English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR)

Report 2017
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Executive summary

This is the fourth annual report from the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR). Much of the national data presented in this report is now also available by Clinical Commissioning Group (CCG), Acute Trust, General Practice (GP) or Local Authority on the Public Health England (PHE) Fingertips antimicrobial resistance (AMR) local indicators or related pages that were launched in April 2016.\(^1\) The AMR local indicators receive more than 4,000 unique visits per quarter and have more than 80 indicators available.

Halving the numbers of healthcare-associated Gram-negative bloodstream infections (GNBSIs) by March 2021 is a key government ambition, announced as a key action in Lord O'Neill’s Review of Antimicrobial Resistance (AMR). In this report, we highlight the year-on-year increased burden (in terms of the number of individuals) of antibiotic-resistant GNBSIs and urinary tract infections (UTIs), though encouragingly the proportion of GNBSIs that are resistant to key antibiotics has remained broadly stable over the last 5 years. This is in contrast to many other countries globally and most likely reflects good antimicrobial stewardship and rare use of cephalosporins and quinolones in the community settings in England.

In 2016, the commonest cause of BSIs was *Escherichia coli*; of these, 41% were resistant to the commonest antibiotic used to treat infections in hospitals (co-amoxiclav) and almost one in five of these bacteria were resistant to at least one of other key antibiotics, though multi-drug resistance (resistance to three antibiotics) remained uncommon (<5%). This suggests that patients with severe infections, including sepsis, who have risk factors for resistant bacteria may require a combination of antibiotics, such as a β-lactam antibiotic and an aminoglycoside, for the first 24 hours of treatment while waiting for laboratory results to guide the choice of optimal therapy. Patient risk factors for resistant bacteria include those who have received prior antibiotic courses, or with a history of recent or recurrent hospital admissions and/or the elderly, especially those living in long-term care facilities. The high levels of AMR also highlight the importance of taking patient clinical samples (especially blood and urine) prior to commencing antibiotics in patients who present with infections to the A&E department or while a hospital inpatient, in order to inform antibiotic treatment after the first 24-48 hours.

This report highlights that AMR was common in the more than 1 million UTIs caused by bacteria identified in NHS laboratories in 2016. Current guidelines recommend that urine samples be sent to the laboratory from those individuals with clinical treatment

\(^1\) https://fingertips.phe.org.uk/
failure, frequent or recurrent UTI or who have a likelihood of a resistant infection. Almost two-thirds of samples were taken in community healthcare settings (General Practice [GP], community hospitals, long-term care facilities). We highlight that trimethoprim resistance is very common in laboratory processed urine samples (34%) but that the current recommended first line treatment, nitrofurantoin is currently effective (3%). This supports the PHE infections guidelines to switch from trimethoprim to nitrofurantoin as empiric treatment for UTI before laboratory results are available.² To improve data on unselected urines, a sentinel surveillance programme with careful sampling from the populations at risk is required.

Between 2012 and 2016, antibiotic prescribing reduced by 5%, when measured as defined daily doses per 1000 inhabitants per day, with declines across the majority of antibiotic groups. However, significant regional variation in antibiotic use continues to occur.

The number of prescriptions dispensed in the GP setting decreased by 13% between 2012 and 2016 (-2% from 2015 to 2016), largely driven by reductions in use of penicillins. Dental practices dispensed 1 in 5 fewer prescriptions in 2016 compared to 2012 and more than 99% of prescribed antibiotics were in accordance with dental treatment guidelines. Secondary care, despite some progress observed in 2015, has not had a sustained reduction in total antibiotic prescribing. However, from 2015 to 2016 hospitals reduced their use of the ultra-broad spectrum antibiotics piperacillin/tazobactam and carbapenems (both -4%). This is the first step in reducing antibiotic use in hospitals and focussing on using these antibiotics appropriately is key to preventing the emergence and spread of carbapenem-resistant Gram-negative bacteria.

The national importance of reducing unnecessary and inappropriate antibiotic use was demonstrated through the development of NHS antimicrobial stewardship initiatives, namely the Quality Premium (QP) from 2014/15 in primary care and Commissioning for Quality and Innovation (CQUIN) from 2016/17 in secondary care. Over the first two years of the QP, 88% of CCGs met their objective to reduce antibiotic consumption and 83% reduced broad-spectrum antibiotic use to the target level. In the first year (2016/17) of the CQUIN, 37%, 33% and 52% of NHS acute Trusts met their objectives to reduce total antibiotic, piperacillin/tazobactam and carbapenem consumption respectively, to 2013/14 levels; though significantly more reduced their piperacillin/tazobactam and carbapenem compared to 2015/16 levels (66% and 67% respectively). The impact of these interventions on infection-related hospital admissions, length of stay and mortality, led by the Imperial College Health Protection Research Unit, will report shortly.

Parallel to the GNBSI work, the Prime Minister announced an ambition to halve inappropriate antibiotic prescribing. This report features the outputs of the joint PHE-Department of Health workshop in this area, where it was recommended that all practice reduce total antibiotic prescribing by 10% by 2020/21 and that secondary care reduce total prescribing by a further 1% and use of piperacillin/tazobactam and carbapenems by a further 3% respectively in 2018/19.

This report highlights the initial results of the point prevalence survey of healthcare associated infections (HCAI) and antimicrobial use (AMU) in acute hospitals, performed in 2016. Despite an older population with increased co-morbidities and surgery, there was no significant change in the prevalence of HCAI or AMU between the last survey in 2011 and 2016. In 2016, one in fifteen patients in acute hospitals had an HCAI and one in three were on antibiotics on the day of survey. A higher level of antibiotic resistance was seen in those with an HCAI compared to the rates observed in the all-patient GNBSI and UTI surveillance data, suggesting that HCAIs are more likely to be antibiotic resistant than community infections. Infections were most prevalent among patients on intensive care units (ICUs). This survey highlights the continuing importance of surveillance of Gram-negative infections, ICU patients and antibiotic use in England.

We also present data on use of and resistance to antifungals in this report. The data highlights the variation in testing performed in laboratories, both reference and clinical, and is the first step to improving surveillance of antifungal resistance.

PHE leads, along with professional and partner organisations, the development and evaluation of antimicrobial stewardship toolkits across the healthcare economy. This report features process evaluations of both the dental and GP toolkits, demonstrating their wide global uptake and utility in helping clinicians prescribe antibiotics appropriately.

ESPAUR has led the development of the Antibiotic Guardian professional and public behaviour change and engagement campaign. We report on the activities to increase engagement and its reach to two thirds of the worlds countries and evaluation of its rollout to other countries. We also present evaluations of webinars and training for healthcare professionals through activities to GPs and hospital staff. ESPAUR has also worked closely with PHE marketing team on the national public campaign, Keep Antibiotics Working, that will launch on 23 October 2017.

As in previous reports, updates from our partner organisations in the ESPAUR Oversight Group are presented, underscoring the importance of cross-working and networking to engage and maximise action to control AMR. Contributions from organisation’s representatives on the ESPAUR oversight group assist us in ensuring we meet the needs of our stakeholders and the NHS.
1. Introduction

The English Surveillance Programme for Antimicrobial Use and Resistance (ESPAUR) was established in response to the UK government’s five-year antimicrobial resistance (AMR) strategy. Over the last four years, it has improved the surveillance and feedback of antimicrobial use (AMU) and resistance data, coordinated PHE’s antimicrobial stewardship (AMS) activity in primary and secondary care and worked across government, devolved administrations, and arm’s length bodies, particularly the NHS.

In the last year ESPAUR has continued to:

- develop, maintain and disseminate robust data for AMU, AMR and AMS
- enable optimal use of this data across healthcare settings, through feedback on the PHE Fingertips platform
- work with research partners to measure the impact of incentives and interventions

In the 18 months since the AMR local indicators profile was launched on Fingertips there have been more than 4,000 unique visits per quarter, with peaks coinciding with new data releases onto the system. There are now 93 indicators on this profile with local data available for individual Clinical Commissioning Groups (CCGs) and Acute Trusts across AMR, AMU, healthcare-associated infections, infection prevention and control and AMS. In addition, there are three indicators on antibiotic use in the National General Practice profiles and similar data sets on the Public Health Outcomes Framework profile using local authority geographical breakdown.

In 2016, following the publication of Lord O’Neill’s Review on AMR, the government announced two new ambitions, namely to half both healthcare-associated Gram-negative bloodstream infections (HA-GNBSI) and inappropriate antibiotic prescribing. This report therefore particularly focuses on the epidemiology and resistance of GNBSI in Chapter 2. Previous sentinel surveillance has demonstrated that approximately half of the BSIs caused by *Escherichia coli* (the most common cause of BSI in England) were caused by an underlying urinary tract infection (UTI). Therefore, it is essential if we are to prevent progression of infections from the urinary tract to the blood that they are treated with the correct empiric antibiotics; current resistance patterns for *E. coli* UTIs are presented. Chapter 2 also highlights the progress on enhancing understanding of the epidemiology of carbapenemase-producing Gram-negative bacteria. These resistant

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4 https://fingertips.phe.org.uk/
5 https://amr-review.org/
bacteria have emerged and spread globally and are now a common cause of hospital outbreaks in England.

Chapters 3 and 4 highlight the progress on reducing total antibiotic use in England. It highlights the excellent response by NHS commissioners, providers and clinicians to the challenge to reduce antibiotic use in England with the work being delivered in partnership with NHS England and NHS Improvement. In the general practice (GP) setting, almost all CCGs are now prescribing less antibiotics (age and sex adjusted) than they were in 2014 and broad-spectrum antibiotics (defined as co-amoxiclav, ciprofloxacin and cephalosporins) now account for less than 10% of all antibiotics prescribed. NHS dental prescribing continues to decrease and in 2016 was 21% less than 2012. In secondary care, considerable reductions in the hospital use of broad-spectrum antibiotics (carbapenems and piperacillin/tazobactam) have occurred; however, total antibiotic prescribing has not yet declined, most likely related to switches from broad-spectrum antibiotics to combinations of two or three narrower spectrum antibiotics. There are new additions in this chapter including a breakdown of community prescriptions by healthcare professional and an exploration of prescribing by consultant specialty in secondary care.

Chapter 5 highlights the outputs and developments in AMS focussing on process evaluations of the dental and GP AMS toolkits. This chapter also describes the methodology for the development of the primary and secondary care prescribing measures to support a 50% reduction of inappropriate antibiotic prescribing.

Chapter 6 explores antifungal resistance and prescribing. This is an emerging threat with the recently identified pathogen *Candida auris*, often resistant to antifungals, having caused outbreaks in English hospitals over the last two years.

Chapter 7 outlines the results of the 2016 point prevalence survey of healthcare-associated infections and antimicrobial use.

Chapter 8 highlights key interventions delivered to public and professionals to improve education, knowledge, and awareness of AMR. This includes on-going activities and outputs related to World Antibiotic Awareness Week, evaluation of the on-going Antibiotic Guardian Campaign, delivery of workshops and training events for healthcare professionals and e-Bug activities, delivering education and training resources for children and young adults.

The final chapter highlights activities delivered by organisations that are represented on the ESPAUR Oversight Group and includes work relating to improving antibiotic use, resistance, stewardship, education and public engagement. The Oversight Group encompasses arm’s length bodies including NHS England, NHS Improvement, Health Education England and the National Institute for Health and Care Excellence (NICE)
and professional organisations including the British Society for Antimicrobial Chemotherapy, Royal Pharmaceutical Society, Faculty of General Dental Practice, Royal Colleges of Nursing, Surgery, Physicians and General Practice, and the British Society of Medical Microbiology. We would like to thank the members of this multi-faceted group, who with their on-going support, encouragement, and constructive feedback ensure that we meet the needs of the healthcare economy and public in our activities.
2. Antibiotic resistance

Introduction

This chapter presents updated data on antimicrobial resistance (AMR) in the Gram-negative pathogens highlighted as the focus for surveillance in the UK 5-year AMR strategy.\(^7\)

As 2017 sees the implementation of a new national ambition to reduce the incidence of healthcare-associated bacteraemias caused by *Escherichia coli*, *Klebsiella* spp. and *Pseudomonas aeruginosa* by 50% (compared to baseline year April 2017 to March 2018) by April 2021,\(^8,9\) there is a particular emphasis on these species. The data on resistance (derived from analysis of isolates from blood) are presented both in terms of trends in resistance to key individual antibiotics and patterns of multi-resistance. For *E. coli*, additional data are presented on patterns of susceptibility testing and resistance in isolates from urinary tract infections (UTIs). Updates are also provided on trends in referral of carbapenemase-producing Enterobacteriaceae (CPE) to the national reference laboratory together with an assessment of less commonly encountered carbapenem resistance genes, the use of the Electronic Reporting System for the enhanced surveillance of carbapenem producers and trends in resistance in *Neisseria gonorrhoeae*.

Other topics covered include pan-aminoglycoside resistance and transferable colistin resistance in Gram-negative bacteria 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. While not included here, updated data on the Gram-positive pathogens included in the national strategy (*Staphylococcus aureus*, *Streptococcus pneumoniae* and *Enterococcus* spp.) and TB that were covered in the 2016 ESPAUR Annual Report, are available in the on-line Appendix accompanying this Report and in the annual report on TB in England,\(^10\) respectively.

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\(^7\) https://www.gov.uk/government/publications/uk-5-year-antimicrobial-resistance-strategy-2013-to-2018


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 two 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 Gram-negative bacteria covered in this report, although any test results suppressed from clinical reports by the sending laboratories are not captured when the data is submitted. In contrast the AMR module contains more comprehensive antibiogram information as it includes results for all antibiotics tested (including results suppressed from clinical reports) for isolates from all clinical sources. However, until the launch of SGSS in 2014, AmSurv had lower laboratory coverage than CoSurv/LabBase2. Therefore, analysis of trends in antimicrobial susceptibility covering years prior to 2014 is currently undertaken using data from the CDR module. In contrast, analysis of the susceptibility of *E. coli* causing UTIs in 2016 was undertaken using data in the AMR module of SGSS.

Hospital microbiology laboratories report antimicrobial susceptibility test results “susceptible”, “intermediate” or “resistant”. These categories are defined as follows\(^{11}\):

- **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
- **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

For the purpose of this report, antibiotic susceptibility test results reported as intermediate or resistant were combined and presented as non-susceptible. For analysis of resistance to more than one antibiotic, multidrug resistance (MDR) was

defined as acquired non-susceptibility to at least one agent in three or more antimicrobial classes.\textsuperscript{12} Susceptibility test results are presented when more than 70\% of specimens were tested for that antibiotic (or combination), unless otherwise specified.

Data on the incidence of \textit{E. coli} bacteraemia were from the national mandatory surveillance scheme\textsuperscript{13} while data on the incidence of \textit{Klebsiella} spp. and \textit{P. aeruginosa} 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 \textit{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.

**Data transparency**

All data presented in this chapter in Figures and Tables are available in the online Appendix in excel format,\textsuperscript{14} with the exception of summaries on \textit{N. gonorrhoeae} which are available in the 2017 GRASP annual report.\textsuperscript{15}

**Results**

**Trends in antibiotic resistance in Gram-negative bacteria causing bloodstream infections**

The five-year trends in resistance to key antibiotics in Gram-negative pathogens causing bloodstream infections, assessed in terms of the proportion of isolates that are non-susceptible, are shown in Figures 2.1 to 2.6.

(a) \textit{Escherichia coli}

The number of cases of \textit{E. coli} bacteraemia reported to the mandatory surveillance system between 2012 and 2016 and the proportion of isolates non-susceptible to key antibiotics is shown in Figure 2.1. In most years typically 80-90\% of isolates had

\textsuperscript{13} https://www.gov.uk/government/collections/escherichia-coli-e-coli-guidance-data-and-analysis#epidemiology
susceptibility test results for each antibiotic (detailed information is provided in the online Appendix).

The proportion of isolates resistant to ciprofloxacin (18.1-18.7%), third-generation cephalosporins (10.8-12.4%) and gentamicin (9.3-10.1%) remained stable over the five year period up to 2016. Resistance to piperacillin/tazobactam, which had increased year-on-year, from 9.6% in 2012 to 11.6% in 2015, showed only a marginal increase to 11.8% in 2016, while resistance to co-amoxiclav, which had increased from 37.3% in 2012 to 42.3% in 2015 decreased to 40.8% in 2016 (Figure 2.1). Carbapenem resistance fluctuated from year-to-year within the range 0.07-0.14%, with between 15 to 32 isolates reported from blood in an individual year, with no consistent time trend.

![Figure 2.1 Number of bloodstream isolates of E. coli reported to the mandatory surveillance scheme and the proportions non-susceptible to indicated antibiotics](image-url)

The proportions of bloodstream isolates of E. coli showing multi-resistance also remained stable between 2012 and 2016 and varied in the range of 3-5%; the highest proportions were seen for combinations of third-generation cephalosporins, quinolones and aminoglycosides and the lowest for third-generation cephalosporins, aminoglycosides and piperacillin/tazobactam (Figure 2.2).

Although the proportions of E. coli blood culture isolates with resistance to either individual or combinations of key antibiotics remained fairly stable between 2012 and 2016, the incidence of E. coli bacteraemia increased year-on-year, from 32,405 cases in 2012 to 40,272 cases in 2016, an overall increase over the five-year period of 24.3% (Figure 2.1). Thus, the burden of resistance as reflected in the estimated numbers of antibiotic-resistant bloodstream infections (derived using the numbers of infections and the proportions of resistant isolates each year shown in Figures 2.1 and 2.2) increased year-on-year. For example, the estimated numbers of ciprofloxacin-resistant infections increased from 5,930 in 2012 to 7,490 in 2016, while infections resistant to third-generation cephalosporins increased from 3,500 in 2012 to 4,995 in 2016. The estimated numbers of infections due to E. coli with combined resistance to third-
generation cephalosporins, ciprofloxacin and aminoglycosides increased from 1,555 to 2,054 over the same period.

![Figure 2.2 Proportion of bloodstream isolates of *E. coli* non-susceptible to combinations of antibiotics](image)

There was regional variation between the four PHE regions (North of England, Eastern and Midlands, London and the South of England) with regard to the proportions of *E. coli* isolates showing resistance, both to individual and combinations of antibiotic classes. Throughout 2012 to 2016, London consistently showed higher resistance to ciprofloxacin (25-27%), gentamicin (14-15%) and third-generation cephalosporins (15-18%) than the other three regions (16-19%, 8-11% and 9-14%, respectively). A more detailed regional breakdown based on the NHS regions is available in the online Appendix.

(b) *Klebsiella* spp.

In 2016 the two commonest species among blood culture isolates of the genus *Klebsiella* were *K. pneumoniae* (81%) and *K. oxytoca* (17%).

As seen with *E. coli*, the overall proportions of isolates of *K. pneumoniae* resistant to individual key antibiotics generally remained stable between 2012 and 2016, with

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resistance to ciprofloxacin, third-generation cephalosporins, gentamicin and carbapenems fluctuating within the ranges 10.0-11.5%, 11.1-12.3%, 7.1-8.9% and 0.8-1.5%, respectively. Resistance to piperacillin/tazobactam, which had increased year-on-year from 13.3% in 2012 to 18.6% in 2015, showed a slight reduction to 17.8% in 2016. Similarly, resistance to co-amoxiclav, which had increased year-on-year from 19.7% to 28.4% between 2012 to 2015, decreased slightly to 27.5% in 2016 (Figure 2.3).

The proportions of bloodstream isolates of *K. pneumoniae* resistant to combinations of antibiotic classes also remained stable between 2012 and 2016, albeit with some year-to-year variation. Multi-resistance varied in the range of 3-8%, with the highest proportions seen for combinations of third-generation cephalosporins, aminoglycosides and piperacillin/tazobactam and the lowest for third-generation cephalosporins, quinolones and piperacillin/tazobactam (Figure 2.4).

**Figure 2.3 Number of bloodstream isolates of *K. pneumoniae* reported to SGSS and the proportions non-susceptible to indicated antibiotics**

Although the proportions of blood culture isolates of *K. pneumoniae* resistant to a number of key antibiotics remained fairly stable between 2012 and 2016, reports of bacteraemia due to *K. pneumoniae* showed an overall increase between 2012 and 2016 (Figure 2.3), indicating that the burden of resistance to these antibiotics as reflected in the numbers of resistant bloodstream infections increased over time. For example, using the numbers of reported infections and the proportion of resistant isolates each year shown in Figure 2.3, the estimated numbers of ciprofloxacin-resistant infections increased from 459 in 2012 to 739 in 2016, while infections resistant to third-generation cephalosporins increased from 510 in 2012 to 790 in 2016. However, in contrast to *E. coli* bacteraemia where reporting of cases is mandatory, reporting of bacteraemia due to
\textit{Klebsiella} spp. was voluntary between 2012 and 2016 leading to incomplete case ascertainment and potential under ascertainment of the burden of resistance.

There was regional variation in the proportions of \textit{K. pneumoniae} bloodstream isolates showing resistance, to key antibiotics. As with \textit{E. coli}, higher proportions of resistant isolates were most commonly seen in London throughout the five year period (2012 to 2016), with this region consistently showing higher resistance to ciprofloxacin (13-18%), gentamicin (11-14%), third-generation cephalosporins (14-19%) and co-amoxiclav (25-36%) each year, compared with the other regions (ciprofloxacin, 8-13%; gentamicin, 5-10%; third-generation cephalosporins, 9-13% and co-amoxiclav, 17-31%). The proportion of piperacillin/tazobactam-resistant isolates was also higher in London in 2015 (22%) and 2016 (21%) compared to the other three regions (17-19% and 17% in 2015 and 2016, respectively), but not in earlier years. London also had the highest proportion of isolates showing resistance to carbapenems in each year apart from 2013, when the North of England had the highest rate. In 2016, 2.2% of \textit{K. pneumoniae} blood culture isolates from the London region were resistant to carbapenems, while the proportions of resistant isolates from the South, East & Midlands and North of England were 0.5%, 0.6% and 0.8%, respectively.

Trends in the proportion of \textit{K. oxytoca} bloodstream isolates resistant to different classes of antibiotics over time are shown in Figure 2.5. Resistance to gentamicin, ciprofloxacin, third-generation cephalosporins and carbapenems was seen in ≤7% of isolates throughout the five-year surveillance period. Resistance to piperacillin/tazobactam and
co-amoxiclav was higher, occurring in 10−15% and 13-20% of isolates, respectively; although the proportions of resistant isolates in 2016 were higher than in 2012, there was no clear trend due to year-to-year fluctuation.

Figure 2.5 Number of bloodstream isolates of *K. oxytoca* reported to SGSS and the proportions non-susceptible to indicated antibiotics

(c) *Pseudomonas* spp.

Resistance of *Pseudomonas* spp. to ciprofloxacin, ceftazidime, piperacillin/tazobactam, gentamicin and to carbapenems remained stable during 2012 to 2016, with the proportion of bloodstream isolates showing resistance falling in the ranges 9.4 to 10.9%, 7.1 to 7.5%, 8.5 to 10.3%, 3.8 to 4.6% and 9.4 to 11.27%, respectively (Figure 2.6). However, apart from a decline between 2012 and 2013, the number of voluntary reports of bacteraemia due to *Pseudomonas* spp., increased year-on-year from 3,364 in 2013 to 4,008 in 2016. Thus, the burden of resistance in terms of resistant infections has continued to rise. For example, based on the data shown in Figure 2.6, the estimated number of infections caused by isolates resistant to ceftazidime increased from 260 in 2012 to 300 in 2016; corresponding numbers of carbapenem-resistant infections were 348 and 429.

Regional variation in levels of antibiotic resistance was again noted, although the magnitude of the variation was low; In 2016, ciprofloxacin resistance ranged between 8 and 10%, while resistance to ceftazidime, piperacillin/tazobactam and gentamicin varied within the ranges of 6 to 8%, 10 to 12% and 3 to 6%, respectively. The largest variation in resistance was seen for carbapenems (with the majority of isolates tested using meropenem), where the proportions of resistant isolates in the Midlands and East region, the North of England, the South of England and London were 9%, 11%, 11%
and 14%, respectively. As seen with *E. coli* and *K. pneumoniae*, London commonly (although not consistently) showed higher levels of resistance to the key antibiotics than the other regions over time.

![Figure 2.6 Number of bloodstream isolates of *Pseudomonas* spp. reported to SGSS and the proportions non-susceptible to indicated antibiotics](image)

Resistance in *E. coli* causing urinary tract infections

Analysis of risk factor data provided via the national mandatory surveillance scheme indicated that about half of patients with *E. coli* bacteraemia had a UTI that was thought to have been the underlying source of the invasive infection. In order to inform the management of patients with UTIs, we outline the antibiotic susceptibility patterns of *E. coli* reported from laboratory-confirmed cases of UTI.

Data on both the proportion of urine isolates of *E. coli* tested against a range of antibiotics that either are or have been recommended as first or second-line treatment options for UTIs and the proportions that are susceptible or resistant are shown in Figure 2.7. Data were available for a total of 1,007,684 urine isolates, of which 61% (n=615,598) were from the community setting (GPs, community care hospitals including genitourinary medicine clinics) and 39% (n=392,086) were from the acute setting. Ninety-eight percent of isolates from both settings were tested for susceptibility to nitrofurantoin (the recommended first-line therapy for lower UTIs in current PHE guidance) and trimethoprim (recommended where there is a low risk of resistance). Of

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the isolates from community and acute settings for which susceptibility test results were available, 2.7% and 3.2% were resistant to nitrofurantoin, respectively; corresponding rates of resistance to trimethoprim were 34% and 37%. Testing of the second-line agents mecillinam and fosfomycin was only reported for 35% and 29% of isolates, with approximately 9% and 4% of tested isolates showing resistance, respectively, with little difference between community and acute settings. Ciprofloxacin is one of the key antibiotics for treating complicated or upper UTI (pyelonephritis) and 82% of isolates had a susceptibility test result with resistance reported for 12% and 15% of urine isolates from community and acute settings, respectively.

Figure 2.7 Proportion of acute hospital and community urine isolates of *E. coli* tested and found to be susceptible or non-susceptible to nitrofurantoin, trimethoprim, co-amoxiclav, quinolones, mecillinam and fosfomycin

The level of testing and the proportions of isolates susceptible or resistant to antibiotics recommended for the treatment of UTIs in children and pregnancy was assessed by analysis of isolates from patients aged <12 years and 16-40 years old (child bearing age), respectively; 95% of cases in the latter group were female. As shown in Figure 2.8, in both age groups, 98% of isolates were tested for susceptibility to nitrofurantoin, of which 1.2% were resistant; corresponding rates of testing with trimethoprim and the proportions resistant were 98% and 32.6% in children and 98% and 31.4% in patients aged 16-40 years. Approximately 82% of isolates from both children and patients aged 16-40 years were tested for resistance to cephalexin, the proportion of resistant isolates in the two age groups being 9.4% and 8.0%, respectively.
Carbapenemase-producing Gram-negative bacteria

Although carbapenem resistance remains low in blood culture isolates of *E. coli* and *Klebsiella* spp. in England, such resistance is nonetheless a significant threat to healthcare, as data from other countries have shown that the prevalence of carbapenem resistance can increase dramatically over short time periods (Figure 2.9).

![Figure 2.8. Proportion of *E. coli* isolated from urine from patients of different age groups tested and susceptible or non-susceptible to nitrofurantoin, trimethoprim, co-amoxiclav and cephalexin](image)

![Figure 2.9 Proportion of blood culture isolates of *K. pneumoniae* resistant to carbapenemems in Europe showing a marked increase in Italy over a 4-year period.](image)
plasmids containing genes encoding carbapenemases. Hence epidemiologically-linked clusters of infection or colonization may involve more than one species of bacteria.

β-lactamase enzymes (including carbapenemases) are classified into four Ambler classes, designated A-D, based on differences in their amino acid sequences. Classes A, C and D enzymes all have serine at the active site while those in class B have a bivalent metal ion, usually Zn$^{2+}$. The carbapenemases known to date are found in Ambler groups A, B or D as shown below:

1. **Class A carbapenemases**: eg. KPC, IMI, SME, SFC, IMI/NMC-A, GES
2. **Class B carbapenemases**: eg. NDM, VIM IMP, SPM
3. **Class D carbapenemases**: eg. OXA-48-like

In the UK, the Standard for Microbiology Investigation (SMI) for Detection of Bacteria with Carbapenem-hydrolysing β-lactamases (Carbapenemases)$^{19}$ recommends that ideally all clinically significant isolates of Enterobacteriaceae should be tested against a carbapenem as the UK seeks to increase the knowledge of the national distribution of carbapenemase producers. Any isolate which appears to be resistant to an indicator carbapenem through an acquired resistance mechanism should then be referred for confirmation; meropenem is the recommended indicator carbapenem by the European Committee on Antimicrobial Susceptibility Testing (EUCAST). Most NHS laboratories in England submit their isolates to AMRHAI, although some PHE Specialist Laboratories offer referral services at a regional level, and then refer selected isolates onwards to AMRHAI.

In 2016, AMRHAI confirmed the presence of at least one carbapenemase in 2,595 Enterobacteriaceae (Figure 2.10), with the ‘big 5’ carbapenemase families (KPC, OXA-48-like, NDM, VIM and IMP) and combinations thereof accounting for >99% of confirmed CPE. Many of these isolates were from screening rather than clinical samples.

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In addition to the ‘big 5’ carbapenemase families, other less common carbapenemase types including GES, IMI, SME and FRI were detected and there is evidence that some are circulating in the UK.

1. GES (Guiana extended-spectrum (GES) β-lactamases can confer carbapenemase or extended-spectrum β-lactamase (ESBL) activity depending on the gene variant. GES carbapenemases have been identified by AMRHAI in *P. aeruginosa* (particularly sequence type [ST] 235) and various species of Enterobacteriaceae since 2012.\(^\text{20}\) Isolates have mostly been sporadic. Exceptions are: (i) a laboratory in the North East that has submitted GES-5 carbapenemase-positive *P. aeruginosa* ST235 since 2012; and (ii) an outbreak involving GES-5-positive *K. oxytoca* in a London hospital in 2015.\(^\text{21}\) Whilst AMRHAI has been able to identify potential markers for GES carbapenemase production in the antibiograms of *P. aeruginosa*, phenotypic detection of CPE producing GES is complicated by the diverse range of carbapenem MICs noted in positive isolates received to date, meaning that some GES carbapenemase-positive isolates may be misinterpreted as ESBL producers with reduced susceptibility to the carbapenems contingent upon porin loss.

\(^{20}\) Hopkins KL et al. GES carbapenemases in Enterobacteriaceae and Pseudomonas aeruginosa in the United Kingdom. ASM Microbe 2016; Boston, Mass.

\(^{21}\) Eades C et al. GES-5 carbapenemase-producing Klebsiella oxytoca causing clinical infection in a UK haematopoietic stem-cell transplantation unit. 26th ECCMID; Amsterdam, The Netherlands
2. IMI carbapenemases have been sporadically identified in AMRHAI submissions since 2010 and are typically restricted to the genus *Enterobacter*. However, AMRHAI recently reported an IMI carbapenemase in a *Klebsiella variicola* isolated in the UK. To our knowledge this is only the second report worldwide of an IMI carbapenemase outside of the *Enterobacter cloacae* complex.\(^{22}\) The *bla*IMI gene may be either chromosomally- or plasmid-encoded depending on the gene variant and once these genes become plasmid-encoded this may facilitate their spread to other Enterobacteriaceae.

3. SMEs (*Serratia marcescens* enzymes) are acquired, but chromosomally-encoded carbapenemases found in some *S. marcescens*. AMRHAI recently reported on the first SME-positive isolates identified by PHE since screening for carbapenemases began in the early 2000s.\(^{23}\) The isolates were genetically unrelated and were from patients with no known epidemiological links to each other or to other countries that have reported SME enzymes, which suggests that SME carbapenemases are circulating in the UK at a very low level.

4. In 2016, AMRHAI identified an *E. cloacae* complex strain that produced a plasmid-encoded FRI carbapenemase – only the second report globally of a FRI family carbapenemase.\(^{24}\) The patient had no recent history of travel abroad and so the source of acquisition of this strain is unknown.

GES, IMI, SME and FRI are all class A carbapenemases and should, in theory, be detectable by any phenotypic method that can detect KPC carbapenemases. However, due to the scarcity of these carbapenemase families it is likely that such methods have not been fully validated. In AMRHAI’s experience, and based on the published literature, the SME and GES families in particular are not reliably detected by all current phenotypic methods. As commercial diagnostics have limited coverage and focus on detection of the “big 5” carbapenemase families, the emergence of these other carbapenemase families potentially poses a problem for infection prevention and control. Isolates that exhibit antibiograms consistent with a class A carbapenemase, but that are negative for KPC in molecular tests should be referred to AMRHAI for extended molecular screening.

Data from AMRHAI demonstrate that most CPE are resistant not only to the carbapenems, but to most other antibiotic classes (Table 2.1). Previous AMRHAI data from 2014 showed that only colistin remained effective against >90% of all CPE.\(^ {25}\) However, analysis of confirmed CPE received in 2016 illustrated that colistin resistance

\(^{25}\) PHE. Carbapenem resistance: implementation of an enhanced surveillance system. Health Protect Rep 2015; vol 9, issue 2.
is emerging, particularly in *Klebsiella* spp. harbouring a non-metallo-carbapenemase or multiple carbapenemases.

Ceftazidime-avibactam (CAZ-AVI) and ceftolozane-tazobactam (CZT-TAZ) are cephalosporin/β-lactamase inhibitor combinations recently licensed for the treatment of multidrug-resistant Gram-negative infections. CAZ-AVI inhibits bacteria with non-metallo- (but not metallo-) carbapenemases and was active against ≥96% of non-metallo CPE referred to AMRHAI in 2016 (Table 2.1). In contrast, CZT-TAZ has activity against ESBL-producing Enterobacteriaceae, and *P. aeruginosa* demonstrating up-regulated efflux and depressed AmpC activity,26 but lacked activity against many CPE isolates in 2016.

Table 2.1: Antibiotic susceptibilities of CPE submitted to AMRHAI, where susceptibility testing was performed, 2016 (n = 708).

<table>
<thead>
<tr>
<th>Antibiotic</th>
<th>Proportion Susceptible(^a), %</th>
<th>Metallo-enzyme producers (NDM, VIM, IMP) (n=261)</th>
<th>Non-metallo-enzyme producers (KPC, OXA-48-like, KPC + OXA-48-like, GES, IMI, SME, FRI-2) (n=422)</th>
<th>Others (MBL + non-metallo-enzymes, NDM + OXA-48-like) (n=25)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>E. coli</td>
<td>Klebsiella spp.</td>
<td>Enterobacter / Citrobacter</td>
</tr>
<tr>
<td>Imipenem</td>
<td></td>
<td>5</td>
<td>2</td>
<td>3</td>
</tr>
<tr>
<td>Meropenem</td>
<td></td>
<td>5</td>
<td>1</td>
<td>3</td>
</tr>
<tr>
<td>Ertapenem</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ampicillin</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Co-amoxiclav</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Piperacillin/tazobactam</td>
<td></td>
<td>4</td>
<td>0</td>
<td>2</td>
</tr>
<tr>
<td>Cefotaxime</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ceftazidime (CAZ)</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ceftazidime/avibactam</td>
<td>(^b)</td>
<td>3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Ceftolozane/tazobactam</td>
<td></td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Aztreonam</td>
<td></td>
<td>20</td>
<td>28</td>
<td>47</td>
</tr>
<tr>
<td>Ciprofloxacin</td>
<td></td>
<td>5</td>
<td>7</td>
<td>15</td>
</tr>
<tr>
<td>Gentamicin</td>
<td></td>
<td>37</td>
<td>21</td>
<td>20</td>
</tr>
<tr>
<td>Tobramycin</td>
<td></td>
<td>28</td>
<td>4</td>
<td>5</td>
</tr>
<tr>
<td>Amikacin</td>
<td></td>
<td>50</td>
<td>40</td>
<td>55</td>
</tr>
<tr>
<td>Colistin</td>
<td></td>
<td>97</td>
<td>93</td>
<td>97</td>
</tr>
<tr>
<td>Tigecycline</td>
<td></td>
<td>96</td>
<td>61</td>
<td>88</td>
</tr>
</tbody>
</table>

\(^a\) Susceptibility defined using EUCAST 2017 breakpoints
\(^b\) Two isolates were susceptible to avibactam alone

active in vitro against ≤50% isolates
active in vitro against >50 & ≤90% isolates
active in vitro against >90% isolates
Enhanced surveillance of carbapenemase-producing strains via the Electronic Reporting System

In response to increasing numbers of carbapenemase producers being confirmed in AMRHAI and on-going isolation of such isolates both in the North West and London regions of England, PHE implemented an Electronic Reporting System (ERS) for enhanced surveillance system of carbapenemase-producing Gram-negative bacteria in England.

The ERS serves three main functions:

i. a system for laboratories to request full characterisation of Gram-negative bacteria where expression of an acquired carbapenemase is suspected
ii. a system to report locally confirmed carbapenemase producers
iii. a system for NHS Trusts to submit enhanced surveillance data

The ERS was launched in May 2015, with a module to capture local molecular testing added in July 2016. Monthly surveillance reports are produced that provide an update on carbapenemase-producing Gram-negative bacteria reported via the ERS, showing cumulative and monthly counts by Acute Trusts and monthly counts of individual mechanisms of resistance. The report is emailed to all ERS users, NHS Directors of Infection Prevention and Control, microbiologists, epidemiologists and PHE HCAI teams.

As of July 2017 there were a total of 790 registered users on ERS with 132 (95%) laboratories having at least one registered user. Monthly ERS usage figures for the period January – July 2017, show that approximately 70% of organisms referred to the AMRHAI laboratory for confirmation of carbapenemase production were received via the ERS. Patient demographics and specimen details are mandatory fields. The enhanced data fields providing risk factor information are added by Trust infection control teams, registered on ERS as ‘Trust users’, following notification of a confirmed case. The completion rate for the enhanced data fields range from 21% to 33%. As of April 2017 there are 216 registered Trust users representing 86 (54%) Acute NHS Trusts.

