AU vs 44.0 AU, $p < 0.00001$) with accuracy remaining unchanged on this collection. For the 1181 isolates tested across 4 reference centres, BYG v2.0 yielded overall sensitivity of 96.3 % and specificity of 99.8 %. Compared with molecular results, 26 false-negative results were observed (OXA-48-like [n=10], NDM [n=5], GES-5 [n=4], VIM [n=3], IMP [n=2] and IMI [n=2]) and 1 false-positive result was reported for one carbapenem-resistant *E. cloacae*. Considering only the 670 isolates tested prospectively, the BYG v2.0 displayed overall positive and negative predictive values of 100% and 98.4% (respectively, 100% and 99.1% in centre A; 100% and 97.5% in centre B; 100% and 97.2% in centre C; and 100% and 98.2% in centre D). No false-positive results were observed, but 5 OXA-48-like, 2 VIM and 1 NDM producer were not detected. Regarding time to positivity, 45% and 85% of CPE detected were positive in 5 and 10 minutes, respectively. Even for OXA-48-like-producers, which are often more difficult to detect phenotypically, 44% were detected within 5 minutes and 89 % within 10 minutes.

Conclusions: The BYG v2.0 is a new highly simplified, rapid and efficient assay discriminating between CPE and non CPE in under 30 min. The real-time quantified electrochemical signal allows the objective and traceable interpretation of the results.

Cysteamine as an antibiotic resistance breaker

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Background: Antibiotic potentiators as adjuncts to antimicrobial therapy are a potential solution to the global challenge of antibiotic resistance. The development of new antimicrobial chemical entities (NACEs) de novo is a lengthy process and so alternative

therapeutic strategies must be developed in the interim. Extending the lifespan and spectrum of activity of current antibiotics could be achieved by co- or concurrent therapy with a compound that can restore its activity against resistant bacteria, the combination of amoxicillin with clavulanate is a currently licensed example of this approach. Some existing drugs with an established clinical history for other indications also have resistance-breaking properties which might be harnessed to provide much needed novel antimicrobial therapy solutions, and have been described as antibiotic adjuvants. Here we investigate the “old” molecule, cysteamine, which has been used to treat the metabolic disease cystinosis for over 20 years and is the subject of current research in the field of cystic fibrosis, to see if it has wider utility as an antibiotic potentiator against MDR pathogens of global concern.

Material/methods: Minimum inhibitory concentrations (MIC) and minimal fungicidal concentrations (MFC) of tested compounds were determined using CLSI standardised broth microdilution techniques (CLSI, refs), and fractional inhibitory concentration coefficients (FIC) were calculated using the CLSI standardised checkerboard technique. Assessment of azithromycin potentiation activity against *Neisseria meningitidis* utilised Etest strips placed upon GC agar plates impregnated with concentrations of cysteamine. Mouse thigh model studies examined microbial burden (cfu/g) of thigh tissue 26 hours post infection. The wax moth *Galleria mellonella* model was also utilised to demonstrate *in vivo* protection from infection.

Results: Here we show that cysteamine can potentiate a wide range of antibiotics from different classes of compounds and can reverse CLSI/EUCAST clinically defined resistance in *in vitro* experiments. We can also demonstrate *in vivo* potentiation of antibiotic efficacy in the *G. mellonella* and mouse thigh model of infection. Cysteamine reversed azithromycin resistance across a number of resistant MRSA isolates, but surprisingly was also capable of potentiating azithromycin activity against Gram negative AMR *Neisseria meningitidis* (shown below) in a strain-specific manner.

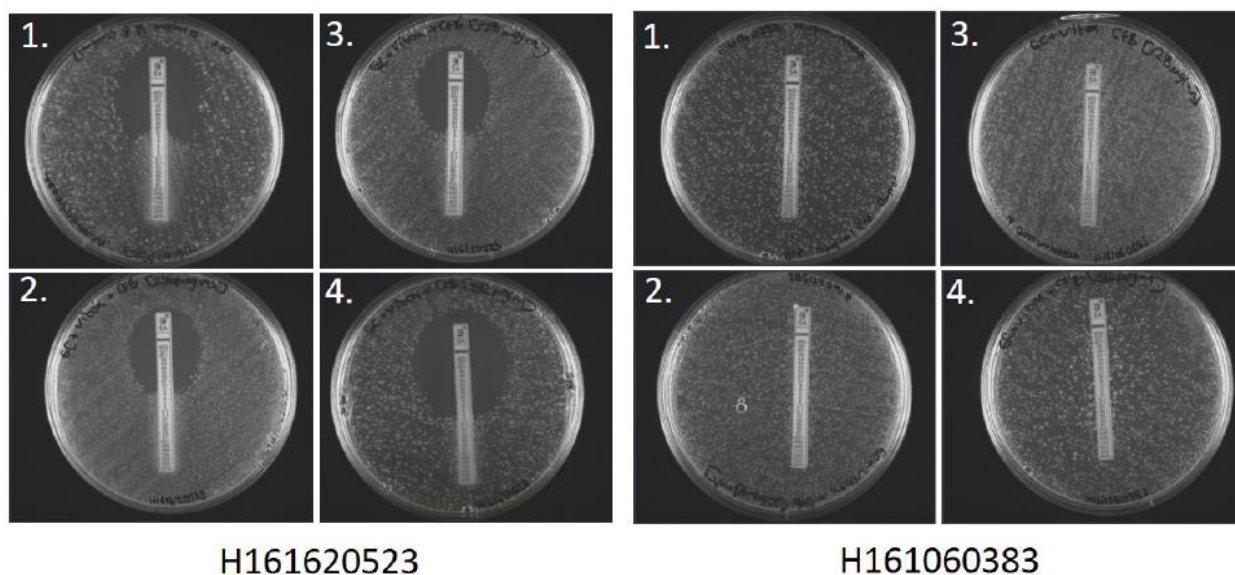


Figure 1: Increased zones of clearance of *N. gonorrhoeae* strain H161620523 can be observed surrounding azithromycin Etest strips on plates with increasing concentrations of cysteamine (1. 0 mg/L; 2. 128 mg/L; 3. 256 mg/L; 4. 512 mg/L) incorporated into GC (+ Vitox supplement) agar, whereas there is no apparent difference for strain H161060383.

Conclusions: Cysteamine has utility as a broad spectrum potentiator of antibiotics. It could be repurposed as an adjunct therapy to extend the useful lifetime of our valuable antibiotics in current clinical practice when treating AMR infections caused by a variety of pathogens.

First identification of 16S rRNA methyltransferases in *Pseudomonas aeruginosa* in the UK

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Background: 16S rRNA methyltransferases (16S RMTases) are an emerging resistance mechanism, and cause high-level resistance (MICs ≥ 256 mg/L) to all clinically-relevant aminoglycosides in Gram negative bacteria. The aim of this study was to screen for 16S RMTase genes (*armA*, *rmtA-H* and *npmA*) among *Pseudomonas aeruginosa* isolates referred to the Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit at Public Health England (PHE) for investigation of unusual resistance, especially carbapenem resistance, and/or typing.

Material/methods: *P. aeruginosa* isolates (n=221) from 2003-2015 displaying pan-aminoglycoside resistance (amikacin, gentamicin and tobramycin MICs of ≥ 64 , ≥ 32 and ≥ 32 mg/L, respectively) were screened for *armA*, *rmtA-H* and *npmA* genes with 2 multiplex PCRs. The isolates were typed using variable-number tandem-repeat (VNTR) analysis and sequence types (STs) were inferred accordingly. Carbapenemase genes were present in 155/221 isolates.

Results: Twenty-two (10.0%) pan-aminoglycoside-resistant *P. aeruginosa* isolates were positive for 16S RMTase genes (Table). Eighteen (81.1%) of these co-produced an IMP, NDM, SPM or VIM carbapenemase, compared with 137/199 (68.8%) of 16S RMTase-negative isolates. Of 6 patients who had a known travel history between 2011-2015, 5 (27.3%) had visited India. The sixth patient, positive for *rmtD* and *bla*_{SPM}, had travelled to Brazil where they were hospitalised. 16S RMTase-positive isolates belonged to 19 VNTR profiles, 5 of which corresponded with high-risk clones ST357 (5 isolates), ST654 (3 isolates) and ST233, ST277, ST773 (one isolate each).

Table: Details of 16S RMTase-positive *P. aeruginosa* isolates

Sample Number	16S RMTase gene	Carbapenemase	Travel History	Hospital	VNTR Profile	Sequence type (ST)
156	<i>armA</i>	Negative (OrpD porin loss)	-	LONDON_1	12, 3, -, 5, 5, 1, 9, 5, 11	-
1	<i>rmtB</i>	NDM	-	LONDON_2	12, 4, 6, 5, 3, 1, 10, 9, 12	ST773
2*	<i>rmtB</i>	VIM	-	LONDON_3	10, 2, 5, 4, 4, 2, 6, 4, 12	-
181*	<i>rmtB</i>	VIM	-	LONDON_3	10, 2, 5, 4, 4, 2, 6, 4, 12	-
43	<i>rmtB</i>	NDM	-	LONDON_4	10, 2, 5, 4, 4, 2, 6, 4, 10	-
180	<i>rmtB</i>	Negative	India	LONDON_5	10, 2, 5, 4, 4, 2, 6, 4, 13	-
17	<i>rmtB</i>	NDM	India	YORK&HUM_1	11, 3, 2, -, 3, 1, 9, 3, 11	ST654
109	<i>rmtB</i>	NDM	India	SOUTH WEST_1	11, 3, 2, -, 3, 1, 9, 3, 11	ST654
107	<i>rmtB</i>	VIM	India	WEST MIDS_1	13, 2, 1, 5, 2, 2, 6, 5, 13	ST357
117	<i>rmtB</i>	VIM	-	EAST_1	13, 2, 1, 5, 2, 3, 6, 5, 11	ST357
128	<i>rmtB</i>	IMP	-	LONDON_6	13, 2, 1, 5, 2, 3, 7, 5, 10	-
129	<i>rmtB</i>	VIM	-	LONDON_7	12, 2, 1, 5, 3, 1, 9, 2, 13	-
136	<i>rmtC</i>	VIM	-	LONDON_8	13, 2, 1, 5, 2, 3, 6, 5, 8	ST357
61	<i>rmtD</i>	NDM	-	LONDON_9	12, 5, 5, 2, 4, 1, 6, 2, 8	-
63	<i>rmtD</i>	VIM	-	LONDON_2	12, 3, 4, 5, 3, 1, 8, 2, 12	ST233
90	<i>rmtD</i>	SPM	Brazil	YORK&HUM_2	9, 8, -, 2, 1, 1, 3, 3, 7	ST277
111	<i>rmtD</i>	VIM	-	NORTH WEST_1	13, 2, 1, 5, 2, 3, 6, 5, 14	ST357
114	<i>rmtD</i>	VIM	No	NORTH WEST_1	13, 2, 1, 5, 2, 3, 6, 5, 14	ST357
144	<i>rmtD</i>	VIM	India	YORK&HUM_2	11, 3, 2, -, 3, 1, 9, 3, 12	ST654
20	<i>rmtF</i>	NDM	-	LONDON_10	11, 3, 2, -, 3, 1, 9, 3, 13	ST654
200	<i>rmtF</i>	Negative (efflux pump)	-	SOUTH EAST_1	11, 2, -, 5, 3, 2, 11, 3, 10	-
209	<i>rmtF</i>	Negative (OprD porin loss and upregulated efflux)	-	NORTH EAST_1	10, 2, 5, 4, 4, 2, 6, 4, 9	-

*Samples 2 and 181 are from the same patient.

Conclusions: This is the first report of 16S RMTase-positive *P. aeruginosa* in the UK. Although the isolates were known to have unusual antibiotic resistance profiles, especially carbapenem resistance, there appears to be an association between 16S RMTases and carbapenemases, as well as a connection with travel to India, where NDM and VIM carbapenemases are known to be circulating. As only 10% pan-aminoglycoside-resistant *P. aeruginosa* isolates harboured 16S RMTase genes, other resistance mechanisms, such as aminoglycoside modifying enzymes, efflux pumps and decreased membrane permeability or a novel 16S RMTase gene not yet identified, were more often responsible for high-level aminoglycoside resistance in the species.

Changing epidemiology of penicillinase producing *Neisseria gonorrhoeae* in England and Wales, 2007-2015

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Keywords: *Neisseria gonorrhoeae*, Penicillinase, Cephalosporins, HIV Seropositivity, Homosexuality Male, Health Promotion

Background: A previous study of the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) found that 27% of penicillinase-producing *Neisseria gonorrhoeae* (PPNG) harboured the TEM-135 enzyme. TEM-135 is 1 amino-acid substitution from an extended-spectrum β -lactamase (ESBL); ESBLs are active against cephalosporins which are the last line treatment for gonorrhoea. This analysis examined trends and risk factors associated with PPNG.

Methods: GRASP is a sentinel surveillance programme which collects consecutive *N. gonorrhoeae* isolates from patients attending 27 specialist sexual health clinics in England and Wales. PPNG was defined as any β -lactamase positive isolate. A test for trend was carried out for the proportion of all isolates with PPNG between 2007 and 2015. Multivariable logistic regression was used to identify risk factors for PPNG stratified by year.

Results: Between 2007 and 2015, the proportion of all isolates that were PPNG increased two-fold (7.6% vs. 15.6%; $p < 0.001$). In 2007-2013, the odds of isolating PPNG were higher in heterosexual men (aOR 2.76; 95% CI: 2.08-3.67 vs. men who have sex with men-MSM), with increasing age (aOR 1.03 per year increase; 95% CI: 1.02-1.04), and in those reporting recent sex abroad (aOR 3.67 95% CI: 2.85-4.71). In 2014-2015, the odds of isolating PPNG were higher in MSM (aOR 1.69; 95% CI: 1.10-2.61 vs. heterosexual men), those of black African ethnicity (aOR 2.23; 95% CI: 1.24-4.02, vs. white ethnicity), and those with HIV positive status (aOR 1.49; 95% CI: 1.13-1.97).

