Public Health England

Protecting and improving the nation's health

English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) 2010 to 2014

Report 2015

About Public Health England

Public Health England exists to protect and improve the nation's health and wellbeing, and reduce health inequalities. It does this through world-class science, knowledge and intelligence, advocacy, partnerships and the delivery of specialist public health services. PHE is an operationally autonomous executive agency of the Department of Health.

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Key facts

- The data in this report covers the calendar years 2010−2014; new data is for the calendar year 2014.
- 95% of NHS hospital microbiology laboratories in England are now submitting data to PHE on the results of antimicrobial susceptibility testing results.

Prescribing

- Total antibiotic consumption (measured as defined daily dose (DDD) of antibiotics per 1000 inhabitants per day) in England has increased by 6.5% from 21.6 DDD per 1000 inhabitants per day in 2011 to 23 DDD per 1000 inhabitants per day in 2014; between 2013 and 2014 total consumption increased by 2.4%.
- Antibiotic prescriptions in primary care, measured as the number of prescriptions dispensed, adjusted for the age and sex distributions in the population, has declined for the last two years and is now lower than the similar measure in 2011 (1.180 items per STAR-PU in 2014 compared to 1.233 items per STAR-PU in 2011).
- Antibiotic use measured in primary care increased when measured by DDD and decreased when measured by prescription, suggesting that longer courses or higher doses are being used.
- Prescribing to hospital inpatients increased significantly by 11.7% and to hospital outpatients by 8.5% between 2011 and 2014.
- Broad spectrum antibiotic use (antibiotics that are effective against a wide range of bacteria) has decreased in primary care to 8.5% and we are the lowest users of cephalosporins and quinolones in the European Union. These antibiotics are more likely to drive antibiotic resistance than narrow spectrum antibiotics.

Resistance

- Between 2010 and 2014 the rate of bloodstream infections caused by *E. coli* and *K. pneumoniae* has increased by 15.6% and 20.8% respectively.
- The number of antibiotic resistant *E. coli* bloodstream infections has increased overall between 2010 and 2014.
- There has been a 23% reduction in *S. pneumoniae* bloodstream infections between 2010 and 2014; this may be related to increased pneumococcal vaccination rates.

Antimicrobial stewardship

- In 2014, 60% of clinical commissioning groups (CCGs) and 87% of NHS acute trusts had reviewed the national antimicrobial stewardship toolkits for primary or secondary care; however, only 13% of CCGs and 46% of acute trusts had implemented an action plan to deliver antimicrobial stewardship activities.

Public and professional engagement

- In 2014, PHE developed and led the UK-wide Antibiotic Guardian campaign to move from raising awareness to stimulating behaviour change in members of the public and healthcare professionals; within the first three months over 10,000 individuals made a pledge towards the prudent use or prescription of antimicrobials on www.AntibioticGuardian.com

Key Messages

1. Overall, antibiotic resistant infections continue to increase. The rate of *Escherichia coli* and *Klebsiella pneumoniae* bloodstream infections increased by 13.5% and 17.2% respectively from 2010 to 2014. While the proportion resistant to key antibiotics used to treat infections has remained constant in *E. coli*, the increased incidence of bloodstream infections means that more individuals have had a significant antibiotic resistant infection. In addition the increases in both the number of *K. pneumonia*e bloodstream infections and the proportion of these infections that were drug resistant means that the number of individuals with antibiotic resistant infections has increased substantially in the last five years.

   However, for other bacteria where there have been targeted interventions to reduce the burden of infection or resistance, we are seeing an impact with declining infection rates or proportion of infections where resistance is detected. For example, the 23% reduction in *Streptococcus pneumoniae* bloodstream infections related to pneumococcal vaccination and the reduction, through effective infection prevention and control within healthcare settings, of *Staphylococcus aureus* bloodstream infections that are resistant to meticillin (MRSA) from 12% to 8% over the last 5 years.

2. Total antibiotic prescribing, measured using defined daily doses, a standardised measure of antibiotic consumption, continues to increase in the NHS, except general dental practice, though with a slower rate of increase from 2013 to 2014 than in previous years. However, antibiotic prescriptions in primary care, measured as the number of prescriptions dispensed, adjusted for the age and sex distributions in the population, has declined for the last two years and is now lower than the similar measure in 2011 (1.180 in 2014 compared to 1.233 in 2011), suggesting higher doses or longer course lengths in general practice prescriptions.

   The majority of antibiotic prescribing occurs in primary care but secondary care prescribes more broad-spectrum antibiotics (antibiotics that are effective against a wide range of bacteria). These antibiotics are more likely to drive antibiotic resistance than narrow spectrum antibiotics. Early evidence suggests that informing prescribers of their prescribing patterns and comparing them to those of their peer professionals may be a factor that helps reduce their antibiotic prescribing. Continued focus by every individual who prescribes, administers and dispenses antibiotics is essential to continue to reduce antibiotic consumption.

3. Antimicrobial stewardship refers to a number of interventions designed to optimise prescribing. These include education, persuading prescribers to prescribe antibiotics appropriately, restricting the prescribing of key antibiotics, and measurement and feedback of antibiotic use. An assessment of antimicrobial stewardship activities in General Practice and Hospitals, showed that acute NHS trusts (hospitals) were more likely to have systems and processes in place than clinical commissioning groups (groups of General Practices that work together to plan and design local health services in England).

   There needs to be increased cross-organisational learning and collaboration regarding the implementation of antimicrobial stewardship activities. Education and training about antibiotic resistance, the effective use of antibiotics and the role of the clinical teams in antimicrobial stewardship needs to be embedded into undergraduate and postgraduate curricula of all healthcare professionals.

4. Antibiotic Guardian, a professional and public pledge-based campaign which aims to increase knowledge of the association between antibiotic prescribing and resistance and to change behaviour accordingly, reached more than 12,000 individuals who had actively engaged and chosen a pledge, in its first six months. These were predominantly healthcare professionals. Further action by the public and healthcare professionals is needed to raise awareness about antibiotic resistance. Everyone can pledge to become an Antibiotic Guardian at www.AntibioticGuardian.com.

   Future public engagement work is essential to educate people as to when and why antibiotics are needed. This should include helping patients to understand the duration of illness for common viral infections (such as colds and flus) that do not require antibiotics and, most importantly, highlighting alternative remedies that can improve their symptoms when they have viral infections that will not improve with antibiotics.

Executive summary

Introduction

The UK published a cross-government five-year antimicrobial resistance (AMR) strategy (encompassing antibiotics) in 2013.[1,2] The overarching goal of the strategy is to slow the development and spread of antibiotic resistance.

Public Health England (PHE) leads on four activities to deliver the AMR strategy, focusing on surveillance, infection prevention and control, antibiotic prescribing practices, and professional and public education and engagement. The English Surveillance Programme on Antimicrobial Use and Resistance, ESPAUR, was established by PHE in 2013 in response to the strategic plan for controlling AMR in the UK published by the Government.

This, the second report from the programme, details trends in antibiotic prescribing/consumption and resistance from 2010 to 2014; highlights the progress in antimicrobial stewardship (AMS) activities in primary and secondary care; and outlines professional and public facing activities that were undertaken in relation to antibiotic education and awareness.

Since the launch of the AMR strategy we have:

- established and improved surveillance data on antibiotic prescribing and AMR
- worked with NHS-England to develop and measure prescribing and improve data collection through the development of an Antimicrobial Prescribing Quality Premium
- performed an assessment of AMS activities and implementation of national AMS toolkits in primary and secondary care
- launched and evaluated an ‘Antibiotic Guardian’ campaign to drive changes in public and professional behaviour around antibiotic use
- developed implementation options for the improved education and training of healthcare professionals
- collaborated with veterinary colleagues and public health organisations in the devolved administrations to publish an integrated UK-wide human and animal ‘One Health’ report on antibiotic use and resistance
- worked with university partners to answer key research questions

[1] Department of Health and Defra. UK five year AMR strategy 2013-2018. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_strategy.pdf

[2] Ashiru-Oredope D, Hopkins S; English Surveillance Programme for Antimicrobial Utilization and Resistance Oversight Group. AMS: English Surveillance Programme for Antimicrobial Utilization and Resistance (ESPAUR). J Antimicrob Chemother. 2013 Nov;68(11):2421-3.

Improvements in surveillance

In the last two years, we have continued to improve antibiotic resistance surveillance by ensuring dedicated resources and improved information technology to enable NHS microbiology laboratories to report all antibiotic testing results to PHE. PHE launched a new web-enabled surveillance system in December 2014 that provides a comprehensive range of modern analytical tools to enable health professionals to securely view laboratory data and produce reports using a simple web interface. Ninety-five percent of NHS hospital microbiology laboratories currently submit routinely generated antimicrobial susceptibility test results to this system. Currently almost 50% of laboratories are automated and capable of producing daily reports. Daily reporting will allow outbreak detection techniques to be developed and rolled out.

We have worked with the NHS Business Service Authority (NHS BSA) and private information technology organisations (IMS Health and Rx info) to collect and collate comprehensive antibiotic consumption data from community (general practice, dental practice, prisons, out-of-hours, walk-in centres, and other community locations) and hospital (acute, mental health, specialist and community) settings to build a comprehensive picture of antibiotic prescribing trends across England.

We have advised NHS England on the development of a Quality Premium for antibiotic use which incentivises CCGs to reduce primary care prescribing of antibiotics, including broad spectrum antibiotics, and for secondary care in the first instance to encourage the validation (checking the quantity) of antibiotic prescribing in acute hospitals, so that future antibiotic use in hospitals can be measured and reduced more accurately.

Surveillance of antibiotic resistance

The incidence of *Escherichia coli* and *Klebsiella pneumoniae* bloodstream infections increased from 2010 to 2014 by 15.6% and 20.8% respectively. The incidence of *K. oxytoca, Pseudomonas* spp.*, Enterococcus* spp.*, Staphylococcus aureus* and *Acinetobacter* spp. bloodstream infections remained constant, while the incidence of *Streptococcus pneumoniae* bloodstream infections has declined. While the proportions resistant to key drugs have remained constant in *E. coli*, the increased incidence of bloodstream infections means that more individuals have had a significant antibiotic-resistant infection. In addition, the increases in both incidence and antibiotic resistance observed in *K. pneumonia*e bloodstream infections means that the number of individuals with antibiotic-resistant infections has increased substantially in the last five years. Resistance in gonorrhoea and tuberculosis (TB) have remained stable, though they remain a significant threat; for example, there was an outbreak of azithromycin resistance in heterosexuals in the North of England in 2014. Table 0.1 reports the proportions of resistance to key antibiotics required for treatment of bloodstream infections, gonorrhoea and TB in 2014 and compares this proportion to the 2010 results.

The enhanced surveillance now undertaken by PHE allows reporting of antibiotic resistance in bacteria isolated from clinical sites other than bloodstream infections. In 2014, for 126,404 isolates of *Enterococcus* spp., the most common well-defined sites of isolation reported were urine/kidney (76.8%) followed by skin/wound (5.5%) and blood (3.3%). The proportion of enterococci from sites other than blood that were resistant to vancomycin (8.1%) was significantly lower than the proportion seen with isolates from blood culture (14.4%). However, this finding should be interpreted with caution as only half the enterococci from sites other than blood were tested for susceptibility to vancomycin, compared to 91% of enterococci from blood cultures.

In 2014, antibiotic susceptibility test results were available for 711,960 isolates of *E. coli* from urine. As urinary specimens should only be sent to the laboratory on clinical suspicion of a urinary tract infection (UTI), this equates to an incidence rate of confirmed bacterial UTI of 1,322 cases per 100,000 population, although the true incidence of clinical UTI caused by *E. coli* is likely to be higher as not all laboratories identify the Gram-negative bacteria in urine to species level and guidelines recommend treatment without microbiological investigation for non-recurrent infections in women. The majority of positive urine cultures were from GP practices (52.4%), other community sources (including care homes and outpatient clinics, 10.6%) and acute trusts (37%). Greater than 96% of isolates from GP practices and acute trusts were tested for susceptibility to trimethoprim and nitrofurantoin, while 83% of isolates from other community sources were also tested against these antibiotics. Resistance to trimethoprim or amoxicillin/ampicillin was seen in over a third and over half of isolates, respectively, in all three settings. However, 97% of isolates from all clinical settings were susceptible to nitrofurantoin. These data may overestimate the extent of resistance, particularly in primary care, as much antibiotic prescribing by GPs is empirical. Although urine samples are submitted for microbiological examination from some patients, the likelihood is that such specimens may be preferentially submitted following initial antibiotic treatment failure, or from patients with histories of repeated or complicated infections who may have received multiple courses of antibiotics.

The detailed reports on enterococcal infections and urinary *E. coli* highlights the importance of laboratory standardisation in testing antibiotics to allow better understanding of antibiotic resistance and improved comparability of resistance across England.

Table 0.1 Antibiotic resistance in key infections, England, 2010−2014

Bacteria	Antibiotic resistance (non-susceptibility) metric	Proportion resistant in 2014 (%)	2014 compared to 2010*
Bloodstream infections			
Escherichia coli	% NS to ciprofloxacin	18.7	↔
E. coli	% NS to cefotaxime and/or ceftazidime	11.1	↑
E. coli	% NS to gentamicin	9.6	↔
E. coli	% NS to imipenem and/or meropenem	0.1	↔
E. coli	% NS to co-amoxiclav	42.0	↑
E. coli	% NS to piperacillin/tazobactam	11.0	↑
Klebsiella pneumoniae	% NS to ciprofloxacin	10.9	↔
K. pneumoniae	% NS to cefotaxime and/or ceftazidime	12.1	↑
K. pneumoniae	% NS to gentamicin	7.5	↔
K. pneumoniae	% NS to imipenem and/or meropenem	1.5	↑
K. pneumoniae	% NS to piperacillin/tazobactam	16.9	↑
***Pseudomonas* spp.**	% NS to ceftazidime	7.4	↔
***Pseudomonas* spp.**	% NS to imipenem and/or meropenem	11.5	↔
Streptococcus pneumoniae	% NS to penicillin	4.2	↔
***Enterococcus* spp.**	% NS to vancomycin	14.2	↑
Staphylococcus aureus	% NS to methicillin	10.0	↓
Acinetobacter spp	% NS to colistin	3.5	↔
Gonorrhoea			
Neisseria gonorrhoeae	% NS to ceftriaxone	0.0	↔
N. gonorrhoeae	% NS to azithromycin	1.0	↔
Tuberculosis			
Mycobacterium tuberculosis	% NS to isoniazid	6.9	↔
M. tuberculosis	% NS to rifampicin and isoniazid	1.3	↔

*The arrows mean the following: ↑statistically significant increase;↓statistically significant decrease;↔ no statistically significant change.
^Due to differences in testing methodology, results cannot be compared. Antibiotic susceptibility test results reported as “intermediate” or “resistant” were combined and presented as “non-susceptible”, as either result would usually preclude treatment of the bacteria with standard doses of the antibiotic.

Surveillance of antibiotic use

In 2014, the majority of antibiotics in England were prescribed in general practice (74%), followed by prescribing for hospital inpatients (11%), hospital outpatients (7%), patients seen in dental practices (5%) and patients in other community settings (3%).

The total consumption of antibiotics in primary and secondary care increased significantly by 6.5% over the four years, from 21.6 defined daily dose (DDD) per 1000 inhabitants per day in 2011 to 23.0 DDD per 1000 inhabitants per day in 2014. Between 2013 and 2014 total consumption increased by 2.4%.

General practice consumption increased by 6.2% when measured as DDD per 1000 inhabitants per day but has returned to 2011 levels of antibiotic prescription items per population suggesting that the amount of antibiotic per course increased either by increasing the course length or increasing the dose per day. Prescribing by dentists decreased by 2.8% when expressed in DDD per 1000 inhabitants per day between 2011 and 2014 and decreased by 7% when expressed as the number of antibiotic prescriptions per population. There was a 5.5% increase in prescribing by other community prescribers from 2011−2014, with an increase of 9.3% occurring between 2013 and 2014. Prescribing to hospital inpatients increased significantly by 11.7% and to hospital outpatients by 8.5% between 2011 and 2014. In 2014, within NHS Trusts, the greatest use occurred in Acute trusts (95%), with Specialist Trusts accounting for 3%, Learning and Mental Health Trusts 1.7% and Community Trusts 0.5%.

Table 0.2 summarises the changes by antibiotic group. Overall, the three most frequently used groups of antibiotics in England in 2014 were penicillins (45%), tetracyclines (22%) and macrolides (15%). Between 2010 and 2014, a significant increase occurred in the use of tetracyclines (13%), sulphonamides/trimethoprim (5%) and the mixed group of other antibacterials (23%). Over the same period, a decrease occurred in the antibiotic consumption of the following groups: other β-lactam antibacterials (-17%), presumed anti-*Clostridium difficile* antibiotics [fidoxamicin, oral vancomycin and oral metronidazole] (-3%), and quinolones (-2%). The decreases in these three groups of antibiotics occurred predominantly in the community.

Conversely, within the hospital setting, broad-spectrum prescribing, particularly carbapenems and piperacillin/tazobactam (regarded as the antibiotics of last resort) increased by 36% and 55%, respectively, between 2010 and 2014. The rate of increase of these antibiotics has slowed; between 2013 and 2014, carbapenems increased by 4% and piperacillin/tazobactam by 7%.

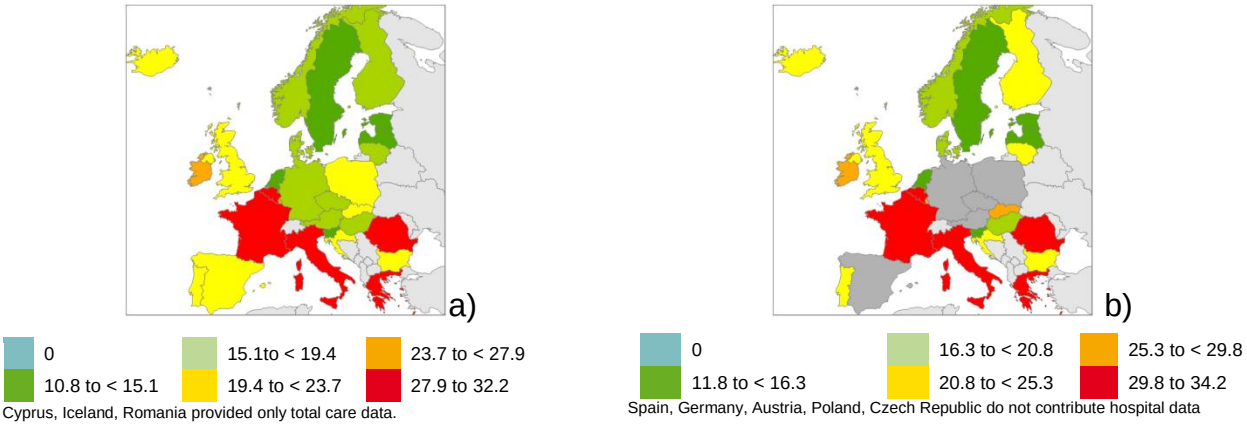
In 2013, the UK remained one of the middle to high prescribing countries for both community and hospital prescribing in comparison to other European Union countries submitting data centrally to the European Centre for Disease Control (Figure 1).

Table 0.2 Summary of antibiotic consumption in general practice and NHS trusts, presented as DDD per 1000 inhabitants per day (with changes compared to 2010*), England, 2010−2014

	General Practice	Compared to 2010	NHS Trusts	Compared to 2010
Broad Spectrum Antibiotics				
Penicillins and enzyme inhibitor	0.9	↑	0.9	↑
Cephalosporins	0.26	↔	0.22	↑
Carbapenems	0.001	↔	0.08	↑
Quinolones	0.3	↓	0.2	↔
Narrow Spectrum Antibiotics				
Penicillins (without enzyme inhibitors)	6.2	↑	1.2	↔
Tetracycline	4.5	↑	0.33	↓
Macrolides	2.7	↑	0.5	↑
Sulfonamides and trimethoprim	1.2	↔	0.4	↑
Proportion of broad spectrum antibiotics/ total antibiotics	**8.5%**	↓	**33.3%**	↑
Total antibiotic use expressed as DDD per 1000 inhabitants per day	17.1	↑	4.2	↑
Total antibiotic prescriptions expressed as items per STARPU^	**1.233**	↔		NA

*The arrows mean the following: ↑statistically significant increase; ↓statistically significant decrease; ↔ no statistically significant change. ^STARPU: Specific Therapeutic Group Age-sex weightings Related Prescribing Units ; comparison with 2010. NA= Not available

Figure 0.1 Geographical distribution for a) community b) community and hospital of antibiotic use, expressed as items per 1000 inhabitants per day, Europe, 2013[3]



Antimicrobial stewardship and public and professional engagement

Good AMS is a cornerstone for both effective treatment of infections and reduction of AMR. AMS programmes contain analysis of local AMR data to guide the development of evidence-based prescribing guidelines, educational resources to improve clinical practices to ensure antibiotics are prescribed appropriately, restrictive and persuasive interventions to use the appropriate antibiotics, and audit and feedback to clinical staff to improve patient care and outcomes against local and national prescribing criteria designed to drive quality improvements. National toolkits have been developed by PHE and partners to support implementation of AMS best practice in England. These are Treat Antibiotics Responsibly, Guidance, Education, Tools (TARGET) for primary care and 'Start Smart, Then Focus' (SSTF) for secondary care.[4,5]

ESPAUR led on four main areas of AMS and public and professional engagement in the 2014−2015 financial year understanding AMS and the use of TARGET in primary care; updating the secondary care SSTF toolkit in secondary care; developing an implementation plan for the AMS competencies; and developing and delivering the Antibiotic Guardian and European Antibiotic Awareness Day (EAAD) campaign for both professionals and members of the public. We have assessed the implementation of AMS toolkits in primary and secondary care through surveys; 100 (68%) of Acute NHS Trusts and 68 (41%) of clinical commissioning groups (CCGs) participated. The key results are outlined in Table 3. The secondary care survey revealed that the role of specialist antimicrobial pharmacists continues to remain embedded within Acute NHS Trusts; 90% of responding Trusts had a specialist antimicrobial pharmacist at a senior level in post. In primary care, prescribing advisors/medicine management pharmacists

[3] European Centre for Disease Control. European Surveillance of Antimicrobial Consumption Network (ESAC-Net), data accessed October 6th 2015. www.ecdc.europa.eu
[4] http://www.rcgp.org.uk/clinical-and-research/toolkits/target-antibiotics-toolkit.aspx
[5] https://www.gov.uk/government/publications/antimicrobial-stewardship-start-smart-then-focus

lead on AMS in 66% of responding CCGs; this role is also undertaken by specialist antimicrobial pharmacists, quality leads, nursing clinical leads and GP clinical leads. With the exception of antimicrobial prescribing policies, primary care is less likely to have implemented formal AMS activities than secondary care

Table 0.3 Comparison of antimicrobial stewardship activities in secondary and primary care, England, 2014

	Secondary care: Acute NHS Trust n=100	Primary care: Clinical commissioning groups n=82
Existence of AMS committee	94%	18%
Written dedicated antimicrobial policy	93%	99%
Action plan/Implemented toolkit	46%	13%
Written education and training strategy	24%	1%
Implemented audits within AMS toolkit	74%	15%

Following the publication of the NICE Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use guidance (NG15)[6], a Stage 2 Patient Safety Alert highlighting SSTF and TARGET was released jointly by NHSE, PHE and Health Education England (HEE) in July 2015. The alert highlighted the importance of addressing AMR through implementation of an AMS programme using the two key national AMS toolkits (TARGET and SSTF) developed by PHE, in collaboration with the NHS and key professional organisations.

Improving education and training regarding antibiotic resistance.

ESPAUR worked with stakeholders to develop options for the implementation of the antimicrobial prescribing and stewardship competencies within both undergraduate and postgraduate healthcare curricula and continued professional development. These recommendations are under consideration by HEE.

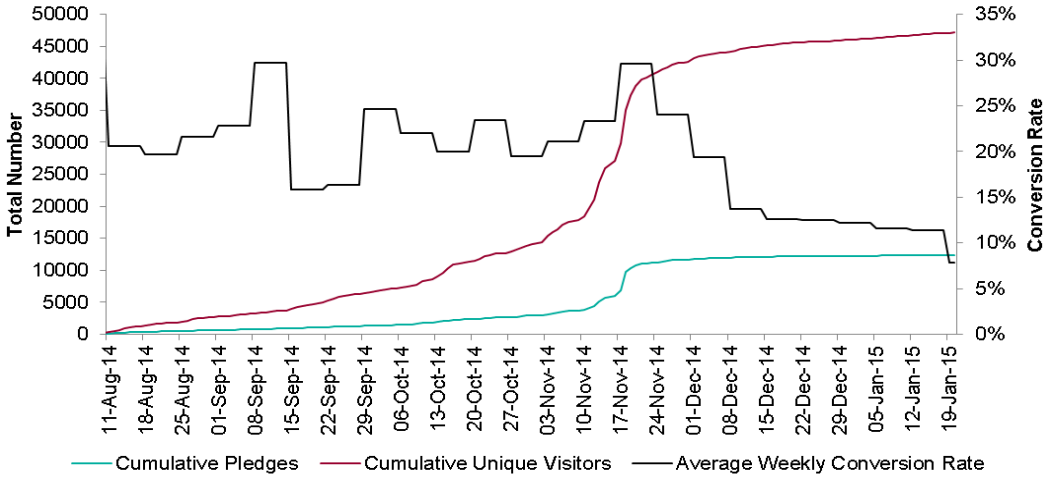
Development and delivery of the Antibiotic Guardian campaign

As part of UK activities for the 2014 EAAD and in support of the UK 5-year AMR strategy, PHE developed the Antibiotic Guardian (AG) campaign 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 objective for the first year was for 10,000 healthcare professionals

[6] NICE. Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use http://www.nice.org.uk/guidance/ng15

and members of the public to choose a pledge on www.antibioticguardian.com by 30 November 2014.

Activities and resources for EAAD and the AG campaign were developed and run by a PHE-led interdisciplinary committee with representation from animal and human health sectors across England and the devolved administrations.



* conversion rate is the proportion of unique visitors who make a pledge

Figure 0.2 Comparison of unique visitors to antibioticguardian.com to the total number of Antibiotic Guardians, between 8 August 2014 and 20 January 2015; conversion rate=26.5% n=12,509 pledges

The campaign goal of 10,000 AGs was met by 30 November 2014 as outlined in Figure 2. The majority of engagement with the AG campaign aligned with EAAD on 18 November with a marked decline in activity after EAAD, demonstrating the importance of a targeted period to engage with professionals and the public. The AG campaign was primarily driven and engaged with by healthcare professionals (69%), with the remaining 31% of pledges provided by the public. The largest group of pledgers were pharmacy teams (22.3% of total AGs) highlighting the engagement of pharmacists in antibiotic campaigns.

A key component of future work will be to evaluate the effectiveness of this campaign in reducing inappropriate antibiotic consumption and prescription by the public and healthcare workers.

Measurement of impact of behavioural interventions and antibiotic resistance awareness campaigns

The PHE and Department of Health Behavioural Insights Team's published a literature review and behavioural analysis in February 2015. The report assessed the evidence about behaviours that support AMS and analysed drivers of those behaviours using a robust theoretical framework. It proposed new and enhanced interventions that have the

potential to reduce the risk of antibiotic resistance. These interventions are grounded in behavioural science, underpinned by a thorough review of the evidence, and have robust theoretical foundations for their mechanism of action. Further reviews and behavioural analyses of current services and interventions to improve AMS are underway to identify opportunities for enhancement through behavioural science.

The behavioural analysis led the Behavioural Insights Teams to run a randomised controlled trial (RCT) during the winter period 2014/15 to reduce antibiotic prescribing by high-prescribing GPs. The RCT tested the independent effectiveness of i) social norm feedback from the Chief Medical Officer, and ii) patient-focused information. Results have been submitted for publication in a peer-reviewed journal. A second behavioural insights intervention trial in primary care based on commitment posters and recorded telephone messages has been developed and is currently being implemented.

Working with veterinary partners

In July 2015 a UK One Health report was published by PHE and ESPAUR in collaboration with the Department for Environment, Food and Rural Affairs (DEFRA) of the Environment's Veterinary Medicines Directorate and devolved administrations.[7] This report set out AMR data for key bacteria that are common to animals and humans and detailed the amounts of antibiotics sold for animal health and welfare and antibiotics prescribed to humans. The report also included recommendations for improvement to national surveillance programmes in order to facilitate better understanding of AMR and effects of antimicrobial use across both settings.

Working with European and global initiatives

PHE continues to work with the European Centre for Disease Control (ECDC) to enhance surveillance on antibiotic prescribing and resistance and have submitted AMR and hospital and community prescribing data to both the European Antimicrobial Resistance Surveillance Network (EARS-Net) and European Surveillance of Antimicrobial Consumption Network (ESAC-Net). PHE staff are also members of the ECDC Technical Advisory Committee for EAAD, advising particularly on resource development. PHE staff have been elected by EU member state experts to join EARS-Net and ESAC-Net coordination committees respectively. The role of committee members is to work closely with ECDC in between the full network meetings, provide advice to ECDC on urgent matters and contribute to the agenda of the regular network meetings and annual reports. The latest EARS-net and ESAC-net surveillance reports are available on the ECDC website.

[7] https://www.gov.uk/government/publications/uk-one-health-report-antibiotics-use-in-humans-and-animals

PHE continues to support the World Health Organisation meetings in relation to AMR and has been invited to attend, present and chair meetings; and has delivered training and laboratory capacity-building workshops over the last year.

PHE's global health team partnered with the Caribbean Public Health Agency (CARPHA) to deliver a two-day workshop, entitled 'Combatting AMR in the Caribbean' on 9 and 10 December in Port-of-Spain, Trinidad and Tobago as part of the PHE-led AMR Commonwealth Laboratory Twinning Initiative. The aim of the workshop was to raise awareness of AMR and to develop a roadmap to address AMR in the region. The full report is available on the CARPHA website and slides from the day are also available.[8]

Developing research relationships with academic partners

In 2014, the National Institute for Health Research (NIHR) funded two Health Protection Research Units (HPRUs) on Healthcare-Associated Infection and AMR at Oxford and Imperial Universities. The HPRUs are research partnerships between universities and PHE and act as centres of excellence in multidisciplinary health protection research in England. A number of research collaborations are in progress and early outputs are highlighted in Chapter 5.

8 Combatting AMR in the Caribbean: A report on the workshop delivered as part of the Commonwealth laboratory twinning initiative to combat AMR. http://carpha.org/downloads/Antimicrobial%20Resistance%20in%20the%20Caribbean.pdf

Future ESPAUR actions:

- continue to enhance antibiotic surveillance through the ongoing validation of NHS Acute trust data; work with dental prescribers and NHSBSA to improve the granularity of available dental data; work with independent sector hospitals to incorporate their antibiotic prescribing data into the national datasets

- work to improve the quality and standardisation of routine antibiotic testing and interpretation of results to ensure improved comparability and robustness to microbiology data to improve treatment of infections and surveillance with NHS-England, Health and Social Care Information Centre (HSCIC), hospital microbiologists and professional organisations

- PHE has developed methods to automate the transmission of microbiology results to the national surveillance systems and will work to increase the proportion of labs providing daily automated reports, as real time data is essential to facilitate rapid detection of clusters/outbreaks of AMR pathogens

- publish locally relevant data on healthcare associated infections, antimicrobial prescribing, AMR and infection prevention and control for primary and secondary care to facilitate the development of local action plans

- develop outputs and perform and evaluate the newly introduced enhanced reporting system (ERS) for carbapenemase-producing organisms

- scope and cost a sentinel surveillance system for UTIs in general practice to determine the true burden of UTIs and the proportion resistant to antibiotics. A sentinel surveillance system for community urine specimens would enable optimisation of UTI guidelines

- continue to work with veterinary partners to deliver the actions outlined from the 2015 One Health report, to improve comparability of surveillance across key drug-bug combinations and antibiotics common to humans and animals

- continue to embed use of tools and resources for optimising prescribing in primary and secondary care, by supporting the implementation of the NICE AMS guidance

- PHE is the custodian for the Standards for Microbiological Investigations (SMI); developed to improve the quality and consistency across NHS and independent sector clinical laboratories. ESPAUR will measure the uptake of these SMI in relation to antimicrobial susceptibility testing through the antimicrobial susceptibility reports on the national surveillance system

- provide expert advice to NHS England to enable the development of commissioning incentives to encourage healthcare providers to achieve the antibiotic prescribing quality measures (APQMs) recommended by the national expert Advisory Group on AMR and Healthcare Associated Infections (ARHAI) for primary and secondary care

- continue to audit uptake and impact of prescribing guidance across the healthcare system and publish the results of submitted AMS audits

- work with the Royal Colleges and professional bodies to identify how best to utilise the appraisal and revalidation system to promote stewardship and embed best prescribing practice

- deliver the Antibiotic Guardian campaign in 2015, engaging the public and professionals in pledging to take action to preserve antibiotics with an aim to reach 100,000 individuals

- review and evaluate the impact of the Antibiotic Guardian campaign in 2015 to inform the development of a sustained approach across the life of the strategy

- facilitate and commission two public debates with the aim to raise awareness of antibiotics and consider ways that the public believe could limit their use

- continue 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

- continue to work with the HPRUs to ensure that research questions and activities are aligned to PHE priorities

Recommendations to organisations

Recommendations to PHE regions and centres

PHE centres should ensure that this report is discussed at meetings, local Quality Surveillance Groups, strategic clinical networks, health protection committees, local infection prevention and control committees, and should support the development of action plans to reduce prescribing.

PHE field epidemiology services should provide access to aggregated AMR data to relevant stakeholders (eg community and hospital based antibiotic prescribing (pharmacy) advisors, directors of public health) based on local geographies.

PHE staff should direct data queries on antibiotic use in CCGs and general practices to the NHS BSA website (accessed via an N3 connection) http://www.epact.ppa.nhs.uk/systems/sys_main_epact.html and the HSCIC website http://www.hscic.gov.uk/prescribing; and Acute NHS Trusts to their own pharmacy data, held within their hospitals.

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 (NG15).

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 promote the use of the national AMR surveillance system to NHS colleagues through the active dissemination of the system weblink https://sgss.phe.org.uk/

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 HWBs are aware of the strategic nature and priority of AMR, and that it receives due attention in the Joint Strategic Needs Assessment and at Health and Wellbeing Boards.

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 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.

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 regional and area 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.

Directors of infection prevention and control (DIPCs), 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 is reporting AMR data to PHE and 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/. 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 for referral to the national reference laboratory. 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 (accessed via an N3 connection) http://www.epact.ppa.nhs.uk/systems/sys_main_epact.html and the HSCIC website http://www.hscic.gov.uk/prescribing. Acute NHS Trusts can review their own pharmacy data, held within their hospitals. In 2016, PHE will develop a data portal where antibiotic prescribing quality metrics can be viewed for both primary and secondary care organisations.

Regional and area team 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.

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 UK published a cross-government five-year AMR (AMR) strategy (encompassing antibiotics) in 2013.[9,10] The overarching goal is to slow the development and spread of antibiotic resistance and to this end it has three strategic aims, namely to improve knowledge and understanding of resistance, to conserve the effectiveness of existing treatments and to stimulate development of new treatments and diagnostics. These strategic aims are underpinned by seven key areas for action as follows:

- improving infection prevention and control practices
- optimising prescribing practices
- improving professional education, training and public engagement
- developing new drugs, treatments and diagnostics
- better access to and use of surveillance data
- better identification and prioritisation of AMR research needs
- strengthened international collaboration

Public Health England (PHE) leads on four of these activities focusing on surveillance, infection prevention and control, antibiotic prescribing practices, and professional and public education and engagement. The English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) was established by PHE in July 2013 to support English actions within the UK 5 year AMR strategy and bring together PHE, the NHS, and independent healthcare providers.

In the last year, the government-appointed economist Jim O Neill has led an AMR review publishing reports evaluating the future burden and cost of AMR. Initial research, looking only at part of the impact of AMR, shows that a continued rise in AMR would lead globally to 10 million people dying every year and a reduction of 2% to 3.5% in gross domestic product (GDP) by 2050.[11] It is estimated that it will cost the world up to 100 trillion USD. This highlights the public health burden of AMR and the critical importance of ESPAUR working to improve surveillance, enable action on prudent prescribing, and raise public and professional knowledge and engagement.

[9] Department of Health and Defra. UK five year AMR strategy 2013-2018. https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_strategy.pdf

[10] Ashiru-Oredope D, Hopkins S; English Surveillance Programme for Antimicrobial Utilization and Resistance Oversight Group. AMS: English Surveillance Programme for Antimicrobial Utilization and Resistance (ESPAUR). J Antimicrob Chemother. 2013 Nov;68(11):2421-3.

