Public Health England

Protecting and improving the nation's health

English surveillance programme for antimicrobial utilisation and resistance (ESPAUR)

Report 2016

About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. We do this through world-class science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. We are an executive agency of the Department of Health, and are a distinct delivery organisation with operational autonomy to advise and support government, local authorities and the NHS in a professionally independent manner.

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Key facts

1. The number of people affected by antibiotic-resistant Gram-negative infections continues to increase
2. The incidence of antibiotic-resistant Gram-negative bloodstream infections is higher in the very young and the elderly, reflecting the higher rate of infection in these age groups
3. Antibiotic use has reduced significantly across the whole healthcare system for the first time
4. Antimicrobial stewardship continues to be embedded and improving in both general practice and hospitals, although further work is needed in community health trusts
5. A new antimicrobial stewardship toolkit has been launched for dental practices
6. By November 2016, more than 33,000 people had become Antibiotic Guardians and had pledged an action to reduce the unnecessary use of antibiotics
7. Professional organisations and stakeholders are engaging with PHE to raise awareness, educate and deliver aspects of the UK AMR strategy

Executive summary

ESPAUR was established by PHE in 2013 in response to the cross-government UK five-year antimicrobial resistance (AMR) strategy.[1]

The aims of ESPAUR are to:

- develop, maintain and disseminate robust data relevant to antimicrobial use (AMU), AMR and antimicrobial stewardship (AMS)
- enable optimum use of this data across healthcare settings
- measure the impact of AMU and AMS on AMR and patient safety

The following key objectives have been achieved this year:

1. Better access to and use of data

A major initiative over the last year has been to make local surveillance data available to stakeholders via Fingertips, a publicly accessible interactive web tool. In April 2015 PHE launched a series of AMR local indicators for England on the Fingertips data portal.[2] Data for more than 70 indicators are now available across three NHS geographies: acute trusts, clinical commisioning groups (CCGs) and GP practices.

2. Improved AMR surveillance

Improvements in data presentation and analysis have been made possible by continual improvements in both the quality and quantity of surveillance data over the last three years through collaborative work with the PHE Field Epidemiology Service and NHS microbiology laboratories.

PHE has developed and implemented an enhanced reporting system (ERS) for carbapenemase-producing organisms (CPO) with the objective of collecting risk factor data.[3] It has developed outputs for the NHS highlighting the trusts which are reporting through this system and the number of CPO from each trust since the system was launched and in the most recent month.

3. Improved AMU surveillance

ESPAUR can now track antibiotic prescribing from each healthcare sector. The dental subgroup of ESPAUR has worked with the Faculty of Dental Public Health, NHS Business Services Authority, PHE and NHS Digital to develop an options paper and plan for improving the granularity of dental prescribing.

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[1] Ashiru-Oredope D, Hopkins S. J, Antimicrobial stewardship: English Surveillance Programme for Antimicrobial Utilization and Resistance (ESPAUR). *Antimicrob Chemother* 2013; 68: 2421–2423

[2] Public Health England fingertips, available from; https://fingertips.phe.org.uk/profile/amr-local-indicators

[3] Freeman R, et al. Enhanced surveillance of carbapenemase-producing Gram-negative bacteria to support national and international prevention and control efforts. *Clin Microbiol Infect* 27 Jul 2016

PHE has worked with NHS England and NHS Improvement to implement the Antibiotic Prescribing Quality Measures advised by the Department of Health (DH) expert advisory committee on Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) into incentives for CCGs and acute trusts.

4. Improved public and professional engagement

ESPAUR launched the 'Antibiotic Guardian' (AG) campaign as a move from engagement to changes in public and professional behaviour around antibiotic use. Process and outcome evaluations were performed and published which 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 increased self-reported knowledge and changed self-reported behaviour, particularly among people with prior AMR awareness.[4,5]

In collaboration with Health Education England, ESPAUR has scoped and developed implementation options related to education and training of healthcare professionals for antimicrobial prescribing and stewardship competencies in undergraduate and postgraduate education and for continuing professional development.

The PHE Primary Care Unit has continued to work with schools to provide education about the spread, prevention and treatment of infection through the ongoing development and delivery of materials on bacteria, antibiotics and AMR through e-Bug, a free educational resource for use in the classroom and at home.

5. Improved antibiotic stewardship

This year a survey assessing the implementation of recommended antimicrobial stewardship interventions in community healthcare trusts was completed and initial results are presented in this report.

ESPAUR developed an antimicrobial stewardship surveillance system including tools to support stewardship audits in acute trusts and these are being used as part of the CQUIN (Commissioning for Quality and Innovation) in 2016/17.

A dental antimicrobial stewardship toolkit has been developed and rolled out by the dental subgroup of ESPAUR in collaboration with Faculty of General Dental Practice and British Dental Association.

[4] Bhattarcharya A et al. A process evaluation of the UK-wide Antibiotic Guardian campaign: developing engagement on antimicrobial resistance. J Pub Health. (2016) doi: 10.1093 (/pubmed/fdw059)

[5] Chaintarli K et al. Impact of a United Kingdom-wide campaign to tackle antimicrobial resistance o-n self-reported knowledge and behaviour change. BMC Public Health. 2016;16:393

6. Development and implementation of antifungal resistance surveillance and stewardship

This year we have also increased our outputs to look at fungal resistance, antifungal consumption and stewardship, as this is an area of emerging concern highlighted by increasing numbers of *Candida auris* infections detected in England and elsewhere.

Key results

Antimicrobial resistance

- between 2010 and 2014 the rate of bloodstream infections caused by *Escherichia coli* and *Klebsiella pneumoniae* increased by 15.6% and 20.8% respectively. Between 2014 and 2015 the number of cases continued to increase; *E. coli* bloodstream infections increased by a further 4.6% and *K. pneumoniae* increased by 9%. Tackling these infections is a key government priority
- the proportions of bloodstream infections resistant to piperacillin/tazobactam (the most frequently used antibiotic for the treatment of sepsis) rose dramatically between 2011 and 2015, from 8.5% to 11.7% for those caused by *E. coli* and from 12.6% to 18.5% for *K. pneumoniae*. These increases in resistance will increase the pressure on clinicians to use carbapenems (which are the antibiotics of last resort) unless alternative treatment strategies are developed. Resistance to other antibiotics used for treatment was largely unchanged
- carbapenem resistance remains low in bloodstream infections in England (*E. coli* 0.2% and *K. pneumoniae* 1.1%), though there continue to be year-on-year increases in the numbers of bacteria confirmed to produce carbapenemases (enzymes that break down carbapenems making them ineffective for treatment), with 1,893 positive referred isolates confirmed in 2015
- incidence of bloodstream infections and infections caused by resistant bacteria are highest in the extremes of life (the very young and the elderly). Interventions to reduce antibiotic resistance that are focused on the very young and the elderly should be prioritised
- in this report we present data on resistance to combinations of antibiotics, highlighting that only 2.5% of *E. coli* and 2.0% of *K. pneumoniae* tested for susceptibility to co-amoxiclav and amikacin were resistant to both. Combinations of antibiotics are thus possible alternatives to single antibiotics for empiric therapy of sepsis, preserving carbapenems and putting less selection pressure on antibiotics such as piperacillin/tazobactam
- there is wide variation in the rates of resistance to antibiotics across England. For example by CCG trimethoprim resistance in Gram-negative urinary tract infection (UTI) ranges from 16.3% to 66.7%; this may be related to variation in sending urine samples for laboratory testing. However, 86% of CCGs have resistance rates greater than 25%, highlighting that trimethoprim can no longer be advised as the first-line empiric antibiotic treatment for UTIs in England
- antimicrobial resistance is stable in pneumococcal and *Pseudomonas* bloodstream infections and tuberculosis and decreasing in *Staphylococcus aureus* infections. However, vancomycin resistance in bloodstream infections caused by *Enterococcus spp*. rose from 10% to 16% between 2011 and 2015

- an outbreak of azithromycin-resistant gonorrhoea, initially identified in Leeds, has spread across England. Laboratories have been notified to screen all gonorrhoea isolates for resistance and affected patients should be followed up to ensure clinical cure and have rigorous tracing of all sexual contact

Antimicrobial prescribing

- total antibiotic consumption (measured as defined daily dose [DDD]) declined significantly between 2014 and 2015 by 4.3%, from 22.9 to 21.8 DDD per 1000 inhabitants per day
- antibiotic prescribing predominantly occurs in general practice (74%), followed by hospital inpatients (11%), and outpatients (7%). The remainder comprised use in dental practice (5%) and other community settings (3%). Decreased antibiotic consumption occurred in general practice, hospitals and dental practices
- antibiotic prescriptions in primary care, measured as the number of prescriptions dispensed, adjusted for the age and sex distributions in the population (Specific Therapeutic group Age-sex Related Prescribing Units [STAR-PU]), has declined for the last four years and is now lower than the similar measure in 2011 (1.11 items per STAR-PU in 2015 compared to 1.23 items per STAR-PU in 2011)
- broad-spectrum antibiotic use (antibiotics that are effective against a wide range of bacteria) continues to decrease in primary care. England now uses the lowest amounts of cephalosporins and quinolones in the EU. These antibiotics are more likely to drive antibiotic resistance than narrow-spectrum antibiotics. However, hospitals continue to increase their antibiotics of last resort currently available: Piperacillin/tazobactam, carbapenems and colistin
- compared with other UK health administrations, England has the lowest primary care prescribing by (items and DDDs). Scotland has the lowest use of last resort antibiotics with England the second lowest use

Relationship between prescribing and resistance

- despite low levels of use of cephalosporins and resistance, the proportion of bloodstream infections resistant to these antibiotics has not changed significantly in the last five years
- the continued increase (50% over five years) in the use of piperacillin/tazobactam, an antibiotic of last resort, is now associated with a significant increase in resistance of both *E. coli* and *K. pneumoniae* bloodstream infections. The proportions of these isolates that are resistant have increased by 50% and 60% respectively, over five years. While this may relate to different antibiotic susceptibility breakpoints used in clinical laboratories, this is nevertheless important as this is the information clinicians use to guide patient treatment
- this highlights the importance of reducing the use of piperacillin/tazobactam, as well as carbapenems, to reduce the emergence and subsequent spread of resistance

Antimicrobial stewardship

- a dental antimicrobial stewardship toolkit was developed and launched, building on work carried out in the North West of England
- a survey of antimicrobial stewardship was performed in community health service trusts. This demonstrated that further work needs to be developed to embed antimicrobial policies, guidelines and education within these trusts

- an evaluation of TARGET resources for primary care was performed. It demonstrated more than 7,000 course completions have occurred since the materials were launched
- ESPAUR developed and piloted a secondary care stewardship surveillance tool. This was subsequently amended and rolled out to support the AMR CQUIN

Public and professional engagement

- PHE continued to develop and lead the UK-wide Antibiotic Guardian campaign as a move from raising awareness to stimulating behaviour change in members of the public and healthcare professionals; by November 2016, more than 33,000 people had pledged an action to become an Antibiotic Guardian at www.AntibioticGuardian.com
- three professional roadshows and a public event were supported and commissioned by PHE
- health education institutions were surveyed to understand how the PHE developed 'antimicrobial prescribing and stewardship competencies' were being embedded in undergraduate curricula of healthcare students. The average implementation rate for all the dimensions was reported as 67% from those who responded
- PHE e-Bug (an educational resource for children and young people, including resources for teachers in line with the national curricula) team launched Beat the Bugs, a six-week course on hygiene, antibiotic and self-care for use by community groups. A pilot occurred for adults with learning disabilities and results found that knowledge, awareness, and behaviour improved. 'e-Bug' now has partners with 26 countries across the world

Antifungal resistance, prescribing and stewardship

- PHE developed antifungal resistance, consumption and stewardship data in collaboration with national experts and professional organisations
- considerable work needs to occur to improve the resistance data being performed in NHS laboratories and submitted to the national surveillance system
- antifungal consumption differs between community and hospitals; the majority of consumption in the community occurs with antifungals (eg terbinafine and griseofluvin) used to treat skin, nail and hair infections. Within hospitals the predominant antifungals are azoles and amphotericin to treat mucocutaneous or invasive disease
- very few organisations have a dedicated antifungal stewardship programme, predominantly due to lack of resources and competing priorities

ESPAUR will continue the work to meet its aim and objectives over the coming year. The oversight group continues to provide expertise, direction and challenge to PHE and others working in this area to ensure that the projects and surveillance meet the needs of the national AMR strategy. The enthusiasm and engagement of the individuals and professional organisations working with ESPAUR allow this output and much more to be delivered.

Recommendations to PHE regions and centres

This report should have a valuable role in supporting the development of action plans to reduce prescribing. PHE centres should ensure that this report is discussed at relevant meetings including those held by local quality surveillance groups, strategic clinical networks, health protection committees and local infection prevention and control committees.

PHE staff should promote the use of the national AMR surveillance system by NHS colleagues through the active dissemination of the system web link (https://sgss.phe.org.uk/) and the data outputs for local AMR Indicators available on the PHE Fingertips web portal: https://fingertips.phe.gov.uk/profile/amr-local-indicators

PHE staff should ensure they are able to direct organisations and individuals to the resources for AMS guidance available for primary care and secondary care from NICE and PHE, including TARGET and SSTF toolkit and the NICE Antimicrobial Stewardship Guidance.

PHE staff should continue to promote the enhanced surveillance and electronic reporting system (ERS) for carbapenemase-producing organisms. The protocol is available at: https://www.gov.uk/government/publications/carbapenemase-producing-gram-negative-bacteria-enhanced-surveillance-ers-user-guide.

PHE staff should use the opportunity to sign up their own staff and to promote with stakeholders, the Antibiotic Guardian call to action: “The Antibiotic Guardian campaign calls on everyone in the UK, the public and the healthcare community to become antibiotic guardians by choosing one simple pledge about how each will make better use of antibiotics and help save these vital medicines from becoming obsolete.” www.AntibioticGuardian.com

Recommendations to local authorities

Directors of public health should ensure that health and wellbeing boards are aware of the strategic nature and priority of AMR and that it receives due attention at their meetings and in the Joint Strategic Needs Assessment.

Directors of public health should work with stakeholders to provide information and advice to the public regarding steps they can take to address AMR.

Directors of public health should work with local healthcare commissioners (via their routine channels for assuring provider quality) to ensure effective clinical leadership and collaboration on AM stewardship by all providers.

Directors of public health should ensure robust arrangements are made to mobilise, monitor and sustain effective multi-agency action by stakeholders from across whole local system, to develop interventions to reduce high prescribing where it occurs in their population.

Directors of public health should ensure that their local commissioners are commissioning microbiology services that follow the Standards for Microbiological Investigations published by PHE as part of the clinical and public health care package for their population. https://www.gov.uk/government/collections/standards-for-microbiology-investigations-smi

Directors of public health should support the development of local AMS collaboratives in line with NICE Antimicrobial Stewardship Guidance (NG15).

Recommendations to NHS organisations

NHS England and NHS Improvement regional teams are requested to disseminate this report to CCG accountable officers and directors of quality, and medicines management teams, medication safety officers and hospital chief pharmacists.

The boards of NHS organisations should review the data available for their organisation on the Local AMR Indicators page of PHE Fingertips. (https://fingertips.phe.gov.uk/profile/amr-local-indicators)

Directors of Infection Prevention and Control (DIPCs) and medical and nursing directors should ensure that they have an active programme of antibiotic resistance and antibiotic use surveillance and that these programmes inform a local AMR strategy and action plan which are reported to the board at regular intervals.

Antimicrobial stewardship and microbiology laboratory teams should ensure their laboratory and pharmacy is reporting AMR and CQUIN data to PHE. They can compare the results of their local AMR surveillance to other hospitals and laboratories in their region through regular access online via https://sgss.phe.org.uk/ and PHE Fingertips site. This should inform their local antibiotic guidelines to optimise prescribing.

Microbiology laboratories should use the enhanced surveillance and electronic reporting system (ERS) for all bacteria with suspected carbapenemase enzymes when referring isolates to the national reference laboratory for confirmatory testing. The protocol is

available at: https://www.gov.uk/government/publications/carbapenemase-producing-gram-negative-bacteria-enhanced-surveillance-ers-user-guide.

CCGs can be directed to review the CCG and general practice data on the NHS BSA website, PresQIPP prescribing resources, open-prescribing, NHS Digital website, and on PHE Fingertips. Acute NHS trusts can review their own pharmacy data, held within their hospitals and the data submitted for the AMR CQUIN on PHE Fingertips site.

Regional pharmacists, heads of medicines optimisation (or equivalent) in CCGs, medication safety officers and chief pharmacists are invited to sign up and promote the Antibiotic Guardian call to action: “Antibiotic Guardian campaign calls on everyone in the UK, the public and the healthcare community to become antibiotic guardians by choosing one simple pledge about how each will make better use of antibiotics and help save these vital medicines from becoming obsolete.” www.AntibioticGuardian.com

Commissioners of NHS services should ensure that the microbiology services they commission follow the Standards for Microbiological Investigations published by PHE as part of the clinical and public health care package for their population.

All healthcare organisations (both community and hospital) should perform a self-assessment of their organisation’s antimicrobial stewardship practice against the NICE Antimicrobial Stewardship Guidance (NG15), and use the toolkit to develop an organisation focussed action plan.

Recommendations to regulatory authorities

Regulatory authorities for all health and social care settings should ensure policies and procedures are in place to monitor the appropriate use of antibiotics, the effective surveillance for antibiotic resistance and that medical, nursing and pharmacy employees are aware of the importance of their actions in this area.

Regulatory authorities should review the pathology services and ensure that they are following the standards for microbiology investigations.

Regulatory authorities should use the data on Fingertips as part of the information assessment process for NHS organisations.

Recommendations to professional organisations

Professional organisations should cascade this report to their members to raise awareness on antibiotic resistance and to help inform individual actions, including pledging to act as an Antibiotic Guardian on: www.AntibioticGuardian.com.

Professional organisations should work with Health Education England to develop effective undergraduate and postgraduate curricula on antibiotic use and resistance for their trainees, members and fellows.

Professional organisations should promote use of resources supporting AMS, such as TARGET and SSTF.

Chapter 1: Introduction

The English Surveillance Programme for Antimicrobial Use and Resistance (ESPAUR) was established by Public Health England (PHE) in 2013 in response to the cross-government UK five-year antimicrobial resistance (AMR) strategy.[6,7] Since the launch of the programme, there has been ever increasing focus on AMR, a reflection of this is that AMR was placed on the UK government risk register in March 2015.[8] The O'Neill review of AMR, which was commissioned by the UK government in July 2014, focussed on the macroeconomic impact and published its final report in May 2016, highlighting key steps that are required to reduce antibiotic demand, stimulate drug development and promote global activity.[9] On 21 September 2016, the UN general assembly passed a resolution on AMR, predominantly aimed at improving country action plans.[10]

The aims of ESPAUR are:

- develop, maintain and disseminate robust data for antimicrobial use (AMU), AMR and antimicrobial stewardship (AMS) implementation
- enable optimum use of this data across healthcare settings
- measure the impact of AMU and AMS on AMR and patient safety

In this introduction we highlight the work undertaken by ESPAUR and provide a summary of actions to meet these aims over the last year.

Better access to and use of data

One of the seven areas for action that make up the UK five-year strategy for tackling AMR involves improving access to and use of surveillance data. A key activity of ESPAUR has been to increase awareness of the available data and to promote action to improve public health by healthcare professionals such as the development of local action plans to reduce AMR.

[6] UK Five Year Antimicrobial Resistance Strategy 2013-18. Available from; https://www.gov.uk/government/publications/uk-5-year-antimicrobial-resistance-strategy-2013-to-2018
[7] Ashiru-Oredope D, Hopkins S. J Antimicrob Chemother 2013; 68: 2421–2423
[8] Cabinet office, National Risk Register of Civil Emergencies, 2015 edition, Available from; https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/419549/20150331_2015-NRR-WA_Final.pdf
[9] Review on Antimicrobial Resistance, https://amr-review.org/
[10] United Nations high-level meeting on antimicrobial resistance; http://www.who.int/antimicrobial-resistance/events/UNGA-meeting-amr-sept2016/en/

ESPAUR data was used to develop infographics for PHE's Health Matters series; this is a resource for public health professionals, which brings together important facts, Figures and evidence of effective interventions to tackle major public health problems. The AMR Health Matters resource is available for download and use at: https://www.gov.uk/government/publications/health-matters-antimicrobial-resistance

A major initiative over the last year has been to make local surveillance data available to stakeholders via Fingertips, a publicly accessible interactive web tool. In April 2015, PHE launched a series of AMR local indicators for England on the Fingertips data portal (Figure 1.1).

a)

b)

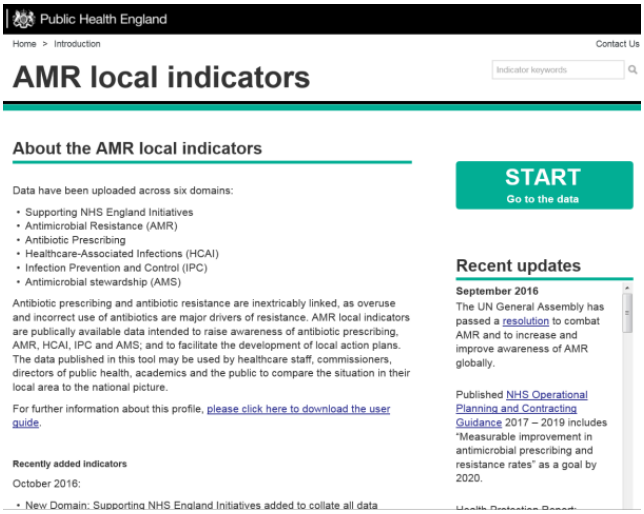


Figure 1.1 Fingertips and AMR: a) Representative presentation of Fingertips home page with link to AMR local indicators[11] b) Fingertips AMR local indicators home page

The AMR local indicators profile comprises six domains, namely:

(i) Supporting NHS England initiatives
(ii) Antimicrobial resistance (AMR)
(iii) Antibiotic prescribing (AP)
(iv) Healthcare-associated infections (HCAIs)
(v) Infection prevention and control (IPC)
(vi) Antimicrobial stewardship (AMS)

[11] Public Health England fingertips, available from; https://fingertips.phe.org.uk/profile/amr-local-indicators http://fingertips.phe.org.uk/

The data available for each domain is broken down geographically and presented at the level of individual NHS acute trusts, clinical commisioning groups (CCGs) or GP practices. Two additional domains collate all the data available for CCGs and acute trusts for ease of viewing. The corresponding data for England as a whole is also presented. This enables users to benchmark their data against both comparabale organisations and the national dataset. The AMR local indicators home page also has a link to a user guide that can be downloaded for ease of reference.

As of November 2016, data for more than 70 quality indicators was available to view, with the geographical breakdown of the data shown in Table 1.1.

Table 1.1: Number of AMR local indicators available in November 2016, by acute trust, clinical commissioning group and general practice

Domains	No of indicators available at indicated geographies		
	Acute Trust	CCG	GP
Supporting NHS England initiatives	7	5	-
Antimicrobial resistance	1	14	-
Antibiotic prescribing	6	7	4
Healthcare-associated infections	21	14	-
Infection prevention and control	4	-	-
Antimicrobial stewardship	2	1	-

The data in the Supporting NHS England initiatives domain is also available in other domains. For ease of use, this domain brings together data relevant to the NHS England AMR CQUIN (Commissioning for Quality and Innovation) goals for 2016/17.[12]

The indicators in the AMR domain include:

a) Trust-assigned and CCG-assigned rates of meticillin-resistant *Staphylococcus aureus* (MRSA) bacteraemia
b) The proportions of *E. coli* from blood tested for susceptibility to key antibiotics (third-generation cephalosporins, ciprofloxacin, gentamicin, piperacillin/tazobactam and carbapenems) and the proportions non-susceptible (apart from carbapenems) by CCG
c) The proportion of *E. coli* (including isolates reported as coliforms) from community urines tested for suscepibility to nitrofurantoin and trimethoprim and the proportions non-susceptible by CCG

[12] NHS England, 2016/17 CQUIN guidance; https://www.england.nhs.uk/nhs-standard-contract/cquin/cquin-16-17/, Publications Gateway Reference 04225,

The indicators in the AP domain include:

a) The defined daily doses (DDDs) of all antibiotics, piperacillin/tazobactam and carbapenems dispensed by acute trusts both per per 1000 admissions and per 1000 occupied bed days
b) Quarterly data from CCGs on the rates for total prescribed antibiotic items both per 1000 resident population and per STAR-PU (Specific Therapeutic group Age-sex weightings Related Prescribing Units; weighted units to allow comparisons adjusting for the age and sex of patient populations) together with12-month rolling values for the same data items
c) Quarterly data from CCGs on the proportion of prescribed antibiotics that are broad-spectrum (ie. cephalosporins, quinolones or co-amoxiclav), together with 12-month rolling values for the same data items and the ratio of trimethoprim to nitrofurantoin prescribing by quarter
d) Quarterly data from GP practices on the rates for total prescribed antibiotic items per 1000 population and per STAR-PU and proportion that are broad-spectrum

The indicators in the HCAI domain include:

a) Data from the national mandatory surveillance programmes for *Clostridium difficile* infection, orthopaedic surgical site infections and bacteraemia caused by *E. coli*, MRSA and meticillin-susceptible *S. aureus* (MSSA). The data is presented for Acute trusts and CCGs over a range of time scales

The indicators in the IPC domain include:

a) The proportion of single rooms (both with and without ensuite facilities) in acute trusts by financial year
b) The cleanliness scores for NHS trusts
c) The proportion of frontline healthcare workers in each acute trust vaccinated against seasonal influenza

The indicators in the AMS domain include:

a) The outcomes of surveys of the national ‘Start Smart Then Focus’ AMS toolkit, AMS reviews performed and submitted to PHE and implementation of AMS action plans in NHS trusts
b) Numbers of Antibiotic Guardians per 100,000 population for each CCG per calendar year

The data in each domain can be viewed in a range of formats including an overview showing counts and rates, interactive maps, spine charts that allow comparisons between areas, and graphs that show temporal trends or allow correlations between pairs of indicators. The data is variably presented over a range of timescales; including financial year, quarter or month. There is a ‘Definitions’ tab that provides comprehensive information about each indicator and the rationale for inclusion. A ‘Download’ tab allows users to download the presented data. Representative data from each domain is presented in the relevant chapters of this report.

Improve AMR surveillance

Improvements in data presentation and analysis have been made possible by continual improvements in both the quality and quantity of surveillance data over the last three years through collaborative work with the PHE Field Epidemiology Service and NHS microbiology laboratories. From September 2013 to September 2016, the number of NHS laboratories reporting antibiotic susceptibility test data to the Second Generation Surveillance System (SGSS, the PHE national surveillance database) has increased from 30% to 98%. This means that there are fewer biases in the system and a wider range of antibiotic resistance data can be reported reliably and consistently from all geographic areas.

During the same time period, the frequency of reporting has also improved, with the proportion of laboratories submitting data on a daily basis having increased from 10% to 82%; of these, 78% can do this as an automated process, requiring minimal to no 'hands on time' from microbiology staff. The improvements in daily reporting mean that PHE can now start work on developing and evaluating statistical methodology to improve the detection of possible outbreaks of drug-resistant infections.

PHE has also worked with NHS England to improve the quality and standardisation of routine antibiotic testing and interpretation of results. This improves comparability and robustness of microbiology data on which infection treatment decisions are made. The following clause is now included in the NHS Standard Contract service conditions[13]:

SC21.2 now states: "The Provider must ensure that all laboratory services (whether provided directly or under a Sub-Contract) comply with the UK Standard Methods for Investigation." With regard to this, PHE is the custodian for the Standards for Microbiological Investigations (SMI), and these standards are accredited by National Institute for Health and Care Excellence (NICE).

PHE has published the development and implementation process of the enhanced reporting system (ERS) for carbapenemase-producing organisms (CPO).[14] It has developed regular outputs for the NHS, highlighting the trusts which are reporting through this system, and the number of CPO organisms from each trust since system inception and in the most recent month. This system is undergoing a formal evaluation, which will define future developments.

[13] NHS Standard Contract 2015/16 Service Conditions, Draft for consultation, https://www.england.nhs.uk/wp-content/uploads/2014/12/nhs-stand-contrct-draft-sc-091214.pdf December 2014

[14] Freeman R *et al*. Enhanced surveillance of carbapenemase-producing Gram-negative bacteria to support national and international prevention and control efforts. Clin Microbiol Infect 27 Jul 2016

Improve antimicrobial use surveillance

ESPAUR can now track antibiotic prescribing/antimicrobial use (AMU) from each healthcare sector.

The dental subgroup of ESPAUR has worked with the Faculty of Dental Public Health, NHS Business Services Authority, PHE and NHS Digital, to develop an options paper and prepare a plan for improving the granularity of dental prescribing, In addition, ESPAUR have worked with the independent sector hospitals to understand their pharmacy systems, and scope how they can contribute to this surveillance programme.

PHE has worked with NHS England and NHS Improvement to implement the Antibiotic Prescribing Quality Measures advised by the Department of Health (DH) expert advisory committee on Antimicrobial Resistance and Healthcare-Associated Infections (ARHAI) into incentives for CCGs and acute trusts.

Improve public and professional engagement

ESPAUR launched the 'Antibiotic Guardian' (AG) campaign to move from engagement to changes in public and professional behaviour around antibiotic use. Before the launch of the 2016 World Antibiotic Awareness Week materials and campaign, more than 33,000 people engaged with this campaign. A process and outcome evaluation was performed and published. [15,16]

Evaluation of the AG campaign has determined that the campaign increased commitment to tackling AMR in both healthcare professionals and members of the public, increased self-reported knowledge and changed self-reported behaviour, particularly among people with prior AMR awareness.[9] This year the AG campaign is working with additional groups including the public through community pharmacy teams, healthcare students, school children and their carers/family to increase the impact and pledges related to these areas.

In collaboration with Health Education England (HEE), ESPAUR has scoped and developed implementation options related to education and training of healthcare professionals for AMP and stewardship competencies in undergraduate, postgraduate education, and continued professional development. PHE is now working to better understand the training needs of healthcare professionals and continues to deliver

[15] Bhattacharya A *et al*, A process evaluation of the UK-wide Antibiotic Guardian campaign: developing engagement on antimicrobial resistance. J Pub Health. 2016 (online)
[16] Chaintarli K *et al* Impact of a United Kingdom-wide campaign to tackle antimicrobial resistance on self-reported knowledge and behaviour change, BMC Public Health. 2016 May 12;16:393

training through local events and webinars in collaboration with NHS Improvement and HEE.

ESPAUR have facilitated two public debates with the aim to raise awareness of antibiotics and consider ways that the public believe could limit their use. Patient stories were developed in collaboration with the British Society for Antimicrobial Chemotherapy as part of the public debates and are available on the Antibiotic Guardian website.

ESPAUR have continued to develop and work with schools through the development and delivery of the materials on antibiotics and AMR, e-Bug, a free educational resource for classroom and home use to learn about bacteria, the spread, prevention and treatment of infection.

Improve antibiotic stewardship

ESPAUR has performed and published an assessment of AMS activities and implementation of national AMS toolkits in primary and secondary care – TARGET and Start Smart then Focus (SSTF) respectively.[17] This year a survey assessing implementation of recommended AMS interventions in community healthcare trusts was completed and initial results are presented in this report.

We have developed an antimicrobial stewardship surveillance system including tools to support stewardship audits in acute trusts and these are being used as part of the CQUIN in 2016/17.

A dental AMS toolkit has been developed and rolled out by the dental subgroup of ESPAUR in collaboration with Faculty of General Dental Practice and British Dental Association.

New work on fungal resistance, surveillance and stewardship

This year ESPAUR have also increased our outputs to look at fungal resistance, antifungal consumption and stewardship as this is an area of emerging concern. This is highlighted by increasing number of *Candida auris* infections detected in England, US and other parts of the world. Antifungal consumption is presented from the available

[17] Ashiru-Oredope et al. Implementation of antimicrobial stewardship interventions recommended by national toolkits in primary and secondary healthcare sectors in England: TARGET and Start Smart Then Focus. J Antimicrob Chemother. 2016;71(5):1408-14. doi: 10.1093/jac/dkv492. Epub 2016 Feb 10.

data in primary care but work is on-going to measure over the counter sales and use in hospitals. Antifungal stewardship is frequently neglected and ESPAUR present initial results from a survey in NHS Trusts.

Launch of the national point prevalence survey on healthcare-associated infections and antimicrobial use in acute hospitals

The aim of the survey is to determine the prevalence of devices, healthcare-associated infections and antimicrobial use in acute hospitals in England. This is the second survey that PHE has led and is occurring in all European countries in 2016-17. PHE has delivered four training events (three traditional face to face events and one webinar) to more than 350 participants from the NHS and independent sector. These covered the point prevalence survey's methodology and case definitions to ensure reliable data collection. More than 200 hospitals across the NHS and independent sector are currently collecting data on their rates of HCAI and AMU, which will be included in next year's ESPAUR report.

ESPAUR hopes that you find the outputs in this report useful in your clinical practice. We thank the members of the ESPAUR oversight group, NHS and independent sector colleagues, professional organisations and the public, for their continued contribution and challenge forwarding the AMR agenda.

Chapter 2: Antibiotic resistance in England

Introduction

This chapter presents updates on trends in AMR in a number of key pathogens. This includes those causing bacteraemia, referrals of carbapenemase-producing Enterobacteriaceae to the national reference laboratory, resistance in tuberculosis (TB), and a national outbreak of gonorrhoea caused by azithromycin-resistant gonococci. New areas covered include an assessment of the burden of bacteraemia due to resistant *E. coli* in patients of different ages, local AMR data via the PHE Fingertips web portal (as part of an initiative to improve feedback of information to stakeholders who are being encouraged to develop local action plans to reduce AMR) and the potential for using combination therapy as alternatives to the use of piperacillin/tazobactam or carbapenems for broad-spectrum empirical antibacterial therapy.

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 PHE) and the national mandatory surveillance schemes for *Escherichia coli* and staphylococcal bacteraemia. Data on carbapenemase-producing Gram-negative bacteria were obtained from the AMR and Healthcare-Associated (AMRHAI) Reference Unit. Data on the spread of azithromycin-resistant gonococci was provided by the PHE Sexually Transmitted Bacteria Reference Unit while data on TB was extracted from the Enhanced Tuberculosis Surveillance System (ETS database).

Results

Bloodstream infections

The five-year trends in resistance to key antibiotics in pathogens causing bloodstream infections are shown in Figures 2.1 to 2.7. For the majority of drug/bug combinations, the proportion of resistant isolates stayed relatively stable with only slight year-to-year fluctuation. Exceptions were resistance to piperacillin/tazobactam, which increased in both *E. coli* and *Klebsiella pneumoniae* from 8.5% to 11.7% and from 12.6% to 18.5%, respectively, and resistance to co-amoxiclav, which increased in the same species from 31% to 42% and from 18.7% to 28.2%, respectively (Figure 2.1 and 2.2). There was also a rise in vancomycin resistance in *Enterococcus* spp. from 10% in 2011 to 16% in

2015 (Figure 2.7). Longer term temporal trends together with information on rates of resistance in NHS regions are provided in Web Appendix 1.[18]

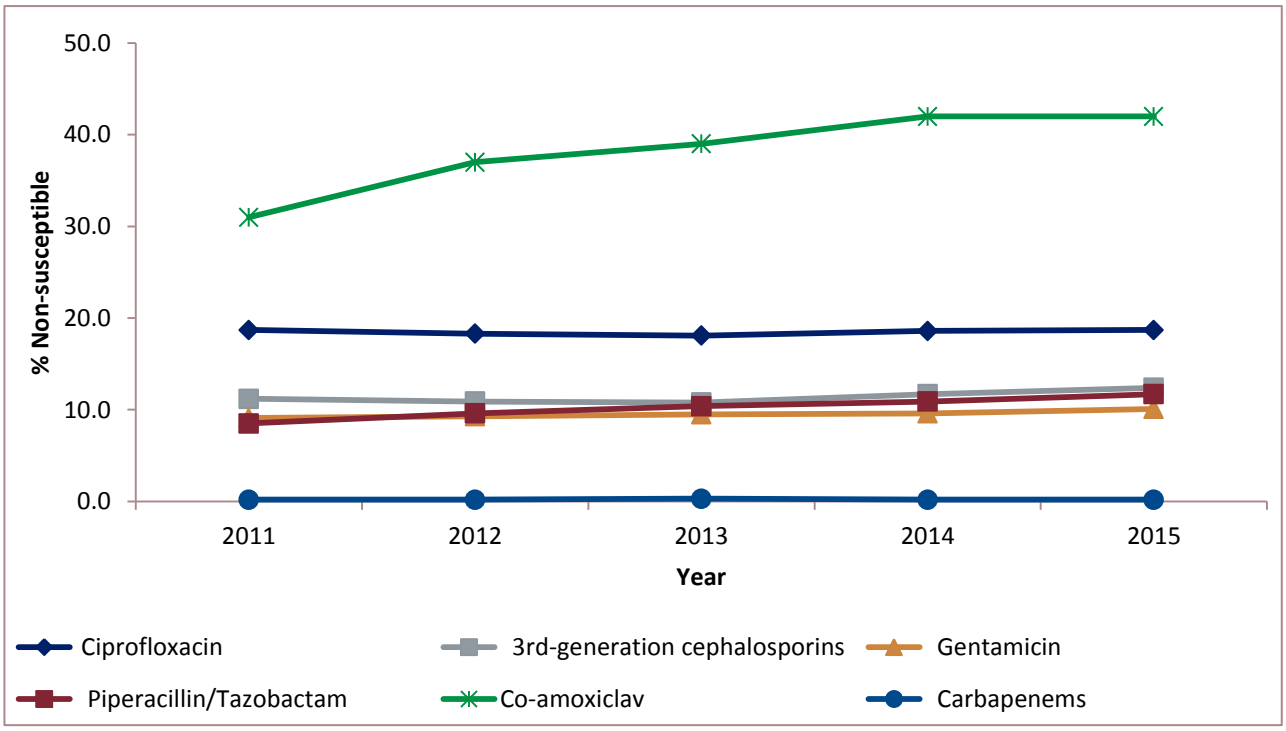


Figure 2.1 Proportions of bloodstream isolates of *E. coli* non-susceptible to indicated antibiotics

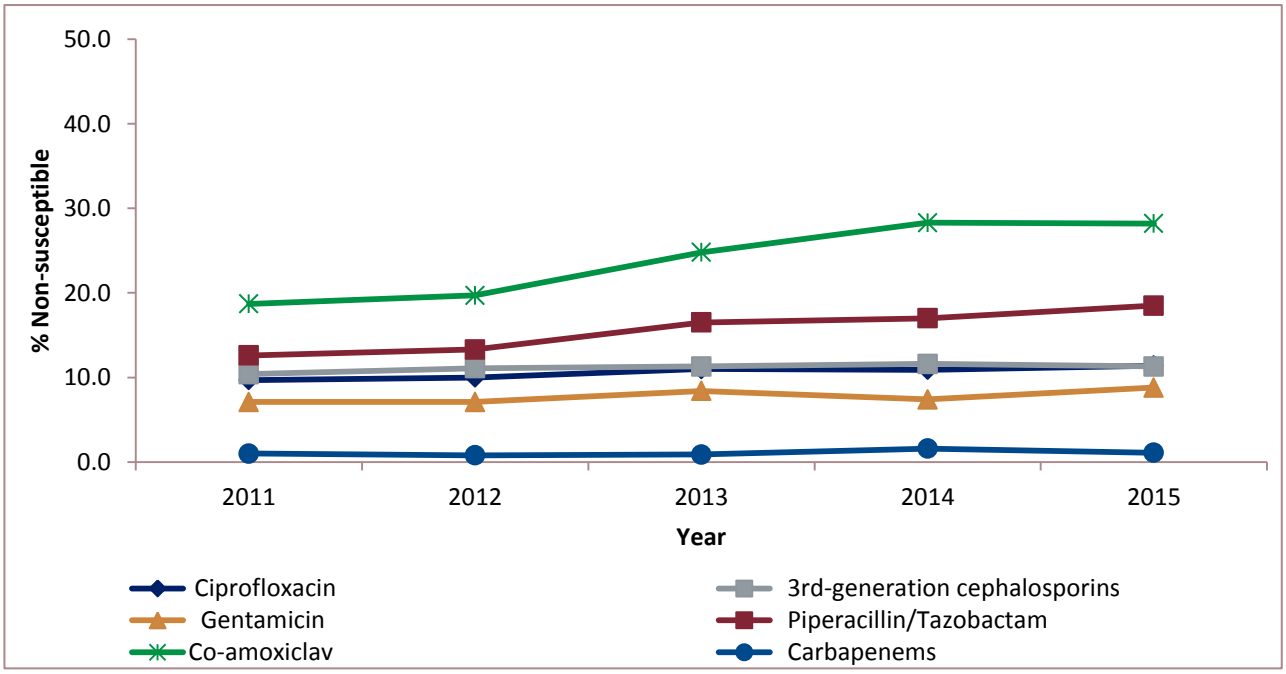


Figure 2.2 Proportions of bloodstream isolates of *K. pneumoniae* non-susceptible to indicated antibiotics

[18] Public Health England; English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 2015. Available at; https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report

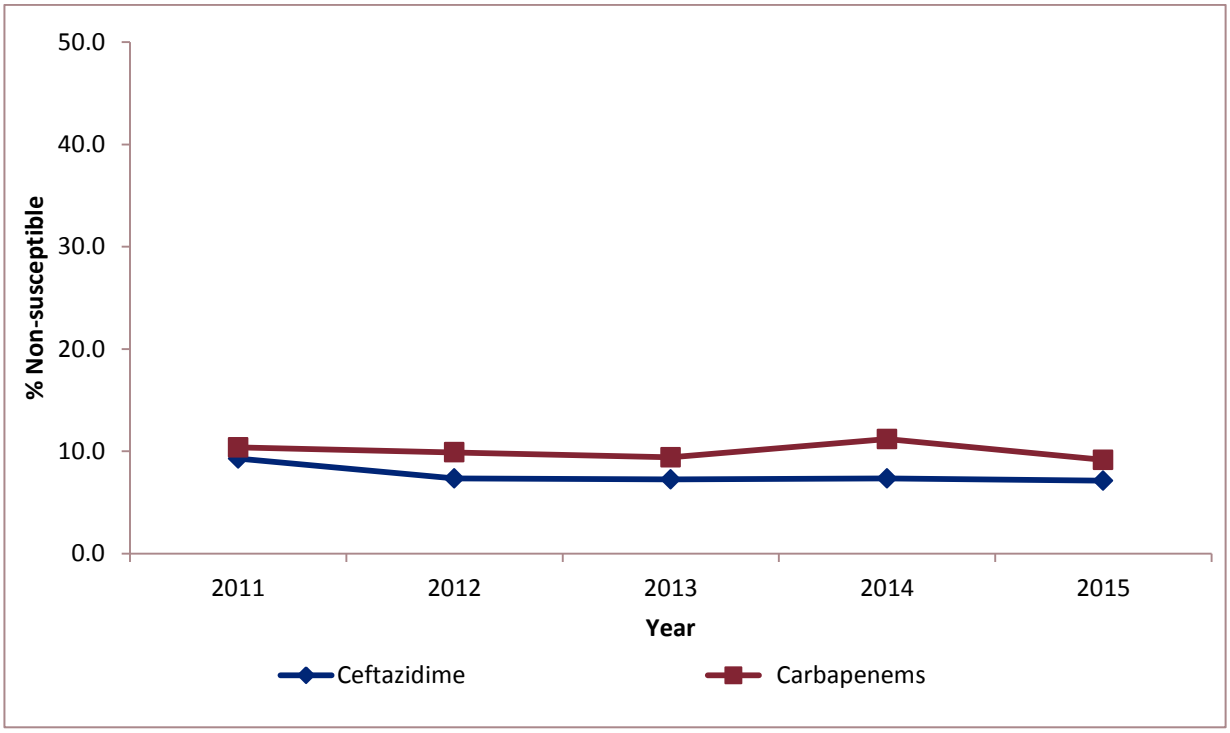


Figure 2.3 Proportions of bloodstream isolates of *Pseudomonas* spp. non-susceptible to indicated antibiotics

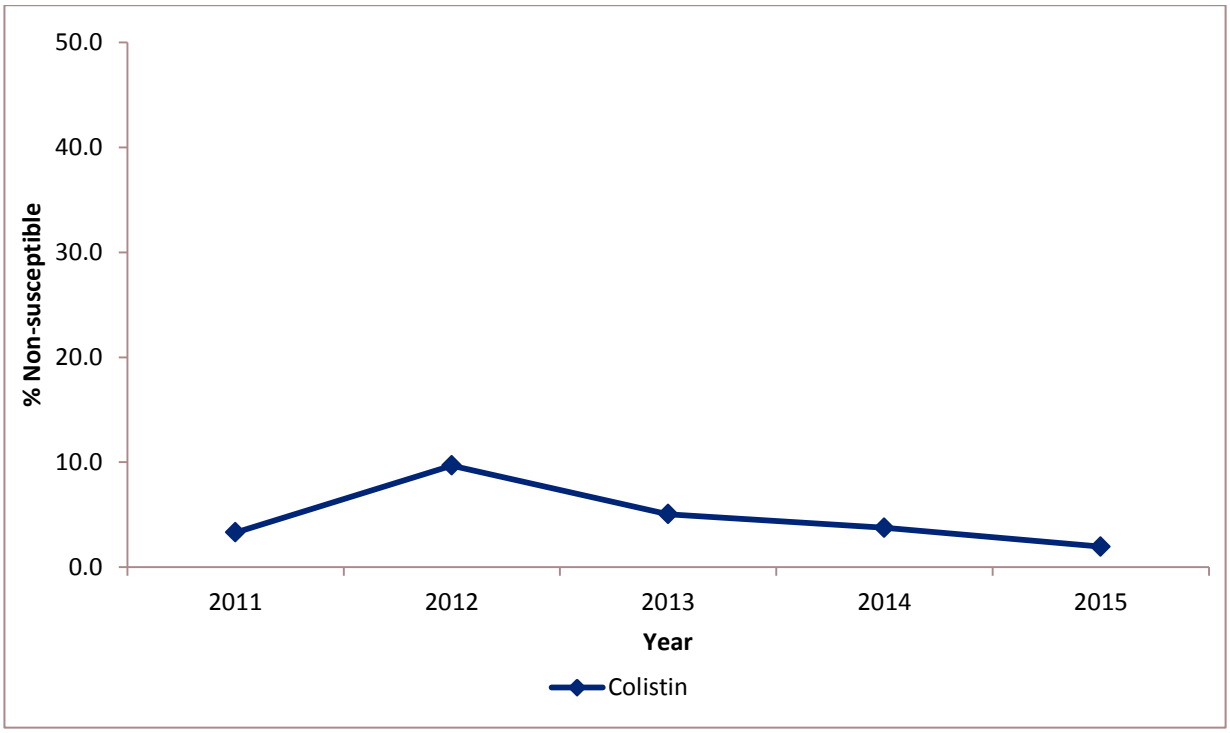


Figure 2.4 Proportions of bloodstream isolates of *Acinetobacter* spp. non-susceptible to colistin

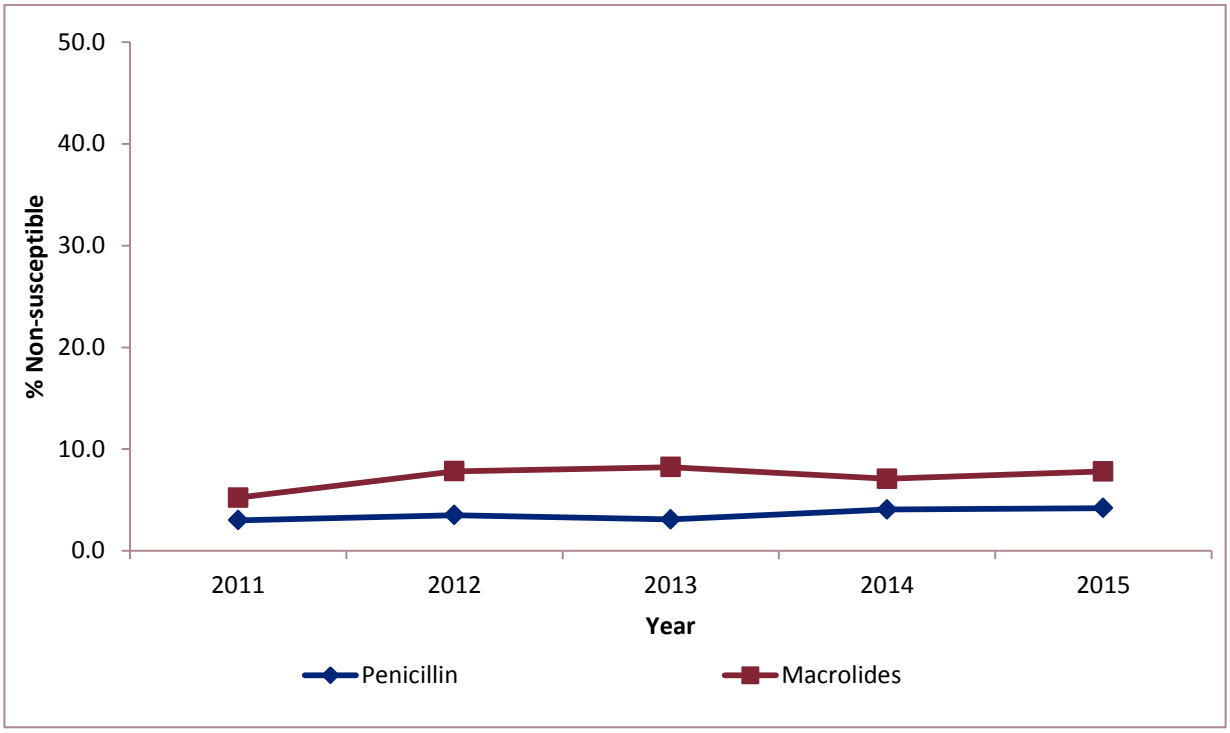


Figure 2.5 Proportions of bloodstream isolates of *S. pneumoniae* non-susceptible to indicated antibiotics

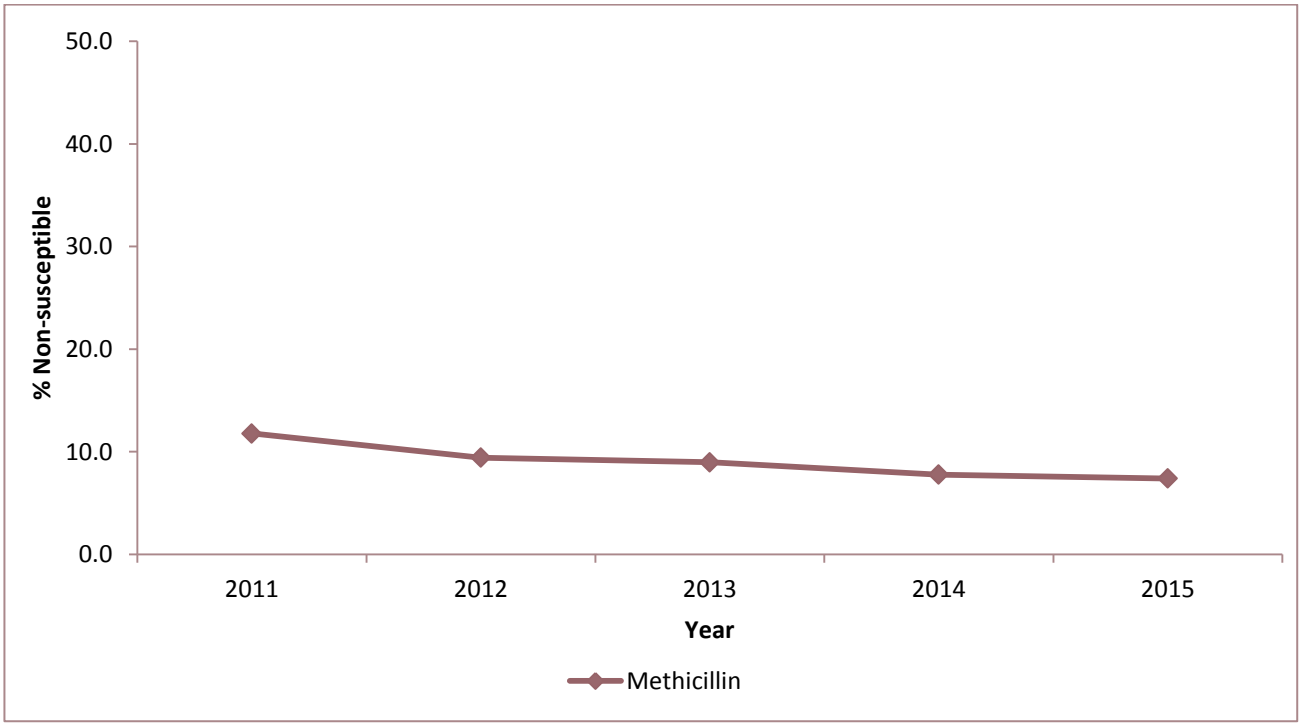


Figure 2.6 Proportions of bloodstream isolates of *S. aureus* non-susceptible to methicillin[19]

[19] Public Health England; Quarterly Epidemiological Commentary: Mandatory MRSA, MSSA and E. coli bacteraemia, and C. difficile infection data (up to April-June 2016) Data available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/551167/QEC_September_2016.pdf

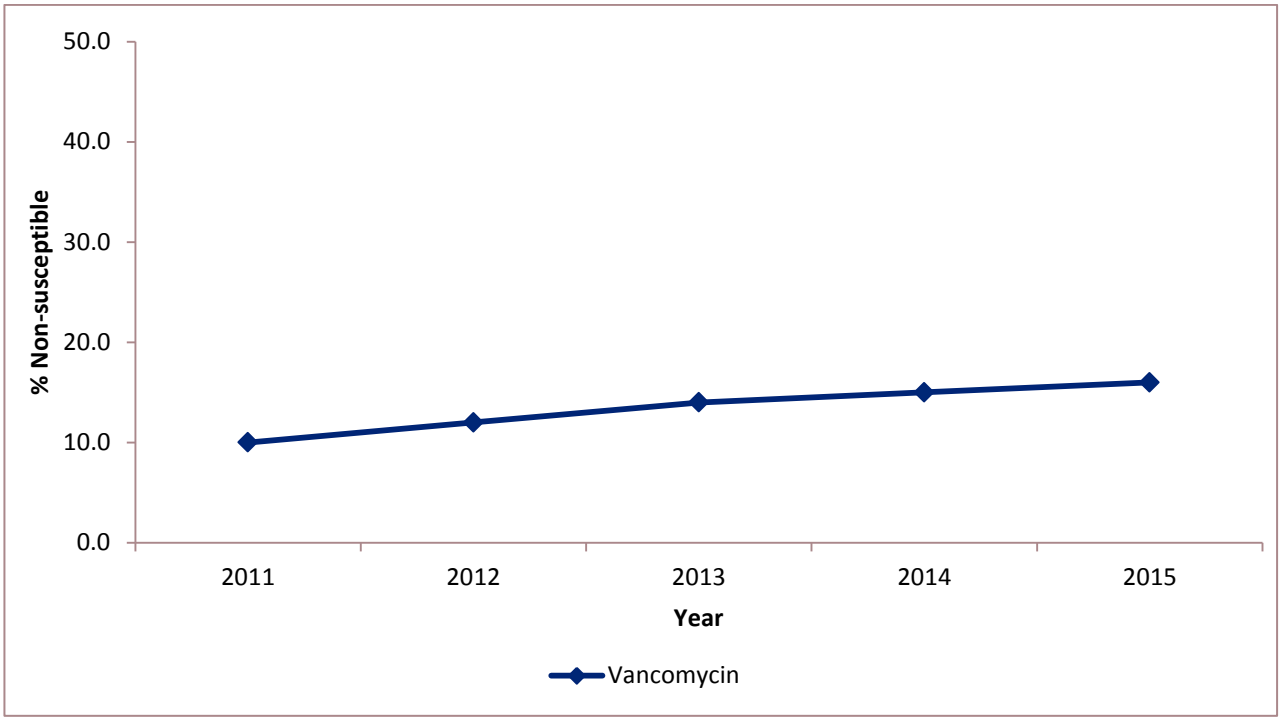


Figure 2.7 Proportions of bloodstream isolates of *Enterococcus* spp. non-susceptible to vancomycin

Increase in the burden of resistance in bloodstream infections due to *E. coli*

Data from the national mandatory surveillance programme showed that the incidence of *E. coli* bacteraemia in England rose from 35,659 cases reported in 2014, to 37,310 cases in 2015, an increase of 4.6%.[20] Therefore, although the proportion of isolates of *E. coli* causing bacteraemia that showed resistance to ciprofloxacin and third-generation cephalosporins remained relatively stable between 2014 and 2015, there was nonetheless an increase in the numbers of isolates resistant to these antibiotics (Figure 2.8). An increase in the numbers of isolates resistant to piperacillin/tazobactam was also noted, reflected both an increase in the incidence of *E. coli* causing bacteraemia and the proportion of resistant isolates in each year. Similar considerations would apply to other Gram-negative bacteria causing bacteraemia, such as *K. pneumoniae*, where the numbers of reports from laboratories in England submitted to PHE on a voluntary basis rose from 6,280 in 2014 to 6,856 in 2015, showing an increase in incidence of 9%.[21] This finding highlights the importance of improving infection prevention and control as a way of reducing the burden of antibiotic-resistant infections. 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.

[20] Public Health England; Quarterly Epidemiological Commentary: Mandatory MRSA, MSSA and *E. coli* bacteraemia, and *C. difficile* infection data (up to April-June 2016) Data available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/551167/QEC_September_2016.pdf

[21] Public Health England; Health Protection Report 2016, *Klebsiella* spp. bacteraemia: voluntary surveillance; Available from; https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/530168/hpr1916_klbsll.pdf.