Discussion: PPNG has increased since 2007 and after 2014 PPNG isolates were no longer associated with recent sex abroad suggesting more local transmission. There is a need to improve health promotion among HIV-positive MSM to reduce spread of PPNG and the potential of ESBL emergence.

Pan-aminoglycoside resistance: the emergence of 16S rRNA methyltransferases in the UK

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Background: 16S rRNA methyltransferases (16S RMTases) are an emerging resistance mechanism, and cause high-level resistance (MICs ≥ 256 mg/L) to all clinically-relevant aminoglycosides in Gram-negative bacteria. The aim of this study was to identify the prevalence of 16S RMTase genes (*armA*, *rmtA-H* and *npmA*) in isolates from the Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit's collection at Public Health England (PHE). These isolates were sent to AMRHAI as they displayed unusual resistance profiles, especially carbapenem resistance.

Material/methods: *Acinetobacter baumannii* (n=550) and Enterobacteriaceae (n=817) isolates from 2004-2015 displaying pan-aminoglycoside resistance (amikacin, gentamicin and tobramycin MICs of ≥ 64 , ≥ 32 and ≥ 32 mg/L, respectively) were screened for *armA*, *rmtA-H* and *npmA* by PCR. Whole genome sequencing (WGS) data, available for 449 Enterobacteriaceae, were analysed to identify 16S RMTase genes and sequence types (STs).

Results: Five hundred and twenty-seven (95.8%) *A. baumannii* and 755 (92.4%) Enterobacteriaceae were positive for 16S RMTase genes (Figure). *armA*, *rmtB*, *rmtC*, *rmtE*, *rmtF* and various 2 gene combinations were identified; no *rmtA*, *rmtD*, *rmtG*, *rmtH* or *npmA* genes were detected. The vast majority (94.5%, 1211/1282) of 16S RMTase-positive isolates also produced a carbapenemase where *bla*_{OXA-23} + *bla*_{OXA-51} (n=490), *bla*_{OXA-23-like} (n=5), *bla*_{OXA-40} + *bla*_{OXA-51} (n = 4), *bla*_{NDM} + *bla*_{OXA-23} + *bla*_{OXA-51} (n=3) and *bla*_{OXA-51-like} (n=2) were found in *A. baumannii* and *bla*_{NDM} (n=527), *bla*_{OXA-48-like} (n=112), *bla*_{NDM} + *bla*_{OXA-48-like} (n=59), *bla*_{KPC} (n=5), *bla*_{VIM} (n=2), *bla*_{GES} (n=1), and *bla*_{NDM} + *bla*_{VIM} (n = 1) were found in Enterobacteriaceae. Four hundred and ninety (93.2%) *A. baumannii* isolates positive for *armA* belonged to international clone II. In Enterobacteriaceae, WGS data demonstrated that *armA*, *rmtB*, *rmtC* and *rmtF* were found in diverse sequence types (STs); 25 *E. coli* STs and 30 *K. pneumoniae* STs were identified. *E. coli* ST410 (19/87, 19.5% total *E. coli* isolates; from 8 laboratories) and *K. pneumoniae* ST14 (111/312, 35.6% total *K. pneumoniae* isolates; from 25 laboratories) were most common. Travel history was available for only 9.8% (125/1282) patients with 16S RMTase-positive isolates; India was the most frequently visited country between 2009-2015 (40/125, 32.0% patients); 32 (80.0%) of these isolates had NDM carbapenemases.

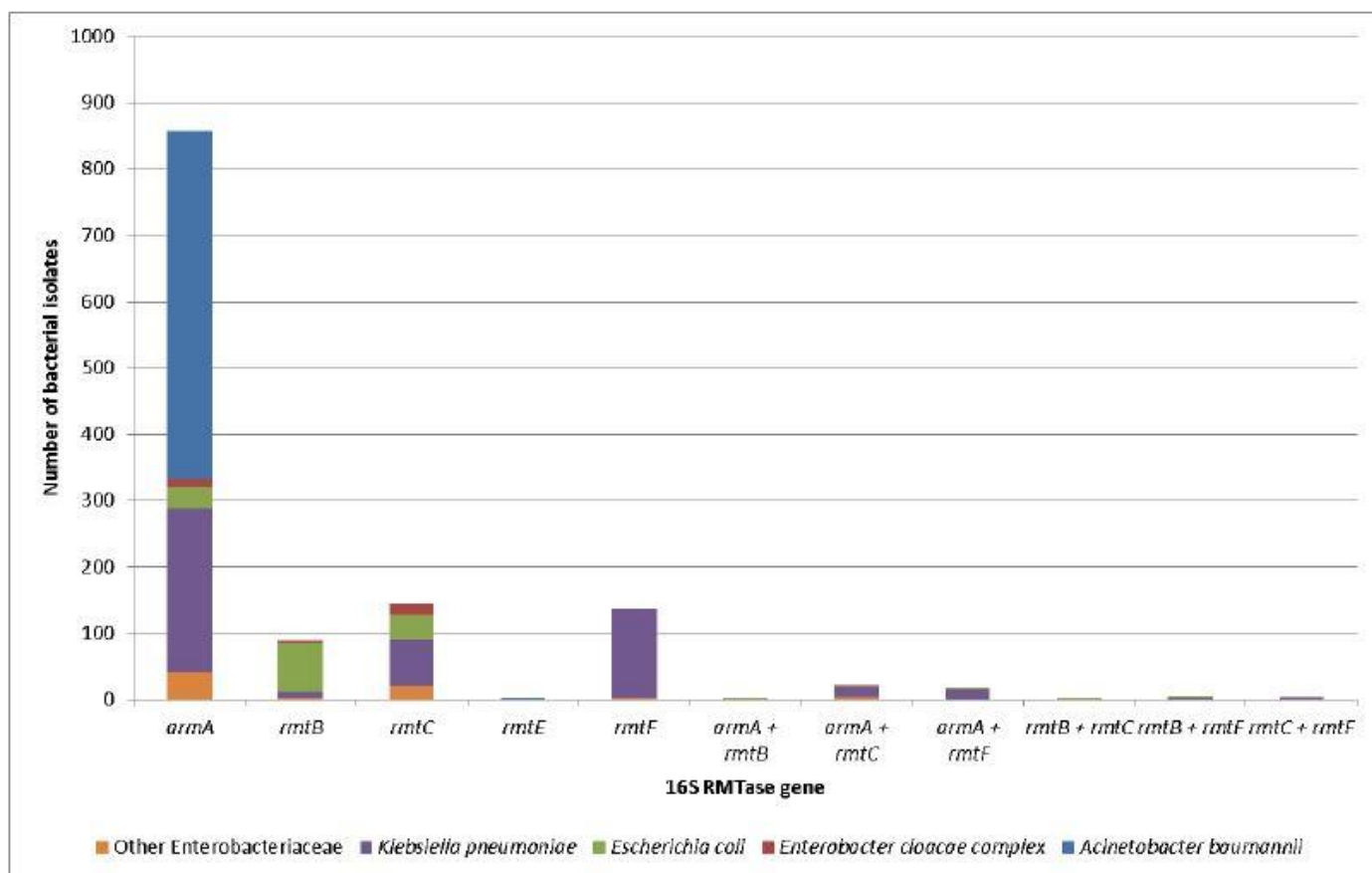


Figure: 16S RMTase-positive isolates broken down by genus/species

Conclusions: 16S RMTase activity has been identified as the major mechanism conferring panaminoglycoside resistance in this group of Gram-negative organisms displaying unusual resistance phenotypes, predominantly carbapenem resistance. This combination of carbapenemase and 16S RMTase genes poses a serious threat to the treatment of multidrug-resistant Gram-negative isolates with already limited treatment options should this combination become more widespread. 16S RMTase genes appear to be spreading through co-selection with carbapenemase genes, which is supported by their carriage in high-risk clones known to be carbapenemase producers such as *A. baumannii* international clone II, *E. coli* ST410 and *K. pneumoniae* ST14.

The evolving face of carbapenemase-producing Enterobacteriaceae: a 5-year review of a London teaching hospital's experience

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Background: The incidence of Carbapenemase-producing Enterobacteriaceae (CPE) has steadily increased over the last decade. However, data regarding risk factors associated with CPE acquisition and the best method of CPE detection is lacking. In

the United Kingdom, the Public Health England CPE toolkit has been used to identify potential cases. We review our experience, as a large London hospital, looking at the epidemiology and evolving detection methods of CPEs within our trust.

Material/methods: We conducted a search of all Barts Health CPE isolates from the period of April 2011 to August 2016 in conjunction with the Antimicrobial Resistance and Healthcare and Associated Infections (AMRHAI) Reference Unit, Public Health England. We reviewed the susceptibility patterns for the 136 CPE cases isolated during this period, to highlight patterns of resistance for different carbapenemase classes, detection methods and identify potential risk factors. Organisms were identified by MALDI-TOF (Bruker, Germany) and automated sensitivity testing performed (Microscan Walk Away System, Siemens Healthcare). All Enterobacteriaceae isolates reported as carbapenem resistant underwent confirmatory testing to determine Ertapenem Minimum Inhibitory Concentration (MIC) by means of an E-test (Biomerieux Clinical Diagnostics). The presence of a carbapenemase was confirmed by multiplex PCR by ARMHAI.

Results: We identified 136 CPE cases during the study period. Of these 60 (44%) were *Klebsiella pneumoniae*, 15 (11%) *Klebsiella species*, 35 (26%) *Escherichia coli*, 18 (13%) *Enterobacter species*, 4 (3%) *Citrobacter species* and 4 (3%) *Serratia species*. AMRHAI confirmed the presence of 92 (68%) OXA-48, 35 (26%) NDM, 6 OXA-48 with concurrent NDM (4%), and 3 (2%) SME carbapenemases. These were isolated across a wide range of clinical specimens. Detection of OXA-48 improved during our study period, in response to an outbreak in 2016. Colorex Supercarba agar was introduced as a screening medium. Review of antibiotic susceptibility patterns demonstrated the previous standard of operation whereby only isolates with a ertapenem MIC >1 were flagged as possible CPEs was an insensitive method for detection of OXA-48 carbapenemases, which can often test susceptible to carbapenems. Isolates resistance to temocillin and tazobactampiperacillin with or without a reduced MIC to ertapenem were flagged as possible CPEs and sent to ARMHAI for confirmation of a OXA-48 enzyme. Contrary to the CPE toolkit guidelines, a history of hospitalisation abroad was not a significant risk factor in the majority of cases, with prolonged length of stay and prior antibiotic use being more prevalent risk factors.

Conclusions: We detected CPEs from a wide range of specimens in patients lacking the convention risk factors for CPE acquisition. OXA-48 and NDM isolates formed the majority of our carbapenemases. As recognition of CPEs has increased, laboratory methods have improved. The use of reduced susceptibility to both temocillin and tazobactam-piperacillin significantly improved detection of OXA-48 carbapenemases.

Activity of ceftolozane-tazobactam against problem non-fermenters sent to the UK reference laboratory - a year's experience

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Background: Ceftolozane-tazobactam (CT) combines a recently-developed cephalosporin with an established beta-lactamase inhibitor. It has been included in the national reference laboratory's standard 'Gram-negative panel' of antibiotics, tested against referred isolates, since July 2015. The first full year's results for non-fermenters were reviewed.

Material/methods: Most isolates are referred owing to resistance to standard agents. On receipt they are identified by MALDI-ToF or, for *A. baumannii*, by PCR of *bla*_{OXA-51-like}. Susceptibility testing is by agar dilution using EUCAST breakpoints, utilising a wide panel of antibiotics to facilitate interpretive reading; metallo-carbapenemase, *bla*_{GES} and (variably) *bla*_{VEB}/ESBL genes are sought by PCR in isolates with phenotypes suggesting their presence.

Results: Among 1431 *P. aeruginosa* tested, 400 and 155 were judged to have moderate and strong elevation of efflux, respectively whilst 151 were inferred to have derepressed AmpC beta-lactamase. CT was active, at its 4+4 mg/L breakpoint, against 100, 95 and 93% of these groups, respectively, compared with 90, 28 and 21% for ceftazidime, which is the most active established beta-lactam vs. the species. By contrast, all of 124 *P. aeruginosa* isolates with MBLs, 29/30 (97%) with ESBLs, and 38/45 (84%) with high-level ceftazidime resistance (MIC >256 mg/L) via uncertain mechanisms were CT resistant, with MICs >16+4 mg/L for over 90% with metallo-carbapenemases or VEB enzymes; MICs for clonal *P. aeruginosa* with GES carbapenemases (n=19) straddled the breakpoint, with most values at 4-4 to 8+4 mg/L. Overall, CT was active at breakpoint vs. 52.1% of *P. aeruginosa* nonsusceptible to ALL relevant established beta-lactams (i.e. carbenicillin, piperacillin-tazobactam, ceftazidime and carbapenems), rising to 80.2% for isolates lacking carbapenemases or ESBLs. Most (86.1%) imipenem-resistant *A. baumannii* (n=302) were resistant to CT at 4+4 mg/L whereas MICs for *B. cepacia* complex (n=77) and *S. maltophilia* (n=86) isolates correlated strongly with those of ceftazidime – previously the cephalosporin with the lowest MICs for both species/groups but were 2-8-fold lower in >80% of cases.

Conclusions: CT is notably active against problem non-fermenters, except *Acinetobacter* spp.; its activity against *P. aeruginosa* with up-regulated efflux or derepressed AmpC is particularly striking. A CT MIC >16+4 mg/L for *P. aeruginosa* predict the presence of a carbapenemase or ESBL.

What is the evidence that previous azithromycin treatment for chlamydia or gonorrhoea is associated with *Neisseria gonorrhoeae* azithromycin resistance?

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Introduction: The prevalence of azithromycin resistance in *Neisseria gonorrhoeae* (NG) including high-level resistance (HL-AziR NG) is increasing in England. It has been suggested that exposure to azithromycin at sub-optimal doses may facilitate development of azithromycin resistance in NG. We investigated whether treatment history for non-rectal chlamydia (CT) or NG (as proxies for azithromycin exposure) in GUM services was associated with susceptibility of NG to azithromycin.