There were 6,208 de-duplicated organisms (by patient and bacterial species) submitted via the national ERS between May 2015 and May 2017, with 4,350 (70%) of these organisms isolated from screening specimens. There were 3,166 confirmed carbapenemase-producing organisms reported on ERS in this period, of which 3,066 were CPE. From July 2016 (the date when the local molecular testing results module was released) to July 2017, 32 laboratories have entered 1,758 results in the local testing fields, with 1,066 bacteria entered with a carbapenemase gene detected by their laboratory.
In terms of the range of carbapenemases reported via the ERS, numbers of CPE producing OXA-48 and NDM carbapenemases increased over this time. In contrast, monthly reports of KPC have shown an overall downward trend apart from a spike in the late summer of 2016 (Figure 2.11), although there have been only a small number of reports on the system from Manchester, despite an on-going issue with KPC-producing *K. pneumoniae* in that area since about 2011.27

![Figure 2.11 Confirmed CPE by month reported on ERS, May 2015 – May 2017](image)

The majority (64%) of CPE reported on the ERS were isolated from rectal/faecal specimens, with 94% of these designated as screening samples (Figure 2.12). There appears to have been an increase in confirmed CPE from rectal/faecal specimens between July and October 2016, which is reflected in a similar increase in confirmed CPE from screening samples in the same period. Urine specimens represent 57% of confirmed CPE clinical samples on the ERS. The next largest groups of clinical specimens with confirmed CPE were blood (10%), sputum (6%) and skin/wound (4%).

The ERS data entry form captures the location of the patient at the time the specimen is taken. The majority of confirmed CPE specimens were taken from patients designated as being NHS Trust inpatients (86%). Confirmed CPE cases from GP practices or walk-in centres, community outpatient centres or nursing homes make-up 5% of the total (Figure 2.13). A summary dataset by Trust is available in the online Appendix.
Resistance in *N. gonorrhoeae* is a major concern globally, as it has emerged for all classes of antimicrobials used for treatment. Previous therapies include penicillin, ciprofloxacin and cefixime, all of which were replaced in the UK as the prevalence of AMR breached the WHO recommended threshold (≥5% of infections resistant to the first line therapy). In March 2017, *N. gonorrhoeae* was included as a high priority on the WHO list of pathogens that require the urgent development of new antibiotics to remain treatable.

In the 2016 GRASP survey, 1,284 isolates of *N. gonorrhoeae* from 25 genitourinary medicine (GUM) clinics were successfully tested for antimicrobial susceptibility and matched to clinical data. With regard to resistance to first-line therapy (combination of ceftriaxone and azithromycin), no isolates were resistant to ceftriaxone (MIC >0.125 mg/L) and there was a decline in the proportion of isolates resistant to azithromycin (MIC >0.5mg/L) from 9.8% in 2015 to 4.7% in 2016. The proportion of isolates resistant to the previous front-line drug cefixime (MIC >0.125 mg/L) increased from 0.4% in 2015 to 1.7% in 2016. Over the same time resistance to ciprofloxacin (MIC >0.06 mg/L) declined from 41.9% to 33.7% and resistance to penicillin (MIC >1.0mg/L or

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β-lactamase positive) decreased from 17.6% to 13.9%. More detailed information is available in the 2017 GRASP annual report.29

Emerging resistance issues

Pan-aminoglycoside resistance in Gram-negative bacteria

16S rRNA methyltransferase enzymes (16S RMTases) are emerging resistance mechanisms found in Gram-negative bacteria that confer high-level resistance (MICs ≥256 mg/L) to all clinically-relevant aminoglycosides. To date, ten 16S RMTase genes have been described: armA, rmtA, rmtB, rmtC, rmtD, rmtE, rmtF, rmtG, rmtH and npmA. Under the auspices of a joint PhD studentship funded by the National Institute for Health Research Health Protection Research Unit in Healthcare-Associated Infections and Antimicrobial Resistance at Imperial College London, PHE’s AMRHAI Reference Unit has been screening referred isolates for other purposes for these genes as their prevalence in the UK is currently unknown.

Almost all Enterobacteriaceae (755/817, 92.4%) and Acinetobacter baumannii (527/550, 95.8%) expressing high-level resistance to all of tobramycin, gentamicin and amikacin (MICs >64 mg/L) were positive for one or more 16S RMTase genes, with armA, rmtC and rmtF being the most common. Amongst positive isolates, the majority (94.5%) also harboured a carbapenemase gene, with NDM being the most common amongst Enterobacteriaceae and OXA-23 (associated with international clone II) amongst A. baumannii. In contrast, only 10% (22/221) of P. aeruginosa exhibiting pan-aminoglycoside resistance were found to harbour a 16S RMTase gene, confirming that other mechanisms, such as aminoglycoside-modifying enzymes, efflux pumps and porin loss are currently more important in this species. Nevertheless, 81.1% of 16S RMTase-positive P. aeruginosa co-produced a carbapenemase (belonging to various families).

Despite the intrinsic bias of the presence of carbapenem resistance related to samples referred to the reference laboratory, ‘high risk’ clones appear to play an important role in the emergence of 16S RMTases in Enterobacteriaceae, A. baumannii and P. aeruginosa. Emergence of 16S RMTases in the UK and their association with carbapenemases poses a serious threat to the treatment of Gram-negative infections.30,31

30 Taylor E et al. Pan-aminoglycoside resistance: the emergence of 16S rRNA methyltransferases in the UK. 27th ECCMID; Vienna, Austria.
31 Taylor E et al. First identification of 16S rRNA methyltransferases in *Pseudomonas aeruginosa* in the UK. 27th ECCMID; Vienna, Austria
Transferable colistin resistance

For serious infections caused by multi-resistant Gram-negative bacteria colistin often remains an important ‘last-line’ option for treatment. Most colistin resistance in the Enterobacteriaceae results from mutations in several different chromosomally-encoded genes leading to modification of the lipopolysaccharide. These chromosomally-encoded forms of colistin resistance are not transferable between strains, with resistance resulting either from de novo emergence or clonal expansion of resistant isolates.

In 2015 the first transferable colistin resistance mechanism encoded by the plasmid-mediated \textit{mcr-1} gene was reported in \textit{E. coli} isolated in China and later described worldwide in various enterobacterial species isolated from the environment, vegetable and meat products, animals and humans. Subsequently, novel variants designated \textit{mcr-2} to \textit{mcr-5} have been reported. Variants \textit{mcr-2} and \textit{mcr-3} were described in \textit{E. coli} from Belgium and China, respectively, while \textit{mcr-4} has been described in \textit{Salmonella} Typhimurium from Italy and in \textit{E. coli} from Spain and Belgium. Novel variant \textit{mcr-5} was reported in a tartrate fermenting \textit{Salmonella enterica} subsp. 	extit{Enterica} serovar Paratyphi B (\textit{Salmonella Paratyphi B dTa+}) in Germany. \textit{Moraxella} spp. have been suggested as a potential reservoir of \textit{mcr} genes, which may be transferred to Enterobacteriaceae following association with mobile genetic elements. \textit{mcr} genes have greater potential for impact on public health than mutational colistin resistance since infection prevention and control measures may not successfully contain the resistance as the \textit{mcr} gene may "escape", transferring among strains, species and genera. Rapid identification of bacterial strains producing \textit{mcr} genes is therefore important for prompt implementation of infection prevention and control measures in order to prevent further spread of resistance.

A retrospective analysis of the PHE archive of whole-genome sequences of ~24,000 bacterial isolates from surveillance collections, submissions to reference services and research projects between 2013 and 2015 identified 15 \textit{mcr-1}-positive isolates consisting of \textit{Salmonella enterica} and \textit{E. coli} isolated from humans and poultry meat. In 2016 AMRHAI started screening for \textit{mcr} genes in Enterobacteriaceae, \textit{Acinetobacter} and \textit{Pseudomonas} spp. confirmed as colistin resistant by the reference laboratory. Up

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35 Yin W et al. MBio 2017; 27:8(3).
to the end of 2016, only three additional mcr-1 positive strains have been identified amongst referred colistin-resistant isolates.

Two of the mcr-1 positive isolates were confirmed CPE (AMRHAI, unpublished data). There are few reports of sporadic clinical carbapenemase-producing organisms confirmed as carrying mcr genes in the literature. However, prior carbapenem usage was found to be a risk factor for carriage of mcr-1-positive E. coli in China,\(^4^0\) suggesting that the association between mcr-1 and carbapenem resistance may become stronger in the future.

**UK participation in international surveillance of AMR**

AMR is a global health threat hence international surveillance is required to fully understand the worldwide epidemiological picture and total burden of resistant infections. The UK currently participates in EARS-Net, a pan-European surveillance system managed by the ECDC and has enrolled in GLASS conducted under the auspices of the WHO.

**EARS-Net**

EARS-Net (originally established as the European Antimicrobial Resistance Surveillance System [EARSS] in 1998), collects and collates data on resistance to key antibiotics in blood culture and cerebrospinal fluid (CSF) isolates of 8 pathogens (S. aureus, E. coli, S. pneumoniae, E. faecalis, E. faecium, K. pneumoniae, P. aeruginosa and Acinetobacter spp.) Data from each country are submitted to ECDC via The European Surveillance System (TESSy) on an annual basis and the collated data, which allow inter-country comparisons of rates of resistance, are published as annual reports\(^4^1\) and also made publically available via the ECDC Surveillance Atlas of Infectious Diseases (Figure 2.14).\(^4^2\)

Historically, data for England was originally obtained from a small number of hospital laboratories that enrolled in EARSS and submitted isolates to the national Reference Laboratory along with paper forms. Subsequently, data for these laboratories was collected from routine laboratory surveillance reports (LabBase/CoSurv). From late 2016, PHE began a recruitment drive to increase participation in EARS-Net, by encouraging laboratories routinely submitting AMR data to SGSS to enrol in the surveillance programme. Work has been done to restructure and automate the data extraction and submission process with the aim of improving data quality and

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timeliness. Laboratories who would like to enrol in EARS-Net are asked to contact PHE at EARS.Net@phe.gov.uk.

Figure 2.14. Proportion (%) of invasive isolates of *E. coli* resistant to quinolones by country in Europe, 2015. Data shown courtesy of the ECDC Surveillance Atlas of Infectious Diseases.

**GLASS (Global Antimicrobial Resistance Surveillance System)**

In May 2015, the 68th World Health Assembly adopted the WHO global action plan on AMR. One of the five strategic objectives of the action plan is to strengthen the evidence base through enhanced global surveillance and research. The GLASS is being established to support a standardized approach to the collection, analysis and sharing of data on AMR at a global level, in order to inform decision-making, drive local, national and regional action, and provide the evidence base for action and advocacy. The UK enrolled in the GLASS programme in July 2017 and is currently establishing a UK GLASS Steering group to discuss data collection and engage with EARS-Net regarding submission of UK data to the GLASS information technology (IT) platform.
Discussion

A major AMR focus of this year’s ESPAUR Report is resistance in Gram-negative bloodstream infections. As highlighted in previous reports the surveillance data continue to show a mixed picture. On the one hand, resistance to key antibiotics assessed in terms of the proportions of isolates that are resistant shows little change over the last few years. On the other hand, increases in the incidence of Gram-negative bacteraemia mean that the burden of resistance, assessed in terms of the numbers of resistant infections continues to show an upward trend. This serves to highlight the importance of infection prevention and control as a key intervention for tackling AMR. Reducing the numbers of infections also reduces the need to prescribe antibiotics, which further serves to reduce the selection pressure for the emergence and spread of resistance. In this regard it is noteworthy that in late 2016 the UK government announced an ambition to reduce healthcare-associated Gram-negative bloodstream infections in England by 50% by March 2021.43 Continuation of the surveillance activities reported here will be essential for monitoring progress in achieving this ambition.

In the present report robust data on the incidence of *E. coli* bacteraemia showing year-on-year increases were available from the mandatory surveillance programme implemented in 2011. In contrast, data on the incidence of bacteraemia due to *Klebsiella* spp. and *Pseudomonas* spp. were only available from SGSS which houses data submitted by hospital laboratories on a voluntary basis. Although ~98% of hospital laboratories supply data, there is nonetheless incomplete case ascertainment. In an effort to improve the collection of data on bacteraemia due to the latter two organisms, PHE have upgraded the Data Capture System (DCS) used by hospital Trusts to report cases of *E. coli* bacteraemia to enable collection of data on bacteraemias caused by *Klebsiella* spp. and *P. aeruginosa*. Further to this, in September 2017, NHS Improvement wrote to NHS Trust and Foundation Trust Chief Executives, Directors of Infection Prevention and Control, Regional Chief Nurses and Regional Medical Directors informing them that mandatory reporting of bacteraemia was being extended to include those caused by *Klebsiella* species and *P. aeruginosa*.44 In support of actions to reduce the rates of these infection, NHS also published two resources, namely a tool to enable providers and CCGs to understand the excess length of stay and number of deaths associated with *E. coli* bloodstream infections and the savings that can be made if infection rates are reduced, together with a map displaying NHS providers and CCGs with the highest and lowest infection rates in 2016/17.45 The extension of mandatory reporting to cover the three commonest Gram-negative pathogens causing bacteraemia will greatly enhance case ascertainment and it is hoped that the timely feedback of

44 https://improvement.nhs.uk/news-alerts/provider-bulletin-20-september/#gramnegativeinfection
45 https://improvement.nhs.uk/resources/preventing-gram-negative-bloodstream-infections/#h2-monitoring-ecoli
more robust local data via PHE Fingertips will be useful to frontline workers in developing and assessing the effectiveness of interventions to reduce these infections.

In addition to surveillance of resistance in bacteraemia, PHE is also expanding surveillance into other disease areas, particularly UTIs. The rationale for focusing on UTIs is that they are one of the most common infections seen in both the community and hospital settings. In addition UTIs are a common source of underlying infection that may seed the blood to cause bacteraemia. Hence better management of UTIs may have the additional benefit of reducing associated bloodstream infections. As shown in this report, rates of resistance to trimethoprim were much higher than those for nitrofurantoin, supporting the national recommendations for use of the latter agent. It must be borne in mind however, that producing robust estimates of rates of resistance in UTIs, particularly in the community, is compromised by the current lack of structured surveillance. Most prescribing for infections in primary care is empirical and the majority of UTIs are not investigated microbiologically, and those that are reflect a biased population such as treatment failures (likely to be due to resistance) or recurrent and/or complicated infections in patients who may have experienced considerable exposure to antibiotics. One approach to tackling this problem is the establishment of a network of sentinel GP practices to undertake prospective surveillance, although such an approach would be expensive and require significant financial resource.

In addition to the above, PHE is working to improve the quality of routinely generated data for other pathogens (together with associated data on antimicrobial susceptibility) reported to SGSS. To this end an audit is planned which will include both the CDR and AMR modules in SGSS, covering data for the period 1 January 2013 to 31 December 2016. The audit will be delivered in three separate, but linked pieces of work comprising: (i) a review of the Laboratory LIMS reporting rules in each laboratory to ensure that organisms required are included and correctly specified. This will initially focus on the 2 most popular systems in England, which currently account for 50% of laboratories; (ii) an audit to compare received reports against the reporting guidelines. Quality issues at specimen level will be examined, including ensuring codes are correctly translated for items such as organisms, specimens and antibiotics; (iii) an audit comparing data held on the LIMS with data received by SGSS for individual laboratories for a subset of organisms. An interim report will be presented in spring 2018 with a full report delivered in the autumn. Issues identified by the audit will serve to inform actions to improve the quality of surveillance data. Other areas of work to improve the quality of surveillance data include the use of data linkage to bring together disparate but complementary information held on different databases, for example linking microbiology data in SGSS with clinical data in HES and outcome data from the ONS. Such combined datasets lend themselves to more sophisticated analyses allowing more complex epidemiological and microbiological issues to be addressed. In the slightly longer term linkage with whole genome sequence data will allow the underlying molecular epidemiology of pathogen spread as well as the spread of AMR to be
investigated in much greater depth. A further advantage of such integrated datasets will be to reduce the need for data to be supplied (often manually) by colleagues in the NHS.

With regard to AMR, there is much concern over the problem of emerging resistance to carbapenems. The data from the UK again gives a mixed picture in that while resistance to carbapenems in clinical isolates of *E. coli* and *Klebsiella* spp. causing bloodstream infections remains low, referral of isolates of CPE to the national Reference Unit continues to increase year-on-year. PHE is working to increase our understanding of the epidemiology of carbapenem resistance by encouraging Trusts to report risk factor information when they submit isolates for confirmation of carbapenemase production. Although PHE has implemented the ERS for enhanced collection of data on confirmed carbapenemase producers, unfortunately as outlined in this report, completion of the enhanced data field is currently undertaken for less than a third of confirmed isolates.

The most significant clinical problems arise when infections are caused by strains of bacteria resistant to multiple antibiotics. Surveillance is thus being expanded to provide updates on trends in multi-resistance. To complement these activities, molecular research is on-going to analyse the underlying genetics of resistance with a particular focus on resistance to carbapenems and aminoglycosides. It is hoped that such a multi-disciplinary approach will provide a broad insight into the underlying epidemiology of the spread of AMR.

One of the seven key areas for action in the UK 5-year AMR strategy is to strengthen international collaboration, as AMR is an global problem requiring an integrated and coordinated international response. PHE has contributed to pan-European surveillance of AMR through its participation in EARS-Net (and its predecessor EARSS) since its inception and will soon be expanding its role by contributing to a broader international programme of AMR surveillance following the formal enrolment of the UK in July 2017 into GLASS conducted under the auspices of the WHO. The UK is widely regarded as being a world leader in terms of surveillance of AMR and by sharing its experience and expertise, PHE will endeavour to make a positive contribution to enhancing surveillance of AMR at an international level.

**Future actions**

Future work will seek to:

- monitor the progress of the national ambition to halve healthcare-associated Gram-negative bacteraemias and assess the impact on the burden of AMR in terms of the numbers of resistant infections
• improve our understanding of the epidemiology and incidence of antibiotic-resistant UTIs with a view to improving the management of UTIs and reducing the numbers of UTIs that progress to bacteraemia
  o assess the feasibility of establishing prospective community-based surveillance of UTIs via a network of sentinel GP practices
  o assess the feasibility of more in-depth analysis of routinely generated laboratory data to look at specific patient groups or settings such as antenatal clinics, children with single/uncomplicated versus multiple/complicated UTIs
• reduce the burden of data entry for the NHS in support of surveillance by developing more sophisticated data linkage and electronic data transfer systems
• undertake an audit to assess the completeness and compliance of reporting to PHE by diagnostic laboratories with a view to improving the quality of routine surveillance data. The audit will include:
  o errors in laboratory rules for reporting to PHE
  o missing data within SGSS
  o incorrect coding
• explore reasons for geographical variation in levels of HCAI incidence and antibiotic resistance in England
• continue to support the UK in its global leadership role through international work and feeding in to the development of GLASS
3. Antibiotic consumption

Introduction

In England, prescriptions for antibiotics are written by medical, dental and nursing professionals in general practice (GP), dental practice, hospitals and other community services (eg out of hours services and walk in centres). Continuous measurement, with the ability to identify the prescriber location (eg hospital, general practice, dental), is essential for tracking antibiotic use over time and determining the effectiveness of antimicrobial stewardship (AMS) programmes in different prescriber populations. It also determines particular antibiotics whose usage is rapidly rising, to help target resources and interventions to curb these increases. An additional feature in this year’s report is the inclusion of a section on hospital departmental prescribing.

Methods

All data in this report is presented by calendar year from 2012 to 2016.

Data source – primary care

Information on the use of antibiotics prescribed in the community was obtained from the NHS Digital (NHSBSA) database. Data are extracted each month as a snapshot in time from the GP Payments system maintained by NHS Digital. As well as general practice prescribing, primary care data also captures data from other community prescribing, which includes walk-in-centres and out of hours services. [See Annex – Chapter 3 for full list]

Data source – secondary care

Information on the use of antibiotics in secondary care was obtained from Quintiles IMS (formerly known as IMS Health). The database held by Quintiles IMS contains information from 99% of NHS hospital pharmacy systems, for drugs dispensed to individual patients and wards. All NHS Trusts were included.

Data source – dental data

Information on the use of antibiotics prescribed in dental surgeries was obtained from the NHS Business Services Authority (NHSBSA) database.
Classification of data

The classification of data on antibiotic use was based on the anatomical therapeutic chemical (ATC) classification system, using the WHO defined daily dose (DDD) for each drug. This is the international classification system aimed at identifying the therapeutic ingredient of all medicines available for human use. Antibiotics for systemic use fall into ATC group ‘J01’. Additionally three oral agents outside the ‘J01’ group that are used to treat *Clostridium difficile* infections were included (fidaxomicin, metronidazole and oral vancomycin).

Denominators

Mid-year populations for each year were extracted from the Office for National Statistics. Hospital admission data for each year was extracted from Hospital Episode Statistics (HES) from NHS Digital.

Trend analysis

National trends in the consumption of antibiotics were assessed for the last five years (2012–2016). A linear regression was applied with the dependent variable being antibiotic consumption in DDD per 1000 inhabitants per day or items per 1000 inhabitants per day and the explanatory variable being year, statistically significant = p<0.05. A statistically significant trend is denoted with the inclusion of †.

Data transparency

All data presented in this chapter in Figures and Tables are available in Excel format in the online Appendix, which additionally includes NHS Area Team data.

Antibiotic grouping

Other β-lactam antibacterials include cephalosporins, carbapenems, and monobactams. Other antimicrobials include glycopeptides, polymyxins, steroid antibacterials, imidazole and nitrofuran derivatives, fosfomycin, linezolid, daptomycin.

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Results

Total consumption of antibiotics in 2016

In 2016, the total consumption of antibiotics in primary and secondary care was 21.4 DDD per 1000 inhabitants per day. There was a statistically significant (p<0.05; denoted by † in the remainder of the chapter) decline of 5.1%† over the last five years, with the main decline occurring between 2014 and 2015 and a further 0.9% reduction from 2015 to 2016 (Figure 3.1). The majority of antibiotics in England were prescribed in the GP setting (74%), followed by hospital inpatients (11%), hospital outpatients (6%), patients seen in dental practice (5%) and patients in other community settings (3%).

Figure 3.1 Total antibiotic consumption, expressed as DDD per 1000 inhabitants per day, England, 2012-2016
Primary care

The highest level of prescribing was in the GP setting and consumption decreased from 17.3 to 15.9† DDD per 1000 inhabitants per day (-8.1%) from 2012 to 2016 with a 2.1% decline being observed between 2015 and 2016. Prescribing by dentists decreased from 1.1 to 1.0† DDD per 1000 inhabitants (-11.5%) between 2012 and 2016, with a decline of -4.9% being observed between 2015 and 2016. There was an increase from 0.59 to 0.73† DDD per 1000 inhabitants (25%) in prescribing by ‘other community prescribers’ from 2012 to 2016, with the largest increase occurring between 2015 and 2016 (12.5%); while this increase is the largest, the other community setting contributes 3.4% of total antibiotic use and the decreases in prescribing in the GP setting were not substantively offset by increases by other community prescribers. Primary care data is also presented as antibacterial items (where each item is an individual antibiotic, more than one antibiotic item could be prescribed at a single consultation).

Secondary care

There was an increase in total secondary care prescribing from 3.58 to 3.81† DDD per 1000 inhabitants per day (6.5%) between 2012 and 2016 with an increase of 2.6% since 2015. There has been an increase in prescribing to hospital inpatients between 2012 and 2016, from 2.27 to 2.43† DDD per 1000 inhabitants per day (6.7%); between 2015 and 2016 prescribing increased from 2.37 to 2.43 DDD per 1000 inhabitants per day (2.3%). Prescribing to hospital outpatients remained broadly stable between 2012 and 2015 but then increased from 1.34 to 1.39 DDD per 1000 inhabitants per day (3.5%) in 2016. The increase in prescribing in secondary care presented as DDD per 1000 inhabitants per day reflects increased hospital activity, including overnight and day-case admissions, outpatient and Accident & Emergency (A&E) attendances; data is also presented by hospital admission in the section on prescribing in secondary care below.
Variation in prescribing by NHS Area Team

In 2016 there continued to be regional variations of prescribing. The lowest rate was observed in Lancashire (16.1 DDD per 1000 inhabitants per day), while the highest rate observed was Merseyside (27.0 DDD per 1000 inhabitants per day). While there is no obvious pattern, areas in the North and North West generally have slightly higher rates of prescribing compared with other areas of the country (Figure 3.2). Full details of Area Team prescribing are presented in the supplementary data.

Figure 3.2 Total antibiotic consumption, expressed as DDD per 1000 inhabitants per day by NHS Area Team, England, 2016
Total prescribing by key agents

The three groups of antibiotics most frequently used in England in 2016 were penicillins (45.0%), tetracyclines (22.1%) and macrolides (14.8%). Between 2012 and 2016 there was an observed decline in the rate of consumption in the following classes: other β-lactam antibacterials (-22.5%), Anti-C. difficile agents (-15.7%), sulfonamides and trimethoprim (-12.3%), penicillins (-7.4%), quinolones (-5.9%) and macrolides (-6.4%). Broadly speaking, overall prescribing was similar in 2015 and 2016, although notable declines were observed in penicillins (-6.2%), other β-lactam antibacterials (-6.5%) and sulfonamides and trimethoprim (-6.5%), while an increase was observed in the group, other antimicrobials (5.8%) (Figures 3.3a and 3.3b).

![Figure 3.3a Total antibiotic consumption by key antibiotic groups, expressed as DDD per 1000 inhabitants per day, England, 2012-2016](image-url)
Penicillins

Penicillins accounted for 45.0% of the total antibiotic prescribing in England in 2016. Although the rate was unchanged between 2015 and 2016, there was a decline in consumption between 2012 and 2016, from 10.4 to 9.6† DDD per 1000 inhabitants (-7.4%) (Figure 3.3a).

Total consumption of penicillins in the GP setting declined between 2012 and 2016 (-11.5%†) while penicillins prescribed in the dental setting also showed a decline (-9.9%†) over the same period. Hospital inpatient prescribing was 2.8% higher in 2016 than it was in 2012, while hospital outpatient prescribing remained broadly stable over the same period. Penicillin prescribing in other community settings increased between 2012 and 2016, from 0.34 to 0.44† DDD per 1000 inhabitants (28.3%), with a 13.5% increase observed since 2015. In 2016 prescribing in other community settings accounted for 4.6% of total penicillin prescribing.

Consumption trends for some commonly used penicillins are shown in Figure 3.4. Co-amoxiclav and amoxicillin consumption decreased by 12.1%† and 10.5%† respectively, between 2012 and 2016; use of co-amoxiclav declined by 5.4% between 2015 and
2016 although amoxicillin use did not change in this period, predominantly reflecting changes in prescribing in the GP setting.

Piperacillin/tazobactam increased between 2012 and 2016 from 0.08 to 0.10† DDD per 1000 inhabitants (23.7%), although a decrease of 3.1% was observed between 2015 and 2016. Phenoxymethylpenicillin and flucloxacillin showed no significant change.

Between 2012 and 2016 use of pivmecillinam increased from 0.01 to 0.04† DDD per 1000 inhabitants (258%), with an increase of 53% being observed between 2015 and 2016. This increasing trend was observed in both primary and secondary care prescribing and is most likely related to changes in PHE guidance for UTI prescribing. Temocillin consumption, while relatively small (<0.01 DDD per 1000 inhabitants per day), increased between 2012 and 2016 (217.9‰), with an observed increase of 51.2% from 2015 to 2016, most likely related to its use as an alternative to carbapenems for suspected or confirmed ESBL infections in hospitals.

Figure 3.4 Consumption of most commonly utilised penicillins, expressed as DDD per 1000 inhabitants per day, England, 2012-2016

47 Details on managing common infections can be found at https://www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care
Cephalosporins

There was a decline in the consumption of cephalosporins from 0.46 to 0.33† DDD per 1000 inhabitants per day between 2012 and 2016 (-28.6%) with a 7.3% reduction being observed between 2015 and 2016. This was almost exclusively due to the decrease in prescribing in the primary care setting, particularly the use of cephalexin in the GP setting; prescribing in secondary care remained unchanged over the five year period (Figure 3.3b, other β-lactam antibacterials).

The top seven agents used in this class are presented in Figure 3.5. There was a decrease in the trend of consumption of cephalexin (-34.7%†), cefradine (-29.7%†), cefuroxime (-15.9%†) and cefaclor (-63.3†) between 2012 and 2016. Ceftriaxone, while only 10% of total cephalosporin use, increased between 2012 and 2016 (53.4%†). Cefotaxime and ceftazidime remained broadly stable over the same period.

Figure 3.5 Consumption of different cephalosporins, expressed as DDD per 1000 inhabitants per day, England, 2012–2016
Tetracyclines

Tetracyclines were prescribed predominantly in the primary care setting (90%). Consumption remained relatively stable between 2012 and 2016 at 4.7 DDD per 1000 inhabitants per day although a reduction in consumption was observed between 2015 and 2016 (Figure 3.3a). An increased trend† in consumption was observed in hospital outpatients and other community setting. Over the same period there was a decline in the trend† of dental prescribing. Hospital inpatient and GP prescribing remained stable over the same period.

The top seven agents prescribed in this class are presented in Figure 3.6. Doxycycline (48.2%) and lymecycline (36.0%) were the predominant tetracyclines prescribed. These two are known treatments for acne, a common skin condition, and the rates of prescribing may reflect this or potentially the use of doxycycline rescue packs for those patients who have frequent exacerbations of chronic obstructive pulmonary disease . There was an increase in the rate of consumption of doxycycline between 2012 and 2016 from 1.94 to 2.28† DDD per 1000 inhabitants per day (17.8%), lymecycline prescribing had a similar rate of prescribing in 2012 and 2016.

Figure 3.6 Consumption of different tetracyclines, expressed as DDD per 1000 inhabitants per day, England, 2012-2016

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48 NHS guidelines for the treatment of acne can be found at http://www.nhs.uk/Conditions/Acne/Pages/Treatment.aspx
49 NICE clinical knowledge summary on chronic obstructive pulmonary disease can be found at https://cks.nice.org.uk/chronic-obstructive-pulmonary-disease#management
Quinolones

There was a decline in the trend of quinolone consumption between 2012 and 2016 (-5.8%)†, although levels of consumption (0.52 DDD per 1000 inhabitants per day) were the same in 2016 as they were in 2015 (Figure 3.3b). Ciprofloxacin was the main quinolone prescribed, accounting for 81.0% of all quinolones, and showed a decline in the trend† of consumption between 2012 and 2016, norfloxacin and nalidixic acid also declined† over the same period. The trend of increased consumption of levofloxacin continued in 2016, and increased by 71.7%† since 2012 and 14.5% between 2015 and 2016 (Figure 3.7).

![Figure 3.7 Consumption of different quinolones, expressed as DDD per 1000 inhabitants per day, England 2012 – 2016](image)

Macrolides

Macrolide use declined between 2012 and 2016 (-6.6%)†; in 2016, total consumption was 3.16 DDD per 1000 inhabitants per day, a reduction of 0.9% from the levels reported in 2015 (Figure 3.3a). The majority of prescribing occurred in the GP setting (80.6%).

The trend in consumption of clarithromycin use continued to increase in 2016 and overall consumption has risen by 10.7%† since 2012. Conversely erythromycin use declined over the same five year period (-42.4%)†, most likely related to practitioners
switching use from erythromycin to other macrolides in accordance with clinical
guidelines and improved tolerability, but also reflecting the use of azithromycin as an
anti-inflammatory for frequent exacerbations of chronic obstructive pulmonary disease
(Figure 3.8). The decline in consumption of erythromycin is a key reason for the
observed decline in macrolides as a combined class.

Figure 3.8 Consumption of different macrolides, expressed as DDD per 1000 inhabitants
per day, England, 2012-2016

Sulfonamides and trimethoprim

Total consumption of this group of antibiotics showed a decline over the five year period
since 2012 (-12.3%†), with a decrease of 6.5% seen between 2015 and 2016 (Figure
3.3a); in 2016, the consumption of sulphonamides and trimethoprim was 1.26 DDD per
1000 inhabitants per day. This decline is reflected in both the GP setting as well as
within inpatient prescribing. Prescribing in outpatients and in other community settings
remained broadly stable between 2012 and 2016.
Nitrofurantoin

The trend in nitrofurantoin consumption continued to increase, with a 17.6%† increase from 2012 to 2016 (including a 5.9% increase between 2015 and 2016); in 2016 nitrofurantoin consumption was 0.96 DDD per 1000 inhabitants per day. This trend was observed in all prescribing settings (Figure 3.9). The most likely explanation is increasing adherence to PHE primary care prescribing guidelines, which changed to recommend this antibiotic as first-line treatment for lower UTIs in adults in 2014.50

Aminoglycosides

Consumption of aminoglycosides remained broadly stable between 2012 and 2016; a slight increase was observed between 2012 and 2014 but consumption subsequently declined in 2015 and 2016. An increase was observed in the trend† of consumption within hospital inpatient and outpatient settings over the five year period. A declining trend† was observed in the GP setting, although aminoglycosides were rarely prescribed in this setting. This class makes up a relatively small amount of the overall prescribing at approximately 0.12 DDD per 1000 inhabitants (0.6% of total prescribing) (Figure 3.10).

50 Details on managing common infections can be found at https://www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care
Trends in consumption of other agents: parenteral glycopeptides and daptomycin

Use of glycopeptides and daptomycin occurred almost exclusively in the hospital setting (98.9%). Despite reductions in MRSA bacteraemia and other infections, the use of parenteral glycopeptides (vancomycin and teicoplanin) and daptomycin continued to increase over the last 5 years from 0.065 to 0.094† DDD per 1000 inhabitants (44.6%) (Figure 3.11), predominantly related to the rise in teicoplanin use. Teicoplanin use may be increasing related to improved access to outpatient parenteral antibiotic therapy and use in surgical prophylaxis (one-third of hospital inpatients on teicoplanin were receiving it as surgical prophylaxis, in the 2016 national prevalence survey). The consumption of daptomycin increased by 83.2%†, though it still remains very low at <0.01 DDD per 1000 inhabitants per day (Figure 3.12).
Figure 3.11 Consumption of glycopeptides and daptomycin, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2012-2016

Figure 3.12 Consumption of different glycopeptides and daptomycin, expressed as DDD per 1000 inhabitants per day, England, 2012-2016
Colistin

Colistin is a last resort antibiotic that is most frequently used for multidrug-resistant infections. Total consumption of colistin varied little between 2015 and 2016 and over the five years since 2012; in 2016, total colistin consumption was 0.073 DDD per 1000 inhabitants per day. However, from 2012 to 2016 there was a declining trend in colistin prescribing in the GP setting, with conversely, an increasing trend observed in prescribing of colistin in the secondary care outpatient setting, most likely related to the new clinical commissioning guidelines for inhaled therapies for adults and children with cystic fibrosis released in December 2014. Using colistin in inpatient and other community settings remained stable over the five year period (Figure 3.13).

Figure 3.13 Consumption of colistin by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2012-2016

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Prescribing in primary care: prescription items from general practice, dentists and other community services

The total amount of antibiotic items prescribed continued to decrease between 2012 and 2016 from 2.17 to 1.88† (-13.4%) antibiotic items prescribed per 1000 inhabitants per day; there was a greater decline in items prescribed compared to DDD, suggesting longer duration prescriptions (potentially as prophylaxis), higher doses of antibiotics per prescription or switches to antibiotics with higher DDD per daily use. In 2016 there was a reduction (-2.2%) in the rate of items prescribed compared with 2015. This decline observed over the five year period primarily reflected changes in primary care prescribing in GP and dental practice settings. Other community settings, while broadly similar to 2012, had an increasing trend in consumption since 2013, though this setting accounted for only 5.3% of prescribing in 2016 (Figure 3.14).

GP prescribing accounted for 86.3% of all antibiotic items in the community in England in 2016, which is similar to levels that have been observed in recent years. Dentists prescribed 8.4% of antibiotic prescription items, while 5.3% was prescribed in other community settings.

Figure 3.14 Antibiotic items by prescriber group, expressed as items per 1000 inhabitants per day, England, 2012-2016
General practice

Penicillins remain the most commonly prescribed antibiotic items in GP prescribing, accounting for 49.8% of all antibacterial prescriptions, followed by tetracyclines (13.1%) and macrolides (12.5%). Use of penicillins in the GP setting declined from 2012 to 2016†; notably the number of prescription items for co-amoxiclav and amoxicillin declined by 31% and 22% respectively. The reduction in penicillin consumption has been a contributing factor for the observed declining rate of total GP antimicrobial prescribing over the last five years. Macrolides, sulphonamides, anti-\textit{C. difficile} agents and other β-lactam antibacterials have also shown a reduction in consumption in the GP setting. Use of tetracyclines and other antibacterials increased over the same period (Figure 3.15).

![Figure 3.15 Antibiotic items prescribed by GP, expressed as items per 1000 inhabitants per day, England, 2012-2016](image-url)
Other community prescribing

Other community prescribing includes diverse prescribing locations. The trend of increased community service prescribing continued in 2016 from 0.088 to 0.100† antibiotic items per 1000 inhabitants (13.7%) between 2012 and 2016 with an increase of 9.4% being recorded between 2015 and 2016. Penicillins (61.9%) are the most common group prescribed in this setting, followed by macrolides (10.6%) and trimethoprim (10.4%).

Among the other community settings, the highest level of prescribing is seen out-of-hours, which accounts for 58.1% of prescribing. Walk-in centre (15.4%) use has increased, though data may be misclassified with urgent care (6.3%) as it will depend on how this is reported to NHSBSA; it may be reported at Clinical Commissioning Group (CCG) level, as standalone centres, or combined within GP cost centre. Since the 2013 NHS re-organisation, there has been reclassification and reconfiguration of these services and therefore comparisons require caution; the trends for each location are outlined in Figure 3.16a and 3.16b.