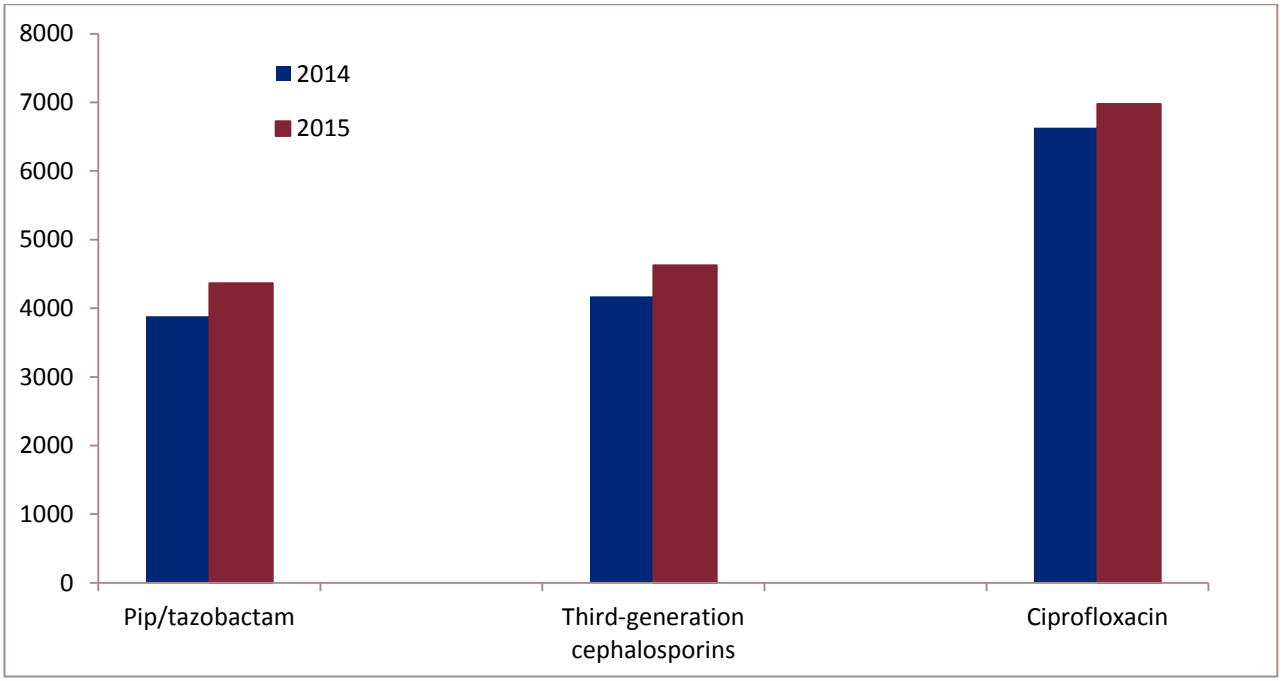


Figure 2.8 Number of bacteraemia isolates of *E. coli* resistant to indicated antibiotics in 2014 and 2015 in England

Incidence of resistance in bloodstream infections caused by *E. coli* in patients of different ages

The risk of bacteraemia is not uniform in patients of different ages. For most pathogens, including *E. coli*, a higher incidence of bacteraemia is typically seen in the very young and the elderly compared to patients of middle years (Figure 2.9). Associated with this, the burden of antibiotic resistant infections will also vary by age. The association of resistance with patient age is complex, as in addition to the varying incidence of infection, blood culture isolates from patients of different ages may vary in terms of the proportion that are resistant to different antibiotics. For example, over the five-year period 2011 to 2015, the proportion of isolates resistant to third-generation cephalosporins was consistently lowest in the <1 year age group and highest in patients aged 1-14 years (Figure 2.10). However, the situation varied by antibiotic with, for example, resistance to co-amoxiclav also being consistently lower in patients aged <1 year but with little difference see between the other patient age groups (data not shown).

Examples of the variation in the incidence of resistance, by age group, for two antibiotic classes, namely third-generation cephalosporins and ciprofloxacin (a quinolone) are shown in Figure 2.11. As with incidence of infection, resistance is highest in the extremes of life. Hence, interventions to reduce antibiotic resistance may need to be focussed on these groups as they are at increased risk of having infections that are resistant to key antibiotics.

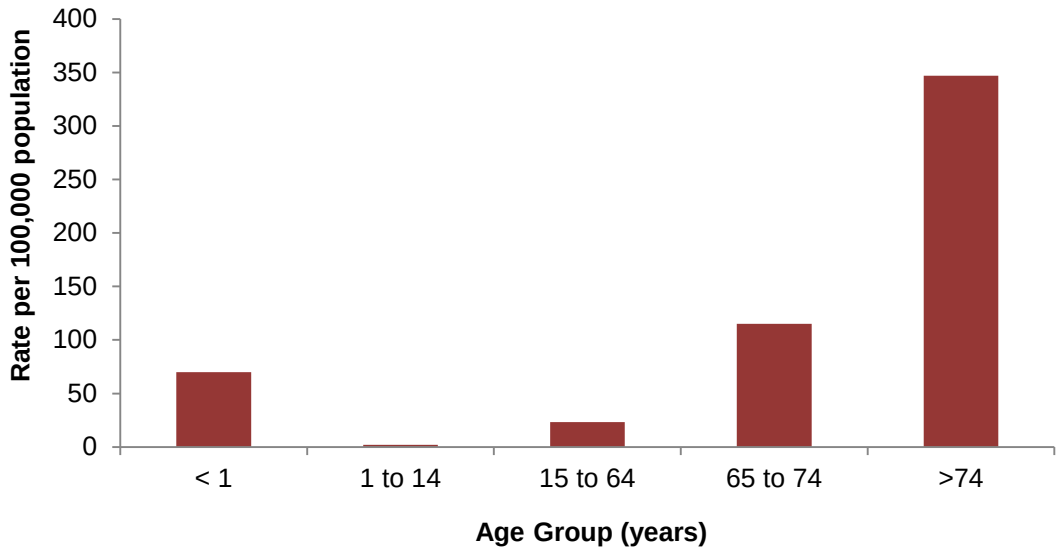


Figure 2.9 *E. coli* bacteraemia rates per 100,000 population by age in 2015 (based on voluntary reports to SGSS)

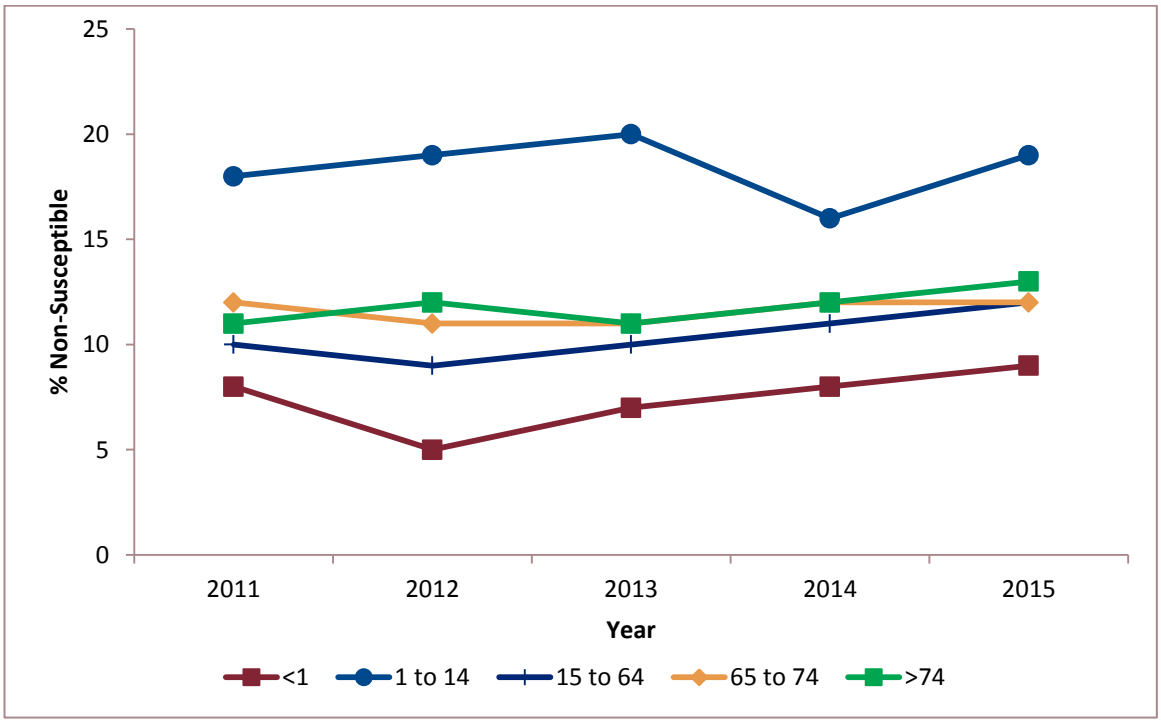


Figure 2.10 Proportion of *E. coli* from blood that are resistant to third-generation cephalosporins in patients of different age groups

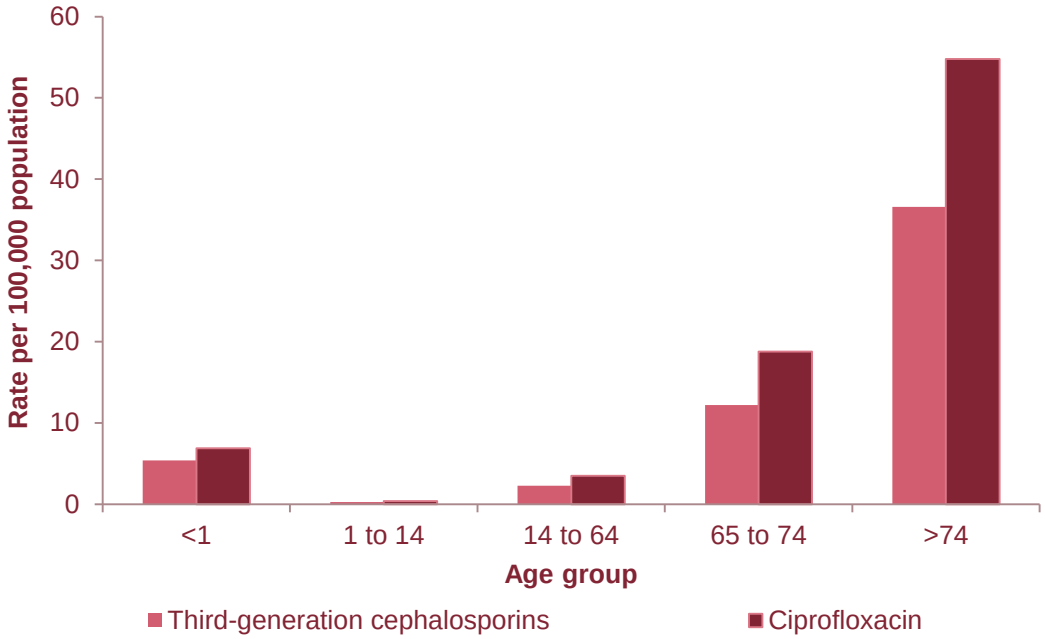


Figure 2.11 Rates of *E. coli* bacteraemia resistant to third-generation cephalosporins or ciprofloxacin in patients of different age groups. Data derived from voluntary reports to SGSS; 85% of isolates were subject to susceptibility tests

Provision of local AMR data on Fingertips

As of November 2016, there are 15 indicators in the 'Antimicrobial Resistance' domain of the AMR local indicators profile in Fingertips. The 15 indicators comprise trust-assigned and CCG-assigned MRSA bacteraemia rates, the proportions of *E. coli* from blood tested for susceptibility to carbapenems, third-generation cephalosporins, ciprofloxacin, gentamicin and piperacillin/tazobactam, the proportions of tested isolates resistant to each (apart from carbapenems), the proportion of community *E. coli* urine specimens tested for susceptibility to trimethoprim and nitrofurantoin, and the proportions of such isolates that are non-susceptible to each. Apart from trust-assigned MRSA, all the other indicators are reported at the level of CCGs.

Some examples of AMR outputs from Fingertips are given below:

1. Geographical variation in the proportions of *E. coli* from blood tested for susceptibility to particular antibiotics and the rates of resistance among tested isolates

National surveillance of AMR involves collation of routinely generated antibiotic susceptibility test results from hospital microbiology laboratories. It is therefore of importance to assess variation in testing policies with regard to which pathogens are tested for susceptibility to which antibiotics. As shown in Figure 2.12, the map tool in the AMR local indicators profile in Fingertips allows easy visualisation of geographical

variation in testing for susceptibility to particular antibiotics, in this case for blood culture isolates of *E. coli* tested for susceptibility to third-generation cephalosporins and carbapenems. The map tool can also be used to show geographical variation in non-susceptibility to tested antibiotics (Figure 2.13).

The colour-coded maps are interactive and running the cursor over the map identifies individual CCGs and gives the proportion of isolates tested and resistant. The map tool also provides an interactive colour-coded histogram that ranks the CCGs in order of the proportion of isolates tested and the proportions resistant. The data in Fingertips indicates that for 95% of the CCGs in England, greater than 90% of the blood culture isolates of *E. coli* are tested for susceptibility to third-generation cephalosporins and carbapenems. Thus, while some geographical areas have scope for improvement, overall, the national picture in terms of susceptibility testing seems robust. If those CCGs which currently have low levels of testing should seek to make improvements, local data can also be formatted graphically to show trends over time, thus facilitating monitoring of progress.

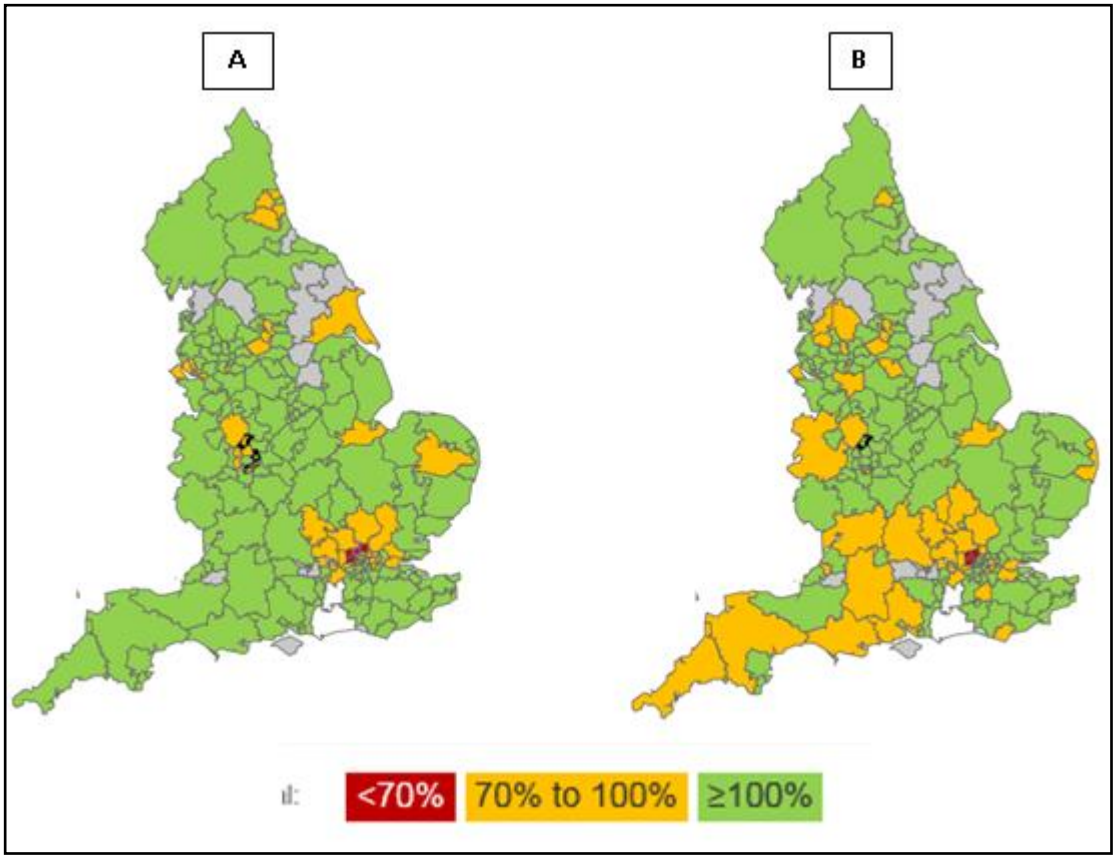


Figure 2.12 Proportion of *E. coli* from blood tested for susceptibility to: (A) third-generation cephalosporins; (B) carbapenems. Data presented by CCG for Q2 2016

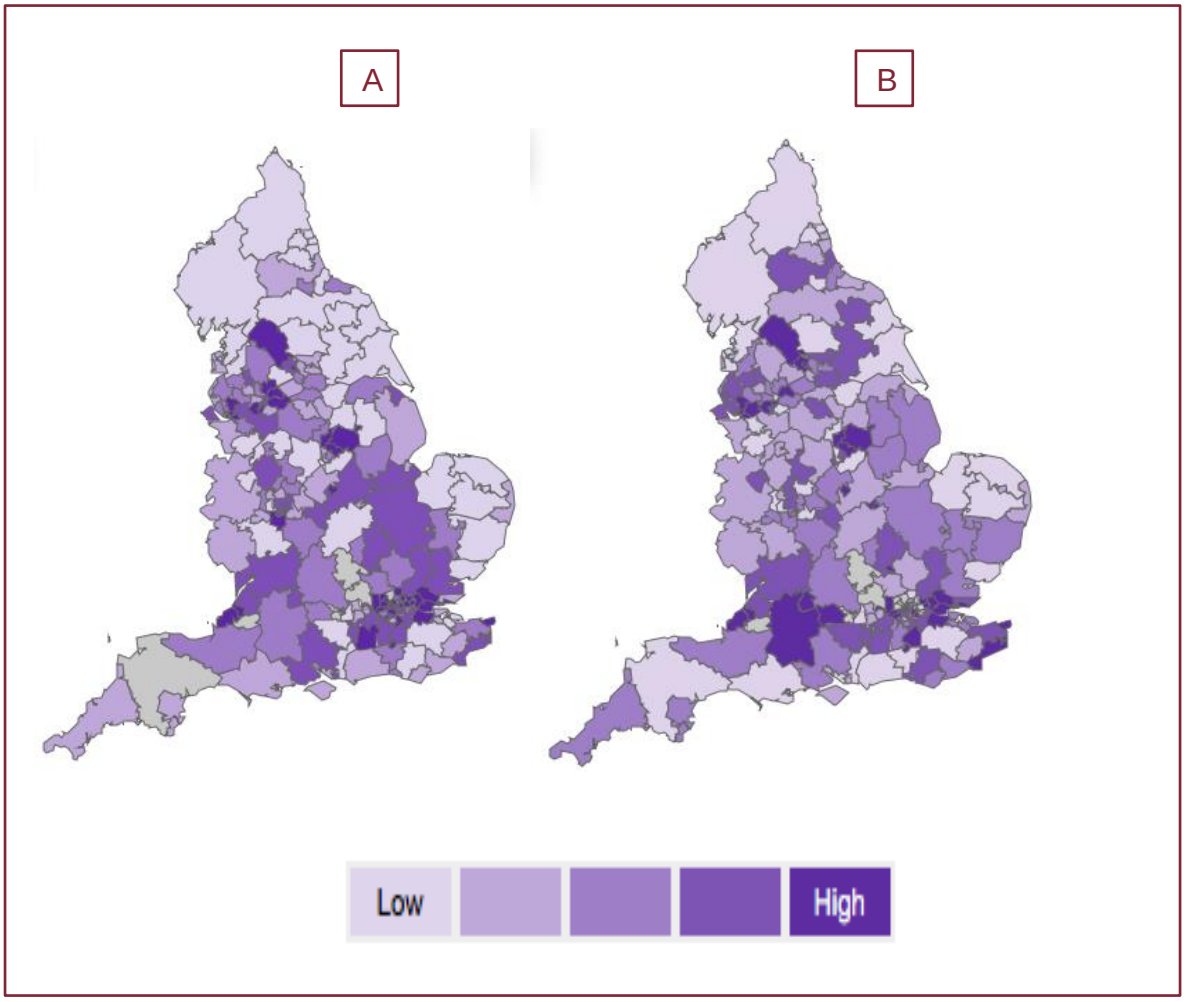


Figure 2.13 Rolling quarterly average proportion of *E. coli* from blood non-susceptible to: (A) Ciprofloxacin; (B) third-generation cephalosporins. Data presented by CCG for Q2 2016. The colour coding for the level of resistance is presented in quintiles

While the levels of susceptibility testing and rates of resistance to particular antibiotics can be mapped and presented at CCG level (based on the patient's residence), a limitation is that comparable data is not currently available at the level of acute trusts. This is because microbiology laboratories may provide a service for more than one hospital, and the location of individual patients from whom blood cultures are taken for testing cannot currently be ascertained with complete certainty. Work is in progress to try to amend the IT infrastructure to address this shortcoming to the system.

2. Susceptibility of *E. coli* from community urine specimens to nitrofurantoin and trimethoprim

Analysis of mandatory surveillance data on *E. coli* bacteraemia indicates that for cases where an underlying focus of infection is reported, about half implicate a urinary tract infection (UTI). Thus, better management of UTIs is seen as a potential intervention to reduce the incidence of *E. coli* bacteraemia. PHE guidance on the treatment of uncomplicated UTIs in the community recommends nitrofurantoin as the preferred first-line therapy. However, analysis of prescribing data indicates that trimethoprim continues to be widely used (see Chapter 3). The rate of resistance to each antibiotic in CCGs across England is shown in Figure 2.14. Rates of resistance to trimethoprim ranged from 16.3% to 66.7%, with 86% of CCGs having resistance rates of 25% or more; the median for England was 29.1%. By contrast, resistance to nitrofurantoin ranged from 0.3% to 12.8%, the median for England being 3.6%. 'Fingertips' also allows trends in resistance to trimethoprim and nitrofurantoin in individual CCGs over time to be easily monitored, as shown in Figure 2.15.

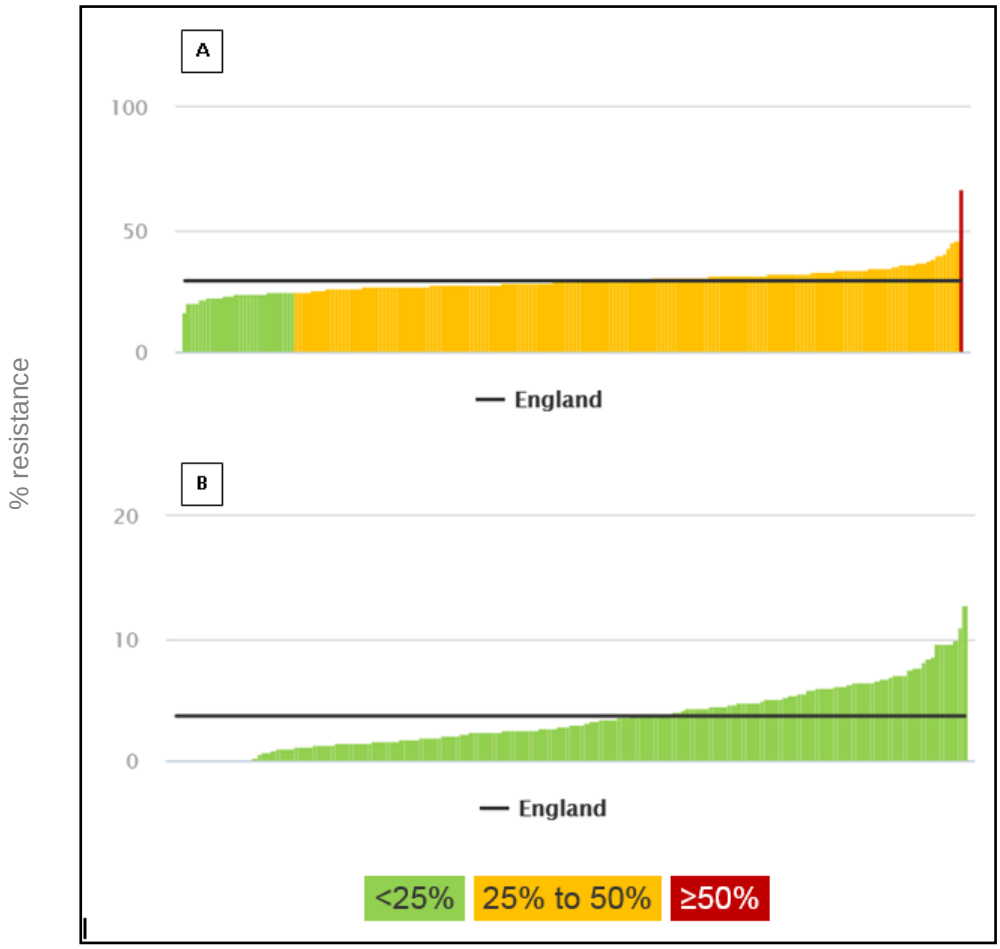


Figure 2.14 Rates of resistance to trimethoprim (A) and nitrofurantoin (B) in *E. coli* from community UTIs by CCG for Q2, 2016. The histograms are interactive and rates of resistance for individual CCGs are shown when the cursor is run over the histogram

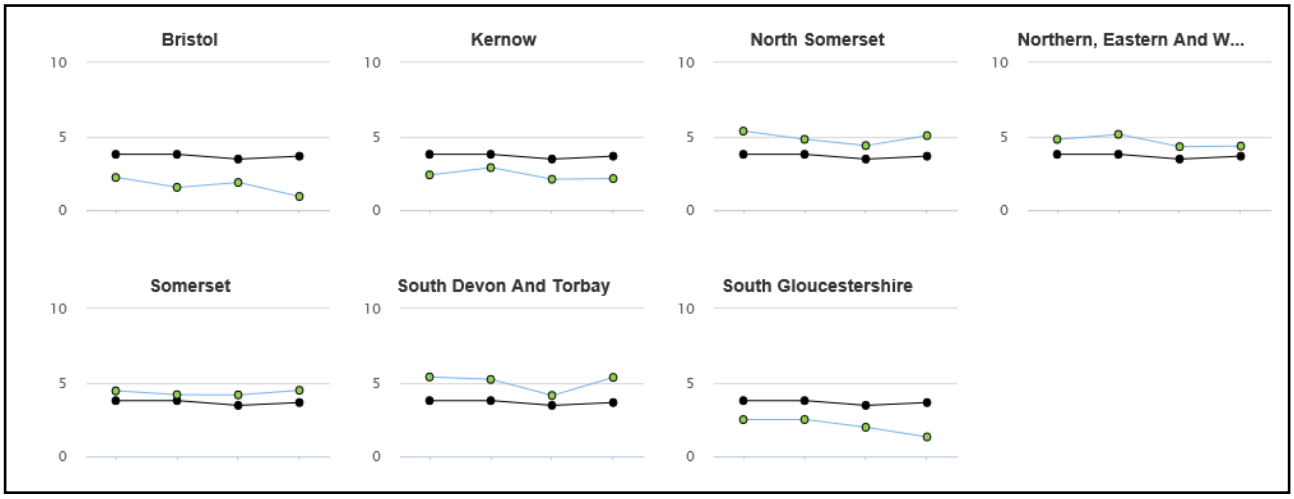


Figure 2.15 Trends in resistance (%) to nitrofurantoin in *E. coli* from community UTIs shown for CCGs in the South West NHS region; data shown by quarter from Q3 2015 to Q2 2016. Blue line, CCG; black line, England

3. Comparison of indicators using Fingertips.

Using the 'Compare Indicators' view tab in Fingertips it is possible to look for potential correlations between different indicators. For example, Figure 2.16 shows a measure of prescribing of trimethoprim against the proportion of *E. coli* from community UTIs that are resistant, with each circle representing an individual CCG. The map is interactive with the identity of each CCG shown when the cursor is pointed at an individual circle.

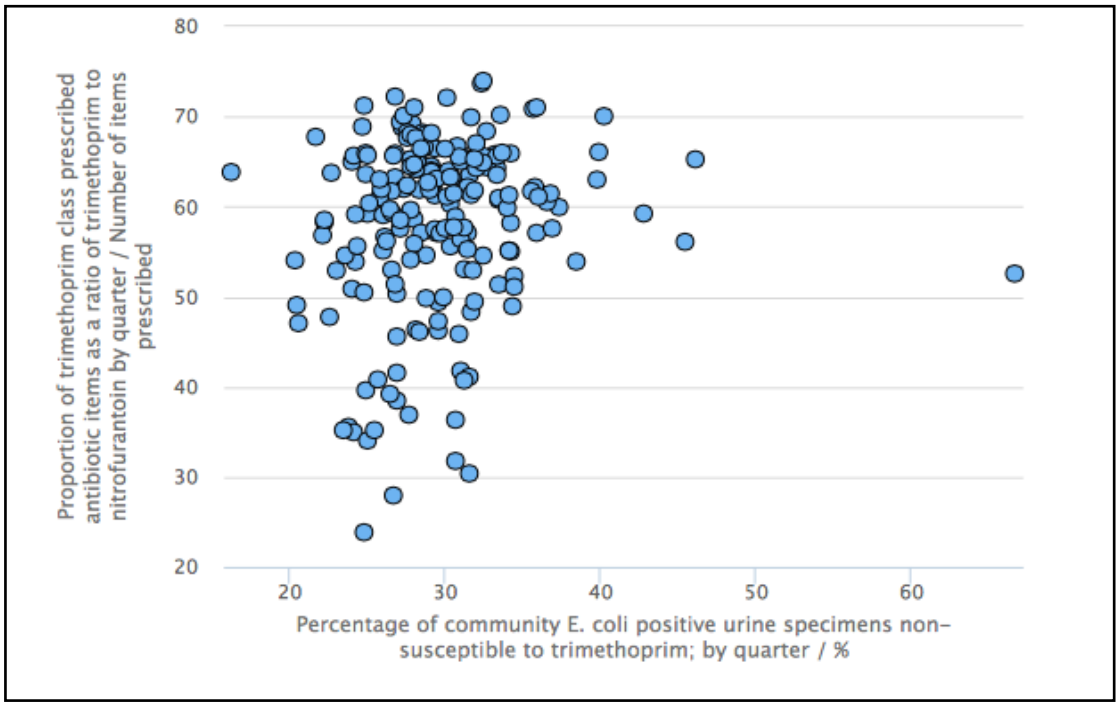


Figure 2.16 Comparison of trimethoprim prescribing against the proportion of *E. coli* from community UTIs that are trimethoprim resistant. Each circle represents a CCG

Surveillance of carbapenemase-producing Enterobacteriaceae

National surveillance data (Figures 2.1 and 2.2) indicate that carbapenem resistance remains uncommon in *E. coli* and *Klebsiella spp.* isolated from blood (≥98% of isolates susceptible). However, data from the PHE Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit show a continued year-on-year increase in the numbers of isolates of Gram-negative bacteria confirmed to produce carbapenemases, with 1,893 Enterobacteriaceae so confirmed in 2015 (Figure 2.17). Carbapenemase-producing Enterobacteriaceae (CPE) appears widely distributed, with isolates having been referred from most UK regions.

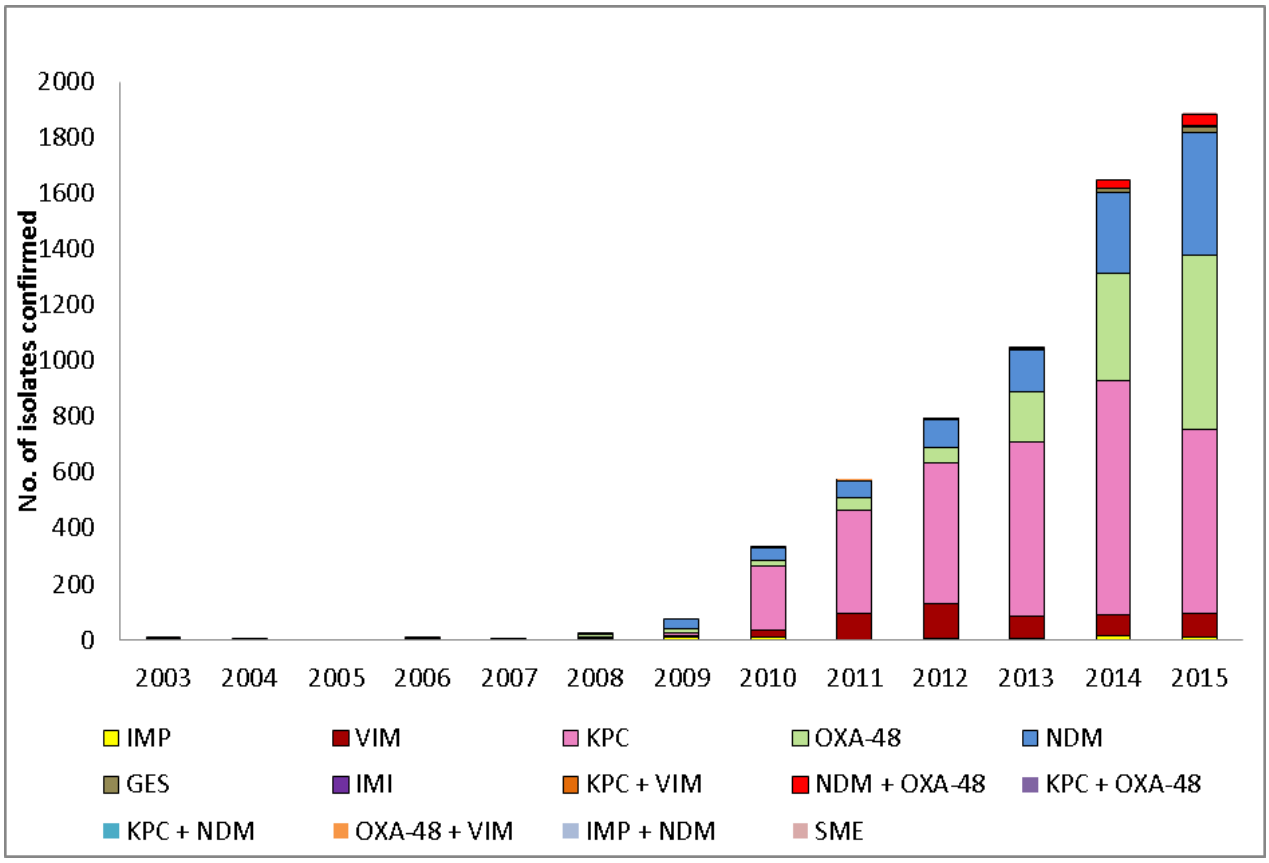


Figure 2.17 Number of isolates referred from UK hospital microbiology laboratories confirmed as carbapenemase-producing Enterobacteriaceae by AMRHAI, 2003-2015

Fewer *Klebsiella pneumoniae* carbapenemase (KPC)-producers were confirmed by AMRHAI in 2015 compared with 2014, because a laboratory in the North West that had previously referred KPC-positive isolates on a regular basis implemented local molecular testing for carbapenemases and referred fewer cases for centralised testing. KPC-producing Enterobacteriaceae (predominantly *K. pneumoniae*) are increasingly

identified in the UK, although without the major outbreaks seen in the North West.[22] Almost two-thirds (64%) of *K. pneumoniae* isolates referred from laboratories outside of the North West and with KPC enzymes belong to clonal group 258, which includes the internationally disseminated lineage sequence type ST258.[23] However, there have been relatively few clusters of infections or colonisations caused by ST258 compared with countries such as Greece, Italy, Israel and the USA, where ST258 has been responsible for large outbreaks. Plasmid spread also plays a role in KPC spread between different strains and genera.

As observed in Europe within the last two years, AMRHAI data indicate an increase in Enterobacteriaceae producing NDM and OXA-48-like carbapenemases. Amongst NDM-producers, the most common hosts (59%) were *Klebsiella spp*. Most belonged to sporadic strains or previously described international lineages (including STs 11, 14 and 15); although there is less evidence for the role of these clones in dissemination of New Delhi metallo-β-lactamase-1 (NDM) carbapenemases than there is for ST258 and KPC enzymes. Instead, diverse plasmids are thought to play a major role in spread of NDM carbapenemases between different strains, species and genera.[24] *K. pneumoniae* belonging to diverse STs were also the most common hosts (55%) amongst OXA-48-like producers referred to AMRHAI. Eighty-one per cent of *K. pneumoniae* (and 65% of total Enterobacteriaceae) carrying 'classic' OXA-48 carried the plasmid pOXA-48a, which has been associated with multiple polyclonal and cross-species outbreaks. In contrast, almost half of all *E. coli* producing OXA-48-like carbapenemases belonged to ST38, which has been shown to carry OXA-48 integrated into the chromosome.[25]

The potential use of antibiotic combinations for empirical treatment

As part of the national strategy to tackle AMR, prescribers are being urged to reduce their prescribing of broad-spectrum antibiotics, particularly carbapenems and piperacillin/tazobactam, with a view to reducing the selective pressure for emergence of resistance to these critically important antibiotics. Empirical treatment of serious infections requires broad-spectrum coverage, and in the absence of single agent alternatives to carbapenems and piperacillin/tazobactam, consideration is being given to the use of antibiotic combinations. In this section we report and compare the proportion of *E. coli* and *K. pneumoniae* isolates that were resistant to aminoglycosides (gentamicin and amikacin), co-amoxiclav, ciprofloxacin or third-generation

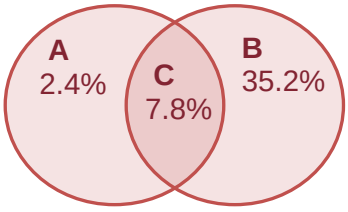
[22] Poole K et al. Active case finding for carbapenemase-producing Enterobacteriaceae in a teaching hospital: prevalence and risk factors for colonization. J Hosp Infect. 2016 Oct;94(2):125-9. doi: 10.1016/j.jhin.2016.06.019. Epub 2016 Jun 29.
[23] Findlay J et al. Editor's Choice: KPC enzymes in the UK: an analysis of the first 160 cases outside the North-West region, J Antimicrob Chemother 2016; 71: 1199-1206
[24] Jain A et al. NDM carbapenemases in the United Kingdom: an analysis of the first 250 cases, J Antimicrob Chemother 2014; 69: 1777-84
[25] Turton JF et al., Clonal expansion of *Escherichia coli* ST38 carrying a chromosomally integrated OXA-48 carbapenemase gene, J Med Microbiol 2016; 65:538-46

cephalosporins, either as single agents or in combination. Isolates were categorised as ‘susceptible’ to antibiotic combinations if they were susceptible to either one or both drugs, and as ‘resistant’ if they were resistant to both individual agents in the combination.

It should be noted that this analysis is based on the use of routinely generated data on susceptibility testing of blood culture isolates reported by hospital microbiology laboratories in England in 2015. However, inter-laboratory variation with regard to which antibiotics are included in routine test panels served to lower the numbers of isolates available for inclusion in the analysis, as only isolates with susceptibility test results for both antibiotics in each combination could be used. In particular it is noteworthy that while 91% of blood culture isolates of *E. coli* reported to SGSS had results for gentamicin, only 51% had results for amikacin. This variation in testing practice may also have contributed to the slight variation in the reported rates of resistance to individual antibiotics when the different combinations are compared, either amongst themselves, or with the data shown in other figures within the report.

(a) Aminoglycoside/co-amoxiclav combinations

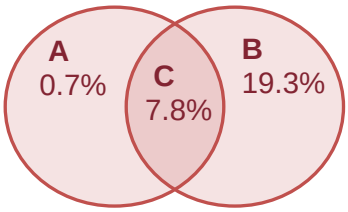
The proportion of blood culture isolates of *E. coli* and *K. pneumoniae* resistant to combinations of gentamicin and co-amoxiclav or amikacin and co-amoxiclav are shown in Figures 2.18 and 2.19 respectively. For *E. coli*, rates of resistance to gentamicin/co-amoxiclav and to amikacin/co-amoxiclav were 7.8% and 2.5% respectively, while for *K. pneumoniae* the corresponding values were 7.8% and 2.0%.



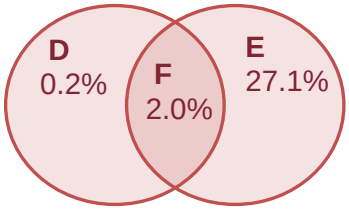
A, Gentamicin
B, Co-amoxiclav
C, Gentamicin/co-amoxiclav

D, Amikacin
E, Co-amoxiclav
F, Amikacin/co-amoxiclav

Figure 2.18 Resistance of *E. coli* to indicated antibiotics



A, Gentamicin
B, Co-amoxiclav
C, Gentamicin/co-amoxiclav

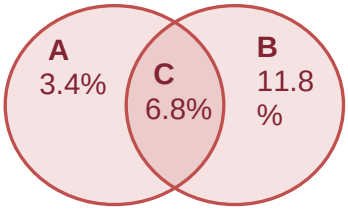


D, Amikacin
E, Co-amoxiclav
F, Amikacin/co-amoxiclav

Figure 2.19 Resistance of *K. pneumoniae* to indicated antibiotics

(b) Aminoglycoside/ciprofloxacin combinations

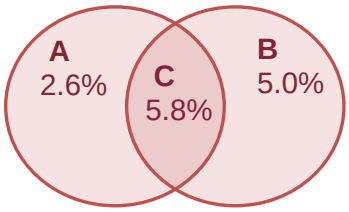
The proportion of blood culture isolates of *E. coli* and *K. pneumoniae* resistant to combinations of gentamicin and ciprofloxacin or amikacin and ciprofloxacin are shown in Figures 2.20 and 2.21, respectively. For *E. coli*, rates of resistance to gentamicin/ciprofloxacin and to amikacin/ciprofloxacin were 6.8% and 2.5%, respectively, while for *K. pneumoniae* the corresponding values were 5.8% and 1.7%.



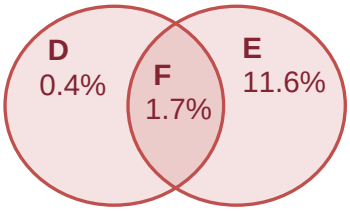
A, Gentamicin
B, Ciprofloxacin
C, Gentamicin/ciprofloxacin

D, Amikacin
E, Ciprofloxacin
F, Amikacin/ciprofloxacin

Figure 2.20 Resistance of *E. coli* to indicated antibiotics



A, Gentamicin
B, Ciprofloxacin
C, Gentamicin/ciprofloxacin



D, Amikacin
E, Ciprofloxacin
F, Amikacin/ciprofloxacin

Figure 2.21 Resistance of *K. pneumoniae* to indicated antibiotics

(c) Aminoglycoside/third-generation cephalosporin combinations

The proportion of blood culture isolates of *E. coli* and *K. pneumoniae* resistant to combinations of gentamicin and third-generation cephalosporins (3GCs) or amikacin and 3GCs are shown in Figures 2.22 and 2.23 respectively. For *E. coli*, rates of resistance to gentamicin/third-generation cephalosporins and to amikacin/ third-generation cephalosporins were 5.1% and 1.3%, respectively, while for *K. pneumoniae* the corresponding values were 5.1% and 1.3%.

A, Gentamicin
B, 3GCs
C, Gentamicin/3GCs

D, Amikacin
E, 3GCs
F, Amikacin/3GCs

Figure 2.22 Resistance of *E. coli* to indicated antibiotics

A, Gentamicin
B, 3GCs
C, Gentamicin/3GCs

D, Amikacin
E, 3GCs
F, Amikacin/3GCs

Figure 2.23 Resistance of *K. pneumoniae* to indicated antibiotics

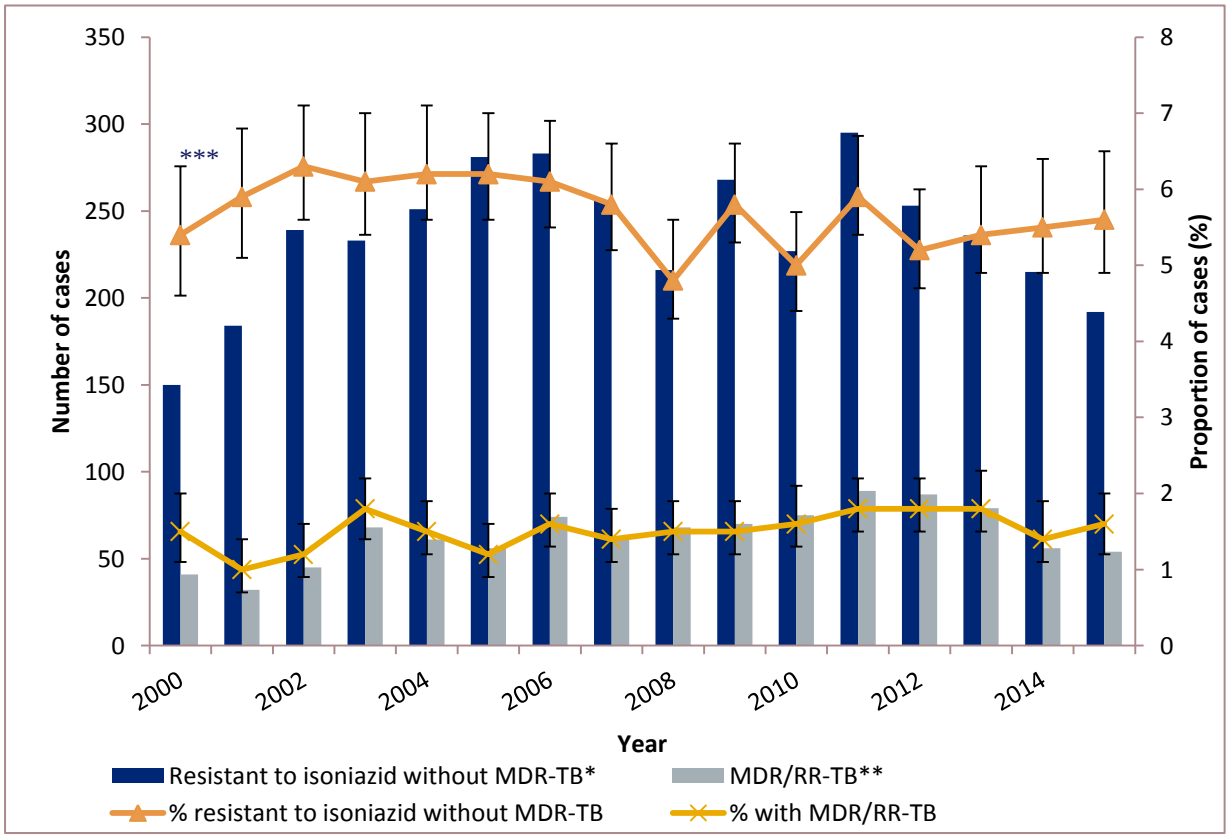
Tuberculosis

In 2015 in England, 5,758 cases of TB were notified, a rate of 10.5 cases per 100,000 population (95% confidence interval (CI) 10.2-10.8). Seventy two per cent (4,087/5,637) of cases were people born outside the UK.

Drug resistance in TB

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

In 2015, drug susceptibility test (DST) results for at least isoniazid and rifampicin were available for 99.4% (3,440/3,460) of culture-confirmed cases notified in England. Among these 7.4% 255/3,440) were resistant to at least one first-line antibiotic, with 5.6% (192/3,440) resistant to isoniazid without multi-drug resistant TB (MDR-TB) (Figure 2.24, Table 2.1). The number and proportion of MDR-TB cases with initial resistance to rifampicin and isoniazid increased from 0.7% (22/3,145) in 2001 to a peak of 1.6% (81/4,967) in 2011, and has since decreased to 1.3% (46/3,440) in 2015 (Table 2.1).



* Culture confirmed cases with DST results for at least isoniazid and rifampicin; and resistant to isoniazid without MDR-TB

** Culture confirmed cases with DST results for at least isoniazid and rifampicin resistant to rifampicin, including those with MDR-TB

*** 95% CI for % resistant to isoniazid without MDR-TB

Figure 2.24 Number and proportion of TB cases with initial drug resistance, England, 2000-2015

TB cases with any resistance to rifampicin, including those with MDR-TB, are hereafter referred to as multi-drug resistant/rifampicin resistant (MDR/RR) TB. The number and proportion of MDR/RR-TB cases increased from 32 (1.0%) in 2001 to a peak of 89 (1.8%) in 2011, and has since decreased to 54 (1.6%) in 2015 (Figure 2.24; Table 2.1). The majority of MDR/RR-TB cases notified in 2015 were non-UK born (90.6%, 48/53), and for those where year of entry to the UK was known, 56.8% (25/44) had entered the UK within the past six years. The most frequent countries of birth of MDR/RR-TB cases were India (7), Lithuania (6) and the UK (5). Cases born in Lithuania had the highest proportion of MDR/RR-TB (16.2%, 6/37). A high proportion of MDR/RR-TB cases in 2015 had at least one social risk factor (16.7%, 8/48).

Table 2.1: Number and proportion of TB cases with drug resistance, England, 2000-2015

Year	Isoniazid resistance without MDR-TB cases*		Rifampicin resistance without MDR-TB cases**		MDR-TB cases		MDR/RR-TB cases#		Proportion of MDR/RR-TB cases that are rifampicin resistant cases without MDR-TB	Extensively Drug Resistant (XDR)-TB cases	
	n	%	n	%	n	%	n	%	%	n	%
2000	150	5.4	13	0.5	28	1.0	41	1.5	31.7	0	0.0
2001	184	5.9	10	0.3	22	0.7	32	1.0	31.3	0	0.0
2002	239	6.3	10	0.3	35	0.9	45	1.2	22.2	0	0.0
2003	233	6.1	19	0.5	49	1.3	68	1.8	27.9	1	0.03
2004	251	6.2	16	0.4	45	1.1	61	1.5	26.2	0	0.0
2005	281	6.2	15	0.3	41	0.9	56	1.2	26.8	0	0.0
2006	283	6.1	20	0.4	54	1.2	74	1.6	27.0	0	0.0
2007	256	5.8	13	0.3	49	1.1	62	1.4	21.0	0	0.0
2008	216	4.8	18	0.4	50	1.1	68	1.5	26.5	2	0.0
2009	268	5.8	11	0.2	59	1.3	70	1.5	15.7	2	0.04
2010	227	5.0	10	0.2	65	1.4	75	1.6	13.3	2	0.04
2011	295	5.9	8	0.2	81	1.6	89	1.8	9.0	6	0.12
2012	253	5.2	10	0.2	77	1.6	87	1.8	11.5	2	0.0
2013	236	5.4	10	0.2	69	1.6	79	1.8	12.7	3	0.07
2014	215	5.5	4	0.1	52	1.3	56	1.4	7.1	3	0.1
2015	192	5.6	8	0.2	46	1.3	54	1.6	14.8	10	0.3
Total	**3,779**	**5.7**	**195**	**0.3**	**822**	**1.2**	**1,017**	**1.5**	**19.2**	**31**	**0.05**

* Culture confirmed cases with DST results for at least isoniazid and rifampicin who are resistant to isoniazid without MDR-TB

** Culture confirmed cases with DST results for at least isoniazid and rifampicin who are resistant to rifampicin without MDR-TB

Culture confirmed cases with DST results for at least isoniazid and rifampicin who are resistant to rifampicin, including those with MDR-TB

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

XDR-TB is defined as resistance to isonaizid and rifampicin (MDR-TB), plus resistance to at least one injectable agent (capreomycin, kanamycin or amikacin) and at least one fluoroquinolone (ofloxacin, moxifloxacin or ciprofloxacin). In 2015, 22.6% (12/53) of the MDR/RR TB cases were resistant to all four first-line drugs (isoniazid, rifampicin, ethambutol, pyrazinamide). Among MDR/RR TB cases, 12 were resistant to at least one injectable agent (amikacin, capreomycin or kanamycin) and 15 were resistant to a fluoroquinolone (ofloxacin, moxifloxacin or ciprofloxacin).

There were 10 initial XDR-TB cases notified in 2015, the highest annual number recorded (Table 2.1). The majority were aged 15 to 44 years (6/10) and non-UK born (7/10). In 2015, three had both an epidemiological and a molecular (identified by Mycobacterial Interspersed Repetitive Units (MIRU) - Variable Number Tandem Repeats (VNTR) clustering) link to another XDR-TB case in England, providing evidence that they acquired TB from recent transmission in England. Overall between 2011 and 2015, the highest number of XDR-TB cases were born in Lithuania (12), followed by a small number from India (3) and the UK (3).

Resistance in *N. gonorrhoeae*

Due to high rates of resistance to previously used drugs including penicillin, tetracycline and ciprofloxacin, current recommended first-line treatment for gonorrhoea is a combination of ceftriaxone and azithromycin. Due to the paucity of alternative agents for treatment, gonococcal resistance to ceftriaxone or azithromycin is a significant public health concern.

In early 2015, the Sexually Transmitted Bacteria Reference Unit (STBRU) at PHE detected an outbreak of high-level azithromycin-resistant gonorrhoea. It was initially detected in Leeds but subsequently spread to neighbouring areas in the North of England, then more widely (Figure 2.25). By the end of 2015, 31 cases had been identified (including one case from November 2014), with a further 17 detected in 2016.

In terms of the epidemiology of the outbreak, the initial cases reported in Leeds were all heterosexual with the majority under 20 years of age. However, later cases noted between November 2015 and February 2016 cases were predominantly men who have sex with men (MSM), from a slightly older age range (18-31), with the majority resident in London or the South East.

Following identification of the outbreak, PHE convened a Level 2 Incident Control Team to actively monitor and respond to the outbreak. Actions taken included the issue of a national alert to microbiology laboratories with a recommendation that all gonococcal isolates be screened for resistance to azithromycin and that resistant isolates should be submitted to the STBRU so that high-level resistance could be differentiated from lower

levels of resistant positives isolated. In addition, PHE issued an alert to clinicians via the British Association for Sexual Health and HIV highlighting the critical need for affected patients to be followed up for test of cure and for rigourous tracing of sexual contacts.

In addition to the outbreak of high-level azithromycin-resistant gonorrhoea, the STBRU reported the first case globally of gonorrhoea treatment failure in a patient receiving the recommended dual therapy of ceftriaxone plus azithromycin.[26] The case, was detected in England in March 2015, was a heterosexual man who acquired the infection in Japan. Although the infecting strain was multi-drug resistant, including resistance to both ceftriaxone and azithromycin, the latter was not high-level resistance. Fortunately, the patient was eventually successfully treated with higher doses of of ceftriaxone plus azithromycin.

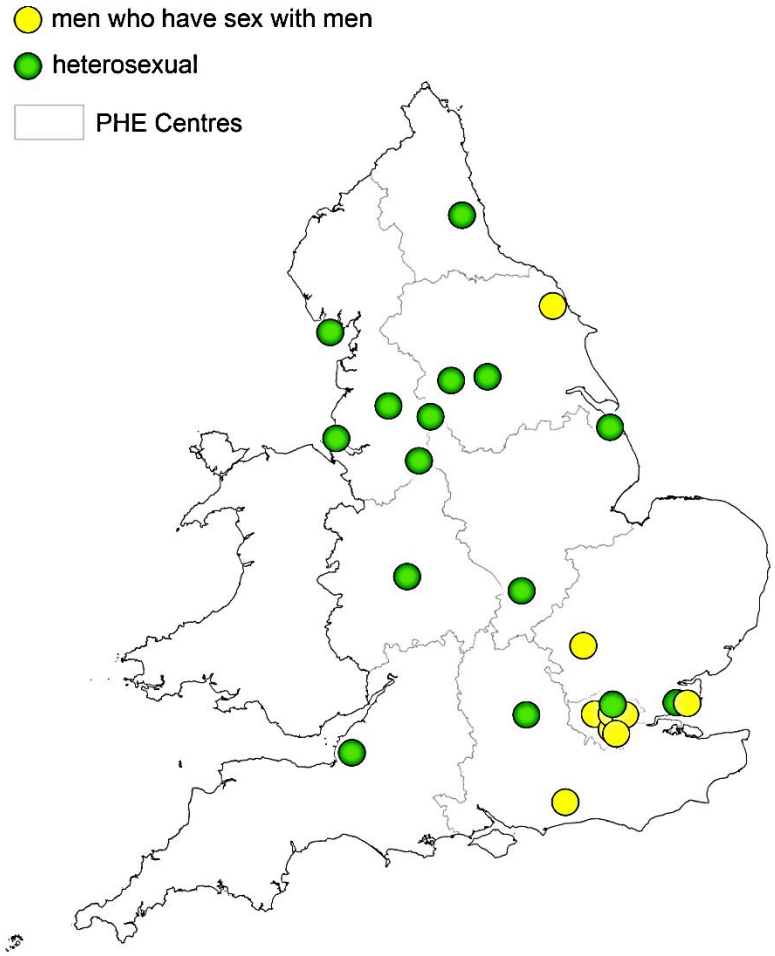


Figure 2.25 Outbreak of high-level azithromycin-resistant gonorrhoea in England (cases detected between November 2014 and August 2016)

26 Fifer H et al. Failure of Dual Antimicrobial Therapy in Treatment of Gonorrhea, N Engl J Med 2016; 374: 2504-6

Discussion

In terms of the threat posed by AMR, the surveillance data show a mixed picture. For the majority of the drug/bug combinations monitored as part of the national surveillance strategy, the proportions of resistant isolates from blood have stayed relatively stable over time, with some (eg resistance to piperacillin/tazobactam and co-amoxiclav in *E. coli* and *K. pneumoniae*) increasing over time but with others such as MRSA showing a decrease. An important caveat to highlight is possible intra-laboratory and inter-laboratory variation in antimicrobial susceptibility testing methodology, which can cause step changes in the reporting of resistance to both clinicians (to act on and plan treatment decisions and empiric guidelines) and to PHE. However, as highlighted previously,[27] while the proportion of isolates of a given species resistant to a particular antibiotic may remain stable, the increasing incidence of bacteraemia, particularly that caused by Gram-negative bacteria such as *E. coli* and *K. pneumoniae* means that the burden of resistance, as measured by the numbers of resistant infections, continues to increase. This highlights the importance of infection prevention and control and it is noteworthy that the strategic focus on reducing Gram-negative bloodstream infections will, if successful, not just reduce the rates of infection per se, but reduce the numbers of resistant infections, which should translate into improved clinical outcomes if infections are more readily treated.

In the face of the relative paucity of new antibiotics, particularly those active against Gram-negative bacteria resistant to many currently available antibiotics, there is concern that the use of carbapenems, which are our drugs of choice for serious infections caused by multi resistant pathogens, may be compromised by emerging resistance. Again, the surveillance data is providing mixed signals. On one hand, resistance to carbapenems among cases of bacteraemia caused by *E. coli* and *K. pneumoniae* remains low, indicating that the use of carbapenems for severe infections has not, as yet, been compromised. However, referrals of CPE to the national reference laboratory continue to increase year on year, and although many referred isolates reflect colonization rather than symptomatic infections, it seems likely that it is only a matter of time before there is an impact on the therapeutic effectiveness of carbapenems. In order to increase our understanding of the epidemiology of carbapenem resistance, PHE launched the ERS for carbapenemase-producing Gram-

[27] Public Health England; English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 2014. Available at; https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report

[27]NHS England. Quality Premium. https://www.england.nhs.uk/resources/resources-for-ccgs/ccg-out-tool/ccg-ois/qual-prem/

[27]NHS England. Anti-Microbial Resistance CQUIN. https://www.england.nhs.uk/nhs-standard-contract/cquin/cquin-16-17/amr-cquin/

[27] NHS England. Sustainability and Transformation Plans. https://www.england.nhs.uk/ourwork/futurenhs/deliver-forward-view/stp/

negative bacteria in April 2015. As indicated above, there is still scope for improved engagement and for more surveillance data to be submitted via the ERS. However, a potential challenge is that with the increasing availability and use of commercial carbapenemase detection tests in the NHS and private laboratories, the confirmation of carbapenemase production in Gram-negative bacteria is becoming incorporated into the routine work of some diagnostic microbiology laboratories who may then no longer submit isolates to the national or regional reference laboratories. The ERS is the only method currently available that allows this locally generated data to be captured and used to inform regional and national trends. Active participation in this surveillance by every trust in the country is therefore vital for building a comprehensive 'picture' of the growing carbapenemase problem in England that will allow us to inform the development of effective infection prevention and control strategies. The longer-term plan is for the ERS to be further enhanced through linkage with electronically stored microbiology data from SGSS, hospital administrative data (Hospital Episode Statistics) and mortality data.