[11] AMR: Tackling a crisis for the health and wealth of nations

Since the launch of the AMR strategy, ESPAUR has:

- established and improved surveillance data on antibiotic prescribing and antibiotic resistance
- improved access and use of surveillance data
- worked with NHS England to measure and improve prescribing in primary and secondary care through the development of an antimicrobial prescribing quality premium, which incentivises clinical commissioning groups (CCGs) to improve the quality of the services they commission
- launched an 'Antibiotic Guardian' campaign, to engage and promote behaviour change among healthcare professionals and the public.
- developed implementation options for the improved education and training of healthcare professionals
- performed an assessment of AMS activities in primary and secondary care
- worked with veterinary colleagues on an integrated 'One Health' approach to antimicrobial usage and resistance surveillance
- worked with university partners to use data to answer key research questions

As we commence the third year of this programme we are delighted to present the progress towards our objectives defined in the 2014 ESPAUR report.[12]

This second report from ESPAUR details trends on antimicrobial usage and resistance from 2010 to 2014, shows developments in AMS and professional/public education and awareness activities, reviews ESPAUR activities and highlights progress made in the last year.

The work of ESPAUR is dependent on many co-operative relationships throughout the NHS, public and private sectors. Key to this are the members of the oversight group, who scrutinise, challenge and collaborate with the PHE staff working on this programme.

[12] English surveillance programme antimicrobial utilisation and resistance (ESPAUR) report, 2014. Available at https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report

Chapter 2: Antibiotic resistance in England

Introduction

Surveillance remains the cornerstone for understanding the epidemiology of antibiotic resistance and for assessing the effectiveness of actions and interventions aimed at reducing its clinical and public health impact. A critical component of surveillance is the dissemination of data following its collection and analysis. In support of this, this report conveys information on the trends in resistance to key antibiotics among a range of pathogens of public health importance, as indicated in the UK 5-year AMR Strategy.

The data on resistance in pathogens causing bloodstream infections is based on the recommendations of the expert Advisory Committee on AMR and Healthcare Associated Infections (ARHAI) as to the pathogens and antibiotics ('drug/bug combinations') that should be the main focus of surveillance in support of the UK 5-year AMR strategy (Table 2.1). The data presented in this report provides a one year update to the national data presented on the key drug/bug combinations included in the ESPAUR report published in 2014. In addition, data is now presented on the secondary ('shadow') list of drug/bug combinations also recommended by ARHAI for potential inclusion in national surveillance. National trend data showing the incidence of bloodstream infections caused by these pathogens and the proportion of isolates of each genus or species resistant to the key antibiotics or antibiotic classes is presented in the main report, with a geographical breakdown providing information on the rates of resistance in NHS regions being provided in Web Appendix 1.

In addition, this chapter presents data on other pathogens or disease syndromes of public health importance and describes enhancements to existing surveillance systems. These include:

i. The incidence and epidemiology of vancomycin resistance in enterococci from blood and other clinical sources
ii. Resistance in *E. coli* causing urinary tract infections
iii. Enhanced surveillance of carbapenemase-producing Gram-negative bacteria
iv. Resistance in tuberculosis (TB)
v. Resistance in *Neisseria gonorrhoeae*, the causative agent of the sexually transmitted infection gonorrhoea.

Methods

Data sources

Bloodstream infections

Data on the susceptibility of each pathogen to key antibiotics from 2010 to 2014 were obtained from the Communicable Disease Report (CDR) module of the Second Generation Surveillance System (SGSS), a national database maintained by PHE. The exception was data on meticillin susceptibility of *S. aureus*, which was obtained from the national mandatory surveillance database held by PHE. The CDR module of SGSS contains data previously held in LabBase2, the forerunner of SGSS.

Data is electronically submitted to SGSS on a voluntary basis by hospital microbiology laboratories in England, who report the results of routine susceptibility testing of bacterial isolates to individual antibiotics as 'susceptible', 'intermediate' or 'resistant'. These categories are defined as follows:

- *susceptible*: a bacterial strain is said to be susceptible to a given antibiotic when its growth is inhibited *in vitro* by a concentration of the drug that is associated with a high likelihood of therapeutic success
- *intermediate*: a bacterial strain is said to be intermediate when the concentration of antibiotic required to inhibit its growth *in vitro* is associated with an uncertain therapeutic outcome
- *resistant*: a bacterial strain is said to be resistant to a given antibiotic when the concentration required to inhibit its growth *in vitro* is associated with a high likelihood of therapeutic failure

For the purpose of this report, antibiotic susceptibility test results reported as 'intermediate' or 'resistant' were combined and presented as 'non-susceptible'.

The report presents the national trends in resistance for the designated drug−bug combinations in England for 2010 to 2014 for isolates obtained from blood. Cases of blood stream infection assigned at regional level are shown in Web Appendix 1. Regional assignment was performed using the patient's residential postcode. Of if not available, their general practitioner's postcode; if neither were available the postcode of the reporting laboratory was used.

Vancomycin-resistant enterococci

Data on the proportion of enterococci isolated from blood that were resistant to vancomycin between 2010 and 2014 were extracted from the CDR module of SGSS. For a more detailed analysis of vancomycin-resistant enterococci, data on enterococci reported to the AMR module of SGSS in 2014 were extracted. Data items collated included species, clinical source, reporting laboratory and susceptibility to vancomycin.

While more extensive data on antibiotic susceptibility is stored in the AMR module of SGSS, fewer laboratories reported to the AMR module in previous years compared to the present. Thus, some retrospective data is less robust compared to that from the CDR module, making the AMR module less suited to retrospective trend analysis at the current time.

Urinary tract infections caused by *E. coli*

Data on *E. coli* isolated from urine in 2014 were extracted from the AMR module of SGSS. Data items collated included source of specimen referral (GP, other community source, acute trust) and susceptibility to nitrofurantoin and trimethoprim first-line agents for treatment of urinary tract infections (UTI). Data on susceptibility to ciprofloxacin, third-generation cephalosporins, piperacillin/tazobactam and carbapenems were also collected to allow comparison with the data on *E. coli* from bloodstream infections.

Carbapenemase-producing Gram-negative bacteria

Data on bacterial isolates confirmed as having genes encoding carbapenemases were provided by the AMR and Healthcare-Associated Infections (AMRHAI) Reference Unit.

Drug resistance in TB

Data on notified cases of TB in England from 2000 to 2014 were extracted from the Enhanced Tuberculosis Surveillance System (ETS database). Clinical teams provide information on TB cases either directly through the web-based ETS system entered at the clinic, or on a case report form entered onto the system at the Health Protection Team level. Data include notification details, demographic information, clinical and microbiological information. Data from all TB isolates sent to mycobacteria reference laboratories for culture between January 2000 and March 2015 were de-duplicated and a summary record was generated from all the isolates from the same individual. These data were then matched to TB case notifications between 2000 and 2014.
Several categories of TB drug resistance are defined as follows:

- *initial resistance*: resistance identified within three months of the first specimen date
- *first-line resistance*: resistance to at least one of the four first line drugs (isoniazid, rifampicin, ethambutol, pyrazinamide) used for standard six month treatment courses.
- *multi-drug resistant (MDR)*: MDR-TB is defined as resistance to at least isoniazid and rifampicin, with or without resistance to other drugs
- *multi-drug resistant/rifampicin-resistant (MDR/RR)*: MDR/RR-TB is defined as resistance to rifampicin including MDR-TB cases
- *extensively drug-resistant (XDR)*: 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 or moxifloxacin)

Drug resistance in *Neisseria gonorrhoeae*

For national surveillance of the incidence of gonorrhoea, data on cases is submitted electronically from genitourinary medicine (GUM) and integrated GUM and sexual and reproductive health clinics to the GUMCADv2 database, which is managed by PHE. National surveillance of antimicrobial resistance in *Neisseria gonorrhoeae* is undertaken via a network of sentinel GUM clinics as part of the Gonococcal Resistance to Antimicrobial Surveillance Programme (GRASP). Over a three-month period each year, isolates from consecutive patients with gonorrhoea attending these clinics are referred to the PHE Sexually Transmitted Bacteria Reference Unit (STBRU) for antimicrobial susceptibility testing. Isolates are linked to demographic, clinical and behavioural data from the clinics for analysis of antimicrobial susceptibility trends in patient sub-groups.

Population denominators

Incidence rates were calculated using the mid-year resident population estimates, provided by the Office for National Statistics (ONS) for the respective years.

Results

Bloodstream infections

The antibiotics for which bloodstream pathogen susceptibility data were collected and analysed are shown in Table 2.1. The third-generation cephalosporins included cefotaxime, ceftazidime, ceftriaxone or cefpodoxime, while the macrolides included erythromycin, clarithromycin or azithromycin.

Incidence of pathogen-specific bloodstream infections

The incidence of bloodstream infections caused by the various pathogens, based on voluntary reporting to SGSS, is shown in Figure 2.1. Of the organisms under review, *E. coli* was the commonest cause of bloodstream infection and showed year-on-year increases, from 45.0 cases per 100,000 population in 2010 to 52.0 cases per 100,000 population in 2014, equating to an overall increase of 15.6%. The incidence of *K. pneumoniae* also increased, from 7.7 cases per 100,000 in 2009 to 9.3 cases per 100,000 in 2014, an increase of 20.8%. In contrast, the incidence of *K. oxytoca, Pseudomonas* spp., *Enterococcus* spp., *S. aureus* and *Acinetobacter* spp. remained relatively constant, while the incidence of S. *pneumoniae* declined by 23.4%, from 7.7 cases per 100,000 population in 2010 to 5.9 per 100,000 population in 2014, probably reflecting the impact of the conjugate pneumococcal vaccine.

Table 2.1 Drug-bug combinations (for isolates from blood culture), England, 2014*

Pathogen	Antibiotic or antibiotic class
Escherichia coli	Ciprofloxacin
	Third-generation cephalosporins
	Gentamicin
	Imipenem/meropenem
	Piperacillin/tazobactam
	Co-amoxiclav
Klebsiella pneumoniae	Ciprofloxacin
	Third-generation cephalosporins
	Gentamicin
	Imipenem/meropenem
	Piperacillin/tazobactam
Klebsiella oxytoca	Ciprofloxacin
	Third-generation cephalosporins
	Gentamicin
	Imipenem/meropenem
	Piperacillin/tazobactam
***Pseudomonas* spp.**	Ciprofloxacin
	Ceftazidime
	Gentamicin
	Imipenem/meropenem
	Piperacillin/tazobactam
Streptococcus pneumoniae	Penicillin
	Macrolides
	Tetracycline
Staphylococcus aureus	Meticillin
***Enterococcus* spp.**	Vancomycin
***Acinetobacter* spp.**	Colistin

* as recommended by the Department of Health expert advisory committee for antimicrobial resistance and healthcare associated infections (ARHAI), 02 October 2014, and agreed by the High Level Steering Group (HLSG) for the UK 5 year AMR Strategy, 27 January 2015

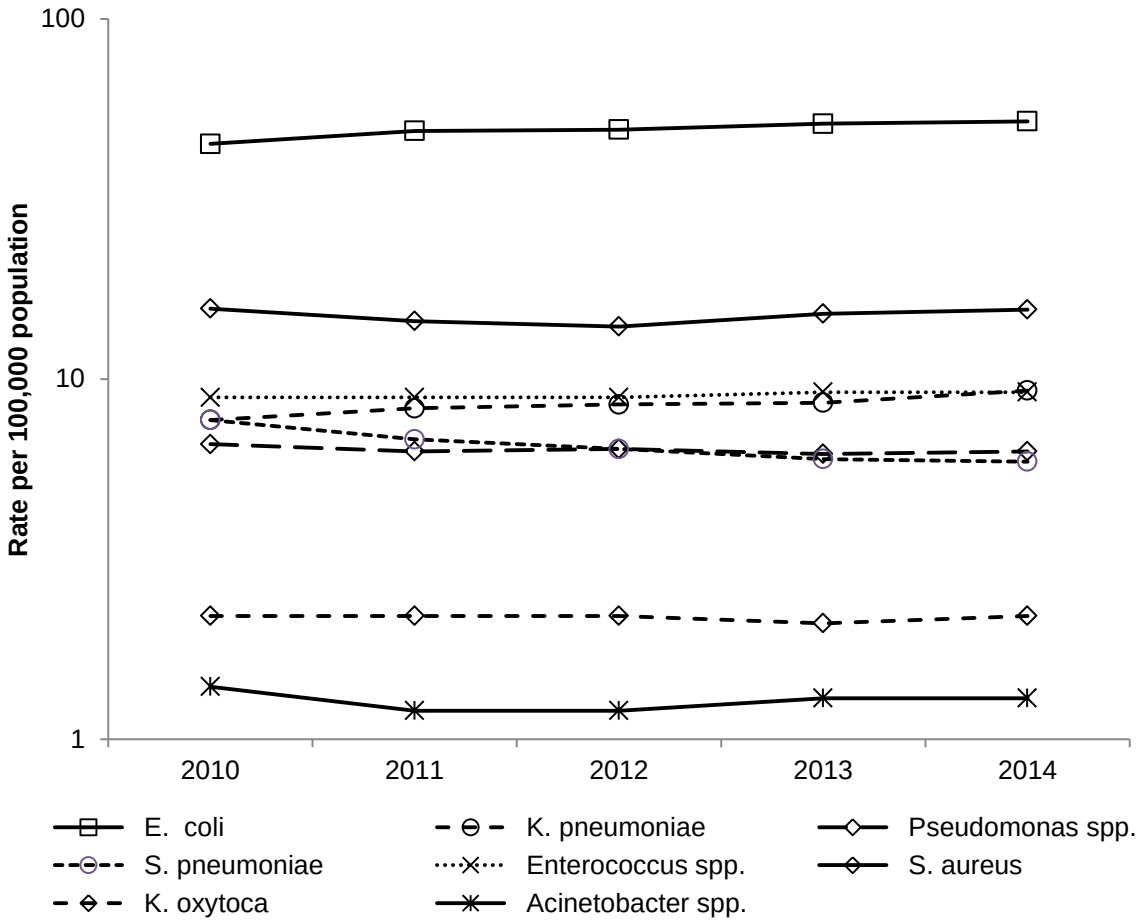


Figure 2.1 Incidence of bloodstream infections due to indicated pathogens, England, 2010−2014

Trends in resistance by pathogen

Escherichia coli

The proportion of *E. coli* bloodstream isolates resistant to different classes of antibiotics over time is shown in Figure 2.2. The proportion of isolates resistant to ciprofloxacin showed little change, ranging from 18% in 2010 to 19% in 2014. The proportion of isolates resistant to gentamicin and to third-generation cephalosporins varied in the range 9−10% and 10−12 %, respectively, while resistance to carbapenems remained uncommon at 0.1% in 2014. Resistance to piperacillin/tazobactam showed a slight upward trend from 8% in 2010 to 11% in 2014, although this increase should be interpreted with caution as data from the National External Quality Assurance Scheme on the criteria used by laboratories for defining resistance, showed a shift from using the Clinical and Laboratory Standards Institute (CLSI) breakpoint of 16 mg/L, to the European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoint of 8 mg/L. The use of a lower breakpoint for categorising resistance could thus potentially increase the proportion of isolates so defined.

Although not shown in Figure 2.2, the trend in the proportions of isolates of *E. coli* resistant to co-amoxiclav (amoxicillin/clavulanic acid) was also investigated. The data showed year-on-year increases as follows: 2010 (24%), 2011 (31%), 2012 (37%), 2013 (39%), and 2014 (42%). However, these data are difficult to interpret with confidence due to laboratories changing from using CLSI testing methods to those of EUCAST. Co-amoxiclav comprises a mixture of amoxicillin and clavulanic acid, and in the CLSI method a fixed 2:1 ratio of the compounds is used while in the EUCAST method varying concentrations of amoxicillin are tested in the presence of a fixed concentration (2 mg/L) of clavulanic acid. It is well documented that the two methods give discrepant MIC distributions. A further confounder is that some laboratories have also used the antibiotic susceptibility testing method advocated by the British Society for Antimicrobial Chemotherapy (BSAC) and the criteria for interpreting the results of disc diffusion tests (ie the diameter of the zone of inhibition of bacterial growth around the disc) was amended between 2010 and 2011 with more isolates likely to have been reported as resistant using the new zone cut off value. Although retrospective analysis of trend data is thus complex, assuming no further amendments to methodology, prospective surveillance of resistance to co-amoxiclav should be feasible.

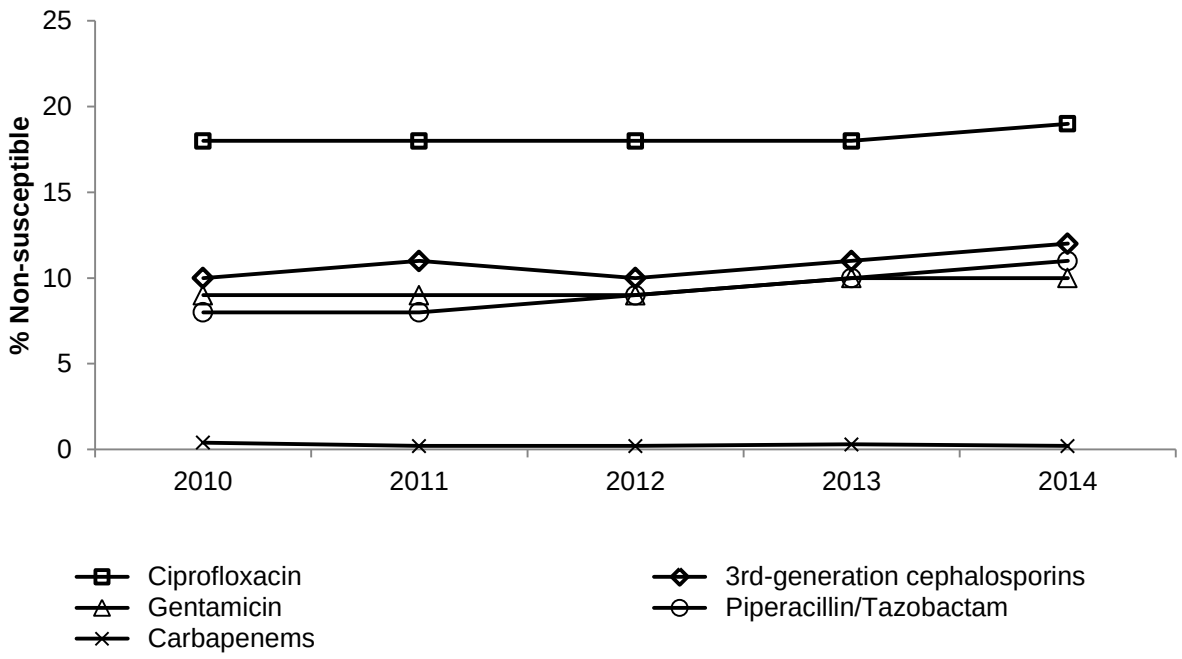


Figure 2.2 Proportions of bloodstream isolates of *E. coli* non-susceptible to indicated antibiotics, England, 2010−2014

Klebsiella pneumoniae

The proportion of *K. pneumoniae* bloodstream isolates resistant to different classes of antibiotics over time is shown in Figure 2.3. Resistance to gentamicin was little changed, from 6% in 2010 to 7% in 2014. The proportion of isolates resistant to

ciprofloxacin increased slightly from 9% in 2010/2011 to 11% in 2013/2014, with a similar slight upward trend also seen for resistance to third-generation cephalosporins, which increased from 10% in 2010/2011 to 12% in 2013/2014. A more pronounced increase was seen for resistance to piperacillin/tazobactam, which increased from 10% in 2010 to 17% in 2014. However the same caveats relating to interpretation of the data as given above for *E. coli* apply here also. Although the proportion of isolates resistant to carbapenems was low, it nonetheless increased from 0.3% in 2010 to 1.5% in 2014.

Klebsiella oxytoca

The proportion of *K. oxytoca* bloodstream isolates resistant to different classes of antibiotics over time is shown in Figure 2.4. Resistance to gentamicin, ciprofloxacin, third-generation cephalosporins and carbapenems was low, being seen in ≤6% of isolates throughout the five-year surveillance period. Resistance to piperacillin/tazobactam was higher occurring in 10−13% of isolates with year-to-year fluctuation.

Pseudomonas spp.

Trends in the resistance of *Pseudomonas* spp. bloodstream isolates to different classes of antibiotics over time is shown in Figure 2.5. For four of the five antibiotics studied, the proportion of resistant isolates was broadly stable over time, being in the range of 9−11% for ciprofloxacin, 7−8% for ceftazidime, 4−5% for gentamicin and 9−11% for carbapenems (meropenem/imipenem). Resistance to piperacillin/tazobactam in contrast showed a slight but significant upward trend, from 6% in 2010−2011 to 10% in 2014, but again this trend needs to be interpreted with caution.

Streptococcus pneumoniae

Data on susceptibility of bloodstream isolates of *S. pneumoniae* are shown in Figure 2.6. The proportions of isolates non-susceptible to penicillin and to macrolides were broadly stable over the five years, being in the range 3−4% and 5−8%, respectively. Resistance to tetracycline showed a slight upward trend from 4% in 2010 to 7% in 2014.

Staphylococcus aureus

The total number of cases of *S. aureus* bloodstream infection reported to the mandatory surveillance programme and the proportion of isolates that were meticillin-susceptible (MSSA) or resistant (MRSA) are shown in Figure 2.7. There was a year-on-year decrease in meticillin non-susceptibility from 12% in 2010 to 8% in 2014.

Acinetobacter spp.

The resistance of *Acinetobacter* spp. bloodstream isolates to colistin was in the range of 4−5% each year with the exception of 2012 when 10% of isolates were reported as resistant. However, due to the wide range of the 95% confidence intervals (4.4−18.8%), this value was not significantly different from the other years.

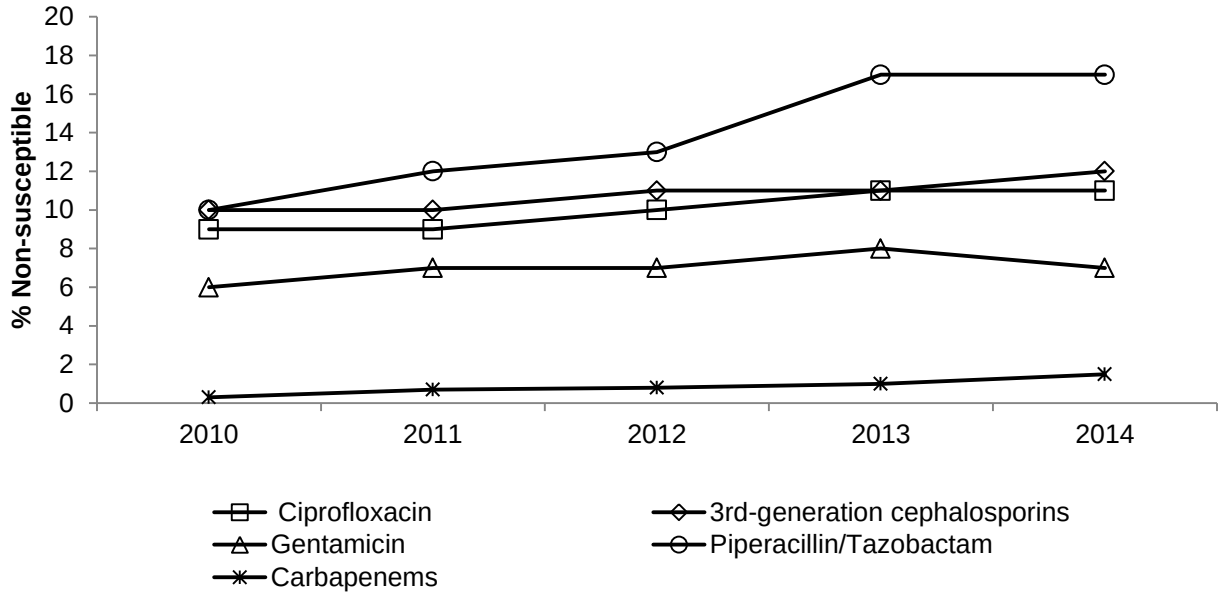


Figure 2.3 Proportions of bloodstream isolates of *K. pneumoniae* non-susceptible to indicated antibiotics, England, 2010−2014

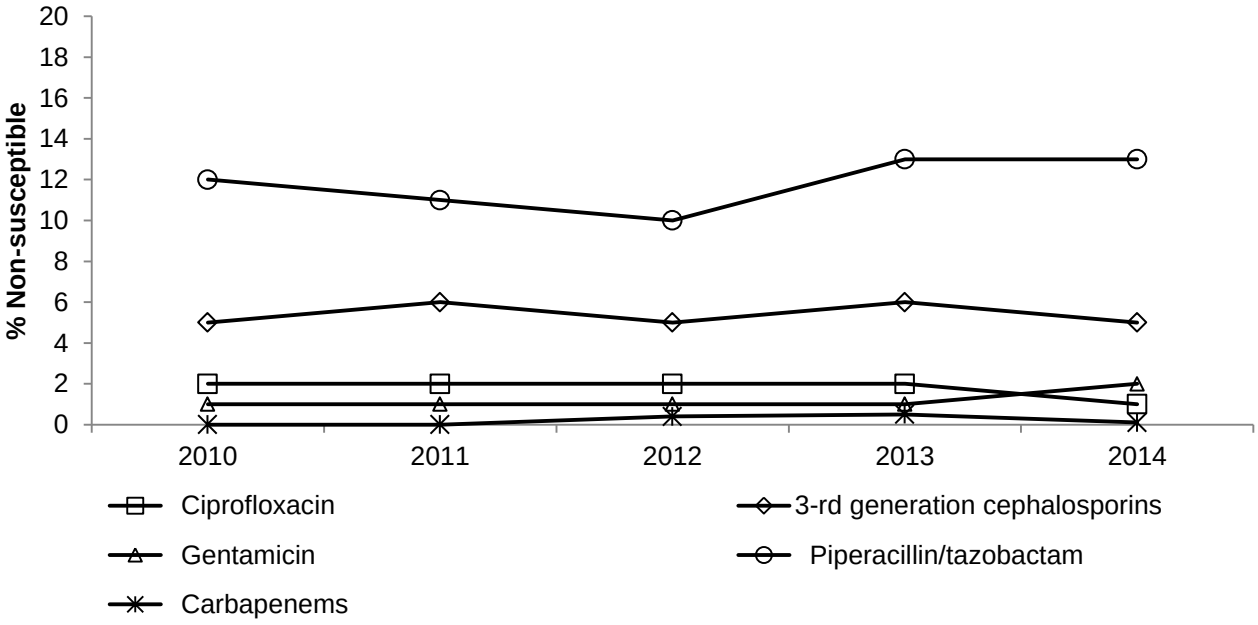


Figure 2.4 Proportions of bloodstream isolates of *K. oxytoca* non-susceptible to indicated antibiotics, England, 2010−2014

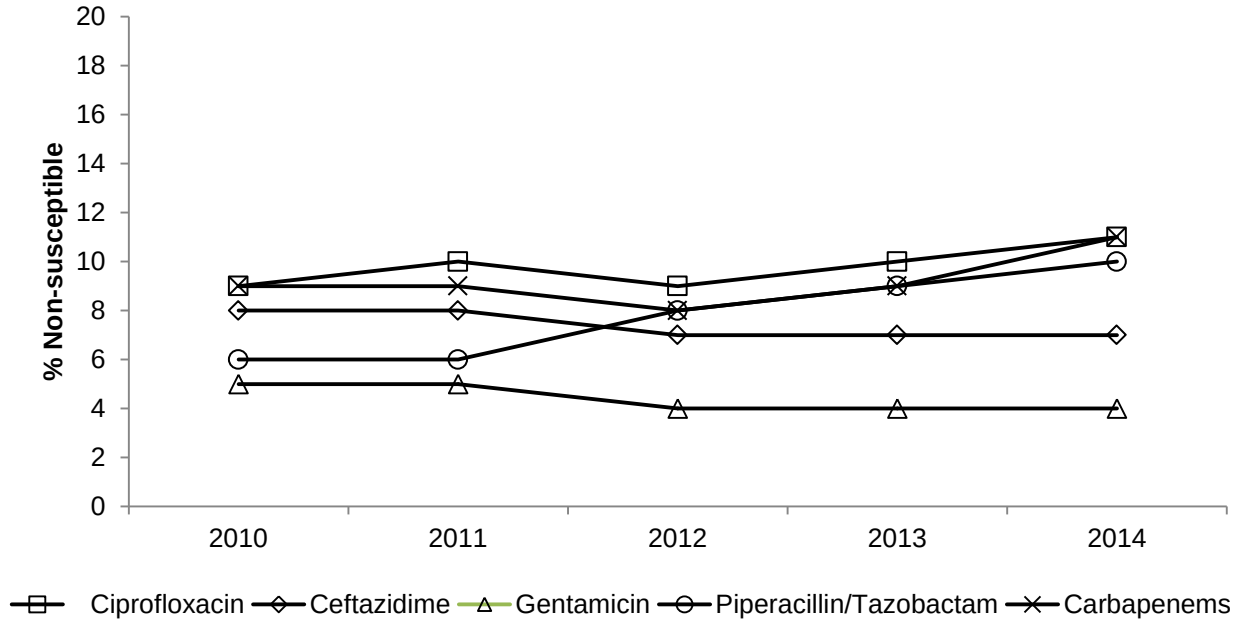


Figure 2.5 Proportions of bloodstream isolates of *Pseudomonas* spp. non-susceptible to indicated antibiotics, England, 2010−2014

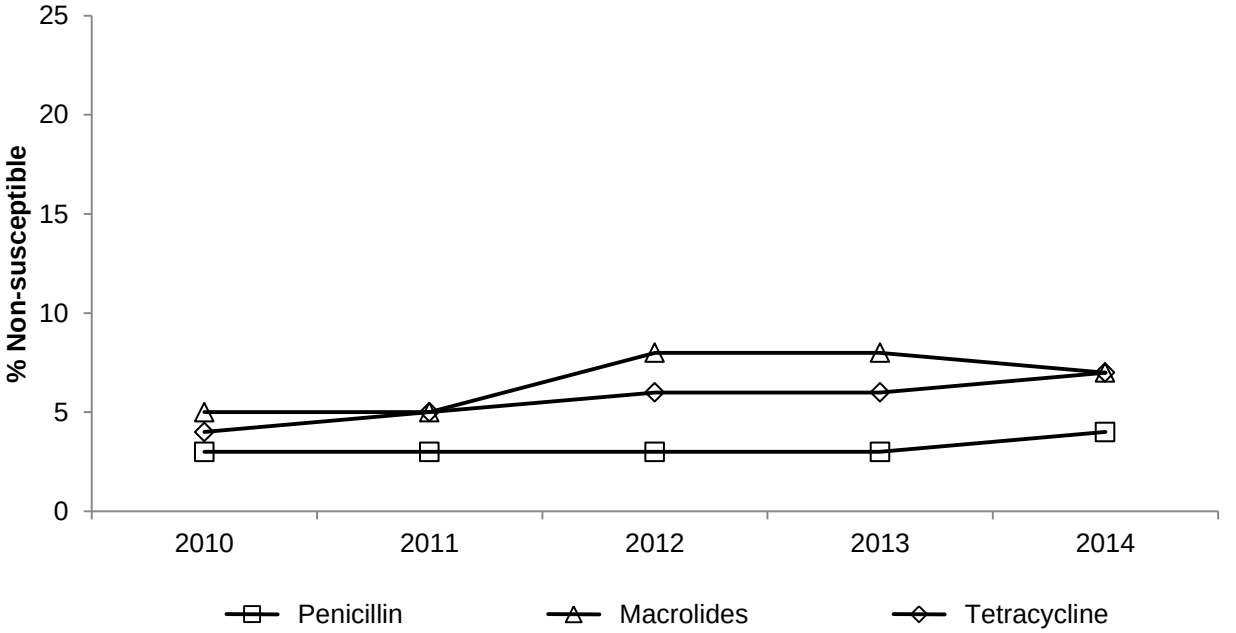


Figure 2.6 Proportions of bloodstream isolates of *S. pneumoniae* non-susceptible to indicated antibiotics, England, 2010−2014

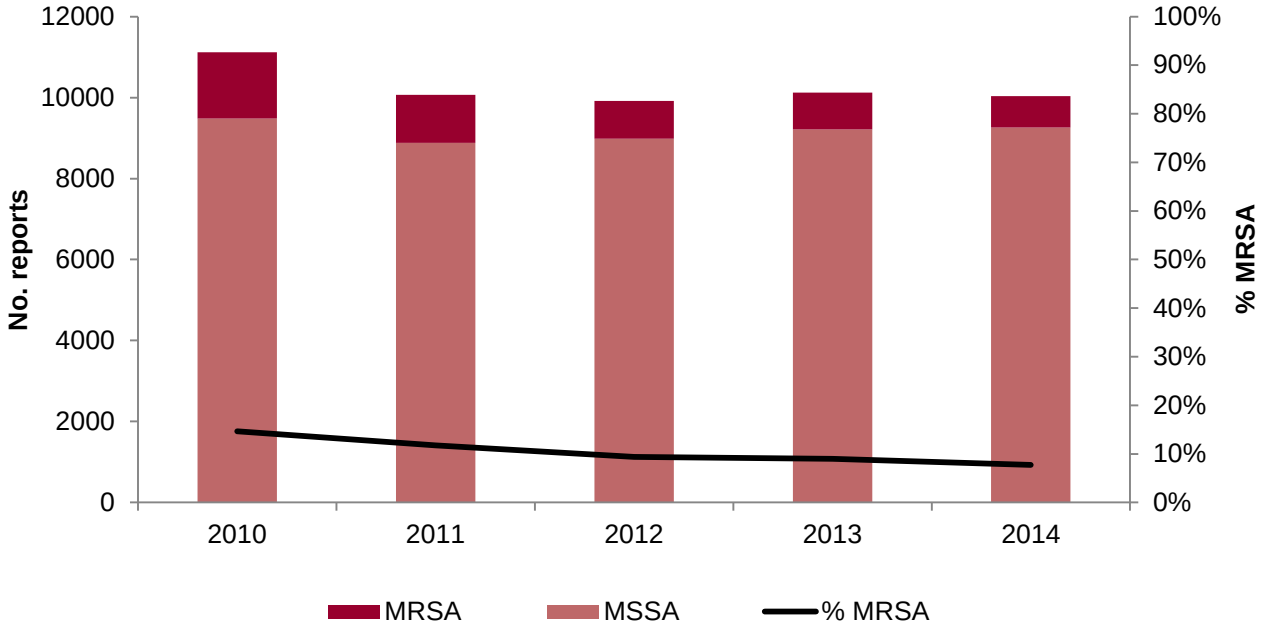


Figure 2.7 Counts of MRSA and MSSA and proportion of total *S. aureus* isolates that are meticillin resistant, England, 2010−2014

Incidence and epidemiology of vancomycin-resistant enterococci

The temporal trend in resistance of *Enterococcus* spp. bloodstream isolates to vancomycin is shown in Figure 2.8. There was an 87.5% increase in the proportion of isolates resistant to vancomycin from 8% in 2010 to 15% in 2014. This in large part reflects a year-on-year increase in the proportion of *E. faecium* isolates (the second most common species of *Enterococcus* from blood) that were resistant to vancomycin, from 17% in 2010 to 25% in 2014.[13] In contrast, only about 2% of *E. faecalis* isolates (the commonest species of *Enterococcus* from blood) were vancomycin-resistant.

While surveillance programmes frequently focus on isolates cultured from blood, enterococci can infect or colonise a range of clinical sites. Analysis of isolates for which antibiotic susceptibility data was reported to the AMR module of SGSS in 2014 showed that for 126,404 isolates of *Enterococcus* spp., the most common well-defined sites of isolation reported were urine/kidney (76.8%), followed by skin/wound (5.5%) and blood (3.3%). A wide range of other anatomical isolation sites (eg faeces/lower gut, 1%, bone, 0.3%; peritoneum, 0.3%; liver/bile, 0.2%) or clinical sources (eg intra-vascular line, 0.5%) were also reported, but the large number of poorly defined sources (eg ‘swab’ 3.5%, ‘tissue’ 1.7%, ‘fluid’ 1.5%, ‘pus’ 0.8%) limits the robustness of the data.