Methods: Descriptive and negative binomial regression analyses of azithromycin Minimum Inhibitory Concentration (MIC) data from 4608 NG isolates collected by the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP) 2013-2015 (matched to GUMCAD data on CT/NG diagnoses) were performed. Descriptive analyses of previous CT/NG among 56 HL-AziR NG isolates (MIC>256 mg/L) was also performed (2013-2016).

Results: Modal azithromycin MIC was 0.25mg/L (1 dilution below the resistance breakpoint) in those with and without history of CT or GC. There were no differences in MIC distribution by previous CT/NG, nor by time since most recent infection (CT: $p=0.97$; NG: $p>0.99$). Among patients with HL-AziR NG, 4 (8%) were treated for CT and 4 (8%) for NG in the previous year, compared to 9% and 13% respectively for all GRASP patients.

Discussion: There was no evidence of an association between previous CT/NG treatment in GUM services and subsequent presentation with an azithromycin-resistant strain. However, 53% of CT diagnoses in 15-24 year olds occur in non-GUM settings therefore further research is needed to explore whether an association with azithromycin exposure in other settings and for other conditions exists.

The emergence and spread of antimicrobial resistant *Neisseria gonorrhoeae* in HIV positive men who have sex with men

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Introduction: In England, men who have sex with men (MSM) who are HIV-positive are disproportionately affected by STIs, in part probably due to HIV sero-adaptive behaviours. *Neisseria gonorrhoeae* (NG) is of particular concern because treatment is threatened by antimicrobial resistance (AMR). In England, AMR NG has typically spread rapidly within sexual networks of MSM. We investigated whether the emergence and/or spread of AMR NG was associated with HIV-positive status.

Methods: The prevalence of NG decreased susceptibility (DS) to ceftriaxone (MIC (mg/L) ≥ 0.015), cefixime (≥ 0.125), and azithromycin AMR (≥ 1) from 2004-2015 was plotted by HIV status to investigate the emergence of DS/AMR using data from England and Wales collected within the Gonococcal Resistance to Antimicrobials Surveillance Programme. Differences were assessed using the Kolmogorov-Smirnov (KS) test. Logistic regression was used to model the association between HIV status and susceptibility to these antimicrobials in separate models adjusting for year.

Results: Among all 5,630 MSM with NG, 25% of samples had DS/AMR to ceftriaxone, 8% to cefixime and 3% to azithromycin. A third (2024/5630) of MSM were HIV-positive. The distribution of prevalence of NG DS/AMR to ceftriaxone, cefixime and azithromycin was similar in HIV-positive and HIV-negative MSM across 2004-2015 ($P > 0.05$ for each antimicrobial). In the logistic regression models, HIV-positive MSM were as likely as HIV-negative MSM to be infected with NG DS to ceftriaxone (DS/AMR prevalence in HIV-positive MSM vs HIV-negative MSM, adjusted odds ratio [95% confidence interval]) 25% vs 25%, 1.0 [0.9-1.1], cefixime 7% vs 8%, 1.1 [0.9-1.4] or azithromycin: 3% vs 3%, 0.9 [0.6-1.2].

Conclusion: From these epidemiological data there is no evidence that MSM with HIV are at greater risk of DS/AMR NG compared to those without HIV. Whole genome sequencing will assist further investigations to explore relatedness of isolates and understand whether distinct populations of NG are spread more efficiently within sexual networks of HIV-positive MSM.

What role does importation play in the spread of antimicrobial resistant *Neisseria gonorrhoeae* in the UK? Associations between antimicrobial resistant strains and recent sex abroad

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Introduction: People living in Britain who have sex abroad are more likely to report sexual behaviour that puts them at greater risk of acquiring STIs, including *Neisseria gonorrhoeae* (NG). Antimicrobial resistant (AMR) NG is a global public health concern, which may emerge de novo or be imported to the UK when individuals infected abroad have subsequent sexual partners at home. We investigated whether patients who reported sex outside the UK ('sex abroad') were more or less likely to be diagnosed with AMR NG.

Methods: Logistic regression was used to model the association between reported recent sex abroad and decreased susceptibility (DS) to ceftriaxone (MIC (mg/L) ≥ 0.015) and cefixime (≥ 0.125) and azithromycin AMR (≥ 1) stratifying by sexual orientation (men who have sex with men (MSM) and heterosexual men and women) from isolates in England and Wales collected within the Gonococcal Resistance to Antimicrobials Surveillance Programme, 2004-2015.

Results: Over 10% of MSM and heterosexuals reported sex abroad. Among heterosexuals, infection with a strain of NG with DS to ceftriaxone was associated with sex abroad after adjusting for potential confounders: ceftriaxone (DS prevalence, adjusted odds ratio (95% confidence interval)): 14%, 1.8 (1.3-2.3). Infection with NG DS/AMR to cefixime or azithromycin was not associated with reported sex abroad after adjusting for potential confounders: cefixime 4%, 1.6 (0.9-2.7); azithromycin 2%, 1.5 (0.7-3.3). For MSM, no association was found between infections with DS/AMR NG and sex abroad.

Conclusion: In the UK, heterosexuals with NG infection who report sex abroad are at a higher risk of DS to ceftriaxone, suggesting that sex abroad might be the source of some AMR NG within heterosexual networks and highlighting the importance of condom use for travellers. In contrast, DS/AMR NG was not associated with sex abroad among MSM, which might reflect established AMR within MSM networks in the UK. Genetic comparison of these isolates using whole genome sequencing might further elucidate how AMR NG is imported and disseminated in the UK.

Does High-Level Azithromycin Resistance Emerge From Low-Level Resistance In *Neisseria Gonorrhoeae*?

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Introduction: High-level azithromycin (Azi) resistance (HL-AziR) threatens gonorrhoea dual therapy (ceftriaxone 500mg and Azi 1g) as it renders Azi ineffective. Between

November 2014-2016, 58 cases of HL-AziR (MIC >256 mg/L) *N. gonorrhoeae* (NG) were detected in England. Whole genome sequencing (WGS) revealed that most HL-AziR isolates were from a single clade (NG-MAST ST9768) with an A2059G mutation in 3/4 or all 4 alleles of the 23S rRNA gene. Lower-level AziR (MICs 1.0–32 mg/L) is commonly associated with a C2611T 23S rRNA gene mutation and *mtrR* promoter mutations. We performed WGS of ST9768 isolates with Azi susceptibility (MICs <0.5 mg/L) or with low-level AziR (MIC 1 mg/L) to investigate their genetic relatedness to the HL-AziR isolates.

Methods: WGS was performed on 7 non-HL-AziR ST9768 isolates from Scotland isolated in 2014. A phylogeny was constructed using the maximum likelihood algorithm based on whole genome variants. Genetic resistance determinants were analysed by mapping the WGS short reads to the 23S rRNA gene.

Results: All ST9768 isolates with Azi MICs of 0.12–1.0 mg/L were part of the same WGS clade as the ST9768 HL-AziR isolates. One susceptible isolate (MIC 0.12 mg/L) had 0/4 mutated (A2059G) 23S rRNA alleles, 5 susceptible isolates (MICs 0.25 mg/L) had 1/4 mutated alleles and 1 low-level resistant isolate (MIC 1.0 mg/L) had 2/4 mutated alleles. No isolates carried the C2611T mutation.

Conclusion: This is the first report of the A2059G mutation in NG isolates with Azi MICs of 0.25–1.0 mg/L. The phylogeny suggested that the HL-AziR ST9768 isolates are descendants of the low-level AziR isolates, which are in turn, descendants of the susceptible isolates. We hypothesise that azithromycin exposure provided selection pressure for 1 or 2 mutated copies of the 23S rRNA gene to recombine with wild-type copies, leading to 3 to 4 mutated copies in HL-AziR isolates. Greater understanding of the prevalent mechanisms of lower level AziR is required as HL-AziR could emerge in isolates with A2059 mutations and eliminate the effectiveness of dual therapy.

Research in antibiotic consumption

Antimicrobial use in cancer patients admitted to hospital in England, 2016

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Introduction: Increasing antimicrobial resistance poses a significant threat to modern day medicine. Antimicrobials are critical for the treatment of infections, particularly in cancer patients who may have compromised immune systems. To improve our understanding of the potential impact of resistance in this patient population, we conducted a study to estimate the proportion of cancer patient admissions involving the use of antimicrobials during 2016 in England.

Methods: Data from the 2016 national point prevalence survey (PPS) on healthcare-associated infections and antimicrobial usage were analysed to ascertain the proportion of cancer patients receiving at least 1 antimicrobial on the day of the survey. Patients on haematology or oncology wards were used as a proxy for cancer diagnosis. Proportion of patients receiving antimicrobials was estimated through application of a random effects model to account for variation by hospital trust.

Results: The PPS contained data from 48,312 inpatients. 1,707 (3.5%) patients were on haematology or oncology wards at time of survey. 926 patients (54%, 95% confidence interval 50–59) received at least 1 antimicrobial. 1,591 antimicrobial prescriptions were captured: 57% were prescribed for treatment and 32% for medical prophylaxis to prevent infection. The most commonly prescribed agents were piperacillin/tazobactam (15%), meropenem (9%) and ciprofloxacin (7%).

Discussion: Antimicrobial resistance has great potential to undermine cancer treatment. Results from this study indicate that a large proportion of cancer patients receive antimicrobials during the course of their treatment. It is essential that antimicrobials remain effective in this patient population.

Investigating the trend in primary care antibiotic prescribing for respiratory tract infections

Sabine Bou-Antoun, Ceire Costelloe, Benedict WJ Hayhoe, Alan P Johnson, Paul Aylin

Objectives: To investigate whether there has been a decrease in total and broad-spectrum antibiotic prescribing for respiratory tract infections in primary care, and whether this reduction is seen in particular age groups.

Method: A descriptive study of the changing trends in antibiotic prescribing in England. The study population includes all patients with a permanent status in up-to-standard English GP practices (ie data reported meets a data quality criteria), who have consulted for acute respiratory tract infections during the study period of April 1st, 2011

– March 31st, 2017. The antimicrobial drugs included in the study are based on antimicrobial drugs listed in the British National Formulary (listed in chapter 5.1 Antibacterial drugs, excluding anti-tuberculosis drugs and anti-leprotic drugs). Sub-group analysis by broad-spectrum and overall antibiotic prescribing and by age group has been completed.

Results: The study population consists of 3,411,367 patients who have consulted with a respiratory tract infection, 2,389,670 of whom were prescribed an antibiotic over the study period, April 2011-March 2017. Trends in the rate of respiratory tract infection consultations which were prescribed an antibiotic have continued to decrease, with the greatest decrease in the past couple of months seen in broad-spectrum penicillins. The results will be discussed with further detail in the presentation.

Conclusions: Findings from the study will provide current estimates of primary care prescribing for respiratory tract infections, in the context of previous trends, and highlights the growing importance of antimicrobial stewardship in primary care.

Age-related decline in primary care antibiotic prescribing for patients with uncomplicated respiratory tract infections following the introduction of the Quality Premium in England: Interrupted time series analysis.

Ceire Costelloe, Kate Honeyford, Mahsa Mazidi, Benedict W.J. Hayhoe, Alison Holmes, Alan P. Johnson, Paul Aylin

The problem: The use of antibiotics globally and in England is widespread and the subsequent presence of bacteria resistant to these antibiotics is increasing. Various international and national policy and initiatives advocate the judicious and appropriate use of antibiotics with the intention of easing the rate of resistance. In 2015/16 the Quality Premium (QP), an England-wide scheme, introduced a financially incentivised measure to reduce unnecessary antibiotic prescribing, a known driver of antibiotic resistance, in primary care by 1% of total antibiotics and 10% broad-spectrum antibiotics. We investigated whether the introduction of the QP was associated with reduced prescribing in primary care for uncomplicated respiratory tract infections (RTIs) and whether this varied by age.

The approach: The study population was obtained from the Clinical Practice Research Datalink database and included patients with a permanent status in up-to-standard English GP practices, who consulted for acute uncomplicated RTIs during the study period of April 1st, 2011 – March 31st, 2017. Consultations were grouped into: acute otitis media, rhinosinusitis, sore throats, upper RTIs, lower RTIs, viral RTIs. Antibiotic prescriptions were linked to a patient's consultation if both occurred on the same day. The antibiotic therapy codes were identified using the British National Formulary subchapter 5.1 (excluding anti-tuberculosis drugs and anti-leprotic drugs). The analyses used a segmented regression of interrupted time series, a strong-quasi

experimental design, fitting monthly data to an Autoregressive Moving Average (ARMA) model to assess the impact of the QP (2015/16) on antibiotic prescribing and broad-spectrum antibiotic prescribing by General Practitioners for RTIs. We examined trends in prescribing for children, adults and elderly.

Findings: Prescribing rates decreased over the study period, with a significant drop in the level of antibiotic prescribing of 14.65 per 1,000 consultations ($p < 0.05$) from April 2015, coinciding with the introduction of the QP. A year after implementation there was a 3% relative reduction in antibiotic prescribing for RTI consultations, with this reduction being sustained after 2 years. There was a concurrent slight reduction in the rate of broad-spectrum prescribing after the introduction of the QP. Antibiotic prescribing of RTI consultations for children exhibited the greatest decline with a 6% relative change in this age group 2 years post-QP. Of the RTI indications studied, the greatest reductions in antibiotic prescribing were seen in patients who consulted for sore throats post-QP. The reduction in antibiotic prescribing did not have a concurrent effect on re-consultation rates.

Consequences: Reviews of the impact of the QP 2015/16 on antibiotic prescribing have not yet examined the specific effect on underlying indications consulted for in primary care or derived age-related prescribing trends. Our results provide support that there was a decrease in antibiotic prescribing, and informs on which groups of patients and infection types have been most affected.