![Figure 3.16a Antibiotic use in other community settings, expressed as items per 1000 inhabitants per day, England, 2012-2016](image-url)
Figure 3.16b Antibiotic use in other community settings, expressed as items per 1000 inhabitants per day, England, 2012-2016

*note Hospital dispensing allocated to other community antibiotics are on FP10(HP), prescriptions issued in hospitals and dispensed in the community

Dental practice

Dental practice prescribing data is available from NHS practices and consultations only.\(^{52}\) From 2012 to 2016, there was a decline in the trend of dental prescribing with a reduction of -21.0\(^\dagger\) in between 2012 and 2016. A reduction of -7.7\(^\%\) was observed between 2015 and 2016 (Figure 3.17). This is a large reduction of approximately 1 in 5 less prescriptions in 2016 compared with 2012. The predominant antibiotics prescribed in 2016 were amoxicillin (66.7\(^\%\)), metronidazole (28.3\(^\%\)) and erythromycin (4.5\(^\%\)) as shown in Table 3.1. Of all items prescribed, greater than 99\(^\%\) of prescriptions were narrow-spectrum penicillins, metronidazole or macrolides, as recommended in dental treatment guidelines.\(^{53}\)

\(^{52}\) http://www.nhs.uk/NHSEngland/AboutNHSservices/dentists/Pages/dental-services-available-on-the-NHS.aspx

Figure 3.17 Total antibiotics prescribed by dentists, expressed as items per 1000 inhabitants per day, England, 2012-2016

Table 3.1: Antibiotics prescribed by dentists, expressed as items 1000 inhabitants per day, England, 2012-2016

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amoxicillin</td>
<td>0.1289</td>
</tr>
<tr>
<td>Metronidazole</td>
<td>0.0561</td>
</tr>
<tr>
<td>Erythromycin</td>
<td>0.0088</td>
</tr>
<tr>
<td>Amoxicillin and enzyme inhibitor</td>
<td>0.0009</td>
</tr>
<tr>
<td>Clarithromycin</td>
<td>0.0002</td>
</tr>
<tr>
<td>Doxycycline</td>
<td>0.0004</td>
</tr>
<tr>
<td>Tetracycline</td>
<td>0.0002</td>
</tr>
<tr>
<td>Other</td>
<td>0.0045</td>
</tr>
</tbody>
</table>

The NHSBSA has worked with PHE to produce a Dental Prescribing Dashboard with increased granularity of data by NHS Area Team.\textsuperscript{54} The dashboard reports the total number of items and net ingredient cost of dental antimicrobial prescribing including the top four antimicrobial items (amoxicillin, metronidazole, erythromycin and clindamycin) as a proportion of all antimicrobial dental prescribing. It also demonstrates that an antibiotic prescription was dispensed after 8.2% of dental treatment courses/ interventions.

\textsuperscript{54} Dental Prescribing Dashboard data are available at http://www.nwph.net/dentalhealth/Prescribing.aspx
Results are reported by individual month including proportions of monthly totals and can be displayed for an individual local team using the drop down selector on the dashboard. Results can be charted by individual antimicrobial item, highlighting figures for a selected local team.

The dashboard provides consultants in Dental Public Health in PHE with insight into dental prescribing so that they can support Local Dental Networks to explore variation in care compared to other areas of England and inform future work with dentists in their locality. This will help to encourage optimal prescribing amongst dentists.

Prescribing in secondary care

Antibiotic prescribing in secondary care peaked in 2013, at 4801 DDD per 1000 admissions. Despite a reduction in 2015, rates of consumption in 2016 returned to similar levels observed in previous years, at 4798 DDD per 1000 admissions (Figure 3.18).

![Figure 3.18 Total Trust prescribing, expressed as DDD per 1000 admissions, England, 2012-2016](image)

However the trend was not the same across all Trust types: between 2012 and 2016, specialist and multiservice Trusts had an increasing trend† of consumption, with a decreased trend† being observed in teaching Trusts; all other Trusts showed minor fluctuations in prescribing but remained broadly similar between 2012 and 2016 (Figure 3.19). See Annex – chapter 3 for Trust type definitions. In 2016, large and teaching Trusts had lower consumption of antibiotics per admission than other Trust types.
Figure 3.19 Antibiotic prescribing, by Trust type, expressed as DDD per 1000 admissions, England, 2012-2016

The increase in antibiotic use observed in 2016 was reflected in the following groups: penicillins, tetracyclines, quinolones and the group other antibacterials. Conversely, the rate of consumption of sulfonamides, macrolides and anti-C. difficile agents declined in 2016 when compared with 2015 (Figure 3.20).
Broad-spectrum prescribing

Within hospitals, the current greatest infection threat is multi-drug resistant Gram-negative bacteria. Therefore the challenge in hospital AMS programmes is to identify patients that may have infection caused by these bacteria, confirm the organism and antibiotic susceptibility pattern rapidly and treat patients with an appropriate antibiotic. Excessive use of antibiotics can be mitigated against by using the shortest duration of therapy possible and using expert review teams to stop or modify a patient’s antibiotic therapy, especially in complex cases. This section discusses the three broad-spectrum antibiotics that are of particular concern in English hospitals, namely, colistin, piperacillin/tazobactam and carbapenems.

Colistin is usually reserved for treating infections caused by bacteria that are known or suspected to be carbapenem resistant. After many years at low consumption levels, use of this antibiotic increased by 62.8%† between 2012 and 2016, with the majority of that increase occurring in 2015. The increase in consumption of colistin was seen in both parenteral and inhalation administration routes (Figure 3.21). Inhalation is used most commonly for infective exacerbations or prophylaxis in patients with bronchiectasis. However the parenteral formulation is also used off-label as a nebulised form in critically ill patients.
There has been an increase in the trend† of consumption between 2012 and 2016 within large, specialist and teaching Trusts, with specialist Trusts having by far the highest rate of consumption, increasing by 61%† between 2012 and 2016 (Figure 3.22). Colistin consumption within medium and small Trusts has remained broadly stable over the same five year period. The rate of consumption in multi-service Trusts has declined for the second year in a row, although the rate is still higher than the rate observed in 2012.

Figure 3.21 Colistin consumption in all Trusts, expressed as DDD per 1000 admissions, England, 2012-2016

There has been an increase in the trend† of consumption between 2012 and 2016 within large, specialist and teaching Trusts, with specialist Trusts having by far the highest rate of consumption, increasing by 61%† between 2012 and 2016 (Figure 3.22). Colistin consumption within medium and small Trusts has remained broadly stable over the same five year period. The rate of consumption in multi-service Trusts has declined for the second year in a row, although the rate is still higher than the rate observed in 2012.
Consumption of piperacillin/tazobactam in secondary care increased between 2012 and 2015 but showed a decline in 2016 (Figure 3.23). While this is promising, the rate of consumption is still 19% higher than the rate observed in 2012. In comparison to 2015, large, medium, multi–service and teaching Trusts observed a decline in the overall rate of prescribing of piperacillin/tazobactam, while small and specialist Trusts both observed an increased rate of consumption (Figure 3.24). All Trust types observed higher rates of prescribing in 2016 compared with 2012.
Figure 3.23 Piperacillin/tazobactam consumption in all Trusts, expressed as DDD per 1000 admissions, England, 2012-2016

Figure 3.24 Piperacillin/tazobactam consumption by Trust type, expressed as DDD per 1000 admissions, England, 2012-2016
Carbapenem use in secondary care declined for the second consecutive year. In 2016 the rate of consumption fell by -4.4% from that observed in 2015; however, carbapenem use in secondary care is still 9% higher in 2016 compared to 2012. Meropenem is still the predominant carbapenem used in secondary care (89.4%) (Figure 3.25).

Figure 3.25 Carbapenem consumption in all Trusts, expressed as DDD per 1000 admissions, England, 2012-2016

All Trust types, with the exception of specialist Trusts, observed declines in consumption in 2016 compared with rates observed in 2015. Large, medium, small and multi-service Trusts had broadly similar rates of carbapenem consumption. Higher rates continue to be observed in both teaching and particularly specialist Trusts (Figure 3.26).
Figure 3.26 Carbapenem consumption by Trust type, expressed as DDD per 1000 admissions, England, 2012-2016

Secondary care – prescribing by department

PHE have analysed the Quintiles IMS data by specialty grouping. The specialties within each group are outlined in Annex – Chapter 3.

Consumption per admission

Between 2012 and 2016 an increase in the trend of consumption was observed within intensive care units (ICU) from 49.4 to 66.0† DDD per ICU admission (33.6%), with a 6.8% increase being observed between 2015 and 2016. However, this increase in DDD per ICU admission may be related, at least in part, to declining piperacillin/tazobactam and carbapenem use and a switch from using a single antibiotic to a combination of 2-3 antibiotics for the same condition (eg rather than using piperacillin/tazobactam to treat intra-abdominal infection, using amoxicillin, gentamicin and metronidazole, and thus increasing the DDD from 1 to 3). Conversely, a decline in consumption was observed within Specialist Medicine, from 4.5 to 3.9† DDD per admission to a Specialist Medicine
Broadly speaking consumption in all other specialist groups remained stable with minor fluctuations (Table 3.2).

### Table 3.2: Total antibiotic defined daily doses per admission in secondary care, by speciality group, 2012-2016

<table>
<thead>
<tr>
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<td>2.1</td>
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</table>

Prescribing of piperacillin/tazobactam and carbapenems in the inpatient setting

Piperacillin/tazobactam and carbapenems are powerful secondary care broad-spectrum antibiotics and are almost exclusively prescribed within the inpatient setting. In 2016 the proportion of all secondary care inpatient prescribing that consisted of carbapenems or piperacillin/tazobactam was below 10% for all departments with the exception of ICU (12.7%) (Table 3.3).

### Table 3.3: Proportion (%) of all prescribing attributed to piperacillin/tazobactam and carbapenems in secondary care, by speciality group, 2012-2016

<table>
<thead>
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<td>1.8</td>
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Between 2012 and 2016 there has been a decline in the proportion of broad-spectrum consumption among all inpatient prescribing within ICU departments (20.3% to 12.7%). Over the same five year period the same comparative proportion increased within Specialist Medicine (8.4% to 9.9%), Orthopaedics (4.0% to 6.3%), AE/non-specific outpatient (1.4% to 2.1%), Obstetrics and Gynaecology (1.0% to 1.8%) and other departments (4.2% to 6.6%). Using the same method of comparison, broad-spectrum use within Geriatrics, General Medicine, Specialist Surgery, Paediatrics and General Surgery remained broadly stable between 2012 and 2016 (Figure 3.26).

Prescribing of co-amoxiclav, quinolones and cephalosporins in in-patients

Co-amoxiclav, quinolones and cephalosporins comprise an additional group of broad-spectrum antibiotics; typically these are prescribed as second-line treatments, frequently following antibiotic susceptibility testing in primary and secondary care. In 2016, the proportion of total prescribing attributable to this group of antibiotics in different departments ranged from 19.8% in ICU to 44.2% in Obstetrics and Gynaecology (Table 3.4).

Between 2012 and 2016 the proportion of all secondary care prescribing consisting of co-amoxiclav, quinolones or cephalosporins increased within Obstetrics and Gynaecology from 38.7% to 44.2%. Over the same period, a decline was observed within Specialist Medicine (21.5% to 20.6%) and Other (28.9% to 23.3%). All other departments observed fluctuations but remained broadly similar between 2012 and 2016 (Table 3.4).

Table 3.4: Proportion (%) of all prescribing attributed to co-amoxiclav, quinolones or cephalosporins in secondary care, by speciality group, 2012-2016

<table>
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<tr>
<td>Specialist medicine</td>
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<tr>
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<td>20.0</td>
<td>19.6</td>
<td>18.9</td>
<td>19.8</td>
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</table>
Antibiotic consumption surveillance

European collaboration

The UK submits data to the European Centre for Disease Prevention and Control on antibiotic consumption. The European Surveillance of Antimicrobial Consumption Network (ESAC-Net) is a European-wide collaboration that monitors rates of antimicrobial consumption. The 2016 data is not yet available. In 2015, the UK ranked 14th lowest out of 29 countries who submitted community data and the second highest of 22 countries who submitted hospital data. While it is useful to compare the data and trends within countries, the reliability of comparisons across countries is less robust and limited by the variation in antibiotics used and the ability in-country to collect all the prescribing data.

Independent Sector

Work with the independent sector to develop antibiotic consumption surveillance continued in 2016. A survey among members of the Association of Independent Healthcare Organisations (AIHO) to collate information on how prescribing data was collected and stored within their organisations was launched in May 2016.

Based on the survey results, ESPAUR developed a pilot project for collecting antibiotic prescribing data from independent sector healthcare organisations. Seven (24%) of the 29 members of AIHO agreed to participate in the pilot and to supply PHE with their organisations’ antibiotic consumption data. Issues around secure data transfer to PHE and classifications systems used (Dictionary of Medicines and Devices Standard; ATC classification) needed to be addressed. Pharmacist leads from four independent sector healthcare organisations, covering more than 90 hospital sites, have already started the process of transferring data. Translation and merging of the provided antibiotic prescribing datasets is currently in progress.

Antibiotic Prescribing Data Warehouse

In October 2015, the ESPAUR Oversight Group initiated a project to develop a single repository for primary and secondary care antimicrobial prescribing data. A PHE project group was established to design and build a prescribing data warehouse.

The data warehouse was initially developed to host primary care prescribing data and processes created to transform and translate the monthly primary care prescribing data collated by NHS Digital. Routines were also developed to incorporate GP population data provided by the NHSBSA. The primary care prescribing data warehouse is updated quarterly to coincide with the release of updated practice population figures.
Historic primary care data from January 2011 onwards was obtained from NHS Digital and loaded into the data warehouse to provide a 6 year data repository. As of July 2017 there were 34 million antibiotic prescribing records in the data warehouse and an archive has been created for all prescribing data from primary care, holding over 720 million records. Following a data validation exercise completed in January 2017, the data warehouse was made available to PHE analysts and scientists.

Following the introduction of the Commissioning for Quality and Innovation (CQUIN) payments framework for 2017/19, the prescribing data warehouse was reconfigured to import prescribing data provided by individual NHS Trusts to support the delivery of this scheme. A template was developed to enable NHS Trusts to record their quarterly CQUIN returns, and this was posted on the NHS England website in March 2017. Reconfiguration of the prescribing data warehouse to accommodate these template files has been completed and the first quarter (April – June 2017) returns were used to pilot the import process.

PHE will also incorporate secondary care prescribing data from Quintiles IMS (formerly known as IMS Health) and this is being modelled for inclusion within the prescribing data warehouse. A secure server has been configured to receive files directly from Quintiles IMS, and the collection and import processes will be automated.

In the second phase of the project, business intelligence applications will be used to link antimicrobial prescribing data, from both primary and secondary care, with other PHE / NHS datasets, including AMR data collated by the PHE Second Generation System (SGSS) and HES data maintained by NHS Digital. Data models will be created enabling on-line reports to be produced that visualise these combined data sources. The project will provide a portal for PHE and subsequently NHS users to access reports that combine prescribing data, routine AMR surveillance data (from SGSS), mandatory HCAI data and enhanced data on carbapenemase-producing Enterobacteriaceae (CPE) collected from the CPE electronic reporting system (ERS; described in Chapter 2).

Discussion

Total consumption of antibiotics continues its downward trend with a -1% reduction between 2015 and 2016. The five year trend of consumption has shown a decline of -5.1% from 22.6 to 21.4 DDD per 1000 inhabitants per day. Antibiotic prescribing is most common in the GP setting where consumption, measured in both DDD (-8.1%), and items (-13.9%), has declined since 2012. Although prescribing in other community settings continues to increase (25% between 2012 and 2016) it remains a relatively small prescribing setting (3.4% of total prescribing). Antibiotic consumption has

increased within secondary care, specifically inpatients over the last five years, which has increased from 2.37 to 2.43 DDD since 2015 (2.3%), when measured by inhabitants per day but the change between 2012 and 2016 when using the hospital activity denominator, admissions was 1.9%, the difference measuring the increased hospital activity relative to the population.

Penicillins (45.0%), tetracyclines (22.1%) and macrolides (14.8%) remain the most common drug classes prescribed in 2016. Over the period 2012 to 2016 a decreasing trend of consumption was observed for penicillins, cephalosporins, quinolones, macrolides, sulfonamides and trimethoprim. An increased trend was observed for nitrofurantoin, glycopeptides and daptomycin.

It is encouraging that piperacillin/tazobactam consumption fell between 2015 and 2016. This is likely to continue to decrease rapidly in 2017 related to the global difficulties in the procurement of piperacillin/tazobactam.\textsuperscript{56} Carbapenem use also declined in 2016, although again it is the first decline after four years of increased consumption and rates still exceed those observed in 2012. The rate of colistin consumption, while similar in 2016 to rates in 2012, showed an increasing trend in secondary care specifically in hospital outpatients; this in particular highlights the requirements for a whole health economy approach as this switch was most likely related to national commissioning guidance with a switch from primary care to secondary care outpatient prescribing, rather than a true change in prescribing.\textsuperscript{57}

In 2016, large and teaching Trusts had lower consumption of antibiotics per admission than other Trust types. These hospitals frequently have a different case-mix compared to other Trust types. Further work exploring specialty-specific prescribing rates within Trust type and the AMS interventions delivered in different Trusts is required to improve our understanding of this observation.

The introduction of specialty level prescribing data gives a more comprehensive understanding of prescribing within secondary care and will allow for more targeted strategy in the future. The rate of prescribing per admissions was highest by far within ICUs which showed an increasing trend in consumption. While this may be of concern, the proportion of all consumption within ICUs that is attributable to broad-spectrum antibiotics has shown a decreasing trend over the same five year period. It is most likely that the reductions in broad-spectrum antibiotics have resulted in increased consumption due to a switch from one broad-spectrum agent to combination therapy with two or three narrow-spectrum antibiotics. In hospitals, the emphasis in the coming years needs to be on the “Then Focus” component of “Start Smart Then Focus” (SSFT)\textsuperscript{58}

\textsuperscript{56} Department of Health advise on piperacillin/tazobactam supply problems. April 2017. \url{http://www.bsac.org.uk/dh-advises-on-piperacillin-tazobactam-injection-supply-problems/}

\textsuperscript{57} Clinical Commissioning Policy for Inhaled Therapy for Adults and Children with Cystic Fibrosis (A01/P/b) is available at \url{https://www.england.nhs.uk/commissioning/wp-content/uploads/sites/12/2015/01/a01-policy-inhld-thrpy-cf.pdf}
in order to ensure antibiotics, if needed, are prescribed for the shortest duration required for an effective clinical outcome and are stopped altogether if an alternative diagnosis explains the patient’s symptoms.

Future actions

ESPAUR will:

• continue to monitor trends in antibiotic prescribing across all sectors, and will explore specific data from the independent sector
• work with dental partners to develop antibiotic prescribing indicators
• monitor the impact of the national public facing AMR campaign on antibiotic prescribing
• via data linkage, determine the impact of primary care antibiotic prescribing on subsequent bloodstream infections
• work with GRASP to explore methods of monitoring antibiotic prescribing for gonococcal infections
• measure specific changes in prescribing related to second-line antibiotics prescribed for urinary tract infections, such as fosfomycin, pivemecillinam
• explore case-mix adjustment of acute Trust antibiotic prescribing to improve benchmarking and quality improvement

Research in antibiotic consumption

Linkage of patient-level antibiotic prescriptions to positive urine microbiology data, England: a pilot study

KL Henderson, B Muller-Pebody, S Hopkins

Increasing antimicrobial resistance in pathogens causing urinary tract infections (UTI) in the community is affecting clinical treatment success, leading to the development of more complex cases of UTIs and potentially bloodstream infections requiring hospitalisation.

We linked patient-level primary care antibiotic prescribing data (1st February–30th April 2014) from NHS Business Services Authority (BSA) electronic records, to Public Health England’s laboratory antibiotic susceptibility surveillance data from bacterial isolates from urine. The purpose was to determine the appropriateness of antibiotic prescriptions of trimethoprim and nitrofurantoin, and inform the next steps of prescribing surveillance.
This is the first pilot of linking national, patient-level antibiotic prescribing data from the community to microbiology data. We found that a third of antibiotic prescriptions for UTIs were repeat prescriptions, and for more than half of those the prescribers did not switch to a different antibiotic. The findings will be presented at the 2017 FIS conference.

Primary Care Antibiotic Prescribing In an Area of North West England, January 2015 – March 2017

Alicia Demirjian, Graeme Rooney, Ceire Costello, Berit Muller-Pebody, Susan Hopkins

Antibiotic prescribing contributes to the spread of antimicrobial resistance (AMR). Public campaigns aimed at improving antibiotic prescribing in primary care have shown variable success, however, the impact of short-term television advertising as a sole media outlet in such campaigns has not been fully evaluated. Our aim is to describe antibiotic prescribing in the ITV Granada coverage area, and determine the impact of a televised AMR campaign in this region.

We performed a descriptive analysis and compared prescribing trends in the target ITV Granada coverage area (comprising 22 CCGs) to those of the partial coverage area (21 CCGs) and the remainder of England, between January 2015 and March 2017. We calculated antibiotic prescribing rates for outpatient antibiotics in number of items per 10,000 population.

A total of 74,683,072 items were prescribed in England between January 2015 and March 2017. Of these, 7,435,777 (10.0%) were prescribed in the target Granada coverage region. Despite an overall decrease in antibiotic prescribing over time, there was a trend for higher antibiotic prescribing in the Granada target and partial coverage areas compared to the remainder of England. This trend displayed an expected seasonality and seemed to follow the national prescribing trend.

This area of North West England is a high-prescribing region and therefore a priority area for potential interventions. Overall antimicrobial prescribing rates in this region have decreased between January 2015 and March 2017, following national trends. A time series model is currently being developed to determine the impact of the regional AMR campaign, Keep Antibiotics Working, on prescribing.

Impact of the universal childhood influenza vaccine programme on antibiotic prescribing rates for respiratory tract infections in primary care in England

Mary Sinnathamby, Berit Muller-Pebody, Fiona Warburton, Graeme Rooney, Katherine Henderson, Rachel Freeman, Susan Hopkins, Richard Pebody
The UK is in the process of introducing a universal childhood influenza vaccine programme, with healthy children in eligible age-groups offered a newly licensed live attenuated influenza vaccine (LAIV). National rollout commenced in 2013/14 with the introduction to two and three year old children and pilots for primary school aged (4–11 years) children. The aim of the vaccine programme is to both directly protect children immunised with influenza vaccine, but also indirectly protect others in the population at higher risk of severe disease such as the elderly and those with underlying clinical risk factors.

Assessment of the impact of the programme in pilot areas where vaccination of primary school aged children was rolled out in the 2013/14 and 2014/15 influenza seasons showed that cumulative primary care influenza-like consultation, emergency department respiratory attendance, respiratory swab positivity, hospitalisation and excess respiratory mortality were consistently lower in targeted and non-targeted age groups, though less for adults and more severe end-points, compared with non-pilot areas.

Influenza infections are associated with a range of secondary bacterial infections, therefore reducing rates of influenza infection in the population may consequently reduce the rates of secondary bacterial infections and thus a concomitant reduction in the prescription of antibiotics for respiratory tract infections may be seen in areas where the childhood influenza vaccine programme has been introduced.

This study, undertaken by PHE’s AMR and Respiratory Surveillance teams, aims to determine whether the incremental introduction of the childhood influenza vaccination programme is associated with different levels of antibiotic prescribing for respiratory tract infections in primary care in pilot areas (where the LAIV was offered to all primary school age children) and non-pilot areas (where the LAIV vaccine was not offered to all primary school age children).

Monthly and yearly (influenza season) aggregated prescription counts for key antibiotic groups used to treat respiratory infections are used by GP practice and by age category to model differences in prescribing levels between pilot and non-pilot areas in influenza seasons prior and post introduction of the programme.

The association between use of different antibiotics and trimethoprim resistance: going beyond the obvious crude association using elastic net regularization and generalized boosted regression models

Koen Bernardus Pouwels, Rachel Freeman, Berit Muller-Pebody, Graeme Rooney, Katherine Henderson, Julie Robotham, Timo Smieszek

59 http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=21256
Background: Studies linking antibiotic usage and resistance at the population level usually focus on crude associations between the resistance against a specific antibiotic and the use of that specific antibiotic or antibiotic class. Confounding by use of other specific antibiotics and the fact that resistance genes are often linked, are typically ignored. In this study we used elastic net regularization and generalized boosted regression models to take into account confounding by other antibiotic groups and at the same time identify potential co-selection mechanisms.

Material/methods: Monthly prescribing data was obtained from NHS Digital, who collate all primary care prescribing data. Positive Enterobacteriaceae records from urine and kidney samples from patients between April 2014 and January 2016 in England were extracted from the comprehensive antimicrobial resistance module (AMR; formerly AmSurv) of Public Health England’s Second Generation Surveillance System (SGSS). Elastic net regularization and generalized boosted regression models were used to evaluate associations between antibiotic prescribing and trimethoprim resistance, both measured at the Clinical Commission Group level.

Results: Between April 2014 and January 2016, 2,487,635 (99%) of 2,513,285 urine Enterobacteriaceae samples were tested for trimethoprim resistance. The most common pathogens identified were *Escherichia coli* (n=1,746,013), *Klebsiella pneumoniae* (n=70,331) and *Proteus mirabilis* (n=40,905). Using both elastic net regularization and generalized boosted regression models, geographical variation in trimethoprim resistance among Enterobacteriaceae urinary samples could be partly explained by geographical variation in trimethoprim, ampicillin/amoxicillin, and combination of penicillins including β-lactamase inhibitors (mainly co-amoxiclav) use. Ampicillin/amoxicillin use had a larger influence than trimethoprim use. Nitrofurantoin was associated with lower trimethoprim resistance levels.

Conclusions: Elastic net regularization and generalized boosted regression models both identified trimethoprim as a predictor of geographical variation in trimethoprim resistance among Enterobacteriaceae urinary samples. Importantly, ampicillin/amoxicillin use seemed to have a larger influence than trimethoprim use, suggesting that co-selection by these antibiotics is an important driver of trimethoprim resistance levels at the population level. The observation that nitrofurantoin was consistently associated with lower trimethoprim resistance levels may indicate that trimethoprim resistance levels could be reversible if trimethoprim use is replaced by antibiotics that have low selection potential, such as nitrofurantoin.
4. Quality improvement initiatives

Introduction

There are two main quality improvement initiatives to reduce antibiotic prescribing, namely the Quality Premium (QP) and the Commissioning for Quality and Innovation (CQUIN) framework. The QP is intended to reward Clinical Commissioning Groups (CCGs) for improvements in the quality of the services they commission and for associated improvements in health outcomes and reducing inequalities, focussing on antibiotic prescribing across CCGs, while the CQUIN framework supports improvements in the quality of services and the creation of new, improved patterns of care across various health provider types, focussing on reducing antibiotic prescribing in acute Trusts.

This chapter outlines the impact of the antimicrobial resistance (AMR)-related quality improvement initiatives led by NHS England and NHS Improvement and supported by Public Health England (PHE), and in particular highlights the results of the 2016/17 QP and CQUIN together with an evaluation of the 2016/17 CQUIN.

Quality premium

NHS England has published a national QP to improve antibiotic prescribing in primary care each financial year since 2015/16.

Almost 2.7 million fewer antibiotics were dispensed in 2015/16 compared to 2014/15, following the introduction of the AMR QP. There were significant and sustained declines in both antibiotic items per 1000 population and antibiotic (NHSBSA use the term antibacterial) items per STAR-PU; STAR-PU (Specific Therapeutic group Age-sex Related Prescribing Unit) is a value used to adjust data to reflect the age and sex of distribution of patients in each practice or CCG. The median antibiotic items per STAR-PU reduced from 1.188 to 1.087 over this 12-month period. The median proportion of broad-spectrum antibiotics (co-amoxiclav, cephalosporins and quinolones) as a proportion of all antibiotic items reduced from 10.8% to 9.6%.

Quality premium 2016/17

The two parts of the 2016/17 QP had specific thresholds as follows:

- part a) reduction in the number of antibiotics prescribed in primary care. The required performance in 2016/17 must either be: a 4% (or greater) reduction on 2013/14 performance OR equal to (or below) the England 2013/14 mean performance of 1.161 antibiotic items per STAR-PU.
part b) number of co-amoxiclav, cephalosporins and quinolones as a proportion of the total number of selected antibiotics prescribed in primary care to either: to be equal to or lower than 10%, or to reduce by 20% from each CCG’s 2014/15 value.

The NHS Business Services Authority (NHSBSA) provided quarterly data on antibiotic prescribing in the community, while PHE openly published QP indicator data on the Fingertips AMR local indicators portal60 and PrescQIPP published data on their antimicrobial stewardship (AMS) hub.61 NHS England and NHSBSA also published monthly an antibiotic QP dashboard that was freely accessible on the NHS England website.62 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.

The TARGET (Treat Antibiotics Responsibly, Guidance, Education, Tools) toolkit Primary Care Unit team have worked with general practitioners, the Royal College of General Practitioners (RCGP) Clinical Innovations Research Centre, the general public, patients, and other stakeholders to inform the need for and to develop resources to support the primary care antimicrobial QP.

To inform general practice (GP) staff about the QP, the TARGET team and Steve Granier, the TARGET clinical champion at the RCGP, have updated the TARGET group presentation. There was also a workshop based around respiratory and urinary tract infection (UTI) clinical scenarios, that aimed to influence all GP staff intentions to prescribe antimicrobials to ensure they were appropriate for infection, by working together as a team; workshop facilitators were actively encouraged to use antibiotic prescribing data from Fingertips or PrescQIPP so that practices may reflect on their antibiotic prescribing data compared to others. The workshop also introduced GP staff to other TARGET antibiotic resources that support the QP. When evaluated in a randomised controlled trial, this educational workshop significantly improved nitrofurantoin prescribing in the practices involved.

Almost 17,600 fewer antibiotics were dispensed in 2016/17 compared to 2015/16 with a continued decline in both antibiotic items per 1000 population and per STAR-PU. Antibiotic prescribing peaked between October and March every year, when colds and flu season occurs (Table 4.1).

60 https://fingertips.phe.org.uk/profile/amr-local-indicators
61 https://www.prescqipp.info/
Table 4.1: Impact of Quality Premium on antibiotic prescribing in CCGs between 2014/15 and 2015/16

<table>
<thead>
<tr>
<th>Financial year</th>
<th>Quarter</th>
<th>Antibiotic items</th>
<th>Antibiotic items per STAR-PU*</th>
<th>Items per 1000 population</th>
</tr>
</thead>
<tbody>
<tr>
<td>2014/15</td>
<td>1</td>
<td>8 937 522</td>
<td>0.28</td>
<td>166</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>8 225 452</td>
<td>0.26</td>
<td>153</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>10 099 553</td>
<td>0.32</td>
<td>187</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>10 090 324</td>
<td>0.32</td>
<td>187</td>
</tr>
<tr>
<td>2015/16</td>
<td>1</td>
<td>8 327 183</td>
<td>0.26</td>
<td>155</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>7 740 602</td>
<td>0.24</td>
<td>144</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>9 051 169</td>
<td>0.28</td>
<td>168</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>9 561 473</td>
<td>0.30</td>
<td>178</td>
</tr>
<tr>
<td>2016/17</td>
<td>1</td>
<td>8 305 125</td>
<td>0.26</td>
<td>154</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>7 806 259</td>
<td>0.24</td>
<td>145</td>
</tr>
<tr>
<td></td>
<td>3</td>
<td>9 266 214</td>
<td>0.29</td>
<td>172</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>9 285 236</td>
<td>0.29</td>
<td>172</td>
</tr>
</tbody>
</table>

*this quarterly metric is different to the antibiotic items per STAR-PU per 12 months

There was progressive success over 2016/17 with 183 of 209 (88%) 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 1.086 from 2013/14 to 2016/17. By March 2017, 174 of 209 (83%) CCGs had met or exceeded the national ambition to reduce prescribing of broad-spectrum antibiotics (co-amoxiclav, cephalosporins and quinolones) as a proportion of total antibiotic prescribing below 10%. The median CCG value for the number of broad-spectrum antibiotics items as a proportion of total antibiotic items reduced from 10.6% to 8.8%. However, significant variation continues to exist across CCGs with two and three fold differences in items per STAR-PU and proportion of broad spectrum antibiotics respectively remaining between high and low-prescribing CCGs.

Quality Premium 2017/19

The 2017/19 QP is focused around 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. These ambitions include:

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

There are three parts to the 2017/19 QP:

Part a) reducing GNBSIs across the whole health economy.
- a 10% reduction (or greater) in all *E. coli* BSIs reported at CCG level based on 2016 performance data
- collection and reporting of a core primary care data set for all *E. coli* bloodstream infections in Q2-4 2017/18. This will require completion of requisite data through the existing PHE Data Capture System (DCS) used for reporting *E. coli* BSIs and the refined data collection for primary care related aspects

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

Part c) sustained reduction of inappropriate prescribing in primary care. Items per STAR-PU must be equal to or below England 2013/14 mean performance value of 1.161 items per STAR-PU

PHE surveillance of *E. coli* shows that 50% of *E. coli* BSI cases related to the urogenital tract and in these 64% of patients had reported at least one UTI in the previous 12 months. Ongoing mandatory surveillance continues to identify previous UTIs as a key risk factor for *E. coli* BSI; therefore the PHE Primary care unit has developed further resources including a TARGET UTI leaflet to share with patients in the consultation (Figure 4.1). This was developed with patients and GP staff, and includes typical urinary symptoms, encourages pain relief and delayed prescribing for milder urinary symptoms explaining the different types of UTI. The UTI leaflet educates patients about self-care and symptoms that would prompt them to consult a health practitioner again, so facilitating the reduction in *E. coli* bacteraemias, and explains how antibiotic resistance arises. TARGET has also produced audit templates for the common infections including UTI, allowing clinicians to determine how their management of urinary symptoms compares to guidance. The template includes Read codes, and also, automatically calculates an individual’s compliance with the management and antibiotic guidance for UTIs.

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### Figure 4.1: Urinary tract infection (UTI) information leaflet

The QP recommendations, leaflet and management of UTI resources are underpinned by the primary care quick reference antibiotic guidance which has been updated to give the latest recommendations and evidence for the treatment of UTI in the community.

The PHE Primary Care Unit team in collaboration with the British Society of Antimicrobial Chemotherapy (BSAC) have developed a series of seven webinars designed to facilitate improved antibiotic use in primary care, highlighting key things clinicians could do in the primary care setting – one of these webinars covered the management of UTI in primary care, and highlighted that at least half of women presenting with urinary symptoms do not have a UTI confirmed on culture. This supports the use of pain relief and delayed prescribing for mild urinary symptoms.

### CQUIN

AMR was one of three national CQUIN indicators for acute care providers 2016/17. The aim of this CQUIN was to reduce antibiotic consumption, to encourage a focus on AMS and to ensure that prescriptions are reviewed within 72 hours of commencing an antibiotic.
AMR CQUIN 2016/17

Part of the CQUIN payment was reserved for submission of consumption data to PHE for years 2014/15 to 2016/17. Payment was also given for meeting the following antibiotic consumption indicators:

- a reduction of 1% or more in total antibiotic consumption against 2013/14 consumption
- a reduction of 1% or more in carbapenem use against 2013/14 consumption
- a reduction of 1% or more in piperacillin/tazobactam use against 2013/14 consumption

The AMR CQUIN also requested that a specific percentage of antibiotic prescriptions were reviewed within 72 hours per 50 antibiotic prescriptions taken from a representative sample across sites and wards:

- 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

ESPAUR, NHS England and NHS Improvement developed an MS Excel template to collect and submit antibiotic consumption data, and an Excel template and electronic survey tool to collect and submit AMS data. These documents were openly published and circulated to all 153 English NHS Acute Trusts to support quarterly data submissions for the AMR CQUIN.64

The number of NHS acute Trusts submitting antibiotic consumption CQUIN data to PHE in quarters one to four of 2016/17 was 139 (91%), 139 (91%), 138 (90%) and 133 (87%) respectively.

64 https://www.england.nhs.uk/nhs-standard-contract/cquin/cquin-16-17/amr-cquin/
In this first year of the AMR CQUIN, 56 (36.6%), 51 (33.3%) and 80 (52.3%) of 153 NHS acute Trusts met their objectives to reduce total antibiotic, piperacillin/tazobactam and carbapenem consumption respectively in 2016/17.

The median total consumption of antibiotics in acute Trusts increased from 4290.31 to 4399.92 Defined Daily Doses (DDD) per 1000 admissions from the 2013/14 CQUIN baseline (Figure 4.2). There were also increases in the median consumption of piperacillin/tazobactam (125.96 to 132.53 DDDs per 1000 admissions) and carbapenems (82.92 to 78.46 DDDs per 1000 admissions) from 2013/14 to 2016/17, though these increases largely occurred prior to the CQUINs commencing in 2015/16 and 2014/15 respectively. Although median consumption for these antibiotics remained above the 2013/14 baseline, the impact of the CQUIN was observed by the decline in consumption within both of these indicators, by 12.2 and 12.0 DDDs per 1000 admissions respectively, from their peaks; 39%, 66% and 67% of Trusts reduced total antibiotic, piperacillin/tazobactam and carbapenem consumption from 2015/16 to 2016/17.

PHE developed the AMS surveillance system (piloted in the East of England) through PHE SelectSurvey, in 2015. Data submission commenced in July 2016. On completion of data entry respondents received an email copy of their responses as proof of submission.

The system collected the following data on a subset of at least 150 antibiotic prescriptions on a quarterly basis

- Number and proportion with evidence of review within 72 hours
- Number reviewed within 72 hours and the proportion of each documented prescribing decision
- Number with indication documented on drug chart

The number of NHS acute hospitals submitting AMS CQUIN indicator data to PHE in quarters one to four of 2016/17 was 129 (84%), 130 (85%), 128 (84%) and 125 (82%) respectively (Table 4.2). The proportion of antibiotic prescriptions reviewed within 72 hours increased quarter on quarter in 2016/17. Although the proportion of acute hospitals meeting the CQUIN target remained high, there was slight decrease from quarter three related to the target increasing incrementally each quarter.