[13] Voluntary surveillance of *Enterococcus* spp. bacteraemia, England, Wales and Northern Ireland: 2014. Health Protection Report; 9 (14). 17 April 2015. Available at: https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/427950/hpr1715_ntrcccs.pdf

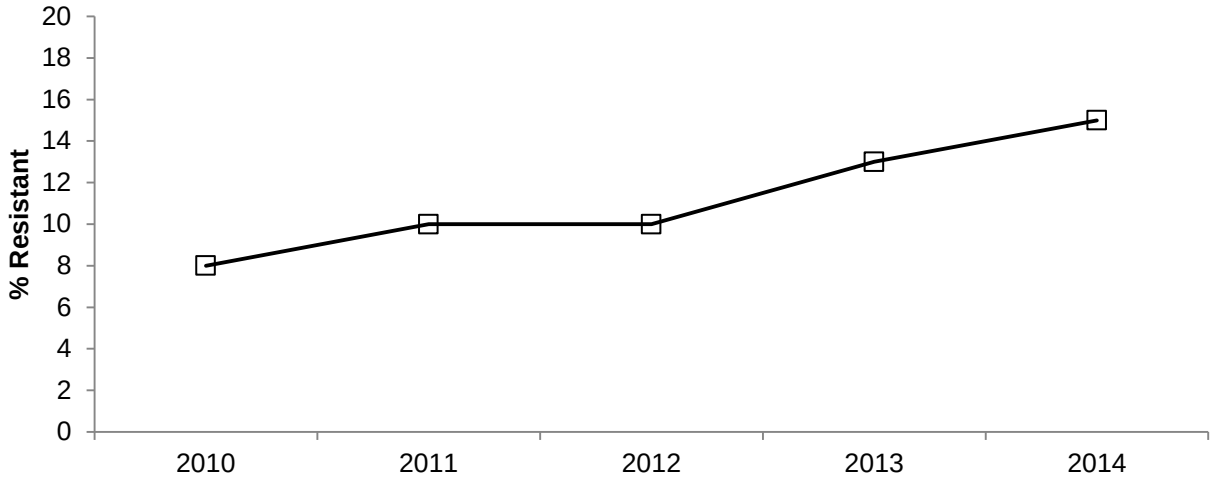


Figure 2.8 Proportion of bloodstream isolates of *Enterococcus* spp. resistant to vancomycin, England, 2010−2014

The numbers and proportions of isolates of *Enterococcus* spp. obtained from blood or from all other sites that were tested for susceptibility to vancomycin, and the proportions reported as resistant in 2014 are shown in Table 2.2.

Table 2.2 Vancomycin resistance among enterococci, England, 2014

Source	No of isolates	% tested	% resistant
Blood	4,186	91.4	14.4
All other sites	122,218	50.1	8.1

The proportion of enterococci from sites other than blood that were vancomycin-resistant (8.1%) was lower than the proportion seen with isolates from blood culture (14.4%). However, this finding should be interpreted with caution as only half the enterococci from sites other than blood were tested for susceptibility to vancomycin, compared to 91% of enterococci from blood cultures. Among 97,086 isolates reported as being from urine/kidney, 43,413 (45%) were tested for susceptibility to vancomycin, of which 3% were resistant.

The numbers and proportions of isolates of different species of enterococci from blood or other sites that were resistant to vancomycin is shown in Table 2.3. *Enterococcus faecalis* was the commonest species identified from both blood culture and other sources. However, detailed analysis of the species identification of enterococci from clinical sources is compromised by the finding that 19% of the isolates from blood and 70% of isolates from sources other than blood were not reported at species level. A further consideration is that *E. gallinarum* and *E. casseliflavus* are intrinsically resistant

to low levels of vancomycin due to the presence of the *vanC* gene. However, about half of the isolates of these species were not reported as vancomycin-resistant, suggesting either they were mis-identified or that the vancomycin susceptibility test result was incorrect.

Table 2.3 Vancomycin resistance among different species of enterococci, England, 2014

Species (Clinical Source)	No (%) of isolates	% tested	% Resistant
(a) Blood			
E. avium	38 (0.9)	89	3
E. casseliflavus*	30 (0.7)	83	52
E. durans	17 (0.4)	100	0
E. faecalis	1699 (40.6)	91	2
E. faecium	1529 (36.5)	94	21
E. gallinarum*	59 (1.4)	86	45
E. raffinosus	17 (0.4)	100	29
E. hirae	3 (0.1)	100	0
***Enterococcus* spp.**	794 (19.0)	88	26
(b) Other sites			
E. avium	175 (0.1)	85	2
E. casseliflavus*	55 (0.1)	84	41
E. durans	32 (<0.1)	88	11
E. faecalis	28489 (23.3)	54	1
E. faecium	7497 (6.1)	90	41
E. gallinarum*	149 (0.1)	80	56
E. raffinosus	117 (0.1)	87	18
E. hirae	10 (<0.1)	90	0
***Enterococcus* spp.**	85694 (70.1)	45	5

* Intrinsic low level resistance to glycopeptides

Urinary tract infections caused by *E. coli*

Data from the mandatory surveillance of *E. coli* bacteraemia indicate that when underlying foci of infection are reported, the urogenital tract predominates, with over half of such reports listing this site. Hence, an understanding of the incidence and epidemiology of UTIs, together with an assessment of the proportion of such infections caused by antibiotic-resistant strains, may not only give greater insight into the burden of UTIs per se, but may lead to interventions that could impact on the occurrence of associated *E. coli* bloodstream infections.

Analysis of reports submitted to the AMR module of SGSS indicated that 711,960 isolates of *E. coli* from urine were subjected to antibiotic susceptibility testing by reporting laboratories in 2014. This equates to an incidence rate of 1,322 cases per 100,000 population, although the true incidence will be likely higher due to under ascertainment of cases given that laboratory testing is recommended in children, or for complicated or recurrent cases in adults and not all urinary bacteria are identified to species level. The isolates were categorised into three groups on the basis of specimen referral, comprising GP practices (n=373,328, 52.4%), other community sources (n=75,303, 10.6%) and acute trusts (n=263,329, 37%). The community sources included care homes and outpatient clinics.

The proportion of isolates from each of the three sources that were tested for susceptibility to a range of antibiotics, and the proportions of tested isolates that were resistant are shown in Figure 2.9. The antibiotics included nitrofurantoin and trimethoprim, as these are first-line agents for treatment of urinary tract infections, and also ciprofloxacin, third-generation cephalosporins, piperacillin/tazobactam and carbapenems, to allow comparison with the data on *E. coli* from bloodstream infections. Greater than 96% of isolates from GP practices and acute trusts were tested for susceptibility to trimethoprim and nitrofurantoin, while 83% of isolates from other community sources were also tested against these antibiotics.

It is reassuring to note that 97% of isolates from all three settings were susceptible to nitrofurantoin. By contrast, resistance to trimethoprim was seen in over a third (35−37%) of isolates, in all three settings.

Amoxicillin is only recommended for treatment of UTI when the infecting strain is known to be susceptible, and it is noteworthy that resistance to amoxicillin was seen in over 50% of isolates from all three settings (data not presented). Rates of co-amoxiclav resistance for UTIs are also not presented as the rates of resistance in urine and blood culture isolates are not readily comparable, due to differences in the interpretation of susceptibility test results for isolates from these sites.

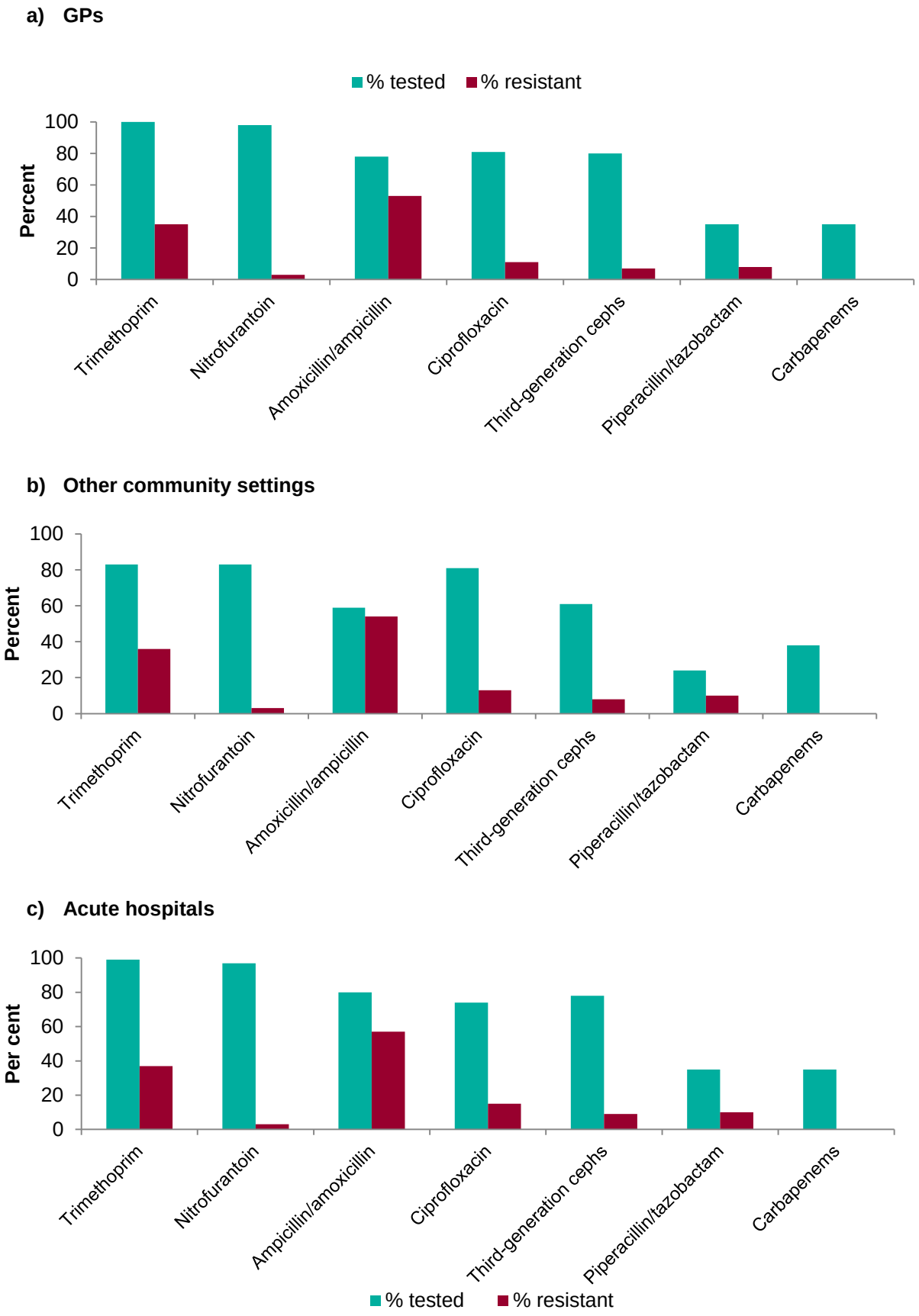


Figure 2.9 Resistance (among the isolates tested) to antibiotics among *E. coli* isolates from urine samples referred from a) GPs, b) other community settings, c) acute hospitals, England, 2014

It should be borne in mind, however, that these data may overestimate the extent of resistance as well as under-estimate the incidence of UTI, particularly in primary care, as much antibiotic prescribing by GPs is empirical. Although urine samples are submitted for microbiological examination from some patients, the likelihood is that such specimens may be preferentially submitted following initial antibiotic treatment failure, or from patients with histories of repeated or complicated infections who may have received multiple courses of antibiotics. Thus the data may be biased towards a cohort of patients with a history of antibiotic use, potentially enriching the sample population for resistant strains.

Surveillance of carbapenemase-producing Gram-negative bacteria

While the data shown above indicate that carbapenem resistance remains uncommon in *E. coli* and *Klebsiella* spp. isolated from blood (≥98% of isolates susceptible), data from the PHE AMR and Healthcare-Associated Infections (AMRHAI) Reference Unit shows a dramatic year-on-year increase in the numbers of isolates of Gram-negative bacteria confirmed to produce carbapenemases, with >1,600 isolates so confirmed in 2014 (Figure 2.10).

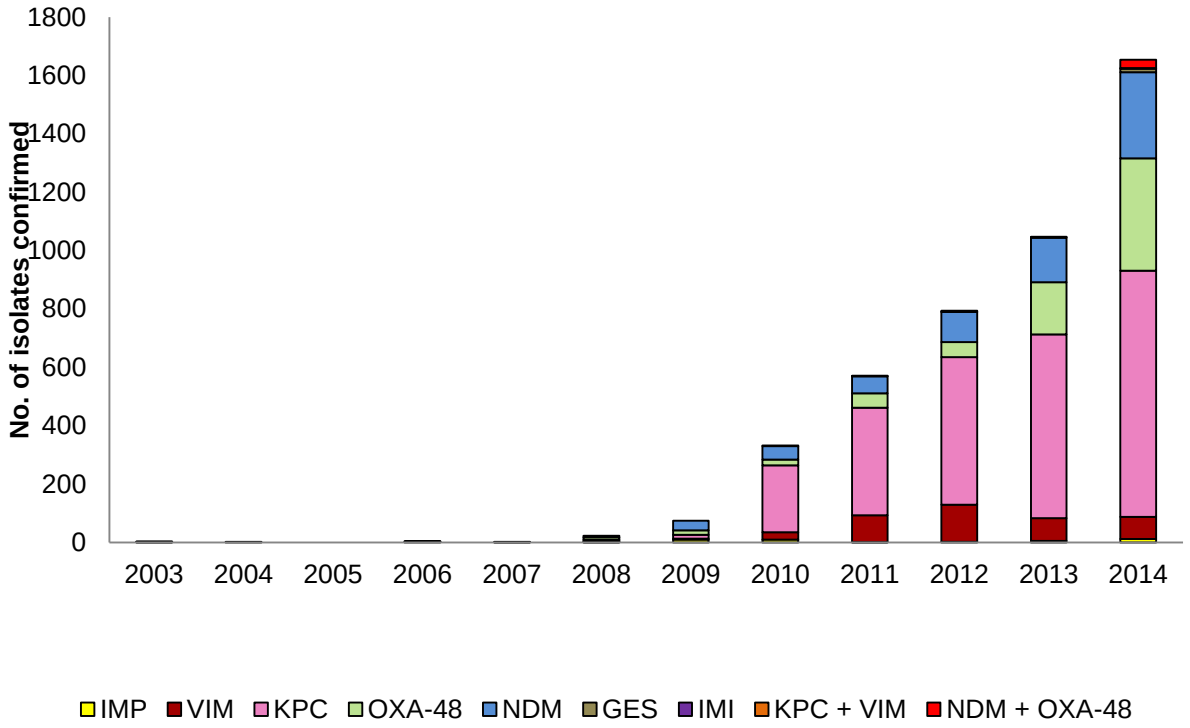


Figure 2.10 Number of isolates referred from UK hospital microbiology laboratories confirmed as carbapenemase-producing Enterobacteriaceae by AMRHAI, 2003−2014

While the above data gives insight into the molecular basis of carbapenem resistance in terms of the types of carbapenemases found, the information provided by laboratories when referring isolates for testing often lacks demographic, clinical and epidemiological detail. This paucity of associated information limits the usefulness of analytical outputs in terms of a key objective of surveillance, namely providing information for action. PHE is addressing this issue by implementing an enhanced reporting system (ERS) for carbapenemase-producing Gram-negative bacteria (see also Chapter 5:).

The ERS, which went live in May 2015, comprises a web-based system that allows laboratories in England to submit surveillance data when requesting full characterisation of Gram-negative bacteria where expression of an acquired carbapenemase is suspected. Data collection is via a two-stage process with patient demographic data, laboratory details and information on the healthcare setting being provided by laboratories at the time of submission of isolates to AMRHAI or a regional PHE public health laboratory. Following confirmation of carbapenemase production, hospital microbiologists or infection prevention and control teams are then requested to provide additional enhanced data including travel history, admission details and potential contact with other patients colonised or infected with carbapenem-resistant organisms. 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.

The results of testing for carbapenemase production undertaken by the PHE national and regional public health laboratories will be made available on the system. When the majority of hospital laboratories are routinely using the system, the availability of the enhanced data set should be of interest to both microbiologists and infection prevention and control teams and will help in a number of settings including the rapid characterisation of outbreaks involving carbapenemase producers. The enhanced data set will also improve our understanding of both local and national epidemiology, particularly with regard to distinguishing nosocomial acquisition from community or foreign acquisition. The data will also input into the evaluation of control measures and contribute to improving the evidence base for setting policy.

Drug resistance in TB

Overall TB case notifications and rates

In 2014 in England, 6,520 cases of TB were notified, a rate of 12.0 cases per 100,000 population (95% confidence interval (CI) 11.7−12.3) (Figure 2.11). Seventy two percent (4,610/6,384) of cases were born outside the UK.

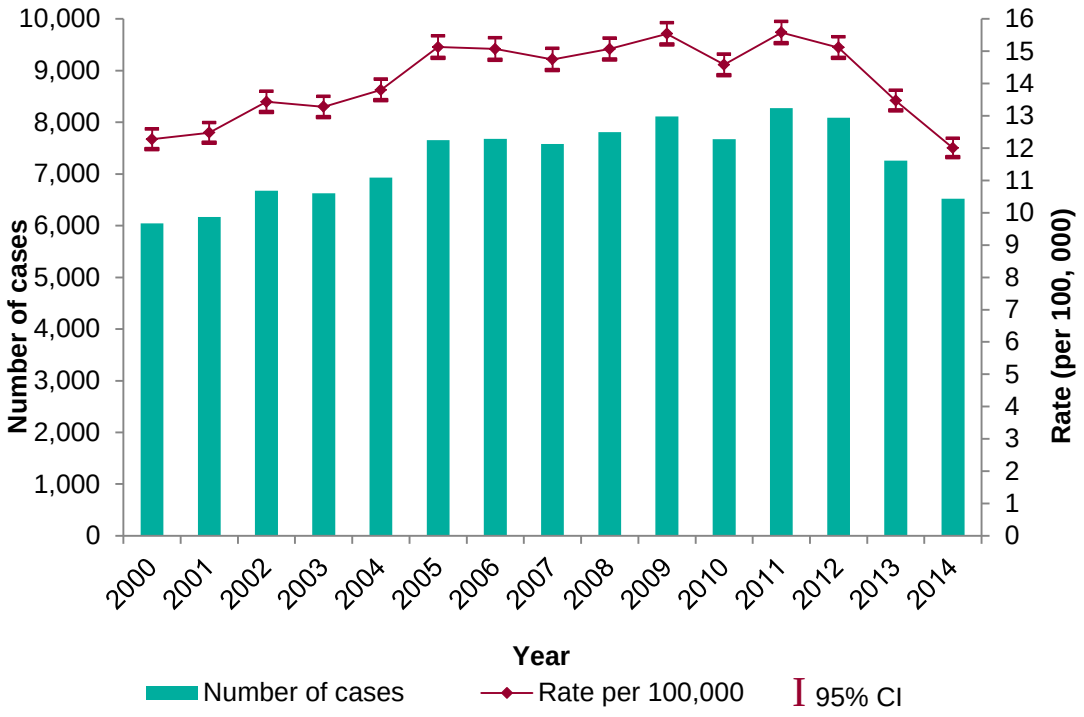


Figure 2.11 TB case notifications and rates, England, 2000−2014

Culture confirmation

Of the TB cases notified in 2014, 60.0% (3,914/6,520) were culture confirmed. A higher proportion of pulmonary cases were culture confirmed compared with extra-pulmonary cases (72.3% [2,482/3,434] versus 46.7% [1,430/3,059]).

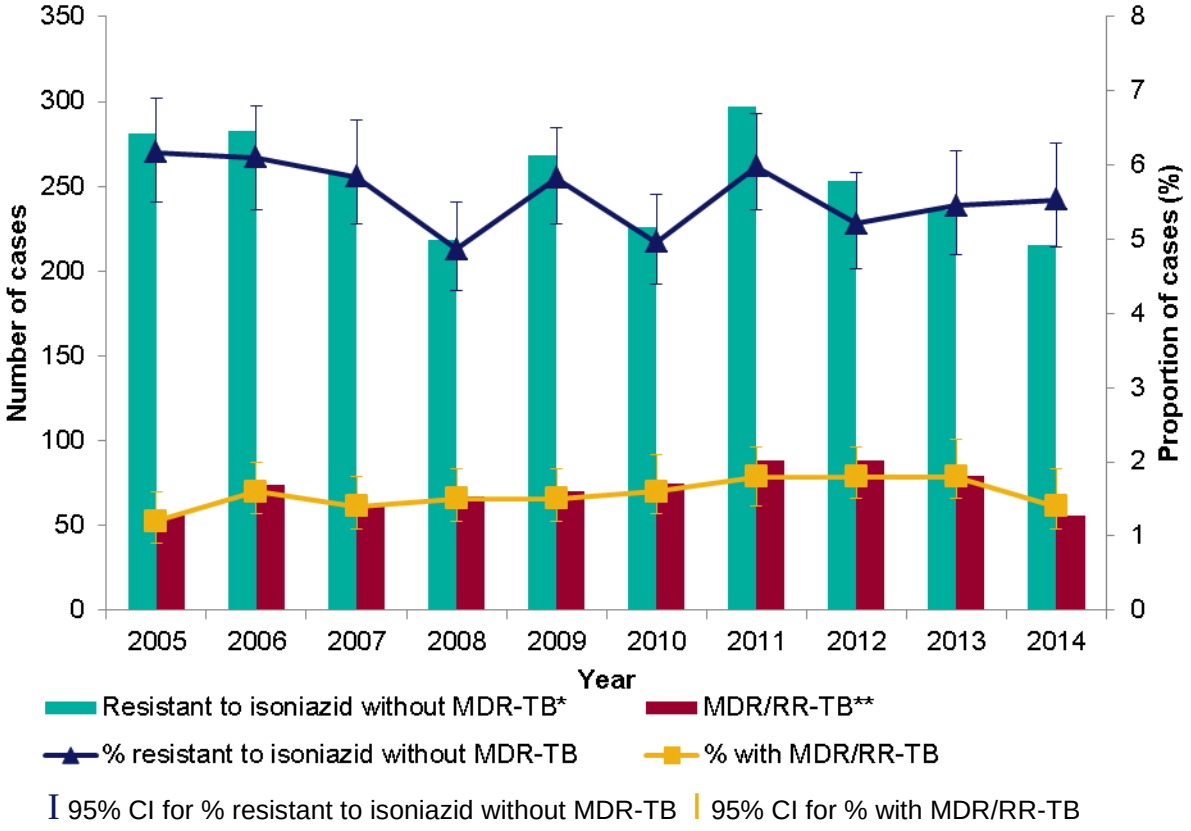
Initial first-line drug resistance

In 2014, drug susceptibility test (DST) results for at least isoniazid and rifampicin were available for 99.4% (3,889/3,914) of culture-confirmed cases notified in England. Seven percent (286/3,889) were initially resistant to at least one first-line antibiotic.

Initial isoniazid resistance without MDR-TB

In 2014, 5.5% (215/3,889) of TB cases had initial resistance to isoniazid without multi-drug resistant TB (MDR-TB), which is similar to previous years (Figure 2.12, Table 2.4).

In 2014, the proportion of cases resistant to isoniazid without MDR-TB was similar in UK born and non-UK born cases (5.4%, 52/967 versus 5.7%, 162/2,833). The most frequent countries of birth of cases resistant to isoniazid without MDR-TB were the UK (52), India (40) and Pakistan (27). A high proportion (18.4%, 34/185) of cases resistant to isoniazid without MDR-TB had at least one known social risk factor (history of past or current drug misuse, alcohol misuse, imprisonment or homelessness).



*Culture confirmed cases with DST results for at least isoniazid and rifampicin 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

Figure 2.12 Number and proportion of TB cases with initial drug resistance, England, 2005−2014

Initial multi-drug resistant/rifampicin-resistant (MDR/RR) TB

The number and proportion of initial MDR-TB cases increased from 41 (0.9%) in 2005 to a peak of 80 (1.6%) in 2011, and has since decreased to 52 (1.3%) in 2014 (Table 2.4).

There were 56 cases with MDR/RR-TB in 2014 (Table 2.4, Figure 2.12). The proportion of MDR/RR TB cases that were resistant to rifampicin without MDR-TB decreased over the past decade from 26.8% (15/56) in 2005 to 7.1% (4/56) in 2014, so in recent years the vast majority of cases of rifampicin resistance were MDR-TB (Table 2.4).

The majority of MDR/RR-TB cases notified in 2014 were non-UK born (88.9%, 48/54) and had entered the UK within the past five years (56.8%, 25/44). The most frequent countries of birth of MDR/RR-TB cases notified in 2014 were Lithuania (11), India (10) and the UK (6). Lithuania had the highest proportion of MDR/RR-TB cases (23.9%, 11/46). A high proportion (16.3%, 8/49) of MDR/RR-TB cases in 2014 had at least one known social risk factor.

Table 2.4 Number and proportion of TB cases with drug resistance, England, 2005−2014

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	XDR-TB cases	
	n	%	n	%	n	%	n	%	%	n	%
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	257	5.8	13	0.3	49	1.1	62	1.4	21.0	0	0.0
2008	218	4.9	18	0.4	49	1.1	67	1.5	26.9	2	0.04
2009	268	5.8	11	0.2	59	1.3	70	1.5	15.7	2	0.04
2010	226	5.0	10	0.2	65	1.4	75	1.7	13.3	2	0.04
2011	297	6.0	8	0.2	80	1.6	88	1.8	9.1	6	0.1
2012	253	5.2	10	0.2	78	1.6	88	1.8	11.4	2	0.04
2013	236	5.5	11	0.3	68	1.6	79	1.8	13.9	3	0.1
2014	215	5.5	4	0.1	52	1.3	56	1.4	7.1	3	0.1
Total	**2,534**	**5.6**	**120**	**0.3**	**595**	**1.3**	**715**	**1.6**	**16.8**	**20**	**0.04**

* 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 XDR-TB

One quarter (14/56) of the MDR/RR-TB cases were resistant to all four first-line drugs. The proportion of MDR/RR-TB cases notified in 2014 resistant to an injectable agent was 12.5% (7/56), and the proportion resistant to a fluoroquinolone was 19.6% (11/56).

There were three initial XDR-TB cases notified in 2014 who were born in India, Lithuania and Romania. This is similar to the two to three cases notified each year between 2008 and 2013 (with the exception of 2011 when there were six cases) (Table 2.3).

Drug resistance in *N. gonorrhoeae*

The rate of gonorrhoea infections reported through the national STI surveillance systems was 64.9 per 100,000 in 2014; more than double the incidence rate in 2010.[14] In 2014, 1,568 samples from 27 GUM clinics that take part in GRASP were successfully tested for antimicrobial susceptibility and matched to clinical data. The 2014 GRASP report is available online.[15]

[14] https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/437433/hpr2215_STI_NCSP_v6.pdf
[15] https://www.gov.uk/government/publications/gonococcal-resistance-to-antimicrobials-surveillance-programme-grasp-report

Resistance to first-line therapy (combination of ceftriaxone and azithromycin)

There were no isolates identified with decreased susceptibility to ceftriaxone and there was a slight decline in resistance to azithromycin from 1.6% in 2013 to 1.0% in 2014. Three isolates from men who have sex with men (MSM), one of the population sub-groups at highest risk of acquiring antimicrobial resistant *N. gonorrhoeae* infection, exhibited high-level azithromycin resistance (MIC > 256 mg/L).

Drug resistance to previous first line therapies

The prevalence of isolates exhibiting decreased susceptibility to cefixime declined from 5.2% in 2013 to 1.4% in 2014. Over the same time resistance to ciprofloxacin increased from 29.3% to 37.3% and resistance to penicillin increased from 18.4% to 22.6%.

Discussion

This report both extends surveillance data on AMR initially presented in the 2014 ESPAUR report and highlights developments and new initiatives aimed at improving surveillance, in support of the UK national strategy for tackling resistance. Surveillance of the antimicrobial susceptibility of common pathogens causing bloodstream infections remains a priority as many surveillance systems in other parts of the world are also focussed on this infection site, allowing both inter-country comparisons and pooling of data to provide the bigger picture in terms of the global threat posed by resistance. Indeed, the World Health Organization is seeking to establish global surveillance of AMR, an initiative that is also actively supported by the UK as part of the national AMR strategy. However, in clinical terms, bloodstream infections may be considered the ‘tip of the iceberg’ with infections at other body sites being much more common. Hence there is a need to expand surveillance activities to include other types of infection in order to get a fuller understanding of the epidemiology of resistance.

Two new areas of surveillance presented for the first time are the occurrence of infections caused by vancomycin-resistant enterococci in sites other than the bloodstream and UTIs caused by *E. coli*. The finding that bloodstream infections comprise only a small proportion of enterococcal infections highlights the value of extending surveillance to isolates from other sites. However, the data presented throw up a number of challenges, particularly the large proportion of isolates from non-blood sites that are not identified to species level. Lack of species identification of bacterial isolates clearly limits the complexity of analysis that can be undertaken, which in turn limits our ability to increase our understanding of the epidemiology of such infections. Lack of species identification in routine clinical microbiology may reflect the dichotomy between using the finite available resources to generate the information required for effective management of individual patients and generation of information that might be applicable to a broader public health agenda.

The other area of new data presentation relates to *E. coli* causing UTIs. This is an important area of work as data from the national mandatory programme for surveillance of *E. coli* bacteraemia indicates that over half the patients where an underlying focus of infection is recorded have a UTI. Thus better management and/or prevention of UTIs may not only decrease the burden of these infections per se, but may also reduce the incidence of subsequent bloodstream infection. However, as highlighted earlier in this report, data on antibiotic resistance among *E. coli* isolated from urine samples from patients in the community may overestimate the proportion of resistant isolates due to likely referral bias. Generation of more robust data on the antibiotic susceptibility of *E. coli* and other pathogens causing UTIs in the community will require the establishment of surveillance involving sentinel GP practices who will refer unselected urine samples for microbiological examination, including susceptibility testing either on a continual routine basis or possibly as a series of point prevalence studies.

Data on drug-resistant TB is also presented in this report. In the past three years there has been a year-on-year decline in the total number of TB cases in England, down to 6,520 in 2014. However, England is still the country with the highest number of TB cases in Western Europe. The proportion of TB cases with drug resistance has remained fairly stable over the past decade, with between 4.9% and 6.2% having initial resistance to isoniazid without MDR-TB and between 1.2% and 1.8% having MDR/RR-TB. While the number of new MDR-TB cases diagnosed each year is small, the significant burden posed by drug-resistant TB should not be underestimated. Treatment of TB entails prolonged antibiotic therapy, with drug-resistant cases requiring treatment for 24 months or longer. MDR-TB treatment comprises complex regimens of multiple antibiotics with high toxicity, so patients require considerable social and clinical support if they are to comply with the treatment regimen in order to achieve a favourable outcome. Infection control for MDR-TB patients can also be challenging, as they remain infectious for considerably longer than patients infected with drug-susceptible strains. Reducing drug-resistant TB is one of the ten key areas for action in the Collaborative TB Strategy for England 2015−2020, and there are several monitoring indicators for drug resistant TB as part of the strategy.[16] Further details on the occurrence and management of TB cases in England can be found in the 2015 PHE annual report.[17]

Treatment of gonorrhoea continues to provide a challenge. Widespread resistance to previous first-line treatment options including penicillin and ciprofloxacin means that these drugs are no longer suitable for empirical therapy. Current treatment guidelines recommend a combination of ceftriaxone and azithromycin and on-going surveillance via GRASP remains crucial to monitoring the efficacy of treatment options and for identifying patient groups at increased risk of infection with resistant strains. Fuller

[16] Collaborative Tuberculosis Strategy for England: 2015 to 2020 available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/403231/Collaborative_TB_Strategy_for_England_2015_2020.pdf

[17] Tuberculosis in England 2015 Report (presenting data to end of 2014) available at https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/464914/TB_Annual_Report_2015.pdf

information on the incidence and epidemiology of gonorrhoea is available in the annual GRASP report published at the same time as this report.[18]

The action point in the UK national strategy for tackling AMR relating to surveillance refers to “better access to and use of surveillance data”. To this end PHE and ESPAUR are working towards improving the feedback and/or availability of data both at national and local levels. The national database SGSS has built-in AMR reporting tools that allow participating laboratories to produce both standard reports on their local data as well as run *ad hoc* queries. In addition PHE Field Epidemiology Service produces a quarterly AMR surveillance workbook providing local data including the number of isolates of particular pathogens tested, trends in the proportion of isolates that are resistant to key antibiotics, and the level of resistance in isolates from different clinical sources. A new initiative to help stakeholders drive local quality improvement is also currently being developed. This initiative aims to help inform stakeholders how to develop local antimicrobial stewardship, resistance and infection control (ASRIC) action plans by providing openly accessible local data as well as information on where to access guidance, educational resources and examples of best practice. By means of initiatives such as this, surveillance of AMR will increasingly achieve its main objective of providing information for action.

[18] Gonococcal Resistance to Antimicrobials Surveillance Programme report 2014 available at https://www.gov.uk/government/publications/gonococcal-resistance-to-antimicrobials-surveillance-programme-grasp-report

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. This year's report presents antimicrobial usage trends concentrating on improved granularity in the data compared to last year, highlighting dental and other community prescribing, in addition to general practice and showing hospital prescribing by Trust.

The chapter also highlights the importance of the unit of measurement including the denominator across different hospital types. Continuous measurement, with the ability to identify the site of the prescription, is essential for tracking antibiotic use over time and determining the effectiveness of AMS programmes. Continuous measurement is especially important for reducing total and broad-spectrum antibiotic use in each area of clinical practice.

There is no one ideal measure that allows the detailed understanding of prescribing. The only unit of measurement that can be combined across all clinical settings at present is the defined daily dose (DDD), which is the internationally recognised unit of measurement of medicine consumption, recommended by the WHO. The DDD is the assumed average maintenance dose per day for a medicine used for its main indication in adults. In general, the DDDs for antibiotics is based on their use in infections of moderate severity. The value of using DDDs is that it allows continuous tracking of total and individual organisation level antibiotic use over time both nationally and regionally, using national and regional populations as a denominator. This is important as AMS programmes and changes in healthcare delivery, may displace prescribing from one area of practice to another eg from general practice, to out-of-hours or walk-in centres, or from hospital outpatients to general practice. The use of DDDs also allows international comparisons, for example with other European countries through data collected by ECDC in the European Surveillance of Antimicrobial Consumption Network (ESAC-Net).

Data on antibiotic use in primary care is also presented using the number of dispensed items. A prescription item refers to a single supply of a medicine prescribed on a prescription form. If a prescription form includes three different antibiotics then it is counted as three prescription items. Items do not, however, provide any indication of the length of treatment or the dose prescribed. It should be noted that data on prescription items is not useful in secondary care, as many drugs may be dispensed to a ward area

in bulk and therefore it is not a measure of single items per prescription per patient. Where possible (ie community prescriptions), the number of antibiotic prescriptions is also measured.

The importance of using both DDD and prescription items, where available, to monitor antibiotic usage is highlighted in Figure 3.1. This shows that while the number of prescription items remained stable in England over the last 15 years, antibiotic usage measured as DDDs increased. This indicates that there have been changes in antibiotic dose per day and/or duration of antibiotic courses.

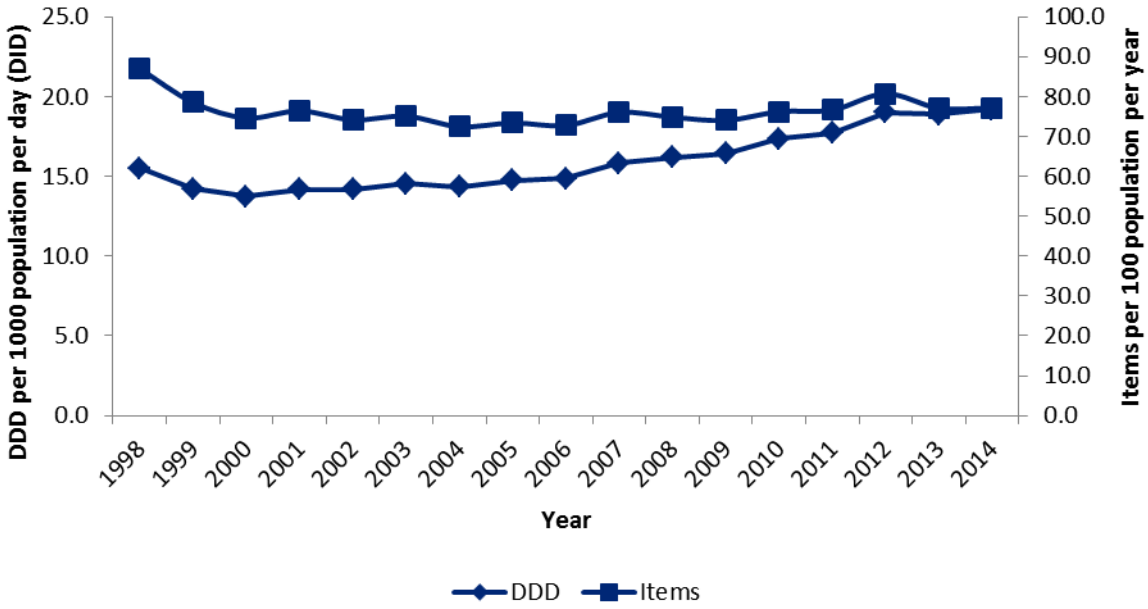


Figure 3.1 Prescriptions dispensed in the community, expressed as DDD per 1000 inhabitants per day and items per 100 inhabitants per year, England, 1998−2014

This chapter also presents the results of the pilot validation of NHS acute trust prescribing data. Currently, antibiotic quantities dispensed by NHS acute trust pharmacies are collected by two independent commercial companies Rx-info and IMS Health. Both IMS Health and Rx-info have in-house quality assurance processes; however, the datasets have not been externally validated. In order to improve the focus on antibiotics, NHS-England included the validation of acute trust prescribing data as part of the Antimicrobial Prescribing Quality Premium for Clinical Commissioning Groups (CCGs) in the 2015/16 financial year. The objectives of the pilot were to develop, test and evaluate the feasibility of the protocol in order to publish the validation protocol for antibiotic use in acute trusts to fulfil the NHS quality premium in 2015/2016.