Estimating inappropriate antibiotic prescribing in secondary care in England: analysis of the 2016 healthcare-associated infection and antimicrobial usage point prevalence survey

Rachel Freeman, Anne Doble, Jasmin Islam, Graeme Hood, Diane Ashiru-Oredope, Susan Hopkins

Background: Overuse of antibiotics has been associated with the development of antibiotic resistance. The UK government has set an ambition to reduce inappropriate antibiotic prescribing by 50% by the year 2020. The aim of our study was to estimate the proportion of inappropriate antibiotic prescribing occurring in secondary care in England.

Methods: We analysed data collected from the 2016 national healthcare-associated infection and antimicrobial usage point prevalence survey was analysed. Analysis was restricted to the 4 commonest conditions: community-acquired pneumonia (CAP), bronchitis, cystitis and pyelonephritis.

Prescribed antibiotic and duration of therapy were compared to national guidelines and expert elicitation to generate a level of agreement between guidance and practice.

Results: There were 5242 patients accounting for 6848 antibiotic prescriptions. The median age of patients was 77 years and 51.8% of patients were female. The most common indication for antibiotics was CAP (4078, 59.6%), followed by complicated cystitis (1010, 14.7%), bronchitis (1006, 14.7%), pyelonephritis (528, 7.7%) and uncomplicated cystitis (226, 3.3%).

Across all conditions, 5131 (65.2%) of antibiotics prescribed were in agreement with national guidelines. 591 (8.6%) prescriptions exceeded the maximum duration recommended in national guidelines.

Conclusions: Our findings suggest that improvements in antibiotic prescribing can be made. A limitation of our study is that it was not possible to ascertain patient co-morbidities from the dataset; further work on estimating comorbidity through modelling McCabe score and linking to datasets that capture Charlson comorbidity index is planned. Our results provide insight into prescribing practices in secondary care and will be used to model estimates of inappropriate prescribing to inform the government's ambition.

Assessing the potential for reductions to inappropriate antibiotic prescribing for surgical prophylaxis in English secondary care, through analysis of the 2016 national point prevalence survey data

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Introduction: In 2016, the UK government set an ambitious target to reduce inappropriate prescribing by 50% by 2020. Within secondary care, antibiotic prescribing for surgical prophylaxis is a potential target area for improvement although the extent of inappropriate prescribing is unknown. This work highlights inappropriate antimicrobial use (AMU) in surgical prophylaxis at a national level and provides estimates for the safe reduction of AMU.

Methods: Data collected during the 2016 national point prevalence survey (PPS) in English secondary care were analysed. Proportion of inappropriate surgical prophylaxis AMU estimates were derived. Appropriateness was assessed based on national guidance, which recommends surgical prophylaxis be given as a single dose with repeated doses for prolonged surgery beyond the half-life of the antibiotic. Prophylaxis was considered inappropriate if administered as more than 2 doses or prescribed for more than 1 day.

Results: The 2016 PPS captured data on a total of 1653 surgical prophylaxis prescriptions, from 75 NHS trusts (n=1112 patients) and 6 independent sector hospitals

(n=54). There were differences observed in the proportion of inappropriate prescribing by hospital type ($p < 0.001$). 40% of prescriptions were administered as more than 1 dose, (31% >2 doses) and 21% were given for over 1 day. The proportion of inappropriate prescriptions varied by age (paediatrics = 65%, adults = 34%; $p < 0.001$).

Conclusion: This work has identified that a considerable proportion of surgical antibiotic prophylaxis in English secondary care may be inappropriate. Surgical prophylaxis therefore represents a key target area for future quality improvement initiatives.

Identifying English practices that are high antibiotic prescribers accounting for comorbidities and other legitimate medical reasons for variation

Hope E, Crump RE, Hollingsworth TD, Smieszek T, Robotham JV, Pouwels KB

Background: Seeing one's practice as a high antibiotic prescriber compared to general practices with similar patient populations can be one of the best motivators for change. Current comparisons are based on age-sex weighting of the practice population for expected prescribing rates (STAR-PU). Here, we investigate whether there is a need to additionally account for further potentially legitimate medical reasons for higher antibiotic prescribing.

Methods: Publicly available data from 7,297 general practices in England between April 2014 and March 2015 were used. We built 2 different negative binomial regression models to compare observed versus expected antibiotic dispensing levels per practice: 1 including comorbidities as covariates and another with the addition of smoking prevalence and deprivation. For both models we used number of STAR-PU's per practice as the offset and subsequently compared the ranking of practices in terms of items prescribed per STAR-PU according to i) conventional STAR-PU methodology, ii) observed – expected prescribing levels using the comorbidity model, and iii) observed – expected prescribing levels using the full model.

Findings: The median number of antibiotic items prescribed per practice per STAR-PU was 1.09 (25th -75th percentile, 0.92-1.25). There was variation in which 1460 (top 20%) practices were identified as the highest antibiotic prescribers by the 3 different methods. The 3 methods agreed on 1134 practices (77.7% of 1460) being high antibiotic prescribers. However, some practices that would be classified as high prescribers using the current STAR-PU methodology would not be classified as high prescribers if comorbidity was accounted for (n=258, 17.7%) and if additionally smoking prevalence and deprivation were accounted for (n=301, 20.6%).

Interpretation: Current age- sex weighted comparisons of antibiotic prescribing rates in England is fair for many, but not all practices. Some practices can legitimately claim that they have a more frail patient population and prescribe, in line with guidelines in

England, more antibiotics than other practices. This new metric that accounts for legitimate medical reasons for higher antibiotic prescribing may have more credibility among general practitioners and, thus, more likely to be acted upon.

A pilot study to investigate antibiotic prescribing in private dental practice.

Nikolaus Palmer and Henry Clover on behalf of the dental subgroup of ESPAUR

Dentists working in NHS primary care account for almost 9% of all the oral antimicrobials prescribed in England, although recent data has shown a reduction in antibiotic prescribing.³ Evidence of the inappropriate use of antibiotics in dentistry is well-documented, contributing to the problem of increasing AMR.⁴⁻⁸ Unfortunately, no evidence is available on the prescribing practices of solely private dental practitioners. It is assumed that private dental practitioners do not use NHS FP10 prescription forms for pharmacies to dispense antibiotics, but rather prescribe using a private prescription or dispense from their own stock.

As there is a clear link between the consumption of antibiotics in both primary and secondary care and the increasing rates of resistance, investigating the prescribing practices of private dental practitioners is a timely and useful task.⁹

Method: A questionnaire was designed to collect demographic information from dentists in private dental practice including eg age, gender and place of qualification . Information was collected on knowledge of the clinical signs and symptoms indicating prescription of antibiotics in conjunction with appropriate clinical treatment; antibiotic of choice for non-allergic patients and patients allergic to penicillin including dose, frequency and duration.

Antibiotic prophylactic regimens (eg for placement of implants) were also investigated in addition to whether a private prescription was provided for dispensing at a pharmacy, or whether antibiotics were dispensed directly to patients from the practice's purchased supply. Information was also collected on the number of times/month antibiotics were prescribed along with whether antibiotic prescribing was audited and against what standards.

The sample selected was a convenience sample utilising private dental practitioners registered to provide services under DENPLAN, the UK's leading dental payment plan specialist. Only dental practitioners providing private treatment were invited to take part. Dental practitioners who provided a mix of NHS and private services were excluded from the study.

DENPLAN administered and distributed the questionnaire to their members utilising Survey Monkey®, an online survey tool, via a link in their monthly e-Newsletter. The

aims of the survey highlighted DENPLAN's ongoing commitment to antimicrobial stewardship and support of the work of Espaur.

All the responses were imported from the SurveyMonkey® excel database into SPSS and analysed.

Results: 3967 emails were sent to DENPLAN members with only 1128 (30.9%) opening the email. 163 dental practitioners clicked on the link in the Monthly e-Newsletter. Of the 163 members who clicked on the link 53 members went on to complete the survey.

Of the 53 respondents 35 (66%) were male and 18 (34%) were female. There was a wide distribution of age ranges with the majority within the 51-60 year age band.

Most of the respondents were aware of the clinical signs indicative of the need for antibiotics. All respondents recognised that an elevated temperature associated with a dental infection necessitated antibiotics with most also recognising gross diffuse swelling (49,92.5%), difficulty in swallowing (47,88.7%) or closure of the eye due to swelling (50,94.3%) require antibiotics as an adjunct to definitive management of the cause. A small number (12,22.6%) would incorrectly prescribe antibiotics for a localised fluctuant swelling where local measures eg incision and drainage are effective. The first choice of antibiotic, where there is no allergy to penicillin, correctly chosen by 49 (92%) respondents was amoxicillin and the majority prescribed the recommended dose of 500mg 3 times daily with 31 (58%) prescribing for the recommended duration of 3- 5 days.

The majority would prescribe metronidazole (34, 64.2%) as an alternative for patients allergic to penicillin as recommended in guidelines. Surprisingly erythromycin would be prescribed by 13(24.5%) as an alternative despite well documented adverse side effects and known levels of resistance. Clarithromycin, a better alternative, would be prescribed by some of the respondents(3, 5.7%). Very few (2, 3.8%) would inappropriately prescribe clindamycin or cephalosporins.

With regard to prophylactic antibiotics a small number (7, 13.2%) of respondents did not provide any prophylaxis or would seek advice from a consultant. The majority (31, 58.5%) used the recommended antibiotic at a dose of 3g 1 hr preop although a range of doses was employed (Table 1). For patients allergic to penicillin clindamycin 600mg 1 Hour preop was used as recommended by the majority who provided prophylaxis for eg implants. Surprisingly metronidazole was prescribed by a small number (10, 18.9%) with clarithromycin and erythromycin also used incorrectly for prophylaxis.

Table 1. Prophylactic antibiotic regimens used by respondents (eg for implants)

1	Antibiotic	2	Dose	3	Frequency	4	Percent
5	Amoxicillin	6	3g 1 hr preop	7	31	8	58.5
9	Amoxicillin	10	3g +500mg 6hrs later	11	5	12	9.4
13	Amoxicillin	14	3g 1hour preop+500mg tds for 5 days	15	1	16	1.9
17	Amoxicillin	18	1g 1hr preop+ 250mg tds for 5 days	19	1	20	1.9
21	Amoxicillin	22	250mg	23	1	24	1.9
25	Pen V	26	2g 1 hr preop+ 1g 6hrs later	27	1	28	1.9
29	Clindamycin	30	600mg 1 hr preop	31	3	32	5.7
33	Metronidazole	34	400mg	35	0	36	0
37	Advice from consultant	38		39	3	40	5.7
41	No prophylaxis given	42		43	7	44	13.2

Of the number of practitioners (26 , 50%) who provided private prescriptions, the majority prescribed < 6 courses of antibiotics /month. Of those who dispensed antibiotics directly(35,66%) most dispensed < 6 courses of antibiotics /month. It should be noted that practitioners provided both private prescriptions to a pharmacy for dispensing and dispensed antibiotics.

When asked whether the respondents carried out audit of their antibiotic prescribing 45% of sample did not presently audit their antibiotic prescribing. Of those that did the majority used FGDP guidance for the standard, with SDCEP and NICE also used.

Conclusions: This study was undertaken as a pilot study to gain some understanding of private dental practitioners knowledge of indications for and their prescribing of antibiotics. Only a very small number of private dental practitioners responded from the convenience sample taken from DENPLAN practices. A more comprehensive study that engages a wider cross section of private dental practitioners may be of value.

From this pilot study it would appear that the majority of the private practitioners who responded are aware of the clinical indications for therapeutic prescribing. Most would prescribe the correct antibiotics at the correct dose/frequency and duration and those that do prescribe prophylactically (eg for implant placement) mostly would prescribe appropriately.

Private dental practitioner prescribing/dispensing of antibiotics/month is generally low with less than prescriptions or courses of antibiotics dispensed/month, approximately half the number of courses prescribed by dental practitioners in NHS practice. Only

55% of this sample audited their antibiotic prescribing, a concern as this is a legislative requirement of the Health and Social Care Act Code of Practice.

Point prevalence audit of care home residents and carers across the UK in the appropriate use of antibiotics

Tracey Thornley, Charlotte Kirkdate, Diane Ashiru-Oredope, Elizabeth Beech, Philip Howard, Heather Elliott, Claire Harris, Alex Roberts

Presented at 78th FIP World Congress of Pharmacy and Pharmaceutical Sciences 2018.

Antimicrobial resistance (AMR) is a major public health problem, causing patient safety issues for individuals and health systems worldwide. There are over 420k people aged 65 years and older living in residential care in the UK¹, of which most of the healthcare needs are provided by the care home staff. Provision of healthcare services for residents in care homes is variable, and can result in disjointed care between carers and NHS healthcare professionals². Patients in care homes are associated with higher rates of antibiotics use, particularly for UTIs³. Providing high quality care for care residents requires close collaboration between NHS healthcare providers and care homes; collecting data in this setting to provide evidence of value can be complex and challenging. Purpose of audit was to understand use of antibiotics in the care home setting, and to identify potential gaps in knowledge and support for carers and residents when using antibiotics; with the aim of identifying how community pharmacy teams can provide additional support.

Point prevalence audit conducted when community pharmacists (n=57) carried out pharmacy advice visits to care homes across the UK between 13th November and 12th December 2017 as part of their routine visits. Anonymised data were recorded electronically by the individual pharmacists capturing type of home (care / nursing / other), number of residents in home on date of visit, number of residents taking antibiotics on that date, whether any antibiotic training was in place for staff, and if the home operated a catheter passport scheme. For patients on an antibiotic; whether they were over 70 years old, if any missed doses, and if so, reason why, type of treatment (prophylaxis / therapeutic), reason for antibiotic, whether the patient was catheterized, where the antibiotic was prescribed, who prescribed it, and whether it was done remotely or in person. Whilst the pharmacists were not asked to make any special interventions as part of the audit, they did record whether they made any clinical interventions based on any information collected. Individual pharmacists sent information they collected to a central point to be amalgamated and analyzed using Excel. Ethics approval was not required as this was an audit conducted on records held by the pharmacy organisation as part of service delivery to residents.