In order to preserve the therapeutic effectiveness of carbapenems and other broad-spectrum antibiotics, efforts are being made to reduce their prescribing in order to reduce the selective pressure for emergence of resistance. However, if prescribing of carbapenems is to be reduced, alternative treatment options will need to be identified. To this end, this report provides some preliminary data showing that antibiotic combinations of amikacin with either β-lactams or ciprofloxacin appear to provide good cover with >98% of bacteraemia isolates of *E. coli* and *K. pneumoniae* being susceptible. Further work, particular in clinical practice, should provide insight into the potential value of these combinations as carbapenem-sparing treatment options.

As alluded to above, interventions to reduce levels of AMR include increased emphasis on infection prevention and control and improved prescribing with a reduction, in particular, in prescribing of broad-spectrum antibiotics. Incentives to achieve these goals include the NHS Quality Premium[28] and CQUIN (Commissioning for Quality and Innovation)[29] payment frameworks as well as the local development of Sustainability and Transformation Plans (STPs),[30] centered on the needs of local populations. Provision via the PHE Fingertips web portal of local data relating to AMR including rates of resistance, as well as data on antibiotic consumption, rates of infection and antimicrobial stewardship activities described in other chapters of this report, will be a valuable tool for those seeking to develop, implement and monitor local action plans for tackling AMR. The provision of local data through Fingertips is a work in progress, with

[28] NHS England. Quality Premium. https://www.england.nhs.uk/resources/resources-for-ccgs/ccg-out-tool/ccg-ois/qual-prem/
[29] NHS England. Anti-Microbial Resistance CQUIN. https://www.england.nhs.uk/nhs-standard-contract/cquin/cquin-16-17/amr-cquin/
[30] NHS England. Sustainability and Transformation Plans. https://www.england.nhs.uk/ourwork/futurenhs/deliver-forward-view/stp/

potential future developments including more detailed analysis of data on resistance to trimethoprim and nitrofurantoin in *E. coli* and coliforms from community urine samples from elderly patients (the over-70s) and rates of resistance of a range of Gram-negative bacteria to key antibiotics in both the acute Trust and community settings.

Two other diseases where AMR is also of concern include TB and gonorrhoea. Although rates of drug-resistant TB have remained fairly stable over recent years, the significant burden this poses should not be underestimated, as cases require prolonged antibiotic therapy lasting 24 months or longer, with complex treatment regimens comprising multiple antibiotics with high toxicity. Infection control for drug-resistant TB is also challenging, as cases may remain infectious for considerably longer than patients infected with drug-susceptible strains. Hence, the surveillance undertaken by PHE is crucially important for monitoring the epidemiology of this important disease. With regard to gonorrhoea, resistance to recommended treatment (ceftriaxone plus azithromycin) is a growing concern as an initial treatment failure due to a gonococcal strain with dual resistance has been recorded. In addition, a protracted outbreak of high-level, azithromycin-resistant gonorrhoea is reported here. Ongoing surveillance work undertaken through the Gonococcal Resistance to Antimicrobials Programme (GRASP) and the reference activities of the PHE Sexually Transmitted Bacteria Reference Unit, will continue to play an essential part in monitoring the spread of this disease.

Future actions

Future work will seek to:

- develop systems for the collection of trust-level rates of Gram-negative bacteraemia and rates of resistance to key antibiotics and make the data available via the AMR local indicators profile in Fingertips
- develop methods for reporting of patterns of multi-resistance in a range of bacterial species
- expand surveillance of AMR to include a wider range of clinical infections
- collect surveillance data on the incidence of a range of infections to monitor impact of reduced antibiotic prescribing
- develop new Fingertips indicators showing the proportion of gonococcal isolates tested for resistance to azithromycin and ceftriaxone

Chapter 3: Antibiotic consumption

Introduction

The consumption of antibiotics is a major driver for the development of antibiotic resistance in bacteria. In England, prescriptions for antibiotics are written by medical, dental, nursing and non-medical prescribers in general practice, other community services, dental practices and hospitals.

Continuous measurement, with the ability to identify the prescriber location (eg hospital, general practice, dental etc), 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 that are rapidly rising to help target resources and interventions to curb these increases.

This year's report presents antimicrobial usage trends across the healthcare economy. This chapter outlines the impact of the NHS Quality Premium (QP) on total and broad-spectrum prescribing in primary care.[31] We demonstrate the utility and data presented on Fingertips in relation to antibiotic prescribing. Progress with improving dental and independent sector prescribing is also summarised.

Methods

All data in this report is presented by calendar year from 2010 to 2015, with the exception of dental data, which is available from June 2010. Data related to the QP is presented for the financial years 2014/15 and 2015/16. The methods were as outlined in previous reports. In addition, we have no longer included information about each antibiotic class as this information can be found in previous reports.[32]

Data source – primary care

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

[31] NHS England. Quality Premium. https://www.england.nhs.uk/resources/resources-for-ccgs/ccg-out-tool/ccg-ois/qual-prem/
[32] Public Health England; English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 2015. Available at; https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report

Data source – secondary care

Information on the use of antibiotics in secondary care was obtained from QuintilesIMS (formerly known as IMS Health).[33] The database held by QuintilesIMS contains information from 99% of NHS hospital pharmacy systems, for drugs dispensed to individual patients and wards. All NHS trusts were included.

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 doses (DDD) for each drug.[34] 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 National Statistics. Hospital admission data for each year was extracted from Hospital Episode Statistics from NHS Digital.

Trend analysis

National trends in the consumption of antibiotics were assessed for the last four years (2012−2015); therefore we can now estimate the potential impact of the AMR strategy and interventions since then, as the baseline year is 2012, the year prior to the strategy. A linear regression was then applied with the dependent variable being antibiotic consumption in DDD per 1000 inhabitants per day and the explanatory variable being year. Statistical significance was $p<0.05$.

Data transparency

All data presented in this chapter in figures and tables is available as a web appendix in excel format. In addition, area team data will be included. This is available in Web Appendix 2.[35]

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[33] For further information; QuintilesIMS website available at http://www.imshealth.com/

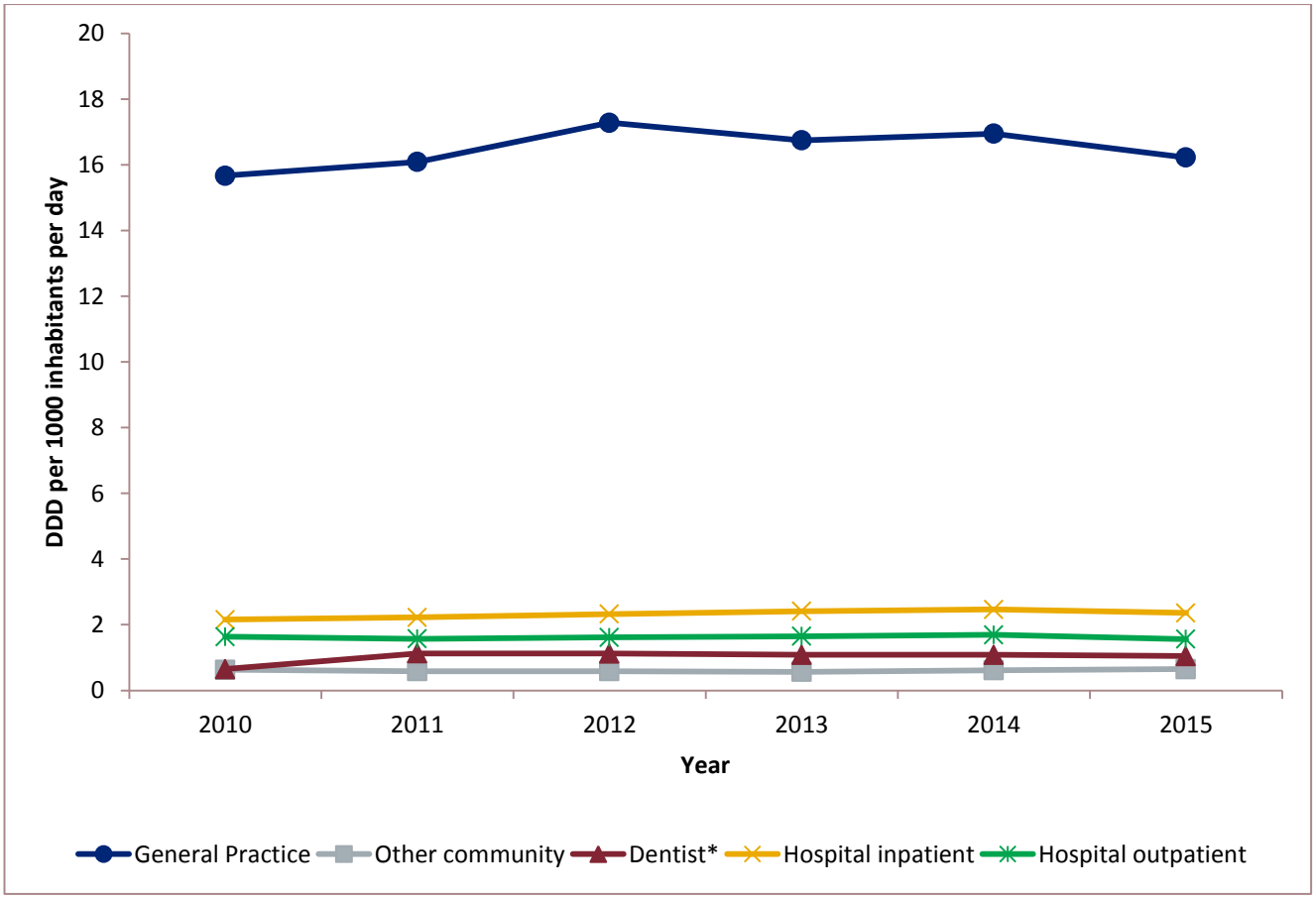
[34] World Health Organisation; Guidelines for ATC classification and DDD assignment 2013 available at http://www.whocc.no/filearchive/publications/1_2013guidelines.pdf

[35] Public Health England; English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 2015. Available at; https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report

Results

Total consumption of antibiotics in 2015

The majority of antibiotics in England were prescribed in the general practice setting (74%), followed by hospital inpatients (11%), hospital outpatients (7%), patients seen in dental practices (5%) and patients in other community settings (3%).
The total consumption of antibiotics, as expressed in DDD per 1000 inhabitants per day in primary and secondary care declined by 4.5% over the last four years (4.3% between 2014 and 2015); from 22.9 to 21.8 DDD per 1000 inhabitants per day between 2012 and 2015 (Figure 3.1).



*Data available from June 2010

Figure 3.1 Total antibiotic consumption, expressed as DDD per 1000 inhabitants per day, England, 2010-2015

Primary care

General practice (GP) was the largest prescribing setting and consumption decreased from 17.3 to 16.2 DDD per 1000 inhabitants per day (- 6.1%) between 2012 and 2015. Prescribing by dentists decreased from 1.12 to 1.04 DDD per 1000 inhabitants (-6.9%) between 2012 and 2015 with a decline of 3.9% being observed between 2014 and 2015. There was an 11.1% increase (0.59 to 0.65 DDD per 1000 inhabitants) in prescribing by 'other community prescribers' from 2012 to 2015, with the largest increase occurring between 2013 and 2014 (8.4%); while this increase is the largest, it contributes less than 4% of total antibiotic use and the decreases in prescribing from GP were not substantively offset by increases in other community prescribers.

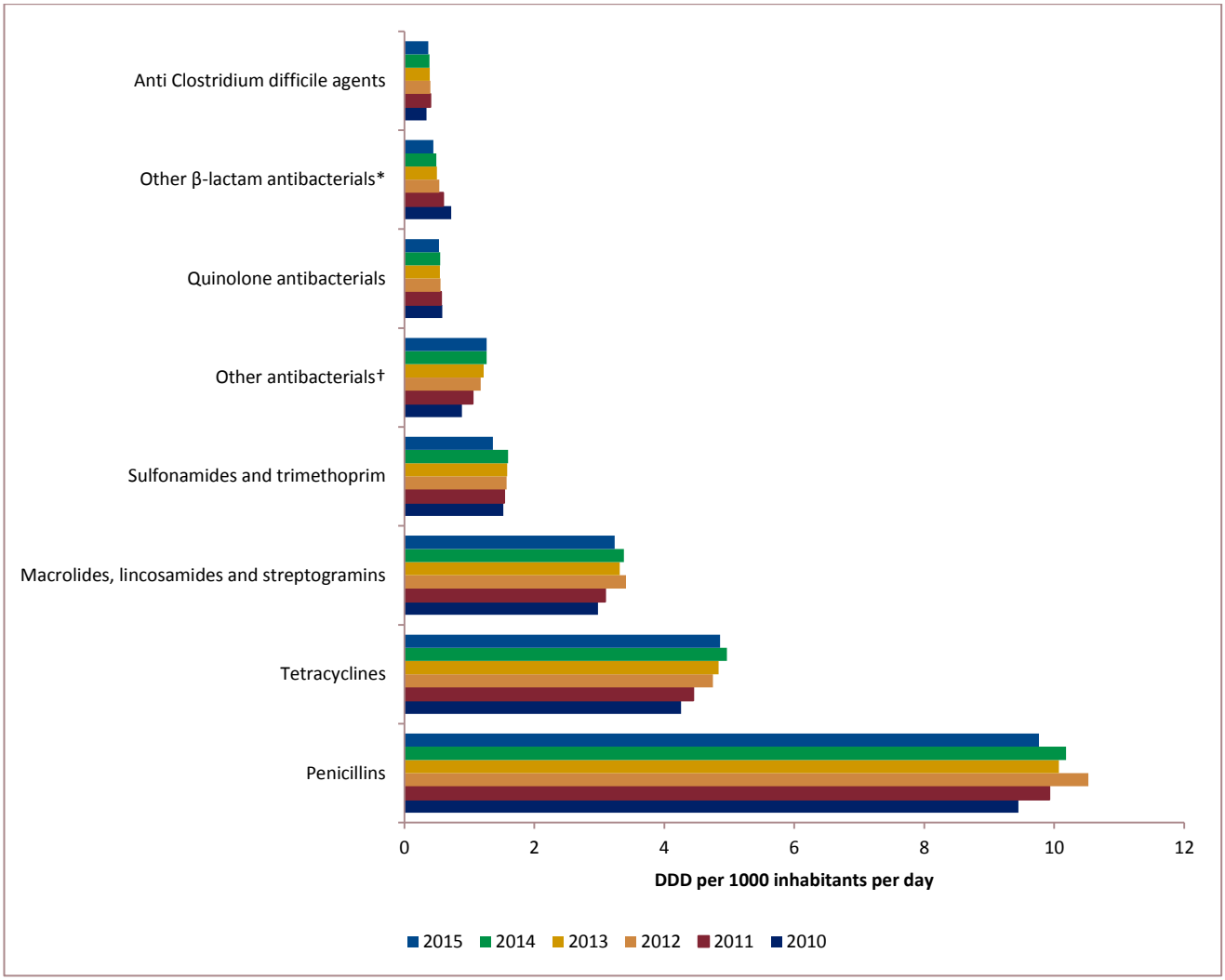
Secondary care

Prescribing in secondary care has been broadly stable between 2012 and 2015. Prescribing to hospital inpatients increased from 2.32 to 2.36 DDD per 1000 inhabitants per day (1.5%) while prescribing to hospital outpatients decreased from 1.61 to 1.56 DDD per 1000 inhabitants per day (-3.3%) over the same four-year period. Prescribing to hospital outpatients and inpatients fell between 2014 and 2015 by 8% and 2% respectively.

Total prescribing by key agents

The three groups of antibiotics most frequently used in England in 2014 were penicillins (44.6%), tetracyclines (22.2%) and macrolides (14.8%) (Figure 3.2).

Between 2012 and 2015, there was an increase in the volume of consumption in the group 'other antibacterials' (7.7%) as well as in tetracyclines (2.3%). Over the same period, there was a decrease in the rate of antibiotic consumption of the following groups: other β-lactam antibacterials (-16.7%), sulfonamides and trimethoprim (-13.4%), metronidazole and oral vancomycin (-9.6%), penicillins (-7.2%), macrolides (-4.9%) and quinolones (-4.8%). Overall drug consumption remained broadly stable, in terms of percentage of each antibiotic class prescribed, between 2012 and 2014.



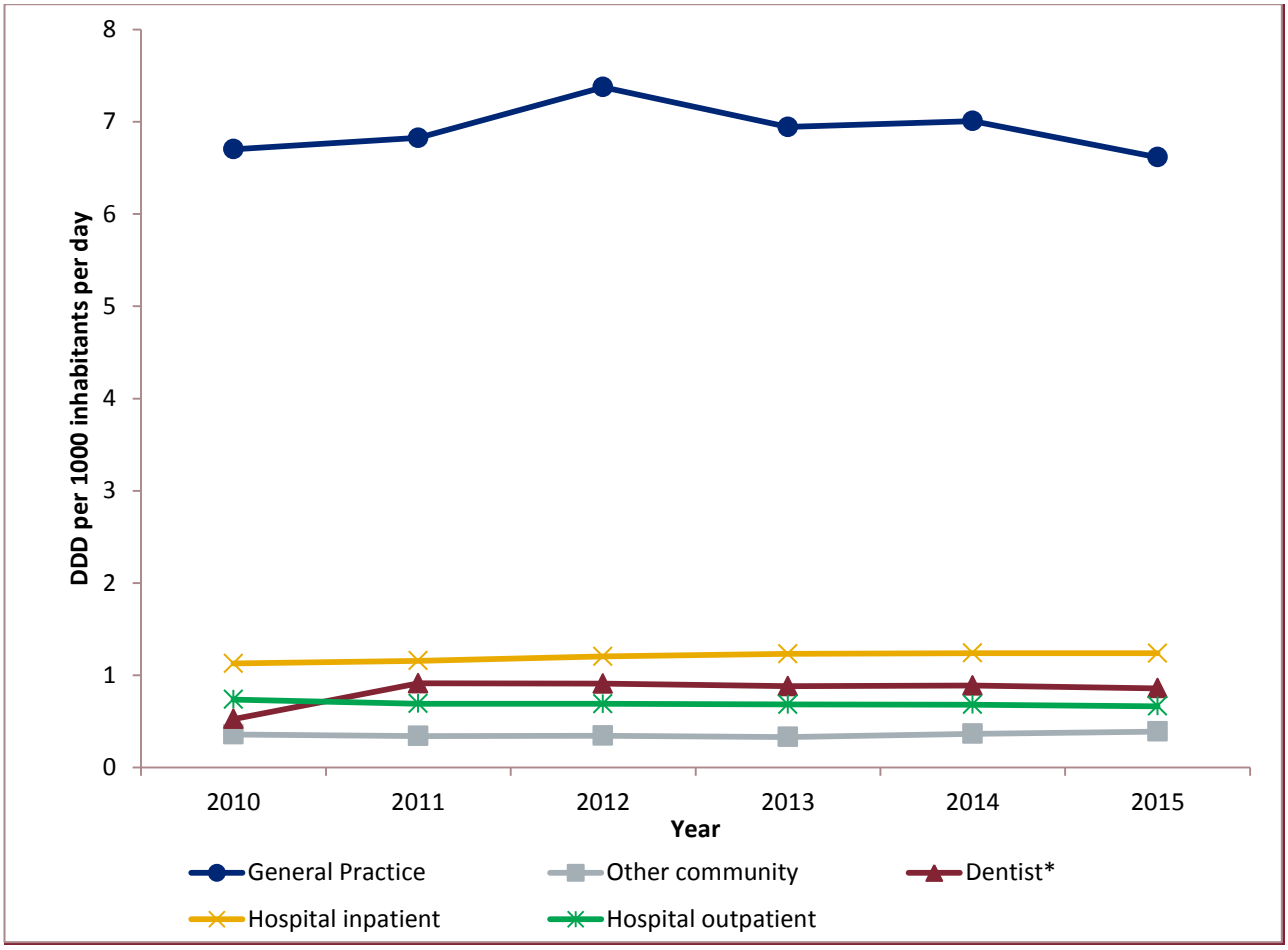
* includes cephalosporins, carbapenems, and monobactams

† includes glycopeptides, polymyxins, steroid antibacterials, imidazole and nitrofuran derivatives, fosfomycin, linezolid, daptomycin

Figure 3.2 Total antibiotic consumption by key antibiotic groups, expressed as DDD per 1000 inhabitants per day, England, 2010-2015

Penicillins

Penicillins accounted for 44.6% of the total antibiotic prescribing in England in 2015, unchanged from 2014. The volume of penicillin prescribed decreased by 7.2% between 2012 and 2015, from 10.5 to 9.8 DDD per 1000 inhabitants (Figure 3.3). Total consumption in GP decreased between 2012 and 2015 by 10.3% while dental prescribing and hospital outpatient prescribing also declined over the same four-year period by -5.5% and -3.7%, respectively. Hospital inpatient prescribing increased 3.0% during 2012-2014 but remained stable between 2014 and 2015. Prescribing in other community settings increased by 13.1% between 2012 and 2015, from 0.34 to 0.39 DDD per 1000 inhabitants; in 2015 prescribing in other community settings accounted for 4.0% of total penicillin prescribing.



*Data available from June 2010

Figure 3.3 Consumption of penicillins, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010-2015

Consumption trends for the most commonly used penicillins are shown in Figure 3.4. The trend analysis demonstrated no significant change between 2012 and 2015, for all antibiotics in this class except piperacillin/tazobactam, which showed significantly increased consumption; this is important because of the rapidly rising resistance outlined in chapter 2.

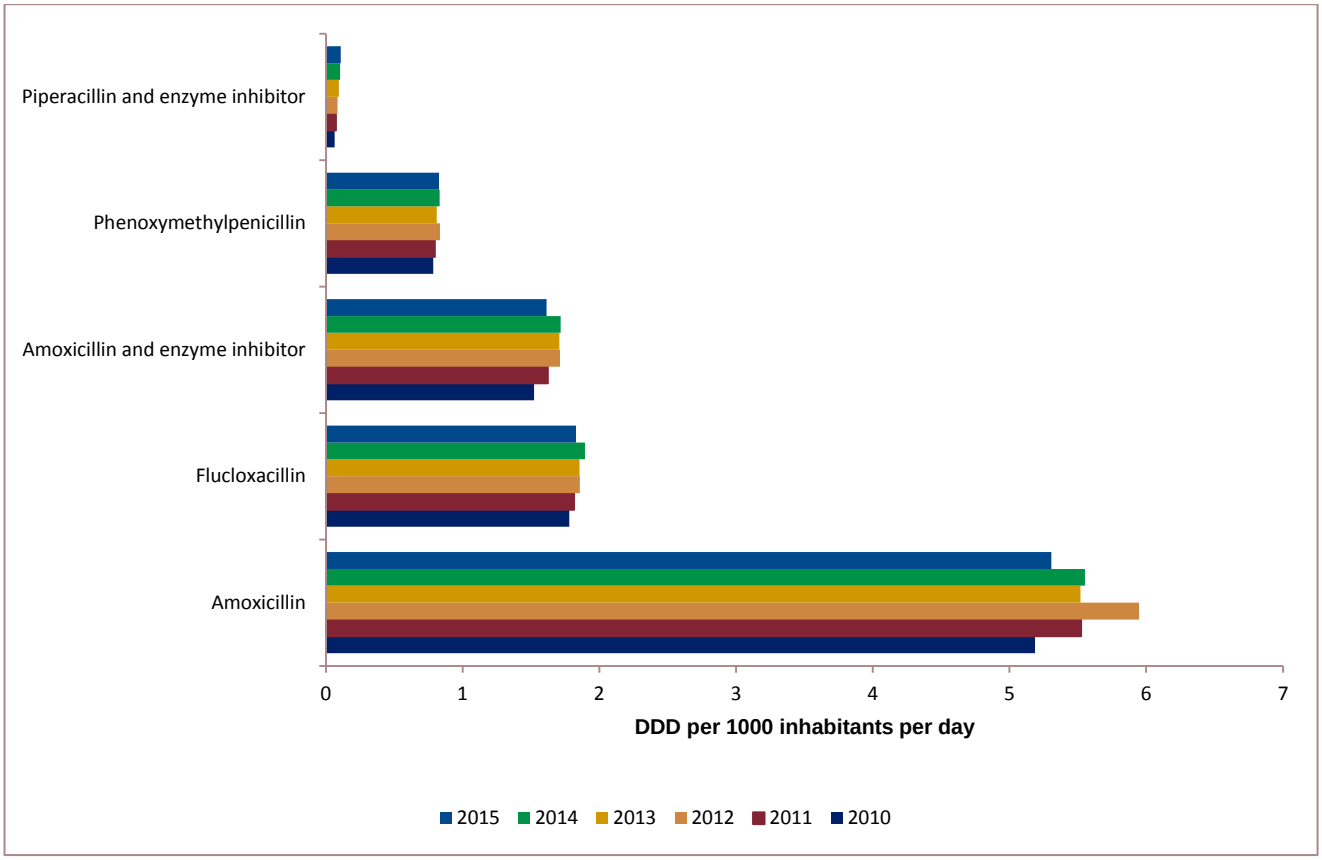
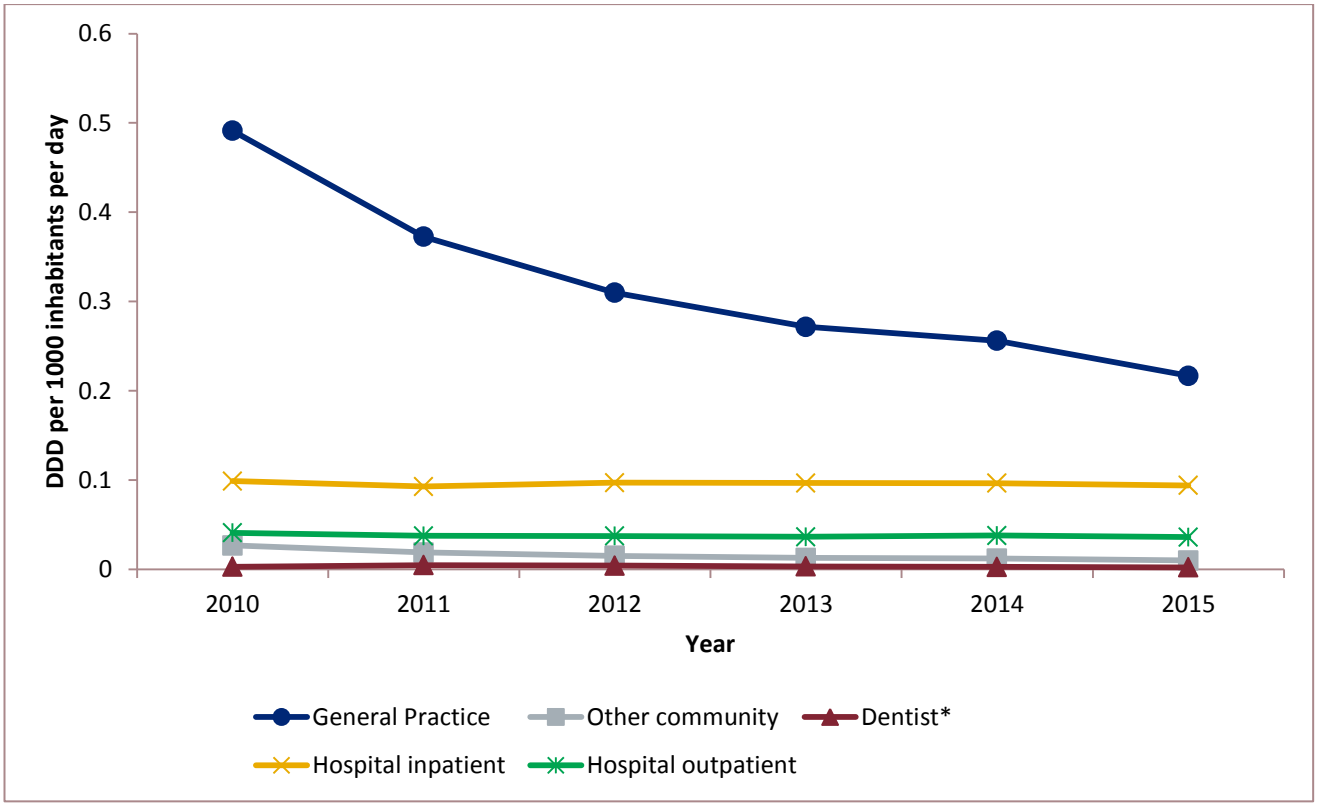


Figure 3.4 Consumption of most commonly utilised penicillins, expressed as DDD per 1000 inhabitants per day, England, 2010-2015

Cephalosporins

There has been a significant and sustained decline in the volume of consumption of cephalosporins between 2012 and 2015 by 9.2% (Figure 3.5).

The top six agents used in this class are presented in Figure 3.6. The use of the oral cephalosporins cephalexin (-25.7%), cefradine (-20.5%) and cefuroxime (-15.9%) declined between 2012 and 2015. Use of the second-generation cephalosporin cefaclor (-54.3%) and the third generation cephalosporin cefotaxime (-1.6%) also declined. Use of the third-generation cephalosporin ceftriaxone consumption increased by 37.4% between 2012 and 2015, though this may be due to the on-going expansion of outpatient parenteral antimicrobial therapy (OPAT) programmes, where its long half-life can facilitate once daily intravenous treatment of patients in their own homes or in other ambulatory settings.



*Data available from June 2010

Figure 3.5 Consumption of cephalosporins, by prescribing location, expressed as DDD per 1000 inhabitants per day, England, 2010-2015

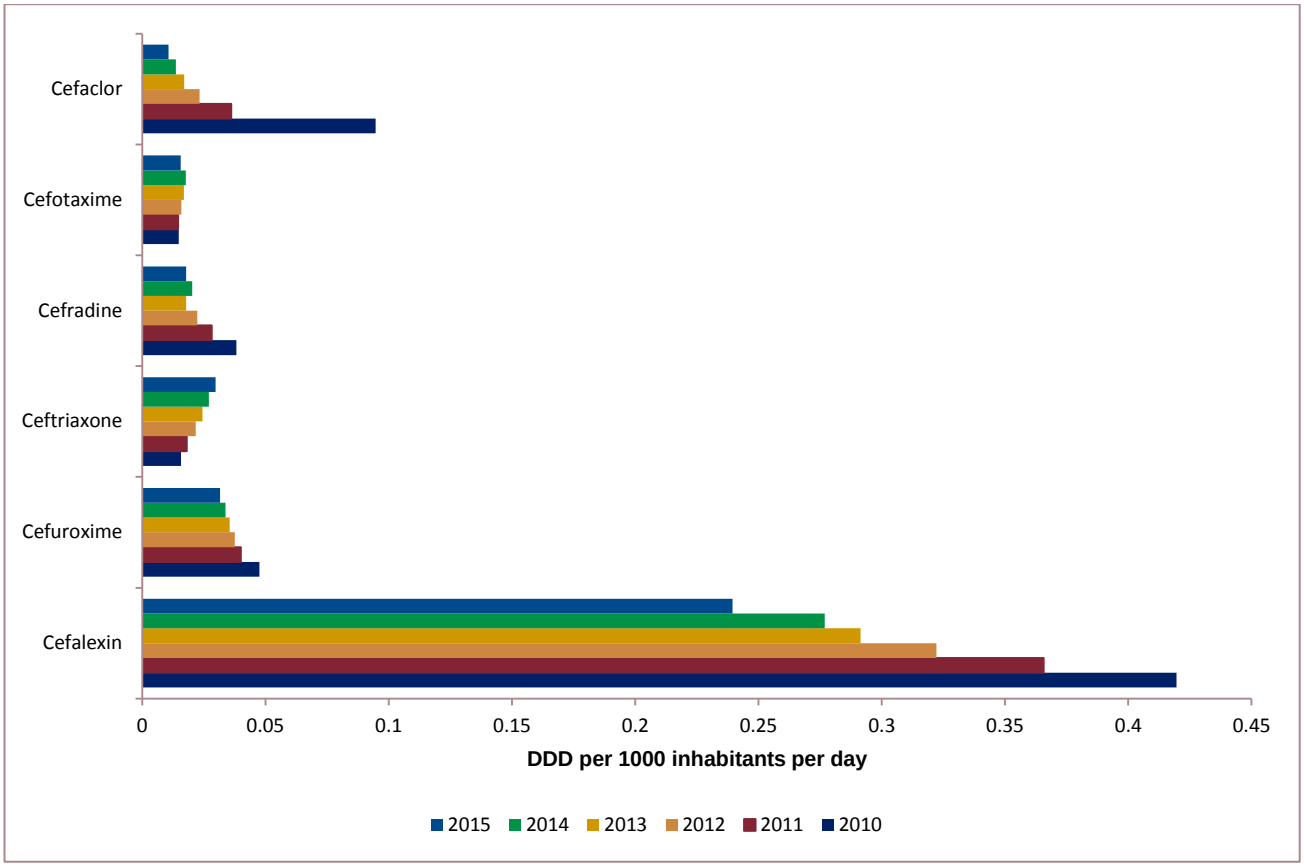


Figure 3.6 Consumption of different cephalosporins, expressed as DDD per 1000 inhabitants per day, England, 2010 - 2015

Carbapenems

Carbapenem use, while only a tiny proportion of total antibiotic use, continues to increase. The vast majority of carbapenem consumption across England occurred within the hospital sector (>99%), with less than 1% of carbapenem consumption related to primary care prescriptions in 2015 (Figure 3.7). A detailed review of carbapenem use in hospitals is within the hospital section.

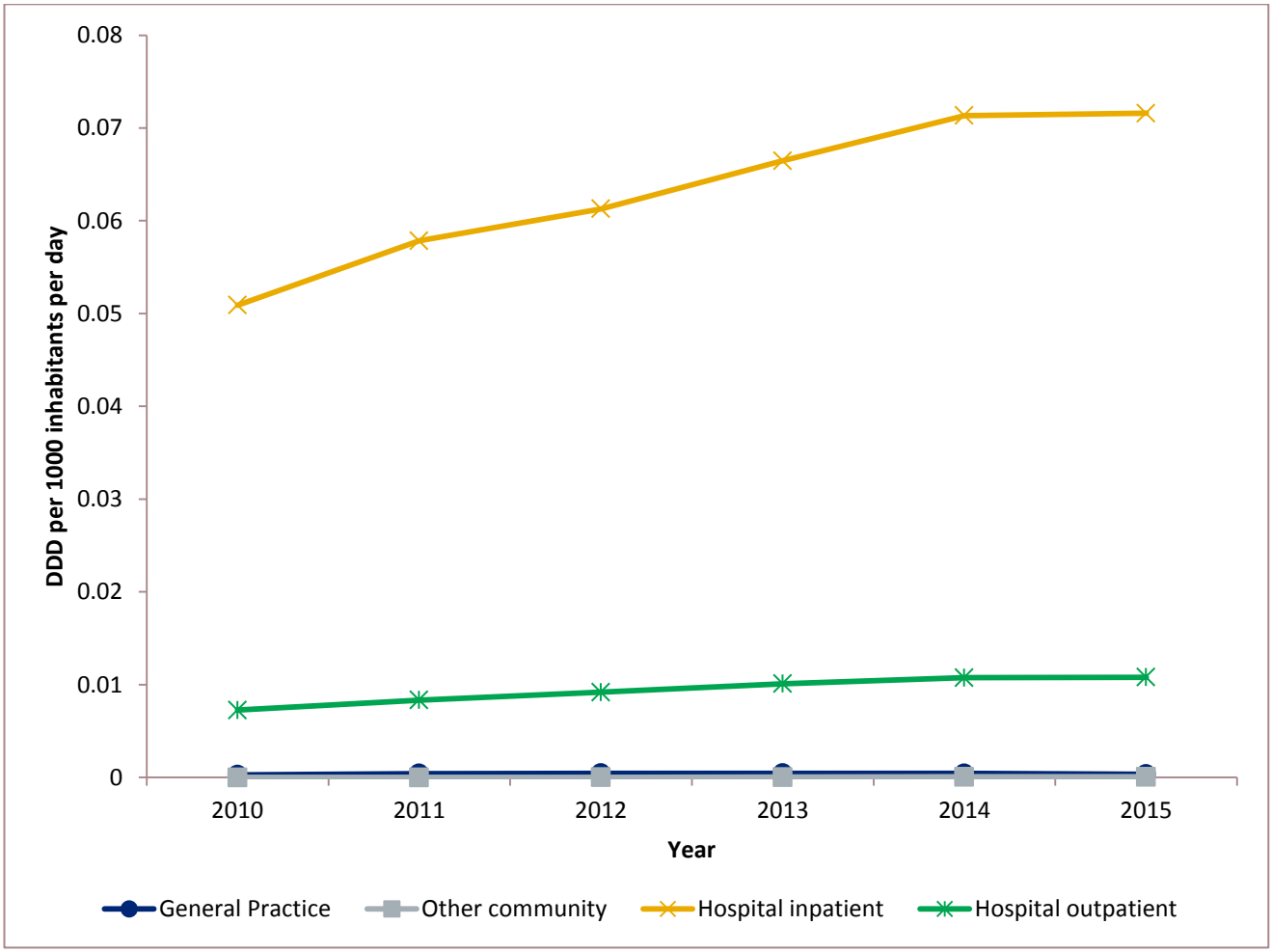
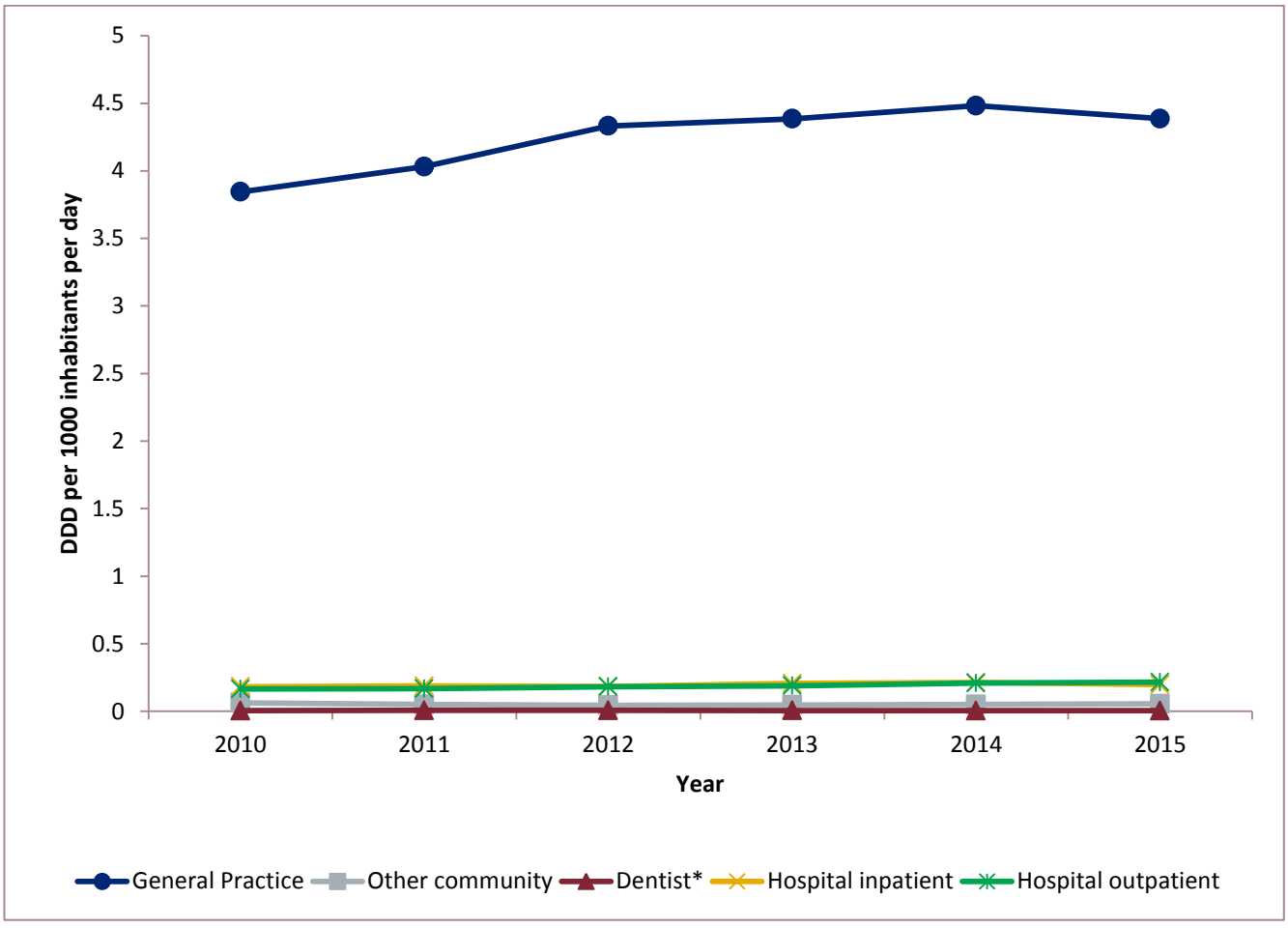


Figure 3.7 Consumption of carbapenems, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010-2015

Tetracyclines

Tetracyclines are still prescribed primarily in the primary care setting (90.3%). Overall, consumption has remained relatively stable between 2012 and 2015 (Figure 3.8). An increased trend in consumption was identified in other community and hospital outpatient settings, although these two make up a relatively small proportion of all tetracycline prescribing.

The top seven agents prescribed in this class are presented in Figure 3.9. In the four years since 2012 the predominant agents consumed were doxycycline and lymecycline (45.9% and 36.7% of tetracycline prescribing) probably reflecting the use of these derivatives as a treatment for acne.



*Data available from June 2010

Figure 3.8 Consumption of tetracyclines, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010-2015

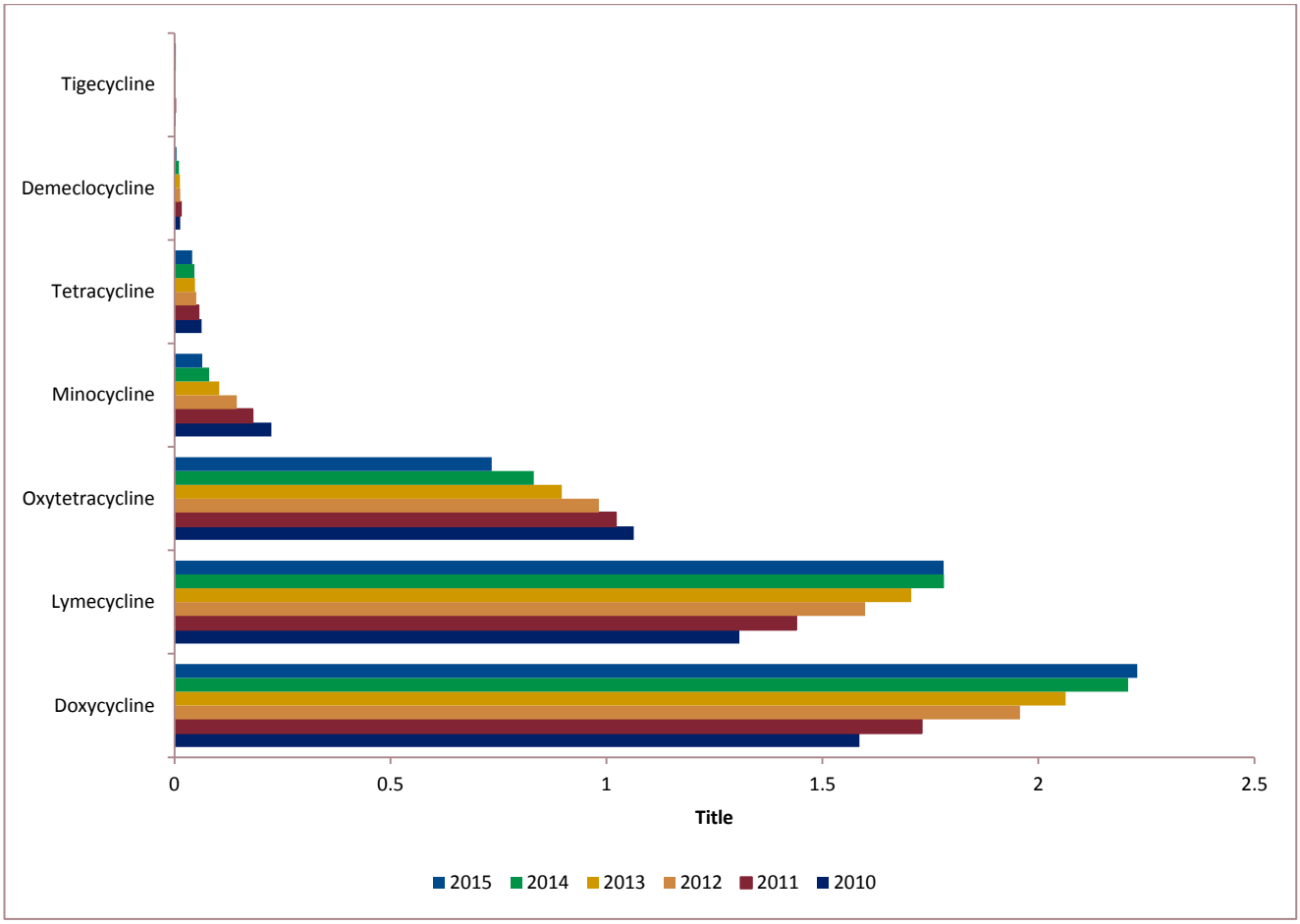


Figure 3.9 Consumption of different tetracyclines, expressed as DDDs per 1000 inhabitants per day, England, 2010-2015

Quinolones

Quinolone consumption has been relatively stable over the period 2012-2015 (Figure 3.10), although there was a slight reduction between 2014 and 2015 (-3.6%).

The main quinolone prescribed between 2012 and 2015 was ciprofloxacin. There has been a trend of increased consumption in the respiratory quinolone, levofloxacin, and this has increased by 53.6% since 2012 (Figure 3.11).

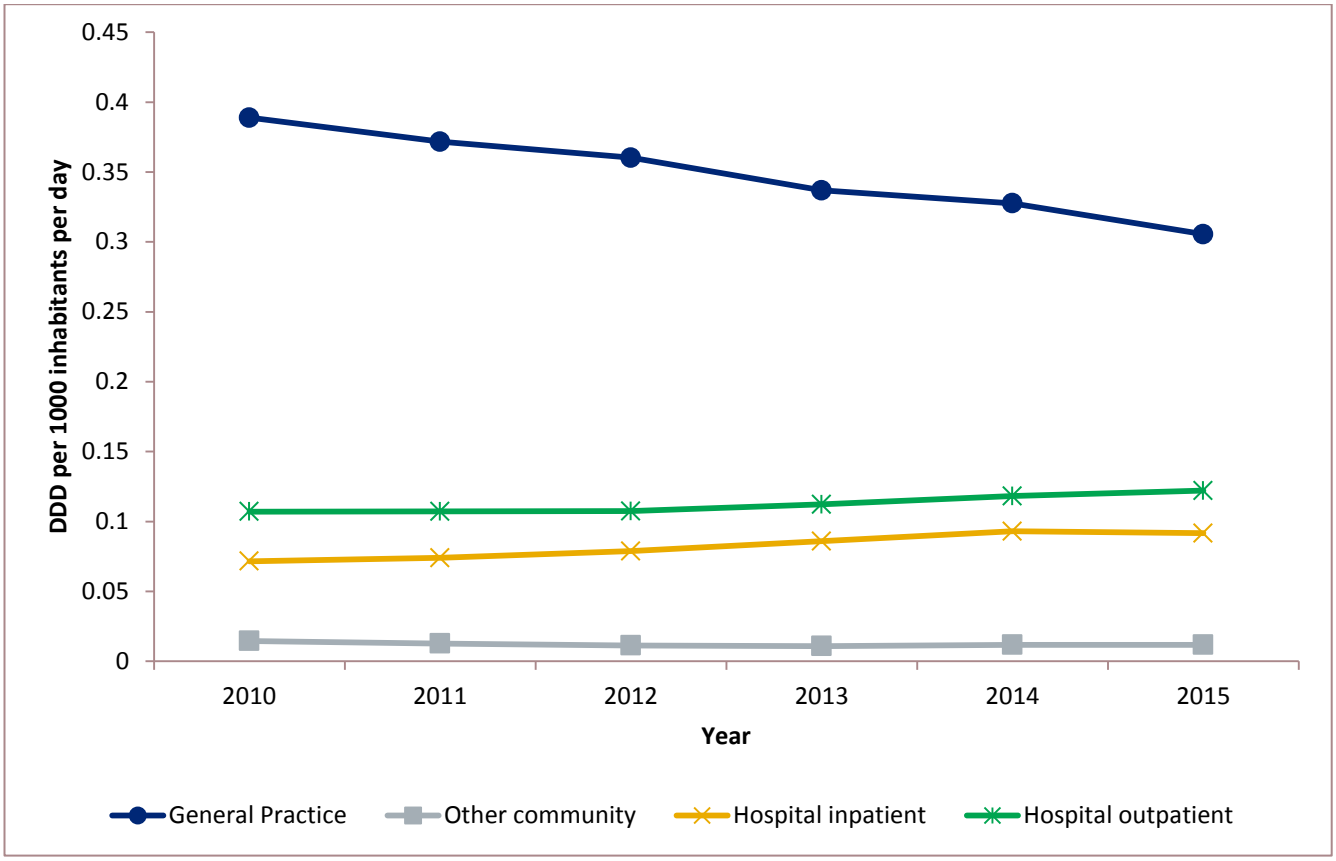


Figure 3.10 consumption of quinolones, by prescribing location, expressed as DDD per 1000 inhabitants per day, England, 2010-2015

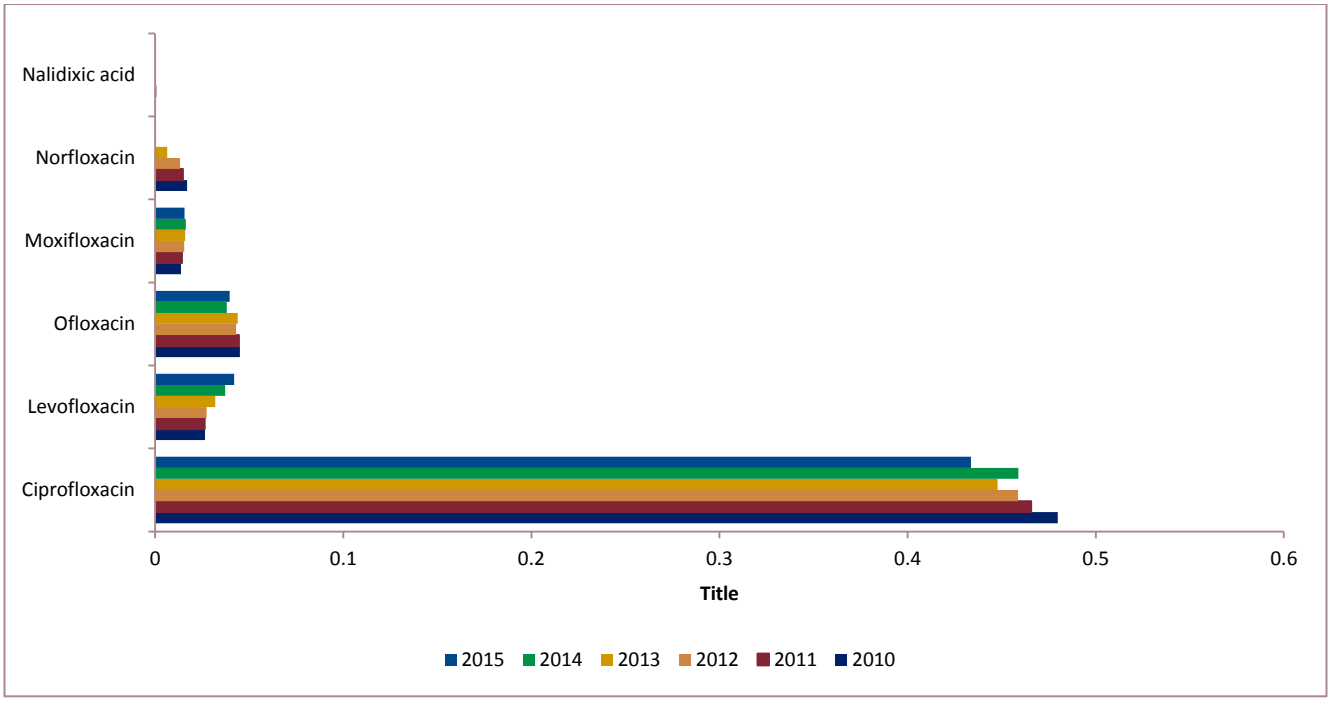
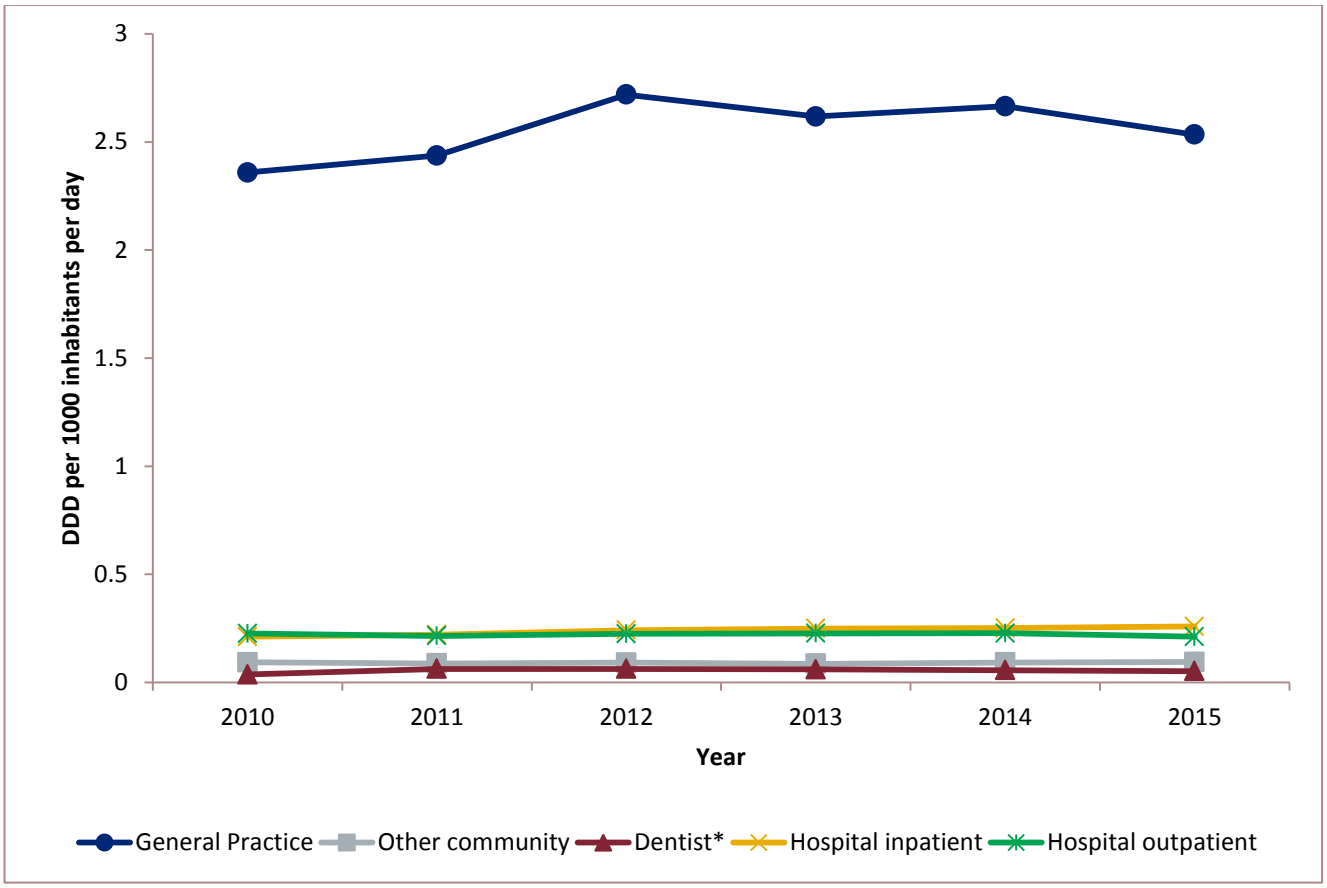


Figure 3.11 Consumption of different quinolones, expressed as DDD per 1000 inhabitants per day, England 2010 - 2015

Macrolides

Macrolide use decreased by 5.7% between 2012 and 2015. The majority of prescribing occurred in general practice, where it declined by 6.8% over the same period (Figure 3.12).

Clarithromycin and azithromycin use has increased since 2012 with a converse fall in erythromycin use, 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 3.13).