Methods

All data in this report is presented by calendar year from 2010 to 2014, with the exception of dentist data, which is available from June 2010.

Data source – primary care

General practice

Information on the use of antibiotics prescribed in general practice was obtained from the NHS Business Services Authority (NHSBSA) database and matched to GP codes on the Organisation Data Service (ODS) from data available under Open Government License (OGL) at HSCIC. NHS prescription services internally audit the prescription data as 97.5% accurate.

Dentist

Information on the use of antibiotics prescribed by dental practitioners was obtained from the NHSBSA database.

Other community

Information on community prescribing and dispensing outside general practice and dentistry (GP out-of-hours services, walk-in centres, urgent emergency care, community health services, hospital services, nursing homes, public health services, hospices and custody services) was obtained from the NHSBSA database and matched to other community service codes on the ODS.

Data source – secondary care

Information on the use of antibiotics in secondary care was obtained from IMS Health. The database held by IMS Health collects information from 99% of NHS hospital pharmacy systems, for drugs dispensed to individual patients and wards. All NHS trusts were included. Individual hospital data is not shown as this forms part of the current confidentiality agreement with IMS Health. Data for individual organisations was categorised by inpatient or outpatient (including day-case, regular day attenders and A&E), where possible, for individual organisations, and then grouped to area team level. This data has not been externally validated at an individual organisation level. Antibiotics included may reflect dispensing from the hospital pharmacy to acute hospital inpatients, urgent care centres and potentially non-acute sites where hospital pharmacies supply drugs.

Classification of data

The classification of data on antibiotic use was based on the anatomical therapeutic chemical (ATC) classification system.[19] 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).

Data definitions

Data is broken down as follows:

- general practice – prescriptions written in general practice by medical and non-medical prescribers
- other – community prescribing and dispensing outside general practice; this largely includes individuals who are in prison, walk-in centres, out-of-hours services, and community care centres and nurses
- dentist – prescriptions written by prescribers in dental practices
- hospital inpatient − prescriptions written by a hospital prescriber (medical, nursing, non-medical prescribers) and dispensed for an individual patient when an inpatient and antibiotics that are dispensed to a ward to be available in emergencies and out of hours
- hospital outpatient – prescriptions written by a hospital prescriber and dispensed by the hospital pharmacy for a patient attending the hospital as an outpatient, at a day unit, A&E, urgent care centre located in the hospital or in a community site with hospital practitioners

As outlined above, data on primary and secondary care use of antibiotics were presented using DDDs. For further details on DDD methodology, please see the WHO Collaborating Centre for Drug Statistics Methodology website at http://www.whocc.no/atc_ddd_index/

CAVEAT: The results shown in this report for primary care oral suspensions and liquids differ from figures published in the ESPAUR Report 2014 as they have been re-calculated following identification of an error in the calculation of DDD. The secondary care co-amoxiclav data from IMS Health was recalculated due to an error in the IMS extraction methods. All data tables have been updated and are available as a web-appendix.

In order to compare results internationally, especially with other data available in Europe, the data was presented as total DDD per 1000 inhabitants per day in England. Additionally, primary care prescriptions were presented as number of items per 1000

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

inhabitants per day and secondary care data as DDD per 100 admissions and per 100 bed-days.

NHS BSA provides quarterly data for indicators on antibiotic prescribing in the community: all antibiotics and broad-spectrum antibiotics (co-amoxiclav, cephalosporins and quinolones). For all antibiotics, the number of antibiotic items per STAR-PU is provided. STAR-PU (specific therapeutic group age-sex weightings related prescribing units) are weighted units to allow comparisons adjusting for the age and sex distribution of patients at each practice .For broad-spectrum antibiotics, the number of broad-spectrum antibiotic items as a proportion of total antibiotic items prescribed is provided. These are available on the information portal of the NHS BSA as part of the medicines optimisations key therapeutic topics (MO KTT). The aim of the comparators is to support organisations and prescribers to review the appropriateness of current prescribing, revise prescribing where appropriate and monitor implementation. The comparators are not intended to be used as targets or performance tables but rather to highlight variation and support local discussion and decisions.

Population denominators

Consumption rates were calculated using 2010, 2011, 2012 and 2013 mid-year resident population estimates, based on the 2011 census for England; 2014 consumption rates are based on 2013 mid-year population estimates since estimates for 2014 had not been released by the time the data were prepared for this report.[20]
Secondary care consumption data was analysed using occupied bed-days (OBD) and hospital admissions as population denominators since there is, as yet, no single agreed method of comparing hospital consumption rates.

Aggregate denominator admission and bed-day data, by five-digit provider code for the calendar years 2010−2014, were extracted from the HES in-patient database using the HES Data Interrogation System (HDIS) and recoded to three-digit Trust level data, with changes in Trust and hospital relationships accounted for over time. Data for individual trusts were then merged to provide an admission and bed-day denominator per Trust type and nationally.

Trend analysis

National and AT trends in the consumption of antibiotics were assessed for the last four years (2011−2014); 2010 was excluded as dental data was unavailable for the entire calendar year. 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 $p<0.05$.

[20] http://www.ons.gov.uk/ons/index.html

Pilot Validation

Fifteen antibiotics which comprised of 85% of total antibiotic use in secondary care along with additional antibiotics that are considered to be of clinical importance were included in the validation protocol. The list of antibiotics validated is outlined in Table 3.1.

An Excel file containing Trust specific spreadsheets was sent by email to a nominated person, usually the antimicrobial pharmacist, within each organisation. Respondents were also asked to submit data that had been extracted directly from the Trust's pharmacy system and not data that had been derived from another source (eg IMS Health, Rx-Info)

Table 3.1 Antibiotics that were validated, England, 2014

Amikacin	Amoxicillin
Amoxicillin / clavulanic acid	Cephalosporins (BNF section 5.1.2.1)
Ciprofloxacin	Clarithromycin
Clindamycin	Daptomycin
Doxycycline	Ertapenem
Erythromycin	Flucloxacillin
Gentamicin	Imipenem with cilastatin
Levofloxacin	Linezolid
Meropenem	Moxifloxacin
Nitrofurantoin	Ofloxacin
Penicillin G	Phenoxymethylpenicillin
Piperacillin-tazobactam	Teicoplanin
Temocillin	Tigecycline
Trimethoprim	Vancomycin

Respondents were asked to return all data entered as unit packs dispensed, for example, and the number of packs or bottles of liquid. Any antibiotic lines which had not been reported by IMS Health were requested to be added at the end of the relevant worksheet.

The following data was to be excluded from any consumption data that each Trust reports:

- antibiotics dispensed to manufacturing units and between one pharmacy store and another pharmacy store within the Trust (ie only antibiotics dispensed to patients or ward stock was included)
- antibiotics dispensed to other Trusts and hospitals that would stock-take independently

Feedback on validation protocol

Staff at acute trusts who returned their validation worksheets were invited to participate in a feedback survey to understand hospital demographics and to share their views on the feasibility and practical issues related to the implementation of the study. The online survey included questions on the practical and feasible aspects of the validation, eg number of hours to complete data validation, ease/difficulty of data collection and validation, staff level of engagement with antimicrobial consumption data, coding or translation table used for calculating antimicrobial consumption, suggestion for improvement of the validation process.

Participants were also invited to join a teleconference to further discuss the validation protocol and agree next steps. The agenda for the teleconference included further feedback of validation results and survey, and comments on updated validation protocol, defining acceptable proportion differences between IMS record and Trust record that required further investigation.

Ethical approval and permissions

Data to be used was provided by IMS health to Public Health England; 99% of hospitals in England contribute to the IMS dataset. As part of development of ESPAUR programme, all acute NHS Trusts in England have given permission for PHE to access their data held by IMS Health for data validation. No patient identifiable information was processed or collected. The survey of participants is part of service evaluation and did not require ethical approval

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.

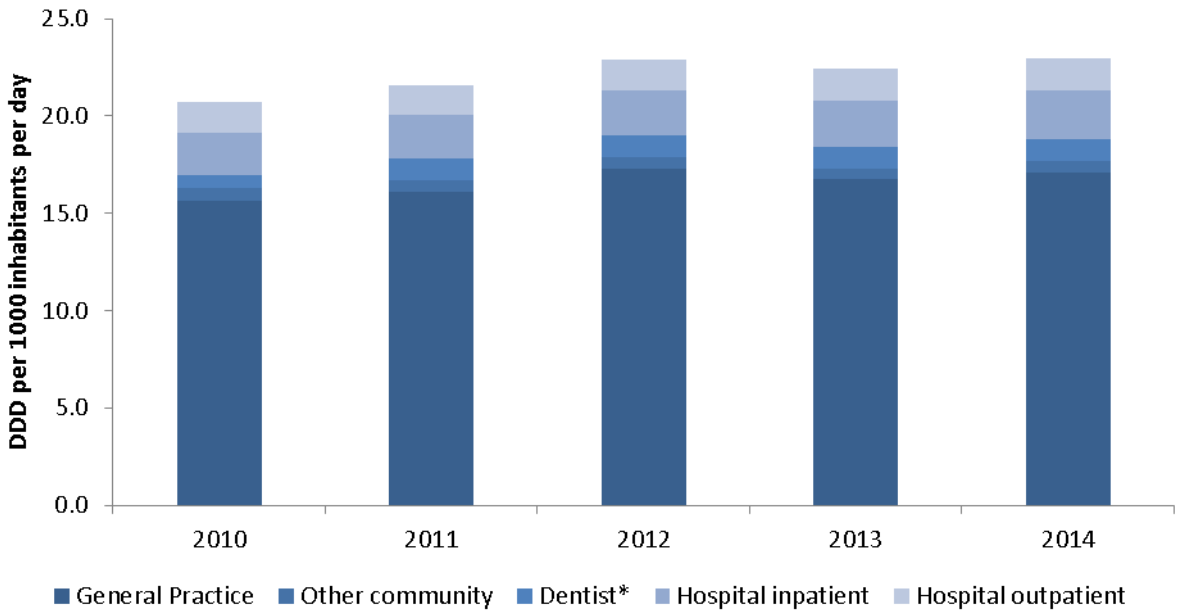
Results

Total consumption of antibiotics

In 2014, the majority of antibiotics in England were prescribed in general practice (74%), followed by prescribing for hospital inpatients (11%), hospital outpatients (7%), patients seen in dental practices (5%) and patients in other community settings (3%).

The total consumption of antibiotics in primary and secondary care increased significantly by 6.5% over the last four years; from 21.6 DDD per 1000 inhabitants in 2011 to 23.0 DDD per 1000 inhabitants in 2014. Between 2013 and 2014, total consumption increased by 2.4% (Figure 3.2).

General practice consumption increased 6.2% (16.1 to 17.1 DDD per 1000 inhabitants) between 2011 and 2014 and 2.1% between 2013 and 2014. Prescribing by dentists decreased by 2.8% (1.13 to 1.10 DDD per 1000 inhabitants) between 2011 and 2014 but increased slightly (0.9%) between 2013 and 2014. There was a 5.5% increase (0.59 to 0.62 DDD per 1000 inhabitants) in prescribing by other community prescribers from 2011−2014, with the largest increase occurring between 2013 and 2014 (9.3%). Prescribing to hospital inpatients increased significantly by 11.7% (2.23 to 2.49 DDD per 1000 inhabitants) and to hospital outpatients by 8.5% (1.57 to 1.71 DDD per 1000 inhabitants) between 2011 and 2014.



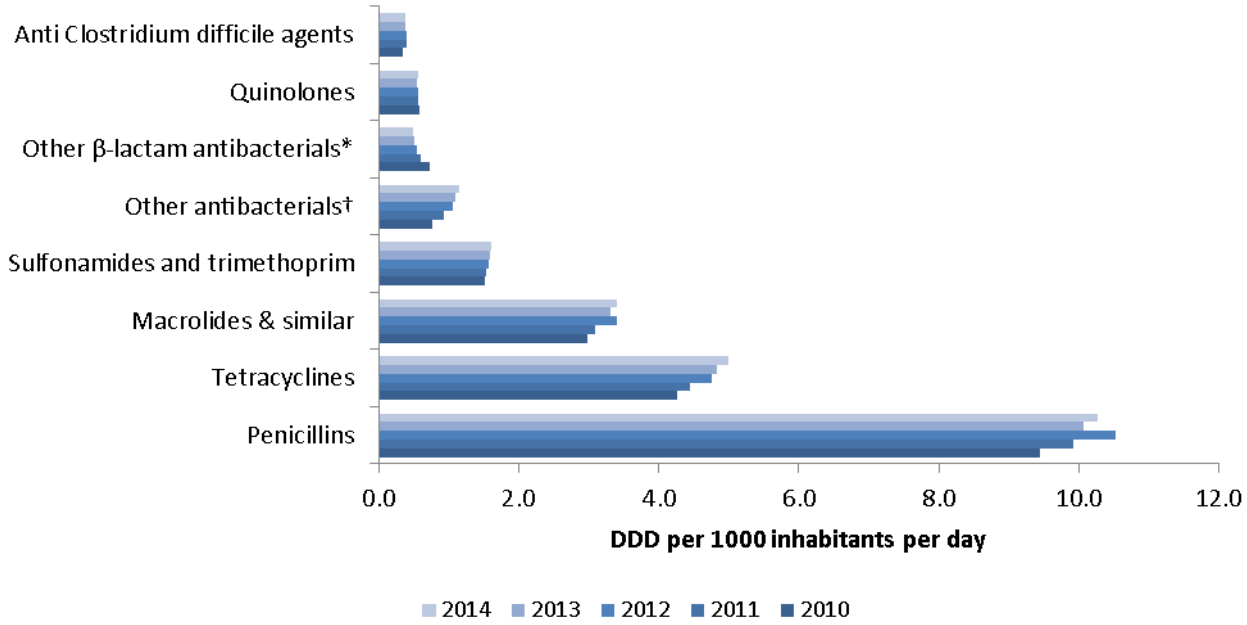
*Data available from June 2010

Figure 3.2 Total antibiotic consumption, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

Total prescribing by key agents

The three groups of antibiotics most frequently used in England in 2014 were penicillins (45%), tetracyclines (22%) and macrolides (15%) (Figure 3.3).

Between 2011 and 2014, a significant increase occurred in the group ‘other antibacterials’ (23%) as well as in tetracyclines (13%) and sulphonamides/trimethoprim (5%). Over the same period, a decrease occurred in the antibiotic consumption of the following groups: other β-lactam antibacterials, which include cephalosporins, carbapenems, and monobactams (-17%), anti-*Clostridium difficile* agents (-3%) and quinolones (-2%).



* includes cephalosporins, carbapenems, and monobactams
† includes glycopeptides, polymyxins, steroid antibacterials, imidazole and nitrofuran derivatives, fosfomycin, linezolid, daptomycin

Figure 3.3 Total antibiotic consumption by key antibiotic group, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

Trends in consumption by antibiotic group

Penicillins

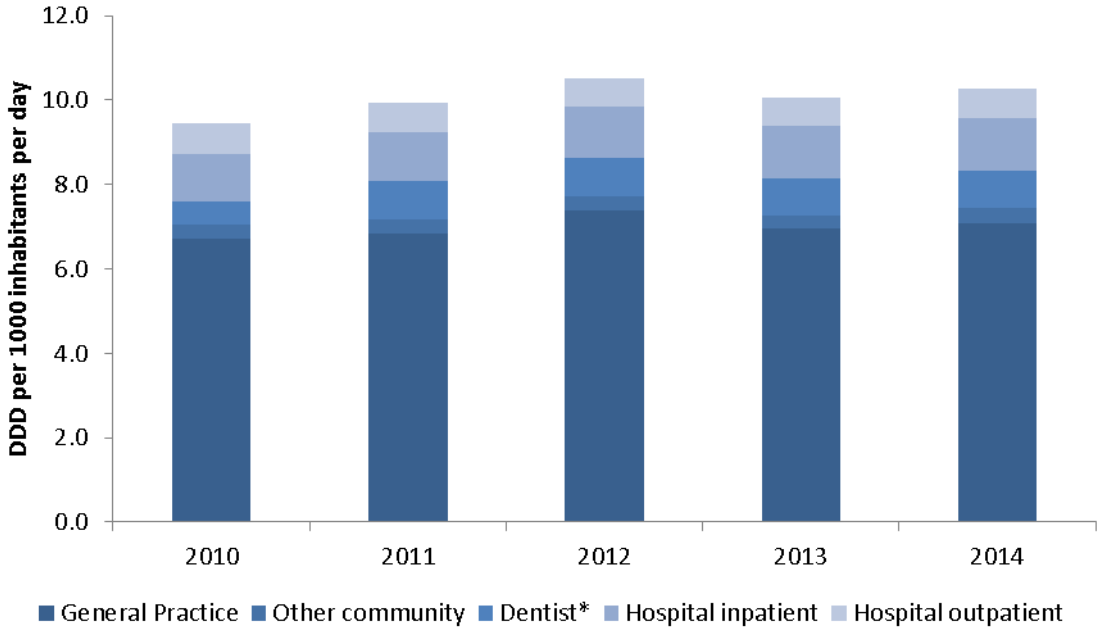
Penicillins include both narrow-spectrum and broad-spectrum agents that are active against a range of Gram-positive and Gram-negative bacteria. β-lactamase-resistant penicillins, predominantly flucloxacillin, are mainly used to treat staphylococcal infections and recommended for the treatment of cellulitis and impetigo. Within the national guidelines, amoxicillin is the primary recommended treatment, where this is indicated, for the majority of upper and lower bacterial respiratory tract infections, while the narrow-spectrum penicillin phenoxymethylpenicillin is recommended for the treatment of non-viral acute sore throat.[21]

The β-lactam/ β-lactamase inhibitor combinations co-amoxiclav and piperacillin-tazobactam are broad-spectrum agents active against a wide range of Gram-positive and Gram-negative pathogens, including anaerobes, with piperacillin having additional anti-pseudomonal activity. In the national community infection guidelines, co-amoxiclav is indicated for the treatment of acute pyelonephritis or animal bites. However, these broad-spectrum agents have a key role to treat hospital sepsis syndromes particularly related to intra-abdominal sepsis or sepsis without a defined source. With the reductions in cephalosporin and quinolone use in England in the last decade, these combination agents have become key agents in many hospital empiric policies.

[21] Management of Infection Guidance for Primary Care. British Infection Association, RCGP and PHE. 2012 available at http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/PrimaryCareGuidance/

Penicillins accounted for 45% of total antibiotic prescribing in England in 2014, increasing by 3.4% between 2011 and 2014 (from 9.9 to 10.3 DDD per 1000 inhabitants) (Figure 3.4). A significant increase occurred in hospital inpatient prescribing (8%) whereas hospital outpatient and dentist prescribing decreased slightly (-0.9% and -1.8% respectively) over the four year period.

Changes in consumption also varied by prescriber from 2013 to 2014: total consumption of penicillins increased by 2% but other community prescribers dispensed 11% more penicillin.



*Data available from June 2010

Figure 3.4 Consumption of penicillin, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

The trends for the consumption of the most commonly used penicillins are shown in Figure 3.5, and demonstrate relative stability overall in England; further review of the β-lactam penicillins in combination with inhibitors will be discussed in the hospital section.

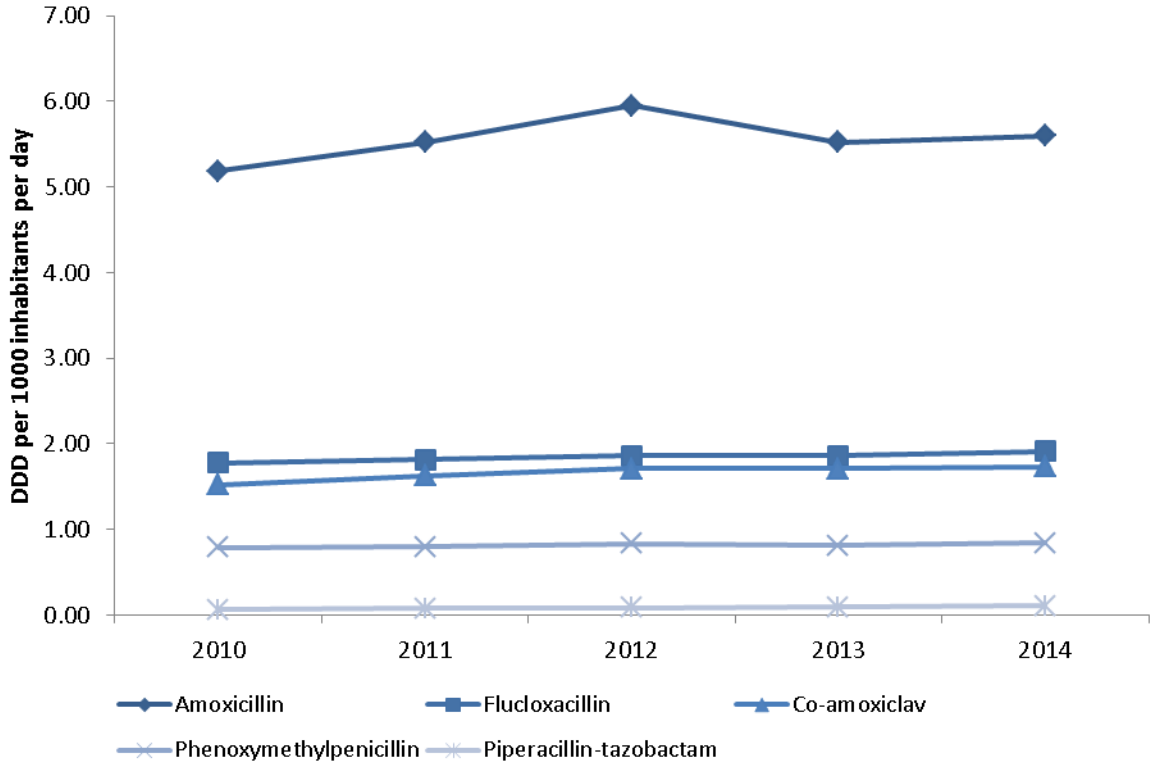


Figure 3.5 Consumption of most commonly utilised penicillins, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

Cephalosporins

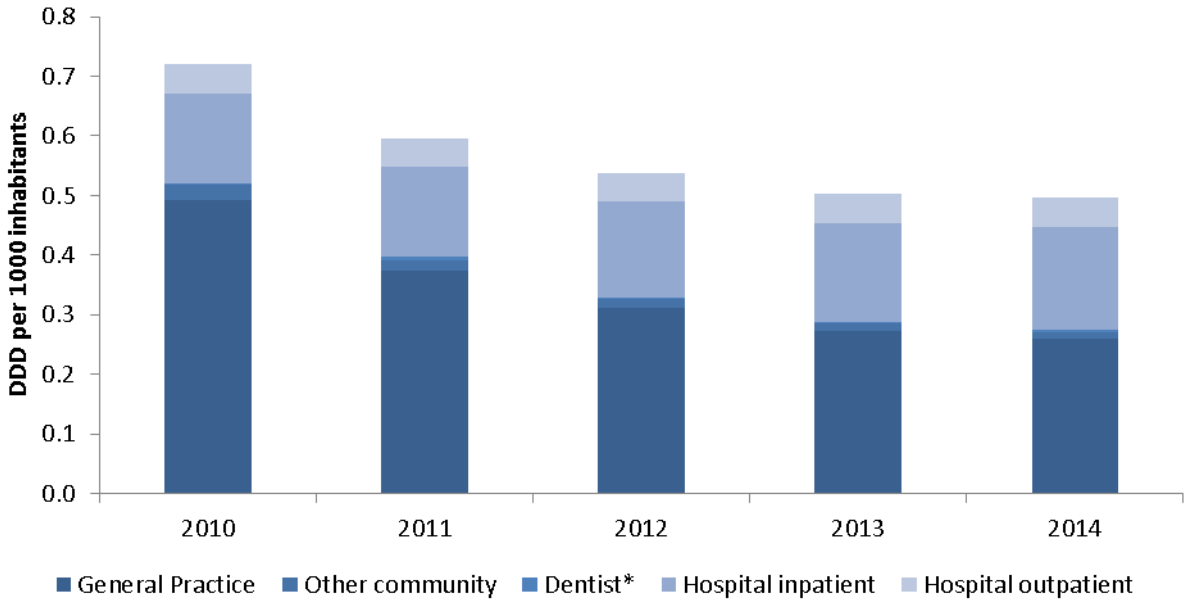
Cephalosporins were first developed in the 1960s and were initially most active against Gram-positive organisms such as staphylococci and streptococci. Subsequently, new generations of cephalosporins were developed that were characterised by improved activity against Gram-negative bacteria. Cephalosporins have demonstrated efficacy in the treatment of hospital and community-acquired pneumonia, intra-abdominal sepsis and urinary tract infections. However, they are recognised to predispose individuals receiving them to *Clostridium difficile* infection and current national guidelines do not recommend their use empirically, with the exception of treatment for meningitis and gonorrhoea.[22] More recently, cephalosporin resistance in gonorrhoea has emerged and the recommended treatment is now a combination of ceftriaxone and azithromycin.[23]

The decline in cephalosporins that occurred between 2010 and 2013 has stabilised with no change in consumption of cephalosporins between 2013 and 2014 (Figure 3.6).

The top six agents used in this class are unchanged from 2013 (Figure 3.7). Oral cephalosporins (cefalexin, cefaclor and cefuroxime) were the predominant

[22] Management of Infection Guidance for Primary Care. British Infection Association, RCGP and PHE. 2015 available at https://www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care
[23] National Guideline on the Management of Gonorrhoea in Adults 2011. Bignell C, Fitzgerald M; Guideline Development Group; British Association for Sexual Health and HIV UK. Int J STD AIDS. 2011;22(10):541-7

cephalosporins consumed, predominantly in the community and use continues to decline. Third-generation cephalosporins (ceftriaxone and cefotaxime) consumption continues to increase, predominantly in hospitals. Ceftriaxone consumption in particular may be increasing due to the ongoing expansion of outpatient parenteral antimicrobial therapy (OPAT) programmes, where its long half-life can facilitate the continuing intravenous treatment of patients in their own homes when required.



*Data available from June 2010

Figure 3.6 Consumption of cephalosporins, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

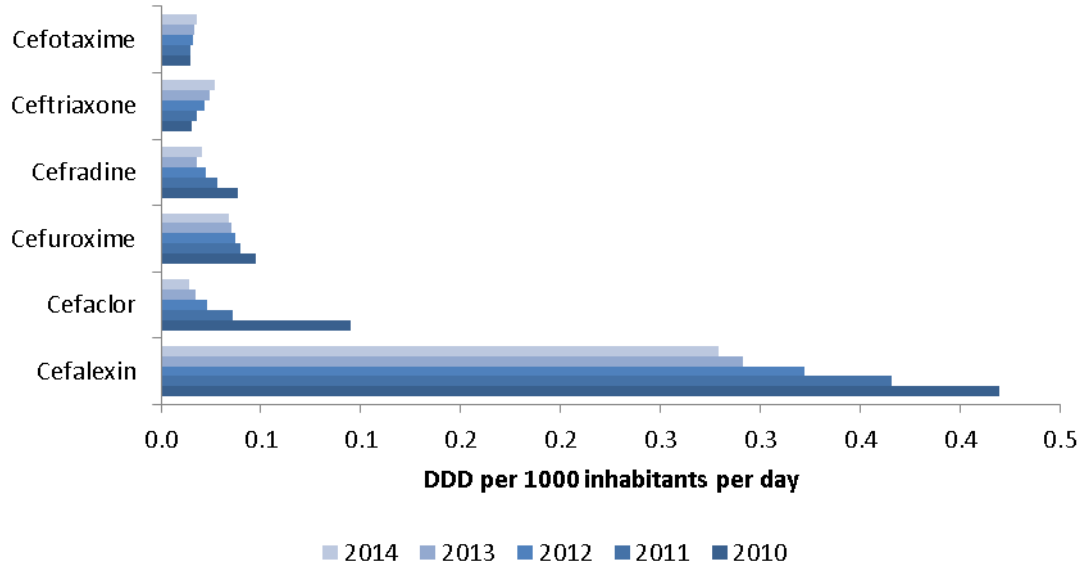


Figure 3.7 Consumption of different cephalosporins, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

Carbapenems

Carbapenems are often described as the antibiotics of last resort, particularly for serious Gram-negative infections. These agents have broad-spectrum activity, with a structure that prevents their breakdown by the majority of β-lactamase enzymes (the enzymes that breakdown other β-lactam penicillins and cephalosporins). However, in recent years, resistance to this antibiotic class has arisen (due to the emergence of bacteria with genes encoding production of carbapenemase enzymes) and is now spreading rapidly worldwide. A major cause of concern is that there are very few new antibiotics in development that are likely to work effectively against all carbapenemase producers.

The use of carbapenems is almost exclusively within hospitals for suspected or confirmed multi-drug resistant Gram-negative infections. Most frequently they are used on intensive care, transplant or cancer units. Ertapenem is administered once per day and patients increasingly complete this treatment at home, if an outpatient parenteral antimicrobial therapy (OPAT) service is available.

Carbapenem usage, 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, with less than 1% of carbapenem consumption related to primary care prescriptions in 2013 (Figure 3.8). Meropenem remains the predominant carbapenem in use (Figure 3.9). A detailed review of carbapenem use in hospitals is within the hospital section.

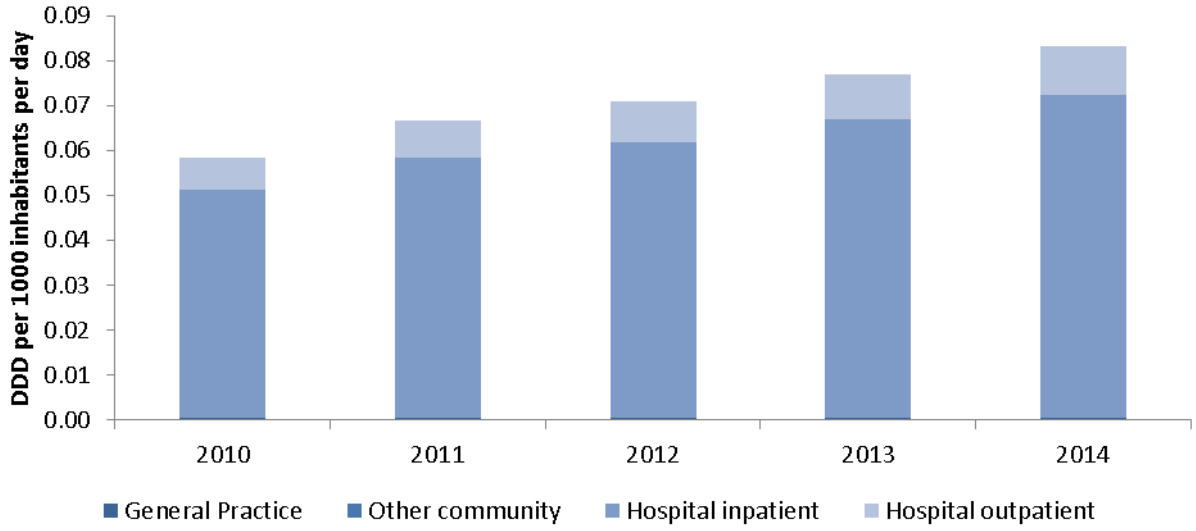


Figure 3.8 Consumption of carbapenems, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

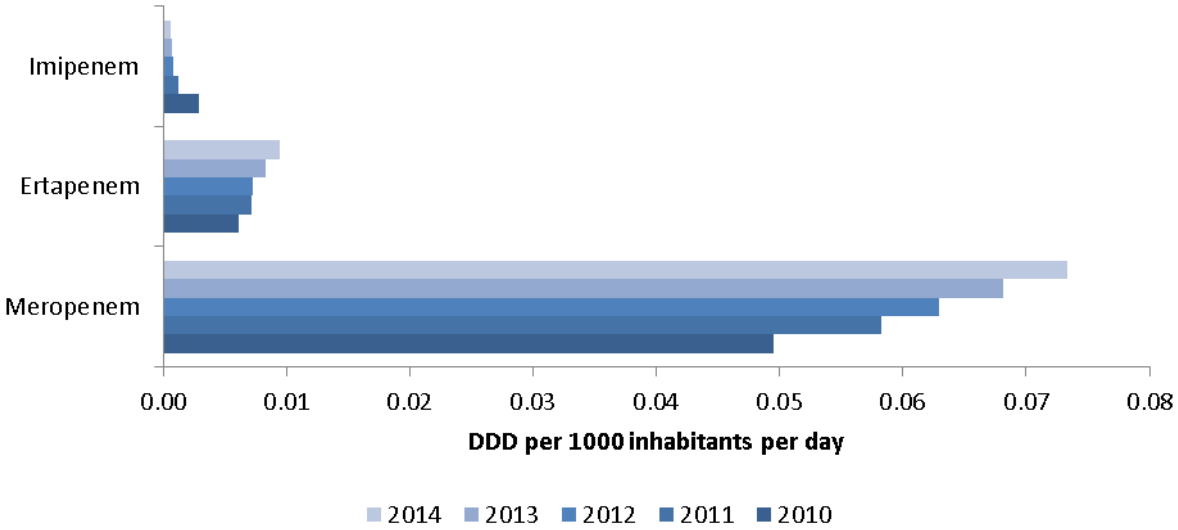


Figure 3.9 Consumption of different carbapenems, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

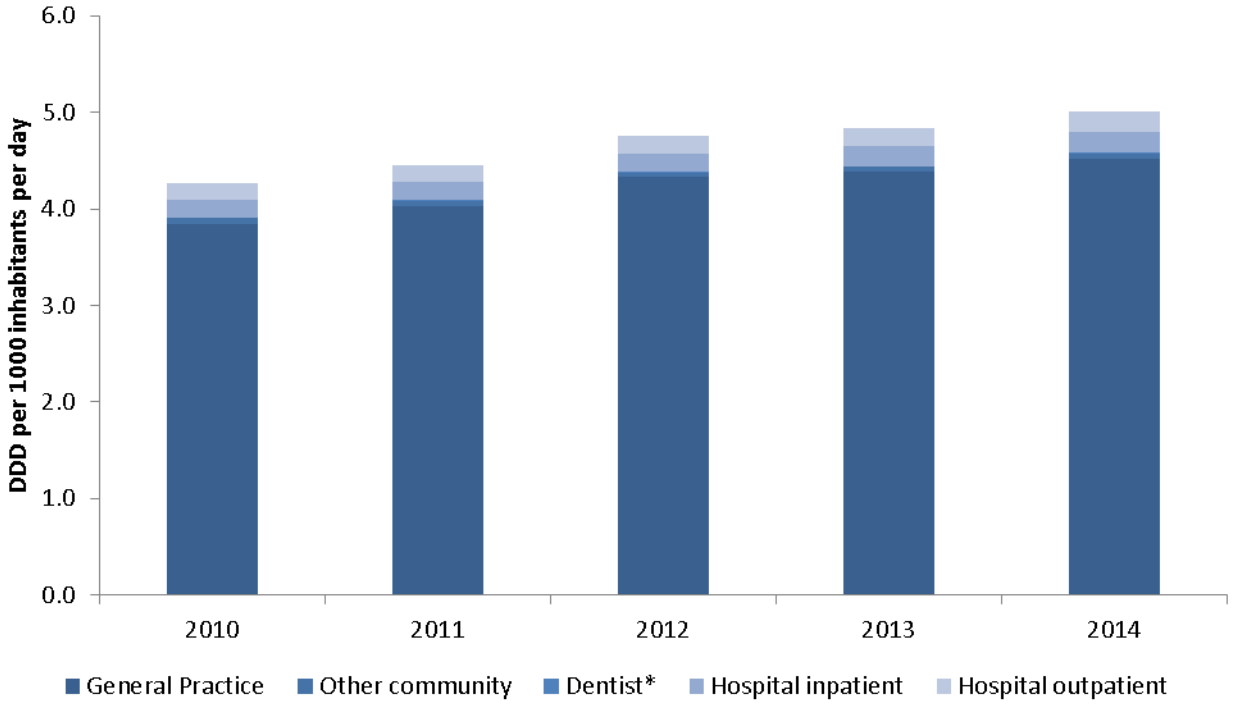
Tetracyclines

Tetracyclines are predominantly used to treat Gram-positive infections. In the national infection guidance for primary care, doxycycline is the alternative agent (first choice is amoxicillin) recommended for sinusitis, bronchitis, exacerbations of chronic obstructive pulmonary disease or pneumonia.[24] The other predominant use of tetracyclines (predominantly lymecycline, oxytetracycline and minocycline) is in skin conditions such as moderately severe acne and rosacea.