Data was analysed for 17,917 residents across 645 care homes. More than 2 thirds of all care homes visited had at least 1 resident on antibiotics on the day of the visit. Mean percentage of residents in care home on antibiotics on day of visit was: 6.3% England (536 homes), 7.6% Northern Ireland (35 homes), 8.6% Wales (10 homes), 9.6% Scotland (63 homes). Of those taking antibiotics, quarter were for prophylactic use. Antibiotic training had been completed in 9.9% nursing homes, and 6.5% care homes (overall 6.8%). Catheter passport scheme was in place for 13.1% nursing homes, and 5.5% care homes (overall 7.1% homes). Majority of antibiotics were prescribed in the home, by a general practitioner, and in person (see Figure 2). Missed doses were recorded for 9.4% of antibiotics prescribed, with refusal by the patient being the most common reason, followed by sleeping. During the audit, pharmacists intervened with 9.5% antibiotics prescribed; 53.4% were for clinical / allergy check; 32.2% were for issues with timing and continuation.

Whilst these results only provide a snapshot in time of antibiotic use within care home, they do help to highlight the use of antibiotics in these environments, particularly for prophylactic use. The majority of antibiotics were prescribed within the care home by the GP, resulting in a heavy resource drain for the NHS. Very few staff had received training in antibiotics, and given the high turnover of staff in this type of sector, can result in problems with maintaining staff knowledge and awareness. Issues were identified with missed doses due to resident refusal or sleeping, and with timing and continuation of therapy, which could have been potentially resolved prior to the situation arising.

Working collaboratively with the community pharmacy team would enable carers to identify early signs of infection with residents and treatment using homely remedies. This gap in knowledge may have contributed to the high numbers of residents being prescribed antibiotics. Training programmes should support staff in self care advice, recognising warning symptoms with minor infections, use of antibiotics; with ongoing support from the pharmacy team. Dispensing of antibiotics for care home residents is done by community pharmacists; the data reinforce the importance of clinical and allergy checks at the point of dispensing to ensure any issues are identified and resolved at an early stage, enabling the resident to have an effective treatment as soon as is needed.

There is a role for pharmacy teams working collaboratively to support the appropriate use of antibiotics within the care home environment. This includes ongoing training and support for carers on self care for residents (recognising warning signs), and practical advice on how to support residents in taking antibiotics (such as timings and dose form). Carers need to work closely with community pharmacists to ensure any allergy issues are identified at point of dispensing.

Research in antifungal resistance, prescribing and stewardship

Prevalence of *Candida auris* in patients admitted to intensive care units in England

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Background: *Candida auris* is an emerging multi-drug resistant fungal pathogen associated with bloodstream, wound, and other infections, especially in critically ill patients. *C. auris* is difficult to eradicate from hospitals, with prolonged outbreaks reported globally. In England, 225 cases have been reported since 2013 (164 colonisations and 61 infections including 31 candidaemias) across 22 hospitals with 3 significant outbreaks in specialist units. MALDI-TOF or genotypic methods are generally required for effective *C. auris* identification. Currently, English hospitals are advised to consider admission screening based on local risk assessment. We piloted universal screening of adults admitted to intensive care units (ICU) to estimate the admission prevalence in the ICU population and inform public health guidance.

Methods: Eight geographically dispersed ICUs, serving ethnically diverse populations reflective of the worldwide distribution of *C. auris*, were selected for inclusion in the study. Multi-body-site screening was used including nose, throat, axilla, perineum, rectal, and catheter urine (where available) for all adult (18+) admissions, between May 2017 and March 2018. *C. auris* identification was performed using Chromogenic agar and MALDI-TOF.

Results: In total 953 adults were screened. All *C. auris* screens were negative (95% CI: 0.00-0.39%). Data linkage and descriptive analysis will be completed by June 2018 to obtain clinical and demographic information about the cohort tested and compare with national indicators.

Conclusions: Based on the low prevalence, we would not recommend universal screening in ICUs in England. Hospitals should continue to screen high-risk individuals (eg previously colonised) in high-risk settings (eg ICUs). All invasive *Candida* infections and isolates from normally sterile sites should be identified to species level.

Further research is needed to characterise risk factors for *C. auris* colonisation and disease.

Azole-resistance in *Aspergillus terreus* and related species: an emerging problem or a rare phenomenon⁸¹

Objectives: Invasive mould infections associated with *Aspergillus* species are a significant cause of mortality in immunocompromised patients. The most frequently occurring aetiological pathogens are members of the *Aspergillus* section Fumigati followed by members of the section Terrei. The frequency of *Aspergillus terreus* and related (cryptic) species in clinical specimens, as well as the percentage of azole-resistant strains remains to be studied.

Methods: A global set (n=498) of *A. terreus* and phenotypically related isolates was molecularly identified (beta-tubulin), tested for antifungal susceptibility against posaconazole, voriconazole, and itraconazole, and resistant phenotypes were correlated with point mutations in the *cyp51A* gene.

Results: The majority of isolates was identified as *A. terreus* (86.8%), followed by *A. citrinoterreus* (8.4%), *A. hortai* (2.6%), *A. alabamensis* (1.6%), *A. neoafricanus* (0.2%), and *A. floccosus* (0.2%). One isolate failed to match a known *Aspergillus* sp., but was found most closely related to *A. alabamensis*. According to EUCAST clinical breakpoints azole resistance was detected in 5.4% of all tested isolates, 6.2% of *A. terreus sensu stricto* (s.s.) were posaconazole-resistant. Posaconazole resistance differed geographically and ranged from 0% in the Czech Republic, Greece, the Netherlands, Turkey to 13.7% in Germany. In contrast, azole resistance among cryptic species was rare (0.2%) and was observed only in 1 *A. citrinoterreus* isolate. The most affected amino acid position of the Cyp51A gene correlating with the posaconazole resistant phenotype was M217, which was found in the variation M217T and M217V.

Conclusions: *A. terreus* was most prevalent, followed by *A. citrinoterreus*. Posaconazole was the most potent drug against *A. terreus*, but 5.4% of *A. terreus sensu stricto* showed resistance against this azole. In Austria, Germany, and the United Kingdom posaconazole-resistance in all *A. terreus* isolates was higher than 10%, resistance against voriconazole was rare and absent for itraconazole.

Determination of the Prevalence of Triazole Resistance in Environmental *Aspergillus fumigatus* Strains Isolated in South Wales, UK

⁸¹ Zoran et. al. Frontiers

Alexandra Tsitsopoulou, Raquel Posson, Lorna Vale, Scarlett Bebb, Elizabeth Johnson, P. L. White

Background/Objectives: Azole resistance in *Aspergillus fumigatus* associated with the TR34/L98H mutations in the *cyp51A* gene have been increasingly reported. Determining the environmental resistance rate has been deemed important when considering front-line therapy for invasive aspergillosis. The aim of the study was to determine prevalence of azole resistance in environmental *A. fumigatus* isolates across SouthWales.

Methods: Over 5 months in 2015, 513 *A. fumigatus* isolates were cultured from 671 soil and 44 air samples and were screened for azole resistance using VIPcheck™ agar plates containing itraconazole, voriconazole and posaconazole. Resistance was confirmed by the CLSI M38-A2 methodology. The mechanism of resistance was investigated using the PathoNostics AsperGenius® Assay.

Results: Screening by VIPcheck™ plate identified azole-resistance in 30 isolates, most of which (28/30) harbored the TR34/L98H mutation, generating a prevalence of 6.0%. Twenty-five isolates had a MIC of ≥ 2 mg/L with itraconazole, 23 isolates had a MIC of ≥ 2 mg/L with voriconazole and 7 isolates had a MIC ≥ 0.25 mg/L with posaconazole. All isolates deemed resistant by VIPcheck™ plates were resistant to at least 1 azole by reference methodology.

Conclusions: There is significant environmental azole resistance (6%) in South Wales, in close proximity to patients susceptible to aspergillosis. Given this environmental reservoir, azole resistance should be routinely screened for in clinical practice and environmental monitoring continued.⁸²

Research in antimicrobial stewardship

Antibiotic consumption in care homes across the United Kingdom; baseline data
Tracey Thornley, Diane Ashiru-Oredope, Andrew Normington, Elizabeth Beech, Philip Howard.

Presented at 78th FIP World Congress of Pharmacy and Pharmaceutical Sciences 2018

Background: Antimicrobial resistance (AMR) is a major public health problem which could ultimately prevent the treatment of common bacterial infections; resulting in simple operations becoming high risk procedures. Antimicrobial resistance is a problem

⁸² Tsitsopoulou et. al. *Frontiers in Microbiology*. June 2018, Vol 9, 1395; doi: 10.3389/fmicb.2018.01395

Worldwide, and international efforts exist to try and deal with the issues. Within the United Kingdom, the Government are committed to supporting the appropriate use of antibiotics, and in 2016, set a target to reduce inappropriate prescribing by 50% by the year 2020¹. Inappropriate use of antibiotics includes prescribing an antibiotic in the absence of evidence or clear rationale of a bacterial infection, and continuation of course beyond recommended guidelines².

Research published by Public Health England has quantified the level of inappropriate prescribing in primary care in England as 20%³; suggesting that levels of prescribing should be reduced to 10% to meet the Government target. There are over 460k residents in care homes in England⁴, the majority of which are elderly and have complex healthcare needs that are exasperated with multiple co-morbidities and medicines related issues surrounding polypharmacy. Nurses and Carers in care homes provide the majority of long term care for older people within the UK, helping residents to live in an environment they can call home where quality of life matters. Providing high quality care for care home residents requires close collaboration between NHS healthcare providers and care homes, supporting both residents and carers themselves. Residents in these settings are known to be associated with higher rates of antibiotics use, particularly for Urinary Tract Infections⁵, a 2016 PPS in Australia reported 9.7% of residents prescribed antibiotics, most frequently for pneumonia, UTI, skin and soft tissue infections⁶.

Within England, annual prescriptions for antibiotics in those aged 75 years and older increased from 142 to 199/100 among those living in a care home⁵. Collecting data in care homes to understand healthcare needs of residents and carers, and provide evidence of value can be complex and challenging as these environments are residents' homes, and not NHS healthcare settings. The objective of this study was to understand the scale of antibiotic use in care homes across the UK, as part of a wider piece of working looking at additional roles of community pharmacists in supporting both residents and carers.

Methods: This was a retrospective longitudinal cohort study. Anonymised data were extracted using SQL query analyser from a national pharmacy chain database on NHS prescriptions dispensed for residents in care homes across the United Kingdom for 12 months from November 2016 to October 2017. Data fields extracted were: anonymised patient identifier, dispensed date, drug name, code, form, strength, pack size, dosage directions and dispensed quantity. Period of treatment was calculated using fields of quantity dispensed and dosage instructions, and was calculable for 75.6% of antibiotics. All analysis was conducted in Excel. Ethics approval was not required as the study was based on an internal audit of anonymised data to help inform service development to the care home resident population serviced by the national pharmacy chain.

Results: Data were analysed for 341,536 residents in care homes across the UK (287,912 England, 28,076 Scotland, 16,409 Wales, and 9,139 Northern Ireland). The percentage of residents receiving any antibiotic during a 12 month period was: 56.6% Northern Ireland, 53.2% Scotland, 48.5% England, and 45.0% Wales. The mean percentage of care home residents on antibiotics each month by Country was 21.4% Northern Ireland, 17.4% Scotland, 16.6% England, and 16.0% Wales, with peaks during months of December and January.

Half of patients (52.1%) were dispensed 1 antibiotic drug type over the 12 month period, a quarter (27.5%) were dispensed 2 types, 12.9% 3, and 5.1% 4 (remaining 2.4% were dispensed between 5 and 10 types). Figure 1 shows the distribution of the number of courses of antibiotics per patient over the 12 month period which is positively skewed, with a median of 2 (full range from 1 to 77). Here, the definition of course could include the same antibiotic being dispensed multiple times over the 12 month period. The top 11 most frequently dispensed antibiotics represent 92.8% of all antibiotics dispensed for residents during this time period. It was possible to calculate period of treatment for 77.0% of these; the results of which are shown in figure 2 (amoxicillin being the highest volume dispensed, and then the remaining antibiotics shown in descending order). Whilst some antibiotics such as amoxicillin had consistent dosage length of between 4-7 days, others such as trimethoprim had wide variability (between 1 and > 28 days)

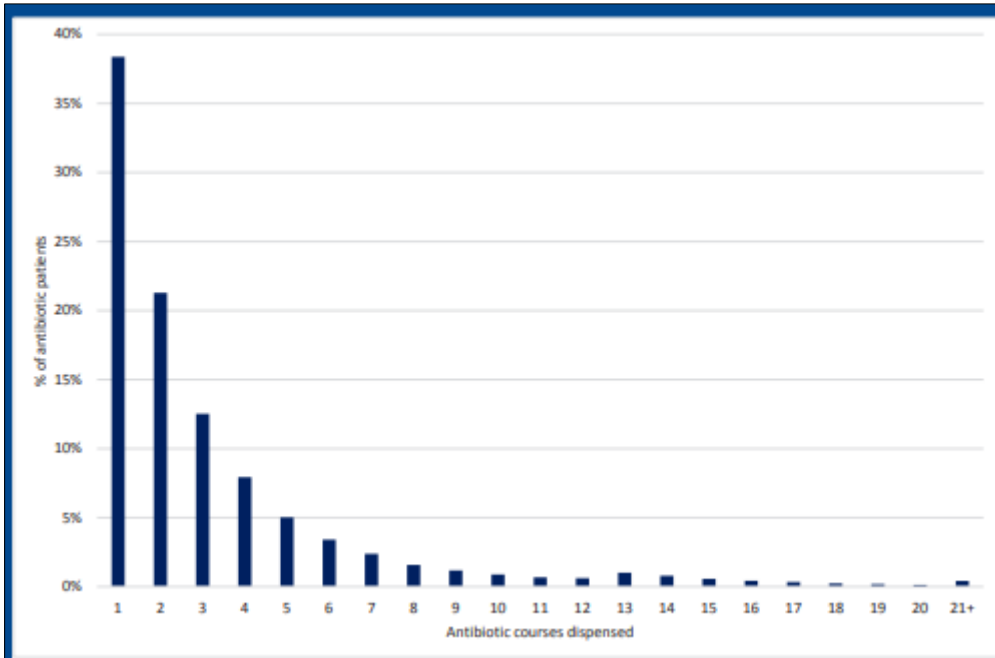


Figure 1. Number of courses of antibiotics per resident over 12 months

Conclusions: Whilst the results presented within this paper are focused on antibiotic use, they highlight the complex needs of some residents within care homes when it comes to these medicines, with some individuals taking multiple courses over 12 months. Rates of antibiotic consumption are higher than seen in previous studies⁶.