**Table 4.2: Review of antibiotic prescriptions within 72 hours in accordance with the 2016/17 AMR CQUIN**

<table>
<thead>
<tr>
<th>Financial quarter</th>
<th>Proportion of antibiotic prescriptions reviewed within 72 hours</th>
<th>CQUIN target (% prescriptions reviewed)</th>
<th>Proportion of NHS acute Trusts meeting AMS CQUIN (n=153)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Quarter 1 2016/17</td>
<td>81.4%</td>
<td>25%</td>
<td>83.0%</td>
</tr>
<tr>
<td>Quarter 2 2016/17</td>
<td>86.5%</td>
<td>50%</td>
<td>83.7%</td>
</tr>
<tr>
<td>Quarter 3 2016/17</td>
<td>89.0%</td>
<td>75%</td>
<td>81.0%</td>
</tr>
<tr>
<td>Quarter 4 2016/17</td>
<td>92.7%</td>
<td>90%</td>
<td>70.6%</td>
</tr>
</tbody>
</table>

The proportion of antibiotic prescriptions where an indication had been documented on the drug chart (clinical notes or electronic record) increased quarter on quarter in 2016/17. The additional data collected on the outcome of the prescribing decision related to Start Smart Then Focus (SSTF) is outlined in Table 4.3; this was not mandatory for the CQUIN 2016/17 but will be collated and presented for the 2017/19 CQUIN.

**Table 4.3: Prescribing decision outcomes for audited antibiotic prescriptions, expressed as percentage of prescriptions reviewed**

<table>
<thead>
<tr>
<th>Documented decision following review</th>
<th>Quarter 1 (n=15057)</th>
<th>Quarter 2 (n=19231)</th>
<th>Quarter 3 (n=19568)</th>
<th>Quarter 4 (n=21243)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Indication documented on drug chart</td>
<td>87.3</td>
<td>91.3</td>
<td>93.2</td>
<td>94.3</td>
</tr>
<tr>
<td>Stopped</td>
<td>9.2</td>
<td>9.9</td>
<td>9.5</td>
<td>9.2</td>
</tr>
<tr>
<td>Continued</td>
<td>61.5</td>
<td>64.2</td>
<td>66.9</td>
<td>67.1</td>
</tr>
<tr>
<td>Switch</td>
<td>10.9</td>
<td>11.4</td>
<td>10.5</td>
<td>9.9</td>
</tr>
<tr>
<td>IV to oral switch</td>
<td>13.9</td>
<td>12.6</td>
<td>12.6</td>
<td>12.8</td>
</tr>
<tr>
<td>Outpatient Parenteral Antimicrobial Therapy (OPAT)</td>
<td>0.5</td>
<td>0.8</td>
<td>0.4</td>
<td>0.2</td>
</tr>
</tbody>
</table>

Data reported to date highlights improvement in the percentage of antibiotic prescriptions with evidence of review within 72 hours, from quarter one to quarter four 2016/17.
Prescribing decision results agree with previous studies which indicated that antibiotic prescribing in England generally started “smartly” but improvements need to be applied to the “focus” component. From June 2017 the proportion of prescriptions with continue, stop and switch decisions is openly published to encourage greater discussion around acceptance to stop or switch antibiotic treatment following review at 72 hours. The results from these audits and data were reviewed and the 2017/19 CQUIN now incorporates further detail.

CQUIN 2017/19

The 2017/19 CQUIN is focused on reducing the impact of serious infections, in particular, antimicrobial resistance and sepsis. For the first time NHS England has published a two year scheme with the aim of providing greater certainty and stability regarding CQUIN goals, thereby giving health communities more time to focus on implementing the initiatives.

Antibiotic consumption and stewardship indicators for the 2017/18 CQUIN are as follows:

- Increasing proportions of antibiotic prescriptions from a subset of patients with sepsis documented and reviewed by a competent clinician within 72 hours
- Reduction of total, piperacillin/tazobactam and carbapenem antibiotic usage (for both in-patients and out-patients) as DDDs per 1,000 admissions by at least 1 or 2% dependent upon previous 2016 reduction performance

Evaluation of 2016/17 CQUIN

A national web-based survey was conducted across acute secondary care Trusts in autumn 2016 to evaluate:

- the implementation of AMS interventions in terms of structures and activity and comparison with the 2014 ESPAUR Survey
- to establish how the CQUIN was perceived by the staff responsible for achieving it at individual Trusts
- to explore which factors may have contributed to whether Trusts achieved the AMR CQUIN components

The survey also sought to evaluate interest amongst secondary care Trusts about taking a part in the NIHR funded programme: Antibiotic Review Kit-Hospital (ARK-Hospital). This programme, led by a network of NHS clinicians and investigators from the Universities of Oxford, Southampton and Brighton, and supported by national organisations includes a clinical trial which aims to deliver substantial reductions in hospital antibiotic use by optimising review and revise of antibiotic prescriptions and reducing antibiotic consumption.

[65](https://www.england.nhs.uk/nhs-standard-contract/cquin/cquin-17-19/)
The survey developed by researchers from ARK-Hospital and ESPAUR was initially piloted across five NHS Trusts before wider-distribution across England. An invitation to participate in a web-based survey was sent on behalf of ESPAUR and ARK-Hospital to all AMS contacts at secondary care NHS Trusts in early December 2016 and remained open until early March 2017. Two follow-up emails and phone contacts were completed to optimise response rate. The survey collected information about adoption of national AMS toolkits, AMS resources and perceptions about the CQUIN. All data extracted from the survey was analysed using SPSS Version 23 (IBM®, UK) and GraphPad Prism™. Ethical approval was not required for this study as this was a survey evaluation to NHS staff; all antibiotic consumption data included was openly available.

The current level of implementation of the secondary care prescribing toolkit SSTF ascertained from the current survey was compared with a previous 2014 ESPAUR survey that included 146 acute secondary care Trusts.66

Responses to the survey to investigate the impact of the CQUIN were received from a total of 116/155 (75%) secondary care acute Trusts across England and included both teaching and district general hospitals (Tables 4.4 and 4.5). Five Trusts completing the survey did not take part in the AMR CQUIN.

The 2016 survey demonstrated the number of Trusts that have reviewed SSTF either formally (62.3%) or informally (22.8%) has remained consistent when compared to the previous 2014 survey (87% Trusts reported reviewing SSTF). The number of Trusts that have implemented a SSTF action plan has increased from 46% in 2014 to 55.3% in the current survey. Almost all respondents (95.6%) reported their Trusts had an AMS committee which met at least quarterly. All AMS committees included a Microbiologist and Antimicrobial pharmacist with varying representation from other healthcare professional groups, including clinical commissioners (from CCGs) or GP representation in 47.4% of responding Trusts. The NICE AMS guidance (Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use) was discussed by 93% of the Trust AMS committee and 82.5% had completed the NICE AMS baseline audit tool. Most respondents (90.5%) had accessed the AMR local indicators data on Fingertips and the majority (71%) had shared this data with their AMS committee. However, only one-third had shared Fingertips data with their Trust board and only 5% reported sharing this data with front-line clinical staff.

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Table 4.4. Overview and comparisons of response rates in previous ESPAUR AMS survey and current survey.

<table>
<thead>
<tr>
<th></th>
<th>2014/15</th>
<th>2016/17</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>%</td>
<td>%</td>
</tr>
<tr>
<td>Proportion of responses received</td>
<td>63</td>
<td>75</td>
</tr>
<tr>
<td>Formally or informally reviewed national AMS toolkits</td>
<td>87</td>
<td>85</td>
</tr>
<tr>
<td>Implementation of AMS Action plan</td>
<td>46</td>
<td>55.3</td>
</tr>
<tr>
<td>Existance of an AMS committee dedicated to reviewing antimicrobial use</td>
<td>94</td>
<td>95.6</td>
</tr>
<tr>
<td>NICE AMS guidance reviewed</td>
<td>*</td>
<td>93</td>
</tr>
<tr>
<td>NICE AMS baseline audit completed</td>
<td>*</td>
<td>83</td>
</tr>
<tr>
<td>AMR local Indicators accessed on Fingertips</td>
<td>*</td>
<td>91</td>
</tr>
</tbody>
</table>

*Not assessed

Table 4.5: Perceptions about impact of AMR CQUIN and reductions in antibiotic consumption in the first six months from launch of AMR CQUIN

<table>
<thead>
<tr>
<th>Part 4a CQUIN achieved</th>
<th>n / total n answered question (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Impact of the AMR CQUIN</td>
<td></td>
</tr>
<tr>
<td>Reduction in Total antibiotic consumption</td>
<td>48/111 (43.2)</td>
</tr>
<tr>
<td>Reduction in piperacillin/tazobactam consumption</td>
<td>41/111 (36.9)</td>
</tr>
<tr>
<td>Reduction in carbapenem antibiotic consumption</td>
<td>61/111 (55.0)</td>
</tr>
<tr>
<td>Perceptions about AMR CQUIN</td>
<td></td>
</tr>
<tr>
<td>AMR CQUIN has changed AMS</td>
<td>58/116 (50)</td>
</tr>
<tr>
<td>AMR CQUIN will help reduce antibiotic consumption</td>
<td>35/116 (30.2)</td>
</tr>
<tr>
<td>AMR CQUIN will reduce antibiotic consumption safely</td>
<td>22/116 (19.0)</td>
</tr>
<tr>
<td>Interest in ARK-Hospital</td>
<td>81/116 (70.6)</td>
</tr>
</tbody>
</table>

Half of the Trusts surveyed felt that the AMR CQUIN had changed AMS activity within their Trusts and a third of respondents felt that the AMR CQUIN would help reduce antibiotic consumption. However, there was no significant change in the numbers of full time equivalents (FTE) for staff (clinicians, pharmacists, nurses, data analysts and administrative support) employed to carry out AMS work at Trusts following the introduction of the AMR CQUIN.
Trusts who felt positive about achieving the AMR CQUIN were more likely to achieve part 4a of the CQUIN in terms of reducing total, piperacillin/tazobactam and carbapenem antibiotic reduction \( (p<0.001) \). Of the surveyed Trusts participating in the CQUIN, 41/111 (36.9\%) achieved the quality measure for piperacillin/tazobactam, 61/111 (55.0\%) for carbapenems and 48/111 (43.2\%) for total antibiotic use. When asked about piloting educational resources to support AMS, 70.6\% of respondents expressed an interest in joining ARK-Hospital.

**Discussion**

**Quality premium**

The reductions achieved through the 2015/16 quality premium have been sustained and further reductions made in 2016/17. However considerable geographical variation in reduction and QP attainment remain. 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 for GP practices to achieve the AMR QP; from resources such as the TARGET toolkit to data portals such as PrescQIPP, NHS England QP monitoring dashboard and PHE Fingertips. The NHS BSAI are launching a new reporting platform for primary care prescribing data and it will include an Antimicrobial Stewardship dashboard to support CCGs and GP stewardship activity by reporting antibiotic prescribing data by age bands. 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.

Both of the 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 two year scheme ensure CCGs will continue to remain focussed on reducing inappropriate antibacterial prescribing.

**CQUIN**

In the first year of the AMR CQUIN acute Trusts successfully turned the tide of year on year increases in antibiotic consumption, especially carbapenems. There were also quarter-on-quarter increases in the proportion of empiric antibiotic prescriptions reviewed within 72 hours, demonstrating increased emphasis on “focussed” AMS.

Since the earlier ESPAUR survey was conducted, AMS committees remain central to delivering AMS and are found within almost all Trusts surveyed. The NICE guidance on AMS and NICE baseline AMS audit tool were both discussed by AMS committees in acute care Trusts in England, although information about how guidance has informed practice was not available. Although the majority of Trusts surveyed had reviewed the
national SSTF toolkit, almost half are yet to implement an action plan locally, despite the introduction of the AMR CQUIN, suggesting an ongoing need for implementation research and continued educational effort around delivering effective AMS. Collaborative research programmes such as ARK-Hospital aim to assist hospitals and determine the effectiveness of this approach.

The number of Trusts accessing local AMR indicators via the Fingertips site is encouraging and suggests that AMS teams are increasingly interested in taking ownership of their data and understanding Trust prescribing patterns, in order to best inform local AMS practice. However, disappointingly this data does not appear to be commonly shared with Trust boards, frontline clinicians, nurses and pharmacists working at acute Trusts who are pivotal in carrying out AMS and successfully achieving the CQUIN. This suggests that other behavioural change strategies are needed to ensure engagement with clinicians and to assist Trusts in achieving their CQUIN aims in 2017-19.

The AMR CQUIN was perceived as an effective tool in reducing antibiotic consumption, but respondents expressed concerns that it would do so safely. The work that is being performed by Imperial HPRU on readmissions, mortality and length of stay following the introduction of prescribing indicators is essential to determine the safety of the CQUIN.

Trusts are encouraged to contact the ARK-Hospital team if their Trust would be interested in participating in the ARK-Hospital NIHR Research programme. Further information available online.67

Future actions

ESPAUR will continue to:

- support the 2017-19 CQUINs and develop resources and tools for hospital implementation
- measure and evaluate the impact of NHS incentives on primary and secondary care prescribing, including unintended consequences
- work with research partners to assess the impact and mediators of the QP and CQUIN. In particular, collaborating with Imperial and Oxford Universities on the ESRC funded grant STEP-Up which will evaluate the QP. Specifically using a mixed methods approach to investigate how commissioners chose to implement the QP, and to determine its cost-effectiveness using standard and novel methods. We are also assessing the impact on the prescribing of antibiotic solutions, as a surrogate for prescribing in children; an abstract from this data was presented in Chapter 3.

67 http://www.arkstudy.ox.ac.uk

89
• explore changes in antibiotic prescribing in acute Trusts, in relation to those who have participated in and those who have not participated in the CQUIN
• extend quality improvement to develop indicators on antibiotic susceptibility testing and improve laboratory practice

Research in prescribing quality improvement

Quantifying inappropriate prescribing in English primary care

Timo Smieszek, Koen B. Pouwels, F. Christiaan K. Dolk, David R. M. Smith, Susan Hopkins, Mike Sharland, Alastair D. Hay, Michael V. Moore, Julie V. Robotham

The aim of this work was to identify and quantify inappropriate antibiotic prescribing in primary care in England, and ultimately to determine the potential for reduction in prescribing.

English primary care data from 2013-2015 recorded in The Health Improvement Network (THIN) database were used. Potentially inappropriate prescribing events in the database were identified by (i) comparing prescribing events against treatment guidelines, (ii) comparing actual prescribing proportions for a set of conditions to ideal proportions derived from expert opinion, (iii) identifying high prescribers and their number of prescriptions above an age- and body-system-specific benchmark.

Applying the most conservative assumptions, 8.8% of all systemic antibiotic prescriptions in English primary care were identified as inappropriate; in a middle scenario, 15.4% of all prescriptions were found to be inappropriate; and in the least conservative scenario, 23.1% of prescriptions were inappropriate. Importantly, all practices included in the analyses had non-zero reduction potentials, ranging from 6.4% to 43.5% in the middle scenario. The conditions which contributed most to inappropriate prescribing were sore throat (23.0% of identified inappropriate prescriptions) and cough (22.2%).

This work demonstrated the existence of substantial inappropriate antibiotic prescribing in English primary care. Not only high prescribers, but all practices should engage in efforts to use antibiotics more responsibly and reduce inappropriate prescribing. Better diagnostic coding, more precise prescribing guidelines and a deeper understanding of appropriate long-term uses of antibiotics would allow identification of further reduction potentials.
Evaluating the impact of the quality premium on antibiotic prescribing in children in primary care

Céire Costelloe, Sabine Bou-Antoun, Lothaire Gerard, Alison Holmes, Susan Hopkins
Work in Progress, Joint PHE and Imperial Health Protection Research Unit in HCAI and AMR Project

Background: Antimicrobial resistance (AMR) is one of greatest problems facing modern medicine. In 2014, the advisory committee on Antimicrobial Resistance and Healthcare-Associated Infection (ARHAI) devised Antibiotic Prescribing Quality Measures (APQM) to curb unnecessary overuse of antibiotics and combat AMR in England. These measures were implemented in April 2015 in the form of a quality premium (QP) awarded to clinical commissioning groups (CCG) for reducing antibiotic prescriptions in primary care.

Objectives: To examine trends in children's syrup antibiotic prescribing in general practitioners’ (GP) practices over time across English CCGs and establish if they have changed post-introduction of the 2015-16 APQMs. To compare prescriptions in CCG that did or did not meet the requirements of the QP.


Findings and interpretation: The study is currently in the analysis phase. Findings from this study could quantify the effect of an AMS intervention, the Antibiotic Prescribing Quality Measures on antibiotic prescribing at the GP practice and at CCG level over time. The study could also serve to provide evidence to support the adoption of and compliance with AMS Programmes in CCGs across England.
5. Antimicrobial Stewardship

Introduction

Optimising prescribing, through the development and implementation of antimicrobial stewardship (AMS) programmes and toolkits is key area two of the UK 5-year antimicrobial resistance (AMR) Strategy.68

This chapter outlines the results from three key projects:

1. Dental sector AMS toolkit
2. Process evaluation of the primary care Treat Antibiotics Responsibly, Guidance, Education, Tools (TARGET) webpages and information leaflets
3. Development of recommendations for primary and secondary care antibiotic prescribing measures to support a 50% reduction in inappropriate prescribing

Additional AMS work supporting the current quality initiatives to reduce antibiotic prescribing were outlined in Chapter 4 while the professional education and engagement work is outlined in Chapter 8.

Antimicrobial Stewardship Projects

Dental Sector AMS Toolkit

A dental AMS toolkit was launched by the dental subgroup of ESPAUR in collaboration with the Faculty of General Dental Practice (FGDP) and the British Dental Association (BDA) in November 2016. As part of the roll out, FGDP, BDA, Public Health England (PHE), the British Society for Antimicrobial Chemotherapy (BSAC) and the Association of Clinical Oral Microbiologists (ACOM) ran a joint social media campaign through a “Thunderclap”69 providing a targeted pledge statement in which users gave permission to be broadcast via their social media accounts (Twitter, Facebook, Tumblr – a blog) on 30 November 2016.

The published toolkit70 includes:

- resources – patient information leaflet, national dental poster and signpost to Antibiotic Guardian website

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69 https://www.thunderclap.it/
70 https://www.gov.uk/guidance/dental-antimicrobial-stewardship-toolkit
English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) Report 2017

- guidance – including signposting to dental antimicrobial guidance
- education and training tools – links to resources on Health Education England and examples of good practice eg Script-3
- audit tools including electronic templates for accurate and easy auditing, Read codes, and action plans

Analysis of the Thunderclap campaign is available online.71

An interim process evaluation was completed for the Dental AMS toolkit. Google analytics data were analysed for all webpage visits and acquisition route via which a visitor arrived at the website. Data were collected between 9 November 2016 and 31 March 2017.

A search of Google using the phrase "dental-antimicrobial-stewardship-toolkit" was conducted to determine the number of websites/pages that include a signpost to the Dental AMS toolkit webpage. Key terms used in social media and Google analytics are included in Annex – Chapter 3.

The predetermined pledge message that was broadcast on Thunderclap with a signpost to the Dental Antimicrobial Stewardship toolkit was:
“Let's keep antibiotics working: I pledge to audit my prescribing when managing oral and dental infections”72

The social media campaign via Thunderclap was supported by 113 social media accounts (112% of goal) and this led to a social reach of 271,229 people (Figure 5.1).

Antibiotic prescribing pledge
by FGDP, BDA, PHÉ, BSAC, ACOM
category: Health

“Let’s keep antibiotics working: I pledge to audit my prescribing when managing oral and dental infections http://thndr.me/CrF Bs n”

Figure 5.1. Final reach and supporters of Thunderclap campaign.

71 https://www.thunderclap.it/projects/49649-antibiotic-prescribing-pledge
72 http://thndr.me/CrF Bs n
The page views and downloads of the poster and leaflet from the .gov website between 9 November 2016 and 31 March 2017 are shown in Table 5.1; 47% of views occurred in November 2016, and the remainder of page views were distributed equally between January and March 2017.

Table 5.1: Total page views and download

<table>
<thead>
<tr>
<th>Page</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dental AMS toolkit page views</td>
<td>5823 (unique page views 3,468)</td>
</tr>
<tr>
<td>Average time on page</td>
<td>167.7 seconds</td>
</tr>
<tr>
<td>Leaflet downloads</td>
<td>784</td>
</tr>
<tr>
<td>Poster downloads</td>
<td>522</td>
</tr>
</tbody>
</table>

The dental AMS toolkit page was accessed from a total of 68 countries. The highest views were from the UK (5076), Australia (145), Canada (80), the USA (73), Spain (46) and Ireland (26). A map of the world demonstrating where the AMS toolkit was accessed from is presented in Figure 5.2. Thirty-five websites were found to signpost to the dental AMS toolkit page and included websites/blogs from UK, Australia and India. User feedback of the dental toolkit is currently in progress.

Figure 5.2: Countries accessing dental AMS toolkit
Process evaluation of TARGET toolkit webpages

The TARGET toolkit is an evidence-based resource to help clinicians and commissioners in England reduce inappropriate antibiotic prescribing. Last year we presented a qualitative evaluation of the materials. This year we have performed a process evaluation of the TARGET toolkit pages of the Royal College of General Practitioners (RCGP) website, to assess the numbers of visitors, the time of year with peak visits and the resources that are the most used.

Google analytics was used to collect participant interaction with the TARGET website; all definitions are available in the social media glossary.

TARGET is the most accessed page on the RCGP website. There have been over 200,000 visits between January 2014 and April 2017 (Figure 5.3). Visits typically increased in the winter months and there was also a surge of activity in the build up to European Antibiotic Awareness Day (EAAD)/World Antibiotic Awareness Week (WAAW) as visitors accessed the site for resources to use.

![Figure 5.3: Total visits to the TARGET webpages, January 14 – April 17](image)

The patient leaflets were consistently the most popular; the number of downloads of each leaflet are outlined in Figure 5.4; in April 2017, 50% of visitors accessed this section directly spending on average 8 minutes on the leaflet pages.
Figure 5.4. Leaflet downloads from the TARGET website, October 2015 – April 2017

There were increases in visits to specific sections of the TARGET website in line with various national initiatives, indicating that GPs turned to the TARGET website to obtain information (Figure 5.5):

- to the audits section of the TARGET website since the launch of the TARGET webinars; the webinars highlighted the importance of audits in prudent antimicrobial prescribing
- to the training modules, audits and urinary tract infection resources following the launch of the 2017/19 Quality Premium (QP)
- to all sections of the website during November each year, related to WAAW
In 2016 the UK government pledged to reduce inappropriate antibiotic prescribing by 50% by the year 2020. The Advisory Committee Antimicrobial Prescribing, Resistance and Healthcare Associated Infection (APRHAI) and PHE were tasked by the Department of Health (DH) to consider the scientific evidence and expert elicitation on inappropriate prescribing levels in both primary and secondary care settings and deliver recommendations for measures to reduce inappropriate prescribing by 50% by end of financial year 2020/21. The UK’s ambition to reduce inappropriate antimicrobial prescribing by 50% by 2020 is to date the most ambitious antimicrobial prescribing ambition of any country worldwide. The USA has pledged to reduce inappropriate antibiotic use by 50% in outpatient settings and by 20% in inpatient settings. Sweden has led the way in reducing inappropriate antibiotic prescribing, by demonstrating a continual decrease in antimicrobial prescribing over the last decade; with total prescribing less than two-thirds that of England in 2016. However, direct comparisons between countries is complex as antibiotic prescribing is associated with many other health and social indicators, such as deprivation, smoking and education.

In September 2016 APRHAI and ESPAUR formed a joint Antimicrobial Prescribing Appropriateness Measures subgroup (Terms of reference and membership are in Annex – Chapter 3).
Candidate measures for primary care ambitions were synthesised using evidence from the PHE antimicrobial prescribing modelling work (Chapter 3 research abstracts). For secondary care, a literature review was performed to establish an appropriate antibiotic prescribing range and used to propose candidate measures. An audit tool for potential use in hospitals was also drafted from findings of the literature review and refined following consultation with specialist infection pharmacists from the UK Clinical Pharmacy Community (UKCPA) Pharmacy Infection Network and the Royal Pharmaceutical Society (RPS) AMR Expert Advisory Group as well as infectious diseases physicians and microbiologists.

A workshop was held in February 2017 to discuss, elicit expert opinion and reach a consensus of which measures should be recommended to the DH expert advisory committee.

**Primary care**

Results from PHE’s modelling work to define antimicrobial prescribing in primary care were presented at the workshop (abstract in Chapter 3). The model identified reduction potentials between 8.8% and 23.1% of all antimicrobial prescriptions, depending on the underlying assumptions. One-third of antibiotic prescriptions were not associated with a diagnostic code and therefore could not be used to determine appropriateness.

Delegates at the Primary Care workshop were asked to interpret and discuss potential reduction scenarios, from most conservative to least, as modelled by PHE. The consensus reached was that at least 20% of antimicrobial prescriptions were currently inappropriate, thus a 50% reduction of inappropriate prescribing would result in a 10% total reduction in antibiotics prescriptions, against 2015/2016 baseline antibiotic prescriptions. It recognised that this target may need to be adapted, if diagnostic coding was improved, to better determine the level of optimal antimicrobial prescribing.

Delegates considered the following range of options and a consensus view was formed on their preferred option.

**Primary care short term:**

- all practices reduce total antibiotic prescribing in the next 12 months by 5% compared to previous year and practices incentivised to improve diagnostic coding for all infections (both treated and un-treated with antibiotics)
- normative-based appropriateness measure (practice level): eg “top quintile practices are inappropriate”
- number of antibiotic items/STAR-PU (Specific Therapeutic group Age-sex Related Prescribing Unit) per 12 months and broad-spectrum antibiotics <10% of total
• appropriateness defined using disease-specific prescribing rates

The consensus reached by the group was the first, ‘all practices reduce total antibiotic prescribing in the next 12 months by 5% compared to previous year and practices incentivised to improve diagnostic coding for all infections (both treated and un-treated with antibiotics)’, though delegates recognised that the NHS may operationalise a target using STAR-PUs.

Secondary care

It is not currently possible to estimate with any reasonable confidence the proportion of antibiotic prescribing in English hospitals that is inappropriate, as the required data from electronic-prescribing directly linked to clinical data is not available nationally. Prescribing of critical broad-spectrum antibiotics increased by 63% for piperacillin/tazobactam and 38% for carbapenems in the five years since 2010 with no clear explanation (resistance to narrow-spectrum agents has been largely stable during this time).

Approximately 5.5% of inpatients and Accident and Emergency attenders are thought to have sepsis. Data from the national point prevalence survey (PPS) of healthcare-associated infection and antimicrobial use performed in 2016 suggested that increases in prescribing of critical broad-spectrum agents were not accounted for by sepsis or septic shock. Approximately 8% of all piperacillin/tazobactam use was prescribed for community-acquired pneumonia (CAP) alone and 22% of almost 3000 patients with a working clinical diagnosis of CAP were treated with the broad-spectrum antipseudomonal antibiotic piperacillin/tazobactam on survey day. The proportion of CAP patients with risk factors for Pseudomonas aeruginosa, related to patients with bronchiectasis or previous hospital admission is estimated to be up to 14%. As the prevalence of P. aeruginosa as a pathogen in CAP is estimated to be less than 1%, at least 8% of CAP patients identified in the PPS were likely treated with piperacillin/tazobactam in the absence of risk factors for P. aeruginosa. This represents 6.8% of all piperacillin/tazobactam prescriptions. This suggests that piperacillin/tazobactam prescribing could be safely reduced by 5% simply by targeting inappropriate use for CAP in patients without risk factors. In the PPS, approximately 20% of carbapenem doses were prescribed for community-acquired infections; 4.3% of patients were receiving a carbapenem (30% of which started on day 0-2 following hospital admission for likely community-acquired infection). Many (~70%) of these prescriptions were for pneumonia, bronchitis (excluding cystic fibrosis), or cystitis/pyelonephritis (i.e. not for sepsis or bloodstream infections) suggesting that up to 21% of carbapenem prescriptions were inappropriate.

However, the PPS does not capture the evidence the diagnosis of community-acquired infections, the rationale for use of broad-spectrum agents nor antibiotic course length.
Individual case note audit of appropriateness of prescribing would enable individual organisations to determine their proportion of inappropriate prescribing. However, this would be resource intensive, requiring large scale co-ordination across acute Trusts and data management/analysis to enable a national understanding of inappropriate prescribing in secondary care.

Reduction targets for financial year 2017/8 were already finalised in the forthcoming CQUIN, therefore discussions for secondary care focussed on 2018/19.

There was general agreement that defined daily doses (DDDs) were sub-optimal for determining inappropriate antibiotic prescribing but were useful for identifying outlier Trusts. A normative approach, whereby high-prescribing hospitals would be required to reduce towards the median or lowest quartile, was not supported because of the lack of information about case mix/acuity which has been shown to affect antibiotic consumption. Evidence for use of shorter courses of antibiotics in relation to patient safety and reduction of antibiotic resistance selection pressure is accumulating for all major infections. Shortening the course length of a typical 7-day course of three times daily antibiotics by just one dose would reduce total antibiotic consumption by 5%, measured in DDD per 1000 admissions.

There was a consensus that the PPS data should also be reviewed for potential indicators of appropriateness and in addition a pilot audit tool should be developed to assess inappropriate prescribing.

In addition the delegates agreed that a goal of a 1% year-on-year reduction is recommended from 2018 until 2020 (data available in 2021) to achieve a total antibiotic reduction of 3% by 2021.

In the absence of new evidence to assess the appropriateness of piperacillin/tazobactam prescribing in English hospitals and in light of the continuing increases in prescribing of piperacillin/tazobactam (63% from 2010 to 2015), the consensus from the group was that a goal of a 3% reduction could be recommended in 2018/19, with this target to be reviewed annually.

In the absence of new evidence to assess the appropriateness of carbapenem prescribing in English hospitals and in light of the continuing increases in prescribing of carbapenems (38% increase from 2010 to 2015), the consensus from the group was that a goal of a 3% reduction could be recommended in 2018/19, with this target to be reviewed annually.

**Recommendations endorsed by APRHAI**

The following were recommended for primary care:
• an antibiotic prescribing reduction target of 10% of antibiotic prescriptions per 1000 population by 2020/2021 (against ‘baseline’ 2015/2016 prescribing, a prescribing target of 3% per financial year), and in order to improve future measures of inappropriate prescribing, is encouraged to improve the use of diagnostic coding for infection consultations. The baseline of 2015/2016 has been selected to mirror the baseline for the ambition to reduce Gram-negative healthcare-associated bloodstream infections by 50%

• APRHAI would meet with leading electronic medical record providers to discuss ways in which diagnostic coding could be improved

The following were recommended for secondary care:

• reduction in total antibiotic consumption by 1%, measured as total antibiotic DDD per 1000 admissions, against ‘baseline’ 2016 for financial year 2018/2019. The baseline of calendar year 2016 has been selected to mirror the baseline currently in use for the CQUIN (Commissioning for Quality and Innovation). A calendar year was used as baseline as the data for financial year was not available at CQUIN launch

• reduction of piperacillin/tazobactam and meropenem consumption by 3%, measured by respective antibiotic DDD per 1000 admissions, for financial year 2018/2019, relative to the ‘baseline’ calendar year 2016 which was selected to mirror the baseline currently in use for the CQUIN. A calendar year was used as baseline as the data for financial year was not available at CQUIN launch

• an assessment of appropriateness using the PPS along with prescribing appropriateness audit of individual patient case notes to ascertain more accurately the proportion of inappropriate prescribing and these data should be used to revise future consumption goals

It should be emphasised that these targets may need to be adapted as a result of emerging evidence on the ultimate level of optimal antimicrobial prescribing.

The targets set will be reviewed by APRHAI annually and revised following analysis of PPS and individual audit data.

Progress towards these goals will be monitored by antibiotic consumption (DDD and prescription items) data and published on the Fingertips website.73

Other key projects

Antimicrobial Stewardship Surveillance tools

73 https://fingertips.phe.org.uk/profile/amr-local-indicators
The AMS surveillance tools developed in 2015 and subsequently used for the 2016 CQUIN were further adapted for the 2017-2019 CQUIN AMR data collection. Further details are provided in Chapter 4.

Future actions

As part of the AMS workstream and in light of the new government ambitions to reduce inappropriate prescribing by 50% by 2020, ESPAUR will undertake the following actions:

- user feedback survey for the dental primary care AMS toolkit currently in progress will be reported in the next ESPAUR report
- the dental ESPAUR subgroup will continue working with the Association of Dental Hospitals to undertake an audit of secondary care prescribing in all dental teaching hospitals in England. The work will be led by a representative of ACOM
- work with local dental networks across England who have committed to tackling AMS within their actions plans
- continue to develop resources and tools for hospital implementation to support the 2017-19 CQUINs
- pilot and evaluate an engagement campaign of the TARGET pharmacy leaflet toolkit with community pharmacists
- develop, pilot and validate tool to assess appropriateness of antibiotic prescriptions in acute hospitals and facilitate data collection and analysis of data in 10 NHS acute hospital organisations
- use the PPS data, to highlight areas of potential inappropriate prescribing in secondary care
- continue to evaluate the impact of NHS incentives on secondary care prescribing by updating the AMS surveillance tool, timely analysis of submitted data and quarterly reporting on PHE Fingertips
- promote the availability of useful analytical tools (eg trend analysis; benchmarking) available via Fingertips to enhance local understanding of relevant data by delivering three webinars, as well as promotion at relevant conference/workshop/meetings and publications
- adapt and pilot the AMS surveillance system for private healthcare providers.
- convene a workshop with CQC, NHS England, NHS Improvement to consider what key principles should considered by clinicians if there is a need to prescribe an antimicrobial remotely
- PHE will work with specialist pharmacists in Community Health Services (CHS) to increase the proportion of CHS trusts that consent to PHE analysing their antibiotic consumption data
Research in antimicrobial stewardship

TARGET Programme

Qualitative study to explore the current and potential for antimicrobial stewardship in English community pharmacies using the Theoretical Domains Framework

Jones LF, Owens R, Sallis A. Ashiru-Oredope D, Thornley T, Francis N, Butler CC, McNulty CAM.

Introduction: Community pharmacists and their staff have considerable potential to contribute to antimicrobial stewardship (AMS) by providing self-care advice and recommending over the counter treatments for common infections, but the barriers and opportunities are not well understood. The aim of this study was to investigate the experiences and perceptions of community pharmacists and their teams around antibiotic stewardship activities.

Method: Qualitative methods (semi-structured interviews and focus groups) were used to gain in depth insights from pharmacists, pharmacy staff, general practitioners (GPs), members of pharmacy organisations and commissioners. The questioning schedule was developed using the Theoretical Domains Framework consisting of 14 behavioural domains.

Results: Participants included eight GPs, 28 pharmacists, 13 pharmacy staff, six representatives from pharmacy organisations in England and Wales, and 2 commissioners.

The domains ‘knowledge’ and ‘skills’ highlighted that pharmacists are knowledgeable and skilled in giving self-care and compliance advice. Analysis of the domain ‘memory, attention and decision-making’ demonstrated that some may not be aware of the impact of giving self-care and compliance advice on antimicrobial resistance (AMR). The ‘environmental context and resources’ domain has highlighted a number of barriers faced in community pharmacy such as lack of time, and misinformation from under skilled staff. Patients’ diagnoses on prescriptions would help inform and improve self-care advice.

‘Professional role and identity’ identified that having the training to provide patient examinations may help pharmacists provide more tailored advice as an additional service. Further clarification is needed on the pharmacists’ role in examining patients, and querying the accuracy and appropriateness of an antibiotic prescription.

Conclusions: Materials are required to support the pharmacists and pharmacy staff role in infection self-care and antibiotic compliance advice. Indication of prescription is needed to enable pharmacists to improve antibiotic advice.
The feasibility and acceptability of the provision of the TARGET Treating Your Infection Urinary Tract Infection (TYI-UTI) information leaflet for women seeking pharmacist advice: a pilot scoping study.

Lecky DM, Karim S, Chughtai S and Hawksworth G.

Background: Interviews with patients and GPs during the development of the TARGET TYI-UTI patient information leaflet highlighted the role of pharmacists in the treatment of UTI. The patient participants discussed seeking advice from the pharmacists for UTIs whilst GPs stated that the pharmacist could play an important role in patient education as some women consult the pharmacists first.

Aim: To assess the feasibility and acceptability of utilising the TARGET TYI-UTI information leaflet in the pharmacy setting.

Methods: Pharmacists from the South West Yorkshire and Humber regions participated in researcher led interviews designed to investigate the pharmacist experience of women with uncomplicated UTIs, their opinion on the TARGET TYI-UTI information leaflet and its potential use in the pharmacy setting. The interview schedule was developed using the Theoretical Domains Framework.

Results: Thirteen pharmacists agreed to be interviewed; work experience ranged from four to 35 years. Finding show that pharmacists consult with women presenting with UTI symptoms on a regular basis. The majority of patients present with a prescription for antibiotics with some seeking advice or even diagnosis prior to a GP visit.

Regardless for the reason of the visit, pharmacists will almost always counsel the patient; usually this is in the form of self-care and safety netting advice; with some providing prevention advice. When dispensing antibiotics, all pharmacists reported discussing the antibiotic and potential side effects with the patient. One of the main patient benefits from the pharmacist consult is that the pharmacist is aware of pharmacodynamic properties of the medication and can counsel the patient appropriately.

Pharmacists found the leaflet educational and empowering for both the pharmacy team and the patient. They felt the leaflet would help overcome potential barriers that may occur during the consult. Many of the pharmacists thought the leaflet did not need to be changed to suit the pharmacy setting but would like it to be available in different languages.

Implications: The high footfall of women in the pharmacy setting with UTI symptoms suggests that pharmacists can play a key role in educating women about self-care and prevention of UTIs. Knowledge and skills, and social motivation are both key drivers for behaviour change. The information in the leaflet can provide the knowledge and skills
women require to self-care and prevent recurrent infection whilst receiving the leaflet (information) from multiple sources (the pharmacy and the GP practice) reinforces key messages and drives social motivation.