Tetracycline use continues to rise across both community and hospital consumption, with an average 3% rise per year (Figure 3.10). However the increases were most pronounced in other community and hospital outpatient prescriptions. Dentists decreased use by 15% between 2013 and 2014.

The top five agents prescribed in this class are presented in Figure 3.11. Over the four years, the predominant agents consumed were doxycycline and lymecycline (42.6% and 35.4%) probably reflecting use as a treatment for acne.

[24] Management of Infection Guidance for Primary Care. British Infection Association, RCGP and PHE. 2015 available at https://www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care



*Data available from June 2010

Figure 3.10 Consumption of tetracyclines, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

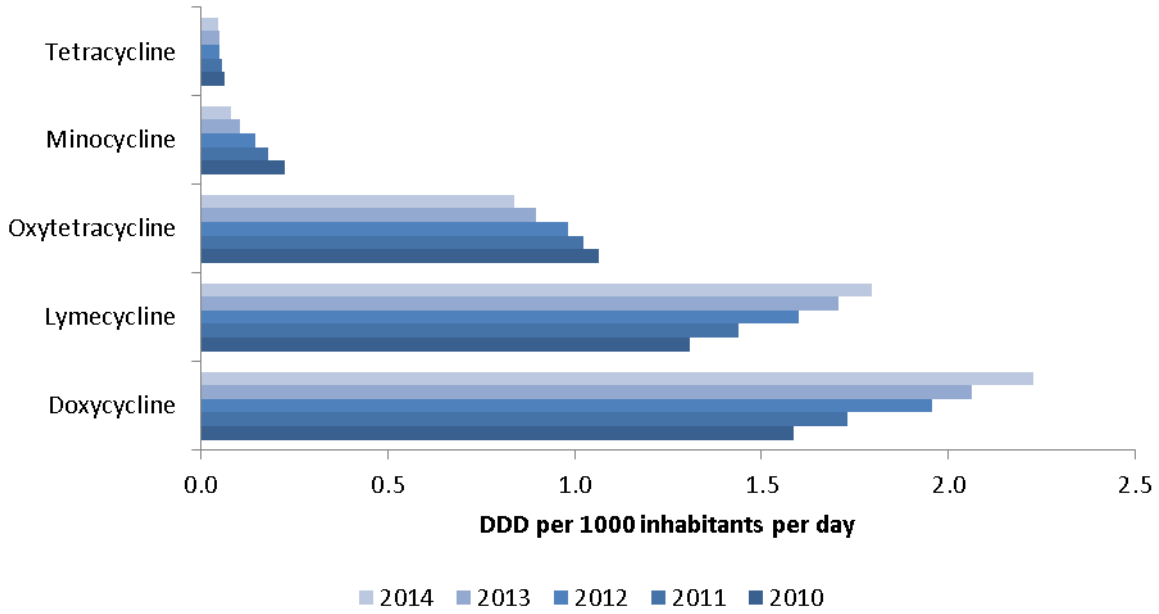


Figure 3.11 Consumption of different tetracyclines, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

Quinolones

Quinolones were developed in the 1960s, initially for the treatment of Gram-negative urinary tract infections. They are broad-spectrum agents active against both Gram-positive and Gram-negative bacteria and frequently used to treat hospital-acquired pneumonia and urinary tract infections. They have excellent oral bioavailability so can be prescribed in tablet rather than injectable form. Many practitioners believe that widespread quinolone use in hospital contributed to the clonal expansion and epidemics of certain bacterial strains. The marked decline in their use has been associated with declining numbers of *Clostridium difficile* and meticillin-resistant *Staphylococcus aureus* (MRSA) infections. In national infection guidelines, ciprofloxacin is recommended only for the treatment of acute prostatitis or pyelonephritis.[25]

Similar to cephalosporins, the decline in quinolone use has now stopped with no change in consumption between 2013 and 2014 (Figure 3.12).

The main quinolone prescribed between 2010 and 2014 is ciprofloxacin. There are continued small rises in the respiratory quinolones levofloxacin and moxifloxacin (Figure 3.13).

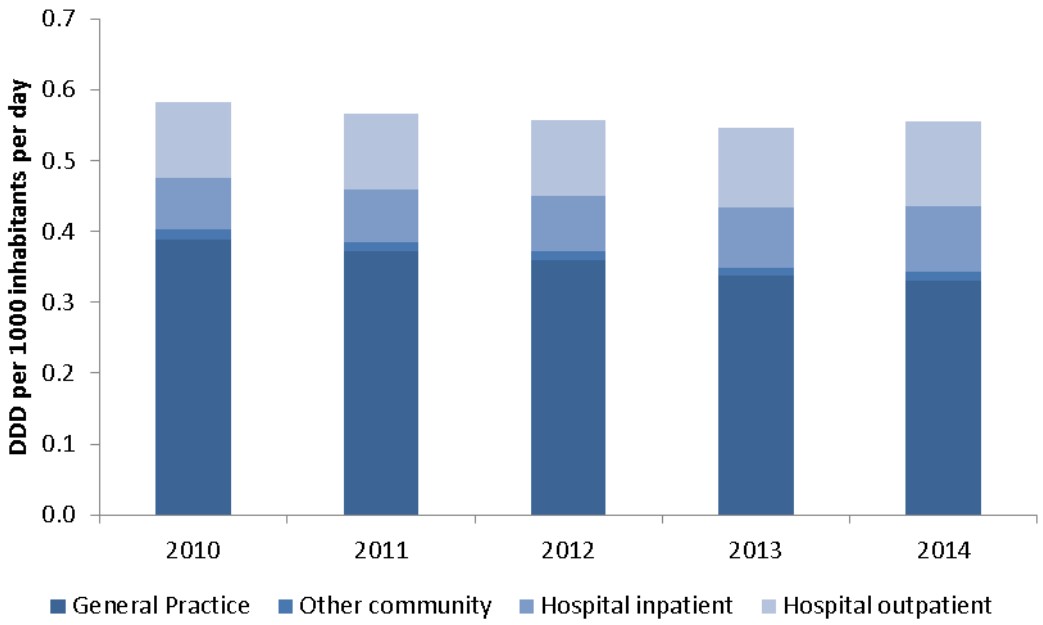


Figure 3.12 Consumption of quinolones, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

[25] Management of Infection Guidance for Primary Care. British Infection Association, RCGP and PHE. 2015 available at https://www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care

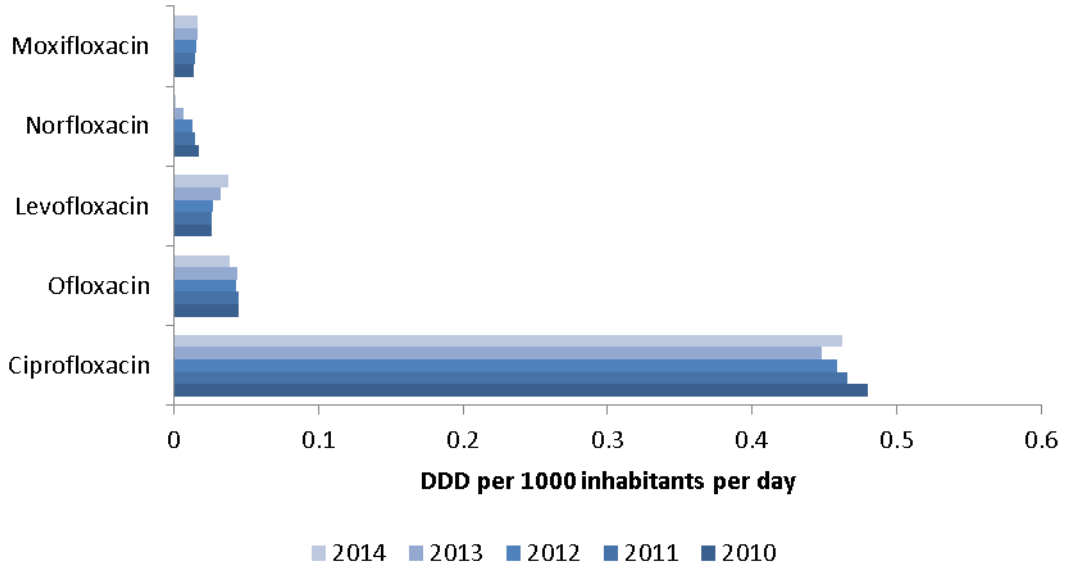


Figure 3.13 Consumption of different quinolones, expressed as DDD per 1000 inhabitants per day, England 2010−2014

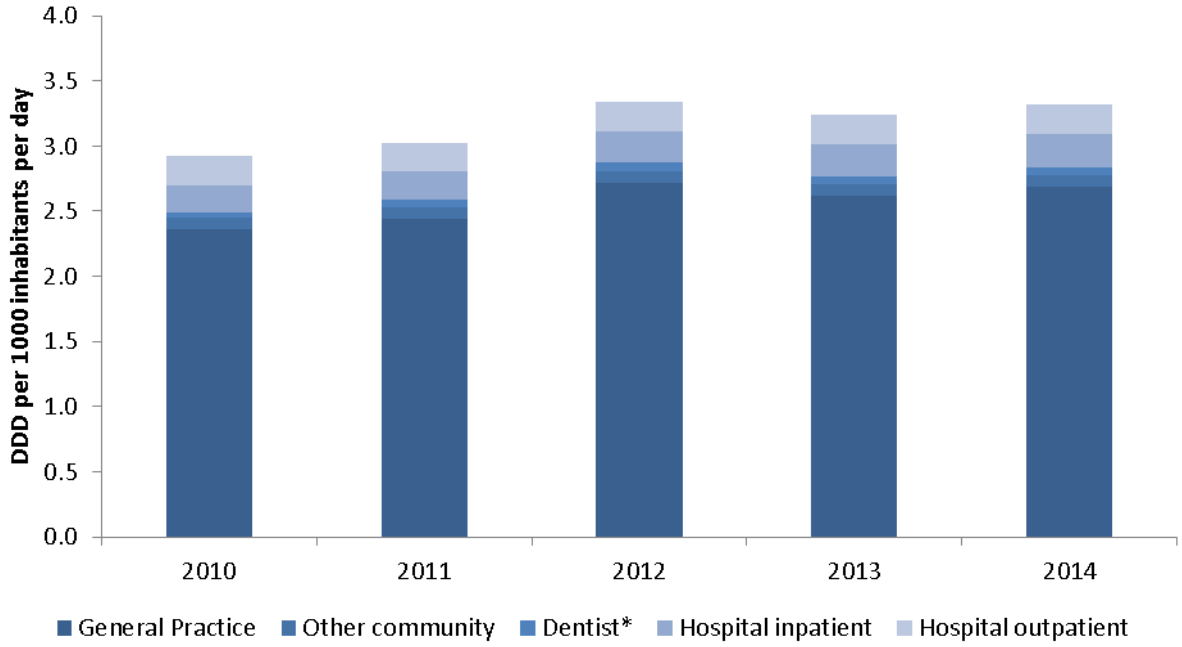
Macrolides

Macrolides are bacterial protein synthesis inhibitors that are active against most Gram-positive species and respiratory Gram-negative pathogens including *Haemophilus* spp., *Bordatella pertussis* and *Moraxella catarrhalis*. Within the national infection guidelines, clarithromycin is recommended as an alternative agent to treat upper and lower respiratory tract infections, where individuals are penicillin intolerant or allergic. This group of agents is also recommended as part of the triple therapy for the eradication of *Helicobacter pylori* and for treatment of *Chlamydia trachomatis* genital tract infections.[26] Azithromycin in combination with ceftriaxone is now recommended as first line treatment for gonorrhoea.

Consumption of macrolides continues to increase in prescriber locations, except dental practice where it has declined by 5% each year since 2012 (Figure 3.14).

Clarithromycin and azithromycin use continues to increase 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, and in addition the use of azithromycin as an anti-inflammatory for frequent exacerbations of chronic obstructive pulmonary disease (Figure 3.15).

[26] Management of Infection Guidance for Primary Care. British Infection Association, RCGP and PHE. 2015 available at https://www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care



*Data available from June 2010

Figure 3.14 Consumption of macrolides, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

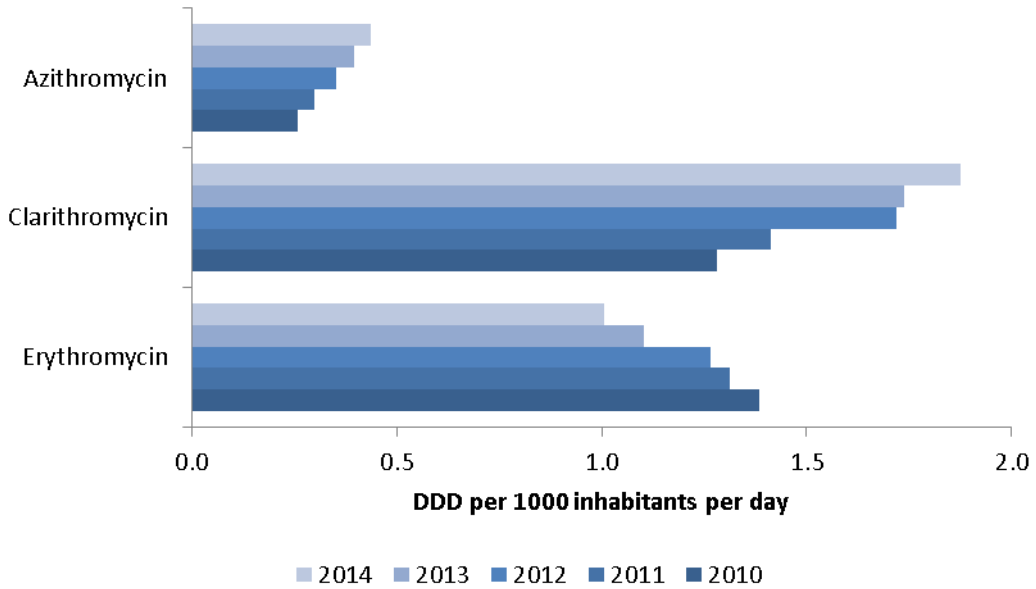


Figure 3.15 Consumption of different macrolides, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

Sulfonamides and trimethoprim

Sulfonamides and trimethoprim can either be used individually or co-formulated. Both antibiotics are bacteriostatic (prevent the growth of bacteria) and act by inhibiting enzymes that are involved in the biosynthesis of folic acid in microbes. They have a wide spectrum of activity against bacteria, fungi and protozoa. In national infection guidelines, trimethoprim is recommended for the treatment of urinary tract infections.[27]

Between 2010 and 2014, total consumption of this antibiotic group continued to rise (Figure 3.16) and England remains one of the highest consumers of sulfonamides and trimethoprim in the EU. Eighty five percent of consumption was trimethoprim monotherapy with the remainder being either sulfonamide or sulfa/trimethoprim combination therapy.

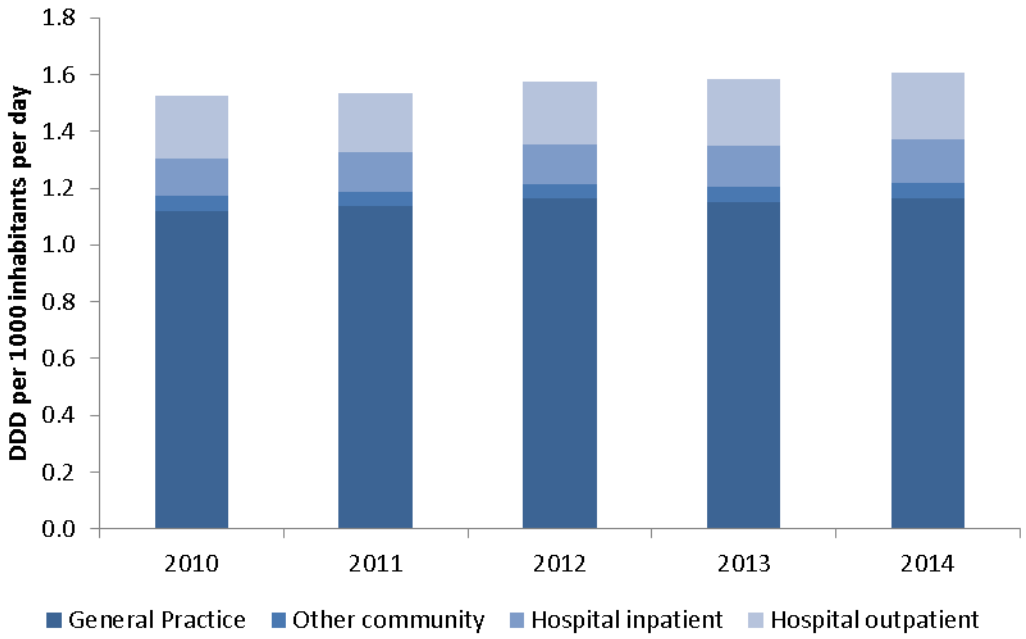


Figure 3.16 Consumption of sulfonamides and trimethoprim, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

[27] Management of Infection Guidance for Primary Care. British Infection Association, RCGP and PHE. 2015 available at https://www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care

Nitrofurantoin

Nitrofurantoin is a key agent in the treatment of community urinary tract infections (UTI). It is recommended for this indication in the national infection guidelines from November 2014.[28]

Nitrofurantoin consumption increased by approximately 50% between 2010 and 2013 but has only increased a further 3% between 2013 and 2014 (Figure 3.17). PHE changed primary care guidelines to recommend this antibiotic as first line treatment in November 2014; this may lead to further increase in use, once CCGs promote its use in local guidance.

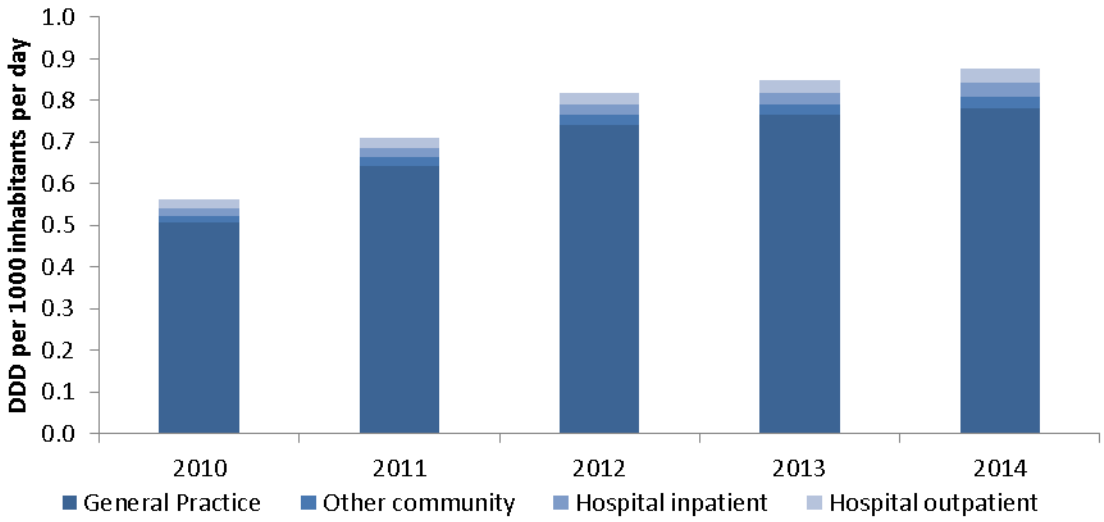


Figure 3.17 Consumption of nitrofurantoin, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

[28] Management of Infection Guidance for Primary Care. British Infection Association, RCGP and PHE. 2015 available at https://www.gov.uk/government/publications/managing-common-infections-guidance-for-primary-care

Aminoglycosides

Aminoglycoside antibiotics are particularly used in treating resistant Gram-negative infections and are frequently used as part of the therapeutic regimen for the treatment of sepsis and urinary tract infections in English hospitals (see Chapter 4).They are also used in combination with either penicillins or glycopeptides for the treatment of serious infections such as endocarditis caused by streptococci or enterococci. The earliest aminoglycoside, streptomycin, was the first antibiotic used against tuberculosis. These agents can also be used in an inhaled form, which is particularly important for preventing exacerbations of infections in individuals with chronic bronchiectasis (lung damage), especially cystic fibrosis.

Consumption of aminoglycosides continues to increase within hospitals and remains stable in general practice (Figure 3.18).

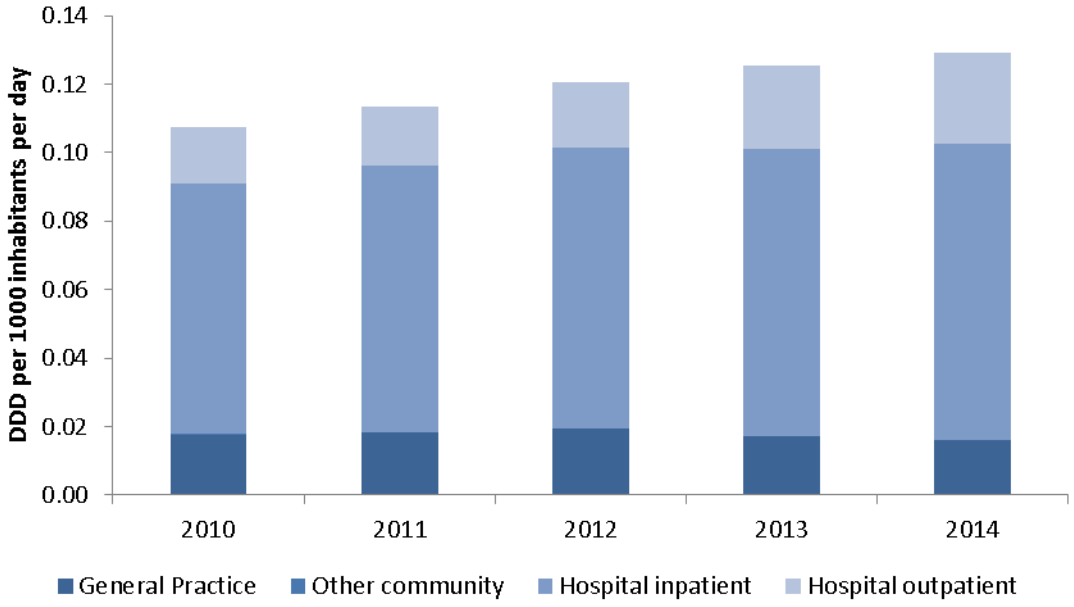


Figure 3.18 Consumption of aminoglycosides, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

Trends in consumption in other agents: glycopeptides and daptomycin

The parenteral (intravenous) form of these antibiotics is used almost exclusively to treat infections due to Gram-positive bacteria that are resistant to other drugs, such as MRSA, enterococci or coagulase-negative staphylococci.

Use of glycopeptides and daptomycin occurs almost completely in the hospital setting. Despite a significant reduction in MRSA bacteraemia and other infections, the use of parenteral glycopeptides (predominantly teicoplanin) and daptomycin continued to increase in the last five years (Figure 3.19 and Figure 3.20). From 2010 to 2014 the consumption of daptomycin has doubled, though still remains very low at less than 0.005 DDD per 1000 inhabitants per day (Figure 3.21). 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 recommended. Teicoplanin use, in particular, may also be increasing related to improved access to OPAT.

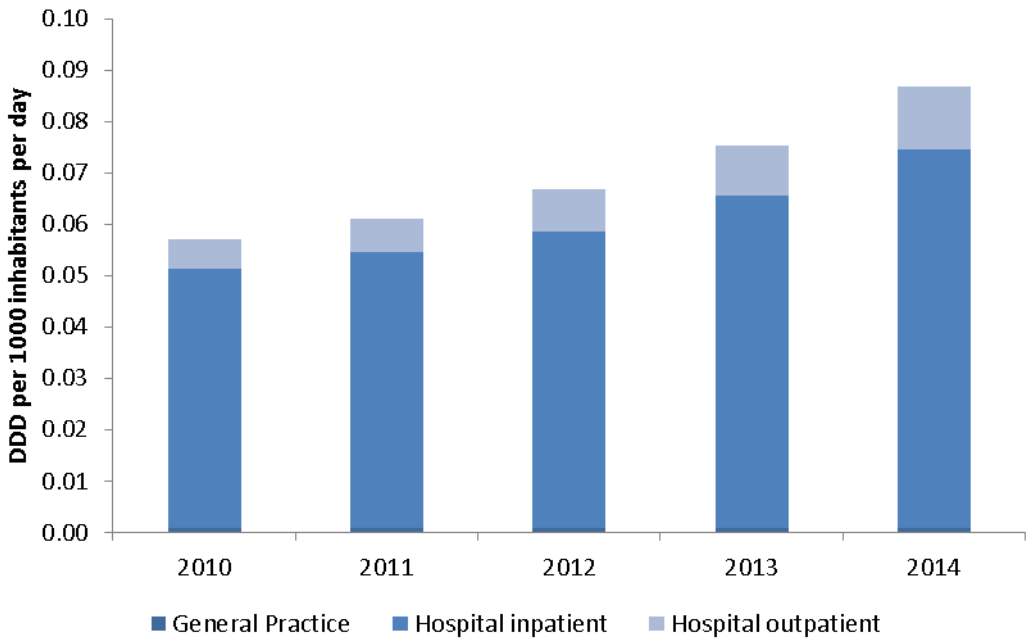


Figure 3.19 Consumption of glycopeptides, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

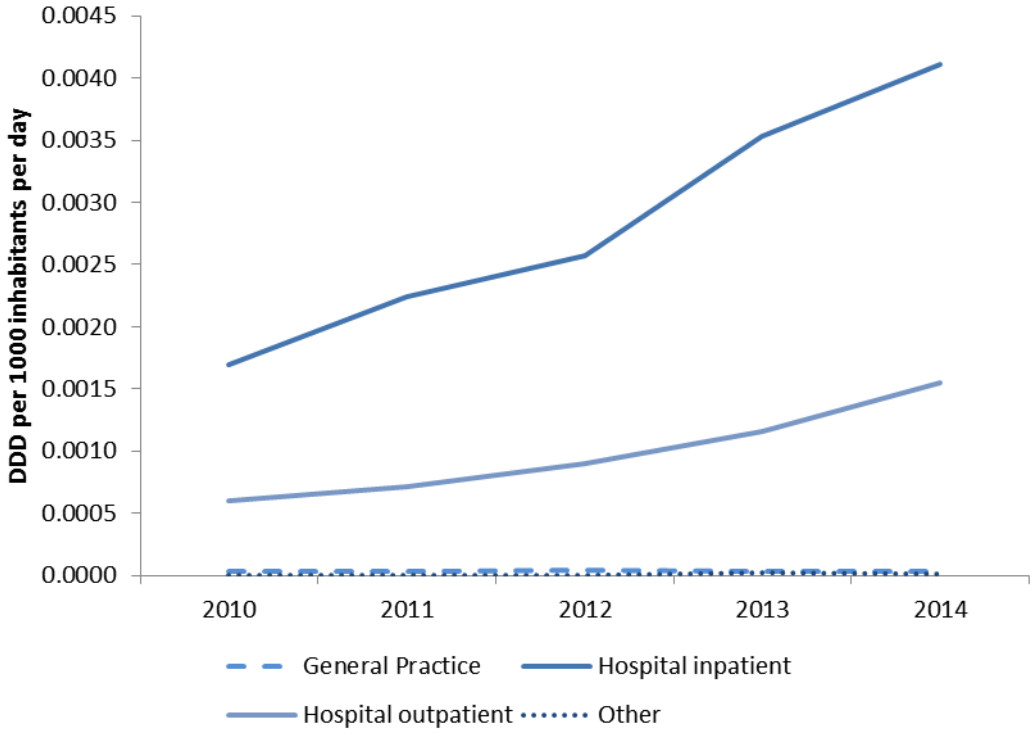


Figure 3.20 Consumption of daptomycin, by prescriber location, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

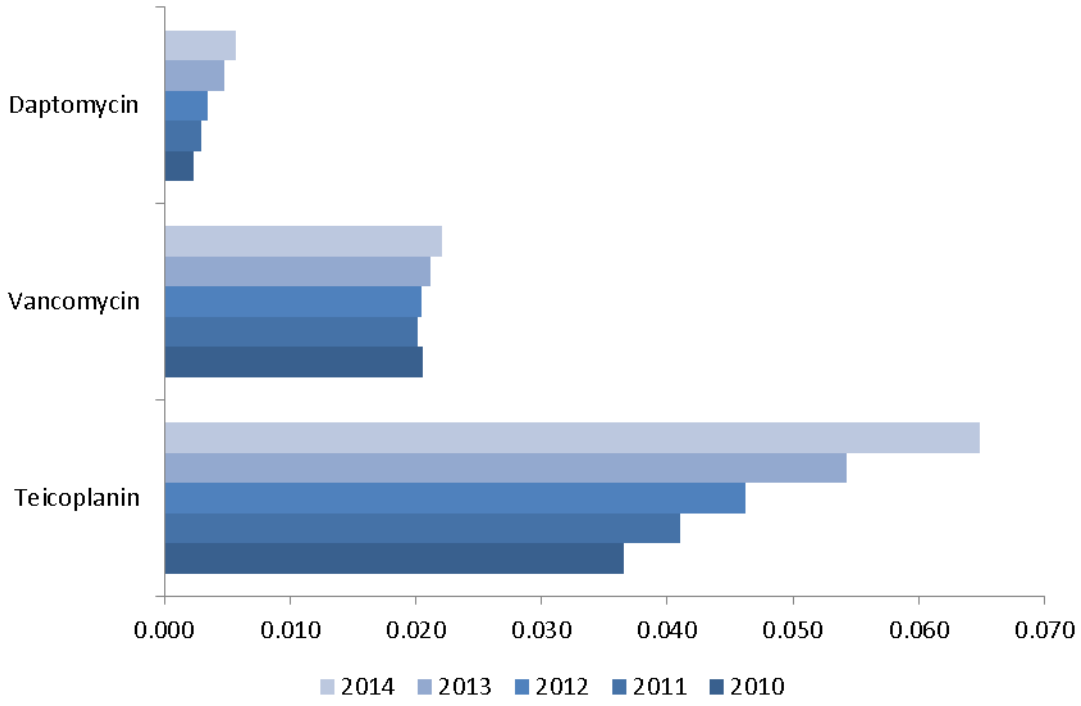


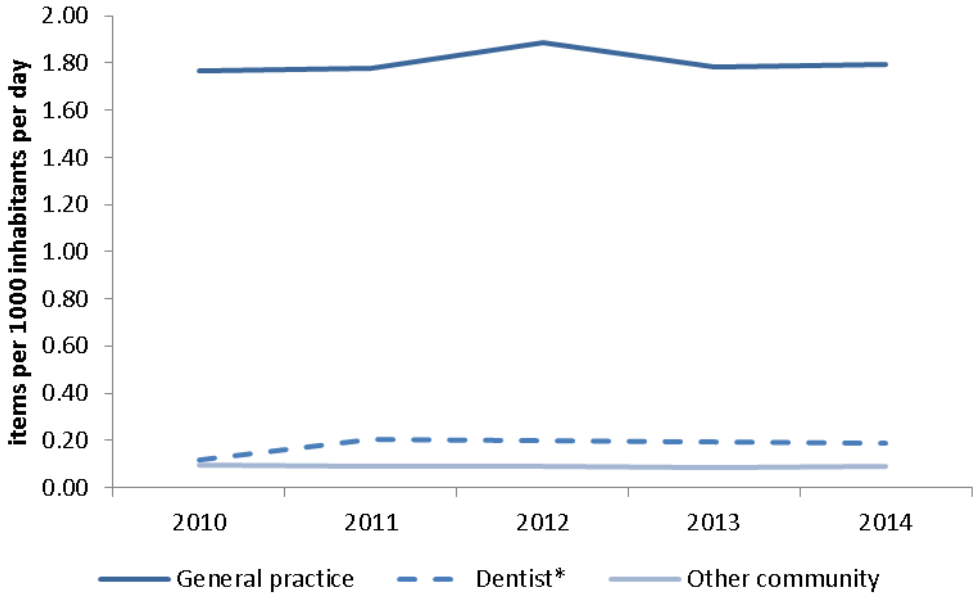
Figure 3.21 Consumption of different glycopeptides and daptomycin, expressed as DDD per 1000 inhabitants per day, England, 2010−2014

Prescribing in primary care: items

General practice, other community services and dentists

The total amount of items (2.07) prescribed per 1000 inhabitants per day stayed stable between 2011 and 2014 but varied by prescriber; general practice and other community services prescribing was unchanged whereas dentist prescribing dropped by 7% (see Figure 3.22) over the same time period.

General practice prescribed 87% of all antibiotic items in the community in England in 2014. Dentists prescribed 9% of antibiotic prescription items and 4% were prescribed by other community services.



*Data available from June 2010

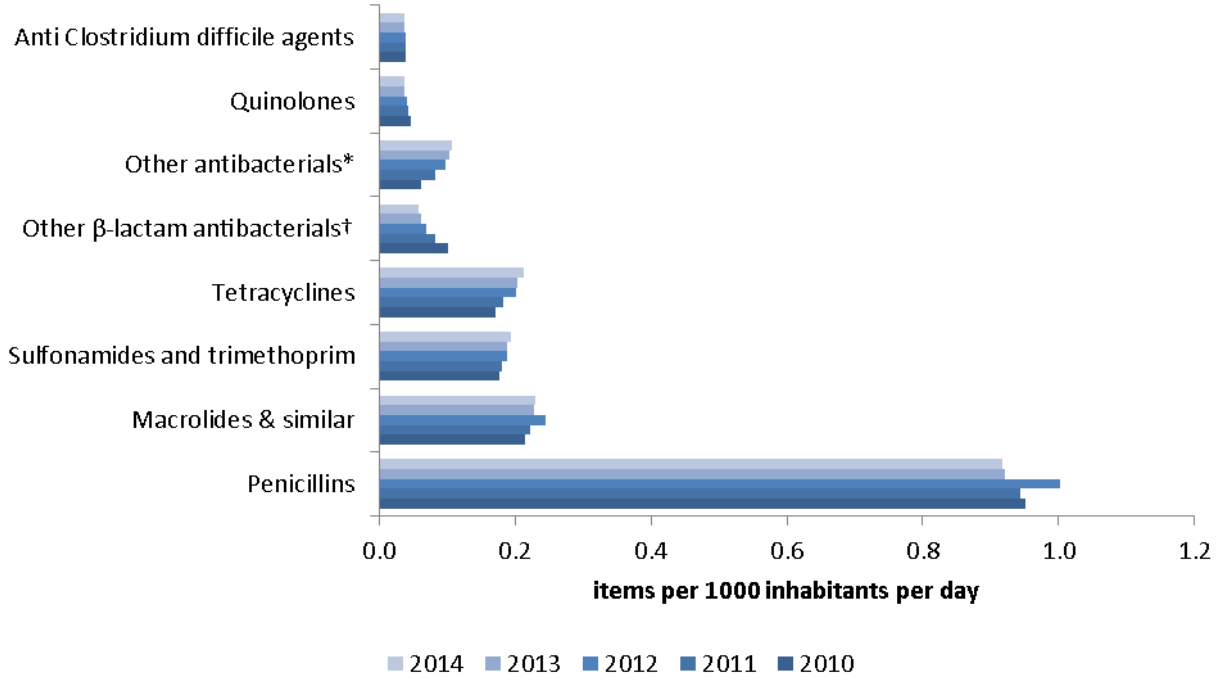
Figure 3.22 Antibiotic items by prescribers, expressed as items per 1000 inhabitants per day, England, 2010−2014

General practice

Penicillins were the most prescribed antibiotic items in general practice (0.9 items per 1000 inhabitants per day) in England in 2014, followed by macrolides and tetracyclines (each 0.2 items per 1000 inhabitants per day).

Total items prescribed per 1000 inhabitants per day increased from 2010 to 2012 and decreased between 2013 and 2014 to return to 2011 levels. Increases in items prescribed occurred for ‘other antibacterials (including aminoglycosides and amphenicols) (30%), tetracyclines (17%), sulfonamides and trimethoprim (7%). The

biggest decreases were observed for ‘other β-lactam antibacterials’ (including cephalosporins and carbapenems) (-30%) and quinolones (-7%) (see Figure 3.23).