Antibiotics can be given in response to unscheduled care which can include prescribing out of hours by healthcare professionals not normally involved in the care of those residents. Pharmacists have a role in supporting the safe and effective use of medicines in care homes, including the use of antibiotics. In 2016 the Government announced the creation of a new Pharmacy Integration Fund (PIF) to enable pharmacists and their teams to spend more time delivering clinical care to patients across NHS settings⁷, including care homes. The fund was created as part of support for the objectives of the Five Year Forward View in delivering efficient and effective care, and supporting integrated working amongst healthcare professionals to support the needs of patients. Integrated working needs to take place amongst healthcare professionals from different disciplines, as well as within disciplines.

Given the acute nature of many antibiotic prescriptions, pharmacists working with care homes need to work alongside pharmacists within the community providing dispensing services to these residents (although with increasing portfolio careers these can often be the same individuals, or within the same teams). Community pharmacy teams dispense acute prescriptions for antibiotics for residents, and can identify potential interactions with current medications, as well as any known allergies. Extending the use of the summary care record would allow pharmacists to provide additional information and advice to residents and carers to enable the antibiotic to be used effectively as part of local guidelines (including period of treatment and associated advice on use). Given the role of carers within the care home environment, there is an opportunity for pharmacy teams to work more closely with them as partners to deliver healthcare to residents, in supporting appropriate and effective use of antibiotics. Pharmacists can also support infection prevention to carers and residents through the national flu vaccination programme

This study provides baseline data of antibiotic use across care homes in the UK, identifying potential areas that pharmacists and their teams can support both residents and carers in the appropriate and effective use of antibiotics. Following the recent focus of pharmacists within care homes as a result of PIF funding, there is an opportunity to consider actions to support carers and residents to tackle AMR across the UK, and revisit the audit at a later date to understand evidence of impact.

Local implementation of national AMS initiatives across Medicines Management teams: a mixed-methods study

Rosalie Allison, Donna Lecky, Elizabeth Beech, Ceire Costelloe, Diane Ashiru-Oredope, Rebecca Owens, Clodna McNulty

Presented at BJGP Research Conference 2018, PHE Health Research and Science Conference 2018, BSAC 2018, PHE Annual Conference 2018, GRIN Conference 2018

Background: The NHS English Quality Premium recommends that inappropriate antibiotic prescribing is reduced; there are a range of national antimicrobial stewardship (AMS) initiatives to support this.

Aim: To assess AMS activities in primary care across England. The findings will be used to inform how the RCGP, NICE, PHE and NHS can help optimise stewardship activities.

Methods: Questionnaire: informed by qualitative data, sent to AMS leads representing all 209 Clinical Commissioning Groups (CCGs) in England in 2017.

Results and Implications: 89% (187/209) of CCGs returned a questionnaire. 82% of AMS leads reported spending only 0.1 whole-time equivalent on AMS activities, as it was only 1 role within a wider remit, so dedicating time is challenging.

Activities reported:

- 99% (167/169) of CCGs had delivered AMS education in the last 2 years: 140 face-to-face; 121 via e-learning
- 99% (184/186) actively promoted the TARGET Antibiotics Toolkit
- 94% (175/186) actively promoted TARGET patient leaflets: 92% The Treating Your Infection (TYI) leaflet
- 90% (166/185) used the PHE managing common infections guidance: 81% (149/185) modify or localise; 41/185 (22%) signpost directly to it
- 86 used CCG audit tools and 82 used TARGET's audit tools
- 85% (142/168) fed back antimicrobial prescribing data to the CCG/CSU board; 100% (169/169) to general practices and 33% (56/169) to out-of-hours providers

Although CCGs reported promoting these AMS activities, there was little evaluation of uptake by primary care practitioners. Future work should focus on measuring AMS uptake; having staff dedicated solely to AMS could facilitate this.

Infectious disease and primary care research – what GP staff say they need

Lecky DM, Granier S, Jenner I, Allison R, McNulty CAM.

Presented at GRIN Conference 2018.

Introduction: The majority of UK antibiotics are prescribed in primary care. Whilst there have been many diagnostic advances and guidance development in recent years, this study aimed to identify where the perceived gaps in knowledge, guidance and research lie, from the prescriber perspective.

Methods: A questionnaire survey and covering letter was disseminated to GPs between May and August 2017.

Results: 428 GP staff responded. Suspected Infection in the elderly (SIE), recurrent UTI (rUTI), surveillance of antibiotic resistance in the community (AMRsur), leg ulcers (LU), persistent cough (pC) and cellulitis (Cel) all fell into the top 6 conditions ranked in order of importance, and the top 6 most frequently named illnesses/conditions respondents felt required further research, evidence and guidance.

Across all 6 conditions, primary care respondent needs were ranked as follows:

1. Need for better evidence base for antibiotic treatment (SIE, AMRsur, Cel)
2. Need for better evidence base for self-care and non-antibiotic treatment (rUTI, pC)
3. Need for improved treatment guidelines for staff (LU)
4. Need for better point of care prognostic tests
5. Need for better clinical scores to help inform management
6. Need for better near patient antibiotic resistance test

Conclusions: This survey has highlighted broad areas for future involvement with primary care although further consultation with staff and other relevant bodies is required. For some conditions, this may be writing/updating/promoting antibiotic prescribing guidance whilst for others highlighting the current evidence base for, or more research into, self-care and non-antibiotic treatment is required.

Development of resources for the management of urinary tract infections (UTIs) in older adults – qualitative findings specific to decision making and current practice in primary care

Leah Jones, Emily Cooper, Amelia Joseph, Rosie Allison, Natalie Gold, Clodna A.M. McNulty

Presented at Infection Prevention Society Conference 2018.

Introduction: To help decrease E.coli bacteraemia and improve antimicrobial use in older adults, we undertook a needs assessment specific to resources around the diagnosis and prevention of UTI using qualitative methods.

Methods: Focus groups and interviews were held with over 118 GP, nursing and residential home staff, and members of the public. Questions explored diagnosis, management, prevention of UTIs and antibiotic use in older adults, focusing on those in care. A UTI leaflet and diagnostic guide were modified iteratively. Discussions were transcribed and analysed using Nvivo.

Results: Many GP staff relied on urine dip sticks to diagnose a UTI in older adults, though some knew this was unhelpful. The high prevalence of asymptomatic bacteriuria was understood by GP staff, but not untrained care home staffs who were fearful of having no diagnostic test. GP staff were also greatly influenced by the consistent use of dipsticks in care homes.

Carers of older adults reported they had an important role in identifying UTIs in older adults by flagging symptoms such as confusion or changes in behaviour to nurses or GP staff. Many would conduct a urine dipstick before contacting the GP.

All staff welcomed the development of diagnostic guidance for UTIs, and complementary information in parallel to information leaflets that could be shared with patients and carers; promoting consistent messages across the care pathway. Hydration and prevention were highlighted as key areas within the resources and participants thought a colourful leaflet with large print could improve patient care.

Conclusions: Resources should highlight the appropriateness of using urine dipsticks in the diagnosis on UTI in older adults with non-specific symptoms, including clear explanations of asymptomatic bacteriuria and possible alternative causes of confusion. Resources on UTI prevention, pyelonephritis and sepsis would be valued by care staff in particular.

‘Urinary tract infections (UTIs); A leaflet for older adults, and carers’, the development of a UTI leaflet for older adults and their carers

Leah Jones, Emily Cooper, Amelia Joseph, Rosie Allison, Natalie Gold, Clodna A.M. McNulty

Presented at Public Health England Conference 2018.

Introduction: Escherichia coli bacteraemia rates are rising with highest rates in older adults. Mandatory surveillance identifies previous Urinary Tract Infections (UTI) and catheterisation as risk factors. Thus, the aim of this work was to help control bacteraemias in older frail patients by developing a patient facing resource covering the prevention, self-care of UTIs and informed by the Theoretical Domains Framework.

Method: Focus groups and interviews were held with care home staff, residents and relatives, GP staff, an out-of-hours service, public panels and stakeholders. Questions explored diagnosis, management, prevention of UTIs and antibiotic use in older adults. The leaflet was modified iteratively. Discussions were transcribed and analysed using Nvivo.

Results: Carers of older adults reported their important role in identifying UTI in older adults by flagging symptoms to nurses or GP staff and undertaking urine dipsticks.

Information needs to be older adult friendly, using larger text, colour and pictures. Participants welcomed and helped to word sections on describing asymptomatic bacteriuria simply, preventing UTIs, causes of confusion and when to contact a doctor or nurse. Carers were optimistic that the leaflet could impact on the way UTIs are managed. Older adults and relatives liked that it provided new information to them. Staff welcomed that diagnostic guidance for UTIs was being developed in parallel; promoting consistent messages.

Conclusions: A final UTI leaflet for older adults has been developed informed by the TDF. See the TARGET website www.RCGP.org.uk/targetantibiotics/

A qualitative study to explore the views of general practice staff on the use of C-reactive protein point-of-care testing for the management of lower respiratory tract infections and in improving antibiotic prescribing.

Charlotte Eley, Anita Sharma, Donna Lecky, Hazel Lee & Cliodna McNulty

Presented at British Society of Antimicrobial Chemotherapy Conference 2018, Public Health England Health Research & Science Conference 2018

Background: C-reactive protein (CRP) testing can be used as a point-of-care test (POCT) to measure inflammatory markers that increase in bacterial infections.

Objective: To explore the knowledge, skills, attitudes and beliefs of general practice staff about CRP POCT in general practice and associated barriers and facilitators to implement CRP POCT for the management of lower respiratory tract infections and improving antibiotic prescribing; in a CCG where CRP POCT was being trialled to improve use of antibiotics for acute cough.

Design and Methodology: A service evaluation of CRP POCT over a 6 month period was previously conducted in 8 practices from a high prescribing NHS CCG in England. The present study followed a qualitative methodology including interviews and focus groups and used the Com-B framework to understand individuals' capability, opportunity and motivation to implement CRP POCT in general practice. All 8 practices from the service evaluation were invited to participate in qualitative interviews. A further 12 randomly selected control practices, which had not used CRP POCT previously, were also invited to interview. Data was thematically analysed and the behavioural framework was developed.

Results: Seven intervention and 5 control practices consented to participate. Participants comprised of 26 general practice staff; 15 General Practitioner's, 5 Practice Managers, 3 Practice Nurses, and 1 Prescribing Pharmacist, Community Matron and Healthcare Assistant. Qualitative data from 11 interviews, 3 focus-groups and 1 hand written response was collected. Participants believed that CRP POCT can

increase diagnostic certainty, help target appropriate treatments, help manage patient expectations and patient demand for antibiotics, support patient education, and improve appropriate antibiotic prescribing. Barriers to implementing CRP POCT include; financial support, time, access to the CRP POCT machine, and the effects on clinical workflow.

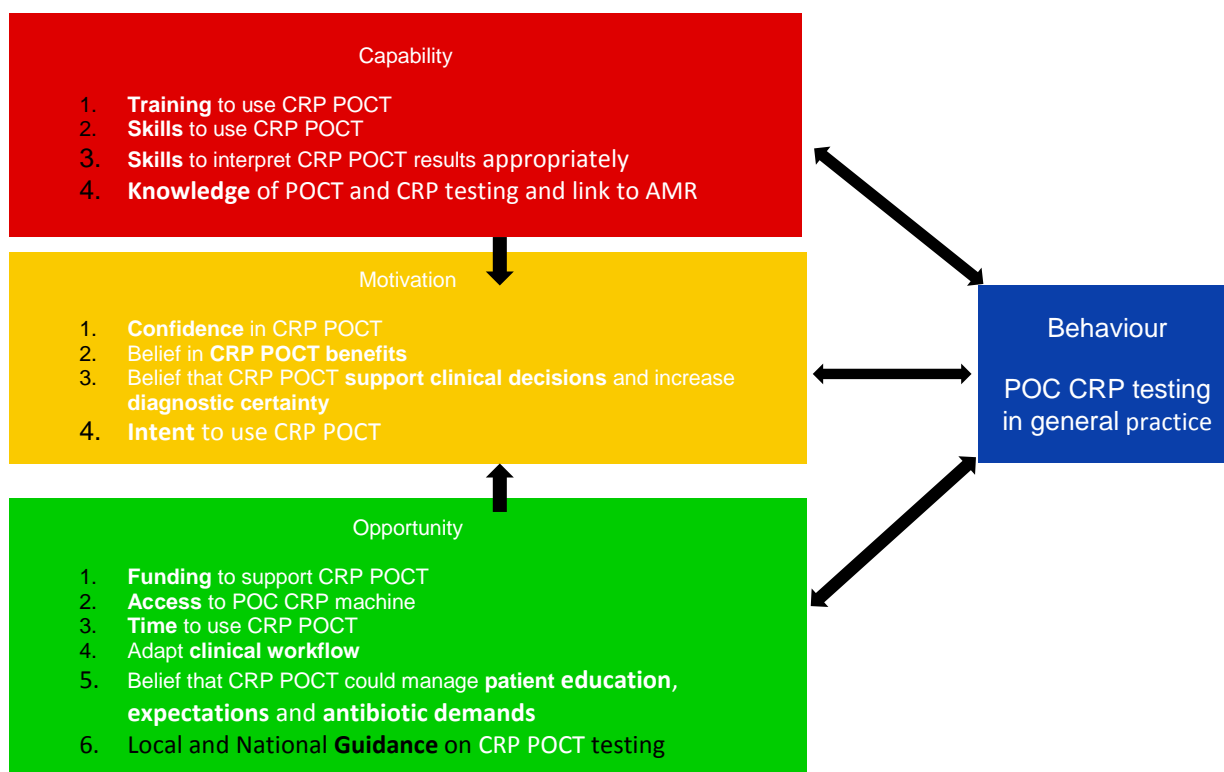


Figure 1: General practice staff's needs to implement the CRP POCT behaviour

Conclusions: CRP POCT was well received by many general practice staff as an additional diagnostic 'tool in your armoury' to support clinical decision making in the management of LRTI. To see an increase in the implementation of CRP POCT, further research into machine development is required, to overcome time, cost and access barriers. Further evidence of the impact of CRP POCT on appropriate antimicrobial prescribing is required to inform future guidance which will be the initial facilitator for behaviour change.