*Data available from June 2010

Figure 3.12 Consumption of macrolides, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010- 2015

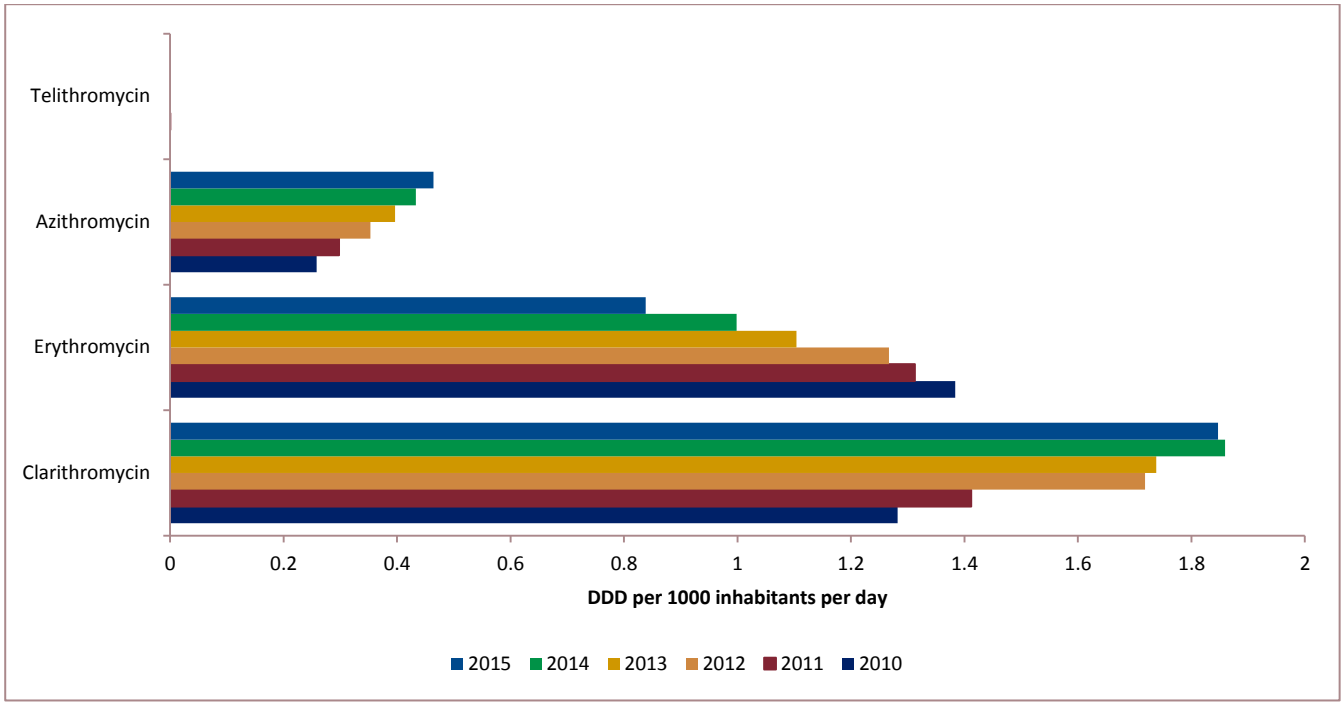


Figure 3.13 Consumption of different macrolides, expressed as DDD per 1000 inhabitants per day, England, 2010-2015

Sulfonamides and trimethoprim

Between 2012 and 2014, total consumption of these antibiotics had steadily increased, but between 2014 and 2015 it declined by 14.5% bringing it to the lowest rate of consumption over the four-year period since 2012 (Figure 3.14).

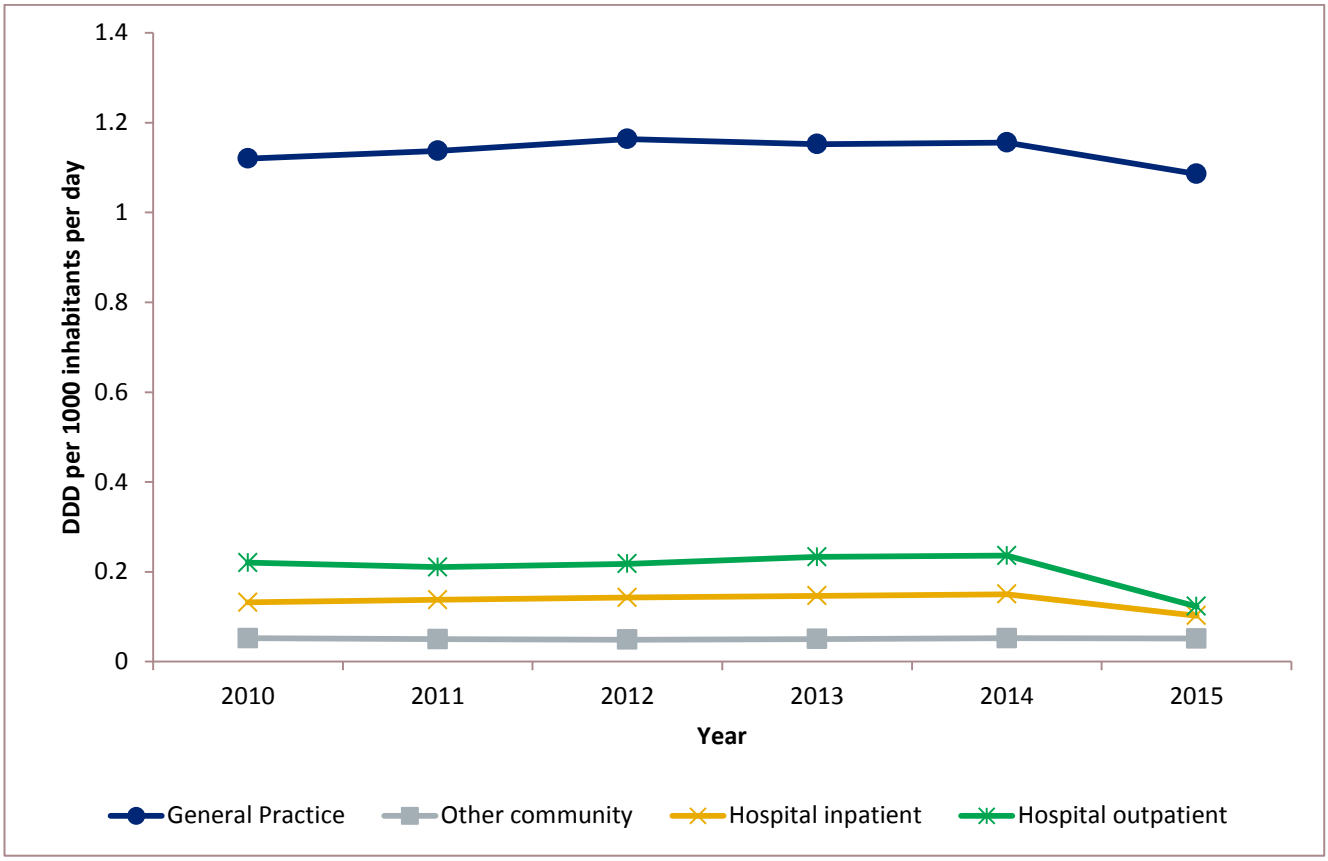


Figure 3.14 Consumption of sulfonamides and trimethoprim, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010- 2015

Nitrofurantoin

The trend in nitrofurantoin consumption showed an increase between 2012 and 2015, which was observed across all prescribing settings that utilise this drug (Figure 3.15). PHE changed primary care guidelines[36] to recommend this antibiotic as first-line treatment for lower urinary tract infections in adults in 2014; this is likely the explanation for the continued upward trend in 2015.

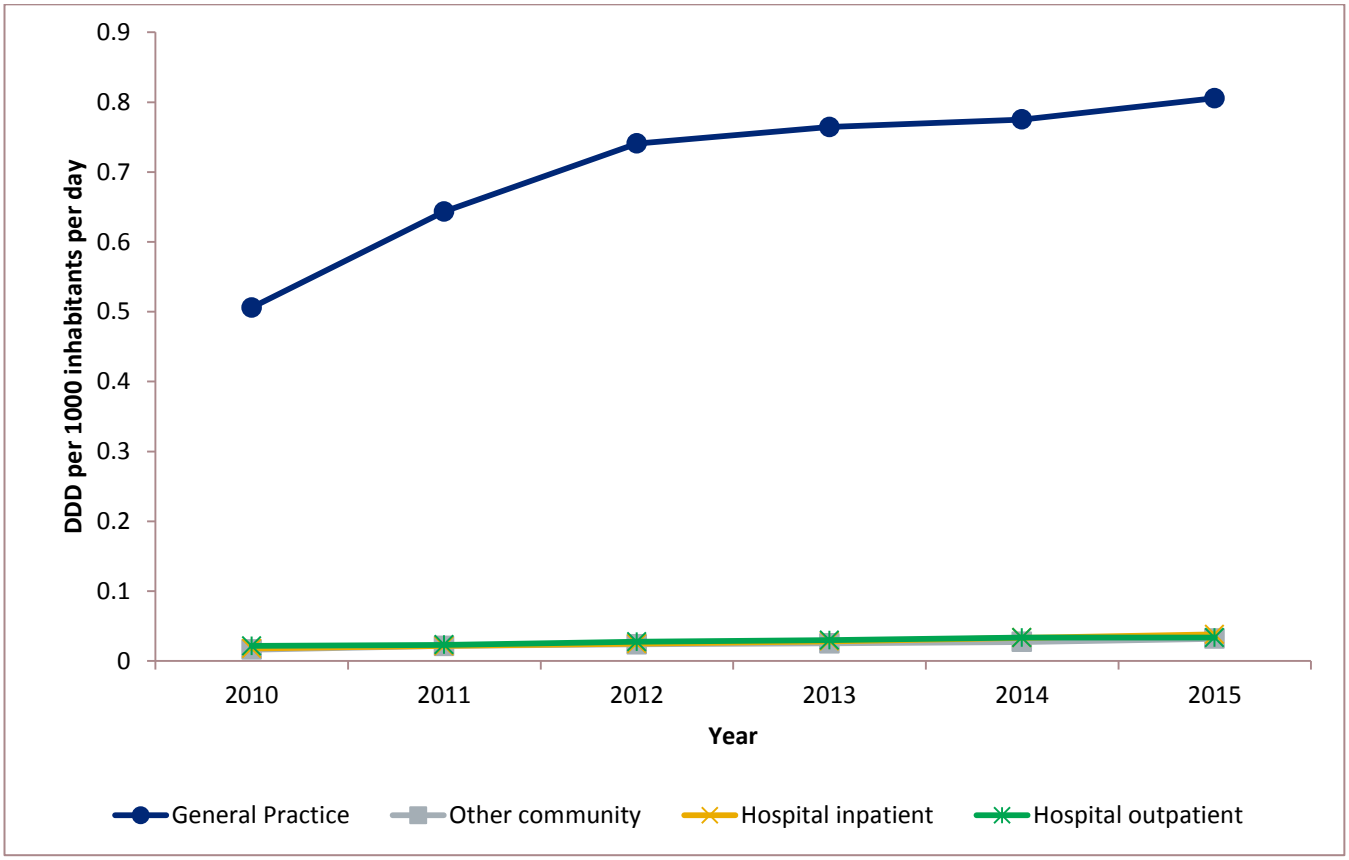


Figure 3.15 Consumption of nitrofurantoin, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010-2015

[36] Public Health England; Managing common infections: guidance for primary care, Available from; https://www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care

Aminoglycosides

Consumption of aminoglycosides remained broadly stable between 2012 and 2015; a slight increase was observed between 2012 and 2014 but consumption subsequently declined in 2015. This class makes up a relatively small amount of the overall prescribing at approximately 0.12 DDD per 1000 inhabitants (Figure 3.16).

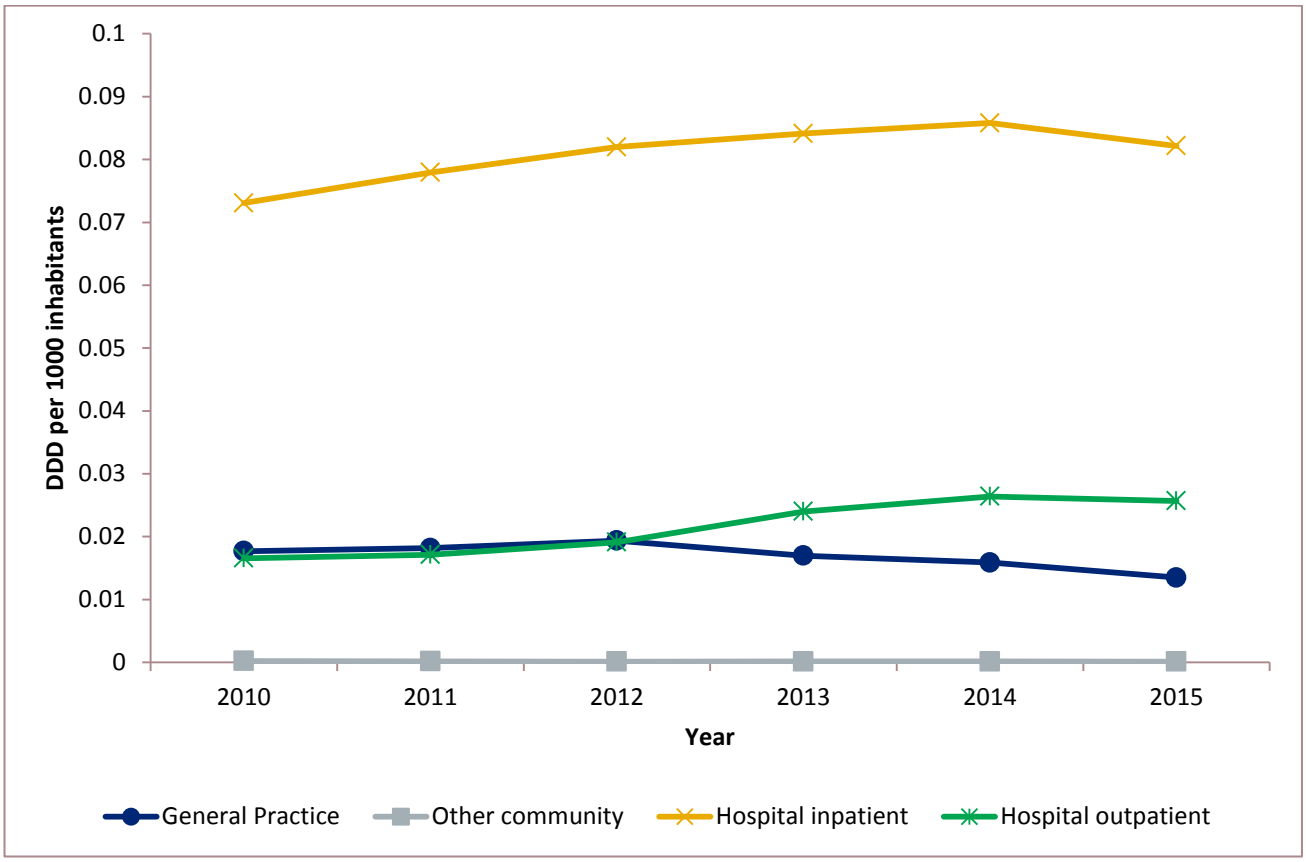


Figure 3.16 Consumption of aminoglycosides, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010-2015

Trends in consumption of other agents: parenteral glycopeptides and daptomycin

Use of glycopeptides and daptomycin occurs almost exclusively in the hospital setting (98.8%). Despite a significant reduction in MRSA bacteraemia and other infections, the use of parenteral glycopeptides (predominantly teicoplanin) and daptomycin continued to increase over the last 4 years from 0.07 to 0.09 DDD per 1000 inhabitants (Figure 3.17) From 2012 to 2015, the consumption of daptomycin increased by 71.5%, though it still remains very low at <0.01 DDD per 1000 inhabitants per day (Figure 3.18). Glycopeptide consumption may be rising due to increased drug doses used per patient per day, with higher target serum concentrations and weight-based doses increasingly being recommended. Teicoplanin use, in particular, may also be increasing related to improved access to OPAT.

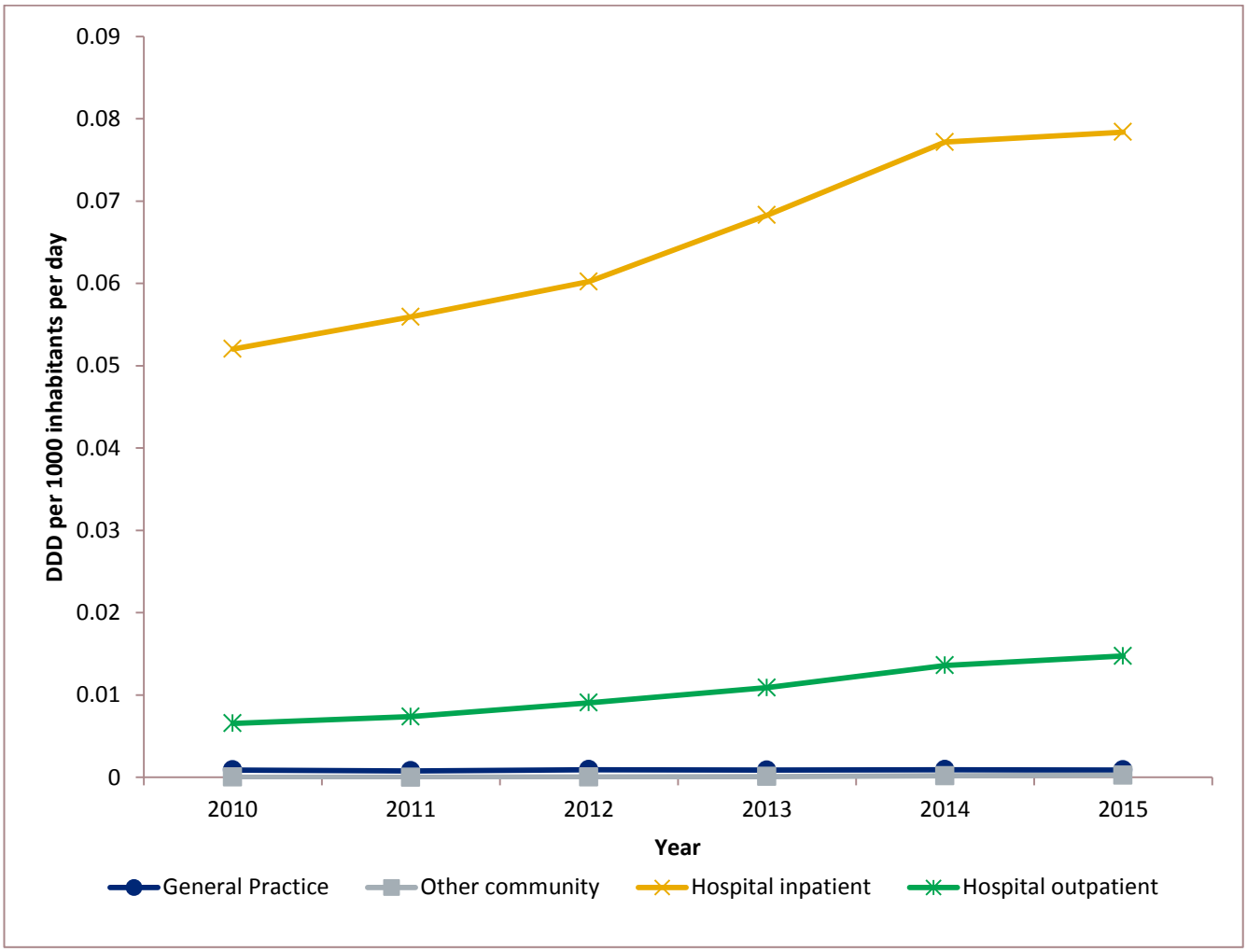


Figure 3.17 Consumption of glycopeptides and daptomycin, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010- 2015

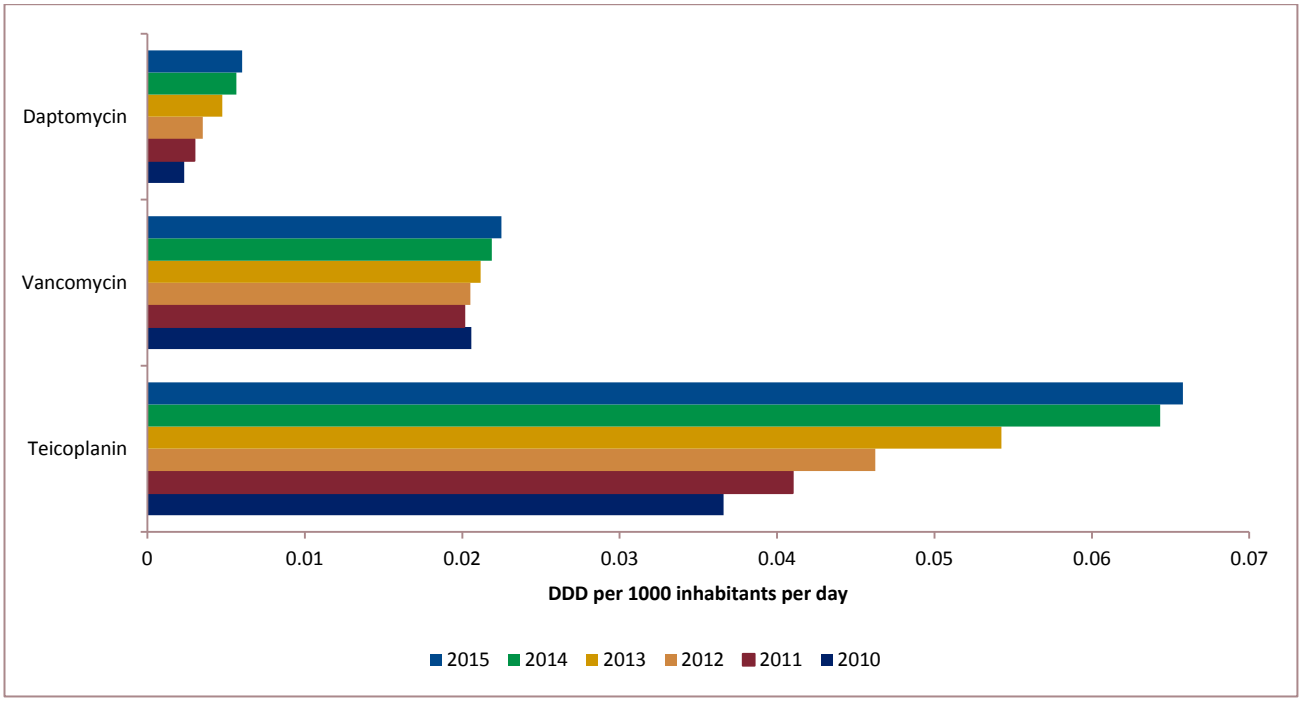
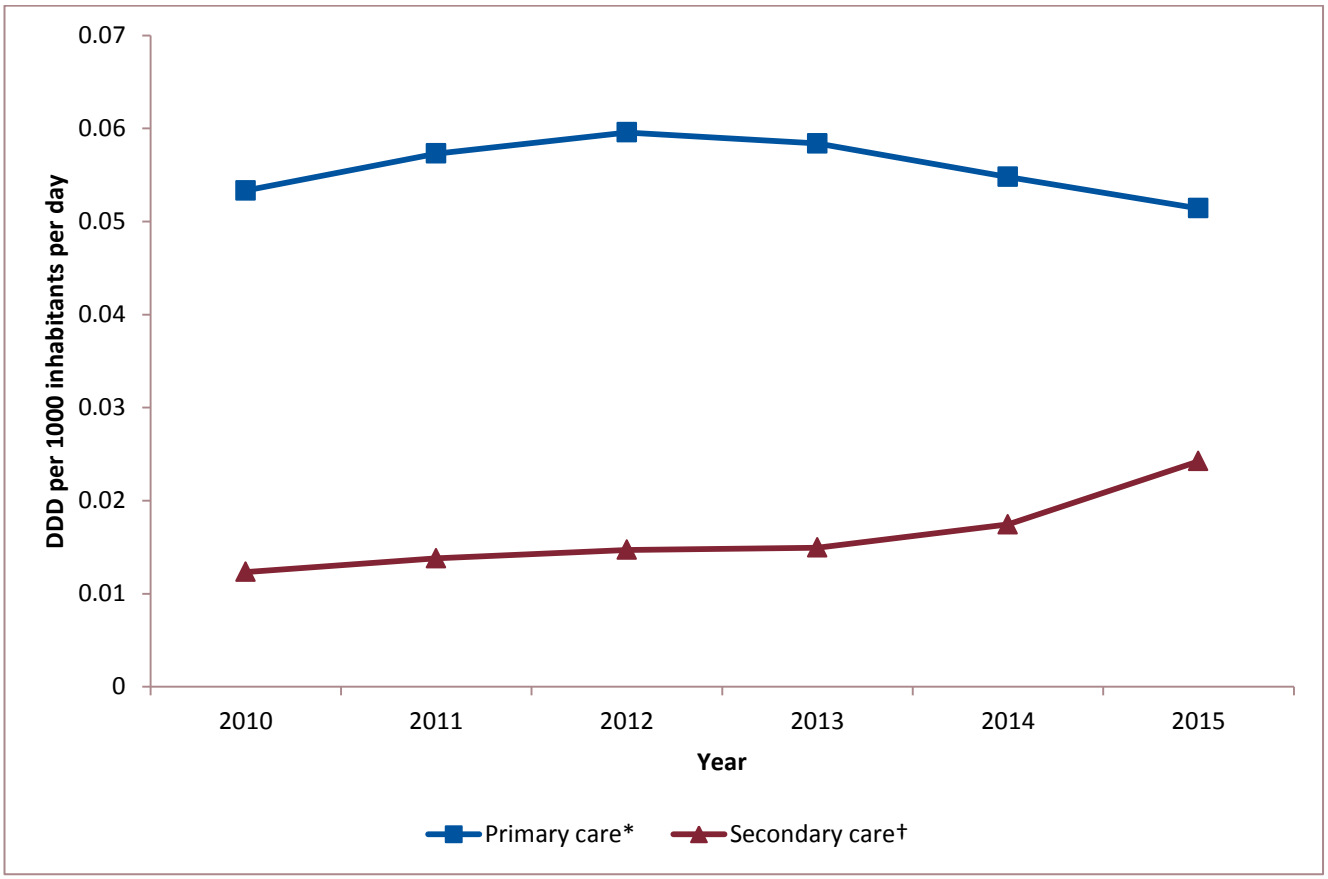


Figure 3.18 Consumption of different glycopeptides and daptomycin, expressed as DDD per 1000 inhabitants per day, England, 2010-2015

Colistin

Colistin is a last resort antibiotic that is often used for multidrug-resistant infections. Since 2012 there has been a decreased trend in colistin prescribing in primary care settings. Conversely there has been a sustained and significant increase in prescribing of colistin in secondary care settings (Figure 3.19).



* Includes general Practice, Dentist and other community prescribing

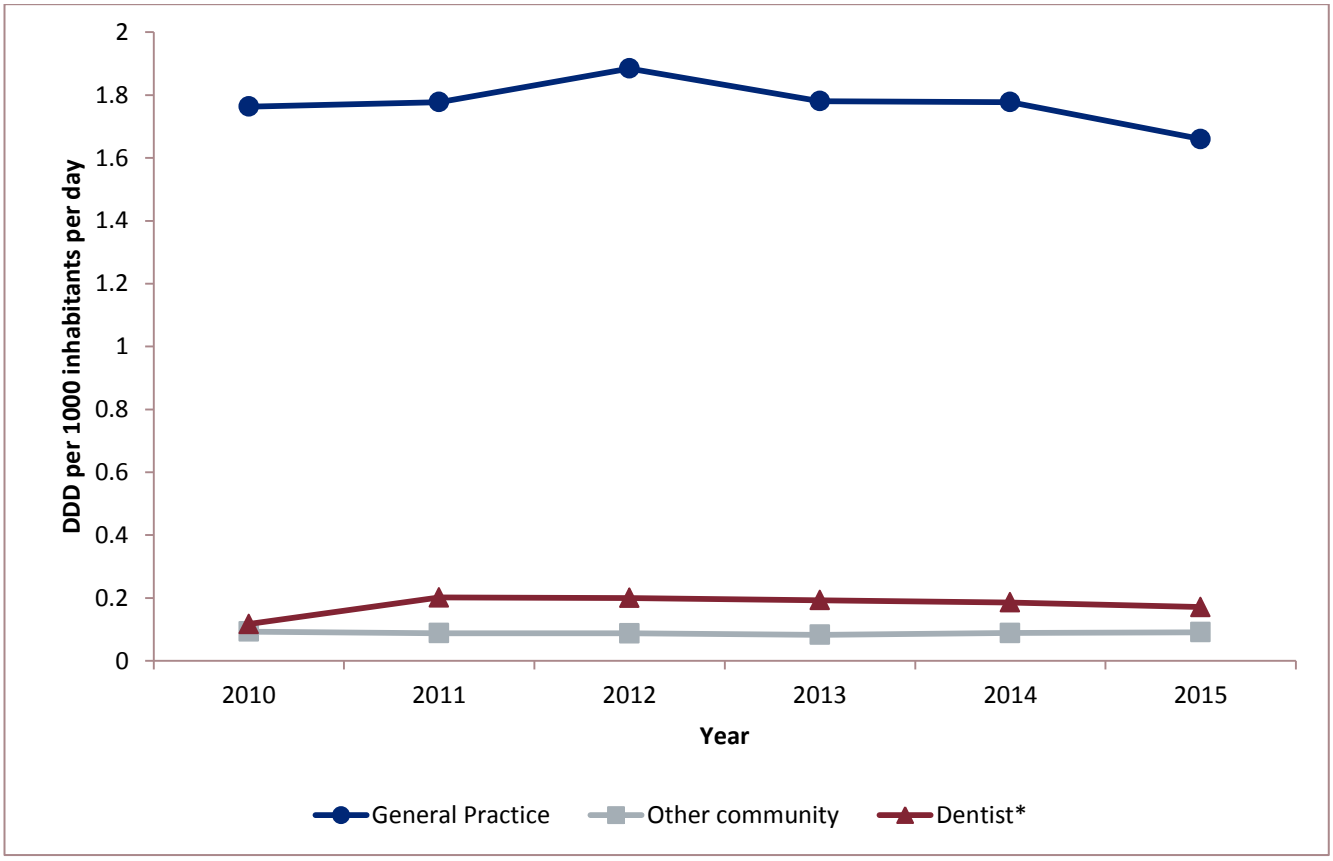
† Includes inpatient and outpatient prescribing

Figure 3.19 Consumption of colistin in primary and secondary care, England 2010 - 2015

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

The total amount of items has shown a trend of decreased consumption between 2012 and 2015 from 2.17 to 1.92 antibiotic items (-11.5%) prescribed per 1000 inhabitants per day. Between 2014 and 2015, there was a reduction (-6%) in the rate of items prescribed. This decreased trend is reflected in the two primary prescribing settings; GP and dentist. Other community setting has had a small increase (3.9%) over the same time period (see Figure 3.20).

GP prescribed 86.4% of all antibiotic items in the community in England in 2015. Dentists prescribed 8.9% of antibiotic prescription items and 4.7% were prescribed by other community services.



*Data available from June 2010

Figure 3.20 Antibiotic items by prescriber group, expressed as items per 1000 inhabitants per day, England, 2010- 2015

General practice

Penicillins remain the most commonly prescribed antibiotic items in GP accounting for 49.8% of prescriptions, followed by tetracyclines (12.6%) and macrolides (12.6%). We have presented this as syndrome-specific prescribing to highlight where changes have occurred in groups of agents prescribed for specific conditions.

Syndrome-specific prescribing

In this section we present the changes in prescribing according to syndrome-specific antibiotics as recommended in the national treatment guidelines published by PHE (Figure 3.21).[37] Overall the greatest impact on prescribing has been observed in the number of antibiotic items recommended for upper and lower respiratory tract infections. More antibiotics recommended for use for urinary tract infections have been prescribed, potentially reflecting re-treatments and increased burden of this condition in the population.

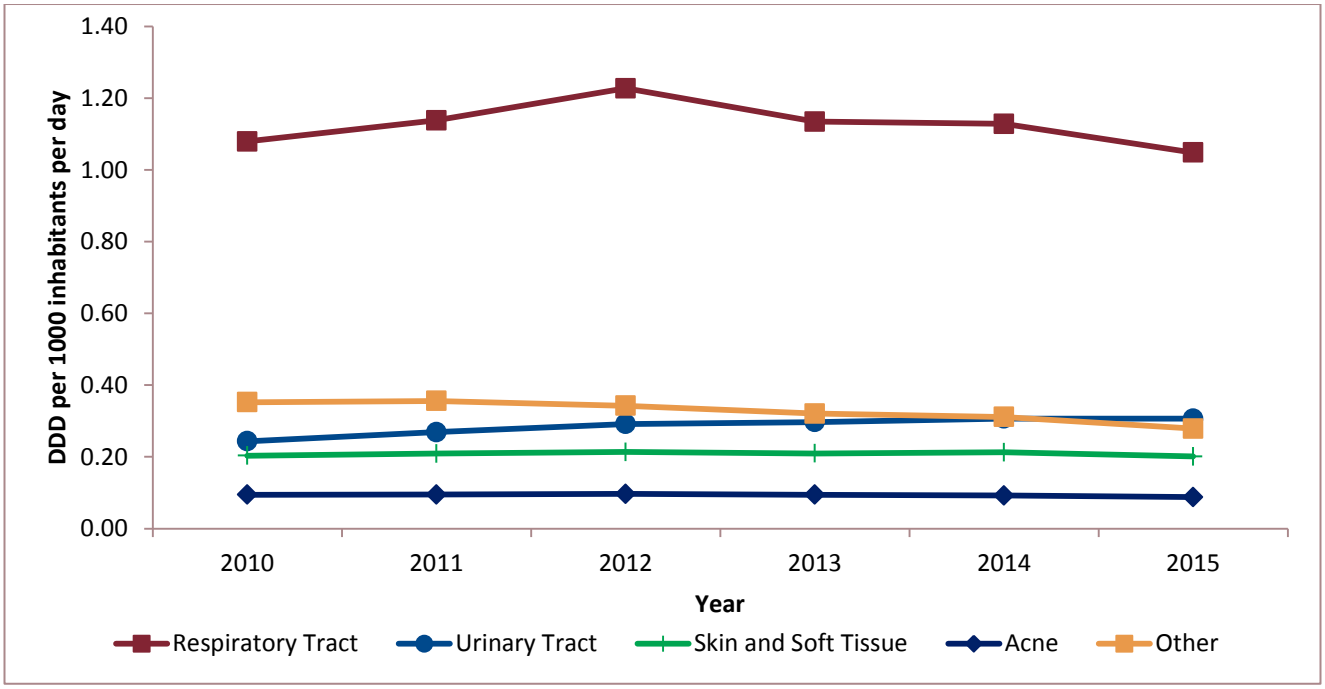


Figure 3.21 Syndrome specific prescribing; items per 1000 inhabitants per day, England; 2010-2015

[37] Public Health England; Managing common infections: guidance for primary care, Available from; https://www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care

There has been no significant change in the antibiotics prescribed for skin and soft tissue infections (flucloxacillin) or acne (tetracycline group, excluding doxycycline from analysis as this is recommended for RTI). The remainder of the antibiotics have seen reductions predominantly in the broad-spectrum antibiotics (co-amoxiclav, cephalosporins and quinolones as described in the QP section).

Respiratory tract Infections

The key antibiotics recommended in the PHE primary care guidelines for upper and lower respiratory tract infections, sore throat and otitis media are outlined in Table 3.1 Overall, there have been year-on-year reductions predominantly driven by reductions in amoxicillin; the macrolide group are unchanged in in terms of prescription items.

Table 3.1: Antibiotics prescribed in the community that are recommended for the treatment of respiratory tract infections (expressed as items per 1000 inhabitants per day)

Antibiotic	2010	2011	2012	2013	2014	2015
Amoxicillin	0.54	0.53	0.57	0.51	0.50	0.45
Phenoxymethylpenicillin	0.12	0.11	0.12	0.11	0.11	0.10
Erythromycin	0.12	0.12	0.11	0.10	0.09	0.07
Clarithromycin	0.08	0.09	0.11	0.11	0.11	0.11
Azithromycin	0.01	0.02	0.02	0.02	0.03	0.03
Doxycycline	0.08	0.09	0.11	0.11	0.12	0.12
Total	**0.87**	**0.86**	**0.93**	**0.84**	**0.83**	**0.76**

Urinary tract infections

The first-line antibiotic treatment for empiric treatment of lower urinary tract infection recommended in the PHE primary care guidelines infections switched from trimethoprim to nitrofurantoin in 2014, as 30% of urinary isolates were resistant to trimethoprim. A change in prescribing with a switch from trimethoprim to nitrofurantoin commenced in 2015 (Table 3.2).

Table 3.2: Antibiotics prescribed in the community that are recommended for the treatment of urinary tract infections (expressed as items per 1000 inhabitants per day)

Antibiotic	2010	2011	2012	2013	2014	2015
Trimethoprim	0.17	0.18	0.18	0.18	0.19	0.17
Nitrofurantoin	0.06	0.08	0.09	0.10	0.10	0.11
Fosfomycin	0.0000	0.0000	0.0000	0.0000	0.0001	0.0002
Pivmecillinam	0.00	0.001	0.001	0.002	0.002	0.004
Total	**0.23**	**0.26**	**0.28**	**0.28**	**0.29**	**0.28**

Other community prescribing

Community service prescribing increased by 3.9% (from 0.088 to 0.091 antibiotic items per 1000 inhabitants) between 2012 and 2015 with the main increase (6.4%) recorded between 2013 and 2014 (Figure 3.22). The penicillin group (61.5%) is the most common group prescribed in this setting, followed by trimethoprim (11.8%) and macrolides (10.7%).

Among the other community settings, the highest level of prescribing is seen out of hours, which accounts for 63.6% of prescribing. There has been a stabilisation in 'other', which reflects improved coding by the NHSBSA (mainly 'community health service') in previous years.

Urgent care and walk-in centre data may be misclassified as it will depend on how this is reported to the NHS BSA; it may be reported at CCG level, as standalone centres, or combined within GP. Since the 2013 NHS re-organisation, there has been reclassification and reconfiguration of these services and therefore comparisons require caution.

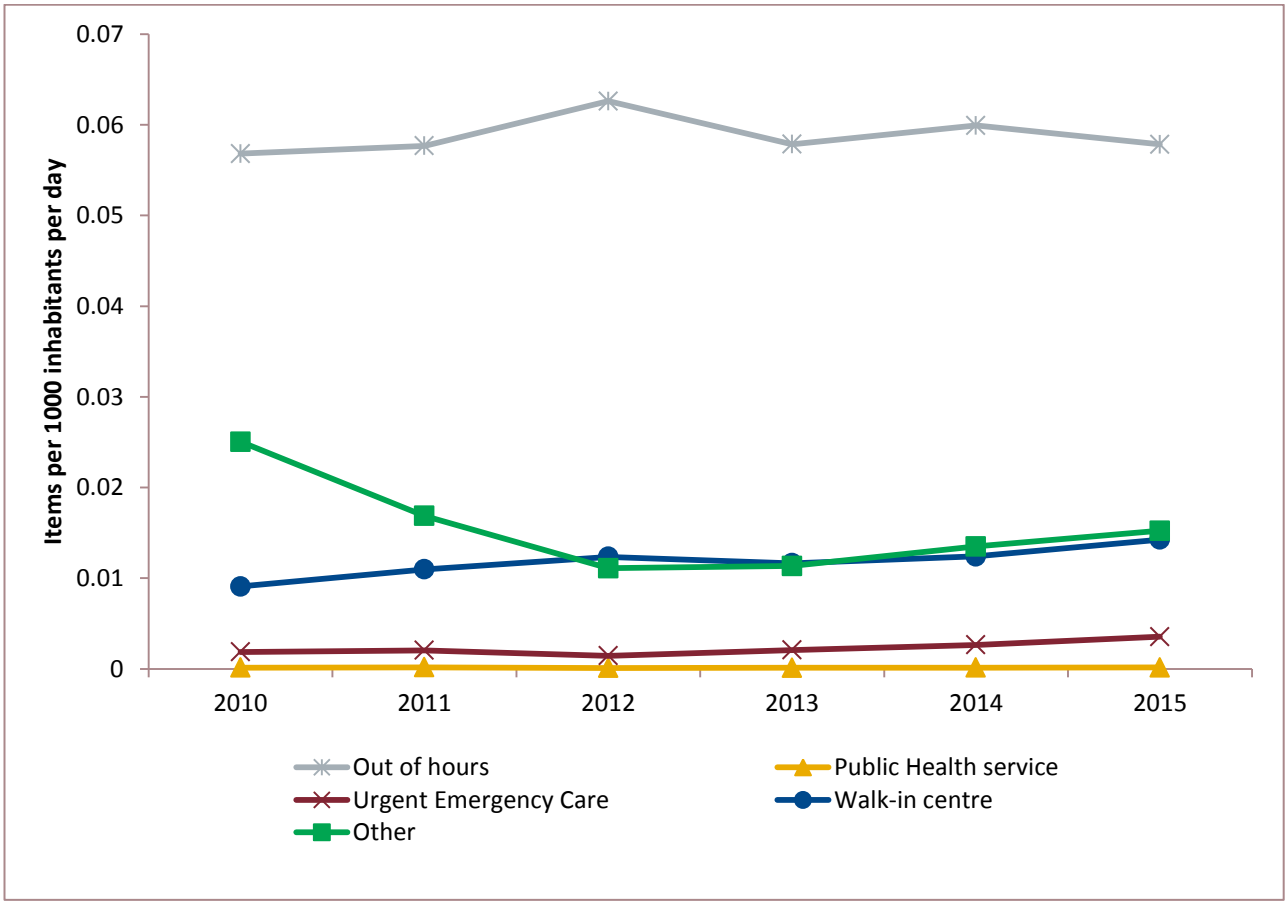
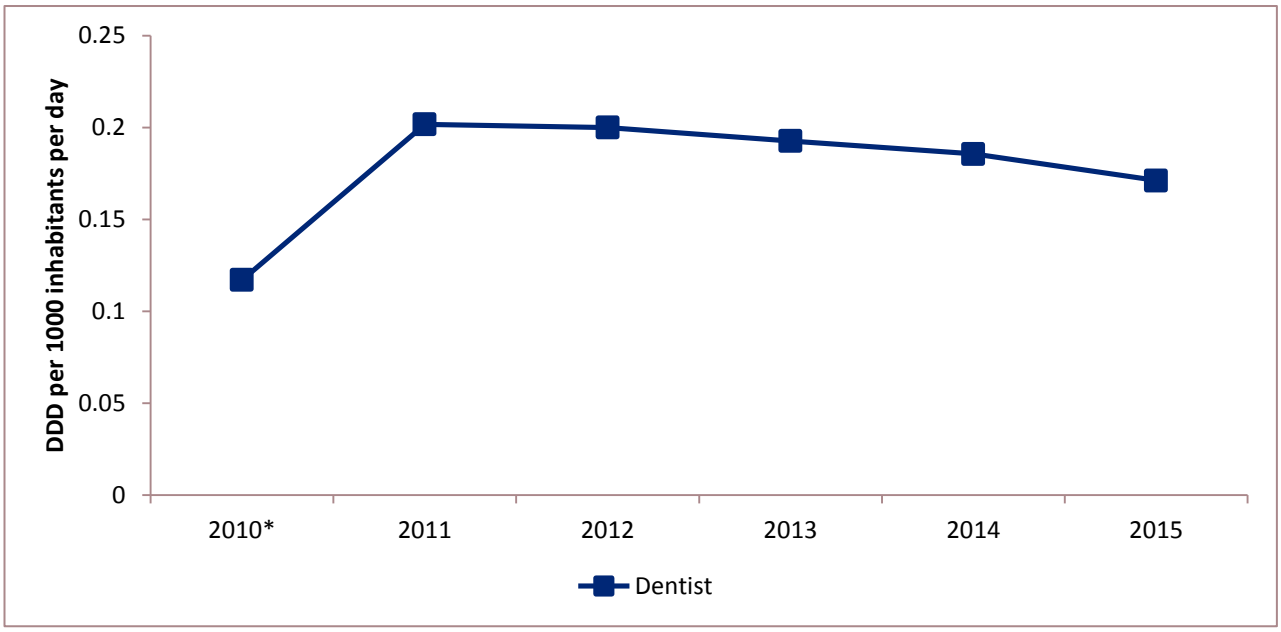


Figure 3.22 Other community antibiotics, expressed as items per 1000 inhabitants per day, England, 2010-2015

Dental practice

From 2012 to 2015, there was a decreased trend in dental prescribing with 14.4% fewer prescriptions in 2015 compared with 2012 (Figure 3.23). The predominant antibiotic prescriptions in 2015 were for amoxicillin (65%), metronidazole (28%) and erythromycin (4%) as shown in Figure 3.27. Almost 99% of prescriptions were narrow-spectrum penicillins, metronidazole or macrolides, as recommended in dental treatment guidelines.[38]



*Data available from June 2010

Figure 3.23 Total antibiotics prescribed by dentists, expressed as items per 1000 inhabitants per day, England, 2010-2015

Table 3.3: Antibiotics prescribed by dentists, expressed as items 1000 inhabitants per day, England, 2011-2015

	Year				
Antimicrobial	**2011**	**2012**	**2013**	**2014**	**2015**
Amoxicillin	0.1298	0.1289	0.1247	0.1206	0.1118
Metronidazole	0.0561	0.0561	0.0543	0.0527	0.0486
Erythromycin	0.0091	0.0088	0.0083	0.0076	0.0067
Amoxicillin and enzyme inhibitor	0.0007	0.0009	0.0009	0.0010	0.0009
Clarithromycin	0.0001	0.0002	0.0002	0.0002	0.0003
Doxycycline	0.0004	0.0004	0.0003	0.0003	0.0003
Tetracycline	0.0002	0.0002	0.0002	0.0001	0.0001
Other	0.0053	0.0045	0.0037	0.0031	0.0026
Total	0.2018	0.2000	0.1927	0.1856	0.1712

[38] Faculty of General Dental Practice (UK); Adult Antimicrobial Prescribing in Primary Dental Care for General Dental Practitioners, Available at http://www.fgdp.org.uk/content/publications/antimicrobial-prescribing-for-general-dental-pract.ashx

Prescribing in secondary care

After five years of increased hospital prescribing, antibiotic consumption, as measured by antibiotics dispensed from hospital inpatient and outpatient pharmacies, using DDD per 1000 hospital admissions decreased by 5% between 2014 and 2015 from 5190 to 4933 DDD per 1000 admissions (Figure 3.24).

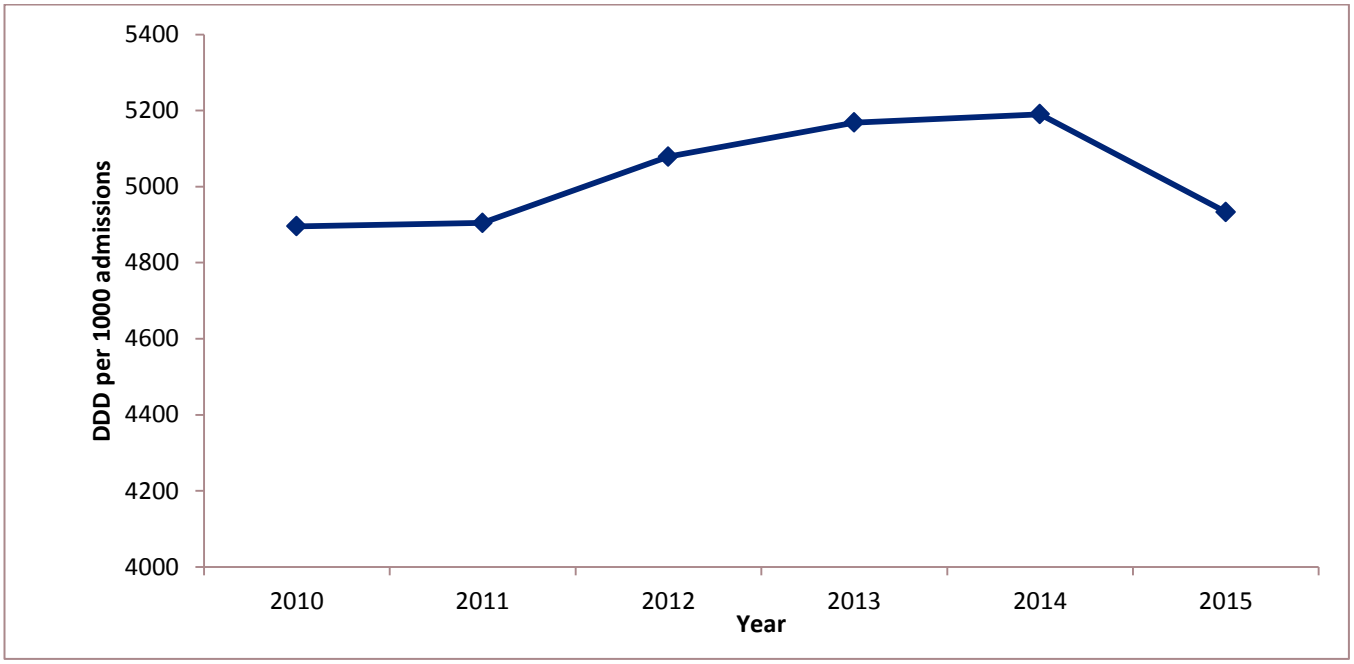


Figure 3.24 Total trust prescribing, expressed as DDD per 1000 admissions, England, 2010-2015

However, this decrease was predominantly driven by decreases in prescribing by teaching hospitals and large and medium trusts remaining static (Figure 3.25). Furthermore multi-service, small and medium sized hospitals had higher antibiotic consumption, expressed as DDD per 1000 admissions than large or teaching hospitals, suggesting potential differences in stewardship activity and longer durations of hospital admissions.

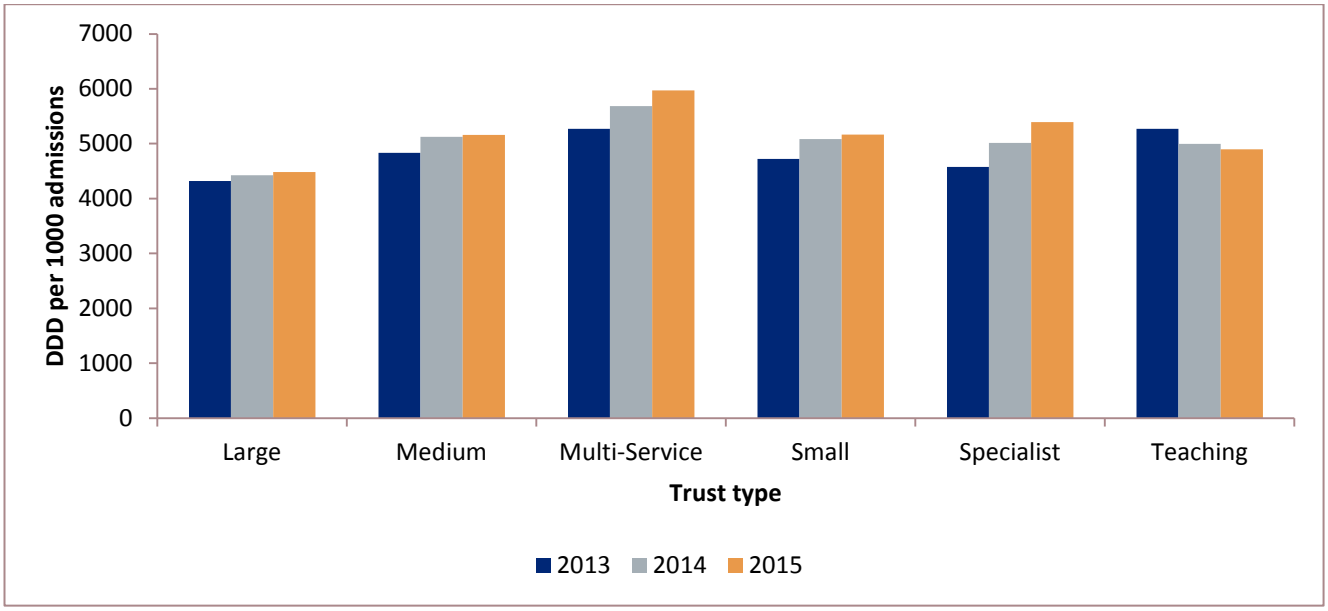
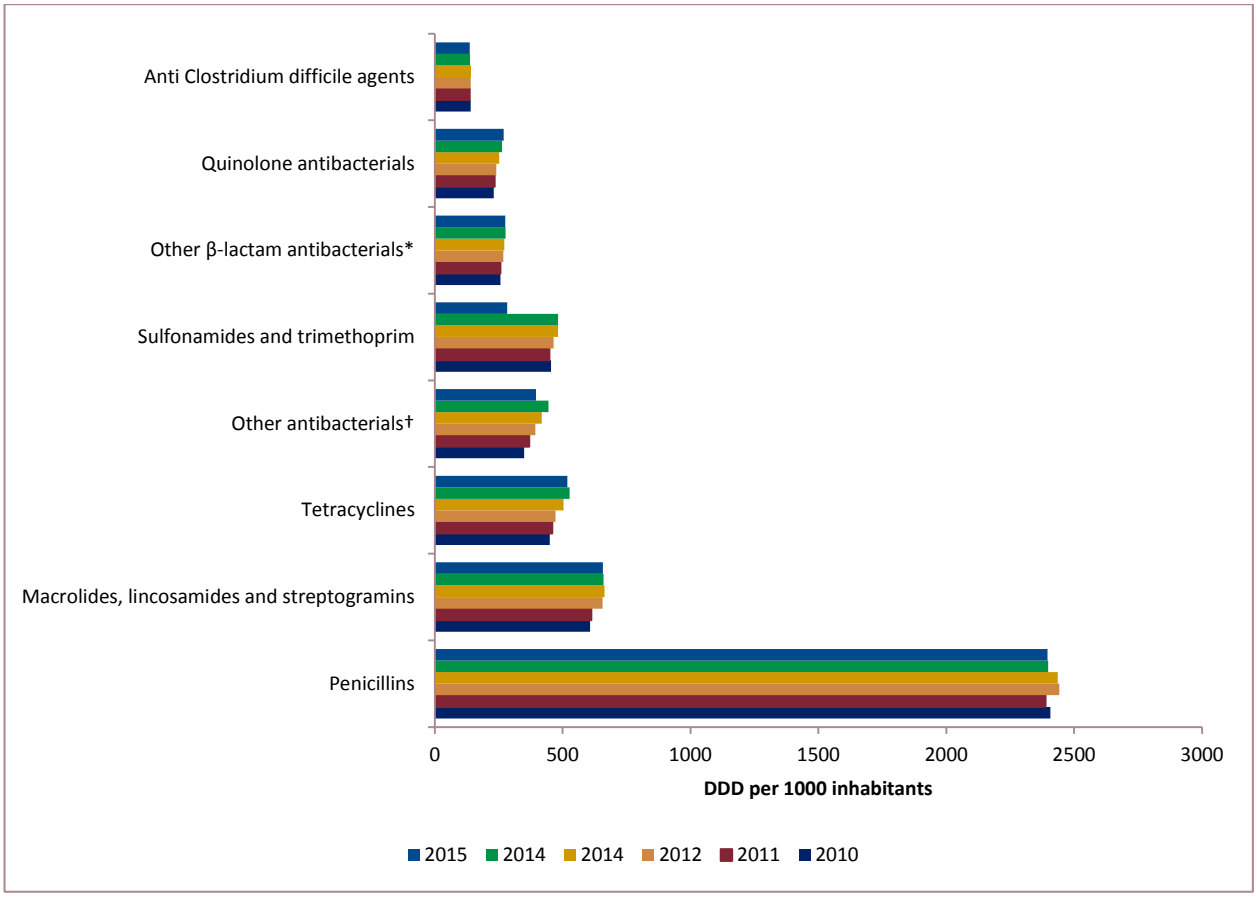


Figure 3.25 Antibiotic prescribing, by trust type, expressed as DDD per 1000 admissions, England, 2013-2015

Between 2010 and 2014, there were incremental increases across all groups each year. In 2015, this increase stopped in almost all groups with particular decreases noticed in the other β-lactam antibiotic groups and the sulphonamides and trimethoprim group.



* includes cephalosporins, carbapenems, and monobactams

** includes glycopeptides, polymyxins, steroid antibacterials, imidazole and nitrofuran derivatives, fosfomycin, linezolid, daptomycin

Figure 3.26 Antibiotic consumption in trusts, by antibiotic group, expressed as DDD per 1000 admissions, England, 2010-2015

Broad-spectrum prescribing

Within hospitals, the current greatest infection threat is multi-drug resistant Gram-negative bacteria, therefore the challenge in hospital antibiotic stewardship programmes is to identify patients and treat patients with effective antibiotics but avoid over-treating them by using the shortest duration possible and using expert review teams to stop or modify antibiotics, especially in complex patients. This section discusses the three broad-spectrum antibiotics that are of particular concern in English hospitals.

Colistin, that is usually reserved for treating bacteria that are known or highly suspected to be carbapenem resistant. After many years at low levels, use of this antibiotic has increased by 30% between 2013 and 2015, with the majority of that increase within the last year. This suggests greater empiric and targeted treatment of carbapenem resistant infections, than we have identified before, in the NHS. Figure 3.27 highlights that the increases were particularly observed in parenteral administration though inhaled colistin has also risen significantly too, which may reflect the increased use of colistin in the treatment of ventilator or hospital-acquired pneumonia with carbapenem resistant bacteria.

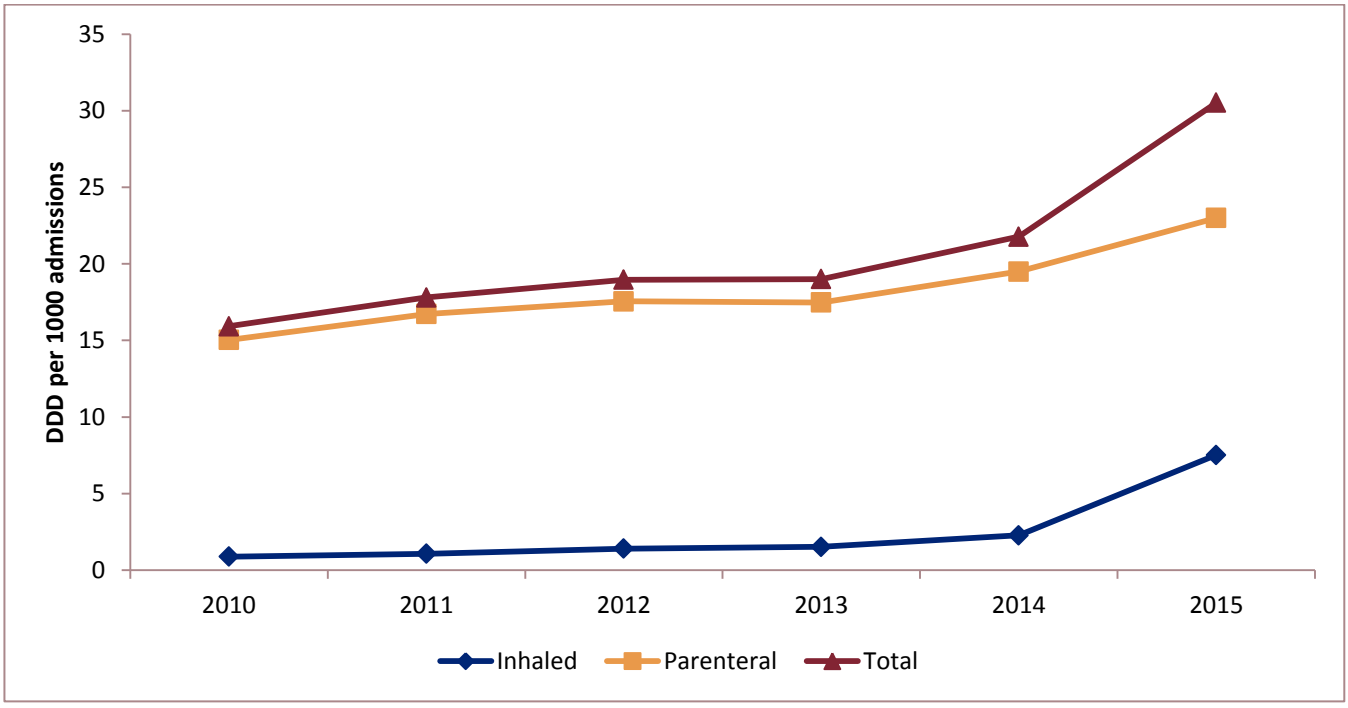


Figure 3.27 Colistin consumption in all trusts, expressed as DDD per 1000 admissions, England, 2010-2015

Unlike overall antibiotic use, specialist and teaching hospitals use much higher amounts of colistin than other trust types (Figure 3.28). This suggests disproportionate burden of suspected or confirmed carbapenem-resistant organisms through patient complexity and/ or prior antibiotic exposure or potential more health-related tourism from endemic countries.