† Includes cephalosporins and carbapenems
* Includes aminoglycosides and amphenicols

Figure 3.23 Key antibiotic groups prescribed by general practice, expressed as items per 1000 inhabitants per day, England, 2010−2014

Quarterly data for antibiotic prescribing indicators in the community are shown in Table 3.2. It demonstrates that total prescribing, adjusted for the age and sex distribution in the population, has stabilised with a significant decrease occurring in quarter 2, 2015. Broad spectrum antibiotic prescribing is also reducing in general practice.

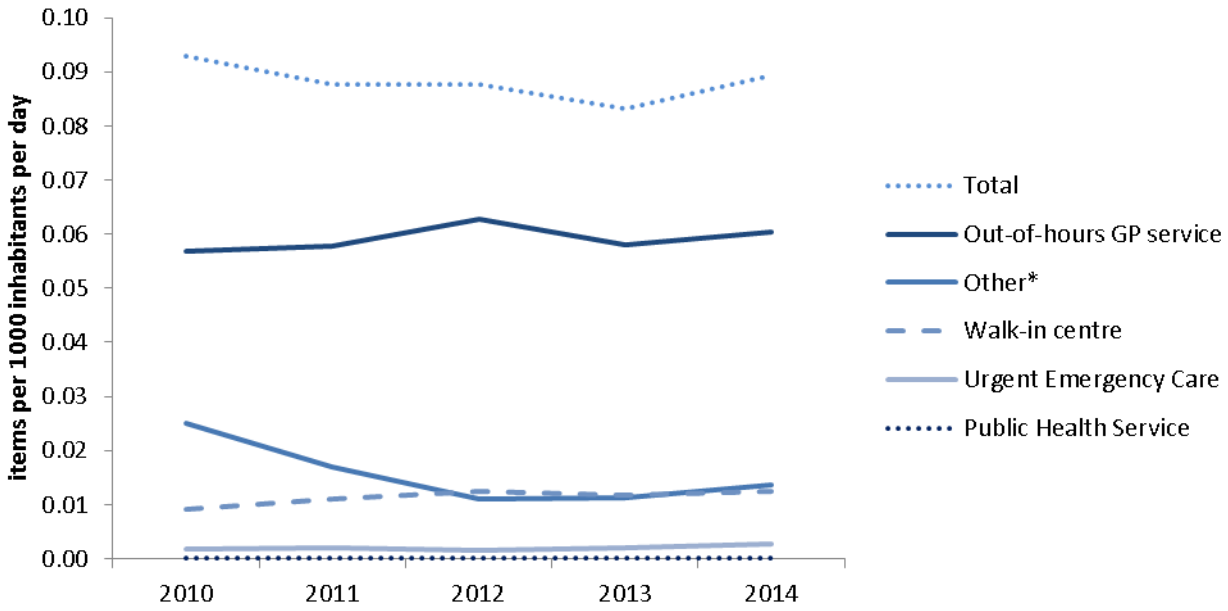
Table 3.2 Total antibiotic items, items per STAR-PU (Specific therapeutic group age-sex weightings related prescribing units) and number of broad-spectrum antibiotic items per antibacterial item prescribed by general practice by quarter, England, April 2013−June 2015

Year	Quarter	Practices (n)	Items	Items per STAR-PU	Items per 1000 population	Proportion of broad-spectrum items antibacterial item
2013	2	9 287	8778566	0.284	163	11.57
	3	9 395	8210129	0.263	152	12.25
	4	9 379	9773275	0.312	181	10.9
2014	1	9 349	9913256	0.316	183	10.6
	2	9 369	8925393	0.284	164	11.23
	3	9 287	8215461	0.261	151	11.86
	4	9 334	10087531	0.319	186	10.11
2015	1	9 288	10077535	0.318	186	9.92
	2	9 271	8316203	0.262	153	10.64

The seasonal effect of antibiotics is observed with higher prescribing of antibiotics in winter months compared with summer months. Comparing the most recent quarter available (quarter 2, Apr−Jun, 2015), to the same quarter in 2014, demonstrates that 610,339 fewer antibiotic prescriptions were dispensed, equating to 11 fewer prescriptions per 1,000 of the population for the same calendar and seasonal period and a 7% reduction. The proportion of broad-spectrum antibiotic items compared to the total number of all antibiotic items prescribed in primary care also dropped in quarter 1 and 2 in 2014 and 3 in 2013 compared to the same quarters in 2013 and 2012, respectively.

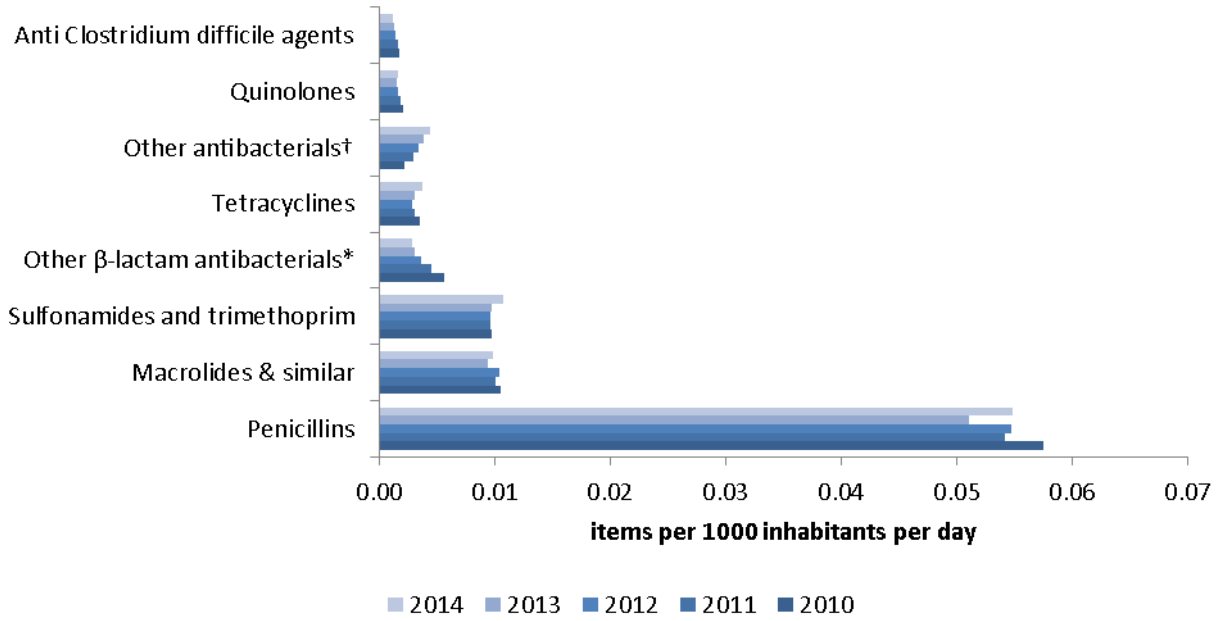
Other community prescribing

Community service prescribing increased by 1.8% (from 0.088 to 0.089 antibiotic items per 1000 inhabitants) between 2011 and 2014 with the main increase (7.6%) recorded between 2013 and 2014 (see Figure 3.24). There is a drop in 'other' related to improved coding by NHS BSA (mainly 'community health service'). Urgent care and walk-in-centre data may be misclassified as it will depend on how this is reported to NHS BSA; it may be reported at CCG, as standalone centres, combined within GP. As organisations have moved from PCT to CCG (April 2013) there has been reclassification and reconfiguration of these services and therefore comparisons require caution.



* includes community health service, hospital service, nursing homes, public health services, hospices, custody services, and unknown

Figure 3.24 Antibiotic items prescribed by other community services, England, 2010−2014

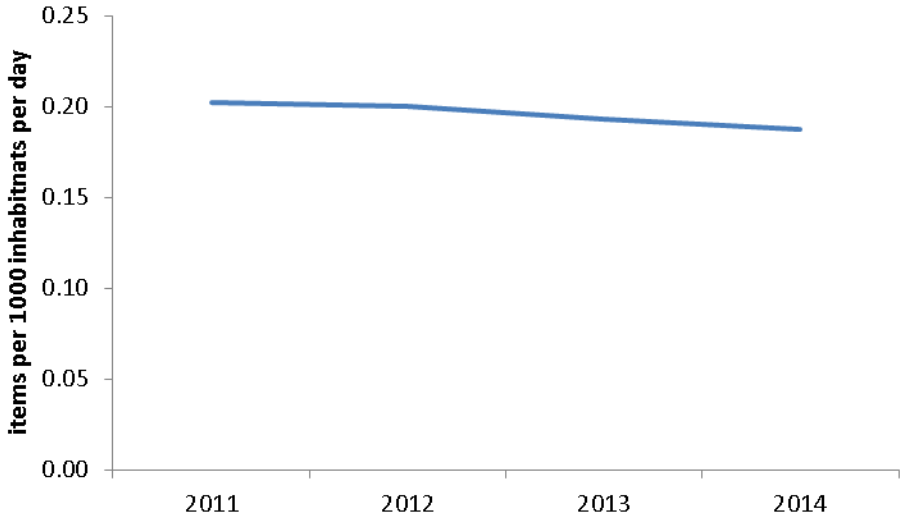


* includes cephalosporins, carbapenems, and monobactams
† includes glycopeptides, polymyxins, steroid antibacterials, imidazole and nitrofuran derivatives,amphenicols, aminoglycosides, fosfomycin, linezolid, daptomycin

Figure 3.25 Key antibiotic groups prescribed by other community services, expressed as items per 1000 inhabitants per day, England, 2010−2014

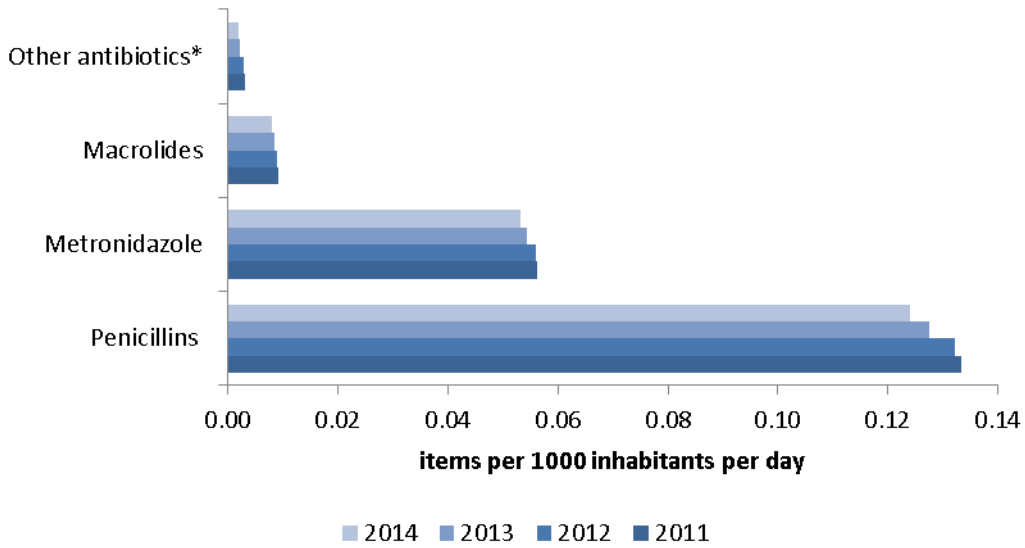
Dental Practice

From 2011 to 2014, there was a 6% decrease (231,038 less prescriptions) in the total number of prescription items prescribed by NHS dental practices (Figure 3.26). The predominant antibiotic prescriptions were for penicillins and metronidazoles, as shown in Figure 3.27. Almost 99% of prescriptions were narrow-spectrum penicillins, metronidazole or macrolides.



† Data for 2010 not shown as only available from June

Figure 3.26 Antibiotic items prescribed by dentists, expressed as items per 1000 inhabitants per day, England, 2011−2014†



* includes lincosamides, 1st generation cephalosporins and tetracyclines
† Data for 2010 not shown as only available from June

Figure 3.27 Key antibiotic groups prescribed by dentists, expressed as items per 1000 inhabitants per day, England, 2011−2014†

Prescribing in secondary care

Between 2010 and 2014, total hospital prescribing has increased by 11% per 1000 inhabitants per day. This prescribing is predominantly related to an increase in inpatient prescribing.

Table 3.3 presents hospital data using both admissions and bed-days, in addition to the total population, as denominators. Between 2010 and 2014, consumption of antibiotics by hospitals expressed as DDD per admission, has increased by 6% compared to 24% per bed-day and 11% per population.

Table 3.3 Total antibiotic consumption in all NHS trusts, using defined daily doses (DDD) and denominators of admissions, bed-days and population, England, 2010−2014

Year	Total DDD (x 10^6)	DDD/ 100 admissions	DDD/ 100 bed-days	DDD/ 100 population
2010	72.9	397	154	138
2011	73.8	398	159	139
2012	77.0	412	166	144
2013	80.0	424	189	149
2014	82.7	421	191	153
Difference 2010- 2014	**13%**	**6%**	**24%**	**11%**

In 2014, 95% of antibiotic consumption was by acute trusts; a detailed breakdown by organisation type is presented in Table 3.4.

Table 3.4 Total antibiotic consumption by trust organisation type, using defined daily doses (DDD), England, 2014

Organisation type	DDD	% total DDD
Acute-Large	22,650,193	27.4
Acute-Medium	18,044,966	21.8
Acute-Small	11,432,453	13.8
Acute-Teaching	26,154,457	31.6
Community	551,574	0.7
Mental Health & Learning Disability	1,372,398	1.7
Specialist - Cancer	509,568	0.6
Specialist - Chest/Heart	733,319	0.9
Specialist - Children	644,915	0.8
Specialist - Ortho/Rheum	157,541	0.2
Specialist - Other	405,900	0.5

The relationship between DDD per admissions and DDD per bed-days differs according to trust type: similar trends are observed in acute and teaching trusts; Community and mental health and learning disability trusts have higher DDD per admission and much lower DDD per bed-day reflecting lower admission numbers and longer lengths of stay in these organisation types. Using admissions data as a denominator gives a better estimate of hospital activity where length of stay is short and outpatient activity frequent, and bed-days is more useful in units where longer lengths of stay are frequent. This highlights the importance of understanding trust activity and is demonstrated in Figure 3.28.

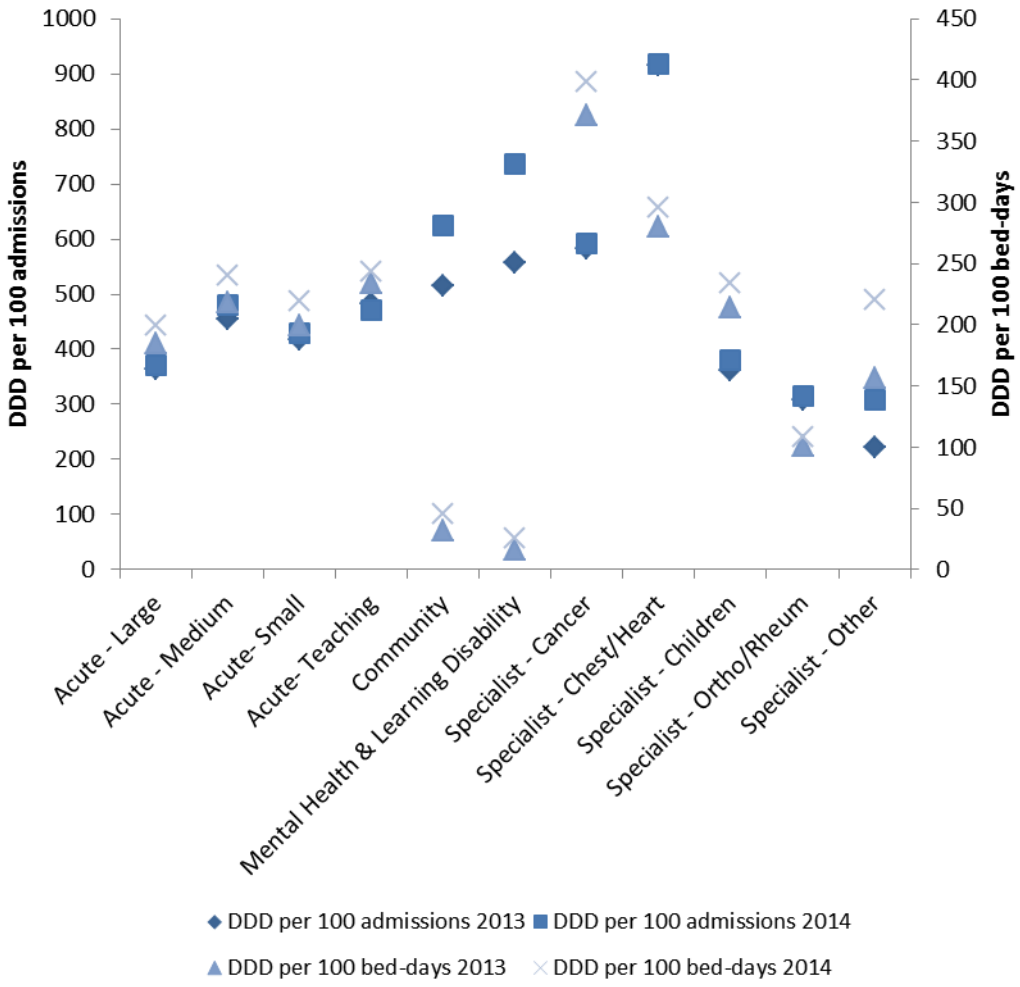
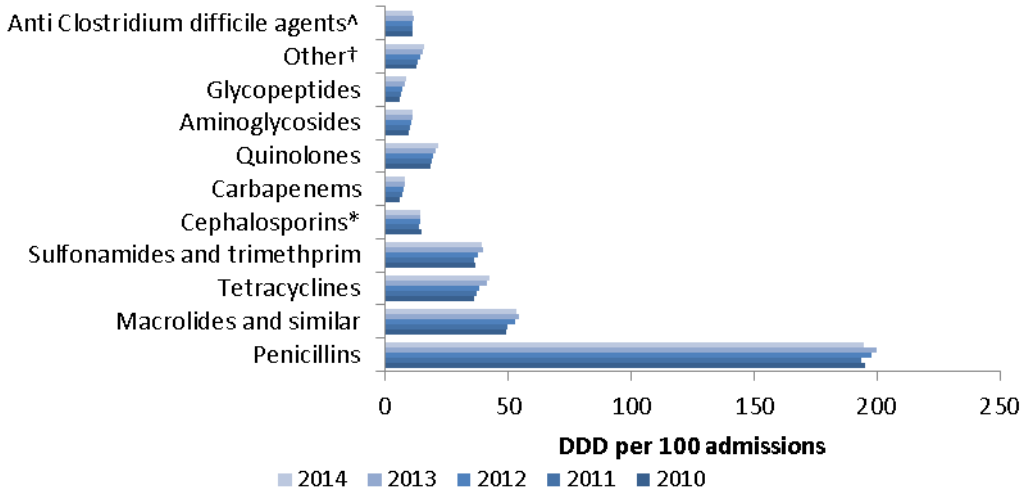


Figure 3.28 Total antibiotic use in NHS trusts, expressed as DDD per 100 admissions and DDD per 100 bed-days, England, 2013−2014

Both macrolide and penicillin consumption decreased in NHS Trusts but use of broad spectrum agents (cephalosporins, quinolones, carbapenems and glycopeptides) continued to increase (Figure 3.29).



* includes cephalosporins and monobactams

† includes polymyxins, steroid antibacterials, imidazole (excluding oral metronidazole) and nitrofuran derivatives,amphenicols, fosfomycin, linezolid, daptomycin

^ includes oral metronidazole, oral vancomycin and fidoxamicin

Figure 3.29 Key antibiotic groups prescribed in hospital, expressed as DDD per 100 admissions per day, England, 2011−2014

The consumption of different antibiotic groups according to type of NHS trust organisation is presented in Figure 3.30.

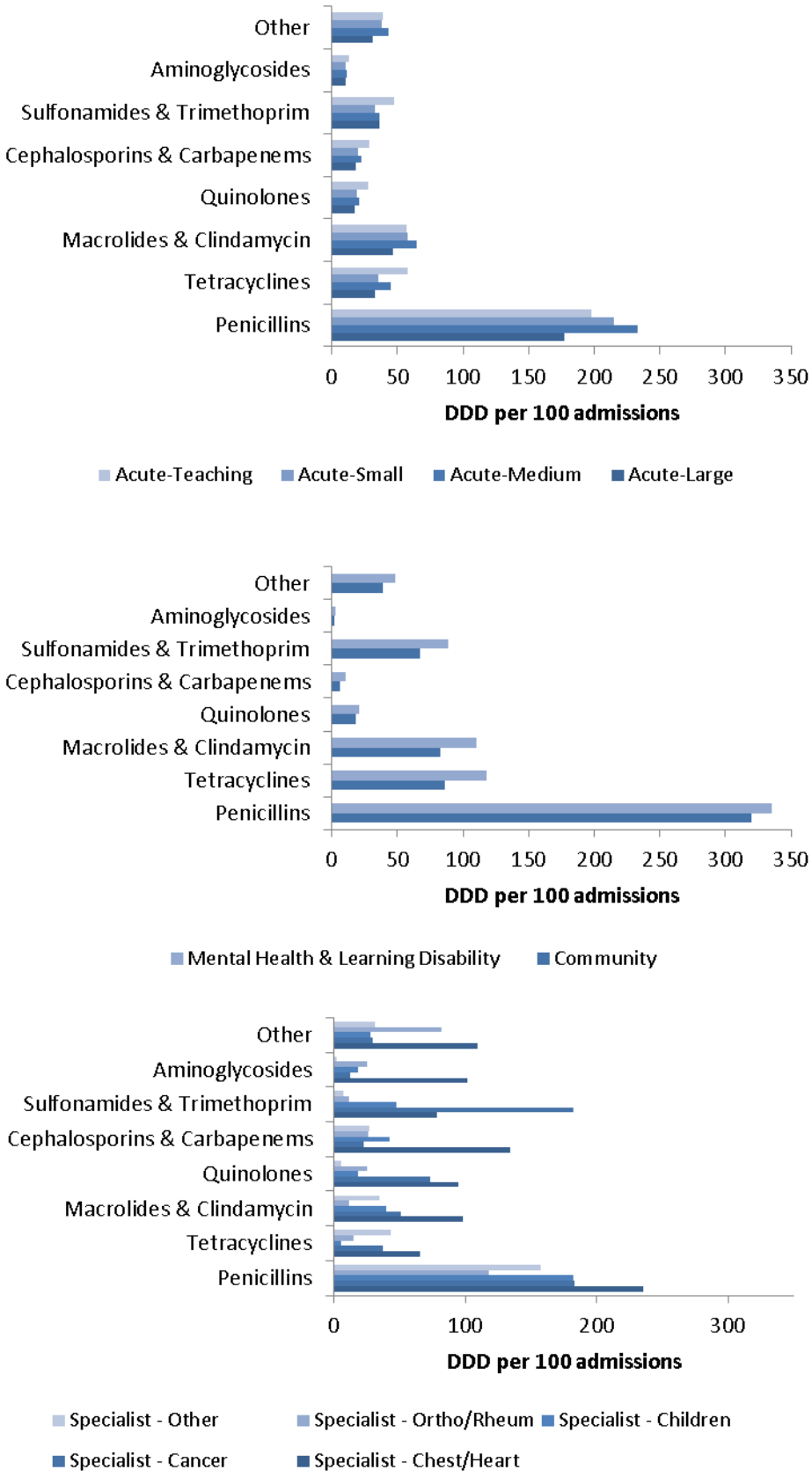
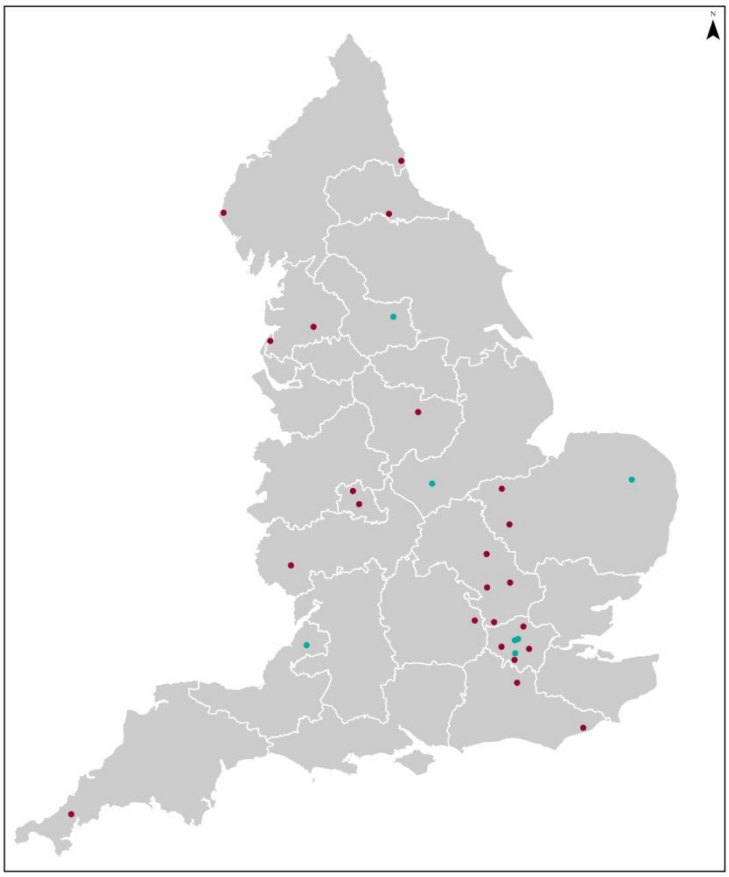


Figure 3.30 Antibiotic group consumption, by trust type, expressed as DDD per 100 admissions, England, 2014

Validation of prescribing in secondary care

Thirty trusts out of the 45 (66.6%) who were sent the pilot study protocol participated in the process. Seven of these 30 trusts were teaching hospitals. The locations of the trusts that participated in the pilot are shown in Figure 3.31. Only 30% of respondents needed to contact the validation team (n=6); email was the most common method of contact (n=5) and four of the six participants had a response within two working days.



- Acute-General Trust
- Acute-Teaching hospital

Figure 3.31 Validation of prescribing data in secondary care pilot sites, England, 2014

Twenty-two trusts responded to the survey (73% response rate). The protocol was completed from data extraction, data entry and data submission by the same individual in 59% of trusts (antimicrobial pharmacist (n=8); pharmacy technician (n=2) or IT pharmacists (n=3)). In the remaining trusts, a pharmacy technician (3) or IT lead (5) obtained the data from the pharmacy system and antimicrobial pharmacist (5); data manager/IT lead (2) or pharmacy technician (1) completed the spreadsheet. Fifty four percent of respondents took under four hours to complete the survey. The breakdown for data extraction and data entry is outlined in Table 3.5. There was an equal split between those that found the process easy, neutral and difficult, often relating to their hospital pharmacy systems and size. Feedback of the validation protocol overall was

that it was easy to follow with 81% selecting neutral, easy or very easy. Further qualitative feedback is presented in Table 3.6.

Table 3.5 Time taken to perform the components of the validation protocol, England, 2014

Time (minutes)	Full validation (n=13)	Data extraction (n=8)	Entry of data (n=8)
0-30	1	5	0
21-60	1	0	0
61-120	1	0	0
121-240	4	1	2
>240	6	2	6

Table 3.6 Written text feedback from participants on the validation protocol and process, England, 2014

"greater clarity on inclusion/exclusion criteria eg issue of pre-packing unit and ED not clear"
"Very complex to match up the data taken from the system and match the descriptors on the spreadsheet. Had to all be done manually and had to be done separately for 2 different sites which took a very long time. Descriptors were not always clear as to what they were referring to (eg ciprofloxacin IV) and there were multiple duplicate descriptors."
"Clarification about different antibiotic lines not included in the worksheet"
"Protocol is clear. We would benefit from being able to submit data by total dose units (eg capsules, vials etc.) rather than number of whole packs. I understand that other Trusts find the opposite is true so perhaps there could be an option?"
"I thought the list of what should or shouldn't be included could have been clearer. The list of antibiotics was odd - some exceptions but other drugs (ie demeclocycline) included. There was a very short deadline for such a large piece of work."
Our data is reported as total number of caps/tabs/vials issued. It was another step to get the number of packs issued. Would be useful to have system that allows you to enter either.

Seven pilot participants participated in the teleconference. This included five antimicrobial pharmacists, one microbiologist and one pharmacy technician. The key feedback from participants from this group session is highlighted below (Table 3.7).

Table 3.7 Group feedback on pilot validation protocol and recommendations for improvements, England, 2014

Two to four hours was sufficient to fully complete the validation process if there were already good systems in place for antimicrobial use data analysis; however for trusts where there were no systems in place, it could take longer than four hours. In the majority of the trusts, a single person completed the full validation process including data extraction and entry onto the spreadsheet. It was recommended that the time to complete the survey be changed to 4−7 hours. There were difficulties in obtaining the data where there had been trust mergers especially if there were two pharmacy systems, and the data had to be combined. There was no simple solution to this but to extract the data from each system separately and then merge it on the data entry sheets. With regards to acceptable differences between locally held and IMS datasets, the group agreed that it was important to ensure that data from both data sets were identical. A 10% difference was considered to be too high. The group suggested and agreed that a 2−3% difference between antimicrobial consumption usage from the IMS data set and the pharmacy system was more acceptable, especially if the IMS data was to be used for benchmarking or target setting.

The following changes to the validation protocol were agreed:

- to include information on the process that trusts need to undertake where differences between trust and IMS data were greater than 3%
- to include details of the help desks for the pharmacy systems within the frequently asked questions section
- to increase the time taken to complete the protocol from 2−4 hours to 4−7 hours
- to add information to the protocol on how to manage missing forms of drugs, including pack sizes

Discussion

Total antibiotic consumption, as measured by DDD, is still increasing though the rate of increase has slowed down with a 2.4% increase between 2013 and 2014 from 21.6 to 23.0 DDD per 1000 inhabitants per day. General practice consumption increased by 2.1%, hospital consumption increased by 3% and consumption by other community services increased by 5.5% though this amounted to the fewest antibiotic prescriptions. Dentists are the only group which decreased consumption but this is also the area with the largest private practice, where prescriptions are not recorded centrally and therefore cannot be measured as accurately as in other clinical areas.

However, in 2014, the largest proportion of antibiotics continues to be prescribed for patients in the community: general practice (74%), hospital outpatients (7%), dental practices (5%) and other community settings (3%). Prescribing in hospitals inpatients accounts for 11% of total consumption. Within NHS trusts, the greatest use occurs in acute trusts (94.6%), with specialist trusts accounting for 3%, learning and mental health trusts 1.7% and community trusts 0.7%.

This demonstrates that the greatest overall reductions in antibiotic prescribing in the country will be generated by reducing community prescriptions, for example a 5% reduction in prescribing by general practice would reduce total DDD by 0.9 per 1000 inhabitants per day compared to 0.21 DDD per 1000 inhabitants per day if hospital prescribing was reduced by 5%. This is potentially achievable as for the first time in the last three years the number of antibiotic prescriptions dispensed in the community declined by 7% from April to June 2015, compared with similar time periods in 2014 and 2013.

The three groups of antibiotics most frequently used in England continued in 2014 to be penicillins (45%), tetracyclines (22%) and macrolides (15%) (Figure 3.3). Between 2011 and 2014, significant increases occurred in use of tetracyclines (13%), sulphonamides/trimethoprim (5%) and the mixed group of other antibacterials (23%). Over the same period, a decrease occurred in the antibiotic consumption of the following groups: other β-lactam antibacterials (-17%), anti-*Clostridium difficile* agents (-3%) and quinolones (-2%). The decreases in these three groups of antibiotics occurred predominantly in the community.

Conversely, within the hospital setting, broad spectrum prescribing continues to increase, particularly those antibiotics of last resort, carbapenems and piperacillin-tazobactam. Between 2013 and 2014, prescription of carbapenems, piperacillin-taxobactam rose by 4% and 7% respectively, with total increases between 2010 and 2014 of 36% and 55% respectively. It is important that acute NHS trusts in particular prioritise AMS and target clinical reviews by specialist infection doctors and pharmacists to patients prescribed broad-spectrum antibiotics to ensure that these continue to be the

most appropriate agents and that alternative antibiotics that can be used to preserve these last resort antibiotics are considered. In this report we have highlighted the differences in prescribing volume and the variation in antibiotics prescribed in different NHS trusts. This highlights and emphasises that the majority of antibiotic prescribing occurs in acute trusts and this is the area that we should continue to focus efforts on AMS.

This is the first time that dental antibiotic use has been reported in detail along with other prescribing settings. There has been a continuous decrease in items prescribed but slight increase in DDD between 2013 and 2014. However less than 50% of the population receive NHS dental care and while this appears unchanged over the previous 24 months, it may be that there are movements of patients and prescriptions to private care, that we are currently unable to measure.[29] Since May 2015, the Faculty of General Dental Practitioners has made their antimicrobial guidelines for dental practice available as open access; this is an excellent initiative to support standardisation and best practice.[30] Local measures, such as drainage of pus through root canals or dental extractions, are the primary modality of treatment. Antibiotics are recommended for oral infections where there is evidence of spreading infection (cellulitis, lymph node involvement, or swelling) or systemic involvement (fever, malaise). Other indications include necrotising ulcerative gingivitis and sinusitis. The commonest recommended antibiotics are penicillins – phenoxymethylpenicillin or amoxicillin. Metronidazole and macrolides are recommended as alternatives in cases of penicillin allergy. In particular the Scottish guidelines state that the routine use of clindamycin or co-amoxiclav has no advantage over these agents for the treatment of standard dental infections. These drugs should only be used as second line treatment for severe spreading infections. Doxycycline is recommended only as treatment for sinusitis. ESPAUR oversight group has developed a dental working group that will explore AMR, antimicrobial use (including data to practice level) and stewardship measures that should be developed and undertaken in England. We will report the outcome of this working group and objectives for future dental surveillance in 2016.

Validation studies are an important epidemiological function within the context of surveillance of antimicrobial consumption and resistance. The pilot validation protocol was successfully developed with 30 acute trusts and modified and improved under their direction. Detailed explanations and clarifications were made to the worked example appendix in the final protocol. All NHS acute trusts have now submitted a dataset to PHE. Analysis is now underway to assess the differences between IMS Health and Rx info datasets. The baseline data that the acute trusts submitted will inform the baseline for measuring the impact of AMS in England in the coming years.

[29] NHS Dental Statistics for England 2014/15. Available at http://www.hscic.gov.uk/catalogue/PUB18129
[30] Antimicrobial Prescribing for General Dental Practitioners, 2014. Available at http://www.fgdp.org.uk/publications/antimicrobial-prescribing-standards.ashx

Improvements in surveillance and reporting driven by ESPAUR to date have focused on antibiotic consumption and resistance. A presentation of antifungal consumption and resistance was provided to the ESPAUR oversight group in February 2015. The group determined that a subgroup was required to identify gaps within current antifungal surveillance and seek to explore and implement improvements to national surveillance programmes.

While the focus of ESPAUR is England it is important to understand the consumption of antibiotics in the European and UK context. Antibiotic consumption across the UK devolved administrations shows similar trends and in the next 12 months we will work with the devolved administrations to develop a joint antibiotic consumption report.

We will also continue to work with ECDC to ensure that the datasets across Europe are enhanced, reliable and comparable. Each country has different insurance, reimbursement and data collection procedures, potentially meaning that data is not as comparable as it should be; for example less than 50% of countries are currently capable of submitting hospital data and the hospital data may only include that from acute care hospitals rather than all hospitals. However, in comparison to the 2013 data that was submitted to the European Surveillance of Antimicrobial Consumption Network (ECDC-Net) at ECDC, the UK remains one of the middle to high prescribing countries for both community and hospital prescribing (Figure 3.32).