Patient education on appropriate treatment for common RTIs using the TARGET Treating Your Infection leaflet: What do the public need to know about antibiotics?
Charlotte Eley, Donna Lecky, Clodna McNulty

Presented at FIS Conference 2017 and RCGP Conference 2017

Background: The TARGET Treating Your Infection leaflet for RTIs (TYI-RTI) is promoted by 92% of CCGs to facilitate patient/clinician conversation about management choices and encourage appropriate use of antibiotics. Sharing information with patients on the usual length of illness and proposed new leaflet column, 'with antibiotics: may only shorten illness by', may increase understanding of the limited value of antibiotics and enable patients to make an informed decision about the value of self-care versus antibiotics.

The study aimed to explore:

- public understanding of illness durations and treatment expectations
- how the public interpret information on the limited value of antibiotics
- health professional's views on the leaflet

Methods: A feasibility study was conducted to hear public and health professional views on the leaflet; 40 patients in 1 general practice waiting room and 43 infection control professionals at a conference. Responses were used to modify the leaflet and questionnaire. Further data was collected at 3 practices across South West England: 43 patient questionnaires completed and qualitative interviews/focus groups were facilitated with 16 general practice staff.

Results:

Public:

- majority (93%) were happy for their GP to discuss the leaflet with them in consultation
- over half did not know how long common RTIs usually last: middle ear infections (79%); sinusitis (71%); cough (60%); sore throat (56%); common cold was 24%
- key messages understood were: antibiotics are not an appropriate treatment for common RTIs, self-care is the best treatment; usual illness duration; consequences of antibiotic overuse
- some patients would still want to take antibiotics for common RTIs especially once introduced to information in the proposed new column; middle ear infection (40%); cough (33%); sinusitis (15%); sore throat (8%); cold (8%)
- majority reported knowing self-care (93%) and over half knew when to get help (60%)
- only 15% had heard of back up/delayed prescriptions

Health professionals:

- facilitators include: increase patient education, reduce re-consultation rates, self-care advice, safety netting, side-effects, and patients have something to take away with them

- barriers included lack of time in a consultation, printing costs
- modifications suggested: increase text size, remove logos, remove 'without antibiotics' from the column heading, do not include the proposed new column 'with antibiotics'

Conclusions: The public and health professionals were positive about the TYI-RTI leaflet. Public education is still needed especially around usual illness durations and the limited value of antibiotics to enable the public to make an informed decision about their treatment and encourage them to follow their health professional's advice.

Research in professional education and training and public engagement

Young people's knowledge about antibiotics and vaccinations and increasing it through gaming: a mixed methods study using e-Bug.

Charlotte V Eley, Vicki L Young, Catherine V Hayes, Neville Q Verlander, & Cliodna A Miriam McNulty.

Published in the Journal of Medical Internet Research; Serious Games
Presented at British Antimicrobial Chemotherapy Conference 2018, Public Health England Health Research and Science Conference 2018

Background: e-Bug, led by Public Health England, educates young people about important topics; microbes, infection prevention and antibiotics. Body Busters and Stop the Spread are 2 new e-Bug educational games.

Objectives: To determine student baseline knowledge, views on the games and knowledge improvement.

Methods: Students in 5 UK educational provisions were observed playing 2 e-Bug games. Before and after knowledge and evaluation questionnaires and student focus groups were completed.

Results: 123 junior and 350 senior students completed questionnaires. Vaccination baseline knowledge was high. Knowledge increased significantly around antibiotic use, appropriate sneezing behaviours, and vaccinations. 26 student focus groups were conducted. Body Busters was 'engaging' and 'enjoyable'; whereas Stop the Spread was 'fast paced' and 'challenging' but increased vaccination and health behaviour intentions.

Conclusion: e-Bug games are an effective learning tool for students to increase knowledge around microbes, infection prevention and antibiotics. Game suggested improvements should help increase enjoyment.

Keywords: e-Bug, gamification, knowledge, antibiotics, vaccines

A mixed methods pilot of Beat the Bugs: A community education course on hygiene, self-care and antibiotics

Charlotte Victoria Eley, Vicki Louise Young, Catherine Victoria Hayes, Gill Parkinson, Katie Tucker, Nina Gobat & Clodna Ann Miriam McNulty.

Published in the Journal of Infection Prevention 2018.

Presented at the Infection Prevention Society Conference 2017, PHE Health Research and Science Conference 2017.

Background: e-Bug, operated by Public Health England and endorsed by NICE, is an international health education resource supporting public education WHO recommendations by educating young people about microbes, hygiene, and antibiotics use. e-Bug collaborated with Kingfisher Treasure Seekers to develop a 6 session course for community groups called *Beat the Bugs* covering: microbes, hygiene, antibiotic use and self-care. A pilot was used to inform further development and evaluation.

Methods: Pilot courses with 9-12 adults with learning difficulties and young parents were delivered by community leaders and observed by researchers. Participants completed before and after knowledge questionnaires. Two participant focus groups and 2 course leader interviews explored views on the course and retention of knowledge.

Results: Completed questionnaires and qualitative results showed an improvement in participant knowledge in each session; microbes and antibiotics sessions showed the greatest knowledge improvement. Self-care showed the greatest knowledge retention and participants reported behaviour change including an increase in appropriate hand-washing and tooth-brushing.

Conclusion: The *Beat the Bugs* course is a useful intervention for communities to give individuals the knowledge and confidence to manage their own infection and change behaviour around hygiene, self-care and antibiotics. *Beat the Bugs* is freely available to download: www.e-Bug.eu/Beat-The-Bugs

Keywords: Antibiotics, self-care, hygiene, community, education

SafeConsumE: Reducing the health burden of foodborne illnesses across Europe through the development of educational resources for 11-18 year olds

Rowshonara Syeda, Public Health England, Vicki Young, Public Health England; Carla Brown, Public Health England; Clodna McNulty, Public Health England; Pia Touboul Lundgren, University Hospital

Nice; Monica Truninger, University of Lisbon; Tekla Iszo, National Food Safety Chain Office; Gyula Kasza, National Food Safety Chain Office

Background: Foodborne illnesses are global and can be life-threatening, with vulnerable groups such as children and the elderly more at risk. WHO (2015) estimate that bacteria, parasites, toxins and allergens in food cause approximately 23 million foodborne illnesses and 5,000 deaths in Europe annually. SafeConsumE is an EU funded, transdisciplinary project involving 32 organisations from 14 countries. e-Bug, operated by Public Health England are leading the work package on developing educational programmes for 11-18 year olds to reduce these foodborne illnesses.

Aim: The project aims to reduce health burden from foodborne illnesses and antimicrobial resistance by changing consumer behaviours through effective tools, communication strategies and food safety policy.

Methods: A needs assessment, involving focus groups and interviews, is being conducted in the UK, France, Portugal and Hungary to determine student and educator's knowledge, decision processes, skills, intentions and beliefs around food hygiene and food safety. Schools of both high and low socioeconomic status have been randomly selected in all partner countries. Data obtained from interviews and focus groups will be transcribed verbatim and imported into qualitative data software NVivo and analysed in accordance with the frameworks Theory of Practices and Theoretical Domains Framework.

Findings: UK data reported that teachers would benefit from additional training on food microbiology and food poisoning and that students' learning may be enhanced by games, interactive activities and role play. Students regarded personal hygiene such as handwashing vital during food preparation but had limited understanding of the causes of foodborne illnesses.

Discussion: These preliminary results highlight the need for new educational resources for students and educators that can improve understanding of food hygiene and may change food hygiene practices, thus helping to reduce foodborne illnesses in the long-term.

Annex Chapter 2: Antibiotic resistance

Methods

Data sources

Data on the antibiotic susceptibility of pathogens causing bacteraemia were obtained from SGSS (Second Generation Surveillance System), a national database maintained by Public Health England (PHE) that contains laboratory data supplied electronically by approximately 98% of hospital microbiology laboratories in England. SGSS comprises 2 modules, a communicable disease reporting (CDR; formerly CoSurv/LabBase2) module and an antimicrobial resistance (AMR; formerly AmSurv) module. The CDR module includes antimicrobial susceptibility test results for bloodstream isolates of the key pathogens covered in this report, although any test results suppressed from clinical reports by the sending laboratories are not captured when the data are submitted. In contrast the AMR module contains more comprehensive antibiogram information as it includes results for all antibiotics tested (including results suppressed from clinical reports) for isolates from all clinical sources. However, when SGSS was launched in 2014, the AMR module had lower laboratory coverage than the CDR module. Although there have been subsequent marked improvements in laboratory reporting to the AMR module of SGSS, analysis of trends in antimicrobial susceptibility for the time period covered by this reporting were undertaken using data from the CDR module.

Hospital microbiology laboratories report antimicrobial susceptibility test results 'susceptible', 'intermediate' or 'resistant'. These categories are defined as follows⁸³:

Susceptible: a bacterial strain is said to be susceptible to a given antibiotic when its growth is inhibited *in vitro* by a concentration of the drug that is associated with a high likelihood of therapeutic success

Intermediate: a bacterial strain is said to be intermediate when the concentration of antibiotic required to inhibit its growth *in vitro* is associated with an uncertain therapeutic outcome at standard antibiotic doses. It implies that an infection due to the isolate may be appropriately treated in body sites where the antibiotic is physically concentrated or when a high dosage of drug can be used

⁸³ Rodloff *et al.* Dtsch Arztebl Int 2008; 105 (69): 657-662.

Resistant: a bacterial strain is said to be resistant to a given antibiotic when the concentration required to inhibit its growth *in vitro* is associated with a high likelihood of therapeutic failure.

The breakpoint criteria for categorising clinical isolates as susceptible, intermediate or resistant to individual antibiotics were those published by the European Committee on Antimicrobial Susceptibility testing (EUCAST).⁸⁴

As patients may have more than 1 positive blood culture taken, blood cultures taken from the same patient that yielded growth of the same pathogen with the same antibiotic susceptibility pattern during a 14-day period from the initial positive blood culture were regarded as comprising the same episode of infection and were de-duplicated.

Data on the incidence of *E. coli* and *Staphylococcus aureus* bacteraemia were from the national mandatory surveillance scheme⁸⁵ while data on the incidence of other pathogens were derived from cases reported to the CDR module of SGSS. As the latter data were provided on a voluntary basis, case ascertainment will have been incomplete. Data on referred isolates confirmed as carbapenemase-producing Gram-negative bacteria were obtained from the Antimicrobial Resistance and Healthcare-Associated Infections (AMRHAI) Reference Unit. Data for resistance in *Neisseria gonorrhoeae* were from the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP), which comprises a network of sentinel genitourinary medicine clinics. Over a 3-month period each year, isolates from consecutive patients with gonorrhoea attending these clinics are referred to PHE's national reference laboratory for antimicrobial susceptibility testing. Isolates are linked to demographic, clinical and behavioural data from the clinics for analysis of antimicrobial susceptibility trends in patient sub-groups.

Estimating the burden of antibiotic resistant bloodstream infections

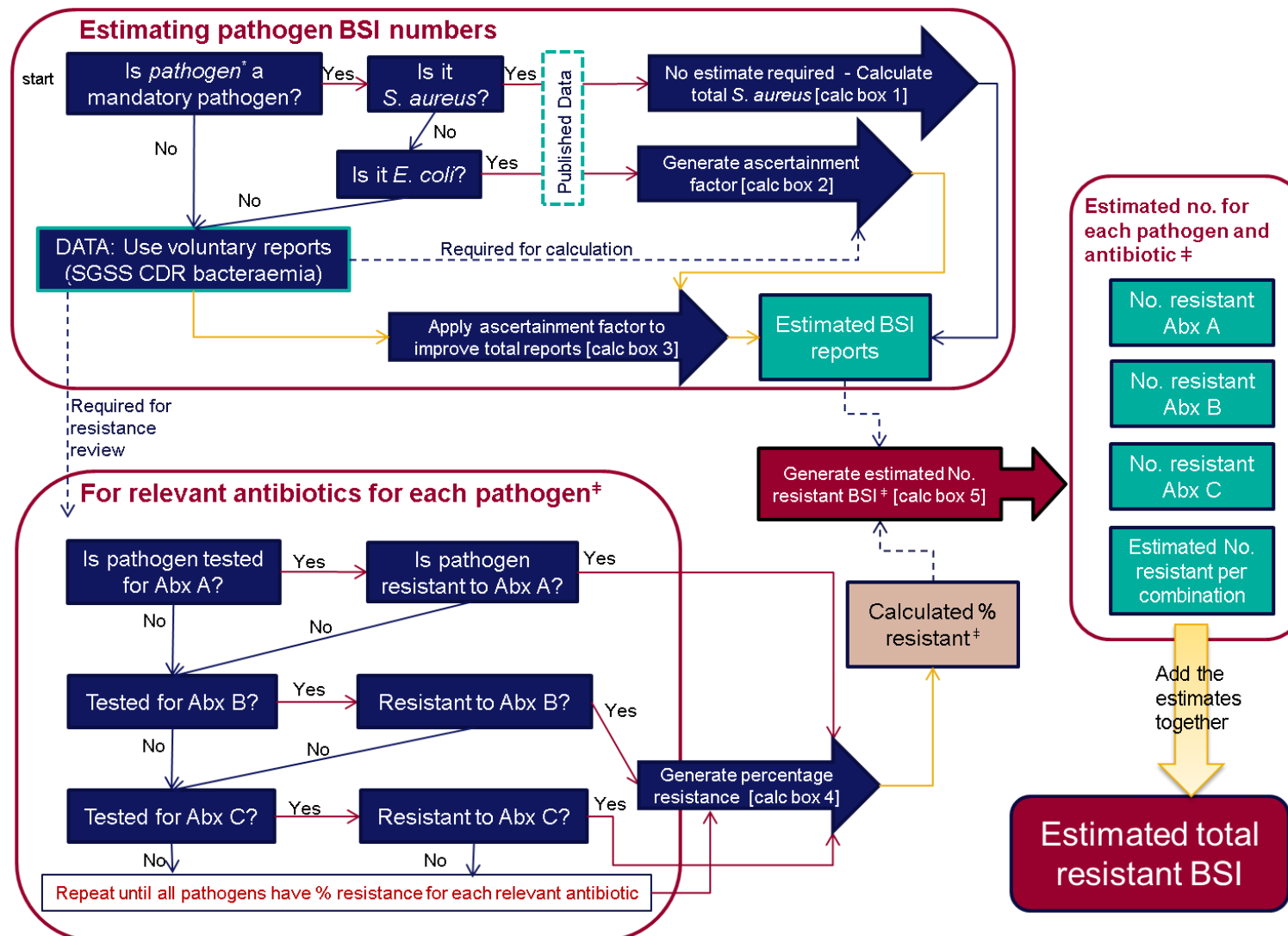
Data used to update the key drug/bug summaries within the ESPAUR report have been utilised to generate an estimated burden of resistant bacteraemia in England. The number of total number of resistant infections is generated by calculating the proportion of the pathogen that have been tested as resistant to an antibiotic, and ensuring that that infection report is not counted in any subsequent antibiotic combinations to avoid double counting (process summarised in annex figure 2.1).