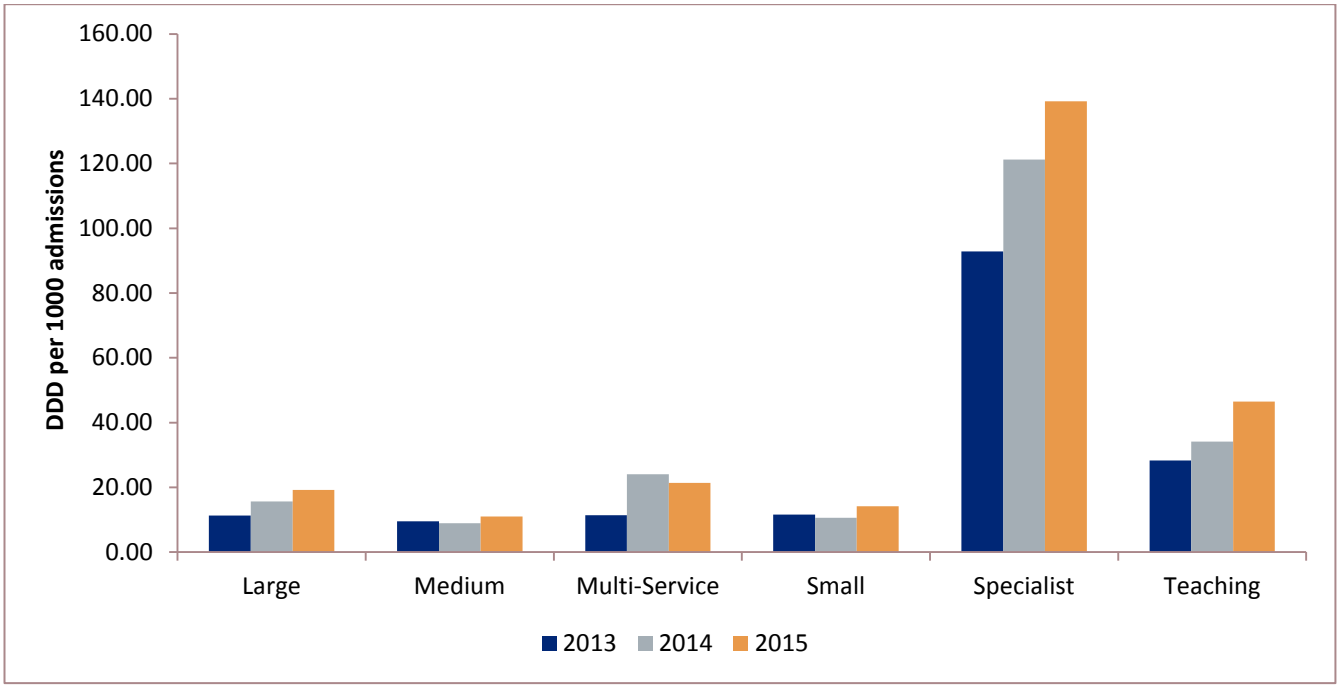


Figure 3.28 Colistin consumption by trust type, expressed as DDD per 1000 admissions, England, 2013-2015

There has been a 62% increase in piperacillin/tazobactam consumption between 2010 and 2015, from 83 to 135 DDD per 1000 admissions (Figure 3.29); this is especially concerning alongside the rapid rise in resistance that has occurred in Gram-negative bloodstream infections, described in Chapter 2.

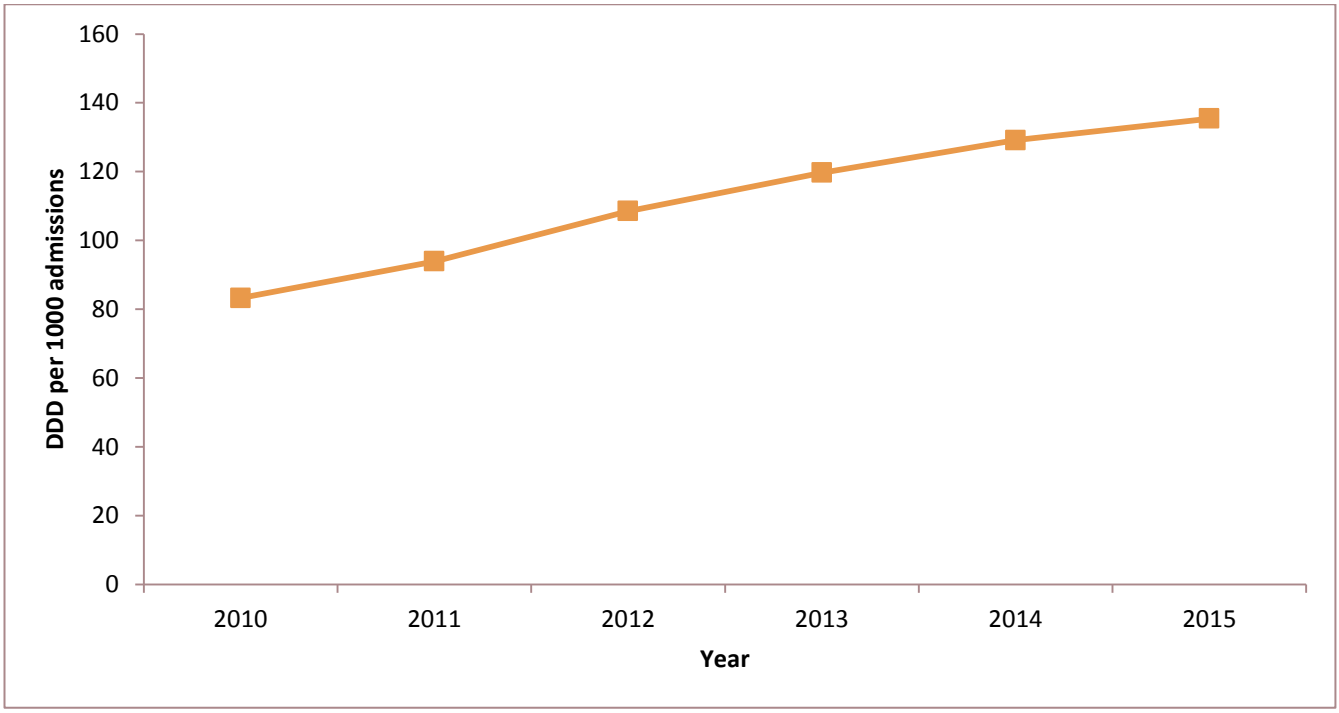


Figure 3.29 Piperacillin/tazobactam consumption in all trusts, expressed as DDDs per 1000 admissions, England, 2010-2015

The increase in use did not occur at the same rate in all hospitals with a more rapid rise occurring in small and medium-sized acute trusts (Figure 3.30).

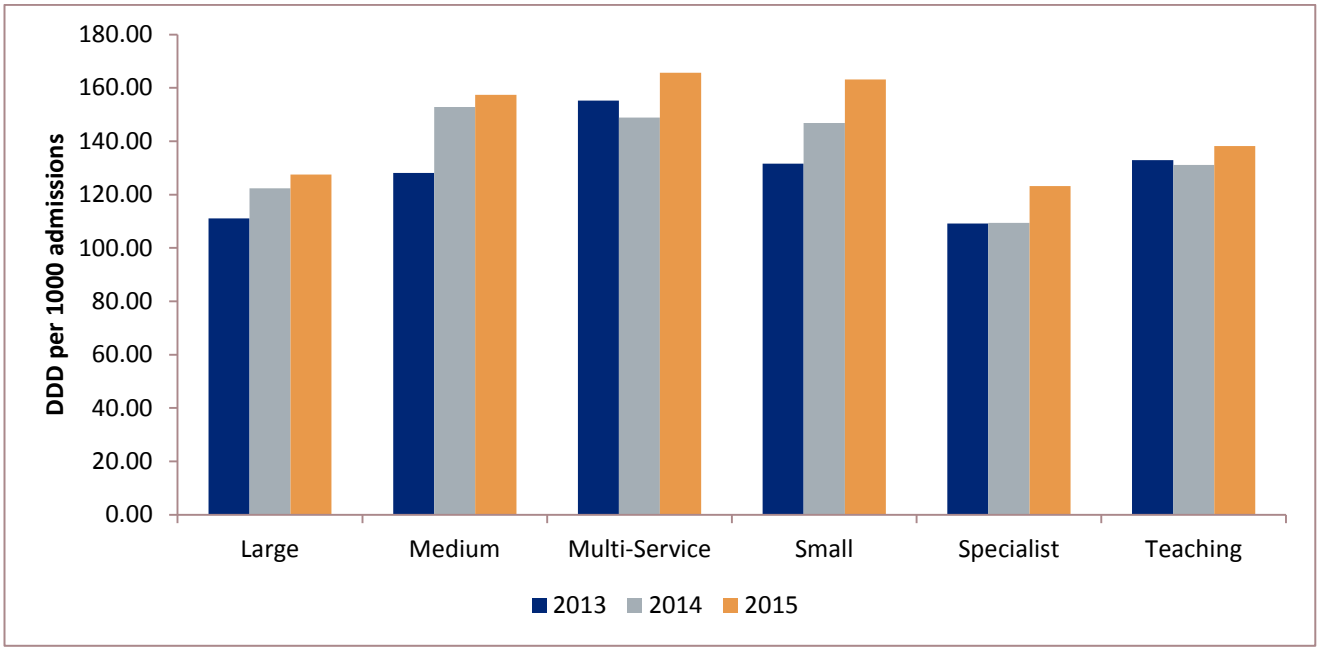


Figure 3.30 Piperacillin/tazobactam consumption by Trust type, expressed as DDD per 1000 admissions, England, 2013-2015

From 2010-2014 carbapenem use rose between 5 -14% per year, though the rate of increase has slowed to just 1% between 2014 and 2015; (Figure 3.31); carbapenem consumption in hospitals increased from 7.5 to 10.4 DDD per 1000 admissions.

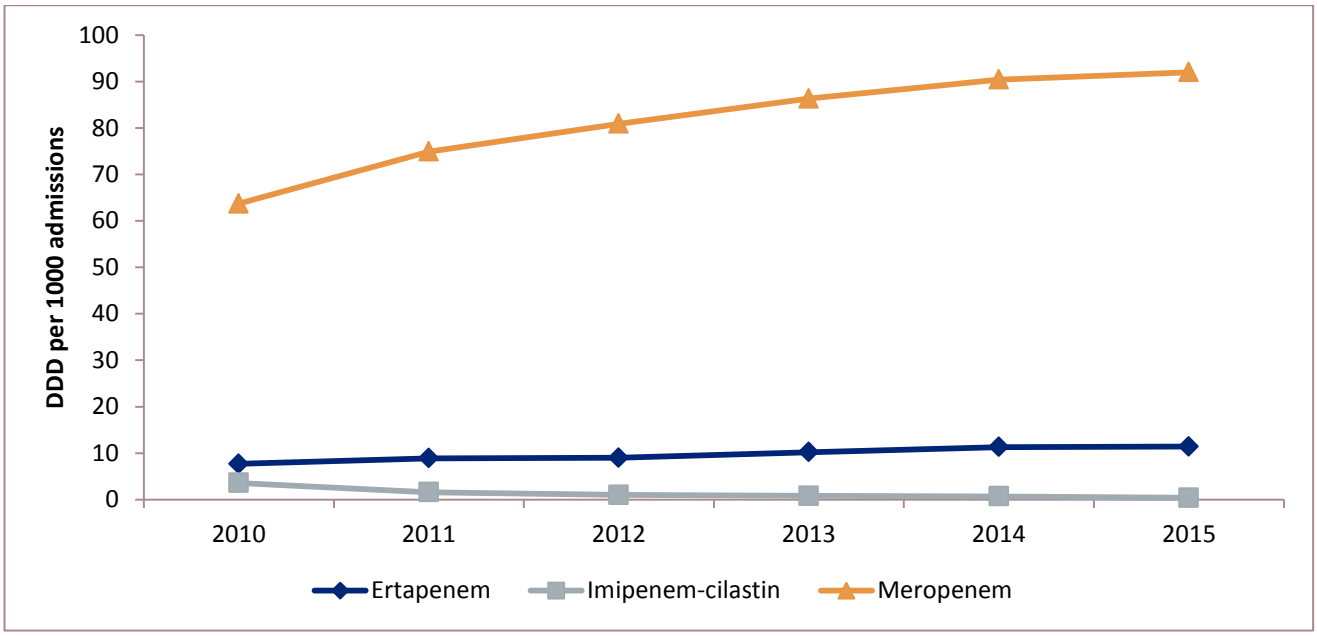


Figure 3.31 Carbapenem consumption in all trusts, expressed as DDD per 1000 admissions, England, 2010-2015

Teaching and specialist trusts reduced use between 2014 and 2015, though the consumption of carbapenems in these organisations remains substantially higher than other trust types (Figure 3.32).

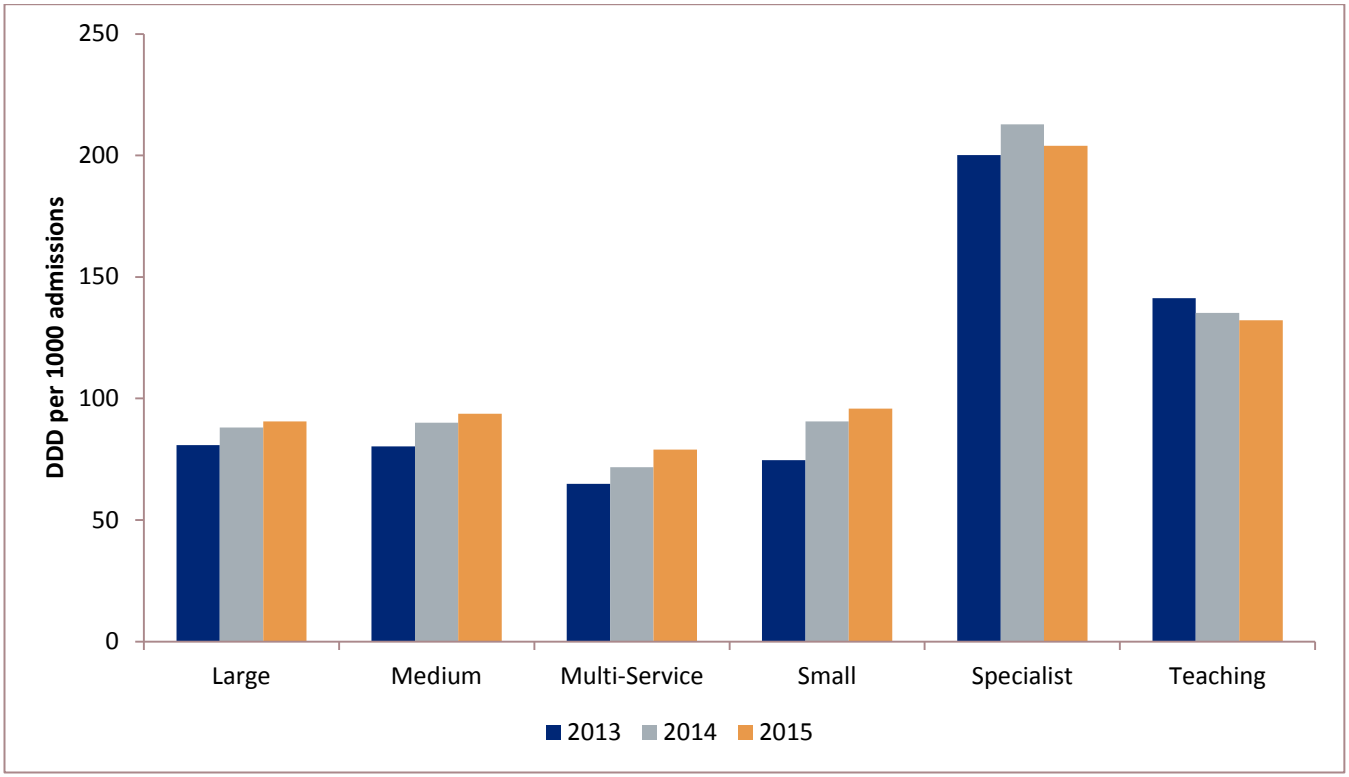


Figure 3.32 Carbapenem consumption by trust type, expressed as DDDs per 1000 admissions, England, 2013-2015

The impact of the Quality Premium on antibiotic prescribing in the community

PHE worked with NHS England to develop a Quality Premium (QP) for antibiotic prescribing in 2015/16.[39] The targets set for each CCGs were aligned to the Department of Health (DH) Expert Advisory Committee on Antimicrobial Resistance and Healthcare-associated Infections (ARHAI's) aspiration to reduce total and broad-spectrum antibiotic use to 2010 levels. The QP is intended to reward for improvements in the quality of the services that they commission and for associated improvements in health outcomes and reductions in inequalities in access and in health outcomes. This was the first ever national incentive to reduce antibiotic prescribing in primary care to support the UK Five Year Antimicrobial Resistance Strategy 2013 to 2018 objective; optimising prescribing practice.

The two parts of the 2015/16 QP had specific thresholds as follows:

- part a) reduction in the number of antibiotics prescribed in primary care by 1% (or greater) from each CCG's 2013/14 value, monitored by items per Specific Therapeutic group Age-sex weightings Related Prescribing Units (STAR-PU). STAR-PU are weighted units to allow comparisons adjusting for the age and sex of patients distribution of each practice and CCG

[39] NHS England. Quality Premium. https://www.england.nhs.uk/resources/resources-for-ccgs/ccg-out-tool/ccg-ois/qual-prem/

- part b) number of co-amoxiclav, cephalosporins and quinolones as a percentage of the total number of selected antibiotics prescribed in primary care to be reduced by 10% from each CCG's 2013/14 value, or to be below the 2013/14 median proportion for English CCGs (11.3%), whichever represents the smallest reduction for the CCG in question

The NHS BSA provided quarterly data on antibiotic prescribing in the community. NHS England and NHS BSA published an antibiotic QP dashboard that was freely accessible on the NHS England website and was published monthly. It provided CCG QP performance data and was intended to be used by both 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. NHS England, NHS Improvement, PHE and Health Education England collaborated to deliver two national AMR workshops for both commissioner and provider organisations.

Almost 2.7 million less antibiotics were dispensed in 2015/16 compared to 2014/15 with a significant and sustained decline in both items per 1000 population and items per STAR-PU. Antibiotic prescribing peaks between October and March each year, when colds and flu season occurs.

Table 3.4: Impact of Quality Premium on antibiotic prescribing in CCGs between 2014/15 and 2015/16

Financial Year	Qtr	Items	Items per STAR-PU	Items per 1000 population
2014/15	1	8 937 522	0.28	165
	2	8 225 452	0.26	151
	3	10 099 553	0.32	186
	4	10 090 324	0.32	184
2015/16	1	8 327 183	0.26	152
	3	7 740 602	0.24	141
	3	9 051 169	0.28	165
	4	9 561 473	0.30	175

There was progressive success over the 12 months with 201 of 208 of CCGs meeting their objective to reduce antibiotic prescription items/STAR-PU by the end of the financial year. The median items per STAR-PU reduced from 1.188 to 1.087 over a rolling 12-month period. One hundred and eighty nine of 209 CCGs met the target to reduce their prescribing of broad-spectrum antibiotics (co-amoxiclav, cephalosporins and quinolones) as a proportion of total antibiotic prescribing by March 2016. The median proportion of broad-spectrum antibiotics reduced from 10.8% to 9.6%. However, significant variation still exists across CCGs with a two-fold difference between high and low-prescribing CCGs.

Using Fingertips AMR local indicators to support NHS incentives

PHE publishes the data to support both the QP in CCGs and GP and the CQUIN in acute trusts. There are seven prescribing indicators available for CCGs.

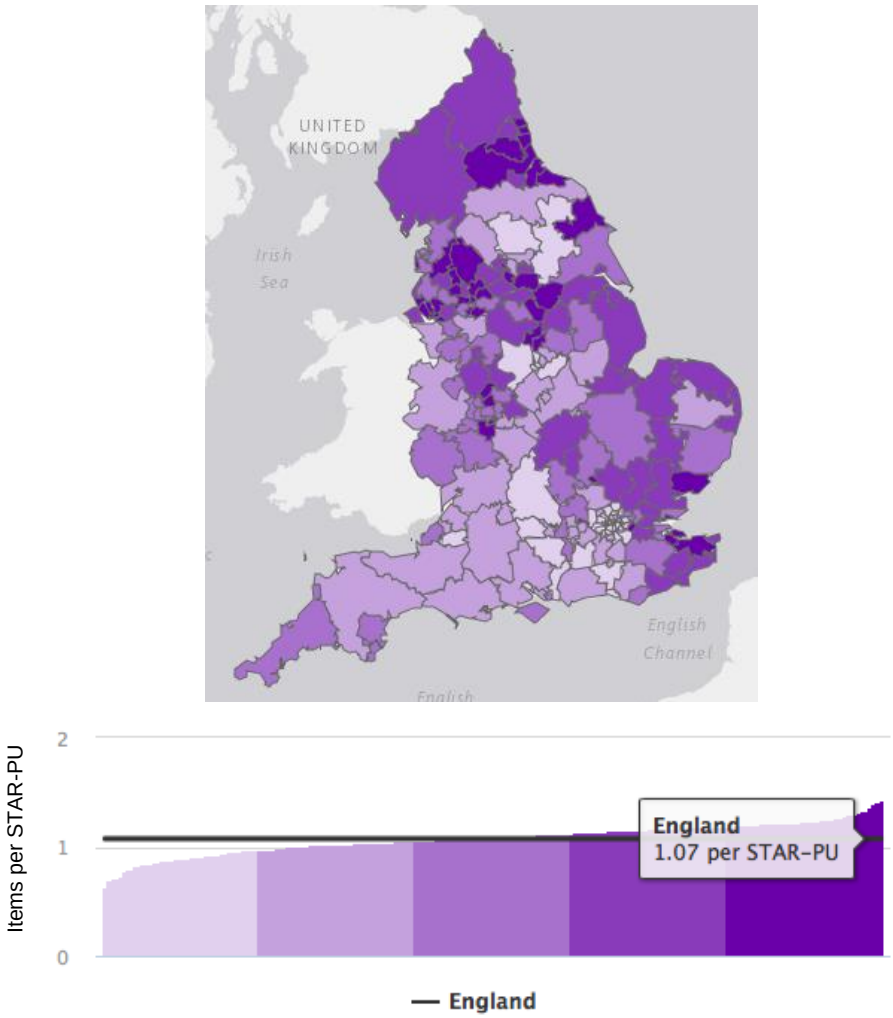


Figure 3.33. Twelve month rolling total number of prescribed antibiotic items per STAR-PU, England, July 2015-June 2016 (map and graph displaying lowest to the highest; hovering over each area on AMR Fingertips displays the CCG area and the numerical output)

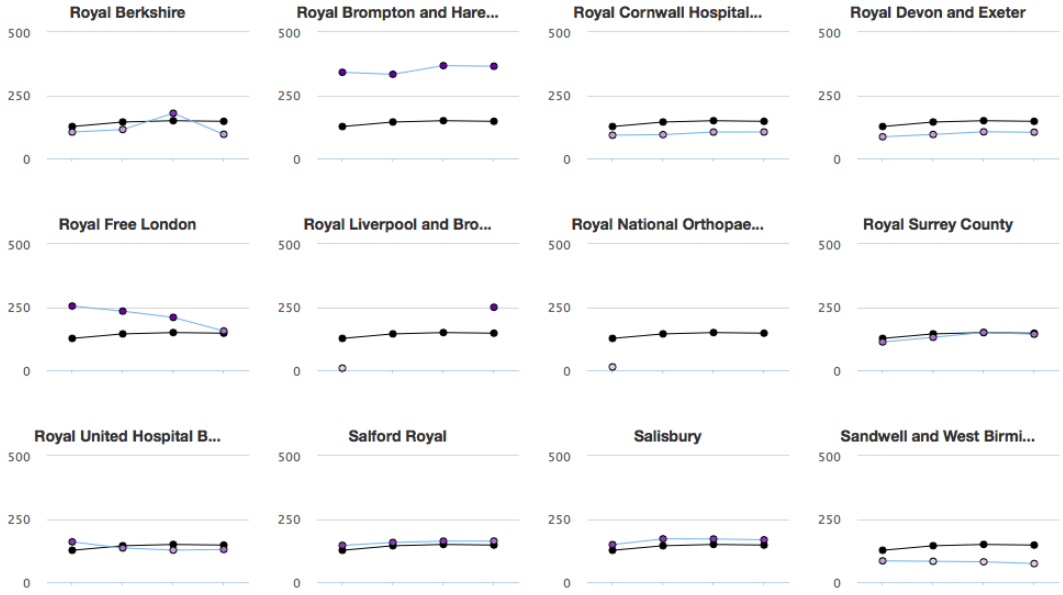
This allows trend and maps to be created so that CCGs can easily compare themselves to their neighbouring CCGs and also similar CCGs based on health measures. For example, Figure 3.33 highlights the variation in items per STAR-PU for the previous 12 months between 0.63 in Camden CCG to 1.44 in Knowsley CCG:

- antibiotic data for Acute trusts is also displayed for the three indicators (total and antibiotics of last resort) that are included in the CQUIN:
- total (inpatient and outpatient) antibiotics dispensed per financial year per 1000 admissions
- piperacillin/tazobactam (inpatient and outpatient) dispensed per financial year per 1000 admissions

- carbapenems (inpatient and outpatient) dispensed per financial year per 1000 admissions

Each acute trust that submits CQUIN data to PHE can review their own trust's progress compared to others. The information can be displayed as trend data, or as spine charts allowing individual organisations to review their progress from local action to reduce antibiotic use and compare their organisations to their peers, providing an opportunity to highlight the acute trusts that are reducing their antibiotic use to potentially learn from. A sample of the trend data for the piperacillin/tazobactam antibiotic use is highlighted in Figure 3.34.

Figure 3.34 Defined daily dose of piperacillin/tazobactam dispensed by acute trusts pharmacies to all inpatients and outpatients per 1000 admissions

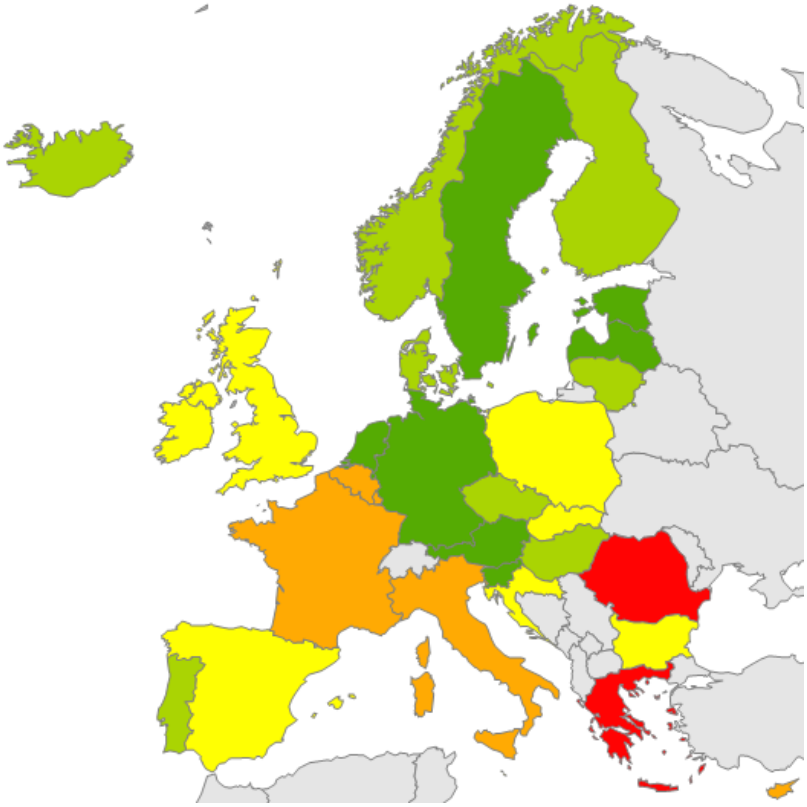


Independent sector

To better improve our understanding of antibiotic consumption across all healthcare sectors, a project on antimicrobial prescribing in the independent sector was initiated at the end of 2015. A letter of participation was circulated to independent sector organisations via the Association of Independent Healthcare Organisations (AIHO) and seven organisations agreed to participate in the project and share their prescribing data with PHE. The project was discussed at the AIHO Pharmacists' Forum and it was agreed that the first step was a survey of independent sector organisations to understand how prescribing data is collected and stored. This data is currently being collated. Once reviewed ESPAUR will develop a method for collecting prescribing data from participating organisations.

Comparisons with other countries

The UK submits data to the European Centre for Disease Control on antibiotic consumption. In, 2014, the most recent year with comparative data, the UK remains in the middle quintile of prescribing (Figure 3.35).



DDD per 1000 inhabitants and per day

	10.578 to < 15.477		15.477 to < 20.375		20.375 to < 25.274
	25.274 to < 30.172		**30.172 to 35.071**		**No data**

Figure 3.35 Consumption of antibacterials for systemic use in the community (primary care sector) in Europe, 2014[40]

England, Scotland and Wales now regularly produce reports outlining hospital and community prescribing (Table 3.5). In 2015, England had the lowest use of antibiotics reported in prescribing items and DDD. Northern Ireland is currently reviewing their data and all four countries data will be included in the 2017 report. Scotland has significantly lower use of the two key antibiotics of last resort (piperacillin/tazobactam and carbapenems) predominantly used in hospitals compared to England and Wales.

[40] European Centre for Disease Prevention and Control; Geographical distribution of antimicrobial consumption, available from; http://ecdc.europa.eu/en/healthtopics/antimicrobial-resistance-and-consumption/antimicrobial-consumption/esac-net-database/Pages/geo-distribution-consumption.aspx#sthash.YAnqEGTr.dpuf

Table 3.5: Antibiotic use compared across the UK health administrations

	Antibiotic items per 1000 population per day (community only)	DDD per 1000 population per day (hospital and community)		
		Total Antibiotics	Piperacillin/ tazobactam	Carbapenems
England	1.79	21.90	0.11	0.08
Scotland	2.00	25.90	0.07	0.05
Wales	2.19	24.27	0.12	0.09

Discussion

There has been significant progress in the last three years in the surveillance, publication and action related to antimicrobial prescribing. Data is available from all NHS-funded antibiotic prescribing settings. Further work is underway to understand prescribing in independent healthcare settings.

Total antibiotic consumption, measured as DDDs, declined significantly between 2014 and 2015 from 22.9 to 21.8 DDDs per 1000 inhabitants per day. Community prescribing from general and dental practice has decreased by more than 6%. GP is the largest prescribing setting and consumption decreased from 17.3 to 16.2 DDDs per 1000 inhabitants. Antibiotic prescribing in primary care measured as the number of prescriptions dispensed per STAR-PU is the lowest level since 2011. (1.110 items per STAR-PU in 2015 compared to 1.233 items per STAR-PU in 2011). Broad-spectrum antibiotic use (antibiotics that are effective against a wide range of bacteria) continues to decrease in primary care. However, hospitals continue to increase their use of antibiotics of last resort, namely piperacillin/tazobactam, carbapenems and colistin. However, the rate of increase of piperacillin/tazobactam and carbapenem use in the hospital sector has slowed.

The impact of the QP including increased transparency and open access to the data has driven clear improvements in prescribing with primary care prescribing nationally having reduced by 7% and back to 2011 levels. This QP is an excellent example of cross-organisation working as it required many organisations nationally and locally to work together to provide data, feedback and expertise. Further evaluations are required to ensure that the cost-effectiveness of the intervention is determined and that the mediators of the QP are understood. This will not only improve the ability to drive further quality improvements but also provide learning on QP impact, not only for AMR but other areas.

Compared with other UK health administration data available, England has the lowest community and hospital antibiotic prescribing. Scotland, However, has the lowest use of last resort antibiotics with England showing the second lowest use.

PHE has now published key antibiotic prescribing quality measures on Fingertips and these measures are the focus of the AMR incentives in both CCGs and Acute trusts. The data presented here suggests that the focus on reducing prescribing is having a positive impact.

The current global median level of antibiotic consumption is 8.54 DDDs per capita per year.[41] England is currently 7% below this level of consumption, at 7.96 DDDs per capita per year. However, we have yet to define the most appropriate level to aim for in this country and further work is in progress by PHE that will help to define where, as a country, we should reduce antibiotic use further.

Future actions:

ESPAUR will

1. Assess the impact of public health campaigns on antibiotic prescribing
2. Continue to work with the independent sector to develop antibiotic consumption surveillance
3. Continue to measure the impact of NHS incentives on primary and secondary care prescribing
4. Continue to submit and work with ECDC and WHO to develop quality measures for antibiotic prescribing
5. Assess the impact of childhood flu vaccination campaign on antibiotic prescribing
6. Start to assess the NHS BSA dataset on age and sex prescribing data
7. Work with research partners to assess the impact and mediators of the QP and CQUIN.

41 Laxminarayan R et al. Achieving global targets for antimicrobial resistance. Science 2016. DOI: 10.1126/science.aaf9286

Chapter 4: Antibiotic stewardship

Optimising prescribing, through the development and implementation of antimicrobial stewardship (AMS) programmes and toolkits is key area 2 of the UK AMR Strategy.[42] This chapter outlines the progress made for community/primary healthcare and secondary care.

Dental sector

The ESPAUR dental subgroup (terms of reference and objectives in Appendix 2) was established in September 2015 on the recommendation of the ESPAUR oversight group, with the aim of exploring options for surveillance, and improving stewardship through prevention, development of resources, audit and education in the dental sector. The key aims in the first year were to understand and improve dental prescribing data, improve cross-sector working and develop a dental AMS toolkit.

Community health services and mental health trusts

PHE has published two national evidence-based AMS toolkits, namely Treat Antibiotics Responsibly, Guidance, Education, Tools (TARGET) and Start Smart then Focus (SSTF), for primary and secondary care respectively. Implementation of these toolkits and associated audits are recommended within the Health and Social Care Act 2008 Code of Practice[43] for the prevention and control of infections, as well as the NICE guidance on AMS (NG15).[44] TARGET provides guidance to help general practice decide when and what antibiotics to prescribe and tools such as patient leaflets to share during consultations. SSTF recommends prompt antibiotic treatment for hospital patients with severe sepsis, along with documentation of the route, indication, dose, duration (RIDD) and post-prescription review at 48-72 hours.

The implementation of these toolkits has previously been assessed in primary care (CCGs) and acute care trusts and but not in community health trusts (CHS) or mental health trusts, creating a gap in our knowledge of antimicrobial use and stewardship in these healthcare settings.

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42 UK Five Year Antimicrobial Resistance Strategy 2013-18. https://www.gov.uk/government/publications/uk-5-year-antimicrobial-resistance-strategy-2013-to-2018
43 The Health and Social Care Act 2008: code of practice on the prevention and control of infections and related guidance. https://www.gov.uk/government/publications/the-health-and-social-care-act-2008-code-of-practice-on-the-prevention-and-control-of-infections-and-related-guidance
44 Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use. NICE 2015. https://www.nice.org.uk/guidance/NG15

A survey was developed to assess AMS activities in community hospitals, which in turn will inform development of AMS guidelines for community hospitals

General Practice and other community prescribers

The TARGET antibiotic toolkit is an evidence- based resource to help clinicians and commissioners in England reduce inappropriate antibiotic prescribing (Figure 4.1). It aims to influence personal attitudes, social norms and perceived barriers to responsible antibiotic prescribing in primary care and encourages action planning and audit. The objectives this year were to perform a qualitative evaluation of the TARGET materials and to explore AMS activities being undertaken in primary care using the Royal College of General Practitioners (RCGP) TARGET e-Learning module's self-assessment tool.

Secondary care: acute trusts

A survey conducted by PHE in 2014 highlighted that the majority of acute trusts completed an antimicrobial point prevalence survey (PPS) at least yearly; with other) audits completed more frequently. In May 2015, the ESPAUR SSTF implementation subgroup recommended that PHE should consider the development of an AMS surveillance system. It aimed to test the feasibility of collecting summary details and results of existing trust AMS audits using Select Survey as the tool. The tool allowed trusts to submit data that had already collected (eg local point prevalence surveys (PPS) and other regular antibiotic audits (eg monthly ward audits); this data would aim to facilitate national benchmarking and sharing of good practice.

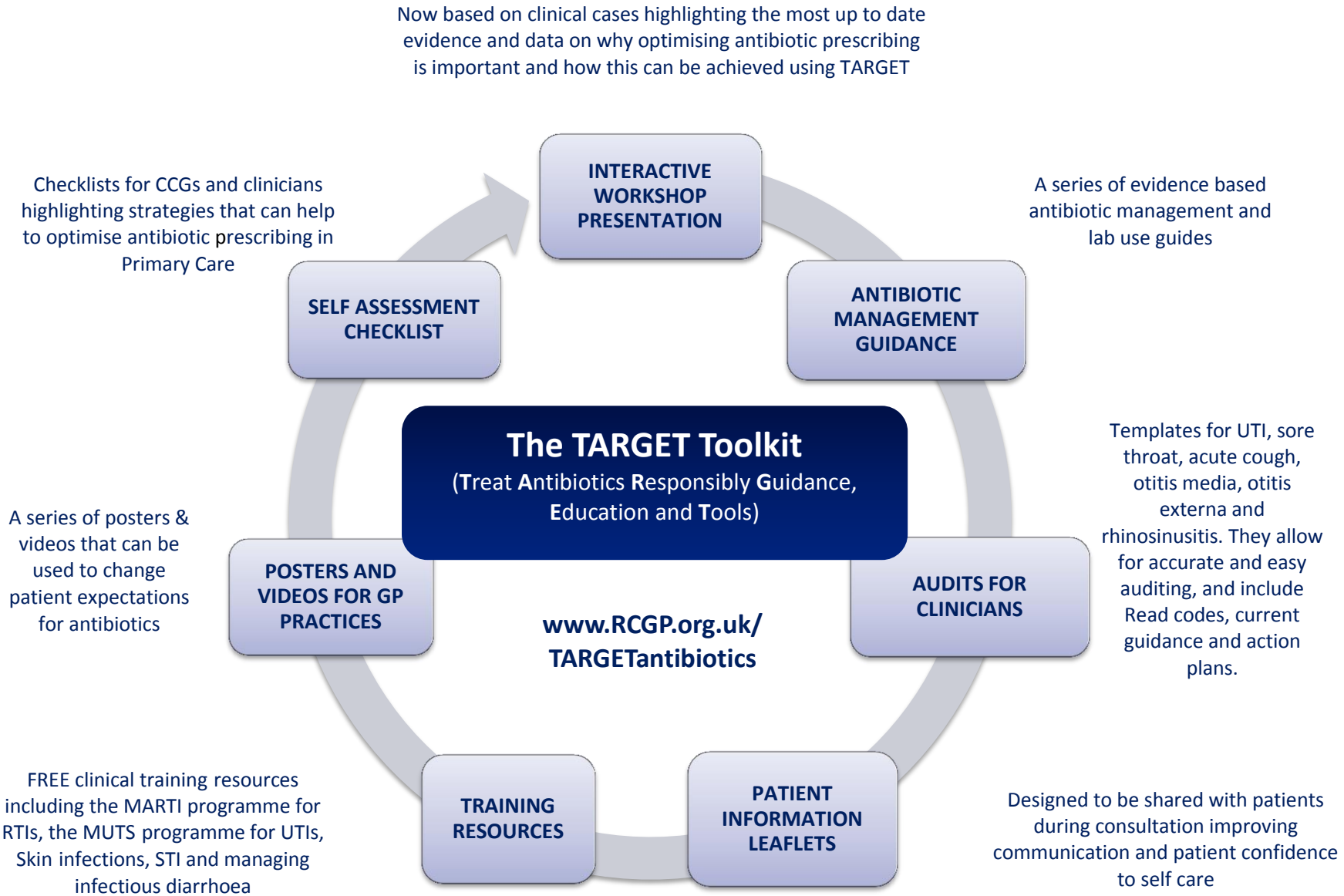

Figure 4.1: TARGET Antibiotic Toolkit

Methods

Development and roll-out of antimicrobial stewardship dental toolkit

The multi-professional/organisation dental subgroup of ESPAUR worked with professional organisations to develop an options appraisal to improve dental prescribing data and develop an AMS toolkit that includes a patient information leaflet, a poster and an audit toolkit. The national toolkit was built on the work carried out in the North West with partners from PHE, local professional networks, local dental committees, academia and supported by the local NHS. The dental subgroup of ESPAUR, which includes representation from a range of organisations, reviewed current evidence available for prudent antibiotic use in dental practice including regulatory documents and national publications. These were used to inform required changes to poster and leaflet components of the local toolkit. The tools were considered during several meetings to reach a consensus concerning clarity, language improvement, relevance and accuracy. A new audit tool was collaboratively developed with Dental Protection, Faculty of General Dental Practice, British Dental Association and PHE.

Community health services baseline stewardship survey

In October 2015, a pilot questionnaire comprising both closed and open-ended questions was sent to six pharmacists practicing in community hospitals. This was an exploratory study to test the relevance and the validity of the content of the questions. Areas covered in the questionnaire were demographics, presence of an antimicrobial pharmacist and an AMS team, existence of antimicrobial guidelines and restricted antimicrobial list and awareness of AMS guidelines in other healthcare settings.

Four pharmacists agreed to participate in this exploratory study, one of whom was a specialist antimicrobial pharmacist. Following this exploratory pilot further revisions were made to the questions; the finalised questionnaire, which was designed as an online survey tool was distributed via the Community Health Services Network to pharmacists in community health services trusts.

The survey was distributed to the 26 CHS trusts in England in February 2016. Responses were analysed using Microsoft Excel. This was a voluntary service evaluation completed by healthcare professionals; ethics approval was not required.

Evaluation of the TARGET Antibiotic Toolkit

Semi-structured interviews with 38 study participants from across England and Scotland, explored local efforts to improve antibiotic prescribing, views on the TARGET materials, and suggested improvements to the toolkit.

Course participants of the RCGP eLearning module 'Antibiotic Resistance in Primary Care' entered data via an electronic self-assessment tool. A report for each respondent compared their results with CCG and national averages. Responses were analysed between November 2014 and June 2016.

Development of secondary care stewardship surveillance tool

This stewardship surveillance tool was developed during 2015 with preliminary testing by pharmacists working in East of England acute NHS trusts. The oversight group also provided comments at the December 2015 ESPAUR meeting.

In March 2016, PHE conducted a national pilot of the AMS surveillance system with the assistance of the regional antimicrobial pharmacists' network, to test the feasibility of centrally collecting details across England.

The web-based tool was circulated to the national antimicrobial pharmacist network across 146 acute NHS trusts for pilot. As this was a voluntary pilot audit completed by healthcare professionals, ethics approval was not required. The results were analysed using Microsoft Excel.

Results

Dental sector

The NHS regional teams commission both primary and secondary dental care services, the majority of care being provided through primary care. Dental practices are independent businesses awarded a contract to provide NHS dental care. There is a mixed economy within many dental practices and private dental care is provided both within NHS practices and in fully private practices.

Details on dental prescribers are not currently captured in prescription data. NHS dental prescribing data is currently only available at national level and at an area team level based on the dispensing pharmacy (though the prescription may not be prescribed in the same area in which it is dispensed), making it difficult to understand the prescribing

patterns of individual practices and hard to know where to target actions in order to effect change.

Antibacterial drugs continue to top the list of items prescribed by dentists in primary care, accounting for 66.4% (3.7 million) of dental prescription items in 2014. There is currently no available information about private prescribing within dental practices.

The ESPAUR dental subgroup has worked with NHS Digital and NHS BSA to develop an options appraisal for future data collection of prescribing from dental practices. This is currently being financially assessed by NHS Digital and NHS BSA, with the aim to introduce more detailed dental prescribing data.

The subgroup has used the network connections of all the group members to foster consistency of message across the system and learn from other best practice. Examples of these include;

- consistent metronidazole dose across the British National Formulary (BNF) for dentists and other guidance. The evidence suggested that metronidazole at a dosage of 400mg three times per day was appropriate for dental infections and consistent with medical prescribing. The work of the subgroup highlighted this evidence and currently the BNF is being updated in line with this guidance

- the dental subgroup considered resources that were already being developed (eg Faculty of General Dental Practice antibiotic prescribing guidance) and worked across the devolved nations (eg Scottish Dental Clinical Effectiveness Programme guidance and Translation Research in a Dental Setting programme and Welsh prescription data granularity)

Development of a primary care dental antimicrobial stewardship toolkit

The working group built on the work carried out in the North West with partners from PHE. Good practice was also noted and incorporated from work previously carried out in Wales, Scotland and through the Faculty of General Practice (FGDP) and the British Dental Association (BDA). The final toolkit includes resources for dental practices; posters and leaflets for patients and signposting to prescribing guidelines. It was published in November 2016 and will be formally launched during World Antibiotic Awareness Week.

Community Health Services

Twenty CHS trusts (77%) responded to the survey. A higher proportion of CHS (25%) have dedicated pharmacy posts focussed on AMS compared to CCGs (5%) and less than acute trusts (94%). Half of CHS have an AMS committee in place, compared with

18% of CCGs and 94% of acute trusts (Table 4.1). While 70% had a dedicated antibiotic policy in place, this is much lower than both CCGs and acute trusts (both >90%).

Table 4.1: AMS Initiatives in community health services trusts

Description	% of Responding CHS trusts (n = 20)
Substantive pharmacy post focussed on AMS	25
AMS committee in place	50
Dedicated antimicrobial policy/management	70

Seventy per cent of CHS have a dedicated antimicrobial policy or management guideline in place compared to 93% of CCGs and 99% of acute trusts. The services provided by the responding CHS trusts varied (Figure 4.2); services included inpatient step up beds (80%); inpatient step down beds (85%) and mental health beds (40%).

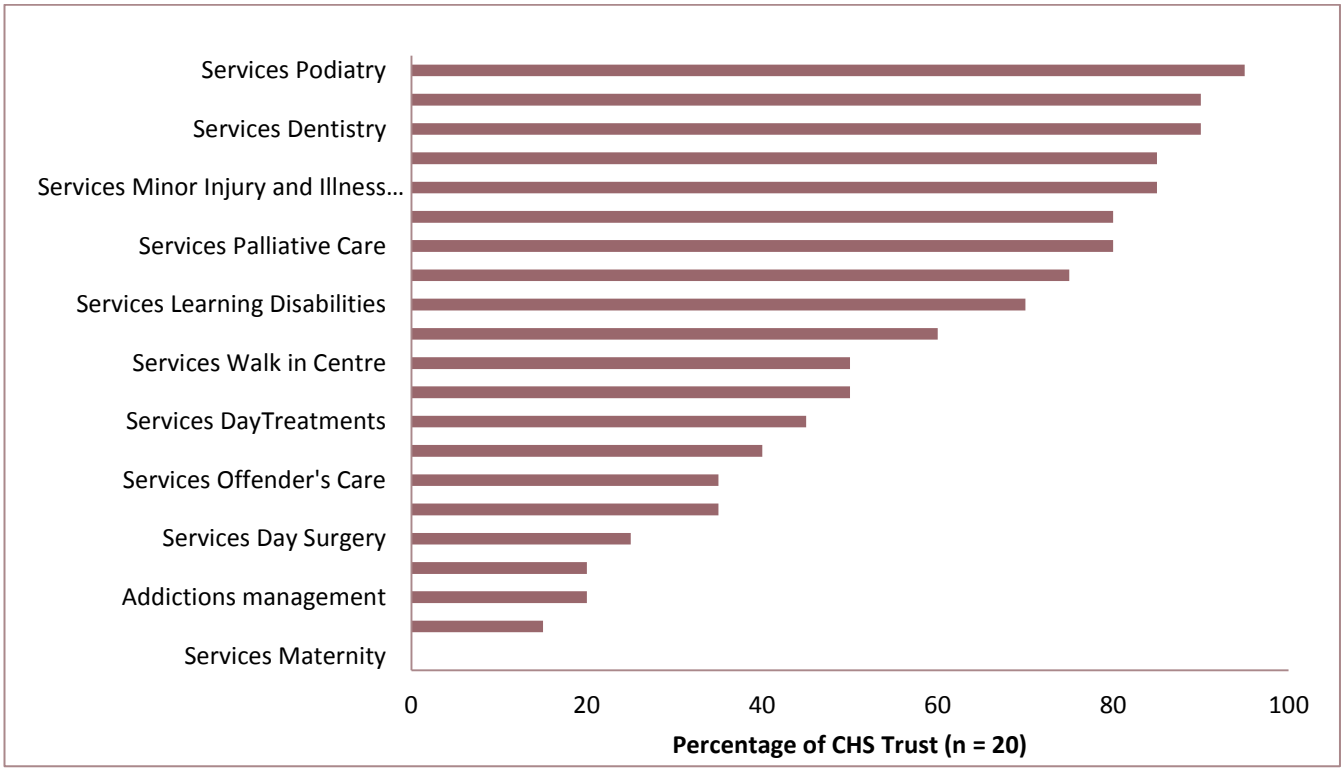

Figure 4.2. Services provided by the responding community health services trusts

In the ten CHS trusts who reported having an AMS committee, the membership of these AMS committees was diverse, with nurses, pharmacists and microbiologists being more commonly represented than other specialties (Figure 4.3).

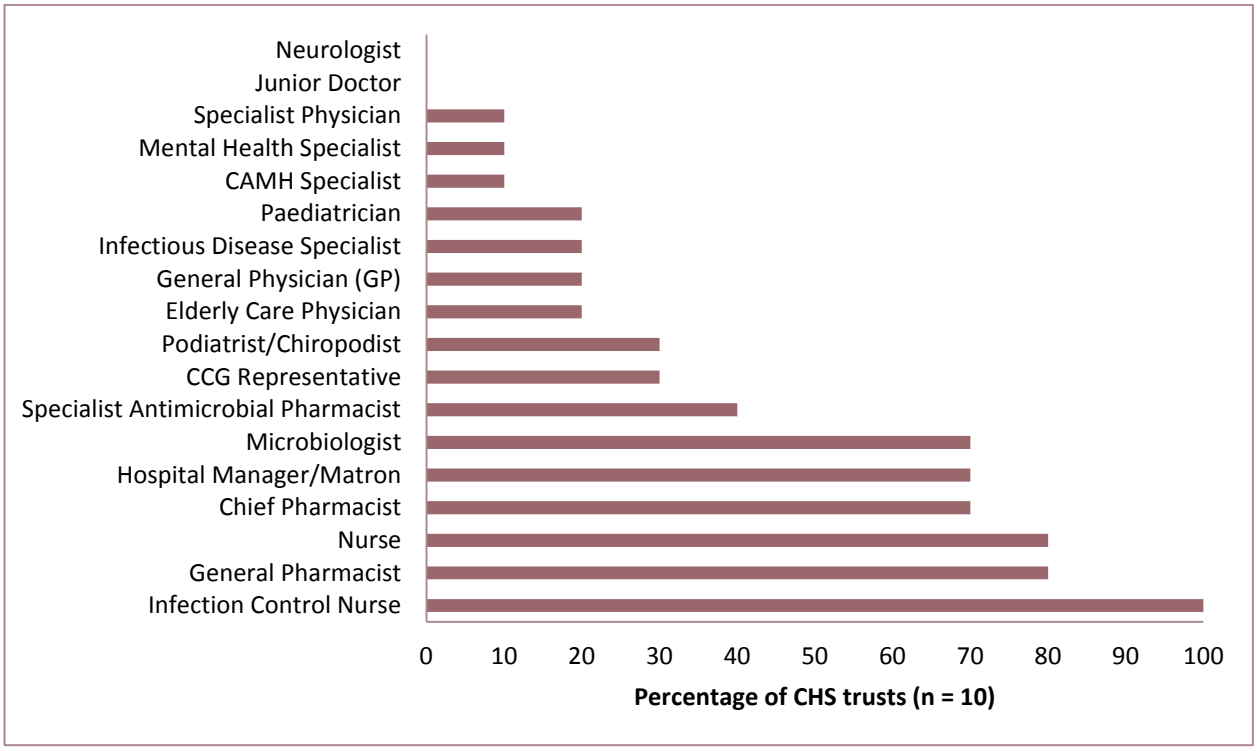

Figure 4.3. Membership of Antimicrobial Stewardship committees in the Community Health Services Trusts

The majority of CHS trusts had an antimicrobial formulary in use. However, for a range of other policies which are routinely implemented in almost all acute trusts, CHS trusts did not have these in place, as outlined in Table 4.2.

Table 4.2: Antimicrobial policies and guidelines in place at the Community Health Services Trusts

Antimicrobial Guideline/Policy	Number of Responding CHS trusts (%) n = 20
Antimicrobial formulary	17 (85)
Empirical antibiotic guidelines	11 (55)
Reserved antimicrobial list	2 (10)
Intravenous to oral switch	3 (15)
Surgical antimicrobial prophylaxis	2 (10
Automatic stop	3 (15)
Separate antimicrobial drug chart/section	3 (15)
Outpatient parenteral therapy (OPAT)	10 (50)

Other key findings of the survey were related to the awareness of the AMS toolkits by the CHS trusts as well as their related actions.

Eighteen (90%) of the responding CHS trusts indicated that they were aware of the primary care AMS toolkit, TARGET; and 15 (75%) were of the secondary care toolkit, SSTF. Fourteen of the responding CHS trusts were aware of both toolkits and of these,

eight had formally reviewed both toolkits. However, less than half had developed action plans and worked with prescribers to improve uptake (Figure 4.4).

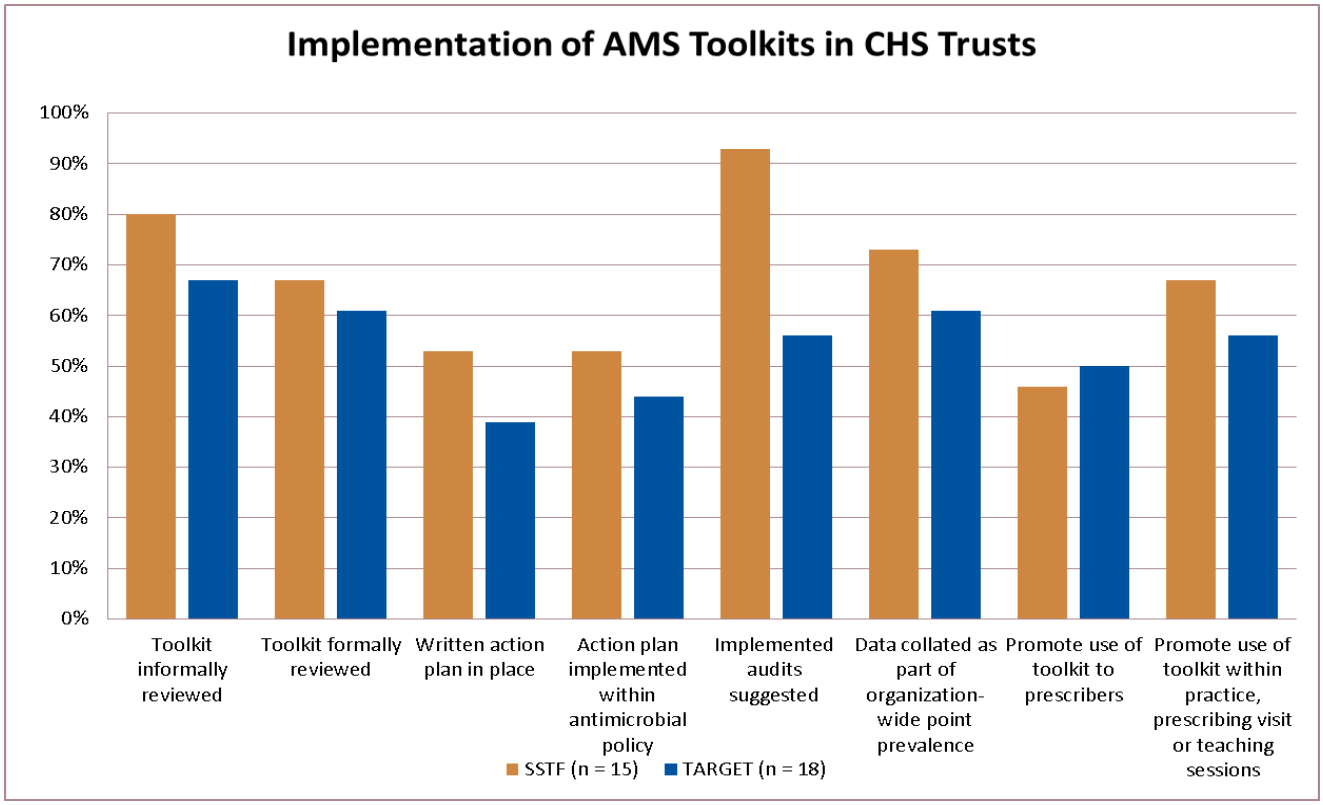

Figure 4.4 The Implementation of AMS toolkits SSTF and Target in CHS trusts

The majority, 90% (18), of CHS trusts were aware of the NICE AMS Guidance (NG15). Of these, 83% (15) had completed the baseline assessment tool. However, only 56% (10) of CHS trusts had developed an action plan as advised in the guidance.