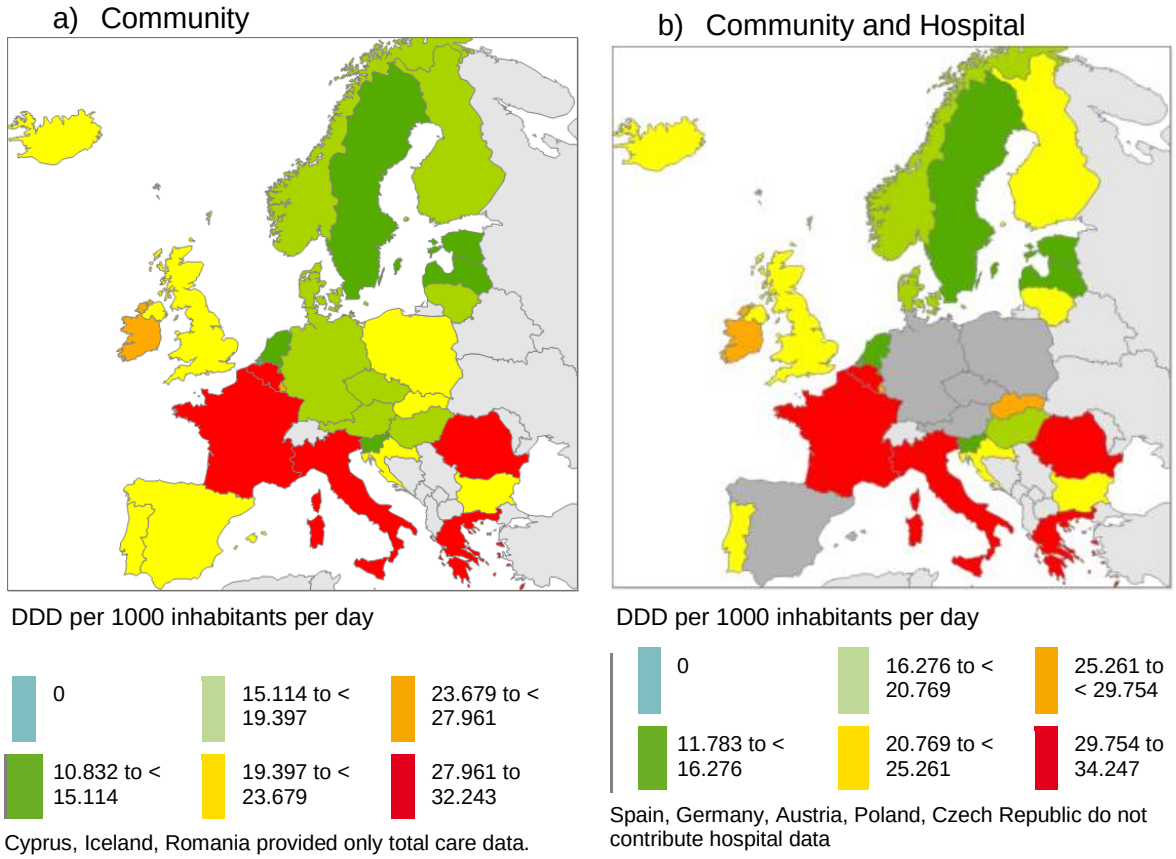


Figure 3.32 Geographical distribution of antibiotics use expressed as items per 1000 inhabitants per day, Europe, 2013

A number of countries cannot currently submit detailed hospital and community data. Given the recent development of England's surveillance systems in this area, we will continue to work with ECDC to improve the quality and comparability of this data across Europe through involvement with ESAC-net.

As part of ESPAUR's remit to support better access and use of surveillance data, antimicrobial consumption data will be used to inform the development of local AMR action plans. Relevant indicators and proposals to establish a data portal for antimicrobial resistance, stewardship and infection control are currently in development and will be rolled out in 2016.

Chapter 4: Antibiotic stewardship and public and professional engagement

Introduction

Key area 2 of the UK AMR Strategy focuses on optimising prescribing through the implementation of AMS programmes. Key area 3 aims to improve professional education and training and public engagement to improve clinical practice and promote wider understanding of the need for more sustainable use of antibiotics.

This chapter outlines the progress made as part of implementing key areas 2 and 3 of the UK AMR strategy. In particular:

- evaluating the use of tools and resources for optimising prescribing in primary and secondary care
- work with Health Education England (HEE) to identify options for implementation of embedding competencies into undergraduate, post graduate and continuing professional development (CPD) curricula
- the Antibiotic Guardian campaign in 2014, engaging the public and professionals in pledging to take action to preserve antibiotics; review and evaluation of the impact of the campaign in 2015 to inform the development of a sustained approach across the life of the strategy

Evaluating the use of tools and resources for optimising prescribing in primary and secondary care

This chapter summarises the results of a national survey to assess the uptake of the TARGET 'Treat Antibiotics Responsibly, Guidance, Education, Tools' AMS toolkit for primary care and AMS activities in primary healthcare settings. The survey on implementation of the secondary care AMS toolkit, Start Smart then Focus (SSTF), was presented at ESPAUR 2014 (ESPAUR 2014) and comprehensive combined results have been submitted for publication in a peer-reviewed journal.

TARGET, which focuses on AMS activities in primary care, was developed by PHE and the Royal College of General Practitioners (RCGP) in 2012 for use by the whole primary care team within general practice or out of hours. It aims to help influence prescribers' and patients' personal attitudes, social norms and perceived barriers to optimal antibiotic prescribing and use. Its resources can be used to fulfil CPD and appraisal requirements.

The Start Smart Then Focus (SSTF) toolkit is a summary of evidence-based AMS practice for use in secondary care settings. It provides information on strategies to improve antibiotic use within secondary care and suggested audit topics to improve practice. Implementing SSTF can help local organisations demonstrate compliance with the Department of Health code of practice on infection control and supports NICE AMS guidance.[31]

Following assessment of the implementation of SSTF in acute care (2014), a multi-professional group was convened by ESPAUR to assess the levers and barriers to embedding and implementing the toolkit in practice. As part of the implementation process; the toolkit was updated based on newly published evidence, expert consensus and user feedback.

Work with HEE to identify options for implementation of embedding competencies into undergraduate, post graduate and CPD curricula

In 2012, the Department of Health expert advisory committee on AMR and healthcare associated infections (ARHAI) and PHE published antimicrobial prescribing and stewardship (AMPS) competences. As part of implementation of the AMR strategy, a joint working group between ESPAUR and HEE was established to develop options for the implementation of the AMPS competencies within both undergraduate and postgraduate healthcare curricula and CPD. To aid their deliberations the working group conducted a survey to identify levers and barriers to implementing the AMPS competencies. The results and future plans are presented.

Deliver and evaluate the 2014 Antibiotic Guardian campaign, engaging the public and professionals in pledging to take action to preserve antibiotics

As part of UK activities for the 2014 European Antibiotic Awareness Day (EAAD) and in support of the UK 5-year AMR strategy, PHE developed the Antibiotic Guardian (AG) campaign 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 objective for the first year was for 10,000 healthcare professionals and members of the public to choose a pledge on www.AntibioticGuardian.com by 30 November 2014.

Activities and resources for EAAD and the AG campaign were developed and run by a PHE-led interdisciplinary committee with representation from animal and human health

[31] NICE Guidelines 15 – Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use https://www.nice.org.uk/guidance/ng15

sectors across England and the devolved administrations. We present an initial evaluation of the AG campaign.

Methods

Evaluating the use of tools and resources for optimising prescribing in primary and secondary care

AMS in primary care:

To assess the uptake of TARGET and AMS activities in primary care, electronic surveys were piloted in 10 CCGs and revised prior to circulation to all 211 CCGs in England in November 2014.

AMS in secondary care:

Update and recommendations for implementing SSTF in secondary care:
Following an update of SSTF by the multi-professional group, the draft updated toolkit was circulated for user feedback in November 2014, to a range of healthcare professionals including junior doctors, nurses, heads of medicines management, senior nurses and clinicians by cascade from the chief pharmaceutical officer for England and NHS England clinical directors. Recipients were asked to provide comments on the updated document and its perceived ease of implementation within their organisations.

Work with HEE to identify options for implementation of embedding competencies into undergraduate, post graduate and CPD curricula

In 2014 a joint working group between ESPAUR and HEE was established to develop options for the implementation of the AMPS competencies within both undergraduate and postgraduate healthcare curricula and CPD.

In February 2015 the working group devised and circulated a survey to the chief executives of professional bodies, royal colleges and local education and training boards (LETBs). The survey aimed to identify resources already available to support professionals demonstrating their competence against the AMPS competencies and levers and barriers to embedding the competences.

The survey may be viewed here: https://surveys.phe.org.uk/AMPSCompetences

Deliver and evaluate the 2014 Antibiotic Guardian campaign, engaging the public and professionals in pledging to take action to preserve antibiotics

The Antibiotic Guardian campaign was developed by a multi-professional group which included lay representation. Using already published evidence, draft pledges were agreed by the group along with the development of a website and video. Prior to formal launch of the website on 13 September 2015, the antibiotic guardian pledges and website underwent a two-month user testing phase with 1,000 individuals including healthcare professionals and members of the public as well as further consultation with behavioural scientists and marketing specialists. Student pledges were added at the request of the Chief Medical Officer on 14 November 2014.

Individuals who pledged on antibioticguardian.com voluntarily provided personal data (name, half-postcode, email) and selected an option for how they had heard of the campaign. Google analytics collected data on all website visits, the proportion which made a pledge, the route via which a visitor arrived at the website and identified unique visitors and location from an IP address. Google analytics data collection began on 08 August 2014, two weeks after the website was accessible online.

The primary outcome of choosing a pledge was assessed by time, location (UK half-postcode) and by pledge groups.

All data was collected through voluntary service evaluation completed by healthcare professionals and the public. Ethics approval was not required.

Survey responses were analysed using STATA (V.13) and Microsoft Excel.

Results

Embed use of tools and resources for optimising prescribing in primary and secondary care

AMS in primary care

Eighty-two CCGs responded to the survey assessing the uptake of TARGET and AMS activities in primary care (response rate 39%). The majority of these had reviewed the TARGET AMS toolkit formally or informally (60%, n=49). Only 13% of respondents had developed an action plan to implement the TARGET toolkit, however promotion of TARGET by prescribing advisor visits and use of TARGET resources, particularly the use of patient information leaflets and educational presentations, were considerably higher at over 50% (Figure 4.1). Although only 12 of the responding CCGs had implemented suggested AMS audits within the TARGET audit plan or collated data as

part of CCG-wide point prevalence surveys, 69% carried out local antibiotic audits. The high levels of local antibiotic audits may be related to CCGs using local prescribing incentive schemes, for antibiotics and other drugs, to influence GP prescribing.

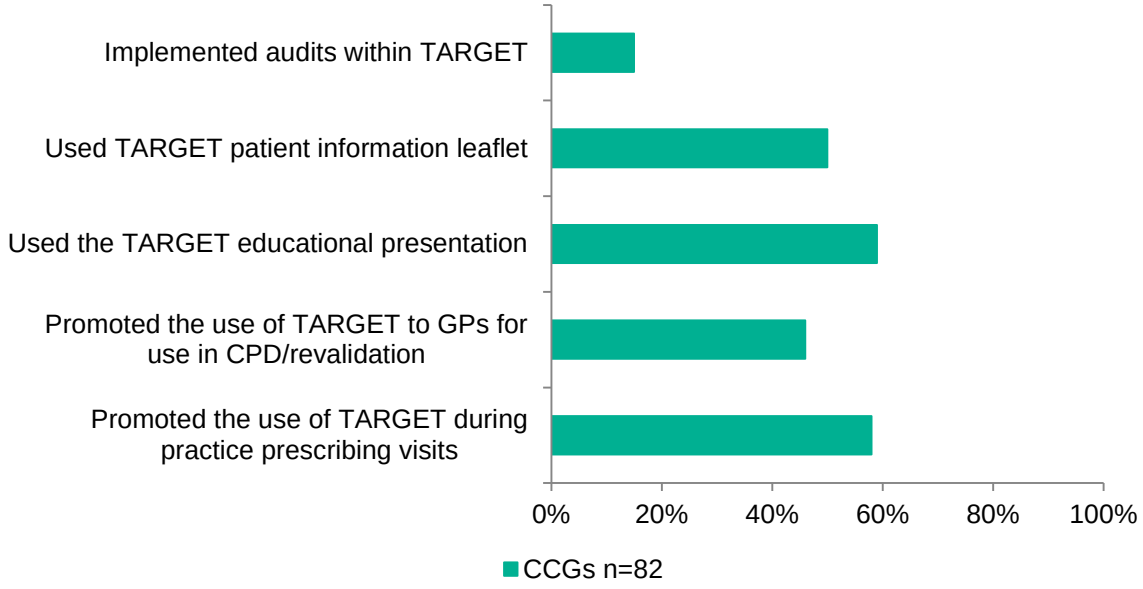


Figure 4.1 Use and promotion of TARGET resources and audits, England, 2014−2015

Adherence to AMS principles is presented in Figure 4.2. Written antimicrobial education and training strategies were rare. In addition, 33% of antimicrobial prescribing and stewardship training conducted was decided by individual CCG trainers. This may have resulted in variable levels of AMS training in primary care.

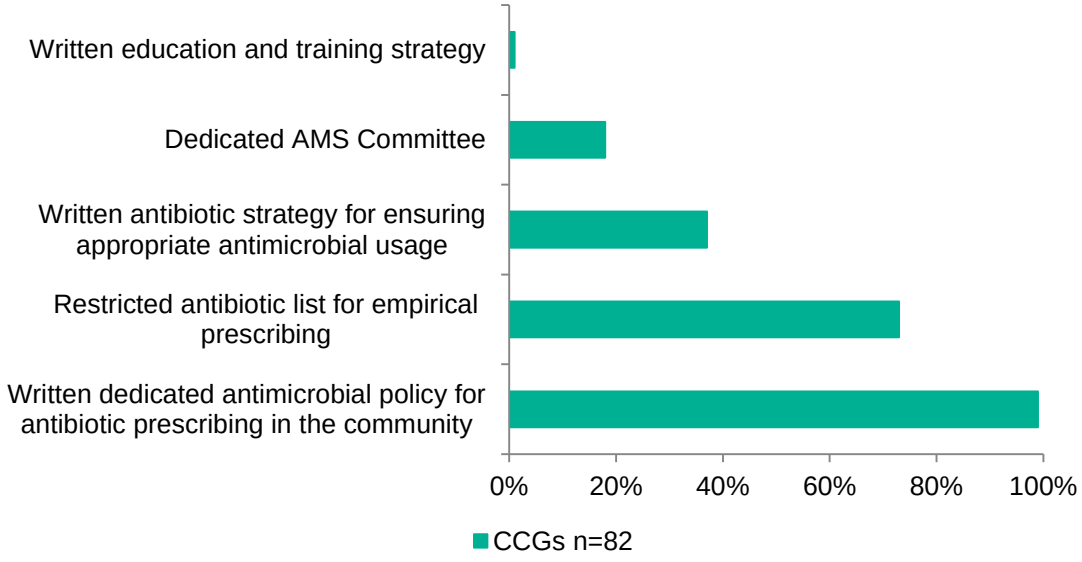


Figure 4.2 Adherence to AMS principles in primary care, England, 2014−2015

Only four CCGs (18%) reported having a specific AMS committee. However the AMS role was also performed by the Drugs and Therapeutics Committee (n=17, 21%), Infection Prevention and Control committee (n=11, 13%) or local acute trusts (n=2, 2%).

Prescribing advisors/medicine management pharmacists led the AMS and prescribing strategy in 54 (66%) responding CCGs, although only four (5%) CCGs had a specialist antimicrobial pharmacist undertaking this role. This role was undertaken by quality, nursing, clinical and GP clinical leads in five (6%), five (6%) and two (2%) CCGs respectively. Specialist antimicrobial pharmacists spent on average four to seven times longer on AMS duties than non-specialists such as prescribing advisor/medicine management pharmacists.

CCGs worked collaboratively with acute trust clinicians such as a microbiologists (n=73, 89%), GP practices (n=71, 87%), community service providers (n=62, 76%) and community pharmacies (n=45, 55%) to deliver AMS. Thirty-nine (48%) responding CCGs did not know of any future plans to develop cross-sector AMS activities with acute trusts, 34 (41%) reported that they would collaborate with acute trusts within the following 1−2 years and nine (11%) CCGs had no future plans.

AMS in secondary care

There were 94 respondents to the SSTF user-feedback survey; 52 (55%) had either formally or informally reviewed SSTF, and 60% of clinicians were not aware of SSTF, indicating that further activities to raise awareness of this national toolkit would be beneficial. Comments received through the user testing process were positive. The predominant comments highlighted that there was a need to clarify which audits should be mandatory, expand the toolkit to antimicrobials (rather than just antibiotics), ensure alignment with surviving sepsis principles, and simplify the expectations of AMS policy.

Table 4.1 Respondent demographics to SSTF user testing survey, England, 2014−2015

Respondent type	No. of responses
Nurse	1
Chief pharmacist	4
Surgeon	6
Lead infection doctor/clinical microbiologist/infectious disease specialist	8
Clinician	12
Junior doctor	14
Lead antimicrobial pharmacist	39
Undefined	10
TOTAL	**94**

Table 4.2 outlines the recommendations made by the SSTF implementation group to further embed SSTF within secondary care based on discussions from four subgroup meetings and results of the user feedback survey.

Table 4.2 Recommendations from SSTF implementation group, England, 2014−2015

1. NHS England should initiate a level 2 patient safety alert on AMS (subject to the necessary approvals) for both primary and secondary care.

2. SSTF and TARGET AMS toolkits should be presented to clinical leaders to raise the profile of these documents at a more senior level.

3. PHE should consider the development of an AMS surveillance system.

4. PHE should consider submitting the SSTF AMS toolkit to NICE for endorsement. The new NICE endorsement programme acts to formally endorse guidance support resources produced by external organisations. The aims of the endorsement programme include ensuring that:
   - users are confident that using an endorsed resource will support implementation of the relevant NICE guidance recommendations or use of the quality standards identified
   - external producers who are developing support resources have the opportunity to work with NICE to ensure their resources are aligned to NICE recommendations

Work with HEE to identify options for embedding competencies into undergraduate, post graduate and CPD curricula

Fourteen organisations responded to the survey. This included local education and training boards ((LETBs) n=6), schools' councils (n=4), professional organisations (n=2) and professional societies (n=2). Twelve were aware of the AMPS competences.

Survey respondents highlighted the following potential barriers to embedding AMS principles in education and practice across the whole healthcare economy:

- public and patient lack of understanding about AMR and expectations of antibiotic treatment;
- the lack of continuity of care;
- the problems in specialist areas with local guidelines;
- the in-grained attitudes of older healthcare professionals;
- the different organisation within medical schools with very variable teaching on antibiotics and AMR; and

- the knowledge and skills of non-prescribing professionals around antimicrobial prescribing may relate to the critical evaluation of another professional's prescribing
- the AMPS competences do not directly allow for this distinction, making some of them less relevant to non-prescribing professionals

The following levers have been identified:

- the commissioning of training courses by LETBs
- Royal colleges who in 2014 published a joint statement (in collaboration with the Faculty of Public Health) on their role in tackling AMR
- the recently published NICE AMS guidance
- the national prescribing framework

The recommendations delivered to HEE from the joint working group are outlined in Table 4.3.

Table 4.3 Recommendations for HEE to implement AMS competencies, England, 2014−2015

1. HEE should inform the four regional directors of education and quality of the variation with which AMS principles are included within undergraduate curricula citing the results of the Imperial College undergraduate curricula survey (once published).

2. HEE should liaise with healthcare regulators to facilitate embedding of antimicrobial prescribing and stewardship competencies into educational curricula. Regulatory documents for undergraduate and postgraduate curricula of each healthcare profession have been identified by the joint PHE/HEE AMPS competencies group.

3. HEE should work with regulatory bodies to explore the possibility of inclusion of antimicrobial prescribing and stewardship principles in professional registration examinations.

4. HEE should consider adapting the current antimicrobial prescribing and stewardship competencies as learning standards on AMR and AMS (not prescribing alone) at different levels for all healthcare staff.

5. HEE should consider facilitating the establishment of network leads to assist with the teaching of antimicrobial prescribing and stewardship and develop core material. This should be seen as a good example of multi-disciplinary working.

6. NHS employers have a key role to play and it is recommended that HEE work with NHS employers to explore how to include AMR and AMS as part of mandatory training for all NHS staff. This can be an extension of infection prevention and control.

7. HEE to explore the best mechanisms through which results of local quality antibiotic prescribing audits are used to influence education and training programmes to enable sustained improvement in AMS.

8. The group understands that embedding the AMPS competencies is dependent on more than education alone. Therefore the group recommends that HEE should work with behavioural insights experts from other agencies and academia to seek to understand how best to achieve behaviour change to incorporate AMS principles.

9. Using the resources identified by the joint PHE/HEE AMPS competencies group HEE should create a freely accessible webpage signposting to educational resources on antimicrobial prescribing, resistance and stewardship which support the learning outcomes of the competencies. This should include a slide set highlighting the key national guidance, toolkits and resources on AMR and AMS. It is envisioned that Higher education institutes may find this a useful resource for delivering learning around AMR and AMS.

10. HEE should explore the possibility of adapting learning materials developed by the Centre for Pharmacy Postgraduate Education (CPPE) for all healthcare professionals.

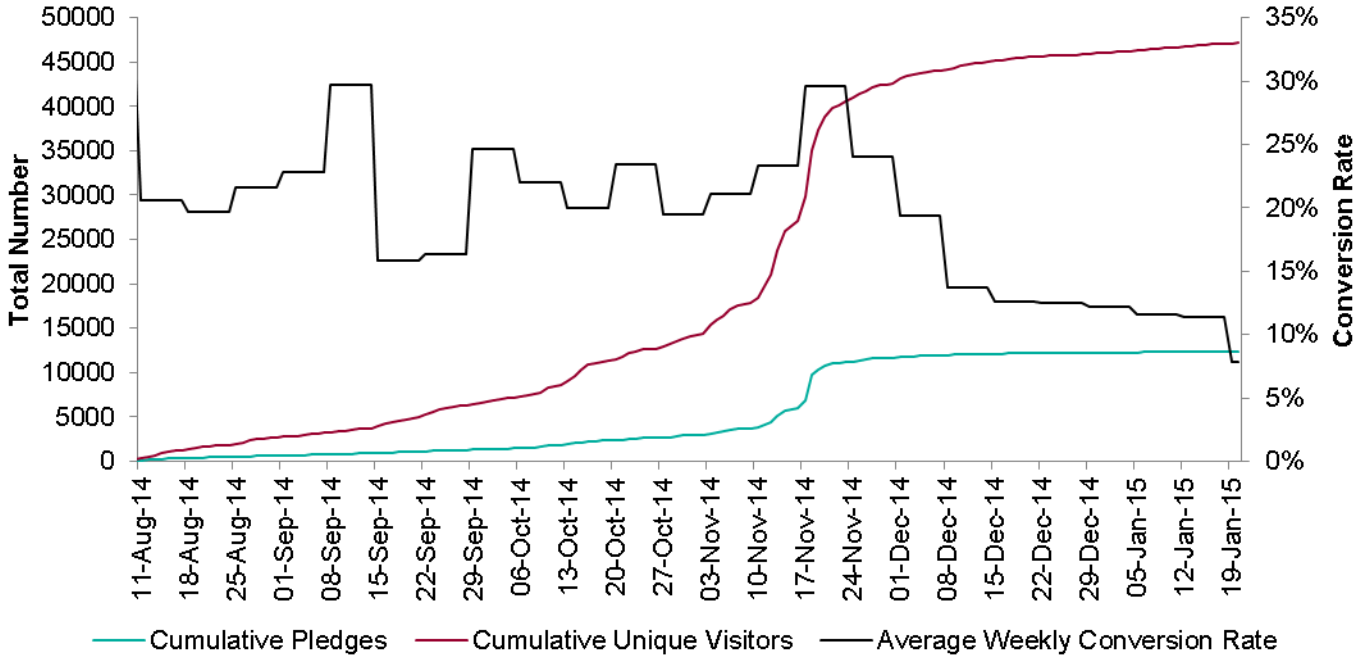
11. HEE should consider submitting the AMPS competencies to NICE for endorsement. The new NICE endorsement programme acts to formally endorse guidance support resources produced by external organisations. The aims of the endorsement programme include ensuring that:
    - users are confident that using an endorsed resource will support implementation of the relevant NICE guidance recommendations or use of the quality standards identified
    - external producers who are developing support resources have the opportunity to work with NICE to ensure their resources are aligned to NICE recommendations

12. HEE should work with NICE during the update of the national prescribing competencies to ensure that AMR, AMS and infection prevention and control continue to feature.

13. HEE should work with the British Pharmacological Society and Medical Schools Council to ensure that AMR, AMS and infection prevention and control are embedded and assessed as part of the Prescribing Safety Assessment (PSA).

Deliver and evaluate the 2014 Antibiotic Guardian campaign in 2014, engaging the public and professionals in pledging to take action to preserve antibiotics

The campaign goal of 10,000 Antibiotic Guardians was met by 30 November 2014 as outlined in Figure 4.3. The majority of engagement with the Antibiotic Guardian campaign aligned with EAAD on 18 November with a marked decline in activity after EAAD.



*overall conversion rate=26.5%; 12,509 pledges; 47,158 unique website visitors

Figure 4.3 Comparison of unique website visitors to the total number of Antibiotic Guardians; antibioticguardian.com, 11 August 2014 to 19 January 2015

There was heterogeneity in the spread of antibiotic guardians across the UK (Figure 4.4). While there was diversity between the UK-nations these differences are not significant. The Antibiotic Guardian website was visited by 47,158 individuals in 156 different countries. Of these, 12,509 became Antibiotic Guardians and at least one pledge was made in 81 countries. The proportion of website visitors who made a pledge on their first visit to the website and became an Antibiotic Guardian provides an overall conversion rate of 26.5%.

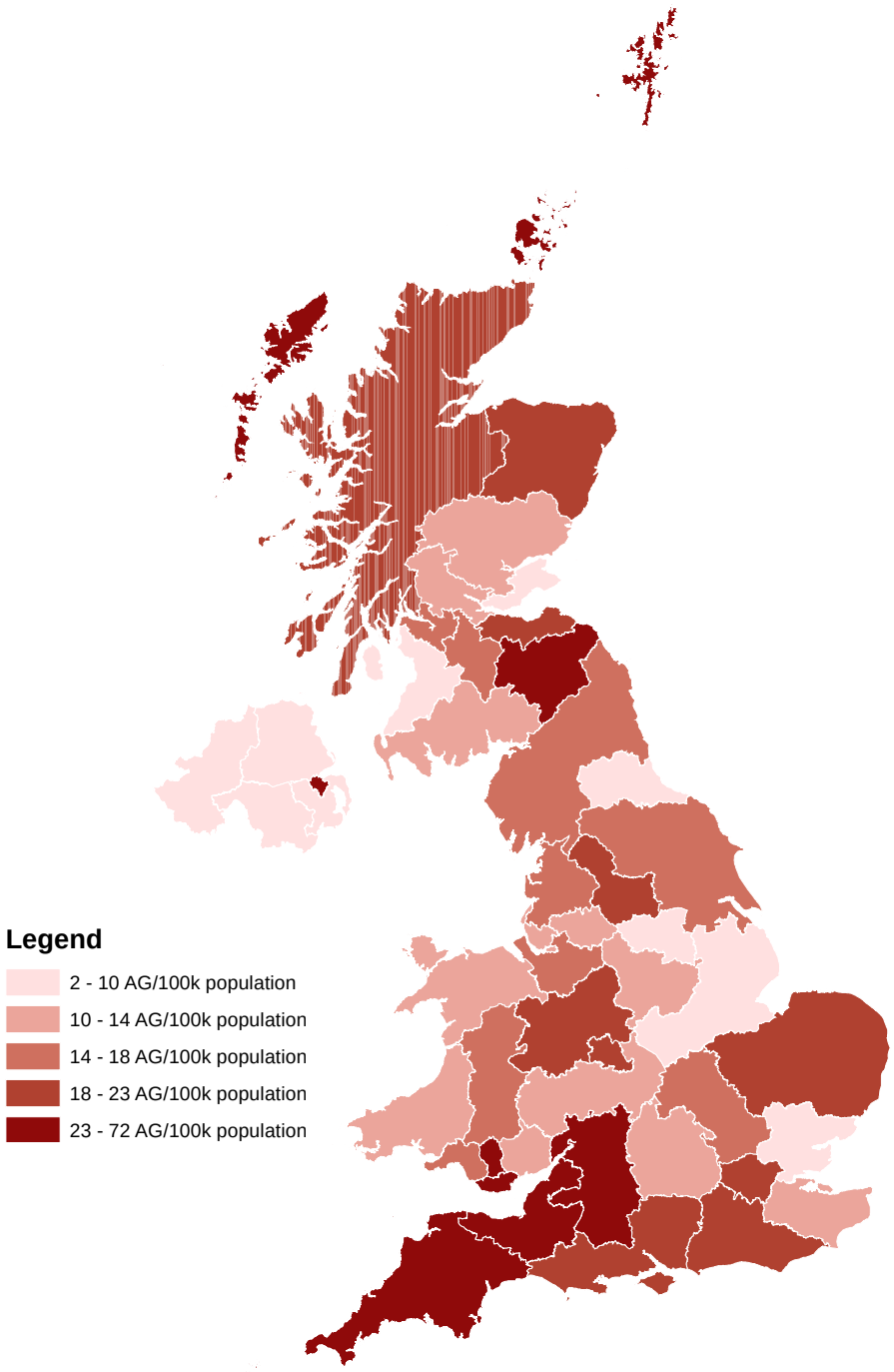


Figure 4.4 Variation of Antibiotic Guardians/100,000 population by NHS area teams/health boards or equivalent, n =11,833, UK, January 2015

The Antibiotic Guardian campaign was primarily driven and engaged with by healthcare professionals (69%), with the remaining 31% of pledges provided by the public (Figure 4.5). The largest group of pledgers were pharmacy teams (22.3% of total Antibiotic Guardians) and adults (21.2%); students represent the third largest target group among the Antibiotic Guardians (8.8%) and are the only group which have pledges in both healthcare professional and public categories.

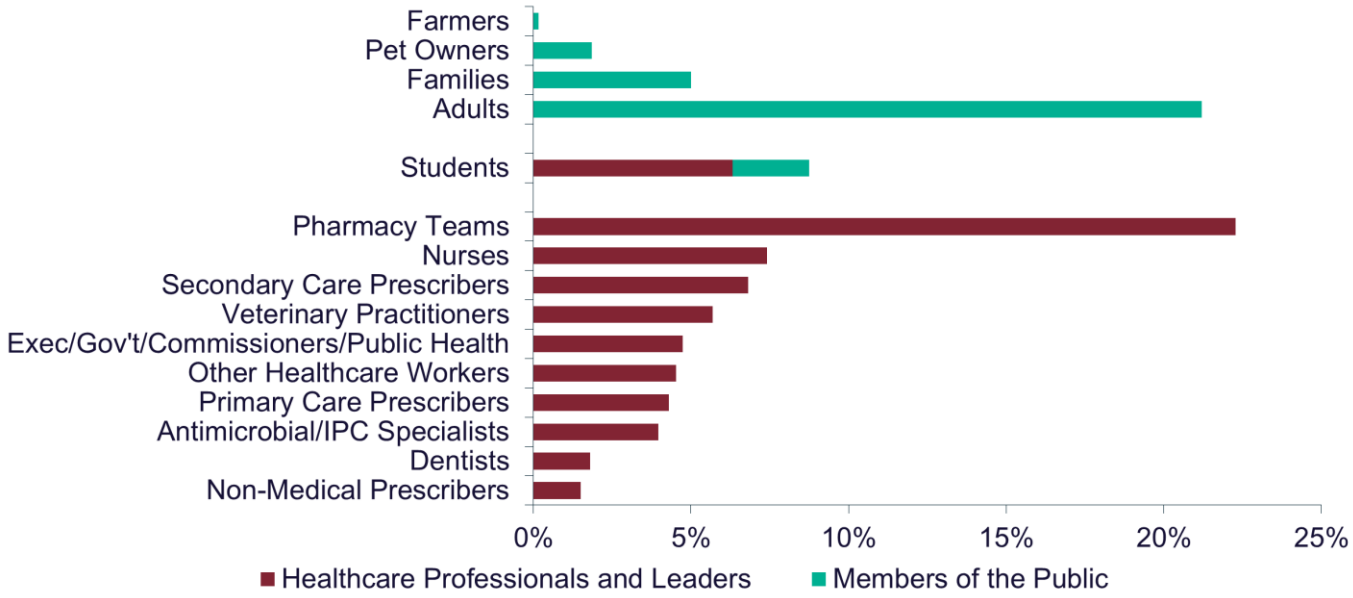


Figure 4.5 Distribution of Antibiotic Guardian pledges by target audiences, antibioticguardian.com, January 2015

Discussion

Over the year, ESPAUR has addressed key actions published in the UK AMR Strategy implementation plan. In particular:

- embed use of tools and resources for optimising prescribing in primary and secondary care
- work with HEE to lead the identification of options for embedding competencies into undergraduate, post graduate and CPD curricula
- deliver the Antibiotic Guardian campaign in 2014, engaging the public and professionals in pledging to take action to preserve antibiotics. Review and evaluate the impact of the campaign in 2015 to inform the development of a sustained approach across the life of the strategy

Optimising prescribing, professional education and training

Key activities completed which have an influence on optimising prescribing in both primary and secondary care include the joint work with HEE to consider options for implementing the PHE and ARHAI antimicrobial prescribing and stewardship competences, and providing the key actions that would enable these competences to be embedded in undergraduate and postgraduate curricula (Table 4.3).[32]

In addition, following recommendation from the SSTF implementation subgroup, a joint NHSE-PHE-HEE stage 2 patient safety alert for SSTF and TARGET was released in

[32] PHE and ARHAI Antimicrobial prescribing and stewardship competencies: https://www.gov.uk/government/publications/antimicrobial-prescribing-and-stewardship-competencies

August 2015 by NHS England.[33] The alert highlighted the importance of addressing AMR through implementation of an AMS programme using the two key national AMS toolkits developed by PHE, in collaboration with the NHS and key professional organisations (Table 4.2).

Implementation of AMS toolkits in primary and secondary care − ninety-nine acute NHS trusts (68% of all acute NHS trusts) and 86 CCGs (41% of all CCGs) participated in two surveys undertaken by PHE on the implementation of AMS toolkits in primary and secondary care. The proportion of trusts and CCGs that had implemented key AMS activities, recommended in the SSTF AMS toolkit for secondary care and the TARGET toolkit for primary care, are shown in Table 4.4.

The secondary care survey completed in 2014[34] revealed that the role of specialist antimicrobial pharmacists continues to remain embedded within acute NHS trusts; 90% of responding trusts had a specialist antimicrobial pharmacist at Band 8a and above in post. In primary care, prescribing advisors/medicine management pharmacists lead the AMS and prescribing strategy in 66% of responding CCGs; specialist antimicrobial pharmacists, quality leads, nursing clinical leads and GP clinical leads had also undertaken this role.

Table 4.4 AMS activities in secondary and primary care, England, 2014−2015

	Secondary care (Acute NHS Trust) n=99	Primary care (CCGs) n=86
AMS Committee	94%	19%
Written dedicated antimicrobial policy	93%	99%
Action plan/Implemented toolkit	48%	13%
Written education and training strategy	26%	1%
Implemented audits within AMS toolkit	79%	15%

In primary care, as well as assessing the implementation of TARGET, the toolkit has been evaluated and materials updated based on results of the evaluation. In addition, a clinical e-module has been developed to support implementation and improvements in its uptake.

The PHE primary care unit is currently developing a webinar series in collaboration with the British Society for Antimicrobial Chemotherapy (BSAC) for microbiologists around

[33] NHS England 2015. Patient safety alert: addressing AMR through implementation of an AMS programme http://www.england.nhs.uk/patientsafety/2015/08/18/psa-amr/

[34] ESPAUR Report 2014. https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report

AMR and AMS in primary care. Furthermore, BSAC in collaboration with the University of Dundee is offering a free six-week massive online open course (MOOC) on AMS.[35]

Other activities to further embed the TARGET toolkit have included:

- working with NHS England to develop the Antibiotic Prescribing Quality Premium for 2015/16. This has led to NHS CCGs focusing on primary care prescribing of antibiotics and AMS activities to support the implementation of the NHS England Antibiotic Quality Premium 2015/16. In addition, to support CCGs, NHS England in collaboration with PHE has delivered three national AMR workshops promoting AMS toolkits and examples of successful practice – these achieved about 75% attendance from representation from commissioning organisations (CCGs and CSUs)
- the Centre for Postgraduate Pharmacy Education (CPPE), University of Manchester, has also run a series of primary care study days with a focus on AMS which members of ESPAUR have contributed to. Also in November 2014 as part of activities for EAAD, CPPE mailed its AMS distance learning publication to all registered pharmacists and pharmacy technicians in England

Public engagement: Antibiotic Guardian

For the first time, using behaviour change strategies, the Antibiotic Guardian campaign has shown evidence of moving from increasing awareness to engagement. Evaluation of the Antibiotic Guardian campaign highlighted that it is an effective tool for increasing knowledge and changing behaviour.

The population bias towards healthcare professionals may be due to the channels which were available to PHE, in particular the significant support for the campaign by NHS and professional organisations with healthcare professionals as their main audience.

The goal for 2015/16 is 100,000 Antibiotic Guardians by 31 March 2016

It is important to have multi-organisation joint action signposting healthcare professionals and staff to the Antibiotic Guardian website[36] to educate non-specialist healthcare professionals on AMR and help them choose a tailored pledge commitment. Following recommendation from ARHAI, all senior healthcare leaders are encouraged to use the Antibiotic Guardian call to action email signature in the week leading up to EAAD.