**Study of local implementation of antimicrobial stewardship activity in primary care**

*Allison R, Lecky DM, Owens R, Beech E, Costelloe C, Ashiru-Oredope D, McNulty CAM.*

Background: The UK 5 Year Antimicrobial Resistance Strategy (2013-2018) states that there are few public health issues of greater importance, in terms of impact on society, than antimicrobial resistance (AMR). Evidence suggests that the use and inappropriate use of antimicrobials is a recognised driver of drug resistant infections and that, in the UK, around 75% percent of antibiotic prescribing occurs in the community. The Advisory Committee on Antimicrobial Resistance and Healthcare Associated Infections (ARHAI) recommends that antibacterial use is reduced and there have been a range of national initiatives to support this aspiration, such as: the NHS England Quality Premium - a CCG based incentive to improve antibiotic prescribing in primary care; national guidance on managing common infections; and TARGET (Treat Antibiotics Responsibly, Guidance, Education, Tools) - to support CCGs and primary care prescribers.

Aim and objectives: The aim of this research is to assess the implementation of antimicrobial stewardship (AMS) activity in primary care across England. More specifically, it has the following objectives:

- to identify the extent and variation in use of antimicrobial stewardship resources at a local level
- to identify ways in which national guidance on managing common infections is adopted and adapted locally
- to assess the extent to which current antimicrobial stewardship resources, systems and process are reported as being successful in supporting the appropriate prescribing of antibiotics

The findings will be used to inform how PHE and NHS Improvements can support CCGs/CSUs to optimise antimicrobial stewardship activities.

Methods: This is a mixed-methods study that involves an iterative process, whereby each stage of the research informs the next. More specifically, it involves: Qualitative interviews: with 11 leads for AMS within CCG/CSU's medicines management teams, to provide a more comprehensive overview of the AMS structures within which local organisations are currently operating and the issues they are currently facing.
Questionnaire: whereby all CCGs in England will be given the opportunity to complete and give more detailed information about current antimicrobial stewardship (AMS) activity in CCGs and primary care across England.

Results and Implications: The structure of medicines management teams varies, with some teams sitting within the CCG and others sitting within a CSU and overseeing multiple CCGs. AMS leads felt that the message of appropriate prescribing was being heard by primary care practitioners, but that prescribers were not connecting this with the bigger picture of antimicrobial resistance as they did not come across this day to day. When discussing knowledge and participation in existing initiatives, TARGET, antibiotic guidance, quality premium, data, benchmarking and feedback, audits, education and incentive schemes were the main initiatives actively promoted by the medicines management teams. The main barriers included: public pressures for clinicians to prescribe antibiotics; workload and capacity; rotation of staff within primary care; clinicians not wanting to make the wrong decision; and lack of understanding. Facilitators for AMS implementation mentioned by participants included: education, specifically mixing up the format, face-to-face from an expert, linking appropriate prescribing to reducing workload; local support such as dedicated staff both within the practice setting but also within the CCG to be responsible for AMS; national campaigns, especially for the general public; integrating resources into clinical systems; better communication strategies; data, feedback and benchmarking as it facilitates discussions; auditing; algorithm-based decision making tools; and national guidance.

The questionnaire phase is on-going and results will be disseminated once complete.
6. Antifungal resistance, prescribing and stewardship

Introduction

Fungal infections in humans range from common, mild superficial conditions such as athlete’s foot or thrush to severe disease that may be life-threatening, such as invasive aspergillosis or candidaemia. Fungal infections are particularly problematic in the hospital setting where patients are vulnerable to infection due to invasive procedures or receipt of immunosuppressive treatment. The emergence and spread of resistance to antifungals in such settings poses a significant threat to our ability to manage seriously ill patients and highlights the importance of monitoring antifungal resistance and the usage of antifungals.

This chapter presents updates on antifungal resistance, with a focus on resistance to key antifungals in the most frequently reported species of moulds (*Aspergillus* spp.) and yeasts (*Candida albicans* and *C. glabrata*) alongside a summary of the fungi that are identified infrequently and emerging resistance within those species. An update is also provided on activities undertaken by PHE in response to the emerging threat posed by *Candida auris*.

For the first time PHE’s national routine antifungal resistance surveillance data are being presented together with datasets provided by PHE’s National Mycology Reference Laboratory (MRL), Bristol, and the Mycology Reference Centre (MRCM), Manchester. Progress has also been made regarding specialty-level antifungal prescribing data. New coverage includes results from the joint PHE, UK Clinical Mycology Network (UKCMN) and British Society for Medical Mycology (BSMM) national survey on laboratory mycology testing capacity74 and an outline of the NHS England Improving Value Antifungal Stewardship Project.

Methods

Data sources – Antifungal resistance

Data on the laboratory reports of *Aspergillus* spp. and *Candida* spp. from 2012 to 2016 were obtained from the Communicable Disease Report (CDR) module of PHE’s Second Generation Surveillance System (SGSS), a national database maintained by PHE. In

addition, antifungal resistance data for *Aspergillus* spp. and *Candida* spp. was provided by the MRL and the MRCM.

PHE’s routine laboratory surveillance and the caveats surrounding data quality have been discussed in earlier chapters, and include:

- incomplete data collection due to reporting on a voluntary basis
- variation in laboratory testing methods
- use of different panels of antifungal agents for the same pathogen between laboratories
- low frequency of antifungal susceptibility testing reported to PHE through routine laboratory surveillance should be noted. This was highlighted within the ESPAUR Report 2016 and led to the recommendation to review the antifungal susceptibility data from UK reference laboratories in parallel.75

The MRL receives referred samples of fungal isolates from NHS trusts, regional mycology reference centres and private microbiology laboratories throughout the UK. In addition, the MRL provides a primary diagnostic service for local laboratories. Samples are received for superficial, subcutaneous, deep-seated and disseminated fungal infections. Patient groups include those with dermatophytosis, chronic obstructive pulmonary disease (COPD) and cystic fibrosis, intensive care unit (ICU) patients and haematology and oncology patients including those who have received solid organ, stem cell and bone marrow transplants. The MRL is the UK coordinating centre for fungal outbreaks.

The MRCM works in partnership with the National Aspergillosis Centre (NAC) and other hospitals to provide laboratory services predominantly for chronic pulmonary aspergillosis patients situated throughout the UK. Laboratory services are also regularly provided for samples from patients following solid organ transplant, those with fungal asthma, COPD or cystic fibrosis, as well as those on extracorporeal membrane oxygenation (ECMO). The MRCM also receives *Aspergillus* spp., *Candida* spp. and other fungal genera from laboratories throughout the North of England, the Midlands, Scotland and Wales.

Within this report, *Aspergillus* species presented are derived from positive identifications in laboratory reports from all specimen sites. *Candida* spp. are reported in two specimen type groups, those from ‘sterile site’ infections (blood, normally sterile fluids or tissues) and those from ‘superficial (eg skin and soft tissue)’ specimen types.

Data presented for *Aspergillus* species by both MRL and MRCM are at a specimen level, and have been de-duplicated to include only one specimen of a particular species per year for a patient. Cultures taken from the same patient that yielded growth of *Aspergillus* within the same calendar year were regarded by both reference laboratories as comprising the same infection episode and were combined, with the most resistant antifungal susceptibility result being retained. Data for *Candida* spp. submitted by MRL is for all isolates irrespective of whether there was two or more isolates per patient per year whereas the MRCM *Candida* spp. data has been de-duplicated to include only one invasive and one superficial specimen (where available) of a particular species per year per patient.

Microbiology laboratories may use different methodologies for determining antifungal minimum inhibitory concentration (MIC) and the cut off points, for classifying an isolates susceptibility (i.e. clinical breakpoints), will vary depending on the method used and the species being tested. Susceptibility results presented in this report from the MRL are based on the Clinical and Laboratory Standards Institute (CLSI) methodology and those from the MRCM laboratory are from the European Committee on Antimicrobial Susceptibility Testing (EUCAST) methodology.

When a clinical breakpoint has been established or changed during the study period the new breakpoint has been applied to all historical specimens where MIC data is available. Where no breakpoints have been defined (for either method), epidemiological cut off points or local interpretation have been used to categorise susceptibility.

For the purpose of this report, antifungal susceptibility test results reported as ‘intermediate’ or ‘resistant’ were combined and presented as ‘reduced-susceptibility’, unless otherwise indicated. Compared to Chapter 2 of this report, a different nomenclature is being used for fungal pathogens since clinicians will still use an antifungal to treat a patient despite raised MIC values but will increase treatment doses accordingly.

**Data sources – Antifungal prescribing**

Information on the use of antifungals in the community was obtained from the NHS Business Services Authority (NHS BSA) database for 2013 until 2016. Information on hospital prescribing was obtained from Rx-info76 for the same time period, which captures data from 86% of all NHS Acute Trusts. The data on antifungal use was derived using the anatomical therapeutic chemical (ATC) classification system.77 Antimycotics for systemic use fall into ATC group ‘J02’.

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76 For further information; RX-Info website available at https://www.rx-info.co.uk/
77 WHO Collaborating Centre for Drug Statistics Microbiology. ATC/DDD Index 2017, available at https://www.whocc.no/atc_ddd_index/
Data analysis - Antifungal resistance

Trends in incidence and resistance are shown at national level for England. Incidence rates are calculated per 100,000 population per year using mid-year population estimates for the respective year.78

PHE’s routine laboratory surveillance (SGSS) reports were analysed for species distribution and trends in incidence rates per 100,000 population, and not for antifungal susceptibility patterns (due to the low level of susceptibility test reporting to PHE though routine reporting79). The majority of antifungal susceptibility test results presented were either from the MRL or the MRCM, or both.

The *Aspergillus* spp.-level resistance summaries provided by the MRL are supplied aggregated for the time period 2008 to 2016 due to the small numbers that are referred annually. The *Aspergillus* spp.-level resistance summaries from the MRCM include the trend between 2012 and 2015.

The *Candida* spp.-level resistance summaries from the MRL are supplied for 2015 only, while the data supplied by the MRCM include trend information between 2012 and 2016.

Data analysis - Antifungal prescribing

Antifungal prescribing data in the community setting are presented as defined daily doses (DDD)80 per 1000 inhabitants per day, using mid-year population estimates for the relevant year.81

Hospital antifungal prescribing data are presented as DDDs per 1,000 hospital admissions per day, using hospital admissions data from Hospital Episode Statistics82 for the relevant year.

79 Chapter 6, ESPAUR report 2016
80 WHO Collaborating Centre for Drug Statistics Microbiology. DDD Definition and General Considerations, available at https://www.whocc.no/ddd/definition_and_general_considera/
Results

Antifungal resistance

Aspergillus species

The incidence of Aspergillus fumigatus isolates identified by PHE’s routine laboratory surveillance for all clinical specimen sites was 3.1 per 100,000 population in 2016, with a slight increase across the five-year time period (2.2/100,000 in 2012) (Figure 6.1). In 2016 less than 10% of A. fumigatus from sterile site isolates included antifungal susceptibility information. All subsequent antifungal susceptibility analyses for A. fumigatus will be using data from the reference laboratories.

A. fumigatus remains by far the most common mould isolated from clinical specimens. Results for other Aspergillus spp. are represented later in the chapter. Compared to the number of routine specimen reported to PHE’s laboratory surveillance system, smaller numbers of A. fumigatus isolates are referred to reference laboratories. However, the incidence of referred isolates to the MRL and the MRCM also increased between 2012 and 2015/2016 (2016 data not available for the MRCM). Only 4% of routinely identified A. fumigatus specimens reported via SGSS are from sterile sites, whereas 24% of all A. fumigatus isolates referred to the MRCM (2012-2015) were from sterile sites.

Reduced susceptibility to any azole was low in A. fumigatus isolates referred to the MRL, with slight increases being recorded in itraconazole and voriconazole resistance between 2012 and 2016. Resistance to these two key triazoles was higher in A. fumigatus isolates referred to the MRCM however decreased from 20.1% to 16.6% and
20.9 to 13.4 for itraconazole and voriconazole respectively, between 2012 and 2015 (Table 6.1). The difference in resistance levels could be due to population bias, with samples referred to the MRCM provided by a cohort of patients with chronic pulmonary aspergillosis. Amphotericin B resistance in *A. fumigatus* remains low at 2% in 2016 (data available from MRCM only). Pan-azole resistance has been recorded, however occurrences remain rare in the UK.83,84,85,86

Table 6.1. Number of referred *A. fumigatus* isolates tested for susceptibility to key antifungals, England, 2012 to 2016 (MRL CLSI method results87 and MRCM EUCAST method results)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Year</th>
<th>MRL - CLSI method</th>
<th>MRCM - EUCAST method</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No. tested</td>
<td>No. (%) with reduced susceptibility*</td>
</tr>
<tr>
<td>Itraconazole</td>
<td>2012</td>
<td>210</td>
<td>3 (1.4)</td>
</tr>
<tr>
<td></td>
<td>2013</td>
<td>346</td>
<td>11 (3.2)</td>
</tr>
<tr>
<td></td>
<td>2014</td>
<td>376</td>
<td>6 (1.6)</td>
</tr>
<tr>
<td></td>
<td>2015</td>
<td>598</td>
<td>39 (6.5)</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td>506</td>
<td>43 (8.5)</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>2012</td>
<td>227</td>
<td>4 (1.7)</td>
</tr>
<tr>
<td></td>
<td>2013</td>
<td>356</td>
<td>8 (2.2)</td>
</tr>
<tr>
<td></td>
<td>2014</td>
<td>428</td>
<td>12 (2.8)</td>
</tr>
<tr>
<td></td>
<td>2015</td>
<td>630</td>
<td>21 (3.3)</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td>531</td>
<td>25 (4.7)</td>
</tr>
<tr>
<td>Posaconazole</td>
<td>2012</td>
<td>47</td>
<td>5 (10.6)</td>
</tr>
<tr>
<td></td>
<td>2013</td>
<td>163</td>
<td>25 (15.3)</td>
</tr>
<tr>
<td></td>
<td>2014</td>
<td>81</td>
<td>3 (3.7)</td>
</tr>
<tr>
<td></td>
<td>2015</td>
<td>119</td>
<td>12 (9.2)</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td>72</td>
<td>5 (6.9)</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>2012</td>
<td></td>
<td>139</td>
</tr>
<tr>
<td></td>
<td>2013</td>
<td></td>
<td>166</td>
</tr>
<tr>
<td></td>
<td>2014</td>
<td></td>
<td>193</td>
</tr>
<tr>
<td></td>
<td>2015</td>
<td></td>
<td>277</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

† isolates with probable treatment failure and/or known mutations causing resistance

*Resistant and intermediate

** Resistant only

87 Any isolate with an MIC of > 1.0 mg/L for itraconazole and voriconazole resistant and an MIC > 0.25 mg/L for posaconazole resistant as it is becoming increasingly clear that patients with isolates above these breakpoints often do not respond to the drugs, moreover they usually have recognisable resistance mutations.
A. fumigatus is the most frequently reported species in clinical specimens, however antifungal susceptibility by Aspergillus spp. varies. Due to low numbers being reported for some of the rarer Aspergillus spp. these data have been aggregated across the period 2008 to 2016 (MRL) and 2012 to 2015 (MRCM; Tables 6.2 and 6.3).

Findings of note are the well-recognised and reported resistance of Aspergillus terreus to amphotericin B\textsuperscript{88} as well as high levels of amphotericin B resistance in Aspergillus versicolor. One hundred per-cent triazole resistance for Aspergillus thermomutatus was seen within the aggregated data from the MRCM, consistent with the high levels of resistance that have previously been reported for this species.\textsuperscript{89} Resistance to itraconazole is also reported for Aspergillus niger.

\textsuperscript{88} Walsh TJ et al. J infect Dis. 2003; 188: 305-319.
Table 6.2: Number of referred *Aspergillus* spp. isolates tested for susceptibility to triazoles, England, 2008-2016 MRL (CLSI method results) and 2012-2015 MRCM (EUCAST method results)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No. tested</td>
<td>No. resistant</td>
</tr>
<tr>
<td>Voriconazole</td>
<td><em>Aspergillus flavus</em></td>
<td>283</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus nidulans</em></td>
<td>39</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus niger</em></td>
<td>164</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus terreus</em></td>
<td>106</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus thermomutatus</em></td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus versicolor</em></td>
<td>22</td>
<td>0</td>
</tr>
<tr>
<td>Posaconazole</td>
<td><em>Aspergillus flavus</em></td>
<td>42</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus nidulans</em></td>
<td>5</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus niger</em></td>
<td>26</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus terreus</em></td>
<td>16</td>
<td>0</td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus thermomutatus</em></td>
<td>3</td>
<td>3</td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus versicolor</em></td>
<td>3</td>
<td>0</td>
</tr>
<tr>
<td>Itraconazole</td>
<td><em>Aspergillus flavus</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus nidulans</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus niger</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus terreus</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus thermomutatus</em></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td><em>Aspergillus versicolor</em></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

* Local interpretation used due to insufficient evidence for EUCAST MIC breakpoint
Table 6.3: Number of referred *Aspergillus* spp. isolates tested for susceptibility to Amphotericin B and caspofungin, England, 2008-2016 MRL (CLSI method results) and 2012-2015 MRCM (EUCAST method results)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>No. tested</td>
<td>No. resistant</td>
<td>No. intermediate</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Aspergillus flavus</em></td>
<td>372</td>
<td>51</td>
<td>-</td>
</tr>
<tr>
<td><em>Aspergillus nidulans</em></td>
<td>42</td>
<td>2</td>
<td>-</td>
</tr>
<tr>
<td><em>Aspergillus niger</em></td>
<td>301</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td><em>Aspergillus terreus</em></td>
<td>115</td>
<td>55</td>
<td>-</td>
</tr>
<tr>
<td><em>Aspergillus thermomutatus</em></td>
<td>3</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td><em>Aspergillus versicolor</em></td>
<td>28</td>
<td>7</td>
<td>-</td>
</tr>
<tr>
<td>Caspofungin</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Aspergillus flavus</em></td>
<td>134</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td><em>Aspergillus nidulans</em></td>
<td>18</td>
<td>5</td>
<td>-</td>
</tr>
<tr>
<td><em>Aspergillus niger</em></td>
<td>83</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td><em>Aspergillus terreus</em></td>
<td>43</td>
<td>0</td>
<td>-</td>
</tr>
<tr>
<td><em>Aspergillus thermomutatus</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><em>Aspergillus versicolor</em></td>
<td>17</td>
<td>3</td>
<td>-</td>
</tr>
</tbody>
</table>

* Local interpretation used due to insufficient evidence for EUCAST MIC breakpoint
Candida species

The incidence of Candida spp. from all clinical specimen sites, assessed using PHE’s routine laboratory surveillance database SGSS (Second Generation Surveillance System), was 81.7 per 100,000 population in 2016, equating to a 38% increase over a five-year time period (59.2/100,000 in 2012). Ninety-four percent of Candida spp. reports through routine surveillance related to isolates from superficial sites in 2016, the proportion of which has remained consistent across the time period; this represents an incidence of 76.0/100,000 population in 2016 (Figure 6.2). In 2016, only 4% of Candida spp. superficial site specimen were referred to the MRCM. The population rate of Candida spp. identified in sterile site specimens was 4.6/100,000 and 17% were referred to the MRCM (Figure 6.3). The incidence of sterile site Candida spp. referrals to the MRCM in 2016 was six times lower than that reported via routine laboratory surveillance, and remained stable over the five year period.

Figure 6.2. Rate per 100,000 population of Candida spp. superficial site patient specimen reports in England (routine laboratory specimens and referrals to the MRCM), 2012 to 2016
Candida albicans remains the most frequently isolated Candida species in both superficial and sterile specimen sites (in both routine laboratory surveillance reports and referrals to the MRCM). Comparisons of the species reported through routine laboratory surveillance to PHE and by the MRCM show that a similar variety of species are being identified, however the distributions of species vary slightly. Between 2012 and 2016, 40-50% of sterile site reports for Candida spp. isolates to PHE have been for C. albicans, contrasting with 61-72% of the MRCM’s sterile site referrals (Figure 6.4).
Each year more than 92% of the routine laboratory *C. albicans* reports to PHE are for isolates from superficial sites, of which very few are routinely tested for antifungal susceptibility (range 3%-7% per year). In the annual report on routine surveillance of candidaemia published in PHE’s Health Protection Report, data showed that antifungal susceptibility was included in 59% laboratory reports, an improvement on 39% of candidaemia reports in 2012. The rest of this section will focus on susceptibility test results in referred isolates (all specimen types) and routine laboratory sterile site specimen reports (published in the annual candidaemia report).

*C. albicans* and *C. glabrata* isolates referred to the MRCM for key antifungal susceptibility testing as well as PHE’s routine laboratory surveillance reports which included susceptibility test results are presented in Tables 6.4 and 6.5.

Table 6.4. Number of *C. albicans* isolates tested for and resistant to key antifungals in England, 2012 to 2016

<table>
<thead>
<tr>
<th>Drug</th>
<th>year</th>
<th>No. tested</th>
<th>No. (%) with reduced susceptibility</th>
<th>No. tested</th>
<th>No. (%) with reduced susceptibility</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>all specimen types [MRCM]</td>
<td>sterile site (blood) specimen (PHE routine laboratory surveillance)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fluconazole</td>
<td>2012</td>
<td>177</td>
<td>9 (5.1)</td>
<td>260</td>
<td>3 (1.2)</td>
</tr>
<tr>
<td></td>
<td>2013</td>
<td>93</td>
<td>7 (7.5)</td>
<td>289</td>
<td>6 (2.1)</td>
</tr>
<tr>
<td></td>
<td>2014</td>
<td>65</td>
<td>5 (7.7)</td>
<td>310</td>
<td>8 (2.6)</td>
</tr>
<tr>
<td></td>
<td>2015</td>
<td>69</td>
<td>6 (8.7)</td>
<td>460</td>
<td>7 (1.5)</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td>210</td>
<td>14 (6.7)</td>
<td>466</td>
<td>16 (3.4)</td>
</tr>
<tr>
<td>Echinocandins*</td>
<td>2012</td>
<td>176</td>
<td>0 (0.0)</td>
<td>152</td>
<td>1 (0.7)</td>
</tr>
<tr>
<td></td>
<td>2013</td>
<td>85</td>
<td>0 (0.0)</td>
<td>225</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>2014</td>
<td>55</td>
<td>0 (0.0)</td>
<td>231</td>
<td>1 (0.4)</td>
</tr>
<tr>
<td></td>
<td>2015</td>
<td>52</td>
<td>0 (0.0)</td>
<td>323</td>
<td>0 (0.0)</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td>91</td>
<td>2 (2.2)</td>
<td>335</td>
<td>12 (3.6)</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>2012</td>
<td>175</td>
<td>0 (0.0)</td>
<td>214</td>
<td>1 (0.5)</td>
</tr>
<tr>
<td></td>
<td>2013</td>
<td>93</td>
<td>0 (0.0)</td>
<td>248</td>
<td>3 (1.2)</td>
</tr>
<tr>
<td></td>
<td>2014</td>
<td>65</td>
<td>0 (0.0)</td>
<td>245</td>
<td>3 (1.2)</td>
</tr>
<tr>
<td></td>
<td>2015</td>
<td>62</td>
<td>0 (0.0)</td>
<td>364</td>
<td>9 (2.5)</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td>213</td>
<td>0 (0.0)</td>
<td>405</td>
<td>6 (1.5)</td>
</tr>
</tbody>
</table>

*Caspofungin only for isolates reported to PHE routine surveillance*

---

Fluconazole-resistance in MRCM *C. albicans* referrals increased slightly from 2012-2015 with a drop in 2016, however the number of isolates with reduced susceptibility remained low (Table 6.4). The small numbers tested over the time period, as well as the variability in numbers tested from year to year (including a large increase in the number of tested isolates in 2016) make these results difficult to interpret. The lower proportion of reduced susceptibility over time in routine laboratory surveillance (sterile site) specimens indicate that more complex specimens were likely to be referred to reference laboratories for further testing (Table 6.4). Echinocandin resistance was not detected in isolates tested by the MRCM except for 2 isolates which showed reduced susceptibility to this group of antifungals in 2016. Resistance to caspofungin was very low in routine surveillance reports but 12 *C. albicans* isolates were reported with reduced susceptibility in 2016. Resistance to amphotericin B was neither reported in any tested *C. albicans* MRCM specimen between 2012 and 2016 (Table 6.4) nor in MRL specimen (2015 only, data not shown). In contrast, low levels of resistance (range 0.5-2.5%) were reported through routine surveillance to PHE.

Table 6.5. Number of *C. glabrata* isolates tested for and resistant to key antifungals in England, 2012 to 2016

<table>
<thead>
<tr>
<th>Drug</th>
<th>year</th>
<th>all specimen types [MRCM]</th>
<th>sterile site (blood) specimen (PHE routine laboratory surveillance)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
<td>No. tested</td>
<td>No. (%) with reduced susceptibility</td>
</tr>
<tr>
<td>Fluconazole*</td>
<td>2012</td>
<td>1</td>
<td>(100.0)</td>
</tr>
<tr>
<td></td>
<td>2013</td>
<td>2</td>
<td>(100.0)</td>
</tr>
<tr>
<td></td>
<td>2014</td>
<td>12</td>
<td>(100.0)</td>
</tr>
<tr>
<td></td>
<td>2015</td>
<td>49</td>
<td>(100.0)</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td>84</td>
<td>(100.0)</td>
</tr>
<tr>
<td>Echinocandins¥</td>
<td>2012</td>
<td>103</td>
<td>(0.0)</td>
</tr>
<tr>
<td></td>
<td>2013</td>
<td>93</td>
<td>(0.0)</td>
</tr>
<tr>
<td></td>
<td>2014</td>
<td>38</td>
<td>(5.3)</td>
</tr>
<tr>
<td></td>
<td>2015</td>
<td>42</td>
<td>(9.5)</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td>50</td>
<td>(0.0)</td>
</tr>
<tr>
<td>Amphotericin B</td>
<td>2012</td>
<td>103</td>
<td>(0.0)</td>
</tr>
<tr>
<td></td>
<td>2013</td>
<td>99</td>
<td>(0.0)</td>
</tr>
<tr>
<td></td>
<td>2014</td>
<td>40</td>
<td>(0.0)</td>
</tr>
<tr>
<td></td>
<td>2015</td>
<td>45</td>
<td>(0.0)</td>
</tr>
<tr>
<td></td>
<td>2016</td>
<td>83</td>
<td>(0.0)</td>
</tr>
</tbody>
</table>

*EUCAST MIC breakpoints for fluconazole testing were established in 2014 and applied retrospectively for the presented MRCM test results for 2012/13

*Caspofungin only for isolates reported to PHE routine surveillance
The proportion of MRCM C. glabrata isolates with reduced susceptibility to fluconazole remained consistent throughout the 5 years at 100% (applying the EUCAST breakpoint established in 2014 retrospectively to test results from 2012/13). However, the proportion of MRL isolates with reduced susceptibility was 31.3% (119/380) (CLSI breakpoint) in 2015 and reduced susceptibility to fluconazole reported to PHE’s routine laboratory surveillance ranged from 23.4% in 2012 to 42.8% in 2016 (Table 6.5); this was most likely related to more resistant samples being referred to MRL and routine laboratories identifying to species level and performing susceptibility testing on isolates from particular patient cohorts. Due to these changes in breakpoints, the interpretation of reduced fluconazole susceptibility trends for C. glabrata is difficult. In addition, neither methodology nor breakpoints used by local laboratories for antifungal susceptibility testing are captured by PHE’s routine surveillance so comparisons with test results from the reference laboratories need to be treated with caution.

The number of echinocandin-resistant C. glabrata isolates remained low throughout the five year period, with resistant specimens reported by MRCM in 2014 and 2015 only (Table 6.5). Echinocandin resistance reported to PHE through routine laboratory surveillance ranged between 1.7% tested blood specimens in 2014 to 6.4% in 2013. In contrast, the MRL reported 12% C. glabrata isolates from sterile sites with reduced susceptibility to the echinocandin caspofungin in 2015 (data not shown).

Other fungal pathogens with intrinsic, emerging and multidrug resistance

The data in Table 6.6 are cumulative data reflecting testing over an eight year period and include the most common of the rare moulds that cause invasive infection, particularly those where there is concern over susceptibility to one or more of the most commonly used systemic antifungal agents. For the purposes of this analysis, the breakpoints selected for amphotericin and caspofungin were: ≤1.0mg/L susceptible and >2.0mg/L resistant; for voriconazole an intermediate category for which isolates may respond was also included: ≤1.0mg/L susceptible, 2-4mg/L intermediate and >8.0mg/L resistant.

Most of these isolates were from deep sites and indicative of invasive infection, with two notable exceptions: (1) Many of the Fusarium spp. tested are from cases of fungal keratitis in contact lens wearers, although it is also the commonest mould isolate from blood cultures in cases of disseminated infection; (2) Some of the isolates, most notably Scedosporium apiospermum and Exophiala spp., are from sputum of colonised cystic fibrosis patients; however, in this setting persistent colonisation can progress to allergic bronchopulmonary mycosis (ABPM) and also to more invasive disease as is often seen with the progression to ABPM following colonisation with Aspergillus spp.

Caspofungin, as a representative of the echinocandin group of agents, had little activity against most of these moulds with the exception of Rasamsonia argillacea which is
increasingly encountered in patients with cystic fibrosis. Most clinical successes with *Rasamsonia* spp., which appears to be innately resistant to voriconazole and often also to amphotericin B, have included the use of the echinocandin group.

There are increasing numbers of cutaneous phaeohyphomycosis cases due to *Alternaria* spp. in patients on tacrolimus following renal transplantations. It is notable that nearly a third of referred isolates are resistant to voriconazole which would be the treatment of choice for most other agents of cutaneous phaeohyphomycosis. Moulds in the genus *Exophiala* are often referred to as black yeasts as they can have a very mucoid appearance. They colonise the lungs of patients with cystic fibrosis and may become invasive; possibly leading to neurotropic brain infection. Occasionally, emergent resistance to triazole antifungal agents is seen within this genus.

*Fusarium* spp. are a common cause of keratitis in contact lens wearers and current treatment includes topical natamycin with or without systemic voriconazole. Isolates of *Fusarium* spp. frequently display resistance to amphotericin B (> 30% isolates) and disseminated infections treated with this agent do not respond well. Many isolates also appear to have intermediate susceptibility to voriconazole, however, voriconazole penetrates well into the eye and is therefore often considered a treatment of choice. Clinical success with either agent may owe much to the immune system recovery of the host. The related pathogen *Sarocladium* (previously *Acremonium*) causes a similar disseminated infection and the referred isolates are frequently resistant to amphotericin B (69%) but more commonly susceptible to voriconazole (11% resistance).

High dose lipid amphotericin B remains the treatment of choice for isolates of the subphylum *Mucoromycotina*, which cause rhinocerebral mucormyosis, pulmonary infection and rapidly invasive cutaneous infections of wounds. Most isolates are susceptible to amphotericin B, but resistant to voriconazole and the echinocandin group. Newer triazole agents such as posaconazole and isavuconazole have shown promise as second-line agents. *Lomentospora prolificans* (previously *Scedosporium prolificans*) shows little susceptibility to any of the currently available agents. The treatment of choice is a combination of voriconazole and terbinafine. In contrast, *Scedosporium apiospermum* is nearly always susceptible to voriconazole (3% resistance) and other triazoles, although often resistant to amphotericin B (53% resistance). *Paecilomyces variotii* and *Purpureocillium lilacinum* have both been implicated in invasive and deep seated infections eg endophthalmitis, as well as colonising the lungs of patients with cystic fibrosis. *P variotii* is almost always susceptible to amphotericin B (6% resistance) but many isolates are resistant to voriconazole (83% resistance), whilst the reverse is true for *P. lilacinum* with 100% resistance to amphotericin B and only 2% resistance to voriconazole.
Table 6.6. Number of referred fungal isolates tested for and resistant to key antifungals in England, 2008 to 2016 (MRL)

<table>
<thead>
<tr>
<th>Drug</th>
<th>Organism</th>
<th>No. tested</th>
<th>No. resistant</th>
<th>No. interm.</th>
<th>% reduced suscept.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Amphotericin B</td>
<td>Alternaria spp.</td>
<td>58</td>
<td>0</td>
<td>-</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Exophiala spp.</td>
<td>134</td>
<td>0</td>
<td>-</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Fusarium spp.</td>
<td>586</td>
<td>201</td>
<td>-</td>
<td>34.3</td>
</tr>
<tr>
<td></td>
<td>Mucoromycotina</td>
<td>249</td>
<td>2</td>
<td>-</td>
<td>0.8</td>
</tr>
<tr>
<td></td>
<td>Lomentospora prolificans</td>
<td>25</td>
<td>25</td>
<td>-</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>Paecilomyces variotii</td>
<td>33</td>
<td>2</td>
<td>-</td>
<td>6.1</td>
</tr>
<tr>
<td></td>
<td>Purpureocillium lilacinum</td>
<td>42</td>
<td>42</td>
<td>-</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>Rasamsonia argillacea</td>
<td>29</td>
<td>15</td>
<td>-</td>
<td>51.7</td>
</tr>
<tr>
<td></td>
<td>Saracladium spp.</td>
<td>55</td>
<td>38</td>
<td>-</td>
<td>69.1</td>
</tr>
<tr>
<td></td>
<td>Scedosporium apiospermum</td>
<td>301</td>
<td>159</td>
<td>-</td>
<td>52.8</td>
</tr>
<tr>
<td></td>
<td>Alternaria spp.</td>
<td>63</td>
<td>4</td>
<td>14</td>
<td>28.6</td>
</tr>
<tr>
<td></td>
<td>Exophiala spp.</td>
<td>126</td>
<td>2</td>
<td>4</td>
<td>4.8</td>
</tr>
<tr>
<td></td>
<td>Fusarium spp.</td>
<td>593</td>
<td>32</td>
<td>338</td>
<td>62.4</td>
</tr>
<tr>
<td></td>
<td>Mucoromycotina</td>
<td>230</td>
<td>163</td>
<td>57</td>
<td>95.7</td>
</tr>
<tr>
<td></td>
<td>Lomentospora prolificans</td>
<td>25</td>
<td>0</td>
<td>16</td>
<td>64.0</td>
</tr>
<tr>
<td></td>
<td>Paecilomyces variotii</td>
<td>30</td>
<td>13</td>
<td>12</td>
<td>83.3</td>
</tr>
<tr>
<td></td>
<td>Purpureocillium lilacinum</td>
<td>43</td>
<td>1</td>
<td>-</td>
<td>2.3</td>
</tr>
<tr>
<td></td>
<td>Rasamsonia argillacea</td>
<td>30</td>
<td>3</td>
<td>27</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>Saracladium spp.</td>
<td>55</td>
<td>4</td>
<td>2</td>
<td>10.9</td>
</tr>
<tr>
<td></td>
<td>Scedosporium apiospermum</td>
<td>304</td>
<td>1</td>
<td>8</td>
<td>3.0</td>
</tr>
<tr>
<td></td>
<td>Alternaria spp.</td>
<td>20</td>
<td>5</td>
<td>-</td>
<td>25.0</td>
</tr>
<tr>
<td></td>
<td>Exophiala spp.</td>
<td>33</td>
<td>30</td>
<td>-</td>
<td>90.9</td>
</tr>
<tr>
<td></td>
<td>Fusarium spp.</td>
<td>81</td>
<td>78</td>
<td>-</td>
<td>96.3</td>
</tr>
<tr>
<td>Voriconazole</td>
<td>Mucoromycotina</td>
<td>45</td>
<td>45</td>
<td>-</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>Lomentospora prolificans</td>
<td>10</td>
<td>10</td>
<td>-</td>
<td>100.0</td>
</tr>
<tr>
<td></td>
<td>Paecilomyces variotii</td>
<td>16</td>
<td>7</td>
<td>-</td>
<td>43.75</td>
</tr>
<tr>
<td></td>
<td>Purpureocillium lilacinum</td>
<td>6</td>
<td>3</td>
<td>-</td>
<td>50.0</td>
</tr>
<tr>
<td></td>
<td>Rasamsonia argillacea</td>
<td>5</td>
<td>0</td>
<td>-</td>
<td>0.0</td>
</tr>
<tr>
<td></td>
<td>Saracladium spp.</td>
<td>11</td>
<td>8</td>
<td>-</td>
<td>72.7</td>
</tr>
<tr>
<td></td>
<td>Scedosporium apiospermum</td>
<td>98</td>
<td>63</td>
<td>-</td>
<td>64.3</td>
</tr>
</tbody>
</table>
Candida auris

Candida auris is an emerging fungal pathogen of global concern for several reasons: (1) it has caused prolonged nosocomial outbreaks on five continents; (2) high case fatality rates have been reported from worldwide case series, usually between 30 to 70% of those infected, though there are no comparable background mortality rates for comparison; and (3) it remains difficult to identify through traditional biochemical methods.

Recent publications highlighted that at least four distinct clades have emerged based on the geographical region from which they were first described – South American, South African, South Asian and East Asian. This emergence is likely independent of each other, based on the many thousands of single nucleotide polymorphisms (SNPs) difference between clades, suggesting some common driving factor for this simultaneous appearance across the globe. However, within each clade there are minimal SNP differences and as such determining transmission dynamics within on-going outbreaks is difficult, with separation of novel introductions versus on-going spread very challenging, even with whole genome sequencing.

From January 2015 to June 2017, there were over 200 detections of C. auris from 20 separate English NHS Trusts and independent providers within England. Three large nosocomial outbreaks have occurred, which despite intensive infection prevention and control measures were difficult to control, though all have now been declared over (14 August 2017). Over 35 other hospitals have received patients known to be colonised with C. auris. Most detections were in colonised patients, picked up through enhanced surveillance in the three affected hospitals, though approximately one quarter were clinical infections including 27 patients who had candidaemias (C. auris bloodstream infections). Importantly, UK look back exercises to date have shown that for patients with clinical infections there was no C. auris attributable mortality.