The implementation of education and training initiatives varied for healthcare professional groups is shown in Table 4.3.

Table 4.3: Implementation of education and training initiatives in responding Community Health Services Trusts

Healthcare professional groups	Percentage of CHS trusts that provide the following eduction and training initiatives to staff members from different professional groups			
	Doctors	Nurses	Pharmacist	Non-medical prescribers
Receive AMS/AMR teaching on induction	50	40	50	50
Provided with antibiotic guidelines on induction	75	55	65	75
Have access to optional e-learning	25	30	25	30
Need to complete mandatory e-learning module	15	10	10	10

Primary Care Prescribers: TARGET toolkit

Analysis of TARGET antibiotics web use statistics indicated steady access to the online toolkit with peaks around World Antibiotic Awareness Week each year. Average monthly views of the online resources were around 6,000 per month. In 2015/16, the lowest month was May at 3,059 views and the highest November at 8,560 views.

A total of 1,415 healthcare professionals completed the online self-assessment tool that is linked to the eModule entitled “Antibiotic Resistance in Primary Care.” Almost all respondents used antibiotic guidance, although only two thirds reported that this was made available to all temporary prescribers. Half had undertaken an antibiotic audit in the last two years with a practice action plan.

Most GPs reported that they used back-up/delayed prescribing and three-quarters used leaflets or posters to highlight the importance of responsible antibiotic use.

Analysis of eModule user statistics and feedback indicated that that the TARGET eModules are useful and remain a popular resource. The number of completed courses from launch until 30 April 2016 are presented in Table 4.4.

Table 4.4: Completed TARGET modules since launch

Course	Completions (from launch to 30 April 2016)	Course rating out of 5	User comments
Antibiotic Resistance in Primary Care (launched Nov '14)	897	N/A	N/A
Managing Acute Respiratory Tract Infections (launched Sep '14)	3617	4.32	"Very clear, factual and direct" "This was interesting with regard to the evidence around delayed prescribing"
Skin Infections (launched Feb '15)	653	4.45	"Just the right amount of information for me. Might have been better to have had more information about prescribing to prevent recurrent herpes simplex." "An excellent overview of the things they never taught me in medical school or after!"
Urinary Tract Infections (launched Nov '15)	2349	4.23	"More thought provoking than I thought it was going to be - useful learning points in managing a common condition in primary care" "Very relevant and good detail and practical advice and learnt quite a few new facts and will alter my practice"
Sexually Transmitted Infections (launched June '15)	263	3.8	"Excellent. Comprehensive and helpful" "Very good but takes more than 2h 10m"

The Primary Care Unit, in conjunction with the Clinical Knowledge Summaries (CKS) and a microbiologist based in Southmead Hospital, are currently performing a systematic review and literature search to update the management and treatment of common infections guidance. The first draft of this guidance, with review of recommendations, references, and rationales are due to be completed by the end of 2016 for stakeholder review.

Secondary care: acute trusts

Development of secondary care stewardship surveillance tool

A total of 33 acute NHS trusts participated in the pilot 12 were teaching hospitals. The majority of pilot participants (94%) had reviewed the NICE AMS guidance, with 79% completing the accompanying baseline assessment tool. All organisations had collected patient level audit/quality improvement data relating to AMS guidance in the previous year; these data were most commonly collected on a monthly (39%) or quarterly (27%) basis. A high proportion of wards were typically surveyed at least once over the past year (51-100%) (Table 4.5).

Table 4.5: Wards surveyed by acute trusts for antimicrobial stewardship audits and prevalence surveys

Types of ward surveyed	% participants surveying this ward type (n=33)
Acute Medicine	94
Non-elective surgery	91
Adult Intensive Care Unit (ICU)	76
Paediatrics (including neonatal and paediatric ICU)	70
Accident and Emergency	21
Obstetrics and gynaecology	70
Day wards (ie. no overnight stay)	12
Elderly	88
Psychiatry	0
Long-term care/Rehabilitation	61

The number of patients surveyed during the last AMS audit within trusts ranged from 98 to 1269 reflecting monthly audits and yearly whole trust point prevalence surveys (Table 4.6).

Table 4.6: Data collected by participants during their most recent AMS data collection/audit

	Total responses (n)	% Trusts that collected these data	Mean number of patients surveyed	Range of patients surveyed
Number of patients surveyed	28	79	649	98-1269
Number of patients on antibiotics	28	96	214	72-757
Number of antimicrobial courses prescribed	27	63	273	74-426

The pilot highlighted that majority of trusts collected data on documentation of indication and stop/review date as recommended by SSTF and NICE guidance. However, fewer collected data on whether review decisions were documented at 48-72 hours, compliance with local guidance, documentation of antimicrobial allergy. Only 14% of trusts collected data on whether culture and sensitivity samples are taken before an antibiotic is started (Table 4.7).

Table 4.7: Information audited by acute trusts; and sample results from recent audits

	Percentage of Trusts that collected these data (n=28)	Mean percentage of patients achieving this indicator in recent audit	Range of the proportion of patients meeting this indicator
Indication documented on drug chart (including severity where appropriate)	90	83	27-100%
Stop or review date documented	93	73	30-99%
Antibiotic courses reviewed with formal documentation at 48-72 hours after initiation of therapy	36	71	10-96%
Compliant with local guidelines (dose, frequency, duration) or reason for non-compliance documented	79	84	30-98.5%
Microbiology samples taken before starting antibiotics	14	58	10-88%
Antimicrobial allergy documented	61	93	30-100%

Less than 20% of trusts collected data on the documented antibiotic prescribing decisions made at 48-72 hours as recommended by SSTF (Table 4.8).

Table 4.8: Prescribing decisions currently being collected by trusts

	Total responses (n)	% participants who collected these data
Stop date	26	19
Continue decision	25	16
Intravenous to oral switch decision	25	12
Oral Parenteral Antimicrobial Therapy decision	25	8
Switched to another antibiotic	25	12

Comments provided by participants

Respondents were given an opportunity to provide further comments on the survey or the subjects covered.

The need for a standardised data collection nationally was highlighted: “I feel that this is urgently required to standardise data collection nationally”; “Any help with potential audit tools and data analysis excel documents would be much appreciated.”

Further details on how data was collected and feedback on the collection tool that was considered during updates: “Our audit tool allows us to audit initiation decisions (Start Smart) and continuation decisions (Then Focus) separately – (we) did this because patients often move clinical team during the course – but it means (for instance) that the numbers behind the 'guideline compliance' % are different from these behind the '48-72 hour review' %”; “Within our trust we analyse data with regards to percentage of antibiotics with stop/review and indication documented (rather than number of patients). This is because patients may have multiple antibiotics prescribed, some may have stop date etc others may not. However, I have adapted info for the purpose of this survey”.

Discussion

In community and primary care, a dental AMS toolkit was developed and launched; the uptake and implementation of AMS recommendations in SSTF and TARGET toolkits by CHS was assessed, and evaluation of the TARGET toolkit was also performed.

In secondary care, an AMS tool was developed and piloted. Following the launch of the AMR CQUIN, which included a request for data on review of empiric prescriptions, the AMS tool was adapted for use as part of the national AMR CQUIN.

Dental

The dental subgroup has made significant progress, bringing together key professional, public health and national organisations. In the first year, the subgroup has assessed and developed an options appraisal for future, more granular, dental prescribing; developed a dental stewardship and audit toolkit, building on local and regional work, and working to improve the professional resources available for education.

Community health trusts

Study results demonstrate that national AMS guidance in England has focused attention on initiatives to improve AMS activity in primary and secondary care. Further work is required to promote delivery of AMS in CHS trusts, working with the CHS trust antimicrobial stewardship teams to ensure local engagement.

The TARGET and SSTF work programmes continue to support AMS in primary and secondary care and further implementation particularly of assessment of review decisions is required.

Secondary care – acute trusts

In April 2016, AMR was included as one of the four national 2016/17 CQUIN indicators. The aim of this indicator is to reduce antibiotic consumption and encourage a prescribing review within 72 hours of commencing an antibiotic. The AMR national CQUIN represents 0.25% of the CQUIN quantum. The specific goals of this indicator are:

- part A: to reduce antibiotic consumption
- part B: encourage a focus on antimicrobial stewardship

The indicator chosen for part B was the percentage of antibiotic prescriptions reviewed within 72 hours from 50 antibiotic prescriptions taken from a representative sample across hospital sites and wards.

The AMS tool developed and piloted in 2015/16, was the data collection tool modified to allow collection of the CQUIN data for analysis. The deadline for the submission of the Part B data for the first quarter was 31 July 2016. In this first quarter, 125 trusts have submitted their CQUIN Part B data via the PHE AMS submission tool. Twelve of these were submitted after the deadline.

Preliminary data shows that from the 125 trusts that had submitted their AMS data for Part B, the national average for percentage of antibiotic prescriptions with indication documented was 88% (range 29 – 100%) and percentage of prescriptions with evidence of review within 72 hours, 81% (range 22 to 100%). The CQUIN data from quarter 1 2016/17 is now available on PHE Fingertips Local AMR data.

Future actions

Dental sector

The dental working group will:

- perform a user feedback and evaluation of the dental primary care AMS toolkit
- use the learning from a previous pilot secondary care audit on dental prescribing to conduct a national audit of antimicrobial prescribing patterns in secondary care. The secondary care audit will be performed using the same methodology previously developed and collated by Association of Clinical Oral Microbiologists
- develop resources aimed at dental practitioners and other associated health professionals by finding examples of good practices from around the UK such as ‘Script’ developed by the Health Education England West Midlands and resources currently in use in Scotland through the Scottish Dental Clinical effectiveness Programme

Community health services

PHE will work with specialist pharmacists in CHS to increase education and training, promoting the HEE introductory AMR e-learning module and developing materials to share across CHS.

TARGET Antibiotics Toolkit

Over the next 12 months the TARGET team will:

- launch a series of interactive webinars series with British Society for Antimicrobial Chemotherapy (BSAC) on how to improve antibiotic prescribing (and subsequent

evaluation). These will be available after the live webinars for personal learning at www.TARGET-webinars.com
- publish a TARGET UTI leaflet – a new 'Treating your infection' for patients with UTIs due to be launched on 30 November 2016
- develop and publish an e-Community pictorial, 'Treating your infection' leaflet
- progress project work with RCGP for advisory input into update of TARGET antibiotics resources and audits

In addition, the following focussed research projects will occur:
- attitudes and behaviours of pharmacists in relation to AMR
- atudy of local Antimicrobial Stewardship implementation (focussing on CCGs)
- evaluation of 'Treating your infection' leaflet delivered via GP clinical systems
- support of C-reactive protein (CRP) service evaluations in Oldham and South Tees
- exploration of reasons for variation in urinary catheterisation in care homes and community settings
- publication of RCT of the effect of the TARGET antibiotics workshop in improving antimicrobial prescribing

Secondary care – acute trusts

As part of the AMS workstream and in light of the new government ambitions to reduce inappropriate prescribing by 50% by 2020; ESPAUR and PHE staff will work with the DH expert advisory committee ARHAI to;
- establish an antibiotic prescribing appropriateness measures task and finish group to develop standard audit tool(s) for the evaluation of appropriateness of antibiotic prescribing in secondary care
- identify the optimal approach to measuring appropriateness of prescribing in the primary care setting

ESPAUR will also:
- collaborate with academic research partners to evaluate hospital stewardship activity in support of the 2016/17 CQUIN
- support the 2017-19 CQUINs and develop resources and tools for hospital implementation
- adapt and pilot the AMS surveillance system for private healthcare

Chapter 5: Professional education and training and public engagement

This chapter outlines key interventions delivered as part of implementing key area 3 of the UK Antimicrobial Resistance Strategy including;

- delivery and evaluation of 2015 Antibiotic Guardian (AG) campaign
- delivery of antimicrobial resistance and stewardship workshops and training events for healthcare professionals
- delivery of public events on antimicrobial resistance for the public
- evaluation of e-Bug – resource for school children

Delivery and evaluation of Antibiotic Guardian

As part of UK activities for the 2015 European Antibiotic Awareness Day (EAAD; 18th November), World Antibiotic Awareness Week (WAAW;16-22 November 2015), and in support of the UK five-year AMR strategy, PHE continued to develop the Antibiotic Guardian (AG) campaign, which aims to move from raising awareness to engagement and stimulating behaviour change. AG is an intervention to improve knowledge and behaviours regarding antibiotic prescribing and antibiotic use among both healthcare professionals and the public through an online action-based pledge system. The impact/evaluation study of AG was published following peer-review and demonstrated that the campaign increased commitment to tackling AMR in both healthcare professionals and members of the public, increased self-reported knowledge and changed self-reported behaviour particularly among people with prior AMR awareness.

Activities and resources for EAAD and the AG campaign were developed and run by a PHE-led multidisciplinary committee with representation from animal and human health sectors across England and the devolved health administrations. Membership of the core planning group can be found in Appendix 4.

Prior to WAAW in 2015, PHE invited organisations to register their antibiotic awareness activities via an online survey. This was accomplished through the dissemination of a short survey where professional bodies and organisations could submit their interest in supporting EAAD and/or the AG campaign in the upcoming year. The registration also served to develop a mailing list of interested bodies to allow the dissemination of relevant information and updates regarding the campaign.

AntibioticGuardian.com

The initial concept for this website and logo was developed jointly by PHE and the British Society for Antimicrobial Chemotherapy, who also kindly provided the initial funding for the website, and continue to support the campaign.

PHE funded further website developments in 2015; the updated website with new pledges and features was available on 13 October 2015. The updates allowed for the inclusion of:

- resource links to relevant information for public and professionals
- patient stories
- meetings and events including the AG roadshows and public debates
- awards: where individuals could submit entries into the first annual AG awards competition to celebrate excellence and innovation in raising awareness and engagement
- a news item for major updates

Other key activities delivered as part of the AG campaign in 2015/16 included:

- letters to NHS (primary and secondary care), professional organisations and local authorities continuing the activities from previous years and encouraging them to take part in the AG campaign and to inform them of WAAW 2015. Similar letters were sent to universities for the first time
- a blog on Health Matters ("10 reasons YOU should be worried about antibiotic resistance")
- at the request of European Centre for Diseases Control (ECDC) PHE and the CMO each filmed a short video detailing the activities undertaken by PHE and the Department of Health (DH) to tackle AMR[45]
- following PHE and DH approach to Penguin Random House UK, the publishers supported AG and WAAW by making a worldwide price reduction to £0.99 from the 16th-22nd November copies of Professor Dame Sally C. Davis's (CMO) book "The Drugs Don't Work" available from all e-book retailers
- PHE published three press releases during WAAW focusing on:
    - New data from ESPAUR.
    - Pet owners partnership with Veterinary Medicines Directorate and Bella Moss targeting pet owners.
    - A call to action for AG through press releases, social media and public engagement.
- a quiz for members of the public, healthcare professionals, students and educators
- EAAD and AG featured in an episode of TV programme 'Doctors', which incorporated EAAD and AG into a storyline focusing on raising awareness of AMR and high prescribing of antibiotics

[45] ECDC EAAD Video Pledge - Public Health England's contribution to fighting antibiotic resistance, Available from; https://www.youtube.com/watch?v=9tE_y83fPGQ

As a result of significant engagement in 2015/16, 37% more organisations registered their planned activities (n=306); compared to 2014/15 (n=193). In both years, 69% were NHS organisations in primary or secondary care. In 2015/16 the second largest group were universities (n=41; 13%) compared to n=4; 2% in 2014/15. Support methods in 2015/16 included actively encouraging all staff/ members to share information and pledge to be an AG (95%), promoting AG messages on social media channels (78%) and issuing press releases incorporating the AG call to action (91%) (Table 5.1).

Table 5.1: Mechanisms of support for Antibiotic Guardian 2015, n=306.

Mechanisms of support by registered organisation	Proportion of organisations who performed this activity
Supporting the AG pledge campaign to achieve 100,000 AGs by 31 March 2016	91%
Displaying and sharing AG materials throughout the winter cold and flu season	92%
Promote AG messages via organisation social media channels, such as twitter and Facebook	78%
Share the new online AG antibiotics quiz to establish a benchmark knowledge measure across the UK	80%
Actively encourage all staff/members to share information and answer the AG call to action	95%
Use the organisation website to share information/AG call to action externally	73%
Issue a media/press release incorporating the AG campaign/call to action	91%

In the 2015 season, between 13 October 2015–31 March 2016, there were 16,173 Antibiotic Guardians; taking the overall total to 31,105. There was at least one pledge from 77 countries across the world, with five or more pledges from 24 countries including South Africa, USA, India, Nigeria, Australia and several countries in Europe.

As shown in Table 5.2 and Figure 5.1, there is variation in the distribution of AGs around the UK.

Table 5.2: Distribution of Antibiotic Guardian pledges in the UK, 2015/16

Country	Count	Population	Proportion of total AGs	Rate
England	12086	53493729	76.27%	22.59
Scotland	824	5313600	5.20%	15.51
Wales	2749	3092036	17.35%	88.91
Northern Ireland	188	1840498	1.19%	10.21
UK	**15847**	**63739863**	**100%**	**24.86**

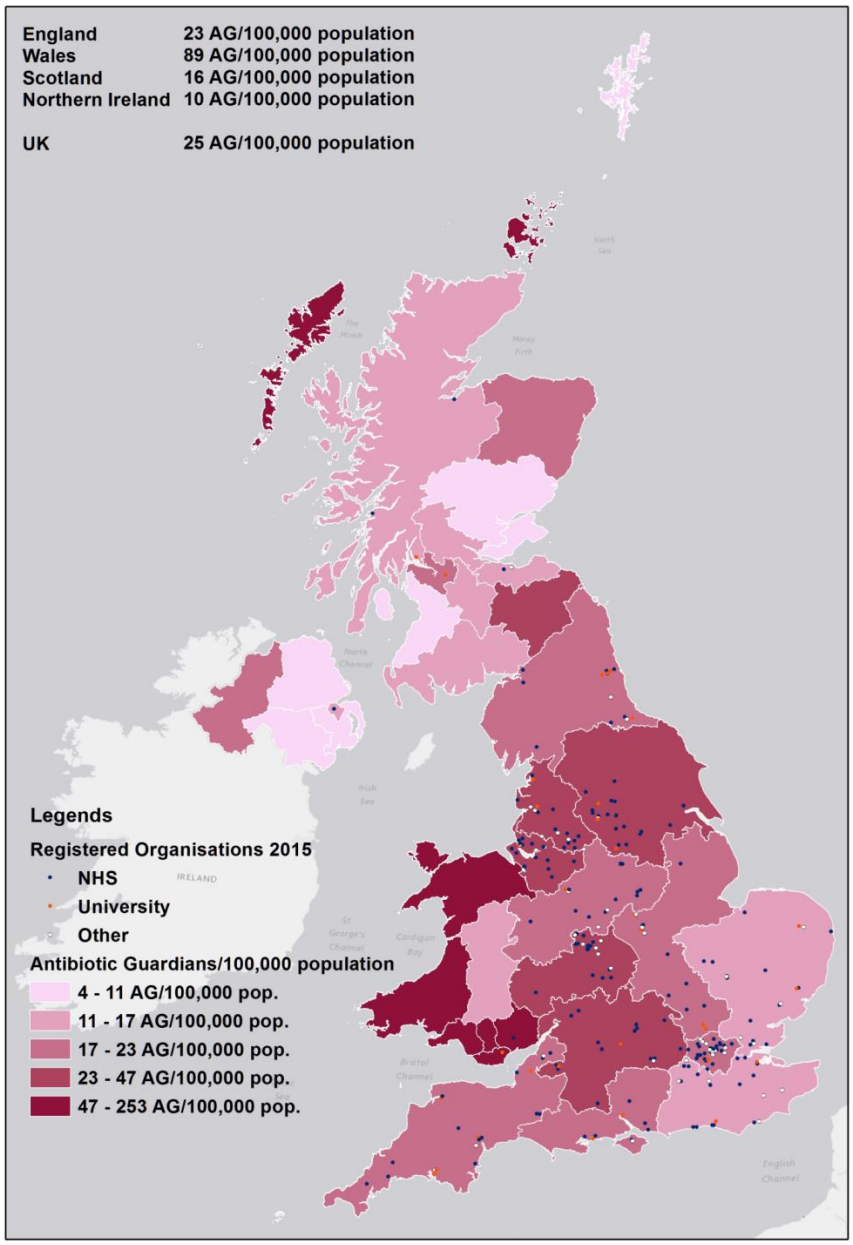

Figure 5.1 Map of new Antibiotic Guardians per 100,000 population by heath boundaries in the UK (n=14,027) and distribution of registered organisations, 2015/16 (n=306)

Based on reported titles, 22% were men, 68% were women, and 10% used the title of Doctor or Professor; 47% were healthcare professionals, 34% were members of the public, 18% were students or educators; a full breakdown can be seen in Figure 5.2.

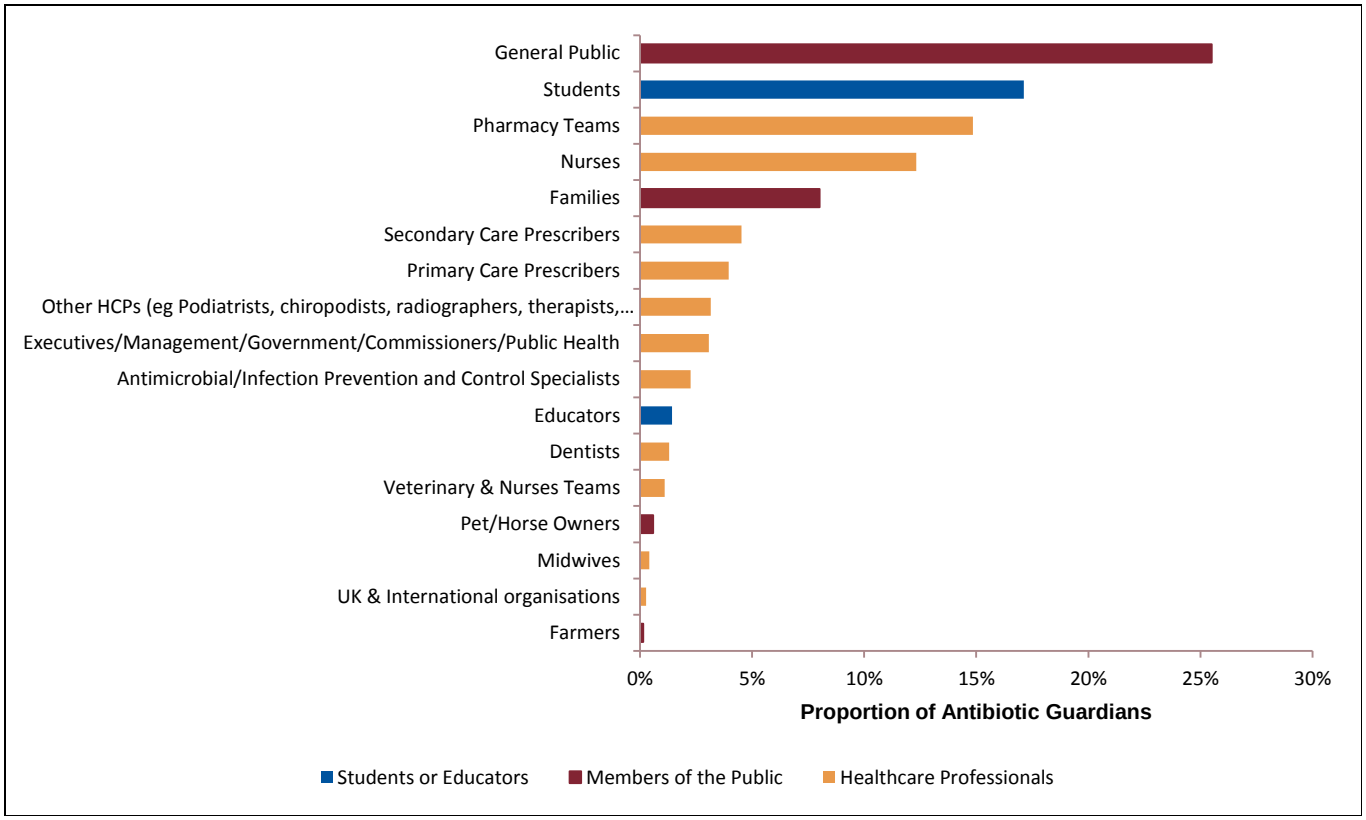

Figure 5.2 Breakdown of those who pledged on Antibiotic Guardian, by professional and public group, 2015/16, n=16173

Assessment of IP addresses highlighted that over half of AGs signed up using the same computer or mobile device as at least one other AG (59%, n=9560/16173 signups using the same IP); between October 2015 and March 2016, there were a total number of 7287 unique IP addresses used. From this we may infer that as many as half of AGs are signing up at a location where individuals have organised some form of activity for encouraging AG sign-ups.

There are marked differences in how healthcare professionals, members of the public, and students reported hearing of the campaign (Figure 5.3).

Of website visits, approximately half (46%) of all unique website visitors were self-directed, 37% were from social media, 15% were from website referrals and 1% were email referrals (n=72,606 website visits).

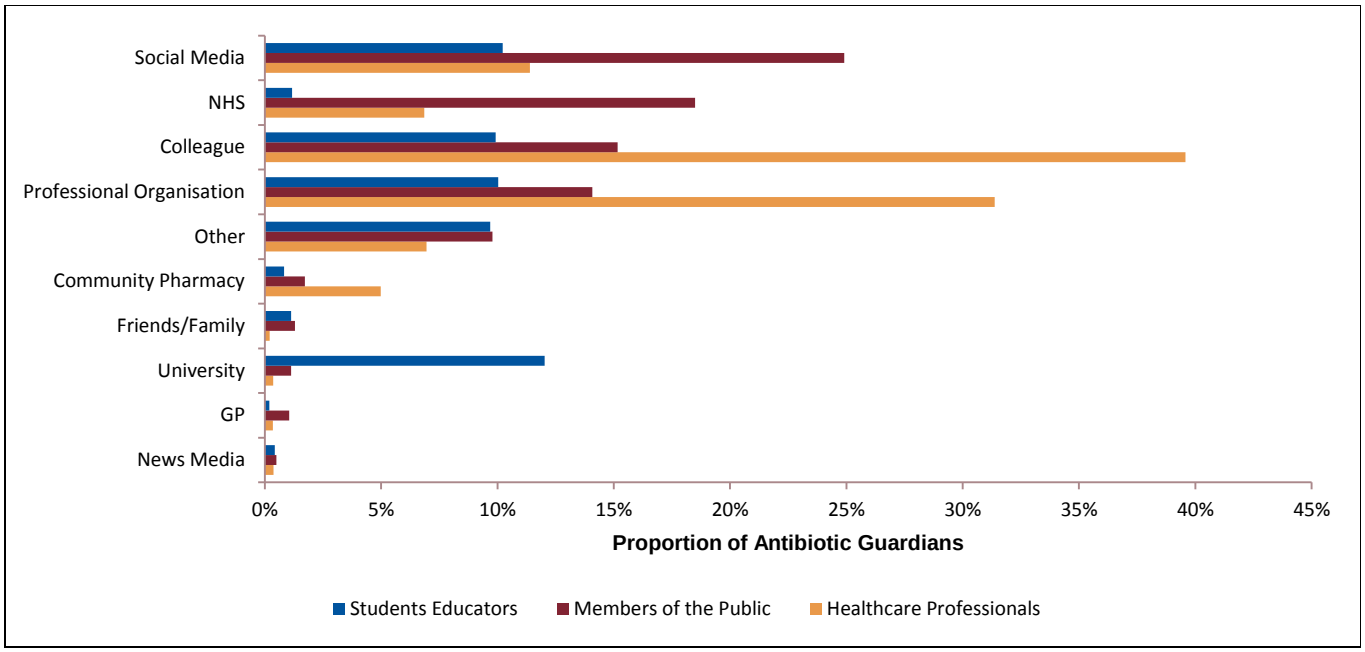

Figure 5.3 How AGs reporting hearing of the AG campaign in 2015/16, n=12821.

Face to face delivery of toolkit resources and educational events

Antibiotic Guardian roadshows, public event and awards

PHE commissioned the social enterprise "4 All of Us" to conduct three professional AMR/AMS workshops (AG Roadshows). The purpose of the roadshows was to deliver guidance, information and resources to multi-professional groups working in GP, acute and community care settings, CCGs and pharmacies. To date four roadshows have been delivered in Leeds, Birmingham and London with a total of 341 registered healthcare professionals, including primary care and secondary care pharmacists' specialist infection/antimicrobial pharmacists' GPs' nurses and academics. Further details and agendas are available via http://antibioticguardian.com/meetings-events/.

Example of topics covered in at the events included:

- an overview of AMR
- strengthening infection prevention and control practices
- AMR: action across Europe
- the Government's stance on AMR
- building laboratory capacity, surveillance networks and response capacity
- antibiotic usage in livestock
- antimicrobial Stewardship including:
    - Guidelines on antimicrobial stewardship;
    - AMS – national update on CQUIN and QP
    - Implementing Start Smart Then Focus
    - How to use and interpret data available locally to influence AMS
    - Case study: how are we doing towards achieving our AMR CQUIN Part A and B objectives
- the impact of 'super gonorrhoea'
- tackling AMR: Engaging with Patients and the Public

- Case Study: Delivering AMR education and training locally through Mosques
- the role of community pharmacists in tackling AMR

Feedback via evaluation forms demonstrated that the event was very well received and attendees found the presentations informative and useful. Further feedback provided highlighted that delegates would be interested to find out how AMS and infection prevention control practices are being incorporated into the curriculum at schools and universities. Additional information on prescribing behaviour in primary care was also requested.

Chief Pharmaceutical Officer's conference

The Chief Pharmaceutical Officer's conference in March 2016 explored equipping pharmacy professionals/leaders to rise to the challenges facing the NHS and included presentations and workshops on AMR. A key part of delivering the AMR strategy as recognised in the UK AMR implementation plan is the creation of local networks of pharmacists involved in AMS across the whole health economy.

This workshop saw details of some of the existing pharmacy led networks that are successfully implementing the UK five-year AMR strategy to inform debate on how pharmacy can take a leadership role in the development of local clinical networks to deliver improvements in AMS across local health economies.

Some of the recommendations for creating local AMR networks which were suggested at the workshop were the necessity for collaborations with multiple organisations, engaging with community pharmacies and local pharmaceutical committees as well the need for chief pharmacists to release pharmacists to allow them to attend network meetings.

Antibiotic Guardian awards

In May 2016, PHE hosted the first AG awards in Birmingham, championing organisations and individuals who have demonstrated achievement in support of AG and its aims during WAAW 2015.

There were seven categories for the awards, with 79 entries received:

- collaborative stewardship
- community
- innovation
- prescribing
- research
- staff engagement
- stewardship

Winning and highly commendable entries can be found on http://antibioticguardian.com/antibioticguardian-awards-winners/

TARGET antibiotic workshops and engagement

Five half-day TARGET educational events took place in early 2016 in Birmingham, Liverpool, Luton, Milton Keynes and Newcastle-upon-Tyne, and were attended by 199 primary healthcare professionals. Workshop evaluations indicate that the workshops were relevant to clinical practice and that participants found them useful. Comments relating to the useful aspects of the workshops include:

- *"*The presentation was very focused and relevant – especially going through by clinical condition" (Luton, 25/02/16)
- "Discussion with colleagues and experts – relevant to everyday practice" (Manchester, 12/01/16)

Workshop sessions have also been held at the North of England AMS event, South West regional events in collaboration with NHS England/Improvement and resources have been made available at national AMS workshops, Antibiotic Guardian roadshows and the PrescQIPP national conference for commissioners.

Together, the RCGP and PHE developed a joint communications plan which enabled the TARGET toolkit to be promoted to thousands of primary health care professionals across the UK through a range of platforms. For 2015-16, this included:

- five articles in the RCGP's newsletter 'Clinical News' which is sent monthly to 50,000 GPs. This includes:
    - May 2015: TARGET Hit or Miss?
    - October 2015: Resisting Patient Demand for Antibiotics
    - November 2015: Ten Top Tips for Talking to Patients about Antibiotic Prescribing
    - January 2016: A Spotlight on the TARGET training presentation
    - March 2016: Spotlight Projects: Tools for Success

- regular mentions in the RCGP's weekly 'Chair's Blog', which is sent to 50,000 GPs and promotion through social media by both the RCGP and PHE.
- RCGP Facebook post illustrating how to use the self-assessment checklist.

AMR public events

PHE/ESPAUR worked with BSAC who were commissioned to organise the public event 'Antibiotic Resistance and You!' to develop two public events held in February 2016 and September 2016. In total, 201 registered for the February event in London and 204 for the event in Manchester (September 2016). The purpose was to have a discussion on the AMR agenda, to educate the public about AMR, inform people of what they can do to tackle the problem, and to explain the collaborative approach. The response received from the roadshow was very positive, with 100% of delegates stating that both the keynote presentations were useful, and that they would recommend the conference to other colleagues.

Delegates requested for the following topics to be discussed at future events:

- practical support for CCGs
- examples of case studies
- methods of engagement for pharmacists
- antibiotic research

e-Bug resources

During the year, e-Bug an educational resource for children and young people which teaches about antibiotics, microbes and hygiene was further developed including new branding, updated content and additional resources including new online games. e-Bug resources include materials for teachers to use in classrooms, such as lesson plans, worksheets and interactive activities. The materials were developed to be in line with the National Curriculum and are all freely available on the e-Bug website (www.e-Bug.eu). e-Bug also hosts resources for students, including online games, quizzes and revision guides. Materials are available for students aged 4-18 years and are outlined in Figure 5.4.

Figure 5.4 e-Bug resources for 4-18 year olds

Work continued with partners across 26 countries to promote key hygiene and antibiotic messages to children across the world. The resources are currently available in 23 different languages including most European languages, Turkish and Arabic. In early 2016, e-Bug held a face to face meeting in London for all international partners. The meeting was attended by 42 delegates representing 17 different countries. The meeting was an opportunity to present the new materials for 15-18 years olds covering antibiotics and vaccinations, and to discuss updates to the e-Bug games.

In 2016, e-Bug launched Beat the Bugs, a 6-week hygiene, antibiotic and self-care course designed for use in the community. The course is fun, interactive and flexible, making it suitable to be run with a range of community groups such as youth groups, young mothers, brownies and guiding groups and adult learning courses. A pilot with adults with learning disabilities found that participants enjoyed the course and the results suggested that knowledge, awareness and behaviour had improved. The full course, as well as each individual session, can be freely downloaded from the Beat the Bugs webpage; http://www.e-bug.eu/beat-the-bugs/

The e-Bug interactive science show was developed into a peer education workshop, in which secondary school students were trained to become peer educators and deliver the activities to their peers. The workshops were evaluated with before, after and knowledge retention questions, as well as qualitative interviews. The results indicate that the workshops are an effective way to improve knowledge in young people, particularly around the antibiotics topic, and that peer educators gain a range of skills through the workshop such as confidence and communication (Young et al., submitted for publication).

Three of the e-Bug online games were also evaluated to assess knowledge and awareness change, and to understand how the games can be improved. The games were able to increase knowledge in some areas and had different levels of enjoyment for the students (Hale et al., submitted for publication). The results identified areas for improvement and these updates were made prior to re-launching the website in HTML5.

Conclusions

The interventions implemented have been shown to increase engagement from healthcare professionals and members of the public in tackling AMR as at 31 October 2016, there were 33,841 Antibiotic Guardians.

Engagement with professional groups and training providers has also led to AMR featuring in published curricular including;

- updated prescribing competency framework for all prescribers, AMR including IPC and AMS features as a distinct competence and includes signpost to the national Antimicrobial Prescribing and Stewardship competences, http://www.rpharms.com/unsecure-support-resources/prescribing-competency-framework.asp?
- 2016 Foundation Doctors curricula for the first time include AMR as part of the training outcomes descriptors.
    - Prescribes and administers oxygen, fluids and antimicrobials as appropriate eg in accordance with NICE guidance on antimicrobial stewardship and sepsis
    - Prescribes according to relevant national and local guidance on antimicrobial therapy, recognising the link between antimicrobial prescribing and the development of antimicrobial resistance

Future plans

The plans for Antibiotic Guardian in 2016/17 are:

- To increase the proportion of AGs who are members of the public and increase the number of healthcare student pledges.
- Carry out focused activity and evaluate impact of campaign with three target groups;
    - Healthcare students
    - Young families
    - The public through community pharmacy
- As part of plans for 2016/17, we will work with the Fingertips AMR team to determine the possibility of making AG rates available by local authority, to improve focus outside the NHS on delivery of this campaign.
- Continue to host further AG roadshows and public debates.

The Independent Review of AMR[46] commissioned by the Government in 2014 and chaired by Lord Jim O'Neill recommended a world-wide awareness campaign. During the year WHO-Europe commissioned PHE to translate the AG programme into Russian (www.antibioticguardian.com/russian) and requests were received for translation into additional languages including French and Dutch. During the following year, we will work to expand AG to include a range of languages that are part of the WHO six international languages.

Continue to work with HEE to improve uptake of AMS education and training for healthcare professionals and health students.

Continue to work with professional organisations to enhance and implement the AMS toolkits through education and training events for healthcare professionals and regular communication through networks.

[46] Review on Antimicrobial Resistance, https://amr-review.org/

Chapter 6: Antifungal resistance, prescribing and stewardship

This year's ESPAUR report extends the surveillance data published in previous reports by presenting data on antifungal resistance, consumption and stewardship for the first time. This follows the establishment of an ESPAUR subgroup on antifungal consumption and resistance surveillance that was established to identify gaps within current antifungal surveillance and seek to explore and implement improvements to the national surveillance programme.

There have been increasing reports of invasive fungal disease, emergence of more intrinsically resistant species of pathogenic fungi and the development of cross-resistance to clinical azoles and critical broad-spectrum antifungals following both long-term exposures of patients to antifungals and environmental use of agricultural azoles.[47,48,49,50] These report increasingly vulnerable patient populations due to complex medical procedures such as transplant surgery or immunosuppressive treatment and the high costs associated with antifungal treatment and prophylaxis, highlight the importance of monitoring antifungal resistance in clinically relevant fungal isolates and usage of antifungals.

This first report on antifungal resistance looks at routinely reported resistance to key antifungals in the most frequently reported species of moulds (*Aspergillus* and *Fusarium*) and yeasts (*Candida albicans* and *C. glabrata*) from clinical isolates.[51] The antifungals presented were chosen by a panel of experts as those where emerging or worrying levels of resistance are being reported. [52,53] The fungal pathogens and antifungals for which susceptibility data were collated and analysed are shown in Table 6.1.

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[47] Azevedo M et al. Genesis of Azole Antifungal Resistance from Agriculture to Clinical Settings. J Agric Food Chem. 2015; 63(34):7463-8

[48] Review on Antimicrobial Resistance. Antimicrobials in Agriculture and the Environment: Reducing unnecessary use and waste. December 2015. Available at https://amr-review.org

[49] Bromley M et al. Occurrence of azole-resistance species of Aspergillus in the UK environment. Journal of Global Antimicrobial Resistance 2(2014) 276-279

[50] European Centre for Disease Prevention and Control, ECDC Technical Report: Risk assessment on the impact of environmental usage of triazoles on the development and spread of resistance to medical triazoles in Aspergillus species. ECDC, 2013.

[51] PHE. Surveillance of Candidaemia in England, Wales and Northern Ireland; 2015. Health Protection Report [serial online] 2016; 10(32): Infection Report.

[52] Verweij P et al. International expert opinion on the management of infection caused by azole-resistant Aspergillus fumigatus. Drug Res Updates. 2015;21-22:30-40

[53] Guarro J. Fusariosis, a complex infection caused by a high diversity of fungal species refractory to treatment Eur J Clin Microbiol Infect Dis. 2013; 32: 1491.

Table 6.1: Fungal pathogen and antifungal agents selected for review

Pathogen (or group of similar)	Antifungal or antifungal class
Aspergillus fumigatus	Azole agents* (voriconazole)
***Fusarium* spp.**	Amphotericin B
	Azole agents †
Candida albicans	Caspofungin
	Azole agents (fluconazole; voriconazole)
Candida glabrata	Echinocandins
	Azole agents

* Excluding fluconazole

† Excluding both fluconazole and itraconazole

We also have included an update on *Candida auris*, a recently identified pathogen which has been detected within NHS hospitals and is known to cause hospital outbreaks, unlike other *Candida* spp.

The emergence of antifungal resistant pathogens such as *C. auris*, high drug costs and the toxicity of antifungal agents highlight the importance of monitoring the use of these drugs. This report brings together for the first time antifungal prescribing data from general practice and NHS hospitals in England.

Amphotericin B has been the main antifungal therapy for invasive mycoses, but other antifungals such as azoles and echinocandins are now considered first-line drugs for many of these infections. In the community, terbinafine and griseofulvin are commonly prescribed systemic antifungals to treat acute and chronic skin and nail infections.

AMS initiatives have largely focussed on antibacterials. However, although antifungal resistance is not currently as predominant an issue as antibiotic resistance, there is a growing realisation of the need to be vigilant and to start addressing concerns around antifungal usage.[54] A number of recent studies have highlighted the importance of antifungal stewardship in hospitals, outlining significant patient benefits, as well as cost-savings.[55,56,57,58,59] The aim of this work was to explore the current status of antifungal stewardship initiatives across NHS acute trusts within England.

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[54] Review on Antimicrobial Resistance. Tackling Drug-Resistant Infections Globally: Final Report and Recommendations. Published May 2016

[55] Standiford HC et al. Antimicrobial Stewardship at a Large Tertiary Care Academic Medical Center: Cost Analysis Before, During, and After a 7-Year Program. Infect Control Hosp Epidemiol 2012;33(4):338-345

[56] Lopez-Medrano F. et al. A non-compulsory stewardship programme for the management of antifungals in a university-affiliated hospital. Clin Microbiol Infect. 2013 Jan;19(1):56-61

[57] Mondain V et al. A 6-year antifungal stewardship programme in a teaching hospital. Infection 2013; 41: 621–8.

Methods

Data sources

Data on the susceptibility of each pathogen to key antifungals from 2011 to 2015 were obtained from the Communicable Disease Report module of PHE's Second Generation Surveillance System (SGSS).

The routine laboratory surveillance and the caveats surrounding data quality have been well discussed in earlier ESPAUR reports (incomplete data collection, as reporting is done on a voluntary basis, variation in laboratory testing methods).[60] The only additional item to note would be that the ability to report antifungal susceptibility results has been possible since 2005; it is only more recently that many NHS laboratories are performing antifungal testing locally rather than sending isolates to the reference laboratory.[61] Pathogenic moulds are identified in laboratory reports from all key specimen types. Within this report, pathogenic yeasts are reported in two specimen groups; those from 'deep' infections (blood, normally sterile fluids or tissues) and those from 'mucosal' specimen types.

For the purpose of this report, antifungal susceptibility test results reported as 'intermediate' or 'resistant' have been combined and presented as 'non-susceptible' in some instances. The benefits and limitations of this method of data presentation are detailed within the discussion section of this chapter.

Data presented are at a specimen level, due to this fact the specimens are de-duplicated for same day patient repeats rather than the 14 day episode grouping that is used when looking at a single specimen type (as in chapter 2). Cultures taken from the same patient that yielded growth of the same pathogen on the same day were regarded as comprising the same episode and were combined, with the most resistant antifungal susceptibility result being retained (where differences existed).

The azole agents included fluconazole, miconazole, itraconazole, posaconazole, econazole, ketoconazole and clotrimazole, some of which are for topical treatment of cutaneous and mucosal lesions only. The echinocandins included caspofungin,

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[58] Valerio M., et al. Evaluation of antifungal use in a tertiary care institution: antifungal stewardship urgently needed. J Antimicrob Chemother 2014; 69: 1993 –9

[59] Micallef C. et al. Introduction of an antifungal stewardship programme targeting high-cost antifungals at a tertiary hospital in Cambridge, England. J Antimicrob Chemother. 2015; 70:1908-1911

[60] Public Health England; English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report 2015. Available at; https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report

[61] Health Protection Report. 2012 Candidaemia. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/399495/candida_HPR_full_report_2012.pdf

anidulafungin and micafungin; any test results where laboratories record the generic ‘echinocandin’ reference were also included within this group as anidulafungin is often used as a sentinel test drug.

Information on the use of antifungals prescribed in the community was obtained from the NHS Business Services Authority (BSA) database from 2013 until 2015. Information on NHS hospital prescribing was obtained from IMS Health for the same time period. The classification of data on antibiotic use was based on the anatomical therapeutic chemical (ATC) classification system.[62] In this scheme, antimycotics for systemic use fall into ATC groups J02 and D01B.

A web-based survey to explore the current status of antifungal stewardship containing fifty closed questions was developed by a consultant microbiologist and antimicrobial pharmacist involved in local antifungal stewardship. Feedback was obtained from the ESPAUR antifungal subgroup and piloted for face validity. It was disseminated to all English NHS Trusts via the following networks: PHE Lead Public Health Microbiologists network, British Infection Association (BIA), UK Clinical Pharmacy Association (CPA) and the East of England antimicrobial pharmacist group. The survey was open for four weeks and reminders were issued at the mid-point.

Data analysis

Trends in incidence and resistance are shown at national level for England from 2011 to 2015. Incidence rates are calculated per 100,000 population per year using mid-year population estimates for the relevant year.[63]

Antifungals are analysed and presented using defined daily doses (DDD) per 1000 inhabitants per day, using the same methodology as Chapter 3.

The antifungal stewardship survey was de-duplicated by Trust and analysed using Excel.

[62] WHO Collaborating Centre for Drug Statistics Microbiology, ATC/DDD Index 2016 Available from; http://www.whocc.no/atc_ddd_index/
[63] Office for National Statistics, ONS population estimates, Available from; http://www.ons.gov.uk/peoplepopulationandcommunity/populationandmigration/populationestimates

Results

Aspergillosis and Fusariosis

Aspergillosis remains the most common invasive mould infection with the vast majority in the UK due to *Aspergillus fumigatus.* Allergic reactions to *A. fumigatus* are more common than invasive infection. There is a spectrum of respiratory infection depending on underlying lung function and immunological state, however, in more susceptible patient groups (eg cystic fibrosis and immuno-compromised patients) the risk of severe disease and poor outcomes are greatly increased. The introduction and availability of triazole (itraconazole, voriconazole, posaconazole and isavuconazole) and echinocandin (caspofungin, micafungin and anidulafungin) antifungal drugs over the last 20 years has been a factor in improving patient survival.[64] The development of resistance in *A. fumigatus* to any of the therapeutic antifungal agents is a threat, with widespread clinical implications for treatment outcomes of patients with systemic infections. In particular there have been many reports of azole resistance in *A. fumigatus* isolates following exposure to azole drugs in particular patients or potentially related to agricultural use of azoles.[65]

The incidence of *A. fumigatus* positive specimens from all sites was 3.2 per 100,000 population in 2015, with a slight increase being noted across the five-year time period (3.0/100,000 in 2011; Figure 6.1). *A. fumigatus* remains by far the most common mould isolated from clinical specimens.

Fusariosis is the second most common mould infection, primarily affecting neutropenic patients; in 2015 the incidence was 1.7 per 100,000 population.[66] While not unheard of, it remains rarely observed in patients with HIV.[67] There are at least 70 species causing fusariosis, but most infections are caused by four species, the most prevalent is *Fusarium solani* species complex (60%) followed by *F. oxysporum* species complex (20%).[68] Table 6.2 shows the susceptibility of *Aspergillus fumigatus* and *Fusarium* spp. to antifungal agents.

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[64] Verweij P *et al*., Azole Resistance in *Aspergillus fumigatus*: can We Retain the Clinical Use of Mold-Active Antifungal Azoles?. Clin Infect Dis. 2016; 62(3)362-8

[65] Azevedo M *et al*. Genesis of Azole Antifungal Resistance from Agriculture to Clinical Settings. J Agric Food Chem. 2015;63(34):7463-8

[66] HPA. Antimicrobial Resistance in England, Wales and Northern Ireland, 2006. London, Health Protection Agency 2007

[67] Nucci F et al. Fusariosis. Semin Respir Crit Care Med. 2015; 36(5):706-714

[68] Guarro F. Fusariosis, a complex infection caused by a high diversity of fungal species refractory to treatment. Eur J Clin Microbiol Infect Dis (2013)32:1491

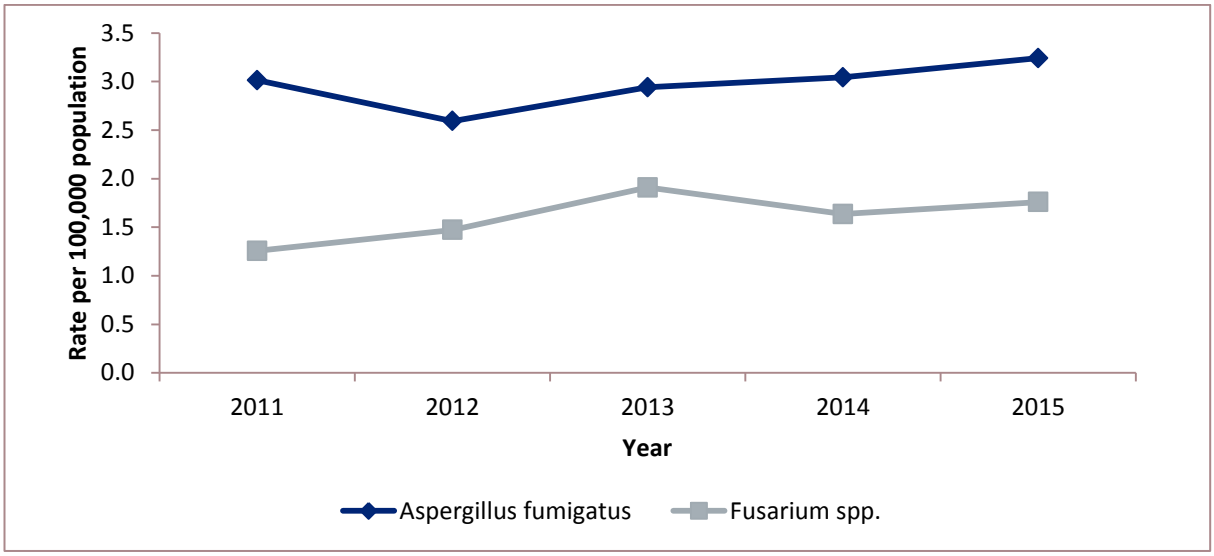


Figure 6.1 Incidence rate (per 100,000 population) of reported culture positive specimens (from all clinical specimens) for *A. fumigatus* and *Fusarium* spp. in England, 2011 to 2015, based on voluntary reporting to PHE

Table 6.2: Antifungal resistance identified in a) *A. fumigatus* and b) *Fusarium spp.* mould specimens, England, 2011-2015, based on voluntary reporting to SGSS

a. *A. fumigatus*

Antifungal	Year	No. reported as tested	% reported as tested	Number resistant	Number intermediate	% Non-susceptible
Itraconazole	2011	19	1%	0	0	0%
	2012	13	1%	1	0	8%
	2013	15	1%	2	0	13%
	2014	25	2%	0	0	0%
	2015	71	4%	5	0	7%
Voriconazole	2011	18	1%	0	0	0%
	2012	17	1%	1	0	6%
	2013	15	1%	0	1	7%
	2014	26	2%	0	0	0%
	2015	76	5%	0	0	0%
Any azole*	2011	19	1%	0	1	5%
	2012	18	1%	2	0	11%
	2013	15	1%	2	1	20%
	2014	27	3%	0	0	0%
	2015	78	5%	5	1	8%

* excluding fluconazole

b. *Fusarium spp.*

Antifungal	Year	No. reported as tested	% reported as tested	Number resistant	Number intermediate	% Non-susceptible
Amphotericin B	2011	6	1%	2	0	33%
	2012	10	1%	2	0	20%
	2013	22	2%	4	0	18%
	2014	6	1%	1	0	17%
	2015	20	2%	6	0	30%
Voriconazole	2011	6	1%	0	1	17%
	2012	11	1%	1	3	36%
	2013	22	2%	0	12	55%
	2014	8	1%	1	3	50%
	2015	20	2%	4	8	60%
Any azole†	2011	6	1%	0	1	17%
	2012	11	1%	2	3	45%
	2013	22	2%	0	12	55%
	2014	7	1%	1	3	57%
	2015	20	2%	7	6	65%

† excluding fluconazole and itraconazole

Identified resistance to any azole (excluding fluconazole) was low in *A. fumigatus* (Table 6.2a). However, antifungal susceptibility test results for *A. fumigatus* isolates were poorly reported to the national routine laboratory surveillance system (less than 5% of reports include test results for itraconazole, voriconazole and other azoles).

A similar picture is seen with susceptibility test reporting for isolates of *Fusarium* spp., with less than 2.5% of reports including results for amphotericin B or voriconazole. Isolates of *Fusarium* spp. frequently displayed resistance to amphotericin B, and intermediate resistance to azole antifungals, including voriconazole, the preferred treatment option for *Fusarium* spp. infection (Table 6.2b).

Candidiasis and Candidaemia

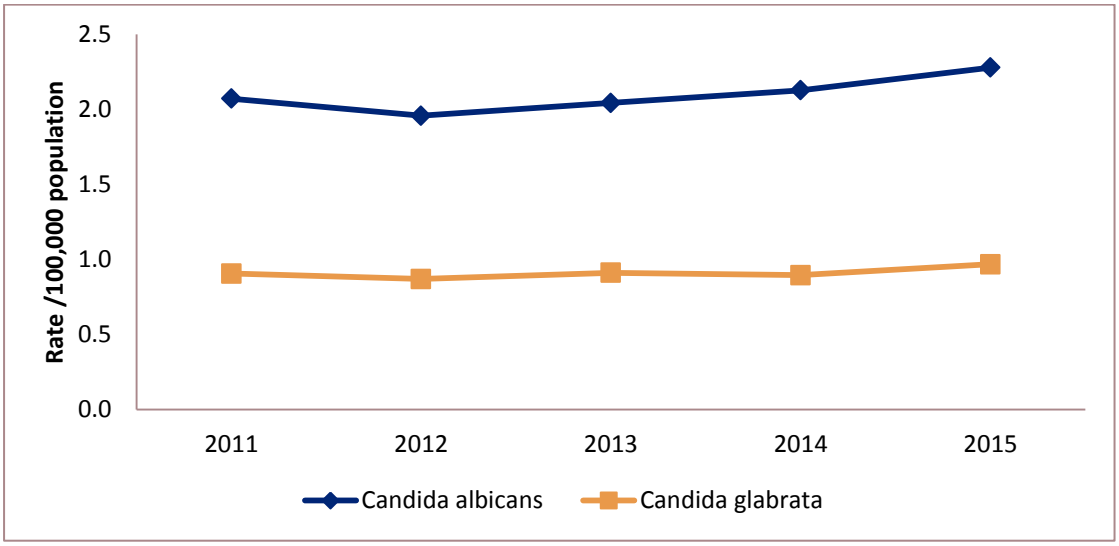
Candida is a yeast and is the most common cause of fungal infections worldwide. Many species are harmless commensals in humans; However, when mucosal barriers are disrupted or the immune system is compromised they can invade and cause disease. *C. albicans* is the most commonly isolated species, and most frequently causes mucosal infections (commonly known as thrush). Systemic infections of the bloodstream and major organs (candidaemia or invasive candidiasis) are particularly important in immuno-compromised patients.

Candida spp. were the 11th most commonly identified organisms in all reported bloodstream infections in England in 2014, comprising 1.5% of such infections; the incidence of candidaemia has been increasing steadily between 2008 and 2015.[69] This has been attributed to an increase in the use of more aggressive therapy practices (eg chemotherapy, organ transplantation and intensive care use). *C. albicans* remains the most frequently isolated yeast from clinical specimens but its relative prevalence has evolved over time with a rise in non-albicans *Candida* (NAC). Fluconazole resistance has been recognised for many years, especially in *C. glabrata* (dose dependent resistance) and *C. krusei* (intrinsically resistant). Echinocandin resistance is increasingly recognised and is mediated primarily through mutations in hot-spot regions of the glucan synthase (FKS) genes.

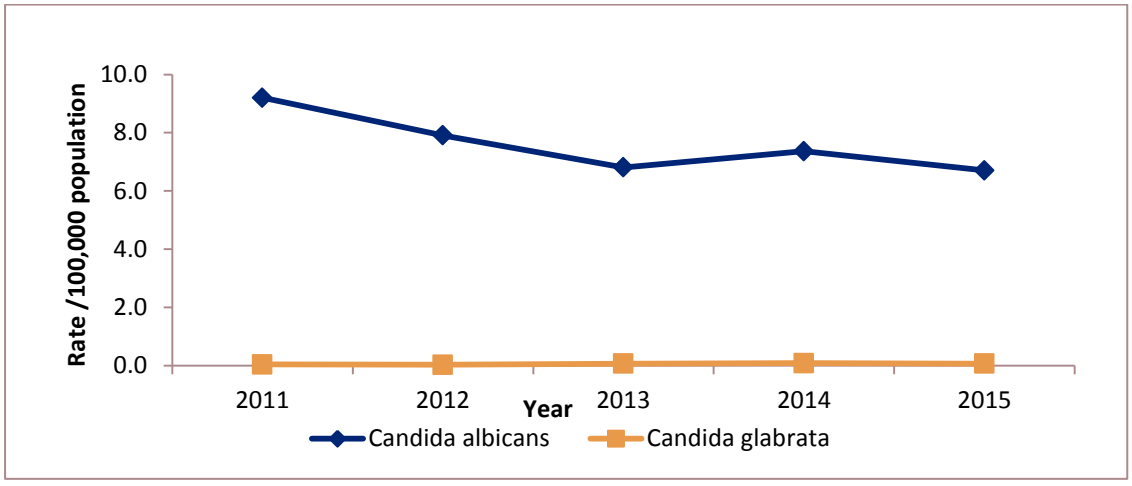
The overall incidence of *C. albicans* isolates from sterile site specimens was 2.3 per 100,000 of the population in 2015, a non-statistically significant increase on the previous four years (Figure 6.3a). There has been a decrease in incidence of *C. albicans* identified in mucosal specimen sites over the same period (Figure 6.3b). The total incidence of sterile site and mucosal site isolates in 2015 was 10 per 100,000 population. The incidence of *C. glabrata* isolated from sterile sites has remained just

[69] Public Health England; Infection report Volume 10 Number 32 Published on: 23 September 2016 https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/555332/hpr3216_cnddm.pdf

below 1.0 per 100,000 population across the five year period (Figure 6.2a), and was less frequently isolated from mucosal specimens with less than 0.01 per 100,000 population reported in 2015 (Figure 6.2b).



a. Sterile Site Specimens



b. Mucosal Specimens

Figure 6.2 Incidence rate per 100,000 population of reported *Candida albicans* and *Candida glabrata* (a) sterile site and (b) mucosal specimen types in England, 2011 to 2015, based on voluntary reporting to PHE

Even though antifungal testing of sterile site specimens of *C. albicans* and *C. glabrata* has increased year on year for each of the key antifungals, still only less than 48% and 56% respectively of reported isolates included antifungal test results in 2015 (Table 6.3). In *C. albicans* isolates from sterile sites non-susceptibility to fluconazole, voriconazole and caspofungin was low between 2011 and 2015 (Table 6.3a). Reported non-susceptibility was consistently higher in the reported mucosal specimens, however, the frequency of mucosal specimens tested for antifungal non-susceptibility remained low (Table 6.4).