⁸⁴ www.eucast.org/

⁸⁵ www.gov.uk/government/collections/escherichia-coli-e-coli-guidance-data-and-analysis#epidemiology

The ascertainment of voluntary CDR module cases when compared with mandatory surveillance reports of *E. coli* (annex table 2.1) was applied for each relevant year to estimate the total number of bloodstream infections for each pathogen (except for *S. aureus* where the mandatory surveillance totals for both MRSA and MSSA were used).

Annex Figure 2.1. Flow diagram for generating the burden of resistant bloodstream infections estimates



* full list of pathogens in Box 1 (next page); full list of numbered 'Calculation Boxes' in Box 2 (next page)
 † per pathogen and antibiotic combination, full list in Box 1 (next page), all estimates are for a given time frame

Box 1	Pathogen	Antibiotic
	<i>E. coli</i>	Colistin AND Carbapenems
	<i>K. pneumoniae</i>	Colistin
	<i>K. oxytoca</i>	Carbapenems
		3 rd generation cephalosporin
		Gentamicin
	<i>Acinetobacter</i> spp.	Colistin AND Carbapenem
		Carbapenem
		Ciprofloxacin & Gentamicin
	<i>Pseudomonas</i> spp.	Colistin
		Carbapenem
		Any three of: Ceftazidime, Piperacillin/tazobactam, aminoglycosides, ciprofloxacin
	<i>Enterococcus</i> spp.	Glycopeptide
	<i>S. aureus</i>	Methicillin
	<i>S. pneumoniae</i>	Penicillin AND macrolides
		Penicillin

Box 2

Calculate 1

Total *S. aureus*:

= no. MRSA mandatory reports*
+ no. MSSA mandatory reports*

Calculate 2

Ascertainment factor %:

= $\left[\frac{\text{no. mandatory } E. coli \text{ reports}^*}{\text{no. voluntary } E. coli \text{ reports}^*} \right]$

Calculate 3

Apply ascertainment factor %:

= no. voluntary *E. coli* reports* x
% ascertainment factor

Calculate 4

Percentage resistant (%):

= $\left[\frac{\text{no. resistant reports} \ddagger}{\text{no. tested reports} \ddagger} \right] \times 100$

*in a given time frame; † pathogen list on next page

‡ per pathogen and antibiotic combination in a given time frame

Table annex 2.1. Ascertainment factor applied to estimate total number of resistant BSI

Year	Mandatory <i>E. coli</i> bacteraemia reports	SGSS <i>E. coli</i> bacteraemia reports	% ascertainment	Ascertainment Factor
2013	33497	27150	81%	1.23
2014	35684	27962	78%	1.28
2015	37382	30524	82%	1.22
2016	40309	33791	84%	1.19
2017	41287	35362	86%	1.17

Data transparency

All data presented in this chapter in Figures and Tables are available in the online Appendix in excel format,⁸⁶ with the exception of summaries on *N. gonorrhoeae* which are available in the 2018 GRASP annual report.⁸⁷

Table of the EUCAST susceptibility category breakpoints⁸⁸

Organism	antimicrobial	EUCAST MIC breakpoints		
		S	I	R
<i>E. coli</i> <i>K. pneumoniae</i> <i>K. oxytoca</i>	ciprofloxacin	≤0.25	0.5	>0.5
	gentamicin	≤2	4	>4
	ceftazidime	≤1	≥2 and ≤4	>4
	cefotaxime	≤1	2	>2
	ceftriaxone	≤1	2	>2
	cefpodoxime	≤1	---	>1
	meropenem	≤2	≥4 and ≤8	>8
	imipenem	≤2	≥4 and ≤8	>8
	ertapenem	≤0.5	1	>1
	piperacillin-tazobactam	≤8	16	>16
	amoxicillin-clavulanic acid	≤8	---	>8
<i>Pseudomonas</i> spp.	ciprofloxacin	≤0.5	---	>0.5
	gentamicin	≤4	---	>4
	ceftazidime	≤8	---	>8
	meropenem	≤2	≥4 and ≤8	>8
	imipenem	≤4	8	>8
	piperacillin-tazobactam	≤16	---	>16
<i>Acinetobacter</i> spp.	Colistin	≤2	---	>2
<i>Enterococcus</i> spp.	Vancomycin	≤4	---	>4
	Teicoplanin	≤2	---	>2
<i>S. aureus</i>	Benzylpenicillin	≤0.125	---	>0.125
	Cefoxitin	≤4	---	>4
	Oxacillin	≤2	---	>2
	Rifampicin	≤0.06	≥0.12 and ≤0.5	>0.5
	Mupirocin	≤1	≥2 and ≤256	>256
	Fusidic Acid	≤1	---	>1
	Gentamicin	≤1	---	>1
	Ciprofloxacin	≤1	---	>1

⁸⁶ www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaurreport

⁸⁷ www.gov.uk/government/collections/gonorrhoea-neisseria-gonorrhoeae-guidance-data-and-analysis

⁸⁸ www.eucast.org/clinical_breakpoints/

www.eucast.org/fileadmin/src/media/PDFs/EUCAST_files/Expert_Rules/Expert_rules_intrinsic_exceptional_V3.1.pdf

	Erythromycin	≤1	2	>2
	Vancomycin	≤2	- - -	>2
<i>S. pneumoniae</i>	Ampicillin	≤0.5	1	>2
	Benzympenicillin	≤0.06	≥0.12 and ≤2	>2
	Erythromycin	≤0.25	0.5	>0.5
	Azithromycin	≤0.25	0.5	>0.5
	Clarithromycin	≤0.25	0.5	>0.5
	Tetracycline	≤1	2	>2

The disk diffusion method for detection of penicillinases is more reliable for identification of methicillin resistance, provided careful adherence to zone diameter and zone edge measurement.

The cefoxitin MIC is a poor predictor for methicillin resistance and the disk diffusion method is more reliable rapid molecular techniques are available to identify the *mecA* and *mecC* genes (MRSA indicators) avoiding the requirement to undertake susceptibility testing for isoxazolympenicillins (such as oxacillin). This information is not captured in these data. Please refer to the mandatory surveillance of MRSA bacteraemia for a full picture of the burden of MRSA in England.

Antimicrobials highlighted in red are used as a proxy or in combination to determine resistance to the antibiotic type.

Annex Chapter 3: Antibiotic consumption

Methods

Data source: primary care

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

As well as prescribing from general practice, the primary care data also includes other community prescribing such as out-of-hours services and walk-in centres. The full list of primary care prescribing is provided in the Annex.

Data source: secondary care

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

Data source: dental data

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

Classification of data

The classification of antibiotics for this report is based on the Anatomical Therapeutic Chemical (ATC) Classification System managed by the World Health Organization (WHO).⁸⁹ Data covered all antibiotics in the ATC group 'J01', (antibiotics for systemic use) and 3 additional oral agents outside the 'J01' group used to treat *Clostridium difficile* infections, namely fidaxomicin (A07AA12), metronidazole (P01AB01) and vancomycin (A07AA09).

⁸⁹ World Health Organisation. Guidelines for ATC classification and DDD assignment. 2013. Available online from: www.whocc.no/filearchive/publications/1_2013guidelines.pdf

This ATC system aims to identify the active therapeutic ingredient of all human medicines and assigns drugs a measure of use known as the Defined Daily Dose (DDD), which is the assumed average maintenance dose per day for a drug used for its main indication in adults. It is important to note however that while the DDD is used as a unit of measurement of drug use, it does not necessarily reflect the recommended or prescribed daily doses used in practice as therapeutic doses for individual patients may vary depending on characteristics such as age, weight, ethnic differences, type and severity of disease and pharmacokinetic considerations.

Antibiotic grouping within the J01 group

Penicillins (' β -lactam antibacterials, penicillins') included extended-spectrum penicillins, β -lactamase sensitive and resistant penicillins, and β -lactamase inhibitors either alone or in combination with penicillins, whereas 'Other β -lactam antibacterials' included cephalosporins, carbapenems, and monobactams.

'Other antimicrobials' included glycopeptides, polymyxins, steroid antibacterials, imidazole derivatives, nitrofurans derivatives, fosfomycin, linezolid and daptomycin.

Denominators

Mid-year populations for each year were extracted from the Office National Statistics (ONS).⁹⁰ Hospital admission data for each year was extracted from Hospital Episode Statistics (HES)⁹¹ from NHS Digital.

Trend analysis

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

Data transparency

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⁹⁰ Office for National Statistics. Population estimates. Available online from:

www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates

⁹¹ NHS Digital. Hospital Episode Statistics (HES). Available online from: digital.nhs.uk/data-and-information/data-tools-and-services/data-services/hospital-episode-statistics

All data presented in this chapter in Figures and Tables are available as a web Appendix in Excel format.

Other community settings categories

Other community settings to category look up table.

Other Community Settings	Setting Category
Other	Other
Walk-in Centre	Walk-in Centre
Out-of-hours	Out-of-hours
WIC and OOH Practice	Out-of-hours
Public Health Service	PH Service
Community Health Service	Community Service
Hospital Service	Hospital
Optometry Service	Other
Urgent & Emergency Care	Urgent Care
Hospice	Hospice
Care Home / Nursing Home	Nursing Home
Border Force	No data reported
Young Offender Institution	Custody
Secure Training Centre	No data reported
Secure Children's Home	Custody
Immigration Removal Centre	Custody
Court	No data reported
Police Custody	No data reported
Sexual Assault Referral Centre	No data reported
Other – Justice Estate	No data reported
Prison	Custody

Trusts definitions

Trusts definitions in the ESPAUR report are based on the Estates Returns Information Collection (ERIC)⁹².

⁹² NHS Digital. Hospital Estates and Facilities Statistics. Available online from: digital.nhs.uk/data-and-information/areas-of-interest/estates-and-facilities/hospital-estates-and-facilities-statistics

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

Department speciality

Department speciality to department group look up table.

Department Speciality	Department Group
Mixed Outpatient Clinics	AE/Non-specific out-patients department
Aseptic unit	AE/Non-specific out-patients department
A & E	AE/Non-specific out-patients department
Psychogeriatric	Geriatrics
Geriatrics	Geriatrics
Intensive Care	Intensive Care Unit
Dermatology	General Medicine
Respiratory/ Chest/ Asthma clinic	General Medicine
Cardiology	General Medicine
Gastroenterology	General Medicine
Coronary care	General Medicine
Rheumatology	General Medicine
Thoracic/ Chest medicine	General Medicine

General Medicine	General Medicine
Endocrinology	General Medicine
Obstetrics & Gynaecology	Obstetrics and gynaecology
Fertility /Genetics	Obstetrics and gynaecology
Orthopaedics	Orthopaedics
Pain Clinic	Other
Radiology	Other
Physiotherapy	Other
Physically Disabled	Other
Rehabilitation/Long stay unit	Other
Pathology Lab	Other
Mental Handicap	Other
Occupational Health	Other
Learning Disabilities	Other
Child Adolescent Psychiatry	Other
Other Wards/ Units	Other
Psychiatry / Mental Illness	Other
Psychiatric Day Hospital	Other
Paediatric ICU	Paediatrics
Neonatal Unit	Paediatrics
Paediatric / Paediatric Surgery	Paediatrics
Acute Internal Medicine	Specialist medicine
Medical Oncology	Specialist medicine
Clinical Oncology (Radiotherapy)	Specialist medicine
A.I.D.S Unit	Specialist medicine
Infectious dis./Isolation	Specialist medicine
Renal Medicine	Specialist medicine
Liver Unit	Specialist medicine
Neurology	Specialist medicine
G.U.M	Specialist medicine
Haematology	Specialist medicine
GUM Medicine	Specialist medicine
Liver (failure) Unit	Specialist medicine
Transplantation Unit	Specialist Surgery
E.N.T.	Specialist Surgery
Cardio-thoracic Surgery	Specialist Surgery
Plastic Surgery	Specialist Surgery
Oral Surgery	Specialist Surgery
Vascular Surgery	Specialist Surgery
Ophthalmology	Specialist Surgery
Urology	Specialist Surgery
Neurosurgery	Specialist Surgery

General Surgery	General Surgery
Breast Treatment & Care	General Surgery
Day Case Theatres	General Surgery
Theatre/ Anaesthetics	General Surgery

Piperacillin-tazobactam supply problems

Piperacillin-tazobactam supply problems [guidance](#).