Sequencing in England at the MRL using a conserved region of the genome that highly differentiates between the clades has shown the introduction of S. Asian (most prominent), E. Asian, and S. African (in one hospital outbreak) subtypes. The MRL has also demonstrated two morphologically distinct forms, with one ‘clumping’ (S. African) versus single cell forms (S. Asian). The aggregative form appears to be less pathogenic in an in-vivo wax moth model. No multidrug resistant strains have been identified to date, though all isolates are resistant to fluconazole, with variable resistance to other drug classes.

A key unanswered question is the background prevalence of colonisation in the general population. To answer this, a pilot survey of patients admitted to ICU was launched in July 2017, with screening of all patients on ward entry to five hospitals serving multi-ethnic populations to determine background rates of colonisation. It is anticipated that at
least 800 patients will be screened, giving a point prevalence estimate with a precision of 0.5%. There remains on-going epidemiological studies to better delineate risk factors for both acquisition and invasive infection, and PHE’s Biosafety Investigation Unit at Porton Down has acquired funding to further investigate the fungicidal activity of a variety of disinfectants and antiseptics. Preliminary work suggests that chlorhexidine without the addition of isopropyl alcohol (IPA) is a less effective method than chlorhexidine with IPA for removing \textit{C. auris} from skin surfaces.\textsuperscript{91} The need for hydrogen peroxide based terminal cleaning has been debated. The national guidance was updated in August 2017, alongside production of a patient information leaflet and guidelines for care in community settings.\textsuperscript{92}

\textbf{Antifungal prescribing}

\textbf{Total consumption of antifungals}

From 2013 to 2016, the total consumption of systemic (oral or parenteral only) antifungals prescribed in general practice and NHS hospitals in England decreased by 19\% from 1.6 to 1.3 DDD per 1000 inhabitants per day. In 2016, 91\% of systemic antifungal prescribing occurred in general practice (Figure 6.5). The decline may be due to a real observation or an increase in over-the-counter (OTC) prescriptions of oral azoles; however, the only systemic antifungal which may currently be prescribed OTC in England is oral fluconazole.

\begin{figure}[h]
\centering
\includegraphics[width=\textwidth]{Total_consumption_of_antifungals_England.png}
\caption{Consumption of total systemic antifungals in general practice and NHS hospitals, expressed as DDD per 1000 inhabitants per day, England, 2013-2016}
\end{figure}


ERRATUM: Please note that an error was identified in the figures published for consumption of antifungals prescribed in NHS hospitals in the ESPAUR Report 2016. The published graphs showed antifungal consumption in “Specialist Trusts” only, not total hospital consumption as stated incorrectly. Please take this into account when comparing antifungal consumption data presented in the ESPAUR Report 2016 with this year’s report.

Prescribing in the community

Total prescribing of systemic antifungals in general practice decreased by 21%, from 1.5 to 1.2 DDDs per 1000 inhabitants per day, between 2013 and 2016. The highest decrease was recorded between 2014/15 (9.0%) compared to 2013/14 (4.8%) and 2015/16 (8.4%) (Figure 6.6).

Consumption of terbinafine, the most commonly prescribed systemic antifungal agent, decreased by 23% between 2013 and 2016 (Figure 6.7). The azoles itraconazole and fluconazole were the second and third most prescribed drugs for treatment of systemic fungal infections over the 3-year period. Itraconazole consumption fell by 4.6% between 2013 and 2016, whereas fluconazole usage increased between 2013 and 2015 before falling by 2.4% in 2016. Of the systemic antifungals shown in Figure 6.7, only oral fluconazole is available OTC medicine and can be sold directly to the patient.
Prescribing in NHS hospitals

Total consumption of antifungals in NHS hospitals increased by 3.1% between 2013 and 2014, but then subsequently decreased by 3.8% and 3.9% between 2014/15 and 2015/16 respectively (Figure 6.8).

Figure 6.8. Total systemic antifungal prescribing in NHS hospital trusts captured by RX-info (131 of 155 NHS Acute Trusts in 2016), expressed as DDD per 1000 admissions (including day cases) per day, England, 2013-2016
Fluconazole was the most prescribed systemic antifungal in NHS hospitals in 2016 with 0.20 DDD per 1000 admissions per day, followed by posaconazole (0.12 DDD/1000 inhabitants/day) and itraconazole (0.10 DDD/1000 inhabitants/day) (Figure 6.9). Only the prescribing of the echinocandins anidulafungin and micafungin increased between 2015 and 2016. Isavuconazole prescriptions are only available for 2016 because this antifungal was only licensed for use in December 2015.

![Bar chart showing systemic antifungal prescribing in NHS hospitals by antifungal group, expressed as DDD per 1000 admissions (including day cases) per day, England, 2013-2016](image)

*Figure 6.9. Systemic antifungal prescribing in NHS hospitals by antifungal group, expressed as DDD per 1000 admissions (including day cases) per day, England, 2013-2016*

When comparing systemic antifungal prescribing for patients at specialty level, ‘Clinical haematology’ had the highest usage per occupied bed (59 DDD/100 admissions/day) in 2016 followed by ‘General Medicine’ (33 DDD/1000 admissions/day) and ‘Nuclear Medicine’ (28 DDD/1000 admissions/day) (Figure 6.10).
Mycology Laboratory Diagnostic Capacity for Invasive Fungal Diseases in 2017: Results of a national survey

Accurate diagnosis and identification to species level of fungal infections is crucial for improving patient outcomes and providing information for antimicrobial stewardship activities. Therefore, ESPAUR's Antifungal Consumption and Resistance Surveillance subgroup agreed in its inaugural meeting that a survey of laboratory testing capabilities for clinically significant fungal pathogens, diagnostics and antifungal therapeutic drug monitoring (TDM) was essential to determine future actions.

The last national survey on the compliance and implementation of the BSMM standards of care for patients with invasive fungal infections was performed in UK hospitals in 2007. In the subsequent 10 years, new BSMM guidelines were published on fungal

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Figure 6.10. Total systemic antifungal prescribing in NHS hospitals for the 20 highest prescribing clinical specialties, expressed as DDD per 1000 admissions (including day cases) per day, England, 2016

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diagnostics and antifungal drug monitoring. The survey was developed by the ESPAUR Antifungal Consumption and Resistance Surveillance subgroup in collaboration with the BSMM and endorsed by the UKCMN. This report provides a summary of the survey results.

Methods

The survey was developed using the BSMM’s 2007 survey questions with amendments and additional questions based on the updated BSMM standards of care for patients with invasive fungal infections, the BSMM’s guidance on therapeutic drug monitoring and PHE’s guidance on diagnosis of C. auris. The survey was launched on 27 March 2017 for 6 weeks and was distributed by email through clinical networks and accessible through websites and newsletters from PHE, the British Infection Association (BIA) and the Royal College of Pathologists (RCPath).

Results

From 27 March to 8 May 2017 a total of 99 responses were received. Seventeen responses were duplicates with respondents based at the same laboratory or hospital/Trust. Out of the remaining 82 responses, 72 were from England, four from Scotland, two from Wales, and one from Northern Ireland, Isle of Man, the Netherlands and ‘other’ respectively.

This report covers responses from England only. Based on the numbers of all laboratories providing a diagnostic mycology service (n=135), the survey response rate was 53% in England. All but one respondent provided information on the type of Trust serviced by the laboratory (Table 6.7).

Table 6.7. Trust types serviced by responding laboratories

<table>
<thead>
<tr>
<th>Trust type serviced by laboratory</th>
<th>Number of laboratories serving hospital type/ respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-teaching</td>
<td>39/71 (55%)</td>
</tr>
<tr>
<td>Specialist</td>
<td>4/71 (6%)</td>
</tr>
<tr>
<td>Teaching *</td>
<td>28/71 (37%)</td>
</tr>
</tbody>
</table>

Figure 6.11 shows the map of where survey respondents (laboratories) were located.

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The results are presented by non-reference laboratories and reference laboratories if applicable. Respondents were able to select more than one response for some questions.

Awareness of updated BSMM standards

Of the 68 respondents 72% were aware of the published BSMM standards.

Yeast/mould speciation

Identification of isolates to species level by microscopy was predominantly carried out by laboratories onsite or centralised for yeast and moulds, 95% and 77% respectively. The use of other methods for fungal speciation including Matrix Assisted Laser Desorption/Ionization (MALDI), VITEK®, analytical profile index (API) identification and chromogenic agar is shown in:
Table 6.8 as aggregated data. 97% of respondents performed at least one of these methods to identify fungi to species level onsite or centralised.

<table>
<thead>
<tr>
<th>Fungal Testing Performed</th>
<th>Test Performed Onsite or Centralised /Respondents (%)</th>
<th>Test Performed in Reference Laboratory /Respondents (%)</th>
<th>Test Performed in Other External or Private Laboratory /Respondents (%)</th>
<th>Testing Not Applicable /Respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yeast Speciation</td>
<td>58/61 (95%)</td>
<td>17/61 (29%)</td>
<td>1/61 (2%)</td>
<td>1/61 (2%)</td>
</tr>
<tr>
<td>Mould Speciation</td>
<td>47/61 (77%)</td>
<td>26/61 (43%)</td>
<td>2/61 (3%)</td>
<td>1/61 (2%)</td>
</tr>
<tr>
<td>Fungal Speciation*</td>
<td>58/60 (97%)</td>
<td>42/60 (70%)</td>
<td>5/60 (8%)</td>
<td>10/60 (16%)</td>
</tr>
<tr>
<td>Yeast Susceptibility</td>
<td>45/57 (79%)</td>
<td>25/57 (43%)</td>
<td>0/57 (0%)</td>
<td>8/57 (14%)</td>
</tr>
<tr>
<td>Aspergillus Susceptibility</td>
<td>3/36 (8%)</td>
<td>30/36 (83%)</td>
<td>0/36 (0%)</td>
<td>7/36 (19%)</td>
</tr>
<tr>
<td>Other Mould Susceptibility</td>
<td>3/26 (12%)</td>
<td>21/26 (81%)</td>
<td>1/26 (4%)</td>
<td>2/26 (8%)</td>
</tr>
<tr>
<td>C. auris Susceptibility**</td>
<td>25/47 (53%)</td>
<td>21/47 (45%)</td>
<td>1/47 (2%)</td>
<td>n/a</td>
</tr>
</tbody>
</table>

*Microscopy only
* Tests other than Microscopy
NB. More than one response possible

Antifungal susceptibility testing

The location of susceptibility testing varied by fungal species. Seventy-nine percent of non-reference laboratories performed susceptibility testing of yeasts locally (on-site or at a central laboratory within the trust) and 43% responded that they refer isolates for testing to a reference laboratory. This compared with only 8% of non-reference laboratories reporting testing Aspergillus spp. locally and 83% referring isolates to a reference laboratory as well as 12% of non-reference laboratories testing other moulds than yeast locally and 81% referring to a reference laboratory.
Table 6.8. Fungal testing for speciation and susceptibility and where performed (excluding reference laboratories)

<table>
<thead>
<tr>
<th>Fungal Testing Performed</th>
<th>Yeast Speciation ¥</th>
<th>Mould Speciation ¥</th>
<th>Fungal Speciation*</th>
<th>Yeast Susceptibility</th>
<th>Aspergillus Susceptibility</th>
<th>Other Mould Susceptibility</th>
<th>C. auris Susceptibility**</th>
</tr>
</thead>
<tbody>
<tr>
<td>Test Performed Onsite or Centralised /Respondents (%)</td>
<td>58/61 (95%)</td>
<td>47/61 (77%)</td>
<td>58/60 (97%)</td>
<td>45/57 (79%)</td>
<td>3/36 (8%)</td>
<td>3/26 (12%)</td>
<td>25/47 (53%)</td>
</tr>
<tr>
<td>Test Performed in Reference Laboratory /Respondents (%)</td>
<td>17/61(29%)</td>
<td>26/61 (43%)</td>
<td>42/60 (70%)</td>
<td>25/57 (43%)</td>
<td>30/36 (83%)</td>
<td>21/26 (81%)</td>
<td>21/47 (45%)</td>
</tr>
<tr>
<td>Test Performed in Other External or Private Laboratory /Respondents (%)</td>
<td>1/61 (2%)</td>
<td>2/61 (3%)</td>
<td>5/60 (8%)</td>
<td>0/57 (0%)</td>
<td>0/36 (0%)</td>
<td>1/26 (4%)</td>
<td>1/47 (2%)</td>
</tr>
<tr>
<td>Testing Not Applicable /Respondents (%)</td>
<td>1/61 (2%)</td>
<td>1/61 (2%)</td>
<td>10/60 (16%)</td>
<td>8/57 (14%)</td>
<td>7/36 (19%)</td>
<td>2/26 (8%)</td>
<td>n/a</td>
</tr>
</tbody>
</table>

¥ Microscopy only
* Tests other than Microscopy
NB. More than one response possible

Susceptibility testing for fluconazole in *Candida* spp. is performed in 77% of non-reference laboratories as seen in Table 6.9. *A. fumigatus* susceptibility testing for all local antifungal treatment is only performed in 15% of non-reference laboratories. Susceptibility testing is recommended for both.

Table 6.9. Fungal susceptibility testing for antifungals used
Laboratories that perform susceptibility testing /respondents (%)

<table>
<thead>
<tr>
<th>Fluconazole susceptibility for <em>Candida</em> spp.</th>
<th>No</th>
<th>11/48 (23%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>37/48 (77%)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Antifungal susceptibility for <em>Aspergillus fumigatus</em>.</th>
<th>No</th>
<th>39/47 (83%)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Yes</td>
<td>7/47 (15%)</td>
</tr>
<tr>
<td></td>
<td>Don’t know</td>
<td>1/47 (2%)</td>
</tr>
</tbody>
</table>

Survey results for questions on susceptibility testing for *Aspergillus* isolates are presented in Tables 6.10 and 6.11. Best practice recommendations are to perform susceptibility testing for all patients, and to store these isolates for a further six months; these occurred in less than 20% and 20% of respondents laboratories respectively.

**Table 6.10. Fungal Susceptibility testing for *Aspergillus* isolates for different patient types.**

<table>
<thead>
<tr>
<th>Aspergillus patient types</th>
<th>Laboratories that perform susceptibility testing for drugs used for treatment /respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Allergic bronchopulmonaryaspergillosis (ABPA)</td>
<td>5/48 (10%)</td>
</tr>
<tr>
<td>Aspergilloma</td>
<td>8/48 (17%)</td>
</tr>
<tr>
<td>Chronic Aspergillosis</td>
<td>8/48 (17%)</td>
</tr>
</tbody>
</table>

NB. More than one response could be selected

**Table 6.11. Storage of *Aspergillus* isolates after initial speciation for treatment.**

<table>
<thead>
<tr>
<th>Aspergillus isolates stored for potential further testing</th>
<th>Laboratories that store <em>Aspergillus</em> isolates for 6 months/respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No</td>
<td>32/40 (80%)</td>
</tr>
<tr>
<td>Yes</td>
<td>8/40 (20%)</td>
</tr>
</tbody>
</table>

*Candida auris*

All 56 respondents who answered the question whether they were aware of the recently emerging *C. auris* replied ‘Yes’. Twenty-five (53%) of 47 responding non-reference laboratories test for the pathogen onsite, 21 (45%) refer isolates to a reference laboratory and one non-reference laboratory responded referral to ‘other laboratory’.

MALDI is being used by 23 (92%) of non-reference laboratories and one reference laboratory to identify *C. auris*. Two (8%) non-reference laboratories reported using VITEK® and one
reference laboratory uses PCR/sequencing. Currently, only MALDI and PCR/sequencing are advised for speciation of suspected *C. auris* (Table 6.12).

**Table 6.12. Onsite tests used to identify suspected *Candida auris***

<table>
<thead>
<tr>
<th>Speciation Testing Methods</th>
<th>Testing used by Non-Reference Laboratory /respondents (%)</th>
<th>Testing used by Reference Laboratory /respondents (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>MALDI</td>
<td>23/25 (92%)</td>
<td>1/2 (50%)</td>
</tr>
<tr>
<td>VITEK (Biochemical test)</td>
<td>2/25 (8%)</td>
<td>0/2 (0%)</td>
</tr>
<tr>
<td>API</td>
<td>0/25 (0%)</td>
<td>0/2 (0%)</td>
</tr>
<tr>
<td>Chromogenic Agar</td>
<td>0/25 (0%)</td>
<td>0/2 (0%)</td>
</tr>
<tr>
<td>PCR/Sequencing</td>
<td>0/25 (0%)</td>
<td>1/2 (50%)</td>
</tr>
</tbody>
</table>

**Therapeutic drug monitoring**

Due to pharmacokinetic variability within patients, which can be as a result of unpredictable absorption, metabolism, drug to drug interactions and compliance, TDM is recommended by the BSMM for certain antifungals to monitor the therapeutic serum concentration and to avoid toxicity issues. There is no evidence to recommend TDM for amphotericin B and echinocandins as plasma concentrations do not relate to tissue concentrations, toxicity or efficacy of the antifungal agents. Fluconazole TDM may be necessary for some rare clinical circumstances such as patients with central nervous system diseases or unstable patients receiving renal supportive care. Isuvaconazole was not licensed when the standards were published (license year: 2015, publication year: 2013).

Advice on TDM is provided by both reference laboratories and by 77% (33/43) of non-reference laboratories.

BSMM guidelines advise TDM for the antifungals in Table 6.13 after dosage change, shift from intravenous to oral treatment and for optimisation during long term therapy. Both reference laboratories complied with the guidance. However, only 45% of non-reference laboratories advise TDM after dosage change, 38% following shift from intravenous to oral treatment, and 63% for optimisation during long term therapy. The current BSMM guideline on TDM of antifungal agents does not recommend TDM for amphotericin B, echinocandins and isavuconazole (as described further above); this was reflected in the responses with very few laboratories advising TDM for any of these antifungals.

Table 6.13 shows laboratories’ adherence to the BSMM guidance on TDM for antifungal drugs.

**Table 6.13. Advice on Therapeutic Drug Monitoring (TDM) for antifungal drugs***
The NHS Improving Value Antifungal Stewardship Project was established in February 2017 with the aim to achieve improved value from NHS England’s spend on antifungals and improved patient safety through reduced adverse effects and standardisation of clinical practice.

The project will develop guidance for NHS England commissioning teams focusing on the following key areas:

- Optimisation of the use of empirical antifungal treatment
- Improvements regarding antifungal diagnostic testing to inform treatment and antifungal stewardship activities
- Reduction of selective pressure and the impact of resistant fungal pathogens
- Increase in use of antifungals with lower acquisition costs

NHS England’s Medicines Optimisation CQUIN (2017-19) will provide an incentive to adopt best practice in antifungal stewardship.

The NHS Improving Value Antifungal Stewardship Group in collaboration with the ESPAUR subgroup97 carried out a scoping exercise to gather information on current antifungal stewardship activities in the NHS.

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97 A list of membership for the ESPAUR subgroup on antifungal consumption and resistance surveillance subgroup is available in Annex – Chapter 6.
Discussion

In the collation of data for the ESPAUR report 2017, we have brought together for the first time antifungal resistance data extracted from PHE’s national routine laboratory surveillance database and information collected by the MRL and the MRCM. The data show incidence rates and antifungal resistance for key *Aspergillus* and *Candida* species and an additional section describes levels of antifungal resistance in rarer fungal pathogens such as *Fusarium* spp., *S. apiospermum*, *Mucoromycotina* spp. and others. Azole resistance among *Aspergillus* and *Candida* species is a worrying trend which threatens clinical treatment of severely ill patients, as well as echinocandin and multidrug resistance among *Candida* spp. such as *C. glabrata*.

Presenting routine laboratory data on antifungal resistance alongside reference laboratory data is an important first step in building the evidence required to improve the understanding of current antifungal resistance trends in England and inform commissioning and implementing of antimicrobial stewardship policies. However, the presented information also highlights limitations of the data used and areas where surveillance activities need to be improved:

- antifungal susceptibility testing by routine as well as reference laboratories is performed using different in-vitro methods and breakpoints (CLSI/EUCAST) for yeasts and moulds. These differences in methodologies impede the ability to merge available datasets and compare antifungal resistance trends across England
- referral patterns of microbiology laboratories including whether fungal isolates are tested locally, recorded by routine surveillance and/or captured by reference laboratories, are poorly defined and may vary widely, possibly resulting in biased isolate samples especially among referred isolates

Better understanding of the captured data and improved harmonisation of antifungal susceptibility testing data is not only essential for improving the quality of national antifungal surveillance but will also be required for the UK’s contribution to European and global surveillance activities.

This chapter also presents data on systemic antifungals prescribed in general practice and NHS hospitals. The addition of specialty-level prescribing data in this year’s ESPAUR report allows a more detailed analysis of antifungal usage in NHS hospitals with a view to inform stewardship activities. The data show a 21% decrease in systemic antifungal prescribing in general practice between 2013 and 2016, mainly driven by fewer systemic terbinafine prescriptions. Despite the subgroup’s efforts, data on OTC sales of antifungal medicines by pharmacists was not available to the group in time to compare trends and help interpret the reduction in antifungal prescriptions by GPs. Total consumption of antifungals in NHS hospitals slightly decreased between 2014 and 2016 although usage of fluconazole and the echinocandins anidulafungin and
micafungin continued to increase over the same time period. The specialty with highest usage of systemic antifungals per 1000 admissions was ‘Clinical haematology’ followed by ‘General Medicine’ and ‘Nuclear Medicine’ in 2016; this is in marked contrast to the specialist antibiotic prescribing outlined in Chapter 3. The lowest usage per 1000 hospital admissions was recorded for ‘Critical Care Medicine’ and ‘Dermatology’. This information on high and low users by specialty needs to inform antifungal stewardship activities and will be shared with the BSMM and relevant mycology networks such as the UKCMN, BIA and the RCPa.

The ESPAUR antifungal subgroup have also published the initial results from the national survey ‘Mycology Laboratory Diagnostic Capacity for Invasive Fungal Diseases in 2017’ which was developed and launched by the ESPAUR antifungal subgroup in collaboration with the BSMM and endorsed by the UKCMN. The survey on the compliance and implementation of BSMM standards of care for patients with invasive fungal infections was based on a similar survey conducted by the BSMM in 2007. A summary of the results and comparison with the previous survey will be shared with the BSMM to help evaluate how adherence to published standards has changed over time and identify areas where increased efforts are needed to improve compliance with published standards.

Compared to the previous survey, the response rate increased from 35% to 52% (72 out of 135 laboratories providing diagnostic mycology service in England). The survey captured compliance with susceptibility testing recommendations and where responding laboratories performed antifungal speciation and susceptibility testing (onsite/centralised/referral to reference laboratory). The survey highlighted areas of concern regarding TDM of antifungal drugs with low adherence to the BSMM’s recommendations. Less than half of all respondents reported advising TDM for flucytosine even though it should be performed in the majority of treated patients due to its well-established concentration–toxicity relationship and emergence of drug resistance when yeasts are exposed to low flucytosine concentrations.

**Future actions**

The ESPAUR subgroup on antifungal consumption and resistance surveillance will continue to work on the following:

- **scoping of harmonisation of breakpoints in collaboration with the National External Quality Assurance Scheme (NEQAS) and the BSMM**
- **develop study to improve understanding of referral patterns of microbiology laboratories regarding fungal isolates**
- **continue to improve transparency and dissemination of antifungal surveillance data, for example by exploring options of presenting antifungal resistance data on PHE’s publicly accessible interactive data portal Fingertips**
• explore and work with the pharmacy sector to combine antifungal prescribing data with data on antifungal agents available without prescription in England

• ensure that results of national survey on ‘Mycology Laboratory Diagnostic Capacity for Invasive Fungal Diseases in 2017’ are being communicated with relevant networks such as UKCMN, BIA and RCPath to inform promotion of best practice in clinical mycology and antifungal stewardship activities

• ensure survey findings on TDM inform BSMM TDM guidelines, which are currently under review

• work with NHS England Improving Value Antifungal Stewardship Project group to perform a scoping exercise to gather information on current NHS antifungal stewardship activities with the aim to achieve improved value from NHS England’s spend on antifungals and improved patient safety through reduced adverse effects and standardisation of clinical practice.

• work with NHS England Improving Value Antifungal Stewardship Project group to develop relevant performance indicators for antifungal usage, validate their use and publish them on platforms such as PHE’s Fingertips data portal
7. Point prevalence survey of healthcare-associated infections, antimicrobial use and antimicrobial stewardship in England

Introduction

Over four million people in Europe acquire a healthcare-associated infection (HCAI) every year, and around 37,000 die as a direct result of the infection. Surveillance of HCAI and Antimicrobial Use (AMU) is an essential part of infection prevention and antimicrobial stewardship. The point prevalence survey (PPS) drives action by providing data on the burden of HCAI and AMU that allows targeted planning and implementing more effective, evidence based policies, surveillance and strategies. This is the fifth national PPS of HCAI and second national PPS of AMU and quality indicators in England.

Objectives

The objectives of the PPS of HCAIs and AMU in acute-care hospitals are:

- to estimate the total burden (prevalence) of HCAIs and AMU in acute-care hospitals
- to describe patients, invasive procedures, infections (sites, microorganisms including markers of antimicrobial resistance (AMR)) and antimicrobials prescribed (compounds, indications) by type of patients, specialties and healthcare facilities
- to describe key structures and processes for the prevention of HCAIs and AMR at the hospital and ward level in EU hospitals
- to disseminate results to those who need to know at local, regional, and national level:
  - to raise awareness
  - to train and reinforce surveillance structures and skills
  - to identify common problems and set up priorities accordingly
  - to evaluate the effect of strategies and guide policies for the future at the local/national/regional level (repeated PPS)
- to provide a standardised tool for hospitals to identify targets for quality improvement

Methods

In England, the PPS ran from 5 September – 30 November 2016. All acute-care hospitals were eligible for inclusion. An acute-care hospital was defined according to national definitions and there was no minimal size of hospital. Only hospitals with all
eligible patient data submitted were accepted for the national report. All patients admitted to the ward before or at 8am and not discharged from the ward at the time of the survey were included in the study with the following exceptions: day case patients, patients undergoing same day treatment or surgery, outpatients, patients in A&E (including those on less than one day support wards), and dialysis patients (day attenders).

An active HCAI (associated to acute-care hospital stay) was defined according to ECDC guidelines, using signs and symptoms, onset and admission parameters:

Signs and symptoms:

- an infection is active when signs and symptoms of the infection are present on the survey date or
- signs and symptoms were present in the past and the patient is (still) receiving treatment for that infection on the survey date

Onset:

- the onset of symptoms was on day 3 or later (day of admission = day 1) of the current admission or
- the patient presents with an infection but has been readmitted less than 48 hours after a previous admission to an acute-care hospital or
  - the patient has been admitted (or develops symptoms within two days) with an infection that meets the case definition of an active surgical site infection (SSI), that is, the SSI occurred within 30 days of the operation (or in the case of surgery involving an implant, was a deep or organ/space SSI that developed within 90 days of the operation) and the patient either has symptoms that meet the case definition and/or is on antimicrobial treatment for that infection devices or
  - an invasive device was placed on day one or day two, resulting in an HCAI before day 3

Admission:

- the patient has been admitted (or develops symptoms within two days) with *Clostridium difficile* infection less than 28 days after a previous discharge from an acute-care hospital

More than 400 participants were trained in preparation for the PPS via a series of face-to-face and online training sessions. Data capture and submission occurred via a secure Web-based application. The system was modelled on the British Society for Antimicrobial Chemotherapy (BSAC) National Antimicrobial Stewardship PPS system.
The system underwent further development to capture all national, hospital, ward and patient data required for the national HCAI and AMU PPS. In addition to retrospective data entry, this system allowed participants to collect and enter data directly onto the system in real-time.

Results

A total of 88 NHS Trusts and 6 independent organisations submitted patient data to the PPS web-based application. Four NHS Trusts were excluded from the results to avoid selection bias as not all eligible patients within the surveyed hospitals were reported. In total, 48,312 patient records were included in the final dataset. The median patient age was 71 years old; 9% of all patients were children aged <16 years old. There were more female patients (54%) than male patients (46%) [see online Appendix]. Twenty four percent of patients included in the survey were admitted with co-morbidities that would reduce their life expectancy (rapidly fatal within 1 year 4.6%; ultimately fatal 1-5 years 19.4%). Peripheral vascular cannula and urinary catheters were common in the population surveyed (42.8% and 20.1% respectively). Central venous catheters and intubation were infrequent (6.6% and 1.9% respectively), except for specialised services [see online Appendix].

HCAI and AMU prevalence by patient specialty

The HCAI prevalence was 6.6% and the AMU prevalence was 37.0%. The patient specialty with the highest HCAI prevalence was Intensive Care Medicine (17.6%), followed by Surgical specialty (8.5%) (Table 7.1). The patient specialty with the highest AMU prevalence was Intensive Care Medicine (51.9%), followed by Medical specialty (40.0%) [see online Appendix].

Table 7.1 HCAI prevalence and antimicrobial use by main patient speciality

<table>
<thead>
<tr>
<th>Specialty</th>
<th>No.</th>
<th>% HAI</th>
<th>% AMU</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>48312</td>
<td>6.6%</td>
<td>37.0%</td>
</tr>
<tr>
<td>Surgical</td>
<td>12812</td>
<td>8.5%</td>
<td>39.5%</td>
</tr>
<tr>
<td>Medical</td>
<td>20942</td>
<td>5.8%</td>
<td>40.0%</td>
</tr>
<tr>
<td>Paediatrics</td>
<td>1630</td>
<td>2.9%</td>
<td>37.2%</td>
</tr>
<tr>
<td>Intensive Care Medicine</td>
<td>1469</td>
<td>17.6%</td>
<td>51.9%</td>
</tr>
<tr>
<td>Gynaecology/obstetrics</td>
<td>3549</td>
<td>2.4%</td>
<td>22.4%</td>
</tr>
<tr>
<td>Geriatrics</td>
<td>6493</td>
<td>5.5%</td>
<td>30.7%</td>
</tr>
<tr>
<td>Psychiatics</td>
<td>12</td>
<td>0.0%</td>
<td>8.3%</td>
</tr>
<tr>
<td>Other</td>
<td>1405</td>
<td>7.8%</td>
<td>20.4%</td>
</tr>
</tbody>
</table>
Distribution of HCAI infection sites

A total of 3,314 defined HCAIs were identified involving 3,174 patients (1.04 HCAIs per patient). Pneumonia/lower respiratory tract infections (LRTIs) (29.2%) were the most commonly reported HCAI infections, followed by urinary tract infections (UTIs) (17.4%) and systemic infections (12.6%) (Table 7.2). Bloodstream infections (BSIs) accounted for 6.6% of HCAIs [see online Appendix].

Table 7.2 Distribution of HCAI sites

<table>
<thead>
<tr>
<th>Site of HCAI</th>
<th>N (patients)</th>
<th>% HCAI (95% CI)</th>
<th>N (HCAI)</th>
<th>Relative % of all HCAI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>3174</td>
<td>6.6% (6.4 - 6.8)</td>
<td>3314</td>
<td>100.0%</td>
</tr>
<tr>
<td>Bloodstream infections</td>
<td>220</td>
<td>0.5% (0.4 - 0.5)</td>
<td>220</td>
<td>6.6%</td>
</tr>
<tr>
<td>Bone and joint infections</td>
<td>40</td>
<td>0.1% (0.1 - 0.1)</td>
<td>40</td>
<td>1.2%</td>
</tr>
<tr>
<td>Cardio-vascular system infections</td>
<td>29</td>
<td>0.1% (0.0 - 0.1)</td>
<td>29</td>
<td>0.9%</td>
</tr>
<tr>
<td>Catheter-related infections w/o BSI</td>
<td>23</td>
<td>0.0% (0.0 - 0.1)</td>
<td>23</td>
<td>0.7%</td>
</tr>
<tr>
<td>Central nervous system infections</td>
<td>28</td>
<td>0.1% (0.0 - 0.1)</td>
<td>28</td>
<td>0.8%</td>
</tr>
<tr>
<td>Eye, ear, nose or mouth infections</td>
<td>95</td>
<td>0.2% (0.2 - 0.2)</td>
<td>95</td>
<td>2.9%</td>
</tr>
<tr>
<td>Gastrointestinal tract infections</td>
<td>244</td>
<td>0.5% (0.4 - 0.6)</td>
<td>244</td>
<td>7.4%</td>
</tr>
<tr>
<td>Pneumonia/LRTI</td>
<td>969</td>
<td>2.0% (1.9 - 2.1)</td>
<td>969</td>
<td>29.2%</td>
</tr>
<tr>
<td>Reproductive tract infections</td>
<td>13</td>
<td>0.0% (0.0 - 0.0)</td>
<td>13</td>
<td>0.4%</td>
</tr>
<tr>
<td>Skin and soft tissue infections</td>
<td>164</td>
<td>0.3% (0.3 - 0.4)</td>
<td>164</td>
<td>4.9%</td>
</tr>
<tr>
<td>Surgical site infections</td>
<td>496</td>
<td>1.0% (0.9 - 1.1)</td>
<td>496</td>
<td>15.0%</td>
</tr>
<tr>
<td>Systemic infections</td>
<td>417</td>
<td>0.9% (0.8 - 0.9)</td>
<td>417</td>
<td>12.6%</td>
</tr>
<tr>
<td>Urinary tract infections</td>
<td>576</td>
<td>1.2% (1.1 - 1.3)</td>
<td>576</td>
<td>17.4%</td>
</tr>
</tbody>
</table>

Distribution of microorganisms isolated in HCAI

Of the 3,314 reported HCAIs, 37.4% (n=1241) had at least one positive microorganism result, with a total of 1,445 microorganisms being isolated. The ten most commonly isolated microorganisms were *Escherichia coli* (18.9%), *Staphylococcus aureus* (17.6%), *Clostridium difficile* (8.1%), *Pseudomonas aeruginosa* (7.8%), *Klebsiella pneumoniae* (4.9%), *Enterobacter cloacae* (2.8%), *Candida albicans* (2.6%), *Enterococcus faecalis* (2.6%), *Proteus mirabilis* (2.4%) and *Enterococcus faecium*.
(2.2%) [see online Appendix]. *E. coli* was the most commonly isolated microorganism in urinary tract infections (50.9%), whereas *S. aureus* was the most isolated microorganism in pneumonia/LRTIs (19.3%), SSIs (30.2%) and bloodstream infections (19.2%).

**Antimicrobial resistance**

AMR data reported for a subset of pathogens causing HAI s are outlined in Table 7.3. For *S. aureus*, 9.7% were resistant to methicillin/oxacillin, and 3.7% resistant to glycopeptides (teicoplanin or vancomycin). A third of *Enterococcus* spp. were resistant to glycopeptides. Resistance of Enterobacteriaceae to third-generation cephalosporins was 19.7%; this was lower in *E. coli* (13.6%) compared to *Klebsiella* spp. (24.7%). Resistance of Enterobacteriaceae to carbapenems was 2.2%, where isolates of *Klebsiella* spp. had no resistance detected and *E. coli* resistance was 2.0%. Of the 91 tested *Pseudomonas* spp. isolates, 13.2% were resistant to carbapenems.

**Table 7.3 Antimicrobial resistance of HCAI for the most frequently isolated pathogens**

<table>
<thead>
<tr>
<th>HCAI</th>
<th>Total</th>
<th>No. tested</th>
<th>% Resistant</th>
</tr>
</thead>
<tbody>
<tr>
<td><em>S. aureus</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Methicillin/oxacillin</td>
<td>252</td>
<td>237</td>
<td>9.7%</td>
</tr>
<tr>
<td>Glycopeptide</td>
<td>252</td>
<td>164</td>
<td>3.7%</td>
</tr>
<tr>
<td><em>Enterococcus</em> spp.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Glycopeptide</td>
<td>99</td>
<td>80</td>
<td>32.5%</td>
</tr>
<tr>
<td>Enterobacteriaceae</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3(^{rd}) gen. cephalosporins</td>
<td>539</td>
<td>446</td>
<td>19.7%</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>539</td>
<td>410</td>
<td>2.2%</td>
</tr>
<tr>
<td><em>E. coli</em></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3(^{rd}) gen. cephalosporins</td>
<td>270</td>
<td>221</td>
<td>13.6%</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>270</td>
<td>196</td>
<td>2.0%</td>
</tr>
<tr>
<td><em>Klebsiella</em> spp.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3(^{rd}) gen. cephalosporins</td>
<td>93</td>
<td>81</td>
<td>24.7%</td>
</tr>
<tr>
<td>Carbapenems</td>
<td>93</td>
<td>78</td>
<td>0.0%</td>
</tr>
<tr>
<td><em>Pseudomonas</em> spp.</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Carbapenems</td>
<td>111</td>
<td>91</td>
<td>13.2%</td>
</tr>
</tbody>
</table>

**HCAI: origin and device-associated**

Of the 3,314 reported HCAIs, 561 (16.9%) were present at hospital admission, of which 350 (62.4%) were associated with the same hospital, 128 (22.8%) with a different hospital, and 83 (14.8%) had an unknown origin. The majority of HCAIs were acquired during the current hospitalisation (78.0%), with the median number of days until HCAI onset being 12 days.
Of the HCAIs associated with a device, 26.0% of patients with pneumonia (n=863) were intubated within 48 hours before infection onset, 45.0% of patients with a urinary tract infection (n=576) had a urinary catheter within 7 days before onset, and 52.8% of patients with a primary bloodstream infection (n=123) had a vascular catheter within 48 hours before infection onset. Of the total 220 bloodstream infections, 97 were secondary bloodstream infections, with the most common origin being from a urinary tract infection (37.1%) [see online Appendix].

**Antimicrobial use: indications and route of administration**

The PPS captured 17,884 patients receiving a total of 25,741 antimicrobials (65.3% were on 1; 27.8% were on 2 and 6.9% were on 3 or more antimicrobials). Documentation of indication in the clinical notes or on the drug charts occurred for 91% of antimicrobials surveyed. The majority of antimicrobials (81.6%) were used to treat an infection (58.1% were for community infections, 22.3% were for hospital infections and 1.2% were for other long-term healthcare-acquired infections). Prophylaxis accounted for 14.2% of use (surgical 7.9% and medical 6.3%). The indication could not be found for 4.1% of antimicrobials [see online Appendix].