Table 6.3: Resistance identified in sterile site (a) *C. albicans* and (b) *C. glabrata* reports, England, 2011-2015, based on voluntary reporting to SGSS

a. *C. albicans*

Antifungal	Year	No. reported as tested	% reported as tested	Number resistant	Number intermediate	% Non-susceptible
Fluconazole	**2011**	229	21%	2	3	2%
	2012	307	29%	1	2	1%
	2013	371	34%	3	3	2%
	2014	403	35%	3	6	2%
	2015	588	47%	4	5	2%
Voriconazole	**2011**	201	18%	0	0	0%
	2012	272	26%	2	0	<1%
	2013	331	30%	2	0	<1%
	2014	335	29%	3	1	1%
	2015	491	39%	3	1	<1%
Caspofungin	**2011**	80	7%	1	0	1%
	2012	182	17%	0	1	<1%
	2013	280	25%	0	0	0%
	2014	295	26%	0	1	<1%
	2015	406	33%	0	0	0%

b. *C. glabrata*

Antifungal	Year	No. reported as tested	% reported as tested	Number Resistant	Number Intermediate	% Non-susceptible
Fluconazole	**2011**	136	28%	37	32	51%
	2012	177	38%	17	21	21%
	2013	194	40%	22	25	24%
	2014	242	50%	42	37	33%
	2015	289	55%	55	56	38%
Voriconazole	**2011**	128	27%	14	1	12%
	2012	168	36%	8	3	7%
	2013	166	34%	14	6	12%
	2014	190	39%	11	7	9%
	2015	240	45%	24	10	14%
Caspofungin	**2011**	63	13%	0	1	2%
	2012	118	25%	1	1	2%
	2013	149	30%	1	5	4%
	2014	187	38%	0	3	2%
	2015	228	43%	2	3	2%

Table 6.4: Resistance identified in mucosal specimen (a) *C. albicans* and (b) *C. glabrata* reports, England, 2011-2015, based on voluntary reporting to SGSS

a. *C. albicans*

Antifungal	Year	No. reported as tested	% reported as tested	Number Resistant	Number Intermediate	% Non-susceptible
Fluconazole	**2011**	32	1%	0	1	3%
	2012	42	1%	2	1	7%
	2013	72	2%	0	0	0%
	2014	96	2%	2	3	5%
	2015	148	4%	6	2	5%
Voriconazole	**2011**	201	4%	0	0	0%
	2012	272	6%	2	0	<1%
	2013	331	9%	2	0	<1%
	2014	335	8%	3	1	1%
	2015	491	13%	3	1	<1%
Caspofungin	**2011**	1	0%	0	0	0%
	2012	18	0%	0	0	0%
	2013	22	1%	0	0	0%
	2014	46	1%	0	0	0%
	2015	86	2%	0	1	1%

b. *C. glabrata*

Antifungal	Year	No. reported as tested	% reported as tested	Number Resistant	Number Intermediate	% Non-susceptible
Fluconazole	**2011**	7	29%	1	1	29%
	2012	5	31%	2	2	80%
	2013	14	36%	2	2	29%
	2014	20	43%	5	3	40%
	2015	23	61%	6	6	52%
Voriconazole	**2011**	4	17%	0	1	25%
	2012	2	13%	0	0	0%
	2013	12	31%	1	2	25%
	2014	13	28%	0	1	8%
	2015	14	37%	5	0	36%
Caspofungin	**2011**	3	13%	0	0	0%
	2012	2	13%	0	0	0%
	2013	6	15%	0	0	0%
	2014	11	23%	0	0	0%
	2015	10	26%	0	0	0%

Candida auris

C. auris was first isolated from a patient in Japan in 2009.[70] Since then *C. auris* has been associated with serious infections (bloodstream, wound, and ear infections). This pathogen has caused prolonged hospital outbreaks in healthcare settings globally; laboratories and clinicians need to be alert to the possibility of this organism and institute control measures rapidly when confirmed.[71]

This yeast species is commonly resistant to the first-line antifungal drug fluconazole, and may also be resistant to other classes of antifungal drugs (including amphotericin B and the echinocandins). Furthermore, *C. auris* isolates can be misidentified by commercial testing kits and equipment most commonly as *Candida haemulonii, Rhodotorula glutinis or Saccharomyces cerevisiae*. Therefore, it is important that presumptive isolates of these species are subjected to further, specialised testing (eg molecular sequencing or matrix-assisted laser desorption/ionization – time of flight (MALDI-TOF) Biotyper analysis).

After sporadic cases of *C. auris* were identified throughout England in 2013 and 2014, PHE was made aware of an on-going outbreak of *C. auris* in a critical care unit in a London hospital. In response, PHE activated an Incident Management Team and issued a briefing note in June 2016, alerting healthcare providers, including microbiologists and infection prevention and control personnel, to the emergence of this fungal pathogen. In addition, guidance was published for the laboratory investigation, management and infection prevention and control of cases of *C. auris*.[72]

[70] Satoh K et al., *Candida auris* sp. nov., a novel ascomycetous yeast isolated from the external ear canal of an inpatient in a Japanese hospital. Microbiol Immunol, 2009. 53(1): p. 41-4.

[71] Lee WG et al., First three reported cases of nosocomial fungemia caused by *Candida auris*. J Clin Microbiol, 2011. 49(9): p. 3139-42.

[72] Public Health England, Guidance, *Candida auris*: laboratory investigation, management and infection prevention and control; https://www.gov.uk/government/publications/candida-auris-laboratory-investigation-management-and-infection-prevention-and-control

Antifungal prescribing

Total consumption of antifungals

From 2013 to 2015, the total consumption of antifungals prescribed in general practice and NHS hospitals in England decreased by 13.3% from 1.5 to 1.3 DDD per 1000 inhabitants per day. During this time period, 99% of prescribing occurred in general practice (6.3).

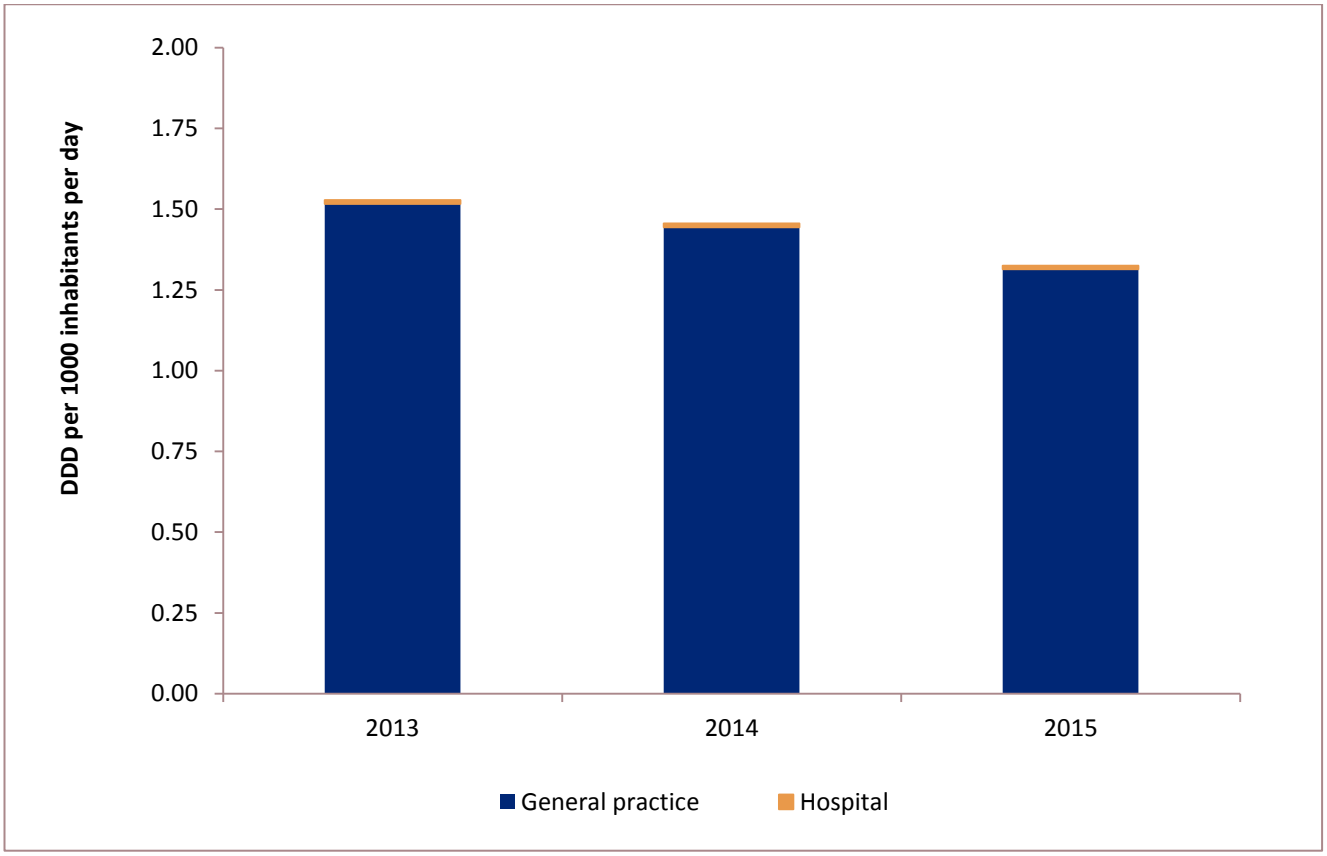


Figure 6.3: Consumption of total antifungals in general practice and NHS hospitals, expressed as DDD per 1000 inhabitants per day, England, 2013-2015

The key systemic antifungals used to treat serious mycotic infections are amphotericin B, azoles and echinocandins. As Figure 6.4 shows, azoles (fluconazole, itraconazole, ketoconazole, posaconazole, and voriconazole) accounted for 98.7% of total consumption in GP and NHS hospitals.

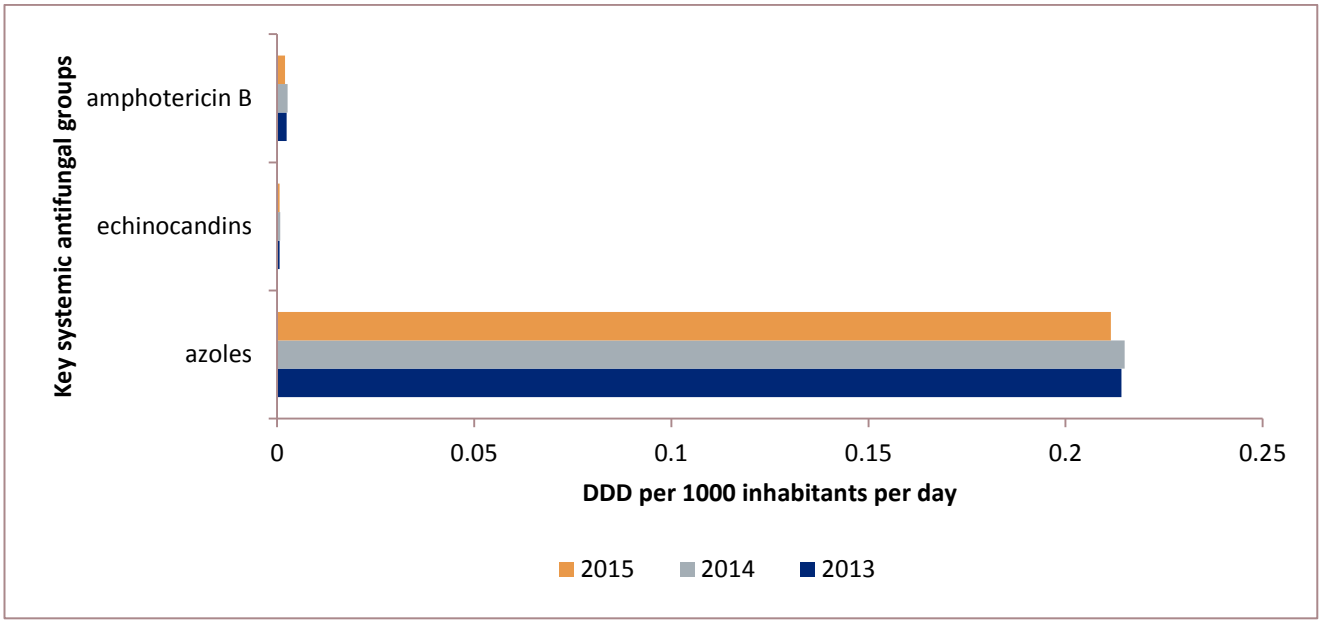


Figure 6.4 Consumption of total antifungals by key systemic antifungal group, expressed as DDD per 1000 inhabitants per day, England, 2013-2015

Prescribing in the community

Total prescribing of systemic antifungals in general practice decreased by 13%, from 1.5 to 1.3 DDDs per 1000 inhabitants per day, between 2013 and 2015 (Figure 6.5).

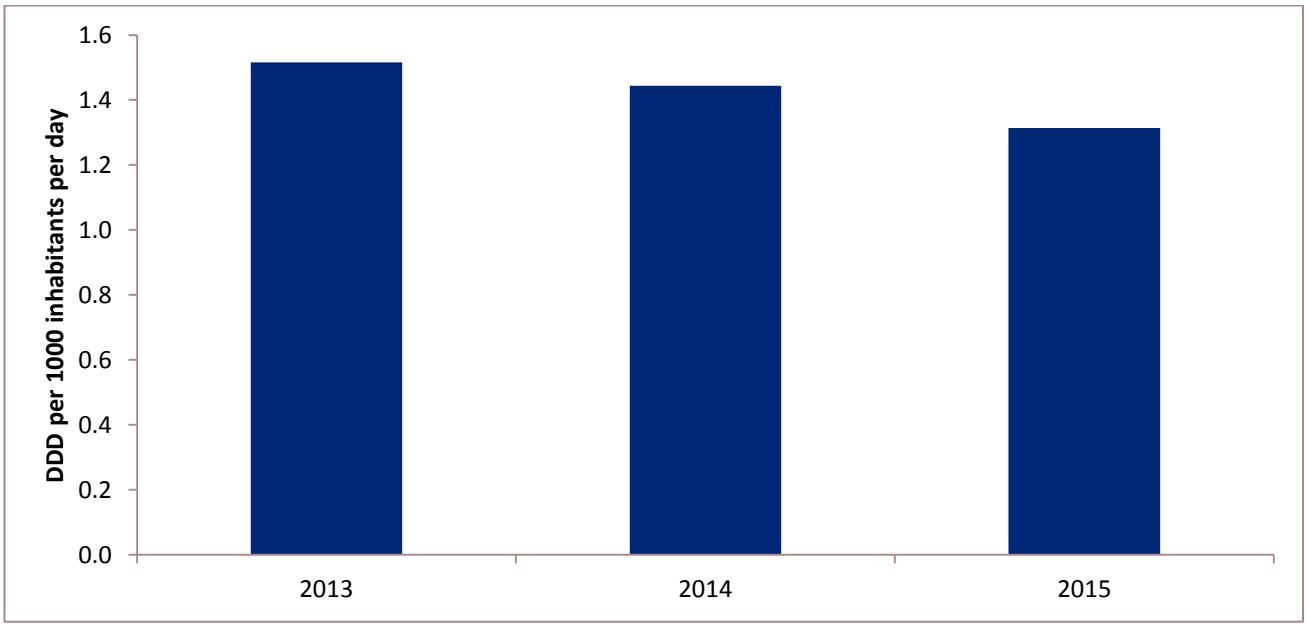


Figure 6.5 Total antifungal prescribing in general practice, expressed as DDD per 1000 inhabitants per day, England, 2013-2015

Terbinafine was the most commonly prescribed antifungal agent, administered orally for the treatment of nail, skin and hair fungal infections, although prescribing reduced by 14% between 2013 and 2015 (Figure 6.6). The only increase in prescribing was observed for fluconazole (4.7%).

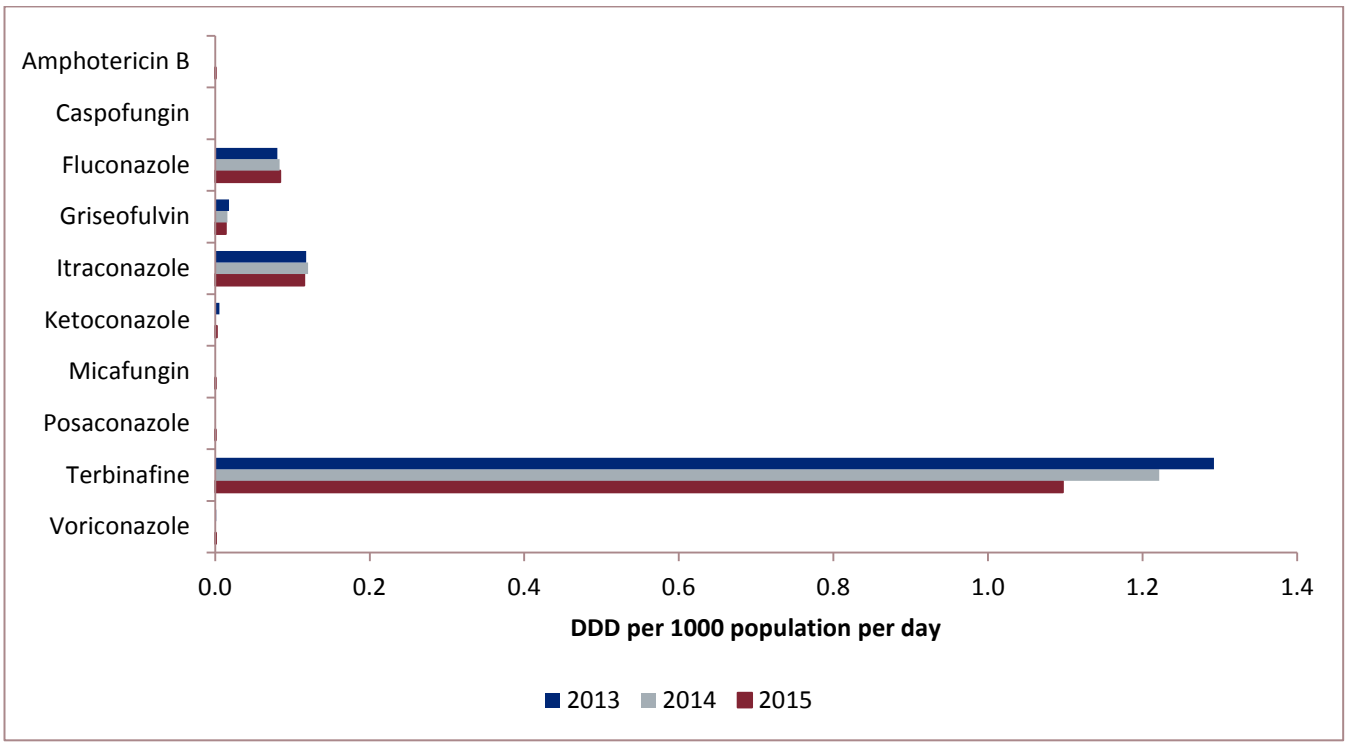


Figure 6.6 Antifungal prescribing in general practice by antifungal group, expressed as DDD per 1000 inhabitants per day, England, 2013-2015

Prescribing in NHS hospitals

Total consumption of antifungals in NHS hospitals decreased by 4.6% between 2013 and 2015 (6.7).

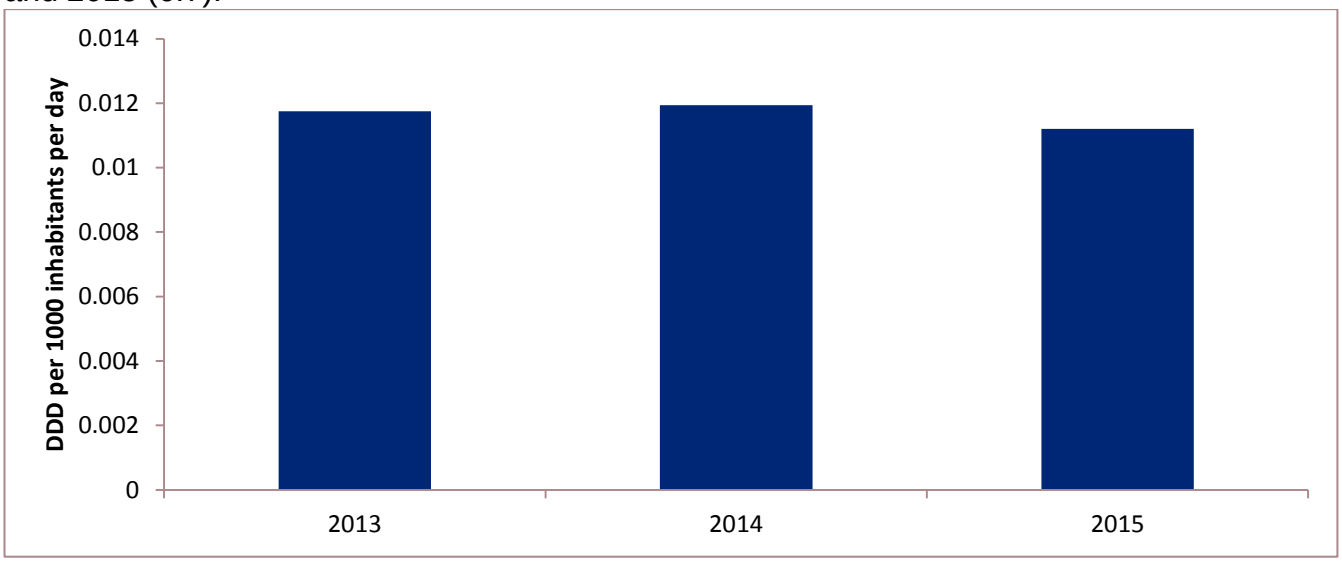


Figure 6.7 Total antifungal prescribing in NHS hospitals, expressed as DDD per 1000 inhabitants per day, England, 2013-2015

The prescribing of fluconazole was the only antifungal that consistently increased (40%) between 2013 and 2015, becoming the most prescribed antifungal in NHS hospitals in 2015 followed by itraconazole and amphotericin B (6.8).

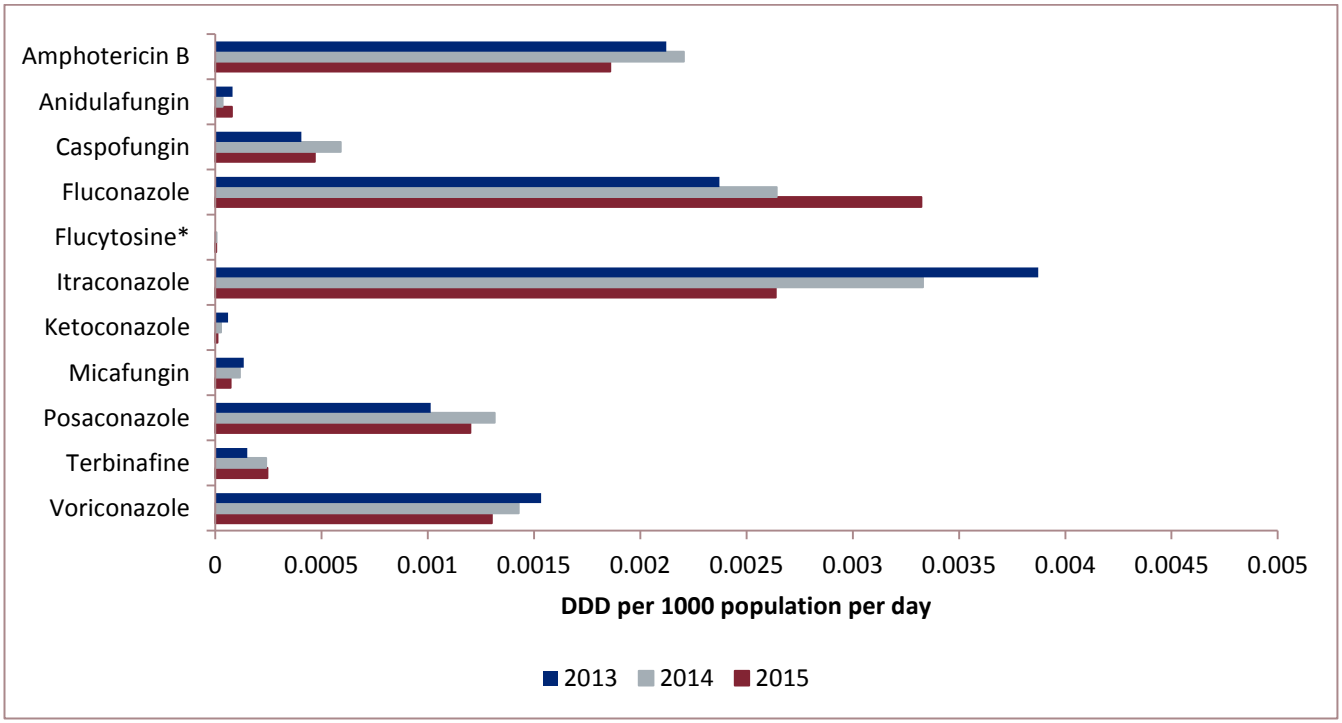


Figure 6.8 Antifungal prescribing in NHS hospitals by antifungal group, expressed as DDD per 1000 inhabitants per day, England, 2013-2015

*Flucytosine: 2013 = 0.000001 DDD/1000 pop/day; 2014: 0.000007 DDD/1000 pop/day; 2015: 0.000005 DDD/1000 pop/day

Antifungal stewardship

There was a 30% response rate to the antifungal survey from acute trusts; 54 individuals working in 47 NHS trusts responded. The main respondents were microbiologists (69%) and a breakdown is provided in Table 6.5 and the proportions of reporting trusts with AFS programmes is outlined in Table 6.6.

Table 6.5: Responding health professionals

	Percentage (n = 54)
Microbiologists	69
Antimicrobial Pharmacist	15
DIPC	4
Infectious Diseases Physician	6
Mycologist	2
Others (Clinical Pharmacy Technician, Microbiology Manager & Microbiology Registrar)	6

Table 6.6: Extent of AFS Programmes in acute trusts

	Percentage (n = 47)
Yes - we have a dedicated antifungal stewardship programme	11
Sort of - we include antifungal stewardship as part of our antimicrobial stewardship programme	43
Not really, but we do monitor antifungal usage	26
No	19

A total of 76% of all responding trusts reported to having fungal guidelines (prophylaxis, treatment or both) and 57% reported that their trust carried out triazole level monitoring (Table 6.7). The 25 trusts that reported to either having a dedicated AFS Programme or carrying out AFS as part of their AMS Programme, reported that the majority of their AFS ward rounds were performed by microbiologists (84%) and pharmacists (54%). The main reasons for starting their AFS Programme were reported to be: to manage antifungal costs (52%), clinical need (48%) and improve antifungal management (40%).

Table 6.7: Table of activities which responding trusts said made up their AFS Programmes

	% with these activities (n = 25)
Have an antifungal stewardship/management team	28
Monitor and report on antifungal use	64
Dedicated antifungal stewardship ward rounds	20
AF team have direct involvement in management of invasive fungal infections (eg candidaemia and aspergillosis	48
Request from clinicians	0

Of the 37 trusts that reported to either having a dedicated AFS Programme, including AFS as part of their AMS Programme or only monitored their antifungal usage, 73% reported that they would do more AFS if they could. However, there were many barriers preventing further AFS work occurring (Table 6.8). A total of 76% of these trusts reported that they would do more AFS if these barriers were removed.

Table 6.8: Table showing the barriers to carrying out AFS which responding trusts reported

	% reporting barrier (n = 21)
Competing priorities	48
Funding by NHS England for high cost antifungal drugs	14
Lack of interest	10
Lack of resources: staff time	67
Lack of resources: expertise	14
Perceived lack of importance	24

Comments provided by participants

- “For a trust of our size, we are fairly targeted and conservative in our antifungal use, as per define data per 100 bed days. We have moved to a more evidence-based threshold for adding in empiric treatment antifungals in haematology patients, as per national guidance”
- “Staff engagement has been one of the areas where we believe we have had the most success, and is showing the programme to be sustainable”

- “Huge impact on appropriate prescribing by implementing a systemic antifungal guideline”
- “Anti-fungal stewardship is challenging in transplant and respiratory patients: transplant team is usually set in their ways as to how they manage their patients and also fear of clinical failure if antifungals are stopped; respiratory team (bronchiectasis and CF) usually rely on radiology findings rather than on biomarkers. Although galactomannan is available … turnaround time is not satisfactory for stewardship. Also, we have problems with funding of this test (currently funded for certain patients) - pathology doesn't have a budget for other patients and other departments (critical care, transplant are not willing to pay)”
- “We used to do weekly antifungal ward rounds with X Microbiologist which were excellent. Since the person left (about a year ago) we haven't resumed these...none of the other microbiologists have the expertise…and perhaps the interest. We also struggle to fit everything in, so lack of time is a major factor. Also the fact that other things have become more 'important'... eg CQUIN for antibiotic reduction so time and effort are currently being directed elsewhere. Antifungals are also hugely complicated so training would be greatly received.....”

Discussion

In this chapter, we have reviewed antifungal resistance data extracted from SGSS, PHE’s voluntary laboratory surveillance database, showing incidence rates and antifungal resistance for the key fungal pathogens *A. fumigatus, Fusarium* spp*., C. albicans,* and *C. glabrata* in England from 2011 until 2015. It has highlighted developments in antifungal resistance surveillance and is an important first step in building the data required to improve our understanding of resistance trends in order to provide an evidence base for antifungal guidance and policy.

The data clearly present challenges. Laboratory reports for moulds and yeasts captured by PHE’s voluntary laboratory surveillance system have steadily increased over the last five years but the numbers of moulds captured are still very small and the proportion of reports including antifungal test results for moulds and yeast isolates from mucosal specimens is too low to allow robust interpretation of trends.

However, between 2011 and 2015, the proportion of sterile site *C. albicans* and *C. glabrata* laboratory surveillance reports including information on susceptibility testing increased in England. This may be in part due to the increased awareness following the production of clinical guidelines in recent years, recommending antifungal susceptibility testing for all *Candida* species isolated from blood[73] and therapeutic drug monitoring (TDM) of antifungal agents[74], and

[73] Cuenca-Estrella M et al. ESCMID guideline for the diagnosis and management of Candida diseases 2012: diagnostic procedures. Clin Microbiol Infect. 2012; 18 (suppl. 7): 9-18

[74] Ashbee HR et al. Therapeutic drug monitoring (TDM) of antifungal agents: guidelines from the British Society for Medical Mycology. J. Antimicrob. Chemother. 2014; 69: 1162-1176

improved laboratory data capture by PHE's surveillance scheme, as well as the increased use of automated antimicrobial susceptibility testing instruments in laboratories across England.[75]

A further limitation is the method of reporting antifungal susceptibility results as 'S', 'I' or 'R', as it will fail to reveal drifts in the minimum inhibitory concentration (MIC). This could be improved by capturing data from other sources, particularly national and regional reference laboratories. One of the problems in interpreting breakpoints and thus providing interpretative categories is that although they have become more closely aligned in recent years there are still differences between those suggested by the Clinical Standards Laboratory Institute (CLSI) and by the European Committee on Antimicrobial Susceptibility Testing (EUCAST). In order to interpret MIC results it is important to know which method was used as many commercial methods still apply CLSI breakpoints.

The capacity and capability of laboratories to accurately identify and test for resistance in fungal pathogens is also largely unknown; the ESPAUR group have taken this on board and will address in the next year. A national survey on the compliance and implementation of the British Society for Medical Mycology (BSMM) standards of care for patients with invasive fungal infections was performed in UK hospitals in 2007.[76]

As new guidelines for fungal diagnostics and antifungal drug monitoring were published recently,[77] the ESPAUR antifungal subgroup agreed that a repeat survey of laboratory testing capabilities for clinically significant fungal pathogens was necessary. A template of the 2007 survey was circulated among the group and relevant updates made. The survey will be circulated through the lead public health microbiologists as a joint PHE/BSMM initiative in November 2016.

With respect to *A. fumigatus*, subtherapeutic concentrations of azoles may allow resistance to emerge, particularly in those treated long term and with large organism loads, as seen in those with chronic pulmonary aspergillosis and aspergillomas.[78] The British Society for Medical Mycology issued recommendations for TDM, but using the laboratory surveillance data for microorganisms does not allow the assessment of whether TDM is occurring[79] There is also increasing concern about cross-resistance in *A. fumigatus* isolates to azoles used in human medicine following exposure to azole drugs used in agriculture.

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[75] Ironmonger D et al. AmWeb: a novel interactive web tool for antimicrobial resistance surveillance, applicable to both community and hospital patients. J. Antimicrob. Chemother. 2013; 68(10): 2406-2413

[76] Schelenz S et al. Standards of care for patients with invasive fungal infections within the United Kingdom: a national audit. J Infect. 2009 Feb;58(2):145-53. doi: 10.1016/j.jinf.2008.12.006.

[77] Schelenz S et al. British Society for Medical Mycology best practice recommendations for the diagnosis of serious fungal diseases. Lancet Infect Dis. 2015 Apr;15(4):461-74. doi: 10.1016/S1473-3099(15)70006-X. Epub 2015 Mar 12.

[78] Howard S et al. Frequency and Evolution of Azole Resistance in *Aspergillus fumigatus* Associated with Treatment Failure. Emerg Infect Dis. 2009 Jul; 15(7): 1068-1076

[79] Ashbee HR et al. Therapeutic drug monitoring (TDM) of antifungal agents: guidelines from the British Society for Medical Mycology. J Antimic Chemother. 2014; 69: 1162-1176.

This is the first time that national antifungal prescribing data for the community and NHS hospital sector have been gathered. Experts from the ESPAUR subgroup on antifungal consumption and resistance surveillance provided input into the presentation and interpretation of the data.

The general trend for antifungal consumption is downward, both in the community and in hospital. As expected, terbinafine prescribing is seen in the community rather than in hospitals, which is consistent with general practice prescribing for superficial fungal infections ie infections of the skin, nails and hair. However, there are significant over-the-counter sales of fluconazole and clotrimazole and mechanisms to capture this data need to be explored.

The usage data for amphotericin B, anidulafungin, caspofungin and posaconazole is variable between 2013 and 2015. Use of itraconazole, ketoconazole and micafungin has consistently decreased whereas use of terbinafine in hospitals has increased over the same time period. Usage data for both posaconazole and voriconazole has shown a downward trend between 2013 and 2015. The only systemic antifungal for which prescribing has increased was fluconazole, both in the community and in hospitals (4.7% in general practice and 40% in hospital prescribing, respectively) over the same time period. The reason for this increase is unclear, although it is unlikely to be related to usage within haemato-oncology units, where the clinical trend has been to address mould infections prophylactically.

However, paradoxically, the data show an overall decrease in the antifungals that are used for mould prophylaxis (itraconazole, posaconazole, voriconazole). Furthermore, the DDD system may not reflect the overall days of therapy given and in some cases, particularly liposomal Amphotericin B the DDD does not reflect the dose used in practice. Further specialty specific consumption data and validation of this data is required to develop an understanding of the underlying trends. It may be that there is significant usage outside of the well-described hospital areas of antifungal usage in haemato-oncology, transplant and intensive care patients.

Potential reasons for the overall decreased usage may be linked to a share in the income benefits realised offered to NHS trusts by local commissioners. The possible move from national specialised commissioning for high-cost antifungal drugs to local tariff based payments may further reduce (inappropriate) antifungal spend.

Rapid real-time diagnostics for invasive fungal infections may also help to reduce use of high cost antifungal drugs which are frequently started prior to laboratory confirmation of infection in profoundly immunocompromised patients. Increasing resistance trends for example for *A. fumigatus* and *C. auris* isolates highlight the importance of preventing

unnecessary use of antifungals and therefore avoiding selection pressure on fungal pathogens.

Although only a minority of trusts conducts AFS programmes, nearly half include AFS as part of routine antimicrobial stewardship activities. Cost and clinical need are the main drivers for AFS. Clinicians believe that the availability of rapid diagnostics and clinical experts in this area could help increase AFS initiatives and reduce the costs and consumption of antifungals.

Future actions

Antifungal stewardship activities should be embedded within practice and mycology diagnostics laboratory capacities enhanced.

The ESPAUR subgroup on antifungal consumption and resistance surveillance will continue to work on the following aims with regards to antifungal resistance;

- combine PHE's voluntary laboratory surveillance dataset with information collected by national and regional mycology reference laboratories
- use the information gathered by the survey on mycology diagnostics laboratory capacity to facilitate interpretation of the captured surveillance data and raise awareness of antifungal diagnostics
- expand the analysis to include those pathogens with intrinsic, emerging and multidrug resistance, such as *C. krusei*, *Scedosporium apiospermum* complex, *Lemontospora prolificans* and *Mucorales* moulds
- explore linkage of laboratory surveillance data to clinical data to enable better clinical use of the reported information
- assess options of presenting antifungal resistance data on publicly accessible interactive data portals such as PHE's Fingertips web portal once reporting and understanding of the laboratory data has improved
- explore and work with IMS Health to develop specialty specific antifungal prescribing datasets
- develop case studies to demonstrate the cost-effectiveness of antifungal stewardship within the NHS

Chapter 7: Stakeholder engagement

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

Association of Independent Healthcare Organisations

Association of Independent Healthcare Organisations (AIHO) is the trade association for independent healthcare providers across the UK.[80] AIHO has existed in its current form since the beginning of 2013, and represents over 200 hospitals that provide services to insured, self-paying and NHS-funded patients. AIHO members vary from large hospital groups to smaller, specialist providers of specific surgeries and treatments.

AIHO and its members are engaging with PHE on several projects:

- participating in the collection of antimicrobial prescribing data project
- taking part in the EU PHE PPS
- identification of private laboratories for inclusion in routine surveillance of infectious disease

Member organisations have:

- implemented Antimicrobial Stewardship and the “Start Smart Then Focus” tool and it is a standing item on the Infection Control Committee’s agenda to raise its status. It is part of the mandatory training agenda
- included in the strategy planning with antibiotic policies updates involving the whole multidisciplinary team
- signed up as Antibiotic Guardians

AIHO members want to participate and support PHE in meeting the AMR strategy objectives. This has highlighted some challenges as the Independent Sector do not always fit neatly into NHS systems. AIHO is engaging with PHE/ESPAUR to increase the understanding of the Independent Sector and identify ways in which to overcome these challenges.

[80] For further details the Association of Independent Healthcare Organisations (AIHO) website is available from; www.aiho.org.uk

British Dental Association

The British Dental Association (BDA) has been at the forefront of efforts to tackle AMR in dentistry by raising awareness, identifying barriers and opportunities to reduce prescribing, and forging inter-professional links to maximise impact. After convening a multidisciplinary expert summit in November 2014 to bring together major players from across the dental, medical, veterinary and pharmaceutical worlds, the BDA published a consensus report highlighting key actions for stakeholders including professional bodies, educators, regulators, individual practitioners and government.[81]

The BDA has been lobbying Government to ensure that the dental contract supports antimicrobial stewardship by providing adequately-resourced treatment time for dental emergencies, enabling practitioners to establish a differential diagnosis and carry out appropriate clinical intervention. This has been supported by the Chief Medical Officer for England. Further information on the BDA's work on AMR Is available via its campaign webpage, which also includes infographics that remind dentists to prescribe responsibly that may be shared via social media.[82]

The BDA continues to work with a wide range of stakeholders within the UK and internationally (through the Council of European Dentists), and published a One Health statement with the British Medical Association, British Veterinary Association and Royal Pharmaceutical Society for EAAD 2015.[83]

British Society for Antimicrobial Chemotherapy

The British Society for Antimicrobial Chemotherapy (BSAC) is an inter-professional organization with over 40 years of experience and achievement in antibiotic education, research and leadership and is dedicated to saving lives through appropriate use and development of antibiotics now and in the future. BSAC publishes the *Journal of Antimicrobial Chemotherapy,*[84] the leading international peer-reviewed journal in its field, and leads *Antibiotic Action*, a UK-led global initiative that seeks to ensure effective antibiotics are researched, discovered and developed for all who need them. BSAC has a programme to facilitate research and development by giving grants and has a very successful meeting's agenda, with events ranging from large conferences for healthcare

[81]British Dental Association; AMR in dentistry summit 10 November 2014 | Consensus report; available from; https://www.bda.org/news-centre/press-releases/Documents/BDA%20AMR%20in%20dentistry%20summit%20consensus%20report.pdf
[82]British Dental Association; AMR in dentistry website available from; https://www.bda.org/amr
[83] British Dental Association; Leading health organisations call for proper use of antibiotics, available from; https://www.bda.org/news-centre/latest-news-articles/leading-health-organisations-call-for-proper-use-of-antibiotics
[84] Journal of Antimicrobial Chemotherapy available from; http://jac.oxfordjournals.org

professionals to small workshops and public debates. The Society engages with a wide range of stakeholders to improve and promote understanding of antimicrobials, including peer organizations, parliamentarians, policy-makers, students and healthcare trainees, scientists, researchers and journalists. Further information on BSAC and its activities can be found on our website.[85]

Specific areas of current activity include the following:

- Antibiotic Action[86]
  Promoting the need for discovery and development of effective antibiotics for all who need them and provision of support for the All Party Parliamentary Group (APPG) on Antibiotics[87]
- Antibiotic Resistance surveillance
  - Monitoring resistance to antibiotics (antimicrobials, antibacterials) within the UK[88]
  - National Antimicrobial Stewardship Point Prevalence System: A N3 server system enabling the collection and provision of reference data on antimicrobial consumption in hospital settings will launch in January 2017[89]
- National Susceptibility Testing Methodology: Providing antimicrobial susceptibility testing and reporting guidance since 1999[90]
- Drug Stability Testing Programme: Providing open access stability data on agents and devices used in infection management[91]
- Massive Open Online Course on AMS: Open access global education for all – over 30,000 registered learners since September 2015[92]

Faculty of General Dental Practice

The Faculty of General Dental Practice (FGDP) provides evidence-based guidance to promote prudent prescribing and antimicrobial stewardship in primary dental care through its 2012 publication," Antimicrobial prescribing for general dental practitioners".[93] The guidance is updated online as new evidence becomes available and is freely available through the FGDPs (UK) Open Standards Initiative.

FGDP has also been at the forefront of social media campaigns within dentistry associated with EAAD and promoting Antibiotic Guardianship. The FGDP (UK)

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[85] British Society for Antimicrobial Chemotherapy website available from; http://www.bsac.org.uk
[86] Antibiotic action website available from; http://www.antibiotic-action.com
[87] All Party Parliamentary Group on Antibiotics (APPG-A) website available from; http://appg-on-antibiotics.com
[88] British Society for Antimicrobial Chemotherapy, Resistance Surveillance Project, website available from; http://www.bsacsurv.org/
[89] National Antimicrobial Stewardship, Point Prevalence system available from; http://www.nas-pps.com
[90] British Society for Antimicrobial Chemotherapy website available from; http://www.bsac.org.uk
[91] British Society for Antimicrobial Chemotherapy drug stability programme website available from; http://www.bsac-dsp.com
[92] British Society for Antimicrobial Chemotherapy British Society for Antimicrobial Chemotherapy available from; http://www.bsac.org.uk/massive-open-online-course-on-antimicrobial-stewardship
[93] Faculty of General Dental Practice (UK) Standards in Dentistry online; http://www.fgdp.org.uk/publications/standardsindentistryonline.ashx

organised and promoted the Thunderclap pledge[94], in collaboration with the Association of Clinical Oral Microbiologists, the BSAC and Antibiotic Action for EAAD 2015 was well supported by the dental profession and achieved a social reach of over 83000.

FGDP has provided a number of press releases highlighting the detrimental overuse of antibiotics, the dangers of inappropriate use and steps that can be taken to keep them working.[95,96]

FGDP is working in collaboration with other primary dental care stakeholders to produce a freely available antibiotic clinical audit tool for practitioners to facilitate embedding antimicrobial stewardship into everyday clinical practice.

Health Education England: Implementation of antimicrobial stewardship competences in undergraduate curricula

Education of healthcare workers and students on rational infection control, antimicrobial prescribing and antimicrobial stewardship is a key part of antimicrobial resistance containment activities. Health Education England (HEE) 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 Antimicrobial Prescribing and Stewardship (AMPS) competences[97] can provide clarity for regulators, education providers and professional bodies to inform standards, guidance and the development of training. The competences consist of five dimensions, namely infection prevention and control, AMR and antimicrobials, the prescribing of antimicrobials, antimicrobial stewardship and monitoring and learning.

A gap analysis/self-assessment survey was sent via HEE local offices to Health Education Institutions to understand how the antimicrobial prescribing and stewardship competencies were being embedded into the undergraduate curricula of healthcare students. The survey was completed separately for each of the courses namely medicine, adult nursing, dentistry, pharmacy, midwifery, independent prescribing courses and allied health professionals. Amongst the questions respondents were

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[94] Thunderclap project; Antibiotic prescribing pledge available from; https://www.thunderclap.it/projects/33157-antibiotic-prescribing-pledge.
[95] Faculty of General Dental Practice (UK), AMR press release available from; http://www.fgdp.org.uk/content/news/fgdpuk-press-release-antibiotic-resistance.ashx
[96] Faculty of General Dental Practice (UK), Pledge to keep antibiotics working available from; http://www.fgdp.org.uk/content/news/pledge-to-keep-antibiotics-working.ashx
[97] Royal Pharmaceutical Society Prescribing competency framework available from; http://www.rpharms.com/unsecure-support-resources/prescribing-competency-framework.asp?

asked about include the healthcare courses they were providing answers for; their awareness of the national AMPS Competencies; which undergraduate or independent prescribing courses specifically include learning content to address the five dimensions of the AMPS competences; the main mode of antimicrobial resistance content delivery; and methods used to evaluate learners' knowledge about antimicrobial resistance content.

HEE received responses from 45 universities who provided responses for 100 different heath courses, including 17 Medical, 13 Pharmacy, 22 Independent Prescribing, 5 Dental, 23 Nursing, 13 Midwifery and 7 Allied Health Professional courses. A total of 86 courses (86%) confirmed they were aware of these AMPS competencies. Overall implementation of each domain, according to professional group, is outlined in Table 7.1.

Table 7.1: Implementation of antimicrobial stewardship competencies in different professional groups

COMPETENCY	*Dent*	*Pharm*	*Med*	*Midw*	*Nur*	*IndPre*	*AHP*
Infection Prevention and Control.	100%	98%	99%	85%	86%	72%	94%
Antimicrobial resistance and antimicrobials	97%	100%	99%	59%	56%	75%	41%
Prescribing antimicrobials.	88%	81%	96%	41%	29%	90%	30%
Antimicrobial Stewardship.	73%	77%	91%	51%	42%	77%	25%
Monitoring and learning	50%	48%	63%	23%	16%	68%	14%
Total average	**82%**	**81%**	**90%**	**52%**	**46%**	**76%**	**40.8%**

Dent = Dentist; Pharm = Pharmacy; Med = Medical doctor; Midw = Midwife; Nur= Nurse, except midwife; IndPre= Independent Prescriber; AHP = Allied Health Professionals

The average implementation rate for all universities and courses was 67% for all the dimensions. This may not be satisfactory for some courses, especially in relation to the levels of professional clinical practice expected from qualified professionals. HEE may have a role in raising awareness nationally via its local offices, individual professional schools councils, professional bodies, regulators and the Royal Colleges.

Further work is required to explore how and what the remaining 54% have done to implement the AMPS competences.

Resources available from HEE on antimicrobial resistance to support AMR education and training

a. A basic introductory free e-learning module*:* Reducing Antimicrobial Resistance. This is available to all health and social care staff – both clinical and non-clinical - in a variety of settings to understand the threats posed by AMR, and ways they can help tackle this.[98]

[98] e-Learning for Healthcare, Reducing AMR, available from; http://www.e-lfh.org.uk/programmes/antimicrobial-resistance

Visit the e-Learning for Health website and visit the “how to access” link for more information.

b. Resources to support GPs and primary care clinicians on antimicrobial resistance. A guide for GPs[99] to AMR involving the Chief Medical Officer and eminent clinicians and an accompanying short informative animation[100] aimed at the public have been produced in partnership with PHE to help all prescribers respond appropriately to patients requesting antibiotics without medical need. Both films provide a short introduction into the risks associated with the over-use of antibiotics, and to encourage appropriate dispersion. It complements the TARGET toolkit, a range of educational materials available to GPs and other prescribers, and was built around some work done by the Wellcome Trust [101] to understand how the public responds to information about AMR.

c. Scoping exercise on embedding antimicrobial prescribing and stewardship competencies (PHE & ARHAI, 2013) within undergraduate and non-medical prescribing curricula. HEE has surveyed higher education institutions about their awareness of the competencies, and how they had embedded them into their undergraduate and postgraduate curricula. They asked about how existing resources may be used to support learning and any perceived gaps in provision. The full report[102] and executive summary[103], set out the results and recommendations for ourselves and external organisations to encourage further adoption of these competencies.

d. Further scoping work to identify whether there are any gap areas in relation to educational resources available to support current prescribers with the responsible prescribing of antimicrobials and if necessary make recommendations to address these gaps is currently underway.

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[99]Health Education England; A GP guide to antimicrobial resistance, available from; https://youtu.be/PkYQJettZVo
[100]Health Education England; Awareness of Antimicrobial Resistance (AMR) Animation available from; https://youtu.be/oMnU6g2djm4
[101] Wellcome trust, Antibiotic resistance poorly communicated and widely misunderstood by UK public, available from; https://wellcome.ac.uk/press-release/antibiotic-resistance-poorly-communicated-and-widely-misunderstood-uk-public
[102] Health Education England, Embedding national antimicrobial prescribing, available from; https://hee.nhs.uk/sites/default/files/documents/Full%20report%20-%20Embedding%20national%20antimicrobial%20prescribing%20and%20stewardship%20competences%20into%20curricula.pdf
[103] Health Education England, Embedding national antimicrobial prescribing, available from; https://hee.nhs.uk/sites/default/files/documents/Executive%20summary%20-%20Embedding%20national%20antimicrobial%20prescribing%20and%20stewardship%20competences%20into%20curricula.pdf

National Institute for Health and Care Excellence

The National Institute for Health and Care Excellence (NICE) continues to provide guidance and advice to support the wider AMS including a new programme of work to develop a suite of prescribing guidelines for the management of common infections in primary and secondary care. These guidelines will primarily be aimed at prescribers but will be valuable to other health professionals and commissioners. In support of this work, the BNF section on antimicrobials will be reviewed to include links to information about regional resistance levels.

In addition to the NICE guideline on AMS systems for effective antimicrobial use (NG15), NICE is currently developing a complementary guideline: AMS changing risk-related behaviours in the general population. To further improve effective antimicrobial stewardship a quality standard (QS121) was published in April 2016, which aims to reduce the emergence of AMR (loss of effectiveness of antimicrobials).

The NICE Key Therapeutic Topics work includes AMS 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 AMR.

Royal College of Physicians

The Royal College of Physicians (RCP) has engaged with the AMR Strategy and the ESPAUR by:

- promoting issues via the Joint Specialty Committee for Infectious Diseases, in partnership with the British Infection Association (BIA) and other organisations (including the RCPath) with a primary interest in infection. This committee reports to RCP Council and advises its parent bodies or other organisations on their behalf, on matters of mutual interest. Its remit includes promoting the coordinated national management of new outbreaks, managing infection education and advice across the hospital setting and advising on antimicrobial resistance, healthcare associated infections and antimicrobial stewardship. The chair of the ESPAUR oversight group is a member for the Joint Speciality Committee
- forming a group to discuss RCP policy initiatives with regard to AMR and sepsis and the relationship between patient safety and Future Hospitals Programme[104]
- communicating and highlighting the importance of appropriate antibiotic prescribing through the RCP President's newsletter and the RCP membership magazine, Commentary

[104] Royal college of Physicians, The Future Hospital Programme (FHP) available from; https://www.rcplondon.ac.uk/projects/future-hospital-programme

- reviewing the postgraduate curricula and highlighting the importance of including topics on AMR and antibiotic stewardship in the curricula and examinations
- highlighting key resources such as the Top Ten Tips HCAI series to our members and fellows with specific tips on effective antibiotic prescribing, postgraduate training, medical prophylaxis and device insertion and care[105]
- supporting AG and European Antibiotic Awareness Day through activity from the RCP on our social media channels including Twitter and Facebook to highlight and raise awareness with our members, fellows and the public

Royal Pharmaceutical Society of Great Britain

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

The RPS has signposted members to resources, information and support on tackling AMR to support them in their practice. We also ensure that AMR is included in all relevant RPS standards and guidance. In 2016 a specific statement on antimicrobial resistance was included in the recently revised Prescribing Competency Framework for all Prescribers.[106]

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 (SEAP). Both groups have provided comment and input across a wide range of work streams relating to antibiotic utilisation and resistance. The SEAP 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.[107]

The RPS has also contributed to work internationally, providing input to the International Pharmaceutical Federation (FIP) report Fighting Antimicrobial Resistance: the contribution of pharmacists.[108]

UK Clinical Pharmacy Association

[105] Royal college of Physicians, HCAI top ten tips, available from; https://www.rcplondon.ac.uk/projects/outputs/hcai-top-ten-tips
[106] Royal Pharmaceutical Society, Prescribing competency framework, July 2016 available from; http://www.rpharms.com/unsecure-support-resources/prescribing-competency-framework.asp
[107] Royal Pharmaceutical Society, New Medicines, Better Medicines, Better Use Of Medicines, May 2014 available from; http://www.rpharms.com/promoting-pharmacy-pdfs/nmbmbu---full-report.pdf
[108] International Pharmaceutical Federation (FIP), November 2015, “FIP issues new resource to arm pharmacy's fight against antibiotic resistance” http://fip.org/www/index.php?page=news_publications&news=newsitem&newsitem=217

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 853 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 update the AMS toolkit for English hospitals and to deliver stewardship in both primary and secondary care. UK CPA have disseminated information from ESPAUR and delivered education on AMS using our online forum, at UKCPA master classes and conferences, in webinars and in sessions 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, performing validation of existing reporting systems (IMS health and Define) and presenting data at FIS 2014 and 2015.

Group members are currently leading the delivery of the CQUIN to reduce total, carbapenem and piperacillin/tazobactam consumption and increase reviews of empiric antibiotic prescriptions in England.

Chapter 8: Research and outputs

This section highlights abstracts of on-going research and outputs that are in development.

Electronic Reporting System (ERS) for carbapenemase-producing Gram-negative bacteria: initial outputs

Rachel Freeman, Dean Ironmonger, Richard Puleston, Katie L. Hopkins, William Welfare, Russell Hope, Peter Staves, Michael Shemko, Susan Hopkins, Paul Cleary, Bharat Patel, Berit Muller-Pebody, Peter Hawkey, Alan Johnson, Neil Woodford, Isabel Oliver

Bacteria resistant to carbapenems pose a significant threat to individual patients as well as to healthcare provision globally. In response to increasing numbers of carbapenemase-producing Gram-negative bacteria identified in the UK (described in Chapter 2), we implemented an Electronic Reporting System (ERS) in England for the enhanced surveillance of these organisms in May 2015 following a pilot project in the West Midlands.

Data on 2,433 isolates from 2,058 patients was submitted via the ERS between May 2015 and April 2016. In addition to isolates that were referred via the ERS to either a regional and/or the national reference laboratory, one organisation submitted their locally-confirmed carbapenemase producers from May 2015–February 2016.

Table 8.1: Proportion of isolates referred to AMRHAI via the ERS as opposed to submission of isolates using paper form requests, May 2015–April 2016

Month/Year	Proportion of isolates referred via ERS (%)
May 2015	10.7
June 2015	27.2
July 2015	26.2
August 2015	22.8
September 2015	19.3
October 2015	24.1
November 2015	24.6
December 2015	41.3
January 2016	64.7
February 2016	62.8
March 2016	62.5
April 2016	67.5

User engagement has continued to improve (Table 8.1). However, further work is required to promote the use of ERS for referring organisms, entering local confirmation test results and increasing the completion of enhanced data received via the system.

An upgrade of the system was rolled-out in July 2016 to add additional functionality and improve the user experience following constructive feedback from laboratories and Trusts over the past 12 months. With the new features, users can now:

- record local molecular test results
- register multiple organisations and user roles
  produce reports for their laboratories and/or trusts

With the increasing availability and use of commercial carbapenemase detection tests in NHS and private laboratories, the confirmation of carbapenemase production in Gram-negative bacteria is rapidly becoming a method for diagnostic microbiology laboratories rather than for reference laboratories. The ERS is the only method currently available that allows this locally-generated data to be captured and used to inform regional and national trends. Active participation in this surveillance by every trust in the country is vital for building a comprehensive picture of the growing carbapenemase problem in England and will allow us to inform the development of effective infection prevention and control strategies.