The majority of antimicrobials were administered parenterally (60.1%) with 39.6% orally administered. Antimicrobial treatment was clinically reviewed at day 2-3 for 80% of antimicrobials prescribed for greater than 2 days. However, only 8.9% of these clinical reviews resulted in an intervention (parenteral to oral switch 5.2%; change to another antimicrobial 3.6%; OPAT 0.1%).

The commonest treatment diagnosis for both community onset and hospital onset infections were RTIs, UTI, or SSIs [see online Appendix].

The commonest antibiotics used in hospitals were co-amoxiclav and piperacillin/tazobactam; these two antibiotics accounted for more than one-quarter of all antibiotics used [see online Appendix]. Meropenem was the 8th most common antibiotic used, accounting for 4% of all antibiotics surveyed.

**Discussion**

The data presented here are the initial results of the PPS performed in acute hospitals, both NHS and independent in England in 2016. This is the fifth national PPS on HCAI and the second national PPS on antibiotic use; the previous PPS was in 2011. These results demonstrate that the inpatient population is older and has a higher risk of dying
compared to the previous survey.\textsuperscript{98} Despite this higher risk population, the proportion of inpatients with an HCAI or on antibiotics does not differ from the last survey.

One in fifteen patients in acute hospitals had an HCAI on the day of the survey and the highest prevalence of HCAI was in the ICU (18%). Pneumonia and LRTIs are the commonest cause of HCAI and UTIs the second most frequent, unchanged from 2011. Only one-third of HCAIs had a causative organism identified at the time of the survey; 35% of bloodstream HCAI were caused by one of the Gram-negative bacteria species that are the focus of the current government ambition.\textsuperscript{99} In this survey \textit{S. aureus} BSI were more prevalent than \textit{E. coli} BSI. This is in contrast to the mandatory surveillance data on these infections where hospital onset (infection on day 3 or greater) in \textit{E. coli} cases are approximately double the number of those caused by \textit{S. aureus}. The reasons why these surveillance programmes result in disparate findings needs more investigation, however, the programmes protocols are quite different with, for example, the PPS recording any infection the patient is still being treated for at the time of the survey, thus infections that require longer therapy durations are more likely to be captured than shorter ones, as is often the case with \textit{S. aureus} vs. \textit{E. coli} BSI.\textsuperscript{100}

It is also important to note that increased resistance was detected in all HCAIs compared to the bloodstream infection data, which encompasses community-onset and hospital-onset infections outlined in Chapter 2. In particular the proportion of \textit{Klebsiella} spp. resistant to third-generation cephalosporins was 25% in those with an HCAI, compared to 12% for \textit{K. pneumoniae} BSIs. This finding is consistent with previous studies demonstrating that more resistant bacteria circulate in the hospital healthcare setting, probably related to higher antibiotic exposure and circulating hospital clones of resistant bacteria.\textsuperscript{101}

One in three patients in acute hospitals were on antibiotics on the day of survey, with the highest prevalence of antibiotic use seen in ICUs (52%). The commonest reasons for antibiotic use were RTIs, SSIs and UTIs in patients where infections started in the community and hospitals. One in twelve patients were on prophylactic antibiotics to prevent surgical site infection. NICE guidance states that patients should receive a single dose of antibiotic(s) before surgery starts, with a second dose intra-operatively only if the operation is longer than the half-life of the antibiotic.\textsuperscript{102} In this survey, almost

\textsuperscript{98} http://webarchive.nationalarchives.gov.uk/20140714095446/http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317134304594
\textsuperscript{99} https://improvement.nhs.uk/resources/preventing-gram-negative-bloodstream-infections/
\textsuperscript{102} Surgical site infections: prevention and treatment. Clinical guideline [CG74] https://www.nice.org.uk/guidance/cg74/
half the patients received antibiotics for longer than the recommended single dose, and 31% received more than 1 day of antibiotic treatment. This requires improvement.

This survey confirmed that acute hospitals and PHE should continue to focus on surveillance and interventions to reduce Gram-negative infections, HCAIs in ICU patients and antibiotic use.

Individual hospital results were shared with hospitals in February 2017, along with a slide set for local dissemination and development of quality improvement initiatives. The national collated results were shared with participating hospitals in August 2017, to allow them to benchmark against their peers who participated. These results have also been discussed with the DH, NHS England and PHE staff.

Future Actions

- submit comparisons of 2011 and 2016 results for peer-reviewed publication, with the consent of participating hospitals
- continue to encourage hospitals to participate in the Infections in Critical Care Quality Improvement Programme (ICCQIP)
- support hospitals to reduce HCAIs, particularly related to the ambition to half healthcare-associated GNBSI programme, led by NHS Improvement
- support the work of the CQUIN to reduce antibiotic use in hospitals, particularly using the data from the PPS to determine measures of inappropriate prescribing
- submit a representative dataset to the European Centre for Disease Prevention and Control to draw comparisons and assess the burden of HCAI and antimicrobial use in acute hospitals across Europe
- work with the DH expert advisory group on Antimicrobial Prescribing, Resistance and Healthcare-associated infections (APRHAI) to consider interventions that may reduce healthcare-associated RTIs
- collaborate with the British Society of Antimicrobial therapy to explore options to facilitate on-going use of the web-based data entry programme to allow hospitals to repeat local PPS at regular intervals and measure quality improvement actions
- present results of the survey to the medical, surgical and nursing Royal Colleges and professional organisations, particularly their specialty-specific prevalence of HCAI and antibiotic use to encourage specialty-specific ownership of infection prevention and control and antimicrobial stewardship actions
8. 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 Strategy (Professional education and training and public engagement) and includes:

- summary of key activities from World Antibiotic Awareness Week (WAAW) and European Antibiotic Awareness Day (EAAD) November 2016
- evaluation of the Antibiotic Guardian (AG) Campaign including expansion beyond the UK, assessment of knowledge of AGs versus published Eurobarometer results and impact of the campaign on attitudes and knowledge
- delivery of antimicrobial resistance (AMR) and stewardship workshops and training events for healthcare professionals
- e-Bug activities, which focus on bacteria, AMR and hygiene education of children and teenagers

World Antibiotic Awareness Week and EAAD 2016: Engaging children, families, healthcare students and community pharmacies

The key goals for the 2016/17 campaign were to increase engagement from three groups:

- community pharmacy: by increasing the number of pharmacy premises who registered planned antibiotic awareness activities during WAAW
- healthcare students: by engaging with universities who offer healthcare courses to run an AMR campaign and nominate local AG champions
- children and families/carers: by developing tailored materials to increase engagement from children and their families/carers via completion of activities, allowing them to earn virtual AG badges

In advance of WAAW and EAAD 2016, PHE invited organisations to register their planned antibiotic awareness activities in order to improve coordination of activities and understand engagement across England. Letters signed by the Chief Executives of Public Health England (PHE) and Health Education England (HEE) and England’s Chief Professional Officers were sent to NHS organisations, local authorities, universities and professional bodies/organisations. The following activities led by PHE in collaboration with a range of organisations occurred: junior and family AG digital badges developed and rolled out in collaboration with the PHE Nursing directorate and e-Bug team in the PHE Primary Care Unit; promotion of new materials including a one-health poster in
collaboration with British Veterinary Association (BVA) and Department for Environment, Food and Rural Affairs (DEFRA) and a new pharmacy poster in co-operation with community pharmacy organisations; and university student badges with healthcare students.

In total, 367 organisations registered planned activities: 30 Universities, 237 Community pharmacy premises and 100 hospitals and primary care organisations.

One hundred and eight individuals began completing activities to earn junior or family AG badges. From February 2017, West Lancashire Scouts, as part of the Scouts Community Impact Programme, worked with PHE to increase awareness of AMR and develop a Scouts AG activity badge, including a sew-on version. The scheme was available to all 13,500 Scouts across West Lancashire and was supported by PHE North West and Lancashire County Council. Other scouting groups that would like to join the scheme or use locally should contact antibiotic.resistance@westlancsscouts.org.uk or visit the website for further details.¹⁰³

Junior and family AG badges were earned after completing educational tasks eg completing educational games¹⁰⁴, or designing a poster after completing learning sessions on the e-Bug website (Figure 8.1 and Figure 8.2). The junior digital AG badges were awarded to children by their school teachers. These continue to be available on Makewaves website.¹⁰⁵

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¹⁰³ https://www.westlancsscouts.org.uk/antibiotic-guardians/
¹⁰⁴ www.e-bug.eu
¹⁰⁵ https://www.makewav.es/badge/4163
Registration for AG activities occurred from 30 Universities. Thirty-three health student societies nominated 100 AG representatives. In collaboration with PHE the healthcare students developed a digital badge for their LinkedIn accounts, which could be earned by completing tasks (Figure 8.3).

**Antibiotic Guardian Champion**

As part of the UK’s activities for World Antibiotic Awareness Week (14-20 November 2016) and European Antibiotic Awareness Day (18 November) healthcare students and pre-registration professionals are invited to become Antibiotic Guardian Champions. Earn your badge by completing the following tasks and sharing your evidence.

Issuer: Know Your Health

Figure 8.3: Healthcare students learning campaign. The digital badges once earned can be linked to students’ LinkedIn accounts.
Google analytics revealed that there were 18,404 page views of the antibiotic awareness resources .gov page between 1 September 2016 and 31 March 2017 with peaks on 11 and 14 November 2016 coinciding with WAAW (Figure 8.4).106

Social media analysis highlighted that during WAAW, there were almost 9,500 tweets by 3,500 participants leading to a social reach of more than 31 million. The Symplur data (analysis of tweets) for the week including the top 10 by mentions, tweets and impressions are outlined in Figure 8.5.

![Internet traffic for antibiotic awareness resources, Sep 2016-Apr-2017](image_url)

**Figure 8.4: Internet traffic for antibiotic awareness resources, Sep 2016-Apr-2017**

**Figure 8.5: Symplur statistics on the hashtag #AntibioticGuardian from 13-19, November 2016.**

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106 [https://www.gov.uk/government/collections/european-antibiotic-awareness-day-resources](https://www.gov.uk/government/collections/european-antibiotic-awareness-day-resources)
In addition, the Centre for Pharmacy Postgraduate Education (CPPE) hosted a web-based learning campaign in collaboration with PHE and other national pharmacy organisations encouraging pharmacy professionals in England to update knowledge about the issues of AMR and HCAI. Four hundred and thirty seven pharmacy professionals engaged with the CPPE learning campaign; 82 completed all four challenges and received their Pharmacy champion badge and 266 individual accounts participated in the Pharmacy Twitter chat. Those who completed all of the campaign challenges (82 pharmacy professionals) were awarded a digital AG Pharmacy Champion 2016 badge (Figure 8.6).

![Antibiotic Guardian Pharmacy Champion badge](image)

Figure 8.6: Antibiotic Guardian Pharmacy Champion badge

Evaluation of Antibiotic Guardian Campaign after three seasons: expansion beyond UK and assessment of knowledge of Antibiotic Guardians versus published Eurobarometer results and impact of the campaign

In 2014, PHE developed the AG behaviour change and engagement campaign in the UK to tackle AMR. This included an online pledge system aimed at healthcare professionals and the public. Process\textsuperscript{107} and outcome\textsuperscript{108} evaluations for the AG campaign published in 2016 showed the wide reach of the campaign and its success in increasing commitment to tackling AMR in both healthcare professionals and members of the public, through self-reported increased knowledge and changed behaviour.

Due to the campaign success, WHO-Europe and Belgian Antibiotic Policy Coordination Committee (BAPCOC) requested to collaborate with PHE to expand the current UK AG campaign to wider European dimension during 2016. This included expanding the AG website with translation into the Russian, Dutch and French languages. Promotion of the AG campaign formed the main focus for WAAW (14 - 20 November 2016) organised by WHO-Europe in Europe.

\textsuperscript{107} Bhattacharya A, Hopkins S, Sallis A, Budd EL, Ashiru-Oredope D. J Public Health (Oxf) 2016; 39: e40–e4

The expansion of AG provided a good opportunity to re-evaluate the campaign to ensure it remained effective at tackling AMR in the UK and Europe and to highlight areas for improvement.

The evaluation studies included:

- demographic and knowledge analysis of 42,457 AGs
- process evaluation of the expansion of the AG campaign across Europe including assessment of AMR knowledge
- impact evaluation of the AG campaign in UK and Europe

In this report we present the interim results and recommendations.

The following analysis occurred:

- A descriptive analysis of:
  - AG pledges made (English language website) between 24 July 2014 and 31 December 2016 provided an update on the campaign after three seasons
  - AG pledges made via the Russian, Dutch and French pages between 1 November 2016 and 31 December 2016 to determine the impact of the translated pages
- The number and proportion of AGs were calculated by year, pledge group, country and how the AG heard of the campaign. The dates of the three years for comparison are year 1: 24/07/2014–31/12/2014, year 2: 01/01/2015–31/12/2015 and year 3: 01/01/2016–31/12/2016

For England, the number and rate of pledges per 100,000 population was also calculated by NHS geographical area (CCGs) and by local authority (the organisation responsible for public health, services and facilities in a particular area) [see online Appendix]. Internet protocol (IP) addresses of AGs were used to identify instances where multiple individuals pledged from a single location.

Data were analysed using Google analytics for number of website visits, acquisition route and conversion rate. Conversion rates were calculated as the proportion of visitors to the website that pledged to become an AG and an adjusted conversion rate was calculated as the proportion of AG pledges from unique website visits. The definitions of these terms are outlined in the social media glossary which can be found in Annex – Chapter 8.

During WAAW 2016, the responses to five questions on AMR knowledge were collected after individuals pledged via a pop-up box survey. The proportion of questions
answered correctly was calculated by pledge group and compared with the published 2016 Eurobarometer survey on antimicrobial resistance.

From August 2014 until December 2016, there were 179,239 unique website visitors with 42,457 English and 367 foreign language pledges (adjusted conversation rate of 23.7%) (Table 8.1). During WAAW 2016, the AG website was visited 14,647 times and 5,120 pledges were received from 59 countries; of those pledges 94.4% originated from the UK with 89.4% from England.

Table 8.1: AG website metrics including conversion rates from 2014 – 2016

<table>
<thead>
<tr>
<th>AG metrics</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>All</th>
</tr>
</thead>
<tbody>
<tr>
<td>Website visits</td>
<td>56,569</td>
<td>67,824</td>
<td>96,833</td>
<td>221,226</td>
</tr>
<tr>
<td>New website users</td>
<td>46,015</td>
<td>54,689</td>
<td>79,620</td>
<td>179,105</td>
</tr>
<tr>
<td>Pledges (all languages)</td>
<td>12,315</td>
<td>15,002</td>
<td>15,507</td>
<td>42,824</td>
</tr>
<tr>
<td>Conversion rate - unadjusted (%)</td>
<td>21.8</td>
<td>22.1</td>
<td>16.0</td>
<td>19.4</td>
</tr>
<tr>
<td>Conversion rate - adjusted (%)</td>
<td>26.8</td>
<td>27.4</td>
<td>19.5</td>
<td>23.9</td>
</tr>
</tbody>
</table>

The number of visitors to the AG site increased each year with peaks during WAAW. The educational YouTube video entitled ‘Will you be an Antibiotic Guardian?’ accessible via the AG website and PHE YouTube channel was viewed 35,827 times with an average view time of 1.33 minutes out of an available 2.02 minutes. The ‘Antibiotic Resistance Playbuzz’ quiz launched on the website in November 2016 was accessed 3,900 times with 628 completions.

At least one AG was present in two thirds of the world’s countries. Country of pledge was added as a new completion field in 2015. In 2015 and 2016, 27,863 pledges were documented from 129 different countries, 96.0% (n=26,758) from the UK, 1.5% (n=427) from the rest of Europe and 2.4% (n=678) from the rest of the world. There was a 95% increase in the number of countries with AGs from 63 countries in 2015 to 123 in 2016.

From 2014 to 2016, the overall rate of AGs in the UK was 62.3 per 100,000 population (95% CI 61.7 – 62.9). There was some variation by country with Wales having the highest rate at 136.3 per 100,000 population (95% CI 132.2 – 140.4), followed by England 61.2 (95% CI 60.5 – 61.8), Scotland 43.7 (95% CI 42.0 – 45.5) and Northern Ireland 23.8 (95% CI 21.6 – 26.1) per 100,000 of the population. Further breakdown by clinical commissioning groups (CCGs) for each year is available from PHE Fingertips AMR local indicators. The total count of AGs and rate per 100,000 population for each CCG and local authorities from 2014 to 2016 is presented in the online Appendix. Local government rates for 2014-2016 ranged from a rate of 3.2 in West Lindsey (95% CI 0.7 – 9.4) to 345.1 in Bath and North East Somerset (95% CI 318.8 – 372.9) per 100,000.
population. Only 6% (n=2,579) of all pledges were re-pledges, suggesting constant new engagement.

For AGs pledging on the UK site, self-direction was the largest acquisition route (49%) with pledges more likely via this route than social media (OR 2.4, 95% CI 2.3-2.5). Fifty-three percent of AGs were healthcare professionals (HCPs). Public and student groups increased their number and proportion of total AGs year on year (Table 8.2). Colleagues were the most common source for hearing about AG (23.0%, n=7359). The public were more likely to hear via social media compared to HCP (OR 3.18, 95% CI 3.0-3.4). AGs pledging on the UK site (including the public) were more likely to answer questions correctly than the Eurobarometer UK group (OR=8.5, 95% CI 7.4–9.9).

Table 8.2: Number and percentage of AG pledges by pledge group from 2014-2016

<table>
<thead>
<tr>
<th>Antibiotic Guardian Group</th>
<th>2014</th>
<th>2015</th>
<th>2016</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>n</td>
<td>%</td>
<td>n</td>
<td>%</td>
</tr>
<tr>
<td>HCP</td>
<td>7803</td>
<td>63.4</td>
<td>7969</td>
<td>53.2</td>
</tr>
<tr>
<td>Public</td>
<td>3429</td>
<td>27.9</td>
<td>4482</td>
<td>29.9</td>
</tr>
<tr>
<td>Students/Educators</td>
<td>1075</td>
<td>8.7</td>
<td>2535</td>
<td>16.9</td>
</tr>
<tr>
<td>Total</td>
<td>12307</td>
<td>100</td>
<td>14986</td>
<td>100</td>
</tr>
</tbody>
</table>

Within HCP AGs, pharmacy team members (33.3%) were the most numerous group, followed by nurses (19.6%) and primary/secondary prescribers (17.6%). Nurses and dentists increased their number who became AGs each year; from 7.5% (n=922) in 2014 to 11.9% (n=1796) in 2016 and 1.8% (n=216) to 2.5% (n=375), respectively. There was a significant increase in the proportion of AG that were students or educators from 8.7% in 2014 to 22.4% in 2016 (p<0.001), reflecting the increased engagement from universities. The highest proportion of students pledging were pharmacy students (45%, n=2991).

Transcribed AG pages became available in November 2016. In the first two months there were 492 unique visitors to the Russian site, 1124 to the Dutch site and 152 to the French site which resulted in adjusted conversion rates of 10.2%, 27.3% and 6.7%, respectively. Unique visitors to the Russian page were mainly from Kazakhstan (32.5%), Russia (12.8%) and the UK (10.2%). In total, Russian speaking countries consisted of 68.9% of unique visitors to the Russian page. For the Dutch and French webpages, the majority of unique visitors were from Belgium, 91.6% and 86.2%, respectively. Within two months of the foreign language AG sites launching, 367 non-English pledges were received: 50 Russian, 307 Dutch and 10 French. The majority of these AGs were from the public (44.7%, n=164) and HCP (44.1%, n=162) compared to students/educators (11.2%, n=41). The Dutch pages received the highest proportion of pledges from the public (46.2%, n=144) whereas the HCP group was the highest pledge group for the French (70%, n=7) and Russian pages (50%, n=25).
Out of 17,965 questions answered in the knowledge survey, 94.2% were answered correctly (n=16,918). The proportion of questions answered correctly was lowest for the Russian pages (78.5%, n=208) compared to the Dutch pages (93.9%, n=1179) and English pages (94.4%, 15,531). The HCP group had the greatest AMR knowledge.

Further insight into the effect of the campaign on behaviour or antibiotic prescribing will be provided by the impact evaluation, which is underway.

The AG campaign continues to have more engagement from healthcare professionals and those with a preceding knowledge and interest in AMR.

Limitations of this process evaluation include lack of knowledge related to the promotional efforts of the campaigns within the different countries and the impact of these activities. No information is available on individuals who viewed the website but did not choose to pledge and gave no reasoning for their decision.

**Antibiotic Guardian Awards**

The AG awards, now in their second year, provide an important opportunity to champion organisations and individuals who support the AG campaign and demonstrate achievement in their work to tackle AMR.

For the 2017 awards, there were 50 entries; 39 were shortlisted across 7 categories following peer-review. The awards ceremony was held on 8 June 2017 at Imperial College London. Further details including shortlisted and winning organisations are available on the AG website.109

**Healthcare students and Antibiotic Awareness Week: a pilot cross-sectional survey in the UK**

Students in all healthcare professions have important roles to play in keeping antibiotics effective. As part of the UK AG 2016 campaign aim to increase awareness of AMR among healthcare students, an online questionnaire was developed to assess knowledge and awareness.

Local survey coordinators at six universities emailed students invitations to an online questionnaire consisting of 25 questions. The questionnaire was also advertised on the AG website and through AG representatives at a further 21 universities. The survey was accessible between 10 October and 17 November 2016. Descriptive statistics were calculated, and comparisons made using t-tests.

Two hundred and fifty-five students from 27 universities were included; the vast majority attended five universities. The course types represented were pharmacy (156), veterinary medicine (71), medicine (12), dentistry (11), physician associate (3), and nursing (2). More than half (57%, 145/255) were in their third year of study or above. Most students planned to work either in primary care (25%, 64/255) or secondary care (43%, 112/255). In the previous 12 months, a third of students had taken antibiotics (34%, 86/252).

Students considered AMR to be a more important global challenge (9.0 on a scale of 1-10; all comparisons p<0.001), than climate change (8.4), obesity (8.0), food security (7.7) and gender inequality (7.3). Almost all students thought AMR was a current national issue (93%, 163/175) that will have a greater impact on healthcare in the future (96%, 167/174). However, fewer students (70%, 122/175) thought that the antibiotics they would prescribe, administer or dispense will contribute to the problem of resistance. Most students (94%, 165/175) thought that it was professionally unethical to prescribe, dispense or administer antibiotics inappropriately or unnecessarily. Almost half of all students had heard of antibiotic or antimicrobial stewardship (48%, 94/196).

Most students wanted more information on how to use antibiotics (75%, 191/255) and 39% wanted more information on AMR (99/255). Forty-two percent (15/36) of students towards the end of their courses (year 4 and above) felt they had sufficient knowledge on antibiotic use for their future practices. All students were aware that bacteria can become resistant to antibiotics (100%, 199/199), but many students also thought that humans and animals could become resistant to antibiotics (40%, 80/199) and (44%, 87/198), respectively.

UK healthcare students were aware of antibiotic resistance, and believed it was an extremely important global challenge. Misunderstandings concerning antibiotic resistance were found, and most students expressed a desire to be better informed.

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

TARGET webinars

During November and December 2016, seven themed webinars developed in collaboration with BSAC were broadcast live weekly. The webinars were subsequently made available as a static resource available online.110

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110 http://www.target-webinars.com/
The seven webinars were:

Webinar 1: Case studies
Webinar 2: Assessing need
Webinar 3: Patient expectations
Webinar 4: Back-up prescribing
Webinar 5: Prescribing in UTI
Webinar 6: Children
Webinar 7: Whole practice

We report how users have interacted with the TARGET webinars / training modules since the webinars were moved to the new platform in January 2017. Data is presented using Google analytics from January to May 2017. It must be noted however that the report only outlines how users have interacted with each of the webinars and other coded pages. Specific page content, eg word documents within each of the pages, were not tagged for tracking. Therefore, whilst we can see how long users may have spent on a particular webinar page, there is no information on any items outside the main text or video that may have been viewed.

Table 8.3: Interaction with the TARGET webinars / training modules

<table>
<thead>
<tr>
<th>Webinar Number</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
</tr>
</thead>
<tbody>
<tr>
<td>Registered for live webinars</td>
<td>772</td>
<td>1170</td>
<td>246</td>
<td>1042</td>
<td>1221</td>
<td>1210</td>
<td>1199</td>
</tr>
<tr>
<td>Watched live webinar</td>
<td>286</td>
<td>205</td>
<td>179</td>
<td>90</td>
<td>120</td>
<td>113</td>
<td>77</td>
</tr>
<tr>
<td>Watched webinar later (until end Dec)</td>
<td>unknown</td>
<td>173</td>
<td>13</td>
<td>17</td>
<td>32</td>
<td>30</td>
<td>26</td>
</tr>
<tr>
<td>Watched webinar later (1/1/2017-31/5/2017)</td>
<td>1,530</td>
<td>1,166</td>
<td>614</td>
<td>671</td>
<td>967</td>
<td>578</td>
<td>549</td>
</tr>
</tbody>
</table>

During this time the webinar website registered 3061 users; 55% of these were new users, 45% returning users. On average these users spent 2min 35secs per session and viewed 2.26 pages accumulating in 11,424 page views from 5,501 individual sessions. Details on specific webinar views in real-time or recorded are outlined in Table 8.3.

The majority of users, 66.5%, accessed the site from Europe, 25.4% from the Americas, 4.3% from Oceania, 3.2% from Asia and 0.53% from Africa. The top 10 countries that accessed the site most frequently are outlined in Table 8.4.
Table 8.4. Most frequent country access to TARGET webinars

<table>
<thead>
<tr>
<th>Country</th>
<th>Sessions</th>
<th>% New Sessions</th>
<th>New Users</th>
</tr>
</thead>
<tbody>
<tr>
<td>United Kingdom</td>
<td>4,230(63.79%)</td>
<td>46.48%</td>
<td>1,966(50.17%)</td>
</tr>
<tr>
<td>United States</td>
<td>1,566(23.62%)</td>
<td>95.21%</td>
<td>1,491(38.05%)</td>
</tr>
<tr>
<td>New Zealand</td>
<td>267(4.03%)</td>
<td>31.09%</td>
<td>83(2.12%)</td>
</tr>
<tr>
<td>Brazil</td>
<td>54(0.81%)</td>
<td>98.15%</td>
<td>53(1.35%)</td>
</tr>
<tr>
<td>Canada</td>
<td>48(0.72%)</td>
<td>89.58%</td>
<td>43(1.10%)</td>
</tr>
<tr>
<td>Singapore</td>
<td>43(0.65%)</td>
<td>11.63%</td>
<td>5(0.13%)</td>
</tr>
<tr>
<td>Jersey</td>
<td>40(0.60%)</td>
<td>7.50%</td>
<td>3(0.08%)</td>
</tr>
<tr>
<td>India</td>
<td>29(0.44%)</td>
<td>72.41%</td>
<td>21(0.54%)</td>
</tr>
<tr>
<td>Qatar</td>
<td>27(0.41%)</td>
<td>14.81%</td>
<td>4(0.10%)</td>
</tr>
<tr>
<td>Australia</td>
<td>19(0.29%)</td>
<td>1</td>
<td>16(0.41%)</td>
</tr>
</tbody>
</table>

Within the UK, most users originated from England (81.85%), followed by Scotland (11.64%), Wales (4.87%) and N. Ireland (1.61%).

The majority of users (42%) accessed the website directly by using the webinar url suggesting prior knowledge of the resource. Thirty-four percent of users found the website as a result of Google’s organic search using a variation of “target webinar”, “back-up prescription protocol” and “how do GPs use back up prescriptions for antibiotics”. Referrals from other websites generated a further 23% of visits. One percent of visits were generated by social media while only 0.1% or 6 visits to the website were referred via email. Webinar 1: Introductory Case Studies was the most viewed webinar since January 2017 with Webinar 7: Common Practice Approach the least viewed (Figure 8.7).
Between 43-49% of users who visited each webinar webpage actually watched the videos spending between approximately 15-25min per viewing the webinars (Table 8.5).

Table 8.5: TARGET webinar webpage and video users

<table>
<thead>
<tr>
<th>Webinar 1: Case studies</th>
<th>Watched video</th>
<th>Webpage visits</th>
<th>Video length</th>
<th>Average view duration</th>
<th>Duration of recording</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>579</td>
<td>1530</td>
<td>00:47:04</td>
<td>00:15:55</td>
<td>00:21:04</td>
</tr>
<tr>
<td>Webinar 2: Assessing need</td>
<td>430</td>
<td>1166</td>
<td>00:49:07</td>
<td>00:19:34</td>
<td>00:20:15</td>
</tr>
<tr>
<td>Webinar 3: Patient expectations</td>
<td>258</td>
<td>614</td>
<td>00:45:35</td>
<td>00:22:08</td>
<td>00:16:07</td>
</tr>
<tr>
<td>Webinar 4: Back-up prescribing</td>
<td>270</td>
<td>674</td>
<td>00:46:09</td>
<td>00:22:14</td>
<td>00:24:03</td>
</tr>
<tr>
<td>Webinar 5: Prescribing in UTI</td>
<td>400</td>
<td>967</td>
<td>00:58:43</td>
<td>00:25:22</td>
<td>00:17:20</td>
</tr>
<tr>
<td>Webinar 6: Children</td>
<td>241</td>
<td>578</td>
<td>00:47:56</td>
<td>00:24:42</td>
<td>00:18:29</td>
</tr>
<tr>
<td>Webinar 7: Whole practice</td>
<td>187</td>
<td>459</td>
<td>00:45:50</td>
<td>00:24:18</td>
<td>00:10:43</td>
</tr>
</tbody>
</table>

TARGET Webinar Participant Reviews – Summary Findings

Webinar viewers had the option of completing a review questionnaire; each of the webinars participants were asked the following questions:

- how informative was the video for this webinar?
- please rate on a scale 1-5 where 1=very informative and 5=very uninformative
- how likely are you to recommend this webinar, or the series, to colleagues?
- please rate on a scale 1-5 where 1=very likely and 5=very unlikely
- was the time of the webinar suitable for you? If not, what time would you prefer?

On average, 93% of participants rated the webinar videos as either quite or very informative (Figure 8.8). Participants found Webinar 4: Back-up prescriptions the most informative, with a 99% positive rating.
Figure 8.8. Participant responses to the question “How informative did you find the webinars?” (n=100%)

Taking the average rating of the webinars combined data, 88% of participants stated that they would be fairly or very likely to recommend the webinars to a colleague. Webinar 4: Back-up prescriptions was the webinar most likely to be recommended with 96% of respondents giving this a positive review (Figure 8.9).

Figure 8.9 Participant responses to the question “How likely are you to recommend the webinars to your colleagues?” (n=100%)
Participants were asked to rate whether the timing of the webinar was suitable with more than half of all participants stating they found the timing acceptable (Figure 8.10).

![Figure 8.10 Participant responses to the question “Was the timing of the webinars suitable for you? (n=100%)”](image)

For those who said no, the majority (41%) stated that they would prefer to review webinar later in their own time. Thirty-seven percent would rather the webinar was shown in the evening (Figure 8.11). Twelve percent of respondents felt that the webinar was too long and that duration should be 15-30mins.

![Figure 8.11. Participants response to preferred timing of the webinar (n=186).](image)
Participants who completed a review questionnaire for any webinar were also asked if they had any suggestions as to how the content or format of the webinar might be improved. Participants across all 7 webinars responded with the suggestions being grouped into 9 different headings (Table 8.6).

Table 8.6. Grouping of participant suggestions as to how the webinars could be improved

<table>
<thead>
<tr>
<th>Suggestion grouping</th>
<th>No. respondents</th>
</tr>
</thead>
<tbody>
<tr>
<td>Good/excellent/no suggestions</td>
<td>102</td>
</tr>
<tr>
<td>More interaction / slides / summary points / guidance</td>
<td>23</td>
</tr>
<tr>
<td>Technical difficulties an issue</td>
<td>18</td>
</tr>
<tr>
<td>Webinars should be shorter</td>
<td>12</td>
</tr>
<tr>
<td>Other suggestions</td>
<td>11</td>
</tr>
<tr>
<td>Liked being able to view the webinar in their own time</td>
<td>2</td>
</tr>
<tr>
<td>Alternative panel member choice</td>
<td>2</td>
</tr>
<tr>
<td>Prefer webinars to be run at evenings/weekends</td>
<td>2</td>
</tr>
<tr>
<td>Alternative suggestion (examine the use of telephone advice services such as NHS Direct or NHS24)</td>
<td>1</td>
</tr>
</tbody>
</table>

The majority of respondents felt that the webinars were suitable as is or had no suggestions. Technical difficulties from poor sound or camera work were initially raised as an issue, however much of this was rectified early in the series. Some of the technical difficulty comments related to users’ connections and not the webinars themselves. Participants reiterated the importance of convenience in the timing and length of webinars, suggesting that they be shorter or run at the weekends when they had more time to participate.

The most frequent suggestions group related to the interactivity of the webinars: participants wanted more interactivity in the form of summary bullets on screen; preferred slides rather than just Q&A; and desired detailed guidance as to how to carry out some of the advice given.

Quite a few of the suggestions could not be easily grouped and have been put into their own group entitled “other” and outlined below:

- “A more generic approach including health professionals from medicine, nursing and allied health and secondary care”
- “Greater emphasis on OOH consultations”
- “Maybe this is a long shot but I often recommend web based materials to patients to look at. Nowadays they all have a smart phone, at least. Is there a place for a link rather than a leaflet (many of which will gather dust)?”
“More specific guidance on safety netting”
“More on 'complicated' UTIs, eg treatment in men, pregnant women or pyelonephritis - but perhaps this will be covered in a later webinar”
“Some discussion on prescribing for men and more about prescribing in pregnancy”
“Some dental specific webinars for prescribing antibiotics for adults and children. They were very informative and interesting, but obviously of limited benefit for myself and my direct colleagues”
“More information about antibiotic use for UTI in children, earaches, and sore throats”
“Not specifically for the webinar, but free access to the leaflets could be helpful too - printing from internet never looks the same with a black and white copy”

Other AMS webinars

Two webinars were delivered in March 2017 and are still available to view on the AG site
- infection and AMR: CQUIN and QP update webinar\textsuperscript{111}
- tackling AMR: Role of Community Pharmacy Teams\textsuperscript{112}

e-Bug activities

e-Bug is an educational resource for children and young people which educates on hygiene, the spread of infection and antibiotics. e-Bug has teacher resources for use in the classroom, to educate students aged 4-18 years on a range of infection topics, including antibiotics and antibiotic resistance. Student resources for use at home are also provided.

The global reach to the e-Bug website and e-Bug antibiotic resources over the last two years, as determined by the visits per continent were analysed and a summary of these are presented in Figure 8.12. The majority of visits to the website are from Europe, with the UK, France and Spain the top three countries with the most visits in the 2016/17 academic year. Data on number of pages per session, average visit duration and the most viewed pages from the top country visits are outlined in Table 8.7. The breakdown of the page views, by page are presented in Table 8.8, along with goals for page views in 2017. Popular web pages were the student games, which were updated and relaunched in 2016, and the antibiotic animation, which is available via You-Tube. Beat the Bugs, a six-week hygiene, infection and self-care course for community groups, was launched in 2016.

\textsuperscript{111} \url{http://antibioticguardian.com/ams-cquin-qp/} (password – CQUINQP)
\textsuperscript{112} \url{http://antibioticguardian.com/community-pharmacy-webinar/} (password – CommunityPharmacy)
126 036 worldwide visits to the e-Bug website in the last academic year (1 September 2016 to 31 August 2017)

Figure 8.12. Visits to the e-Bug website between 1st September 2016 and 31st August 2017.

Table 8.7. e-Bug website visits from different countries

<table>
<thead>
<tr>
<th>Country with most visits</th>
<th>Visits</th>
<th>Pages/session</th>
<th>Avg visit duration (mins)</th>
<th>Most viewed page</th>
</tr>
</thead>
<tbody>
<tr>
<td>UK</td>
<td>32 532</td>
<td>9.09</td>
<td>05:52</td>
<td>England junior student games page</td>
</tr>
<tr>
<td>France</td>
<td>13 003</td>
<td>6.38</td>
<td>04:29</td>
<td>French teacher homepage</td>
</tr>
<tr>
<td>Spain</td>
<td>9925</td>
<td>2.96</td>
<td>02:07</td>
<td>Spanish junior quiz game</td>
</tr>
<tr>
<td>United States</td>
<td>7992</td>
<td>6.43</td>
<td>05:05</td>
<td>England junior student games page</td>
</tr>
<tr>
<td>Denmark</td>
<td>4705</td>
<td>7.74</td>
<td>05:02</td>
<td>Danish junior student games page</td>
</tr>
</tbody>
</table>
Table 8.8. Page views to the e-Bug website and e-Bug antibiotic resources

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>1 Sep 2015 - 31 Dec 2015</td>
<td>1 Sep 2016 - 31 Dec 2016</td>
<td>1 Sep 2017 - 31 Dec 2017</td>
</tr>
<tr>
<td>e-Bug website (all pages)</td>
<td>297,059</td>
<td>331,436</td>
<td>350,000</td>
</tr>
<tr>
<td></td>
<td>85,647</td>
<td>100,721</td>
<td></td>
</tr>
<tr>
<td></td>
<td>31 Dec 2015</td>
<td>31 Dec 2016</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e-Bug student games (all pages with 'games' in url)</td>
<td>70,146</td>
<td>79,409</td>
<td>90,000</td>
</tr>
<tr>
<td></td>
<td>17,853</td>
<td>24,509</td>
<td></td>
</tr>
<tr>
<td></td>
<td>31 Dec 2015</td>
<td>31 Dec 2016</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>e-Bug antibiotic animation (youtube video views)</td>
<td>30,526</td>
<td>46,282</td>
<td>60,000</td>
</tr>
<tr>
<td></td>
<td>8,290</td>
<td>12,743</td>
<td></td>
</tr>
<tr>
<td></td>
<td>31 Dec 2015</td>
<td>31 Dec 2016</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Beat the Bugs homepage (webpage)</td>
<td>n/a</td>
<td>1,066</td>
<td>1,500</td>
</tr>
<tr>
<td></td>
<td></td>
<td>493</td>
<td></td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antibiotic peer education lesson (webpage)</td>
<td>191</td>
<td>267</td>
<td>350</td>
</tr>
<tr>
<td></td>
<td>64</td>
<td>101</td>
<td></td>
</tr>
</tbody>
</table>
At-Bristol Science Centre evaluation

Last year, e-Bug worked alongside the At-Bristol Science Centre to develop activities for students and families to run in the Science Centre Live Lab area. The activities aimed to increase knowledge on antibiotics, antibiotic resistance and treating common infections. The activities included resources from the e-Bug teaching packs, and information on AG.

Over six weeks in 2016, children who visited the At-Bristol Science Centre with their school or families took part in an antibiotic activity. The ability of the activities to improve knowledge on antibiotics was evaluated through knowledge change questionnaires. Before, and immediately, after the activity, participants completed a short true/false questionnaire (Table 8.9). The antibiotic activity was delivered to small groups of participants by Science Centre staff. The questionnaires were analysed using mixed effects logistic regression to look for knowledge change.

The activity was divided into three stations:

- **Research in the lab:** Students study agar plates and learn about different types of microbes, antibiotics and antibiotic resistance
- **The GP visit:** Students listen to GP patient consultations for infections in which patients are and are not prescribed antibiotics
- **Looking after yourself:** Students learn how to stop the spread of infection through hand washing and the use of tissues

Six primary schools and children who attended with family or home educators participated. Sixty-nine before questionnaires and 54 after questionnaires were completed by participants aged between 7 and 14 years. Baseline knowledge of antibiotics was low with less than 50% of participants answering 5 of the 8 questions correctly prior to the start of the activity. The greatest knowledge improvement came in the question “The more we take antibiotics, the more antibiotic resistant bacteria develop”. This had the lowest knowledge prior to the activity. Topics with lower knowledge improvement included not taking antibiotics for coughs and colds. Participants were asked if they had heard of the AG campaign – five responded ‘yes’ in the before questionnaire which increased to 10 in the after questionnaire. Statistically significant improvement in knowledge occurred for questions 1, 3, 4, 7 and 8 (Table 8.9).
Table 8.9. The knowledge questionnaire, correct answers and resulting p values

<table>
<thead>
<tr>
<th>Question</th>
<th>Correct Answer</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>1  All bacteria are bad</td>
<td>FALSE</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>2  If you have a cold you should take antibiotics</td>
<td>FALSE</td>
<td>0.18</td>
</tr>
<tr>
<td>3  Bacteria are becoming resistant to antibiotics</td>
<td>TRUE</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>4  The more we take antibiotics, the more antibiotic resistant bacteria develop</td>
<td>TRUE</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>5  Most coughs and colds get better without antibiotics</td>
<td>TRUE</td>
<td>0.98</td>
</tr>
<tr>
<td>6  You should keep leftover antibiotics to treat infections in the future</td>
<td>FALSE</td>
<td>0.3</td>
</tr>
<tr>
<td>7  Catching a sneeze with a tissue will stop the spread of microbes</td>
<td>TRUE</td>
<td>0.005</td>
</tr>
<tr>
<td>8  We all have a role in helping to tackle antibiotic resistance</td>
<td>TRUE</td>
<td>0.003</td>
</tr>
</tbody>
</table>

This study highlights the ability of the e-Bug activities to significantly improve knowledge on bacteria, antibiotic resistance and the spread of infection in the science centre setting. The results suggest e-Bug should be used outside of schools to educate a wider audience, including families, on antibiotics.

**e-Bug Train the Trainer sessions**

Over the 2016-17 academic year, e-Bug has piloted a free train the trainer workshop for educators and community groups leaders. The training covers all aspects of e-Bug, including the development of the materials, how to access and use the materials, and how to adapt the materials for different settings. The training aims to give educators and community leaders the knowledge, skills and confidence to use e-Bug in their work. Hands on activities are demonstrated and participants have the opportunity to ask questions and discuss how they plan to implement e-Bug in their organisation.

Participants are given reading prior to the training, which covers the background information for the topics included in e-Bug. Educators who complete a short multiple choice test at the end of the session can become approved e-Bug educators. Approved educators can use the approved educator badge valid for 1 year and have their name and location appear on the e-Bug website. By undertaking e-Bug activities throughout the year, the approval status can be renewed.
So far the training has been delivered to over 60 healthy schools leads, teachers, school nurses, NHS health and wellbeing teams, community leaders, family practitioners and community workers. Feedback from the 6 pilot workshops has been very positive with participants enjoying the interactive elements of the training session and discussions around implementation. On average, participants rated the workshop overall as 4.6/5.

Over the next year the e-Bug team will be offering the training to more regions across England, for example through local councils that can offer in-school training programmes on health.

Beat the Bugs

In November 2016, e-Bug launched the Beat the Bugs community hygiene and self-care course. The course covers an introduction to microbes, hand and respiratory hygiene, food hygiene, oral hygiene, antibiotics and a final session on self-care. Educating communities on hygiene and self-care is important to discourage inappropriate use of antibiotics.

Beat the Bugs has been piloted in two community groups: adults with learning difficulties and young mothers at a Children’s Centre. Participants completed before and after knowledge questionnaires and sessions were observed by researchers to increase validity and monitor fidelity. Follow-up participant focus groups and course leader interviews were also conducted at both venues to explore their views on the course.

Quantitative results showed an improvement in participant knowledge in each session with microbes and antibiotics sessions reporting the highest improvement in knowledge. Qualitative results revealed that participants had retained knowledge, particularly around self-care demonstrating an increase in appropriate hand washing and tooth brushing behaviours.

The Beat the Bugs course can be used as a tool for the public and community groups to increase awareness and change behaviour around hygiene, self-care and antibiotics. The course aims to increase the public’s confidence and knowledge on managing their own infections to subsequently reduce inappropriate antibiotic use. The Beat the Bugs course is freely available to download online.113

113  www.e-Bug.eu/Beat-The-Bugs
Future work

World Antibiotic Awareness Week and Antibiotic Guardian

ESPAUR will:

- finalise and publish results of the impact evaluation of AG campaign
- aim to increase the number of registered organisations for WAAW by 10%
- facilitate the development of AG pledges in Turkish following commission by WHO-Europe and Turkish government
- aim to publish the proportion of AGs by local authority on PHE Fingertips Public Health Profiles
- collate and publish case studies of local antibiotic awareness/engagement campaigns and actions taken by organisations shortlisted for AG awards on AG and .gov websites
- work in collaboration with the PHE marketing team to align Keep Antibiotics Working (public facing media campaign and resources) and AG
- focus on embedding developed resources for community pharmacy, healthcare students, junior/family AG. Change junior AG to young AG and create an AG participator badge
- consider a nationwide implementation of the healthcare students survey to assess knowledge, attitudes and behaviour
- Consider how to:
  - implement ECDC’s EAAD toolkit for professionals in hospitals and other healthcare settings
  - further promote e-Bug, TARGET resources and the dental AMS toolkit
  - further promote the NHS Improvement and PHE improvement resource to reduce Gram negative blood stream infections
  - share the patient stories developed by BSAC for PHE as part of AG public events

TARGET and eBug

Activities for EAAD 2017:

- launch a new antibiotic lesson plan for secondary schools students’ ages 11-14 years. The lesson includes a card game and statement sorting task, in which students gain an understanding of what antibiotics are and what they can be used for. Students will also learn the mechanisms for how bacteria can travel from person to person, what students can do to prevent the spread of infection and how bacteria can develop resistance
- offer e-Bug Train the Trainer sessions during October. These will be offered to local authorities, educators and community group leaders. The sessions will give a
background to e-Bug, including how it was developed and the resources that are available. Interactive activities will be demonstrated and there will be opportunity for discussion around the activities and how they can be adapted for different groups

- on 15th November 2017, run an e-Bug session with schools in collaboration with Manchester University and present e-Bug and TARGET to stakeholders across Northern Ireland in collaboration with the Public Health Agency
- Antibiotic activities will be run at the At-Bristol Science Centre during the school autumn term.

Other future work:

- e-Bug are leading a work package in SafeConsumE, a European Commission Horizon2020 funded research programme which aims to reduce the health burden from foodborne illnesses by changing consumers’ behaviour. The work package will develop educational materials for senior students and young adults on the topic of food hygiene. During 2017/18, a needs assessment with educators and students will take place to understand how food hygiene can be improved in young people through education in schools. This will take place in four countries across Europe and the results will be used to develop new e-Bug educational resources for school aged children
- The e-Bug team, and researchers in Cardiff and Manchester will pilot a peer education intervention in the 2017-18 academic year, training medical and pharmacy students from Cardiff and Manchester Universities, respectively, to deliver existing e-Bug peer education antibiotic activities to sixth-form science students in schools. These students will then in turn act as peer educators and cascade the information to other 16-18 year olds in their school and their families. The activities seek to improve knowledge, change intentions around antibiotic use, and give young people the confidence to self-care for mild infections. Quantitative and qualitative data will be collected to evaluate the intervention
- The new e-Bug online educational games Stop the Spread and Body Busters will be evaluated to assess their ability to change students’ knowledge and increase awareness on antibiotics and the spread of infection. Junior and senior students will complete knowledge questionnaires before and after playing the games, and focus groups will be undertaken to collect user feedback, suggestions for improvements and to understand how the games have changed awareness on the topics
- The e-Bug team will evaluate the teacher pages of the e-Bug website and the results will be used to appraise the current quality and inform any future changes, modifications and additions to the website. The evaluation will include questionnaires and task-scenario completion exercises to understand how easily users navigate around the website
Research in professional education and training and public engagement

Omnibus Research Findings

Public knowledge about antibiotics, their use and resistance to inform antimicrobial stewardship programmes: 2014 and 2017 surveys

McNulty CAM, Lecky DM, Marshall D, Butler CC.

Background: The DH antimicrobial resistance strategy has stressed the need to educate the public. To help monitor AMS effects we aimed to determine the public's reported knowledge and use of antibiotics, and management of infections over time.

Methods: Face to face household survey was used with representative sample of 1,625 individuals >15y in January 2014 and 1,691 in 2017. To increase the number of respondents for the questions about back-up / delayed antibiotics, these were asked for two consecutive weeks with 3385 respondents. Data are weighted to match the profile of the population.

Results and implications: In 2017 83% participants agreed bacteria, and 35% viruses, can “effectively be treated with antibiotics”; (2014: bacteria 77%, viruses 40%), and 84% agreed that “most coughs, colds and sore throats get better on their own without the need for antibiotics”. We may be better to use this syndromic approach and severity when discussing the need for, and value of, antibiotics with patients.

There was ongoing misunderstanding of antibiotic resistance and immunity. In 2017 44% agreed “that taking antibiotics weakens your immune system.” 43% agreed “that Healthy people carry antibiotic resistant bacteria”, 50% that “antibiotic resistant bacteria can spread easily from person to person”, 58% that people can “carry antibiotic resistant bacteria for over a year”, and 76% “Taking antibiotics when you don't need them encourages bacteria that live inside you to become resistant” were true. Statements with greater understanding such as ”Taking antibiotics when you don't need them encourages bacteria that live inside you to become resistant” would be useful for clinicians to use in consultations, as trust that health care staff know when patients need antibiotics remains high and similar to 2014. Younger and lower social grades remain the most likely to have misconceptions and need more information.

In 2017 one-seventh of the general public 14% of them were fully aware of what a delayed /back-up antibiotic prescriptions was, with a further 7% knowing either the name or something about the practice. The North (30%) and south West (18%) were significantly more likely to be fully aware than all other areas. 165/3385 (5%) reported being given a delayed/back-up antibiotic prescription within the last 12 months – this was significantly higher in women (6%) than men (4%), and older participants than those 16-24 years. There were no differences by social grade, area, or education.
Slightly more in 2017 (were supportive of delayed/backup antibiotics for throat, ear or urine infections (41%, 43% and 46% of 3,385 respectively in 2017, compared to 36%, 38% and 38% in 2014). There is still a great opportunity to increase support for back-up antibiotics, as over half of the general public remain undecided or against using them. The higher awareness in the North may be because there has been much AMS activity by the North of England Commissioning Support (NECS) using the TARGET Treat Your Infection leaflet to promote back-up prescribing compared to other areas. The higher awareness in the South West may be because research trials of delayed antibiotic prescribing have been undertaken in several areas within the South West, but not all. The 969 (74%) participants reporting cough, throat, ear, sinus, chest infection or flu symptoms in the last year were asked: “Thinking of your MOST RECENT illness which of the following actions, if any, did you take as a result?” A third reported that they carried on most of their usual activities or work (33% with no variation with age, but significantly higher in social grade AB, or higher education)), or took non-prescription medications available over the counter (34%). One fifth (18%; women 21% vs men 14%) took other honey or herbal remedies, or took extra rest (23%, under 34 years more likely and if single or no children). Less than one-in-twenty sought advice from friends, colleagues or family, although this was significantly higher in younger participants 16-24 years (12%).

42% of participants who had taken antibiotics or had an infection in the last year did not recall being given any information about either by a health professional. One-fifth were told how to take antibiotics but far fewer about other things related to them. About One-tenth recalled being given some advice about their symptoms.

There is an opportunity to increase advice to patients in the pharmacy and family setting through leaflets. Resources should be readily available in GP surgeries, as this is the venue most of the general public seek advice.

Acknowledgements: We would like to thank, Rebecca Howell-Jones, Anna Quigley, Sarah Shepherd, Diane Ashiru-Oredope, and Christine Roberts for advising on questionnaire development, and the public who answered the questionnaire.

e-Bug Programme research abstracts – work completed and in progress 2017

Educating children and families on antibiotics and antibiotic resistance: an evaluation of a science centre activity

Young VL, Barber A, Gomez-Gutierrez M, Eley C, Hayes C, Ashiru-Oredope D, McNulty CAM, Klinger C

Background: e-Bug is an educational resource for children and young people which educates on hygiene, the spread of infection and antibiotics. The e-Bug resources
include materials for use in classrooms such as lesson plans and interactive activities, as well as games and online materials for children to access at home. e-Bug worked alongside the At-Bristol Science Centre to develop activities to run in the Science Centre Live Lab area. The activities aimed to increase knowledge on antibiotics, antibiotic resistance and treating common infections. The activities also included information on Antibiotic Guardian, a public campaign to increase awareness and knowledge on antibiotic resistance which includes Junior and Family Antibiotic Guardian digital badges.

Methods: The ability of the activities to improve knowledge on antibiotics was evaluated through knowledge change questionnaires. Children visited the At-Bristol Science Centre with their school or families and were asked to complete a short questionnaire before and after viewing the activity. The questionnaires were compared to look for knowledge improvement.

Results: The e-Bug antibiotic activities ran in the At-Bristol Science Centre for 6 weeks. In total, 69 before questionnaires and 54 after questionnaires were completed by children aged between 7 and 14 years. All 8 questions showed an improvement in knowledge. The greatest knowledge improvement came in the question ‘The more we take antibiotics, the more antibiotic resistant bacteria develop’, which had the lowest knowledge prior to the activity. Baseline knowledge of antibiotics was low, with 5 of the 8 questions having less than 50% of children answering correctly before the activity.

Conclusion: The e-Bug activities are able to improve knowledge on antibiotics within community settings such as Science Centres and Museums. These activities should be used outside of schools to educate a wider audience, including families, on the important topics of antibiotics and antibiotic resistance.

Pilot evaluations of Beat the Bugs: A community education course on hygiene, self-care and antibiotics

Eley CV, Young VL, Hayes C, Parkinson G, Tucker K, and McNulty CAM

Background: e-Bug, operated by Public Health England, is an international health education resource for children teaching about antibiotics, hygiene and infection. An estimated 80% of all antibiotics are prescribed in the community and 50% of these are unnecessary. e-Bug collaborated with Kingfisher Treasure Seekers, to develop a 6 week community hygiene and self-care course called Beat the Bugs covering: an introduction to microbes, hand and respiratory hygiene, food hygiene, oral hygiene, antibiotics and a final session on self-care. Educating communities on hygiene and self-care is important to discourage inappropriate use of antibiotics.
Methods: Before and after knowledge questionnaires were completed during two pilot courses; one with adults with learning difficulties and one with young mothers at a Children’s Centre. Sessions were observed by researchers to increase validity and monitor fidelity. Follow-up participant focus groups and course leader interviews were conducted at both venues to explore their views on the course.

Results: Quantitative results showed an improvement in participant knowledge in each session; microbes and antibiotics sessions reported the highest improvement in knowledge. Qualitative results revealed that participants had retained knowledge, particularly around self-care. Participants reported behaviour change including an increase in appropriate hand washing and tooth brushing.

Conclusion: The Beat the Bugs course can be used as a tool for the public and community groups to increase awareness and change behaviour around hygiene, self-care and antibiotics. The course aims to increase the public’s confidence and knowledge on managing their own infections to subsequently reduce inappropriate antibiotic use.

The Beat the Bugs course is freely available to download from the e-Bug website www.e-Bug.eu/Beat-The-Bugs. Course feedback will be used to improve the course prior to further pilots. Beat the Bugs supports current e-Bug resources in implementing NICE guidance NG63 to improve public knowledge and behaviour around hygiene, self-care and antibiotic use.

A mixed method evaluation of educator’s views on CPD training to learn about the e-Bug health education resource (submitted to Technology, Pedagogy and Education)

Eley CV, Young VL, Hayes CV, McNulty CAM

Introduction: e-Bug is an international educational resource for educators to teach children about microbes, hygiene and antibiotics. The e-Bug training module was developed for educators to increase knowledge about e-Bug and to provide the skills to optimise use of the resources. This study aimed to explore educators’ views on the e-Bug educator training module and to determine its effectiveness in assisting educators with the delivery of health topics using e-Bug.

Methods: Educators were invited to complete an online evaluation survey after completing the e-Bug training module. The online survey consisted of 15 Likert Scale and open ended questions. Quantitative data was analysed using Microsoft Excel software. Two qualitative semi-structured focus groups with educators were conducted to explore their views on the training module. Qualitative data was thematically analysed.
Results: 100 participants completed the training and online evaluation survey. Survey respondents rated their overall impression of the e-Bug training as very good or good (88%). 80% of respondents stated that their perceived knowledge of e-Bug improved after completing the training. Qualitative data analysis reported four main themes; attributes of the e-Bug training (value, functionality, appearance and future development), perceived educator self-development (knowledge, confidence and skills), promotion and accreditation of educator training, and the delivery of educator training. Educators provided suggestions for modifications to the training module including; ensuring training is compatible on all devices and incorporating images, videos and quotes into the training.

Conclusions: Educators view the e-Bug training module as a valuable CPD resource for improving educator knowledge, confidence and skills to teach children about important health topics.
9. Stakeholder engagement

This chapter describes organisations activities that are represented on the oversight group that have engaged with PHE/ESPAUR to meet the AMR strategy objectives.

The British Dental Association

The British Dental Association (BDA) continues to play a leading role in efforts to address AMR in dentistry nationally and internationally. The reduction of prescribing that is incongruent with published guidelines remains a major focus, both in supporting dentists to optimise their practice and in influencing national policy to address contractual issues, such as a lack of funded emergency treatment time, that create pressure to prescribe inappropriately.

The BDA collaborated with the ESPAUR Dental Subgroup and Faculty of General Dental Practice to develop the dental AMS toolkit for primary care, launched on EAAD 2016. The toolkit, comprising a dental practice poster, patient information leaflet and prescribing audit tool, is available via the BDA website; the poster was also distributed as an insert in the British Dental Journal alongside an editorial highlighting the importance of collaboration in addressing antimicrobial resistance. In support of the One Health agenda, the BDA co-ordinated social media activity with the British Medical Association and British Veterinary Association for EAAD 2016.

The BDA has engaged with NICE to ensure that prescribing guidance on antibiotics for oral conditions is appropriate and promotes antimicrobial stewardship, whether patients present to dental or medical practice.

Internationally, the BDA works with European partners through the Council of European Dentists and is increasingly engaged in global discussions via involvement with the Science Committee of the International Dental Federation (FDI) and by participating in World Health Organisation events.

British Society for Antimicrobial Chemotherapy (BSAC)

The British Society for Antimicrobial Chemotherapy (BSAC) is committed to supporting ESPAUR and implementation of the UK 5-year Strategy on Antimicrobial Resistance. BSAC supports members of the UK and global healthcare communities with a range of open access online educational resources that include online courses such as the Massive Open Online Course on Antimicrobial Stewardship (MOOC-AS) Point Prevalence Survey course and Gram Negative Infection Courses. Working independently and in partnership with the British High Commission Science and Innovation Programme, BSAC is providing translations of the MOOC-AS, accessed by
over 42,000 learners to date, in Mandarin, Russian and Spanish and is developing a bespoke course for delivery across Africa. Through Antibiotic Action and a global network of Antibiotic Action Champions BSAC seeks to educate and support both health care professionals and the public in their understanding of AMR and the appropriate and effective use of antibiotics.

BSAC hosts a national susceptibility testing centre at Cardiff and is actively supporting harmonisation of testing methodologies with the EUCAST method. The BSAC national Resistance Surveillance Programme (bacteraemia and resistance) is the longest running sentinel surveillance scheme in Europe, one output of which is access to researchers of a large library of isolates.

The Society produces a range of evidence based guidance, with guideline development groups currently working on Therapeutic Drug Monitoring, Multi-Drug Resistant Gram Negative Organisms, Drug Stability Testing, MRSA – Prevention and Treatment and Outpatient Parenteral Therapy: Good Practice Recommendations.

BSAC works collaboratively both nationally and internationally. The Society developed and gifted software to Public Health England for 2017 point prevalence survey exercise, acts as Secretariat to the All Party Parliamentary Group on Antibiotics, continues to work on the Antibiotic Guardian Campaign which the Society originally co-developed and underwrote, is a member of the Learned Society Partnership on AMR, is a founder member of the Conscience for Antimicrobial Resistance Alliance, established to monitor implementation of the United Nations Declaration on AMR and a partner on the EU Innovative Medicines Initiative DRIVE-AB Project.

In summary BSAC is working on a range of initiatives and collaborations both within the UK and across the globe to support implementation of national and global strategies on AMR, and is fully committed to continue doing so.

Care Quality Commission

The Care Quality Commission continues to regulate against The Health and Social Care Act 2008. Entering the next phase of our inspection program has provided an opportunity to review our approach to the Code of Practice on the Prevention and Control of Infections. Working together with other bodies such as PHE, HEE and NHSI we are updating and strengthening our approach across all sectors of health and

social care in line with the code of practice. More information about CQC’s next phase of inspection is available on the CQC website.

From late 2016 concerns about the remote prescribing of antibiotics were raised in the media and published literature.\textsuperscript{115,116,117} CQC began a program of inspection of online providers of primary care in response to patient safety concerns. This inspection program has identified a need for additional clarification of best practice for remote prescribing of antibiotics. CQC is sharing intelligence and collaborating with PHE to agree principles of good practice in this area. These principles will inform CQC’s ongoing inspection process. CQC has committed to support PHE and NICE to incorporate remote prescribing considerations into the upcoming antimicrobial prescribing guidance being published in 2017/18 and will support the development of any further specific guidance in this area.

Faculty of General Dental Practice (UK)

Promoting appropriate antimicrobial prescribing in dentistry, and raising awareness of the need for antibiotic stewardship among the profession, continues to be a major focus of the Faculty of General Dental Practice UK (FGDP(UK)).

Over the last year, FGDP(UK) has been promoting awareness and use of the dental AMS toolkit, which it co-developed with the British Dental Association, Public Health England and other partners. This included writing to all its members highlighting the launch of the audit tool (developed by FGDP, BDA and Dental Protection), writing a feature in the Primary Dental Journal about the toolkit, and distributing 5,000 copies of the Antibiotics Don’t Cure Toothache poster in A3 size to its members and subscribers through the journal. It has created and promoted a dedicated Antibiotic Stewardship webpage, which has been viewed over 4,000 times and not only co-hosts the toolkit, but explains the scale, nature and relevance of the problem of antimicrobial resistance 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 is made available to dentists in hard copy, as an e-book and freely on the FGDP website, where it has been viewed 45,000 times in the last year and over 86,000 since launching there in 2015. Work has also begun with the Faculty of Dental Surgery to extend FGDP(UK)’s prescribing guidelines to cover secondary care dentistry. FGDP(UK) set up a social media


\textsuperscript{116} Boyd S et al. Obtaining antibiotics online from within the UK: a cross-sectional study. Journal of Antimicrobial Chemotherapy 2017;72(S): 1521-1528

\textsuperscript{117} A Killelea et al. The scandal of the online pills trade which is threatening everyone’s safety. Mirror [Internet] 2017. Available from: http://www.mirror.co.uk/news/uk-news/scandal-online-pills-trade-threatening-9801828
Thunderclap for EAAD 2016, on which the BDA, PHE, BSAC and the Association of Clinical Oral Microbiologists collaborated, and which achieved a social reach of over 270,000.

FGDP(UK)’s AMR Lead, Dr Nick Palmer is the editor and co-author of the FGDP guidelines and represents the Faculty at meetings of the ESPAUR Dental Sub-group and ESPUAR Oversight group. The Faculty engaged with NICE on a range of relevant guidelines and quality standards it is developing, such as those on managing common infections and acute sinusitis.

The Faculty has also responded to recent confusion in the national media over antibiotic prescribing advice to reassure the profession that the Faculty’s guidance already advises review of antibiotic use for dental infections after 2-3 days, and discontinuation of antibiotics if there are no further indications of active infectious disease.

Health Education England

Education of healthcare workers on rational infection control, antimicrobial prescribing and antimicrobial stewardship is a key part of antimicrobial resistance containment activities. Health Education England is responsible for ensuring that our future workforce has the right numbers, skills, values, cultural sensitivities and behaviours to meet patients’ needs and deliver high quality care.

The Health and Social Care Act 2008 code of practice on the prevention and control of infections and related guidance states that providers should ensure that all prescribers receive induction and training in prudent antimicrobial use and are familiar with the antimicrobial resistance and stewardship competencies. A survey was disseminated to the system to identify what learning materials and resources are currently available to support prescribers with learning and education around antimicrobial prescribing, with an aim to identify any gaps, perceived or otherwise. Sixty-one percent of respondents confirmed that all prescribers within their organisation receive induction and training in prudent antimicrobial use and 40% confirmed prescribers are familiar with and/or given the antimicrobial resistance and stewardship competencies.

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The visibility and uptake of the free introductory e-learning session on antimicrobial resistance\textsuperscript{121}, that has a particular focus on infection prevention and control, was evaluated to assess individual and organisational buy-in and usage. The findings of this work shows that awareness of the introductory e-learning session on antimicrobial resistance is good and respondents found this session beneficial in raising healthcare worker awareness of antimicrobial resistance.\textsuperscript{122}

**National Institute for Health and Care Excellence (NICE)**

NICE is working with Public Health England on antimicrobial prescribing guidelines. Each guideline will focus on managing a common infection and offer evidence-based guidance for how antimicrobials should be used to treat the infection across primary and secondary care. The aim is to encourage the responsible use of antimicrobials thereby helping to slow the development of antimicrobial resistance. A Public Health Advisory Committee is producing these guidelines and an interim process guide has been developed. Guidelines for the first 3 topics are planned to publish in the 2017/18 business year with sinusitis (acute) due for publication in October 2017. The guideline presentation includes a visual summary of the recommendations, a guideline and an evidence review. The visual summary presents the recommendations in a diagram on a single page allowing users to access the guidance quickly. In support of this work, the BNF section on antimicrobials will be reviewed to reflect the new guidelines.

In January 2017, NICE published a guideline Antimicrobial stewardship (AMS): changing risk-related behaviours in the general population (NG63). This aims to help 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 developing Antimicrobial Prescribing Advice to support the appropriate use and stewardship of new antimicrobials. The presentation format for this advice has been developed based on the current evidence summary process. The first advice is on Ceftazidime-avibactam (Zavicefta) and is due to be published in October 2017.

NICE’s current Medtech innovation briefings are developed to support the use of innovative medical devices, diagnostics and digital technologies, including those that

\textsuperscript{121} e-Learning for Healthcare, Reducing AMR, available from; http://www.e-lfh.org.uk/programmes/antimicrobial-resistance

\textsuperscript{122} Health Education England, An evaluation of our antimicrobial resistance introductory e-learning session, and national infection prevention and control training

relate to the antimicrobial stewardship agenda. They can be used to support early implementation and further evidence generation of new technologies. Over the past year, MIBs were published on FebriDx for C-reactive protein and Myxovirus resistance protein A testing in primary care (July 2017), eazyplex SuperBug kits for detecting carbapenemase-producing organisms (Feb 2017), QuikRead go for C-reactive protein testing in primary care (Sept 2016) and Alere Afinion CRP for C-reactive protein testing in primary care (Sept 2016).

NICE is also collaborating with the Department of Health (DH) on a research project exploring the assessment of new antimicrobials with high potential to address unmet need. This will consider the potential value that NICE Technology Appraisals can contribute to the appropriate use and stewardship of new antimicrobials. The research is being delivered by the DH Economic Evaluation Policy Research Unit (EEPRU) at the University of York. The DH has been charged with developing 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 payment models.

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.

The Royal Pharmaceutical Society

The Royal Pharmaceutical Society (RPS) is committed to supporting ESPAUR as part of the UK cross-government AMS Strategy. Their Chief Executive, Paul Bennett, President, Ash Soni, and national Boards for England, Scotland and Wales have also all stated their personal commitment to supporting this vital work.

The RPS supports pharmacist members with resources, information and support on AMS to support them in their practice. We also ensure that AMS is included in all relevant RPS standards and guidance. In 2017 the RPS will be hosting a GB wide national campaign on antimicrobial stewardship with resources and messaging to pharmacists and their teams, as well as consumers, about the important role pharmacists can play with antimicrobial stewardship.

The RPS also has two expert groups providing expertise, advice and thought leadership in this area, the RPS Antimicrobial Expert Advisory Group and the RPS Pharmaceutical Science Expert Advisory Panel (PSEAP). Both groups have provided comment and input across a wide range of work streams relating to antibiotic utilisation and resistance. The PSEAP has worked to implement the recommendations to stimulate new antimicrobial development and improve AMS as set out in the RPS report The New
Medicines, Better Medicines, and Better Use of Medicines document.\(^{123}\) The RPS is also continuing to develop the RPS AMS portal\(^{124}\) which signposts to learning and resources about antimicrobial stewardship.

The RPS has also contributed to work internationally, contributing to the Pharmaceutical Group of the European Union (PGEU) paper “The Community Pharmacist Contribution to Tackling AMR”\(^{125}\) and the forthcoming revised statement of policy from the International Pharmaceutical Federation (FIP) on the control of antimicrobial medicines resistance.

**UK Clinical Pharmacy Association**

UK Clinical Pharmacy Association (CPA): Pharmacy Infection Network (PIN) is the representative body for antimicrobial/infection specialist pharmacists and pharmacy technicians in the UK and has 306 members. The group is represented on ESPAUR by a committee member who sits on the oversight group and the AMS sub-committee.

PIN has engaged with PHE/ESPAUR to deliver stewardship in both primary and secondary care, sharing information with members and delivering education on AMS both online via a forum and webinars and at UKCPA master classes and conferences and at the Federation of Infection Societies (FIS) national conferences. We also work locally within our own healthcare communities to raise awareness of AMR and the need for stewardship with medical professionals and members of the public.

The group has taken a key role in advancing antimicrobial consumption reporting in secondary care and delivering reductions in total, carbapenem and piperacillin/tazobactam consumption and increases reviews of empiric antibiotic prescriptions as part of the AMR CQUIN in England.

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124 http://amsportal.org/

Acknowledgements

Chapter 1: Introduction
Susan Hopkins, Alan Johnson

Chapter 2: Antibiotic resistance
Rebecca Guy, Katie Hopkins, Katy Town, Dean Ironmonger, Richard Puleston, Neil Woodford, Alan Johnson

Chapter 3: Antimicrobial use
Graeme Rooney, Dean Ironmonger, Susan Hopkins

Chapter 4: Quality improvement initiatives
Emma Budd, Cliodna McNulty, Elizabeth Beech, Phillip Howard and Diane Ashiru-Oredope

Chapter 5: Antimicrobial stewardship
Diane Ashiru-Oredope, Donna Lecky, Jasmin Islam, Caroline Purslow, Kieran Hand, Alistair Hay, Mike Sharland, Cliodna McNulty, Sandra white, Martin Llewellyn, Susan Hopkins

Chapter 6: Antifungal resistance, prescribing and stewardship
Rebecca Guy, Katie Owens, Elizabeth Johnson, Andrew Borman, Malcom Richardson, Riina Rautema-Richardson, Caroline Moore, Colin Brown, Katherine Henderson, Samir Agrawal, Rohini Manuel, Colin Richman, Philip Howard, Silke Schelenz and Berit Muller-Pebody on behalf of the ESPAUR subgroup on antifungal consumption and resistance surveillance

Chapter 7: Point prevalence survey of healthcare-associated infections, antimicrobial use and antimicrobial stewardship in England
Katherine Henderson, Rachel Freeman, Susan Hopkins

Chapter 8: Professional Education & Training and Public Engagement
Diane Ashiru-Oredope, Vicki Young, Donna Lecky, Oliver Dyar, Cliodna McNulty, Susan Hopkins

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Annex Chapter 3: Antibiotic consumption

Department speciality to department group lookup table, ESPAUR report, 2016.

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Trust definitions ESPAUR report, 2016
These definitions are based on the definitions provided for the Estates Returns Information Collection 2016/17.\(^{126}\)

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<tr>
<th>Trust</th>
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<tr>
<td><strong>Acute Small/Medium/Large</strong></td>
<td>Sites that provides a range of inpatient medical care and other related services for surgery, acute medical conditions or injuries (usually for a short term illness or condition). Treatment Centres providing inpatient facilities are classed as General Acute Hospitals.</td>
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<tr>
<td><strong>Acute Teaching</strong></td>
<td>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.</td>
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<tr>
<td><strong>Acute Specialist</strong></td>
<td>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.</td>
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<tr>
<td><strong>Acute Multiservice</strong></td>
<td>Sites where two 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.</td>
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\(^{126}\) http://hefs.hscic.gov.uk
Annex Chapter 5: Antimicrobial stewardship

Terms of Reference and Membership

ARHAI Antibiotic Prescribing Appropriateness Measures (APAM) task-and-finish group for secondary care

Background
The UK government stated at the G7 meeting in Japan that the UK will cut “inappropriate prescribing in the UK by half by 2020”.

There are currently no baseline data for level of appropriateness in England. This paper highlights the key challenges to establish an appropriate antimicrobial prescribing range nationally. For example, existing international, national and local antibiotic prescribing guidelines are not optimal with regard to identifying appropriate antibiotic prescribing in secondary care.

Subgroup Terms of Reference

1. To develop standard audit tools for the evaluation of appropriateness of antibiotic prescribing in secondary care
2. To consider options for frequency, intensity, resourcing and mechanisms of audit data collection, feedback and reporting
3. To develop an antibiotic guideline specification including standards to define appropriate prescribing with a view to using such a specification to commission or inform guideline writing (for example, by NICE).
4. To facilitate the collection of appropriateness data to establish a national baseline for secondary care

Members: Kieran Hand (proposed joint chair (ARHAI)); Diane Ashiru-Oredope (joint chair) (ARHAI/PHE); Susan Hopkins (PHE), Mike Sharland (ARHAI); Philip Howard (NHS Improvement); Elizabeth Beech (NHS Improvement); Cliodna McNulty (PHE); RPS Antimicrobial Expert Group rep(s); UKCPA Pharmacy Infection Network Rep(s); Chief Pharmacist Rep, NHS microbiologist; PHE Regional Microbiologist/AMR Lead; Epidemiologist; NICE

Timeframe: By March 2017
Annex Chapter 6: Antifungal resistance, prescribing and stewardship

The full list of current subgroup membership is:

- Berit Muller-Pebody
- Colin Brown
- Rebecca Guy
- Philip Howard
- Elizabeth Johnson
- Rohini Manuel
- Andrew Borman
- Diane Ashiru-Oredope
- Caroline Moore
- Riina Rautema-Richardson
- Malcolm Richardson
- Colin Richman
- Silke Schelenz
- David Denning
- Phillip Howard
- Richard Barton
- David Enoch
- Christianne Micallef
- Rakhee Patel
- Samir Agrawal
Annex Chapter 8: Professional education & training and public engagement

Social media and google analytics glossary

- **visit/visitor**: Used to denote a person accessing the website (AntibioticGuardian.com)
- **traffic**: A summary term used to describe visitors (unique or repeated) accessing the website
- **goal**: A custom specific visitor outcome/action set by the administrator within Google analytics; in this case, the outcome was a visitor clicking the submit button after completing the pledge form
- **IP address**: A unique digital signature used on the internet to identify a computer/mobile device; these can be used to distinguish geographic location and between unique and repeat visits
- **unique visits**: The first time an IP address accesses the website, this is used as a proxy for individuals; additional visits using the same IP address are categorised as repeats; this method cannot distinguish between multiple people who may share a single device
- **total website visits**: Every time the webpage is accessed it counts as a new visit; this method accounts for multiple/repeated visits on a single device
- **referral/directed**: A link that directs individuals to AntibioticGuardian.com; these can be found on another website, in an email or in a social media post and do not include self-directed traffic
- **self-directed**: When a visitor directly accesses a website via their browser through a search engine using search terms such as ‘antibiotic guardian’ or by typing in AntibioticGuardian.com in the browser bar; the visitor has not accessed the website from a referral link
- **social media channels**: A summary term to describe online media sharing platforms such as twitter, Facebook, LinkedIn or Google+
- **conversion rate**: The proportion of visitors who take a specific action (goal) during a period of time; in this case, the proportion of visitors who made a pledge and became AGs
- **acquisition**: The directed or self-directed route that visitors use to arrive at a website; this paper considered social media, email, website referrals and self-directed traffic
- **adjusted conversion rate**: The proportion of AG pledges from unique website visits