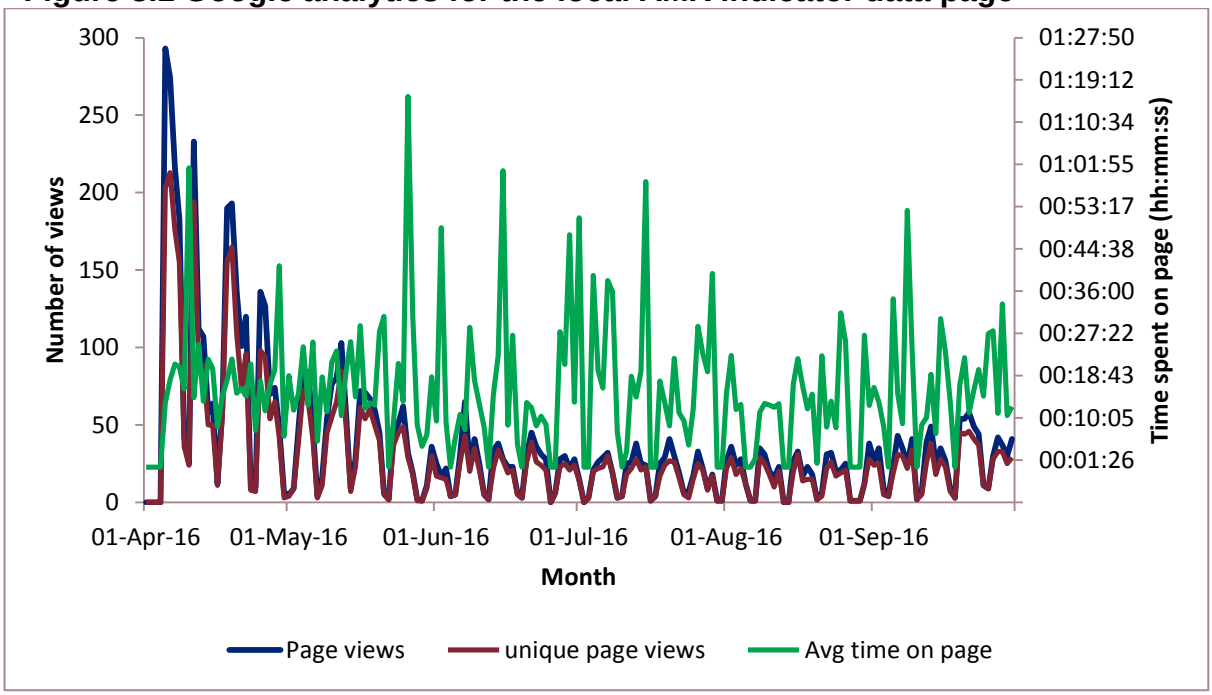
Launch of PHE Fingertips AMR local indicators: initial uptake evaluation

Alan P. Johnson, Berit Muller-Pebody, Emma Budd[1], Diane Ashiru-Oredope, David Ladenheim, Doris Hain, Russell Hope, Alex Bhattacharya, Suzanne Elgohari, Rebecca Guy, Katherine Henderson, Richard Puleston, Graeme Rooney, Simon Thelwall, Edgar Wellington, Theresa Lamagni, Susan Hopkins

Launched on the PHE Fingertips web portal in April 2016, AMR local indicators are publically available data intended to raise awareness of AMR, antimicrobial prescribing, healthcare associated infections, infection prevention and control and AMS. These data can facilitate the development of local action plans and support specific national quality improvement programmes. AMR local indicators published to date are derived from existing data sets that PHE holds centrally or is able to access with permission; they pose no additional burden on the NHS.

Initial evaluation based on Google analytics demonstrated that the AMR local indicators portal received a high number of visitors (4243) in the first eight weeks of operation, of which 3,267 were unique views. The portal had an average of 72.8 visitors per day with the highest page views (274) on Day 2 after launch. However, there was a month-on-month decline in page views from April 2016 to July 2016. (Figure 8.1)

Figure 8.1 Google analytics for the local AMR indicator data page



PHE will continue to monitor the rate of AMR local indicator portal page views per month. A full evaluation of AMR local indicators on fingertips will be conducted following one year of operation. This will include an assessment of who is using the AMR indicators and what they are used for in their organisation.

Point Prevalence Survey on healthcare-associated infection and antimicrobial use in English acute trusts

Rachel Freeman, James Vaudrey, Karen Shaw, Diane Ashiru-Oredope, Katherine Henderson, Susan Hopkins

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 HAI and AMU is an essential part of infection prevention and antimicrobial stewardship. The point prevalence survey drives action by providing data on the burden of HCAI and AMU which allows targeted planning and implementing more effective, evidence based policies, surveillance and strategies.

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

- estimate the total burden (prevalence) of HCAIs and AMU in acute care hospitals;
- describe patients, invasive procedures, infections (sites, microorganisms including markers of antimicrobial resistance) and antimicrobials prescribed (compounds, indications)
- describe key structures and processes for the prevention of HAIs and antimicrobial resistance at the hospital and ward level in EU hospitals

- disseminate results to those who need to know at local, regional and national levels

In England, the PPS began on the 5 September and will end on 30 November 2016. In preparation for the PPS we have trained more than 400 participants via a series of face to face and online training sessions, this included an online seminar to approximately 120 participants (live count online on the day).

Of the 138 participants who replied to the post-training survey, 76 of these participants attended the WebEx training. Forty two participants (35%) responded that the online training was more convenient, an equal number of participants (42/138, 35%) prefer face to face training. Of the respondents, 76% (85/111) would be happy to use web based training for future training with the point prevalence survey.

Data capture and submission will occur via a secure Web-based application. The system is modelled on the British Society for Antimicrobial Chemotherapy (BSAC) National Antimicrobial Stewardship PPS system. The system has undergone further development to capture all ward and patient data required for the national HCAI and AMU PPS. In addition to retrospective data entry, this system allows participants to collect and enter data directly onto the system in real-time.

The results of the PPS will be included in the 2017 ESPAUR report.

TARGET [Treat Antibiotics Responsibly, Guidance, Education, Tools] RCT: A modified McNulty-Zelen design randomised controlled trial to evaluate the effect of the TARGET Antibiotics Toolkit

McNulty CAM, Hawking MKD, Jones LF, Owens RJ, Francis N, Butler C, Moore P, Charlett A, Lecky DM

This study aims to determine whether a one hour TARGET GP practice workshop results in the provision of fewer antibiotic prescriptions, compared to controls with usual support from their CCG. Practices in 4 CCGs were stratified by area, ethnicity, antibiotics dispensed and list size, then randomly allocated to intervention or control. All intervention practices were invited to receive a TARGET workshop. Total oral antibacterial items /1000 patients, items of oral co-amoxiclav, cephalosporins, quinolones, trimethoprim plus nitrofurantoin /1000 patients were analysed for the years before and after the workshop. Results show that there were significant reductions in amoxicillin and ampicillin use after the workshops and a significant increase in nitrofurantoin use.

The GOTARGET Study: Qualitative evaluation of the TARGET Antibiotics Toolkit to improve antimicrobial stewardship in primary care

Jones LF, Hawking MKD, Owens RJ, Lecky DM, Francis N, Butler CC, Gal M, McNulty CAM

This study explores prescriber and stakeholder opinions of the TARGET Antibiotics resources. Semi-structured interviews were conducted with 38 study participants from across England and Scotland. Interviews explored local efforts to improve antibiotic prescribing, views on the TARGET materials, and suggested improvements to the Toolkit. Interviews were audio recorded, transcribed and thematically analysed. The majority of prescribers had positive views on the Toolkit, for example:

"I think they're very useful (The TARGET resources), it's a useful base and very clear information on the TARGET website… this feels that it's very well contained, and easy to follow. It's quite quick to go through, so it's not particularly time consuming but also with really good clear information." – GP M9

There were many suggestions for improvement to each of the resources including allocation of time at the end of the workshop for action planning, simplification of the patient leaflet for individuals with learning difficulties, integration of the leaflet on to GP systems where possible, and increasing exposure with wider promotion.

"It's just that I feel I've stumbled across something I would have liked to have had earlier." – GP M4 (On the TARGET Antibiotics Toolkit)

"…now, everything comes off the computer doesn't it? You're in the consultation and that's what you hit the button for, the patient doesn't need antibiotics and you explain why and out it comes, I would have thought that would be useful." – GP M11 (On integrating the Treating Your Infection leaflet onto GP systems)

Self-assessment of antimicrobial stewardship in primary care: analysis of self-reported practice using the TARGET Primary Care Self-Assessment Tool

Owens RJ, Jones LF, Moore M, Pilat D, McNulty CAM

This analysis explores responses to questions within the Primary Care Self-Assessment Tool, a precursor to the RCGP Antibiotics in Primary Care eModule. The tool enables prescribers to assess their antimicrobial stewardship, and provides a baseline for prescribers to assess their behaviour in comparison to others in their CCG and nationally, and to determine changes in their practice over time. The course participants enter data via an electronic Self-Assessment Tool and we analysed responses between November 2014 and June 2016. 1415 healthcare professionals completed the online tool. Preliminary results indicate that nearly all respondents used antibiotic guidance for the treatment of common infections. Half reported undertaking a

practice-wide antibiotic audit in the last two years and keeping a written record and practice action plan. Most GPs reported that they used back-up prescribing when appropriate. Results indicate that antibiotic guidance and back-up prescribing are used by most prescribers. However, to help optimise antimicrobial use GP staff need to also make guidance available to temporary prescribers, perform regular audits with action planning, and maximise patient focused strategies. Professional education and use of this tool should be encouraged locally to monitor AMS.

Self-assessment of antimicrobial stewardship in primary care: analysis of self-reported practice using the TARGET Primary Care Self-Assessment Tool (abstract presented at PHE conference 2016)

Owens RJ, Jones LF, Moore M, Pilat D, McNulty CAM

Introduction: The Primary Care Self-Assessment Tool, one of the resources within the TARGET Antibiotics Toolkit (www.rcgp.org.uk/targetantibiotics), enables prescribers to assess their antimicrobial stewardship. It provides a baseline for prescribers to assess their behaviour in comparison to others in their CCG and nationally, and to determine changes in their practice over time.

Method: Course participants of the RCGP eLearning module 'Antibiotic Resistance in Primary Care' enter data via an electronic Self-Assessment Tool. A report for each respondent compares their results with CCG and national averages. We analysed responses between November 2014 and December 2015.

Results: 1415 healthcare professionals completed the online tool. 98% of respondents used antibiotic guidance for the treatment of common infections, although only 63% reported that this was made available to all temporary prescribers. 54% reported undertaking a practice-wide antibiotic audit in the last two years and 57% kept a written record and practice action plan - 94% of GPs reported that they used back-up/delayed prescribing when appropriate. Sixty four per cent had a strategy in place to avoid patients re-consulting with other clinicians to obtain antibiotics. Seventy one per cent used patient focused strategies to highlight the importance of responsible antibiotic use. The majority of respondents, 71%, had undertaken an antibiotic related educational module.

Conclusion: Antibiotic guidance and delayed prescribing are used by most prescribers. However, to help optimise antimicrobial use GP staff need to also make guidance available to temporary prescribers, perform regular audits with action planning, and maximise patient focused strategies. Professional education and use of this tool should be encouraged locally to monitor AMS.

TARGET RCGP Spotlight Project 2015/16

Hayman J, Owens RJ, Jones LF, RCGP CIRC team, McNulty CAM

Aims: To increase uptake and awareness of the TARGET Antibiotics Toolkit through both a series of events and various communication platforms. To further update and develop various tools within the toolkit, with a focus on the group presentation, development of further audits and the Treating Your Infection Patient Leaflet.

Educational workshops: Five half-day educational events took place between January and March 2016, Birmingham, Liverpool, Luton and Newcastle-upon-Tyne, and attended by a total of 199 primary health care professionals. Workshop evaluations show that delegates found the workshops to be educational and relevant to clinical practice.

Communications plan: Together, the RCGP and PHE developed a joint communications plan which enabled the toolkit to be promoted to thousands of primary health care professionals across the UK through a range of platforms. For 2015-16, this included:

- five articles in the RCGP's newsletter 'Clinical News' which is sent monthly to 50,000 GPs. This includes:
    - May 2015: TARGET Hit or Miss?
    - October 2015: Resisting Patient Demand for Antibiotics
    - November 2015: Ten Top Tips for Talking to Patients about Antibiotic Prescribing
    - January 2016: A Spotlight on the TARGET training presentation
    - March 2016: Spotlight Projects: Tools for Success
- regular mentions in the RCGP's weekly 'Chair's Blog', which is sent to 50,000 GPs and Promotion through social media by both the RCGP and PHE
- support for European Antibiotics Awareness Week, including a TARGET banner on the RCGP home page (TARGET banner repeated throughout year)

Analysis of web use: Quarterly analysis of TARGET Antibiotics web use statistics indicates steady access to the online toolkit resources with peaks around World Antibiotic Awareness Week. Average monthly hits on the TARGET online resources were 5,634 per month in 2015 and were 6,084 for the first quarter in 2016.

e-Bug: Launch of new HTML5 website development and new games with incentives to visit other parts of the website

Young V, Scholes T, Leighton B, Cooper S, Hayes C, McNulty CAM.

The e-Bug student website was re-launched in May 2016 in HTML5 with refreshed content and new online games. The update now enables the website and content to be viewed on all mobile devices such as tablets and mobile phones. The 'Body Buster' and

‘Doctor Doctor’ games were updated with new content and levels, based on feedback received from students, educators and e-Bug partners. A new game, Stop the Spread, was also launched which teaches the importance of using a tissue to stop the spread of infection and the importance of vaccinations. Usage statistics for the e-Bug website was monitored before and after the launch of the HTML5 website. Although the number of visitors to the website stayed roughly the same in the 6 weeks prior to launch, compared to 6 weeks post launch (13,328 compared to 12,150), the number of pages views increased by 33% (81,370 to 108,326). The number of pages viewed per session also increased 45% (4.8 to 6.95) and the average visit duration increased from 3 mins 55 sec to 4 min 51 sec. These results suggest the new website and games are more engaging as visitors are staying on the website for longer and looking at more pages. An evaluation of the new and updated games will take place to assess their ability to increase knowledge and awareness of the topics covered.

The usage statistics for the e-Bug website were monitored by Google Analytics between September 2015 and July 2016. The statistics show the website had over 129,000 visits, from over 96,414 visitors. Visitors viewed an average of 5.97 pages per session, with an average session duration of 4 minutes 38 seconds. Visitors accessed the website from 216 different countries. The majority of visitors were from the UK and visited the English website, although countries such as Spain, France and Hungary were also frequent visitors. The most popular teacher resources on the website were the senior student ‘Sexually transmitted infections’ resources and the junior student ‘Introduction to microbes' resources. On the student websites, the most popular resources were the online games.

Game evaluation data (Abstract from the paper submitted to the Journal of Medical Internet Research)

Hale AR, Young VL, Grand A, McNulty CAM

Background: e-Bug is a pan-European educational resource for junior and senior school children that contains activities covering prudent antibiotic use and the spread, treatment, and prevention of infection. Teaching resources for children aged 7-15 years are complemented by a student website that hosts games and interactive activities for the children to continue their learning at home.

Objective: The aim of this study was to appraise young people’s opinions of three antibiotic games on the e-Bug student website by exploring children’s views and suggestions for improvements, and analysing change in awareness about the learning outcomes. The three games selected for evaluation all contained elements and learning outcomes relating to antibiotics, the correct use of antibiotics, and bacteria and viruses.

Methods: A mixed methodological approach was undertaken. 153 pupils aged 9-11 in primary schools and summer schools in the Bristol and Gloucestershire area completed a questionnaire with antibiotic and microbe awareness questions, before and after playing three e-Bug games for a total of 15 minutes each. The after questionnaire also contained open-ended and Likert scale questions. In addition, six focus groups with 48 students and think-aloud sessions with four students who had all played the games were performed.

Results: The questionnaire data showed a significant increase in awareness for 2 out of 7 questions, while all questions showed a small level of increase. The two areas of significant knowledge improvement focused around the use of antibiotics for bacterial versus viral infections, and ensuring the course of antibiotics is completed. Qualitative data showed that the e-Bug game 'Body Busters' was the most popular game, closely followed by ‘Doctor Doctor’, with 'Microbe Mania' being the least popular.

Conclusions: The conclusions of this study show that two of the e-Bug antibiotic educational games are valuable. The ‘Body Busters’ game effectively increased antibiotic awareness in children and had the greatest flow and enjoyment for children. The ‘Doctor Doctor’ game also resulted in increased knowledge, but was less enjoyable. The ‘Microbe Mania’ game had neither flow nor knowledge gain and therefore needs much modification and review. These games, especially the ‘Body Busters’ and ‘Doctor Doctor’ games should be promoted to schools and families. The results from the qualitative part of this study will be very important to inform future modifications and improvements to the e-Bug games.

Beat the Bugs community resources

Young VL, Tucker K, Parkinson G, Francis N and McNulty CAM, on behalf of the Beat The Bugs development group

Education of the public is a key driver in the fight against antibiotic resistance. Through education we can raise awareness, increase knowledge and modify intentions around antibiotic use and self-care.

e-Bug, led by PHE, educates children and young people on hygiene, the spread of infections and antibiotics. e-Bug is expanding into the community to groups outside schools, including hard to reach adults. In line with NICE guidance we aim to increase awareness around antibiotics and hygiene.

e-Bug have worked alongside the Kingfisher Treasure Seekers community group to develop Beat The Bugs: a 6-week hygiene course for different types of community settings. The course covers an Introduction to Microbes, Hand and Respiratory

Hygiene, Food hygiene, Oral hygiene, Antibiotics and a final session on self-care and action planning.

During a pilot course with adults with learning disabilities we collected feedback from participants and the course leader. The sessions were observed for fidelity by members of the e-Bug team.

The results from the pilot indicate the course was flexible and improved knowledge and awareness in vulnerable adults. Qualitative feedback identified that the number of visual components and interactive activities should be increased and reading decreased. Based on this feedback, updates and improvements will be made and the course will be rolled out to a range of community groups.

This e-Bug community course will be a very useful addition to the e-Bug resources, to help implement NICE guidance 2016 to improve the public's knowledge and behaviour around hygiene, self-care and antibiotic use.

ESBL prevalence study data in community

McNulty CAM, Lecky DM,Xu-McCrae L, Nakiboneka-Ssenabulya D, Chung K-T, Nichols T, Thomas HL, Thomas M, Alvarez-Buylla A, Turner K, Shabir S, Manzoor S, Smith S, Crocker L, Hawkey P.

Background: Extended-spectrum β-lactamase-producing Enterobacteriaceae (ESBLPE) and carbapenemase-producing Enterobacteriaceae (CPE) cause infections worldwide, but there are no large studies estimating prevalence or risk factors for colonisation with these bacteria within general populations.

Methods: We collected stool specimens and questionnaires from a stratified random sample of adults in selected general practices across England in 2014. We estimated the prevalence of colonisation with CTX-M ESBLPE and CPE, and investigated potential risk factors.

Findings: The estimated prevalence of CTX-M ESBLPE varied across study areas (Shropshire 4·9%, Southampton City 9·2%, Newham 12·7%, Heart of Birmingham 16%). Risk factors for colonisation with CTX-M ESBLPE included being born in India, Pakistan, Bangladesh or Sri Lanka (South Asia; aOR 5·4, 95% CI 3·0-9·7), Afghanistan (aOR 46, 95% CI 9·6-218) or the Middle East (aOR 4·7, 95% CI 1·3-17·0), and travel to South Asia in the last year (aOR 2·9, 95% CI 1·8-4·8) or: Africa, China, South or Central America, South East or Pacific Asia or Afghanistan (aOR 2·6, 95% CI 1·7-4·1). We estimate that being born in South Asia accounted for 24% of all those colonised.

The dominant ESBLPE was blaCTX-M-15 (134 of 204) 66%. Only 0.1% of participants (2/2430) were positive for CPE.

Interpretation: ESBLPE are established in the general population in England. We found the main risk factors for colonisation are travel to, or being born in, areas of the world with high prevalence of ESBLPE. These risk factors should be considered when choosing empirical antibiotic treatment for possible infections caused by Enterobactericaeae.

Funding: This paper is independent research commissioned and funded by the Department of Health Policy Research Programme (Ref. 041/0038S).

Inadequate culture provision for *Helicobacter pylori* revealed in an audit of microbiology laboratories across England, reveals a need for a strategy in this area if we want adequate surveillance of AMR for this very difficult to treat organism

Allison R, Lecky DM, Bull M, Turner K, Godbole G, McNulty CAM.

Background: Current guidance from the National Institute for Health and Clinical Excellence (NICE) recommends that clinicians test for *Helicobacter pylori* using a carbon-13 urea breath test or a stool antigen test, or laboratory-based serology where its performance has been locally validated. Recommended first-line treatment suggests a proton pump inhibitor (PPI) with dual antibiotic therapy.

Aim: To assess whether microbiology laboratories across England comply with NICE guidance and to determine the number of laboratories performing culture and antibiotic susceptibility testing, which will inform decisions on future national *H. pylori* antibiotic resistance surveillance strategies?

Method: In 2015, questionnaires were sent, by e-mail, to 170 Clinical Pathology Accreditation (CPA) labs in England. All non-responding labs were contacted and requested to complete the questionnaire by e-mail or telephone.

Results: Of the 121/170 (71%) labs that responded, 96% provide a *H. pylori* testing service: 78% perform on site and 13% refer elsewhere.
In line with NICE guidance: 95% of labs comply by testing with stool antigen or urea breath test for *H. pylori*. Five labs do not comply as they perform serology or biopsy urease tests first-line (4/5 encourage urea breath tests in their acute trusts).
Cultures and antibiotic susceptibility performed: 23% of labs perform *H. pylori* cultures on site; 46% refer biopsy specimens to another lab (39/43 (91%) refer to the Helicobacter Reference Unit (HRU)).

Of the 22 labs undertaking *H. pylori* cultures; two processed ten specimens/week; others ≤1specimen/week. Nine labs undertake antibiotic susceptibility on site; nine refer elsewhere (8/9 to the HRU).
Eight of nine labs that reported testing for antibiotic susceptibility in-house commented on the antibiotics tested: metronidazole-7/8 labs (88%); clarithromycin-6/8 labs (75%); amoxicillin-7/8 labs (88%); tetracycline-5/8 labs (63%); levofloxacin-2/8 labs (25%).
The results of this audit are promising as the majority of centres provide a non-invasive option as their first-line diagnostic test.

Conclusions: As very few laboratories are routinely performing culture of biopsy specimens to investigate antibiotic susceptibility, an English culture based surveillance system would probably need centralised culture. However, a stool specimen based surveillance system using PCR would be very possible.

The development of a "TARGET antibiotics" UTI leaflet to improve communication in GP consultation around the diagnosis and management of urinary symptoms and UTIs with patients. Increasing self-care and reducing antibiotic use, bacteraemia and recurrence

Lecky DM, Thomas J, Butler C, McNulty CAM

Objectives: UTIs are one of the most common bacterial infections seen in General Practice, accounting for many antibiotic prescriptions. A recent study stated 95% of women consulted a health professional, and 74% reported being prescribed an antibiotic, yet only 63% reported taking them. Unnecessary prescribing of antibiotics could be minimised by improving syndromic-based diagnosis and facilitating communication between the GP and patient in consultation. Enhanced communication may also improve self-care and reduce recurrence of *E. coli* bacteraemia.

Method: We undertook two focus groups and interviews with women who had experienced recent urinary symptoms as well as telephone interviews with GPs. We explored women's attitudes to and experiences of self-caring for their urinary symptoms and women's needs from a GP consultation. We also explored GPs perception of time spent in consultation with patients, exploring antibiotic resistance, information shared, guidelines used and common consultations. In addition we discussed the content of the "TAREGT antibiotics" leaflet to be shared with patients during consultation about possible urinary symptoms and UTIs and this was discussed with all participants.

Results: Women valued an explanatory leaflet that they could share in consultation and take home, giving advice on their diagnosis of their urinary symptoms, self-care and prevention measures. Women were unlikely to recall being given advice on self-care and information whilst in consultation. Women had little understanding of the different

types of UTIs and did not attribute antibiotic resistance to the overuse of antibiotics. Younger women had a higher expectation to be prescribed antibiotics for their urinary symptoms while older women relied more on commonly known self-caring measures such as: hydration and hygiene.

Conclusions: An explanatory leaflet would be a useful tool to encourage better patient diagnosis, the relationship between antibiotic use and resistance as well as self-care and prevention of urinary tract associated symptoms. Simple messaging could help patients re-evaluate the risk of antibiotics. GPs should be encouraged to explore their patient's knowledge, share information on self-care and prevention measures and antibiotic resistance when in consultation.

Management and treatment of common infections guidance

The management and treatment of common infections guidance provides recommendations regarding the diagnosis, management and treatment of a wide range of common infections seen in primary care. Recommendations are made on the best available evidence, and the guidance is reviewed every three years, or less, if there are significant developments in the field. This guidance covers a range of: upper respiratory tract infections, lower respiratory tract infections, urinary tract infections, meningitis, gastrointestinal tract infections, genital tract infections, skin and soft tissue infections, eye infections and dental infections.

Quick reference diagnostic guides

Due to the success of the antibiotic guidance, further quick reference diagnostic guides have been developed for other common infections, for use by GPs and laboratory microbiologists. There are currently nine diagnostic guides available, and these are also reviewed and updated every three years, or more often if there are significant developments in the field. The information provided focuses on the diagnosis of infection, and also provides information regarding recommended management strategies and antimicrobials for treatment. The quick reference diagnostic guides cover: abnormal vaginal discharge, *Chlamydia trachomatis*, fungal skin and nail infections, infectious diarrhoea, *Helicobacter pylori*, Methicillin-resistant *Staphylococcus aureus* (MRSA), Panton-Valentine Leukocidin *Staphylococcus aureus* (PVL-SA), urinary tract infections, and venous leg ulcers.

Guidance updates

The quick reference diagnostic guides and antibiotic guidance are currently undergoing review and update. Below is a list of when the guidance was last reviewed, and when it will next be due for review:

- Management and treatment of common infections: last full review 2012; currently under review
- Abnormal vaginal discharge: last review 2013; currently under review
- *Chlamydia trachomatis*: last review 2011; currently under review
- Fungal skin and nail infections: last review 2011; for review 2017
- Infectious diarrhoea: last review 2015; for review 2018
- *Helicobacter pylori*: last review 2016; for review 2019
- Methicillin-resistant *Staphylococcus aureus* (MRSA): last review 2009; for review 2017
- Panton-Valentine Leukocidin *Staphylococcus aureus* (PVL-SA): last review 2009; for review 2017
- Urinary tract infections: last review 2011; for review later 2016
- Venous leg ulcers: last review 2016; for review 2019

All of the guidance is available online at: https://www.gov.uk/government/collections/primary-care-guidance-diagnosing-and-managing-infections.

Current work

The Primary Care Unit, in conjunction with the Clinical Knowledge Summaries (CKS) and a microbiologist based in Southmead Hospital, are currently undergoing a full systematic review and literature search to update the management and treatment of common infections guidance. The first draft of this guidance, with review of recommendations, references, and rationales, is to be completed by mid-October 2016, to be sent to external stakeholders for review. The comments will be reviewed and any necessary changes will be made to the guidance, so that it is ready for upload to the PHE.gov website by March 2017, at the latest.

The *Helicobacter pylori* quick reference diagnostic guide is currently being reviewed for endorsement by the British Society for Antimicrobial Chemotherapy, the Royal College of Nursing, and the British Society of Gastroenterology. Any comments received will be reviewed for the guidance to be uploaded by the end of October 2016. Both the abnormal vaginal discharge and *Chlamydia trachomatis* quick reference diagnostic guides are being reviewed together, and teleconferences have been arranged with STI specialists in Public Health England and the Royal College of General Practitioners. Changes have been made to the guidance and search terms for a thorough literature search have been developed. The PCU is aiming for upload by January 2017, at the latest. The process of developing the guidance has also recently been presented as an oral presentation and poster presentation at the PHE annual conference.

Future work

The PCU is aiming to continue reviewing the quick reference diagnostic guides, in order of need. The next to be reviewed will be urinary tract infections, as there have been significant developments in the duration of antimicrobial treatment of UTI in adults. In

the future, the aim of the PCU is going to be on the quick reference diagnostic guides, so more of these will be developed, with the next one being discussed on acute sore throat. There is also discussion of writing two papers for publication: one on the amount of dyspepsia seen in GP practices across the South West, and the utilisation of the PHE *Helicobacter pylori* quick reference diagnostic guide, and one on the process of developing the guidance and the importance of this work.

Appendices

Appendix 1

Terms of Reference - English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Oversight Group (December 2013, Updated May 2015)

1.0 Issue

1.1 The English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR), was established in July 2013[109]. Its terms of reference have been updated in light of actions agreed by PHE to support English actions within the UK 5 year AMR strategy.

2.0 Membership

2.1 This oversight group will provide strategic oversight, development and input into the objectives of the ESPAUR.

2.2 Membership of the group will comprise a consortium of stakeholders from the NHS – primary, secondary and mental health trusts and also national and professional bodies. Membership will be subject to invitation and drawn from a range of fields, interested organisations and professional bodies who have expertise/interest in AMRS, epidemiology, data capture and analysis. Actual members will be nominated by the professional organisations/stakeholders and individuals may represent more than one body.

2.3 The following organisations will be represented on the oversight group

1. Public Health England (represented by individuals with appropriate expertise from within the National Infection Service and Health Protection Directorate including HCAI and AMR, AMR Delivery Programme Board, Behavioural insight, Public Health Strategy, Primary Care Unit and Statistics, Modelling and Economics Departments)
2. Department of Health (DH)
3. NHS England
4. DH Expert Advisory Committee on HCAI and Antimicrobial Resistance (ARHAI)
5. Health & Social Care Information Centre
6. IMS Health and Rx-Info Ltd (Define)
7. British Society for Antimicrobial Chemotherapy
8. UK Clinical Pharmacy Association: Infection Management Group
9. Care Quality Commission
10. NICE Medicines and Prescribing Centre
11. British National Formulary

[109] http://www.ncbi.nlm.nih.gov/pubmed/24027247

12. Pharmaceutical Advisers Group
13. Royal Pharmaceutical Society - Frontline Chief Pharmacist & community pharmacist
14. Royal Colleges of Nursing, Pathologists, Physicians, General Practitioners, Surgeons and Paediatrics and Child Health
15. Patient/lay representation
16. Independent/private sector healthcare - independenthealthcare.org.uk
17. NHS Improvement
18. Veterinary Medicines Directorate – DEFRA
19. Faculty of General Dental Practice

2.4 Representatives from surveillance programmes within the Devolved Administrations hold observer status on the ESPAUR oversight group with the aim of fostering strong links and shared learning.

2.5 Other individuals, organisations and groups may be invited as appropriate to individual meetings and sub-groups.

3.0 Aims and Objectives

3.1 The aims of the ESPAUR oversight group are to:

I. Develop and maintain robust data information and surveillance/monitoring systems for antimicrobial use, in order to measure the impact of surveillance systems and antimicrobial stewardship on antimicrobial resistance and patient/public safety.
II. Develop systems and processes to optimise antimicrobial prescribing across healthcare settings

3.2 The objectives of the ESPAUR will focus on delivering objectives within the UK Five-Year Antimicrobial Resistance Strategy.

3.3 With respect to surveillance, the oversight group will work with other PHE Teams to:

I. Participate in the integration and analysis of varying antimicrobial usage datasets across primary and secondary care;
II. Contribute to development of the real-time monitoring and measurement systems for antibiotic consumption in primary and secondary care with a view to supporting antimicrobial stewardship in the NHS and the independent sector;
III. Review the systems developed to ensure that the antimicrobial usage data can be linked with *C. difficile* rates and other bacterial resistance surveillance data; Enhance data analysis of carbapenems and other Critically Important Antibiotics in the NHS and the independent sector;
IV. Develop quality measures for optimal antimicrobial prescribing in primary and secondary care (APQMs) and implement systems to measure these;
V. Advise on the development and implementation of methods to monitor the clinical outcomes including any unintended consequences; for example increased prescribing of particular antibiotics;
VI. Work with other stakeholders, HPRUs and PHE behavioural insights/social marketing teams to measure the impact of approaches and initiatives to change public and professional behaviour around antimicrobial consumption, prescribing and management of antibiotic allergies.
VII. Work with stakeholders to promote a one-health approach to reporting antimicrobial consumption and resistance

3.4 With respect to antimicrobial stewardship (AMS), the oversight group will work with other PHE Teams to:

I. Contribute to the development of evidence-based interventions aimed at changing professional and public behaviours around prescribing and demand for antimicrobials to improve patient safety and outcomes related to antimicrobial prescribing;

II. Advise on the evaluation and embedding of tools and resources for optimising prescribing in the following settings:
- Primary care
- Secondary care
- Community (community hospitals, nursing homes and long term care facilities)
- Out of Hours & Urgent Care

III. Advise in Embed delayed/backup prescribing within primary care settings.

IV. Contribute to the guidance for providers on linking antibiotic formulary to local susceptibility data and improve feedback mechanism for decision support systems/tools (for example the British National Formulary);

V. Contribute to the development of an AMS surveillance system;

VI. Assist in the delivery of EAAD and the antibiotic guardian campaign and work with partners to evaluate these;

VII. Provide advice on the measurement of public awareness on AMR and attitude towards antimicrobial consumption;

VIII. Continue to work with HEE to embed national antimicrobial prescribing and stewardship competences and curricula development;

IX. Contribute to the review of antimicrobial resistance and stewardship training programmes;

X. Work with other stakeholders, HPRUs and PHE behavioural insights/social marketing teams to embed research outcomes into clinical practice across each setting.

3.5 Collaboratively the oversight group will:

I. Deliver the key components of the annual report from the ESPAUR.

II. Ensure that the outputs inform the national research agenda in this area

III. Evaluate and assess the impact of initiatives developed

4.0 Governance

4.1 The Chair of the PHE AMR Delivery Board will be the Executive Lead for the ESPAUR and ensure it meets DH requirements.

4.2 The work plan of the group will be agreed by the PHE HCAI & AMRS Programme Board and endorsed by the DH and ARHAI.

4.3 The Chair of the oversight group will be nominated by the Executive lead for the ESPAUR and will be responsible for ensuring the delivery of the specific objectives and work plan. The deputy chair will be the PHE pharmacist lead/ESPAUR project lead.

4.4 Task and finish subgroups for individual specialist areas will be developed, consisting of oversight group members and additional experts. The subgroups will report to the oversight group at set intervals on outputs

4.5 A risk and issues register will be updated quarterly

5.0 Meetings

5.1 The ESPAUR will meet at least three times per year with further sub-groups and teleconferences as required. It will require a quorum of at least 50% of members to attend. At the discretion of the Chair, meetings may be convened by teleconference (TCC). Remuneration for member expenses shall be claimed from members' own organisations.

5.2 In addition to the above topics, the ESPAUR will consider matters it deems appropriate to fulfil its responsibilities. The ESPAUR may invite assistance from independent experts and advisors to assist them on matters.

6.0 Reporting Structure/Outputs and communications

6.1 The ESPAUR will provide quarterly updates to the PHE AMR Delivery Board and yearly reports to the DH and NHS England. Once per year the Chair of the ESPAUR will attend ARHAI and report on the progress against the objectives.

Membership - English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Oversight Group (January 2016)

Dr Susan Hopkins; ESPAUR Chair; PHE Healthcare Epidemiologist; Royal College of Physicians
Dr Diane Ashiru-Oredope; ESPAUR deputy chair. PHE Pharmacist Lead, AMR Programme; PHE - AMRS & HCAI Pharmacist Lead
Mr Martin Astbury; RPS Community Pharmacy rep
Ms Maree Barnett; Department of Health
Dr Nicholas Brown; British Society for Antimicrobial Chemotherapy
Mr Brian Brown; Care Quality Commission
Ms Sue Carter; Pharmaceutical Advisors Group
Dr Tim Chadborn; PHE - Behavioural Insights
Dr Andre Charlett; PHE - Statistics; Modelling and Economics Dept
Mr Stephen Dobra; DH - Analytics
Ms Sue Faulding; Health and Social Care Information Centre
Ms Rose Gallagher; Royal College of Nursing
Dr Lourda Geoghegan; Public Health Agency Northern Ireland
Ms Lene Gurney; Independent Sector
Dr Kitty Healey; Veterinary Medicines Directorate
Dr Maggie Heginbothom; Public Health Wales
Ms Fran Husson; ESPAUR Lay member
Dr Dean Ironmonger; PHE - AMR and HCAI Dept
Prof Alan Johnson; PHE - HCAI and AMR Dept
Mr David Ladenheim; PHE - HCAI and AMR Dept
Dr Micheal Lockheart; Health Protection Scotland
Dr Cliodna McNulty; PHE - Primary Care Unit
Dr Micheal Moore; Royal Society of Genral Practitioners
Dr Berit Muller-Pebody; PHE - AMR and HCAI Dept
Dr Isabel Oliver; PHE - Field Epi Services
Dr Nick Palmer; FDGP
Dr Bharat Patel; PHE - Public Health Microbiology regions
Dr Richard Puleston; PHE - Field Epi Services
Mr Colin Richman; RX Info
Dr Keith Ridge; NHS England
Dr Julie Robotham; PHE - Economic Modelling
Mr Richard Seal; NHS Trust Development Authority
Prof Mike Sharland; ARHAI
Mr Pete Stephens; IMS Health
Ms Kate Towers; British National Formulary
Ms Tracy Parker; Department of Health
Mr Jonathan Underhill; National Institute of health and Care Excellence
Prof John Watson; Department of Health - Deputy Chief Medical Officer

Mr Tony West; Royal Pharmaceutical Society
Ms Laura Whitney; UK Clinical Pharmacy Association
Dr Sandra White; PHE - Health and Wellbeing (Dental)
Dr Neil Woodford; PHE - AMRHAI
Prof Tony Young; Royal College of Surgeons

Appendix 2

Terms of Reference – Dental Subgroup - English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) (November 2015, Updated October 2016)

1.0 BACKGROUND

1.1 Dental prescribing currently contributes just under 10% of antibiotic prescriptions issued in the primary care setting in England. Some 3.7 million antibiotic prescriptions were dispensed by pharmacists from NHS dental prescription forms (FP10D) in England during 2014. Currently prescribing data at a practice level is not routinely available and there are no systems in place to collate at an individual practitioner level

1.2 The ESPAUR oversight group has determined that a subgroup was required to focus on expanding surveillance of antibiotic consumption in the dental sector.

2.0 PROPOSED TERMS OF REFERENCE

2.1 The ESPAUR dental subgroup will develop a collaborative action plan describing roles, responsibilities and time frames which will;

2.2 Improve data granularity of dental prescribing by:

- Exploring antibiotic consumption data sets currently available across the dental sector
- Identifying current gaps in antibiotic consumption data available and options for closing the gaps
- Identify data sharing agreements that may be required
- Produce a report to define a dental surveillance output and frequency.

2.2 Improve prescribing within dental practice through:

- Review of antibiotic dental prescribing guidance from across the UK
- Sharing best practice of interventions where there has been improvements in dental prescribing
- Share learning from behaviour change insight work undertaken with other health professionals
- Development of a ‘toolkit’ of ways to improve dental prescribing in England based on NICE guidance

2.3 Promote initiatives to improve patient awareness regarding utilisation of antibiotics for dental infections

2.4 The subgroup structure:

2.4.1 Primary Care:
2.4.1.1 Prescribing data and Analysis
2.4.1.2 Stewardship Toolkit

2.4.2 Secondary Care:
2.4.2.1 Statement about the prescribing data
2.4.2.2 Prescribing audit - in progress

2.4.2.3 Resistance data
2.4.3 Professional E&T underpins everything but will be a separate working group/stream
2.4.3.1 Script (primary care and secondary care)
2.4.3.2 Webinars/podcasts

2.4.4 Multi-system AMR collaboration also underpins everything but will be a separate working group/stream

3.0 MEMBERSHIP

- Sandra White; PHE (Chair)
- Nikolaus Palmer; Faculty of General Dental Practice
- Susie Sanderson; British Dental Association
- Diane Ashiru-Oredope; PHE
- Susan Hopkins; PHE
- Elizabeth Beech; NHS England/Devon CCG
- Sejal Hansraj; PHE
- Rachel Freeman; PHE
- Yvonne Dailey; PHE Regional/British Association for Study & Community Dentistry
- Graham Mitchell; NHS Business Services Authority
- Noha Seoudi; Association of Clinical Oral Microbiologists (ACOM)
- Janet Clarke; NHS England
- Tara Renton; Faculty of Dental Surgery
- Martin Woodrow; British Dental Association
- Henry Clover; private dental sector (Denplan)
- Catherine Rutland; private dental sector (Denplan)
- Charles Alessi; PHE Special Advisor
- Adam Roberts; Dental Schools Council
- Nicholas Taylor; Health Education England
- Karen Elley; Health Education England
- Finton Grant; Health and Social Care Information Centre
- Gill Davies; PHE
- Wendy Thompson, GDP/Researcher

4.0 ROLES AND RESPONSIILITIES OF THE MEMBERS

- Members are charged with determining the views of the stakeholders they represent and relaying these thoughts during discussions.
- Members need to carry authority from their individual organisations or have described mechanisms, for outcomes to be delivered within their individual governance systems
- All members should nominate a suitable deputy if they cannot attend a meeting. The chairman will ensure that each member has the opportunity to contribute to the discussion
- Secretariat support will come from the ESPAUR team
- Members will ensure that should they leave their current role, a replacement to represent their organisation, will be offered to the group.

5.0 ORGANISATION OF THE SUBGROUP

- The subgroup will meet on a quarterly or as appropriate basis.
- The chair of the steering group will agree the agenda with members input.
- The agenda and papers will be distributed to members and those in attendance not less than three working days in advance of the meeting.

6.0 CHAIR AND VICE CHAIR

6.1 PHE working groups must be chaired by representatives of PHE. The Chair of the working group will be the PHE national lead for Dental Public Health. The vice-Chair will elected from the group.

7.0 ACCOUNTABILITY

- The subgroup will be accountable to the ESPAUR oversight group
- All members will complete a declaration of interest form.

8.0 REVIEW OF TERMS OF REFERENCE

8.1 The arrangements set out in these Terms of Reference will be reviewed after 1 year.

Appendix 3

Terms of Reference – English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Oversight Group - Antifungal Subgroup (January 2016)

1.0 BACKGROUND

1.1 A presentation of antifungal consumption and resistance was given to ESPAUR in February 2015. The oversight group determined that a subgroup was required to focus on expanding surveillance of these pathogens.

2.0 TERMS OF REFERENCE

2.1 The remit of the antifungal surveillance subgroup will be:

I. Explore the current state of diagnostics for fungal infections through a survey of laboratories

II. Explore antifungal resistance data sets currently available

III. Explore antifungal consumption data sets currently available across primary and secondary care

IV. Identify current gaps in antifungal consumption data available

V. Identify data sharing agreements that are required

VI. Produce a report to define a fungal surveillance output and frequency

3.0 MEMBERSHIP

3.1 ESPAUR oversight group members will work with UK Clinical Mycological Network (UK CMN) Core Project Team

- Berit Muller-Pebody (Chair PHE)
- Diane Ashiru-Oredope (Pharmacist Lead, AMR Programme PHE)
- Rebecca Guy (Senior Scientist, HCAI&AMR Dept. PHE)
- Elizabeth Johnson (Director, PHE Mycology Reference Laboratory)
- David Denning (Professor of Infectious Diseases in Global Health University, Hospital of South Manchester)
- David A Enoch (National Infection Service, Public Health England Microbiology Laboratory, Addenbrooke`s Hospital)
- Christianne Micallef (Pharmacy Department, Addenbrooke`s Hospital Cambridge, University Hospitals NHS Foundation Trust)
- Samir Agrawal (Senior Lecturer and Honorary Consultant, Barts Health NHS Trust)
- Rohini Manuel (Consultant Medical Microbiologist, Public Health Laboratory London)
- Silke Schelenz (Consultant in Microbiology and Infection Control, Royal Brompton Hospital, Chair UK Clinical Mycology Network)
- Peter Stephens (Quintiles IMS, formerly IMS Health)
- Rakhee Patel (Lead Antimicrobial Pharmacist, Darent Valley Hospital, Dartford & Gravesham NHS Trust)
- Emma Budd (Scientist,HCAI&AMR Dept.PHE)
- James Vaudrey (Higher Executive Officer, AMR Programme, PHE)
- Susan Hopkins (Chair of ESPAUR, AMR Programme, PHE)

Appendix 4; European antibiotic awareness day (EAAD) planning groups and membership lists

WAAW/EAAD/AG Core planning group members		
First name	Surname	Organisation
Diane	Ashiru-Oredope	Public Health England: AMR Programme Chair
Aliya	Rajah	Public Health England: AMR Programme Secretariat
Matthew	Abbott	4 all of us
Georgie	Agass	Department of Health: Communications
Elizabeth	Beech	NHS: Prescribing Advisor, Bath and East Somerset Clinical Commissioning Groups
Nick	Brown	British Society for Antimicrobial Chemotherapy/NHS
Scott	Buckler	4 all of us
Tim	Chadborn	Public Health England: Behavioural Insights
Rob	Daracott	Proprietary Association of Great Britain & Self-Care Forum
Matthew	Dolan	Northern Ireland
Steve	Eldridge	Veterinary Medicines Directorate
Carole	Fry	Public Health England: AMR Programme
Brendan	Healy	British Society Antimicrobial Chemotherapy/NHS
Margaret	Heginbothom	Wales
Paula	Higginson	Centre for Pharmacy Postgraduate Education
Cliodna	McNulty	Public Health England: Head of Primary Care Unit
Michael	Moore	Royal College of General Practitioners
Jill	Moss	Bella Moss Foundation
Susan	Paton	Scottish Antimicrobial Prescribing Group
Rhian	Pound-McCarthy	Wales

Lauren	Rellis	Public Health England: Social Media
Jacqueline	Sneddon	Scotland
Sam	Spindlow	Public Health England: Social Media
Jenny	Thorne	Wales: Head, Healthcare Associated Infections & Blood Safety Branch
Victoria	Wells	British Society Antimicrobial Chemotherapy: Science Communicator
Sally	Wellsteed	Department of Health
Libby	Whittaker	Proprietary Association of Great Britain & Self-Care Forum
Camilla	Wiuff	Scotland
Laura	Woodward	Public Health England: Communications

WAAW/EAAD/AG Pharmacy planning group		
First name	Surname	Organisation
Diane	Ashiru-Oredope	Public Health England: AMR Programme
Aliya	Rajah	Public Health England: AMR Programme
Matthew	Abbott	4 All of Us
Elizabeth	Beech	NHS Bath and Somerset Clinical Commissioning Group
Jessica	Bland	British Pharmaceutical Students' Association
Saran	Braybrook	Herefordshire Clinical Commissioning Group
Scott	Buckler	4 All of Us
Beenish	Chaudhry	British Pharmaceutical Students' Association
Harpal	Dhillon	RPS Antimicrobial Resistance Expert Advisory Group
Tess	Fenn	Association of Pharmacy Technicians UK
Chris	Ford	Pharmacy Voice
Alison	Hemsworth	NHS England
Paula	Higginson	Centre for Pharmacy Postgraduate Education
Nigel	Hughes	Community Pharmacy West Yorkshire

Osenadia	Joseph-Ebare	Kings College London
Viola	Lewis	Royal Pharmaceutical Society
Melinda	Mabbutt	Pharmaceutical Services Negotiating Committee
Amit	Parekh	British Pharmaceutical Students' Association
Neal	Patel	Royal Pharmaceutical Society
Lauren	Rellis	Public Health England; Social media
Gul	Root	Public Health England: Lead Pharmacist, Health and Wellbeing Directorate
Rosie	Taylor	Pharmacy Services Negotiating Committee
Tracey	Thornley	RPS AMR Expert Advisory Group
Robbie	Turner	Community Pharmacy West Yorkshire

Junior and Family Antibiotic Guardian planning group		
First name	Surname	Organisation
Diane	Ashiru-Oredope	Public Health England: AMR Programme
Aliya	Rajah	Public Health England: AMR Programme
Wendy	Nicholson	Public Health England: PHE National Lead Nurse children & young people
Sharon	Ashley	Makewaves
Georgia	Flynn	Radiowaves
Lauren	Rellis	Public Health England; Social Media
Matt	Rogers	Digital Me
Vicki	Young	Public Health England: E-bug Project Manager

Antibiotic Guardian health students planning group		
Name	Course	University
Aditya Aggarwal	Dentistry student 4th year	Liverpool John Moores University
Alex Perry	Pharmacy student 4th year	UCL School of Pharmacy
Carla Bodagh	Pharmacy student 4th year	Kings College, London
Holly Hill	Veterinary Medical student 5th year	University of Nottingham
Jessica Bland	Pharmacy student 3rd year	UCL School of Pharmacy
Kingsley Appiah	Medical student 3rd year	Kings College London
Lara-Turiya Seitz (graduated)	Newly qualified Pharmacist,	The Queen Elizabeth Hospital King's Lynn
Osenadia Joseph-Ebare	Pharmacy student; 3rd year	Kings College London
Sana Sheykhzadeh	Pharmacy student 2nd year	UCL School of Pharmacy
Teslimat Ajeigbe	Dentistry 4th year	Liverpool John Moores University
Tracy Ndungu	Pharmacy student 3rd year	Kings College London
Ashleigh Smith	Adult Nursing 2nd year	Kings College London
Beenish Chaudhry	Pre-registration Pharmacist	University of Leicester School of Pharmacy
Gabriella Raimo	Adult Nursing 2nd year	Kings College London
Faith Matungamidze	Pharmacy student 3rd year	Liverpool John Moores University
Rachel Lee	Medical student 2nd year	Rachel Lee
Suky Singh	Pharmacy student 2nd year	University of Nottingham

Glossary

Antimicrobial
An antimicrobial is a drug which is capable of reducing the growth of, or destroying, micro-organisms, including pathogens.

Antifungal stewardship (AFS)
AFS is set of antimicrobial stewardship actions which relate specifically to antimicrobial drugs which treat fungal infections.

Antimicrobial resistance (AMR)
AMR is resistance of a microorganism to an antimicrobial drug which was previously effective against it. This may affect treatment of this microorganism and the infections caused by it.

Antimicrobial stewardship (AMS)
AMS is a coordinated program of actions which aim to reduce the unnecessary use of antimicrobials. Good AMS includes selecting appropriate drugs which work effectively against micro-organisms, and optimising the dose and duration of a treatment to cure an infection, whilst minimising toxicity and conditions for selecting resistant bacterial strains.

All party parliamentary groups (APPG)
An APPG is a cross-party group, run by and for members of the houses of Commons and Lords. This may include individuals and organisations from outside of Parliament

Anatomical therapeutic chemical (ATC)
The ATC classification system and the Defined Daily Dose (DDD) as a measuring unit are recommended by the WHO for drug utilization studies.

Clinical commissioning groups (CCGs)
CCGs were created following the Health and Social Care act in 2012. They are clinically led statutory NHS bodies which plan and commission healthcare services in their area. They replaced Primary Care Trusts.

Confidence interval (CI)
A CI is a range of values defined so that the true value of a population parameter fits within it, given an assigned probability (normally 95% or 99%).

Carbapenemases
Carbapenemases are a set of enzymes which commonly break down carbapenems and β-lactam antibiotics. This includes a broad range of antibiotics including penicillins.

C-reactive protein
C-reactive protein is a ring shaped protein produced in the liver and found in the bloodstream. This protein can become elevated after infection, injury or inflammation.

Defined daily dose (DDD)
The DDD is the assumed average maintenance dose per day for a drug used for its main indication in adults. It is defined by the WHO Collaborating Centre for Drug Statistics Methodology.

Drug susceptibility test
Drug susceptibility testing is a set of methods for determining the level to which microorganisms are resistant or sensitive to a particular antibiotic.

Enterobacteriaceae
Enterobacteriaceae is a large family of gram negative bacteria commonly found in the intestines, soil, water and on plants. This family includes both non-pathogenic and pathogenic species. (Including *E. coli*)

Escherichia coli
E. coli is a species of rod-shaped bacteria which is able to live in the digestive tract of humans. Most strains are not harmful; however, some are able to cause infections which can cause symptoms including diarrhoea, stomach cramps and fever.

Gram negative bacteria
Defined by ‘Gram’ staining of their cell wall, Gram negative bacteria are a large group of bacteria including *Klebsiella, Acinetobacter, Pseudomonas aeruginosa*, and *E. coli.*

Healthcare-associated infections (HCAI)
HCAIs (or HAIs) are any infection acquired curing the course of receiving treatment in a healthcare setting.

Infection prevention and control (IPC)
IPC is a healthcare discipline concerned with the practice and policy of reducing the rate of infection, normally within healthcare settings. This practice includes hygiene methods, decontamination and personal protective equipment.

Klebsiella pneumoniae
A species of rod-shaped bacteria which is able to live in the digestive tract of humans, it can be found as part of the normal flora of the mouth, skin, and intestines. This species is associated with infections of those with a weakened immune system, and can cause pneumonia.

Multi-drug resistant (MDR)
MDR organisms are resistant to a variety of antibiotics, normally this includes resistance to at least one drug in three or more antibiotic categories.

Minimum inhibitory concentration
The lowest concentration (amount in solution) of an antimicrobial drug required to prevent the growth of a specified pathogen/micro-organism.

Mycobacterial interspersed repetitive units (MIRUs)
MIRUs are short, repeated, genetic sequences found in multiple places within the genome of *Mycobacterium tuberculosis.* They are used to identify the strain of the microorganism.

Meticillin resistant / susceptible *Staphylococcus aureus* (MRSA/ MSSA)
MRSA / MSSA are both coccal shaped bacterium of the same species. They are commonly found in the nose, skin and respiratory tract. They can cause skin and invasive infections. MRSA is commonly resistant to a variety of common antibiotics.

non-albicans *Candida*
non-albicans *Candida* is a family of fungal *Candida* species outside of the *Candida albicans* species which is commonly associated with thrush (candidiasis). Non-albicans species are associated with increased resistance to antifungal drugs.

New Delhi metallo-beta-lactamase (NDM) 1
NDM-1 is an enzyme (protein) which causes resistance to a variety of antimicrobials by breaking them down, (especially β-lactams). This is coded on the NDM-1 gene.

Pan drug resistant
Pan drug resistant organisms are resistant to all antibiotic drugs, in all antibiotic categories.

Point prevalence survey (PPS)
A PPS is a study of the number of people in a population with a disease over a predetermined time period. This is divided by the number of people in the overall population.

Quality premium (QP)
The QP scheme is about rewarding clinical commissioning groups (CCGs) for improvements in the quality of the services they commission.

Quality surveillance groups (QSG)
QSG bring together different parts of health and care economies locally to routinely share information and intelligence to safeguard the quality of care patients receive.

Randomised controlled trial (RCT)
An RCT is a study design which assigns participants to two groups randomly (a control group and an experimental group). This allows researchers to compare the two and limit outcomes which are not part of the trial.

Respiratory tract infections (RTI)
RTIs are any infectious disease of the upper or lower respiratory tract. Upper includes the nose, sinuses and throat; lower includes the airways and lungs.

Sustainability and transformation plans (STPs)
STPs show how local health services will evolve and become sustainable over the next five years as part of the Five Year Forward View.

Tuberculosis (TB)
TB is a disease caused by *Mycobacterium tuberculosis* which is a species of rod-shaped gram positive bacteria. This can cause latent or active infections which affect the lungs.

Urinary tract infection (UTI)
UTIs are any infectious disease of the urinary system. This includes the kidneys, ureters, bladder and urethra. Most are associated with the bladder and urethra.

Variable number tandem repeats (VNTR)
VNTRs are a short sequence of repeating genes which exist within a genome. They are found in the genomes of many differing species and can be used to identify individuals or species.

Extensively drug resistant (XDR)
XDR organisms are resistant to a very wide variety of antibiotic drugs. Usually this includes resistance to at least one antibiotic in all but two or fewer antibiotic categories. (ie. one or two categories are still effective)

Abbreviations

AFS	Antifungal stewardship
AG	Antibiotic guardian
AIHO	Association of independent healthcare organisations
AMP	Antimicrobial prescribing
AMPS	The antimicrobial prescribing and stewardship
AMR	Antimicrobial resistance
AMRHAI	Antimicrobial resistance and healthcare associated infection reference unit
AMS	Antimicrobial stewardship
AMU	Antimicrobial use
AP	Antibiotic prescribing
APPG	All party parliamentary group
ARHAI	Antimicrobial resistance and healthcare-associated infections
ATC	Anatomical therapeutic chemical
BASH	British association for sexual health
BDA	British dental association
BIA	British infection association
BNF	British national formulary
BSAC	British society for antimicrobial chemotherapy
BSMM	British society for medical mycology
CCGs	Clinical commissioning groups
CHS	Community health services
CHT	Community health trusts
CI	Confidence interval
CLSI	Clinical standards laboratory institute
CMO	Chief medical officer
CPA	UK Clinical Pharmacy Association
CPA	Clinical pharmacy association
CPE	Carbapenemase-producing enterobacteriaceae
CPO	Carbapenemase-producing organisms
CQUIN	Commissioning for quality and innovation
CRP	C-reactive protein
CSU	Commissioning support units
DDD	Defined daily dose
DH	Department of health
DST	Drug susceptibility test
E. coli	*Escherichia coli*
EAAD	European antibiotic awareness day
ERS	Enhanced reporting system
ESPAUR	English surveillance programme for antimicrobial utilisation and resistance
ETS	Enhanced tuberculosis surveillance
EUCAST	European committee on antimicrobial susceptibility testing
FDPH	Faculty of dental public health
FES	Field epidemiology service
FGDP	Faculty of general dental practice
FIS	Federation of infection societies
GNB	Gram negative bacteria
GP	General practice
GRASP	Gonococcal resistance to antimicrobials surveillance programme
HCAIs	Healthcare-associated infections
HEE	Health education England
IPC	Infection, prevention and control
K. pneumoniae	*Klebsiella pneumoniae*
KPC	*Klebsiella pneumoniae* carbapenemase
MDR/RR	Multi-drug resistant/rifampicin resistant
MDR-TB	Multi-drug resistant TB
MIC	Minimum inhibitory concentration
MIRU	Mycobacterial interspersed repetitive units
MRSA	Meticillin resistant staphylococcus aureus
MSM	Men who have sex with men (demographic)

MSSA	Meticillin susceptible *staphylococcus aureus*
NAC	non-albicans *Candida*
NDM	New Delhi metallo-beta-lactamase 1
NHSBSA	NHS business services authority
NICE	National institute of health and care excellence
OPAT	Outpatient parenteral antimicrobial therapy
PHE	Public health England
PHE FES	PHE field epidemiology
PIN	Pharmacy infection network
PPS	Point prevalence survey
QP	Quality premium
QSG	Quality surveillance groups
RCGP	Royal college of general practitioners
RCP	Royal college of physicians
RCT	Randomised controlled trial
RIDD	Route, indication, dose, duration.
RTI	Respiratory tract infections
SGSS	Second generation surveillance system
SMI	Standards for microbiological investigations
SSTF	Start smart then focus
STAR-PU	Specific therapeutic group age-sex related prescribing units
STBRU	Sexually transmitted bacteria reference unit
STP	Sustainability and transformation plans,
TARGET	Treat antibiotics responsibly, guidance, education, tools
TB	Tuberculosis
TDM	Therapeutic drug monitoring
UTI	Urinary tract infection
VNTR	Variable number tandem repeats
WAAW	World antibiotic awareness week
XDR	Extensively drug-resistant (XDR)

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Chapter 7;
Authors on each Abstract

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