[35] MOOC on AMS: https://www.futurelearn.com/courses/antimicrobial-stewardship
[36] Antibiotic Guardian website: http://antibioticguardian.com

Future plans and opportunities

Following the publication of the NICE guidance on AMS, key activities for implementation and embedding of national AMS toolkits will include:

- seeking endorsement for the national AMS toolkits (both TARGET and SSTF) from NICE and working with NICE to ensure implementation of the guidance across the health and social care system
- working with primary and secondary care providers to ensure they have AMS strategies/action plans in place and are completing the recommended audits
- increasing local and national championing and promotion of the SSTF and TARGET toolkits to increase awareness and improve uptake across primary and secondary care providers; utilising local and national meetings and professional networks to support the embedding of the toolkits into practice
- development of AMS in other healthcare settings including dentistry, community health services, nursing homes and mental health trusts
- continuing to work with NHS England to extend the use of commissioning incentives, the CCG Quality Premium and a national CQUIN, to influence antibiotic prescribing and AMS activities in 2016−17
- working with the Chief Pharmaceutical Officer of England to explore options for establishing local networks of antimicrobial pharmacists, to link secondary and primary care and to align antimicrobial stewardship practices from 2015

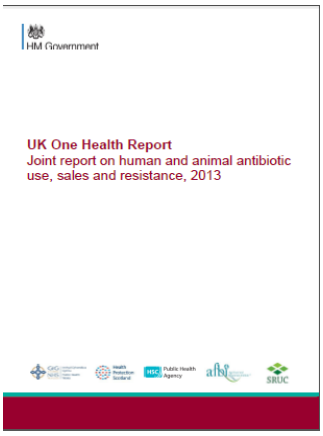
To aid further implementation of the AMPS, competencies work is currently underway within HEE to take forward the implementation of the competencies for healthcare staff through the development of an introductory module on AMR using the published competences as the basis for module development. A gap analysis of AMR teaching within undergraduate courses is also currently underway. Royal colleges, professional bodies, higher education institutes, the NHS and CCGs also have a key role.

The Antibiotic Guardian campaign is the first public health campaign in the UK to demonstrate measurable engagement in tackling AMR. From 2015, the Antibiotic Guardian campaign will be extended throughout the cold and flu season. However this would require sustained effort and outreach from PHE and partner organisations. Future work to develop the campaign should investigate how to best engage with target audiences and embed this new initiative within both public and professional spheres.

Chapter 5: Research and outputs

This chapter highlights secondary uses of the surveillance data collected. It has been utilised in other reports and by researchers to develop hypotheses and interventions to inform public health actions.

UK One Health Report: Joint report on human and animal antibiotic use, sales and resistance, 2013



Antibiotics are critical for treating infections in human and veterinary medicine, and increasing resistance in bacteria is considered a major threat in both fields. Resistant bacteria from animals and humans can transmit in both directions (Figure 5.1). Thus an integrated – one health − approach to surveillance and action is needed.

ESPAUR commenced work with the Defra AMR Coordination (DARC) Group and the Department of Health Expert Advisory Committee on AMR and Healthcare-associated infections (ARHAI) in 2014 to develop a one health report encompassing AMR and consumption data across the human and veterinary sectors in the UK.

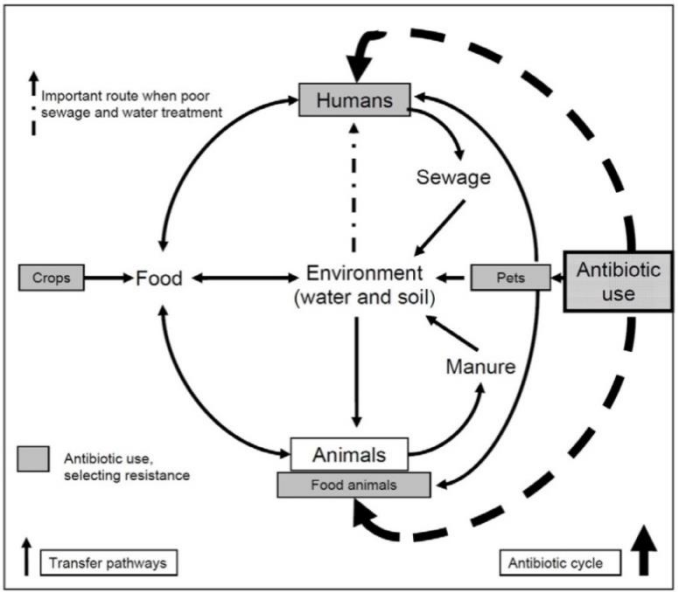


Figure 5.1 Interactions between humans, animals, food, environment and antibiotics. Interactions occur across local, regional, national and international boundaries with movement of humans, animals, and food within and between countries

The One Health Report brings together UK data on antibiotic resistance in key zoonotic (salmonella and campylobacter) and indicator (*Escherichia coli*) bacteria and on the amount of antibiotics sold for animal health and welfare, and antibiotics prescribed to humans, with the following aims:

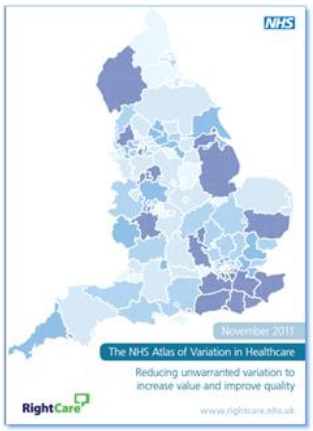
- to encourage further joint working between the human and animal sectors
- to identify the emerging and current antibiotic resistance threats in three key bacteria in humans and animals
- to identify differences in surveillance methodology and data gaps that limit our ability to compare trends between the two fields, both within the UK and across Europe
- to evaluate available data from humans and animals side by side and begin to assess the relationship between antibiotic sales, use and resistance across the two sectors
- to develop recommendations to improve the surveillance of antibiotic use and resistance in humans and animals

The One Health report is an important first step in building the data required to develop coordinated antimicrobial use and resistance surveillance activities in human and animal health across the UK and Europe.

The report has highlighted key public health recommendations for national human and animal organisations to take forward. The next report, planned for 2016, will report on the progress towards these recommendations.

The UK One Health report 2013 is available as a downloadable PDF
https://www.gov.uk/government/publications/uk-one-health-report-antibiotics-use-in-humans-and-animals

NHS Atlas of Variation in Healthcare 2015



The third NHS Atlas of Variation, detailing widespread variation in the quality, cost, activity and health outcome of healthcare in the English NHS, was published by PHE in collaboration with NHS England and NHS Right Care in September 2015.

The NHS atlas uses routinely available data to present selected indicators with the aim of highlighting unwarranted variation, encourage comparisons between NHS service providers and therefore action improvements leading to better outcomes for patients in England. The Atlas features indicators for three specific themes

- evaluation of under- and over-use
- preference-sensitive care
- better value (quality and outcomes per person-cost)

The selected indicators relate to PHE's priority areas: AMR, obesity, smoking, harmful drinking, best start for children, dementia, and tuberculosis. Data for each of the indicators is displayed as a column chart and map to show variation in terms of magnitude and geographical location within England. The commentary associated with each map ("Options for action") suggests possible course of action to reduce unwarranted variation and improve quality of care.

Antimicrobial prescribing data for indicators 1 and 2 in the Atlas was provided by ESPAUR:
Map 1: Mean number of defined daily doses (DDDs) of antibiotics prescribed in primary and secondary care per day per population by NHS area team, 2013
Map2: Percentage of all antibiotic prescription items in primary care that were for key antibiotics by CCG, 2013

Maps 1 and 2 demonstrated significant variability in total antimicrobial use in primary and secondary care and in primary care prescribing of broad-spectrum antibiotics across England in 2013 (as published in ESPAUR report 2014). 'Options for action' recommends NHS service care providers use this data to benchmark their antibiotic use and compare local data with regional and national trends. The section also refers to the quality measures for antibiotic prescribing that have been developed by the Department

of Health expert advisory committee on AMR and healthcare associated infection (ARHAI).[37]

The NHS Atlas of Variation in Healthcare 2015 is available as a downloadable PDF http://www.rightcare.nhs.uk/index.php/nhs-atlas/ and as an online interactive version http://www.rightcare.nhs.uk/atlas/2015_IAb/atlas.html

[37] Advisory 1/2152374732/18606265032/Committee on AMR and Hospital Acquired Infections (ARHAI). Recommended Antimicrobial Prescribing Quality Measures. 2014. https://app.box.com/ARHAI-Minutes-Papers/1

Chapter 6: Research abstracts

Clinical and epidemiological characteristics of new epidemic *Clostridium difficile* strains

Kate E. Dingle, Phuong Quan, Xavier Didelot, David W. Eyre, Nicole Stoesser, David Griffiths, Alison Vaughan, Warren Fawley, Jane Freeman, Kirsti Morris, Damian Mawer, Jessica Martin, Sherwood Gorbach, Ellie Goldstein, Dianne Citron, Peter Stevens, Philip Howard, Susan Hopkins, Mark H. Wilcox, Timothy E. Peto, A. Sarah Walker, Derrick W. Crook.
Lead by Oxford Health Protection Research Unit in HCAI and AMR
European Society for Clinical Microbiology and Infectious Diseases, 2015

Introduction

Nosocomial outbreak-associated *C. difficile* isolates are typically resistant to one or more commonly used antimicrobial drugs. The difficulty of controlling such strains in the healthcare setting is illustrated by hypervirulent PCR-ribotype 027 (multilocus sequence type ST1) which emerged as a clinical problem and spread worldwide soon after acquiring fluoroquinolone resistance. Additional fluoroquinolone resistant lineages which pre- or post-date ST1(027) also cause outbreaks or high incidence endemic *C. difficile* infection (CDI) in various geographic locations, highlighting the enduring and evolving nature of the problem.
Multiple policies aimed at curtailing the UK CDI epidemic were introduced in October 2007. A marked decline in CDI incidence soon followed, however since several interventions were introduced simultaneously, their relative contributions to the decline are unclear.

Objectives

The objective of this study was therefore to understand the impact of one specific policy, the restriction of fluoroquinolone prescribing.

Methods

Epidemiological data and whole genome sequences (WGS) for 2,049 *C. difficile* clinical isolates from Oxford, UK collected between September 2006 and August 2013 were studied. ST and fluoroquinolone resistance genotypes were extracted from the WGS. The incidence of fluoroquinolone resistance was examined overall, and by genotype for seven years, starting 1 year prior to fluoroquinolone restriction. Lineage-specific (ST) phylogenies were constructed using ClonalFrameML, onto which fluoroquinolone resistance genotype was mapped. Additional genomes from clinical isolates collected concurrently in Leeds (n=1,024) were included in the phylogenies and specific lineages were further supplemented with clinical isolates from Montreal (n=89) and Calgary

(n=30), Canada, and Italy (n=13); from Oxford asymptomatic or ELISA negative patients (n=76) and from healthy Oxford infants (n=59).

Results

A striking decline in incidence of all fluoroquinolone resistant lineages; ST1(027), ST42(106), ST3(001) and ST37(017) occurred in Oxford after fluoroquinolone use was restricted. This decline accounted for the overall fall in CDI incidence, since the incidence of fluoroquinolone sensitive lineages was unchanged. Phylogenetic analyses revealed fluoroquinolone resistant clonal expansions had occurred in these four lineages, and these clades were geographically structured. This phylogeny is consistent with infrequent nosocomial introductions of fluoroquinolone resistant strains, followed by rapid, localised transmission. In contrast, the phylogenies of fluoroquinolone sensitive lineages lacked geographic structure, consistent with frequent introductions and infrequent nosocomial transmission. Phylogenies including additional fluoroquinolone sensitive isolates from Oxford asymptomatic patients and healthy infants further supported the idea that sensitive strains are infrequently acquired nosocomially.

Conclusion

These data are consistent with previous findings indicating symptomatic patient to patient transmission, point source or secondary spread in only a minority (35%) of CDI cases. They indicate the importance of maintaining UK fluoroquinolone restriction, and suggest that this policy could be usefully applied elsewhere.

Effect of increased trimethoprim/nitrofurantoin prescribing on the incidence and antibiotic susceptibility patterns of E. coli bacteraemia nationally at GP practice level (2011−2014)

Hannah Lishman, Ceire Costelloe, Susan Hopkins, Berit Muller-Pebody, Russell Hope, Rebecca Guy, Alan Johnson, Paul Aylin, Alison Holmes
Work in Progress, Joint PHE and Imperial Health Protection Research Unit in HCAI and AMR Project.

Background

Bloodstream infections are a major cause of infectious disease morbidity and mortality both nationally and internationally. Between 2012 and 2015 the incidence of *E. coli* bloodstream infections in England increased by 10.4% from 60.4 to 66.23 per 100,000 population. The most commonly reported probable source of *E. coli* bacteraemia in England is urinary tract infection (UTI), with approximately 48% of *E. coli* bacteraemia suspected of originating from a UTI. In a recent meta-analysis, it was found that individuals who were prescribed an antibiotic for a UTI became colonised or infected with bacteria resistant to that antibiotic, with the likelihood being highest within the first

month post treatment. Given that rates of bloodstream infection (both caused by antibiotic susceptible and resistant bacteria) have increased each year, as have the rates of antibiotic prescribing, with the majority of prescribing occurring in primary care, this study aims to quantify the association between antibiotic prescribing for UTIs and the incidence and antibiotic susceptibility patterns of *E. coli* bacteraemia originating from a UTI.

Methods

This is a national ecological study with GP practice being the unit of analysis. The study population is all female adult (18+ years of age) patients with a reported *E. coli* bacteraemia in England between July 1st, 2011 and Dec 31st, 2014 with the primary focus of the bacteraemia being recorded by a clinician as a UTI. The study population has been restricted to women as men with UTIs are typically classified as complicated UTI cases and may therefore receive therapies alternative to trimethoprim and nitrofurantoin.

The study is using primary care trimethoprim and nitrofurantoin prescribing data (the two main antibiotics prescribed for uncomplicated UTIs) obtained from the NHS Business Services Authority (NHSBSA) database and antibiotic susceptibility reports for *E. coli* isolates from blood and urine from Public Health England (PHE)'s Second Generation Surveillance System (SGSS) linked to PHE's *E. coli* bacteraemia mandatory surveillance data. Only urine cultures from calendar year 2014 have been used for linkage as this time period is most reliable for urine culture data. All variables have been aggregated to GP practice level.

A longitudinal analysis is first being completed to look at the correlation between GP prescribing levels of trimethoprim and nitrofurantoin (counted together) and the rates of *E. coli* bacteraemia in women over time. Secondly, additional longitudinal analyses will determine the correlation between GP prescribing levels of nitrofurantoin and trimethoprim and rates of *E. coli* bacteraemia/UTIs in women resistant to these antibiotics (respectively).

Findings and Interpretation

The study is currently in the analysis phase. Our patient population includes 32,791 adult female patients with an *E. coli* bacteraemia with the primary focus of infection being recorded as the urinary tract, 22,768 of which have linked blood culture data and 1,113 of which have linked urine culture data (from 2014 only for the urine cultures). Findings from this study could potentially quantify the effect of different antibiotic prescribing patterns (low/medium/high prescribing of trimethoprim and nitrofurantoin) on the incidence of bloodstream infections at the GP practice level over time. The study could also serve to provide evidence to support the adoption of and compliance with Antibiotic Stewardship Programs in primary care Trusts across England.

Antibiotic prescribing trends and patterns among out of hours providers, England, 2010−2014

Michael Edelstein, Thara Raj, Susan Hopkins
Public Health England

Introduction

AMR (AMR) is a global public health threat, resulting in increased morbidity and mortality. In England, publicly funded clinical commissioning groups (CCGs) locally commission Out-of-Hours (OOH) services to provide primary healthcare outside general practice (GP) opening hours. National surveillance reported a 32% increase in antibiotic prescription in community services other than GP between 2010- 2013. We aimed to describe antibiotic prescribing patterns and trends among OOHs between 2010-2014.

Methods

We estimated the proportion of CCGs with OOH data available in the national prescribing database; described and compared antibiotic prescribing by volume, seasonality and trends in GP and OOH, using linear regression; and compared the proportion of broad-spectrum to total antibiotic prescriptions in OOHs with their respective CCGs in terms of seasonality and trends, using binomial regression.

Results

Data were available in 143/211 (68%) CCGs. Prescription volume in OOH represented 3.2% of GP antibiotic prescription volume (range 3.1-3.3% in individual years) and peaked (as did GP) each year in December. Prescription volume was stable over time (p=0.4). Proportion of broad-spectrum antibiotics prescriptions in OOH increased when it increased in the CCG they operated in (regression coefficient 0.99; 95%CI 0.94-1.06). Compared with GP, the proportion of broad spectrum antibiotics prescriptions in OOH was consistently higher but decreased both in GP and OOH (-0.57%, 95% CI -0.54;-0.6 and -0.76%, 95%CI -0.59;-0.93 per year respectively).

Conclusion

OOH prescribing volume was stable over time, and followed similar seasonal patterns to GP. OOH antibiotic prescribing reflected the CCGs they operated in but with relatively more broad-spectrum antibiotics than GP, although with a narrowing gap. Understanding factors influencing prescribing in OOH will enable the development of tailored interventions promoting optimal prescribing in this setting.

Provision of social norm feedback to high prescribers of antibiotics in general practice: a pragmatic national randomised controlled trial

Michael Hallsworth[1,4], Tim Chadborn[2], Anna Sallis[2], Michael Sanders[1,5], Daniel Berry[3], Felix Greaves[2], Lara Clements[2]; Sally C Davies[3]

[1] Department of Health Behavioural Insights; [2] Public Health England Behavioural Insights; [3]The Department of Health; [4] Imperial College London; [5] Harvard Kennedy School

The teams recently evaluated two population interventions to reduce antibiotic prescribing among 1,581 GP practices whose prescribing rate for antibiotics was in the top 20% in their area. A national randomised controlled trial was used to develop robust evidence of the effectiveness of each intervention independently. One intervention was a letter from England's Chief Medical Officer providing social norm feedback that the practice was prescribing antibiotics at a higher rate than 80% of practices in their area (along with a leaflet on antibiotic prescribing). The other intervention was patient-focused information that linked unnecessary antibiotic use to future personal consequence (along with a similar leaflet). The letter was a fraction of the cost of the patient-focused information.

The key outcome monitored from September 2014 to April 2015 was the rate of antibiotics dispensed (per 1000 weighted population). The inclusion of a group of GP practices that did not receive the interventions enabled the experts to definitively calculate the effect of each intervention. Use of publicly-available prescribing data enables low-cost and robust evaluation of public health interventions. This work will provide strong evidence of the independent effectiveness and return-on-investment of two behavioural interventions designed to reduce antibiotic prescribing in primary care. Results have been submitted for publication in a peer-reviewed journal.
The Behavioural Insights teams are now working with the NHS Business Services Authority and NHS England to implement and further test evidence-based behaviour change messages into routine and automated feedback to GPs.

The PHE Behavioural Insights Team are currently recruiting GP practices to a randomised controlled trial to test the effect of commitment devices and automated telephone messages, designed using behavioural science, on antibiotic prescribing rates. This trial will run over the winter 2015/16 and report in the autumn 2016 (NHS prescribing data publication is lagged by three months).

Development of a national electronic reporting system for the enhanced surveillance of carbapenemase-producing Gram-negative bacteria in England

Rachel Freeman, Dean Ironmonger, William Welfare, Susan Hopkins, Russell Hope, Paul Cleary, Bharat Patel, Peter Hawkey, Neil Woodford, Alan Johnson, Richard Puleston
Public Health England
European Scientific Conference on Applied Infectious Diseases Epidemiology, 2015

Background

Carbapenem resistance poses a significant threat to healthcare provision globally. Accurate and timely data will play a crucial role in controlling the spread of resistance. We developed a surveillance system to describe and monitor changes in the epidemiology of infections and colonisation by carbapenemase-producing Gram-negative bacteria. Carbapenem resistance is complex, therefore effective surveillance of it is challenging. Our approach detailed here has attracted the interest of several other countries facing similar challenges.

Methods

A working group designed a surveillance system to capture enhanced surveillance data, providing functional specifications for the system developer. To ensure rapid development and minimise costs, we recommended the adaptation of an existing regional pilot system into a national surveillance system.

Results

The resulting surveillance system utilises web-based case data capture, integrated into an established national microbiology reference service for the characterisation of carbapenem-resistant Gram-negative bacteria. To account for variations in isolate referral and testing practices across England, the system design ensures that data can be recorded at all stages of the referral process. The system uses a two-stage data submission process: patient demographic data, laboratory details and healthcare setting are provided prospectively by the laboratory for each isolate submitted. Enhanced data on patient travel history, admission details and potential contact with carbapenemase-producing Gram-negative bacteria is provided retrospectively by hospital infection prevention and control teams. The surveillance system will be further enhanced through linkage with electronically-stored microbiology, administrative and mortality data. Reference microbiology results are made available to stakeholders via the system.

Conclusion

Our approach allowed for rapid system development, at minimal cost, and integrated the surveillance programme into existing practice. We anticipate this will improve acceptance and increase participation.

Modelling seasonality in *Klebsiella* spp. in long-term care facilities

Alicia Rosello*, Esther Van Kleef, Dean Ironmonger, Carolyn Horner, Susan Hopkins, Andrew Hayward, and Sarah Deeny
*PHE funded UCL PhD student
Epidemics[5.] Fifth International Conference on Infectious Disease Dynamics, 2015

Introduction

Klebsiella spp. are considered an important threat to human health due to the high virulence found in community-associated clones, the emergence of multidrug-resistance in hospital-associated clones and their ubiquity in the environment. AMR (AMR) is a sizeable problem in long-term care facilities (LTCFs), where infections are common and antibiotic prescribing is high.

Methods

The AmSurv surveillance system captures the antibiotic susceptibility of bacteria isolated from both community and hospital samples that are analysed in reporting laboratories in England. Since December 2012, all laboratories in the West Midlands region report to AmSurv. *Klebsiella* isolated from urine samples from patients over 70 years of age sent to laboratories in the West Midlands between April 2010 and March 2014 were selected for analysis. The postcodes of patients from which the samples were taken were matched against the postcodes of LTCFs registered by the Care Quality Commission to determine LTCF residence. The weekly counts of *Klebsiella* isolated from clinical urine specimens were de-duplicated to one per person per week.

Results

During the study period 1,319 *Klebsiella* urine clinical samples were reported. A median year-on-year increase of 19.5% (IQR=-9.8%-87.4%) was observed. The data were aggregated into weekly counts and seasonality was explored through a generalized linear Poisson model that accounted for the increasing trend observed over the study period and differences between LTCFs. Each week of the study period the counts were 1.004 times higher than that of the previous week (95%CI=1.003-1.005). A peak was observed in August, when the cases were 1.4 times higher than in January (95%CI=1.1-1.8).

Discussion

Future work will include the exploration of the remaining variation in these data through statistical modeling of the clustering of AMR bacterial infections in time as a proxy for transmission in LTCFs and will account for the increasing trend observed over the study period and seasonality.

Appendix A: ESPAUR oversight group – terms of reference

Terms of Reference – Updated May 2015
December 2013

English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) Oversight Group

1.0 Issue

1.1 The English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR), was established in July 2013[38]. 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 Health Protection and Microbiology Services, HCAI and AMR, AMR Delivery Programme Board, Behavioural insight, Public Health Strategy, Primary Care Unit and Statistics, Modelling and Economics Department)
2. Department of Health (DH)
3. NHS England
4. DH Expert Advisory Committee on HCAI and AMR (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

[38] 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 Trust Development Authority
18. Monitor
19. Veterinary Medicines Directorate – DEFRA
20. British Dental Association/*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 AMS on AMR 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 AMR Strategy.

3.3 With respect to surveillance, the oversight group will:

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 AMS 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 AMS (AMS), the oversight group will:

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 AMR 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.

Appendix B: List of abstract publications, publications and presentations

Date	Authors	Title	Where
21/11/2015	Ashiru Oredope D; Budd EL; Bhattacharya A; Din N; McNulty CAM; Beech E; Murdan S; Hopkins S	Implementation of TARGET and antimicrobial stewardship activities in English primary care	Federation of Infection Societies
21/11/2015	Budd E, Ladenheim D, Kontrimaite U, Ashiru-Oredope D.	User-Feedback on the antimicrobial stewardship toolkit for Secondary care in England; Start Smart then Focus	Federation of Infection Societies
21/11/2015	Ashiru-Oredope D, Budd E, Flint J, Bryne G, Brown N.	Embedding the national antimicrobial prescribing and stewardship competences into healthcare	Federation of Infection Societies
21/11/2015	Bhattacharya A, Chaintarli K, Gobin M, Ingle S, Budd E, Oliver I, Ashiru-Oredope D.	The Antibiotic Guardian campaign: Moving from antimicrobial resistance awareness to engagement and behaviour change.	Federation of Infection Societies
18/11/2015	Ashiru-Oredope D; Hopkins S	Antimicrobial resistance: moving from professional engagement to public action.	J Antimicrob Chemother. 2015 Nov;70(11):2927-30.
11/11/2015	Chaintarli K, Ingle S, Bhattacharya A, Ashiru-Oredope D, Gobin M, Oliver I	Evaluation of the Antibiotic Guardian campaign	ESCAIDE
14/09/2015	Bhattacharya A, Ashiru-Oredope D, Budd E, Chaintarli K, Gobin M, Sallis A, Oliver I, Hopkins S.	Developing a UK-wide antimicrobial resistance campaign: moving from awareness to engagement	PHE Conference 2015
14/09/2015	Chaintarli K, Ingle S, Bhattacharya A, Ashiru-Oredope D, Oliver I, Gobin M	Evaluation of the Antibiotic Guardian pledge campaign: evidence of behaviour change	PHE Conference 2015
14/09/2015	Budd E, Bhattacharya A, Beech E, Micallef C, Ladenheim D, McNulty C, Hopkins S, Ashiru-Oredope D.	Antimicrobial Stewardship activities in England: Informing a baseline for the UK 5 year AMR strategy	PHE Conference 2015
14/09/2015	Ashiru-Oredope D, Madhani M, Lacey S	Assessing the impact of implementing quality improvement measures on antimicrobial stewardship (AMS) at a district general hospital	Royal Pharmaceutical Society Conference 2015
14/09/2015	Ashiru-Oredope D, Budd E. Beechc E, McNulty C, Micallef C. Ladenheim D, Bhattacharya A, Hopkins S	Evaluating the implementation of national antimicrobial stewardship toolkits for primary and secondary care in England	Royal Pharmaceutical Society Conference 2015
16/06/2015	Muller-Pebody B, Ladenheim D , Fuller C , Ashiru-Oredope D, Hopkins S.	Validation of national hospital antimicrobial consumption data in England	Antimicrob Resist Infect Control. 2015; 4(Suppl 1): P172
25/04/2015	Ashiru-Oredope D	Combating anti-microbial resistance - information for action	Clinical Pharmacy Congress
24/04/2015	Ashiru-Oredope D, Bhattacharya A, Budd E, Hopkins S, Spindlow S	Moving from raising awareness to increasing engagement: European Antibiotic Awareness Day activities in the United Kingdom	European Congress of Clinical Microbiology and Infectious (ECCMID)
24/04/2015	Ladenheim, D, Ashiru-Oredope, D, Muller-Pebody B, Fuller C, Hopkins, S.	Developing a national protocol to validate antimicrobial prescribing data in acute hospitals in England	Clinical Pharmacy Congress

15/04/2015	Ashiru-Oredope D, Budd E, Bhattacharya A, McNulty C, Beech E, Micallef C, Ladenheim D, Reacher M, Hopkins S.	A national approach to improving antimicrobial stewardship: Evaluating the implementation of national antimicrobial stewardship guidance in primary and secondary care in England	European Congress of Clinical Microbiology and Infectious (ECCMID)
01/04/2015	PHE, HPS, PHW, HSCPHA, AFBI, SRUC and VMD	One Health Report	Gov.UK
18/03/2015	Ashiru-Oredope D, Bhattacharya A, Budd E, Hopkins S, Spindlow S	Analysis of the Antibiotic Guardian campaign: a national campaign to act as catalyst for behaviour change toward antimicrobial resistance	PHE Applied Epidemiology Scientific Meeting
18/03/2015	Ashiru-Oredope D, Bhattacharya A, Budd E, Hopkins S	Surveillance of Surgical prophylaxis practice in NHS Trusts	PHE Applied Epidemiology Scientific Meeting
25/02/2015	Ashiru-Oredope D, Bhattacharya A, Budd E, Hopkins S, Spindlow S	Antibiotic Guardian: Developing a UK pledge campaign for European Antibiotics Awareness Day	WHO AMR Workshop
25/02/2015	Cichowska A, Ashiru-Oredope D	Evidence for policy: England's Response to AMR	WHO AMR Workshop
13/01/2015	Bhattacharya A, Budd E, Ashiru-Oredope D	EAAD 2013 Evaluation Report	Gov.UK
26/11/2014	Ashiru-Oredope D, Bhattacharya A, Budd E, Hopkins S, Spindlow S	Antibiotic Guardian: Developing a national pledge campaign for European Antibiotics Awareness Day	Federation of Infection Societies
26/11/2014	Ashiru-Oredope D, Bhattacharya A, Budd E, Guy R, Muller-Pebody, B, Johnson A, Hopkins S	Developing the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) - One year on	Federation of Infection Societies
26/11/2014	Ashiru-Oredope D, Micallef C, Ladenheim D, Bhattacharya A, Budd E, Hopkins S	Evaluating the implementation of the national antimicrobial stewardship guidance: Start Smart then Focus	Federation of Infection Societies
03/11/2014	Ashiru-Oredope D, Bhattacharya A, Budd E	The Antibiotic Guardian Campaign	GovToday: Reducing HCAIs
13/10/2014	Ashiru-Oredope D, Elderidge S, Gledhill R, Moss J, Bhattacharya A,Hopkins S	Veterinary Practitioners as Antibiotic Guardians	One Health Conference: Royal Society of Medicine
10/10/2014	ESPAUR writing committee	English surveillance programme antimicrobial utilisation and resistance (ESPAUR) report	Gov.UK
06/10/2014	Ashiru-Oredope D, Higginson P	Community Pharmacists at Antibiotic Guardians	The Pharmacy Show

In Press	
Ashiru Oredope D; Budd EL; Bhattacharya A; Din N; McNulty CAM; Micallef C; Ladenheim D; Beech E; Murdan S; Hopkins S (On behalf of the English Surveillance Programme for Antimicrobial Utilisation and Resistance)	Implementation of national antimicrobial stewardship toolkits in primary and secondary healthcare sectors in England: TARGET and Start Smart then Focus
Bhattacharya A, Hopkins S, Sallis A, Budd E, Ashiru-Oredope D	A process evaluation of the UK-wide Antibiotic Guardian campaign: developing engagement on antimicrobial resistance
Chaintarli K, Ingle S, Bhattacharya A, Ashiru-Oredope D, Oliver I, Gobin M	Evaluation of the Antibiotic Guardian campaign to help tackle antimicrobial resistance

Appendix C: Glossary

Antibacterial
A drug that destroys or inhibits the growth of bacteria. The action of the drug may be selective against certain bacteria.

AMS
AMS is a key component of a multifaceted approach to preventing emergence of AMR. Good AMS involves selecting an appropriate drug and optimising its dose and duration to cure an infection while minimising toxicity and conditions for selection of resistant bacterial strains.

AMR
AMR (AMR) is resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it.

Antimicrobials
An antimicrobial is a drug that selectively destroys or inhibits the growth of micro-organisms.

Bacteraemia
The presence of bacteria in the bloodstream.

Bioavailability
The amount of a drug that reaches the tissue(s) of the body where it is required to act.

Carbapenemases
Enzymes that hydrolyze (destroy) carbapenems and other β-lactam antibiotics, especially in members of Enterobacteriaceae family are increasing worldwide and an emerging threat.

Carbapenems
Carbapenems are broad-spectrum β-lactam antibiotics, in many cases the last effective antibiotic against multiple resistant Gram-negative bacterial infections.

Case ascertainment
The determination of a case or episode using surveillance, for example determination of cases of antibacterial resistance.

Clostridium difficile
A toxin producing bacterium which can cause severe diarrhoea or enterocolitis. This most commonly occurs following a course of antibiotics which has disturbed the normal bacterial flora of the patient's gut.

Director of Infection Prevention and Control (DIPC)
The DIPC is a highly visible, senior authoritative individual who has executive authority and responsibility for ensuring strategies are implemented to prevent avoidable HCAIs at all levels

in the organisation and provides assurance to the Board that systems are in place and correct policies and procedures are adhered to, across the organisation, to ensure safe and effective healthcare.

Empiric therapy
Prescription of an antibacterial before the causative agent of an infection is known.

Enterobacteriaceae
A family of Gram-negative bacilli that contains many species of bacteria that normally inhabit the intestines. Enterobacteriaceae, that are commonly part of the normal intestinal tract flora, are referred to as coliforms.

Enterococcus
A bacterium which normally colonises the human bowel.

Extended-spectrum β-lactamases (ESBL)
Extended-spectrum β-lactamases (ESBL) are enzymes produced by bacteria making them resistant to penicillins and cephalosporins. Resistance to third- generation cephalosporins in *E. coli* (and other Enterobacteriaceae) is a broad indicator of the occurrence of ESBLs.

Incidence
The number of new events/episodes of a disease that occur in a population in a given time period.

Indication
An infection that indicates the requirement for antibacterial therapy.

Infection
Invasion and multiplication of harmful micro-organisms in body tissues.

Micro-organism
An organism that is too small to be seen by the naked eye. Microorganisms include bacteria, fungi, protozoa and viruses.

MRSA (meticillin resistant *Staphylococcus aureus)*
A strain of *Staphylococcus aureus* that is resistant to meticillin and other penicillin and cephalosporin antibiotics.

MSSA (meticillin sensitive *Staphylococcus aureus)*
A strain of *Staphylococcus aureus* that is sensitive to meticillin.

Normal flora
The micro-organisms that normally live in or, on the body, and contribute to normal health. When antimicrobial agents are used to treat infections, there are changes to the normal flora which may reduce their ability to treat the infection.

Parenteral
A route of drug admission that is not oral, commonly used to denote drug admission by injection.

Prevalence
The total number of cases of a specific disease in existence in a given population at a certain time.

Prophylaxis
Any means taken to prevent infectious disease. For example, giving antibiotics to patients before surgery to prevent surgical site infections.

Reliability
Measure of repeatability (and agreement) of HCAI diagnosis by different data collectors.

Surveillance
The systematic collection of data from the population at risk, the identification of infections using consistent definitions, the analysis of these data and the dissemination of the results to those who collected the data, those responsible for care of the patients and those responsible for prevention and control measures.

Third generation cephalosporins
Third-generation cephalosporins have a broad-spectrum of activity and further increased activity against Gram-negative organisms.

Appendix D: Abbreviations

Acronym	Full Name
AMC	Antimicrobial consumption
AMR	AMR
AMRHAI	AMR and healthcare associated infections reference unit (PHE)
ASP	AMS programme
AT	Area team
ARHAI	AMR and healthcare associated infections
ASTRO-PU	Age, sex and temporary resident originated prescribing unit
BAPCOC	Belgian Antibiotic Policy Coordination Committee
BNF	British National Formulary
BSAC	British Society for Antimicrobial Chemotherapy
CAP	Community associated pneumonia
CCG	Clinical commissioning group
CIAs	Critically important antibiotics
CMO	Chief Medical Officer
CPE	Carbapenemase-producing Enterobacteriaceae
CRO	Carbapenem resistant organism
DARC	DEFRA AMR committee
DDD	Defined daily dose
DEFRA	Department for Environment, Food and Rural Affairs
DH	Department of Health
DIPC	Director of Infection Prevention and Control
EAAD	European Antibiotic Awareness Day
EARS-net	European AMR Surveillance Network
ECDC	European Centre of Disease Prevention and Control
ESAC-net	European Surveillance of Antimicrobial Consumption Network
ESBL	Extended-spectrum β-lactamases
ESPAUR	English Surveillance Programme for Antimicrobial Utilisation and Resistance
EU	European Union
HSCIC	Health and Social Care Information Centre
HAP	Hospital associated pneumonia
HCAI	Healthcare associated infection
HES	Hospital episode statistics
IPCC	Infection Prevention and Control Committee
NHS BSA	NHS Business Services Authority
NHS England	National Health Service England
OOH	Out of hours
PHE	Public Health England
PPS	Point prevalence survey
RTI	Respiratory tract infection
ScotMARAP	Scottish Management of AMR Action Plan
SGSS	Second Generation Surveillance System

SSI	Surgical site infection
SSTF	Start Smart Then Focus (prescribing guidance)
STAR-PU	Specific therapeutic group age-sex related prescribing units
STRAMA	Swedish Strategic Programme for the Rational Use of Antimicrobial Agents and Surveillance of Resistance
TARGET	Treat antibiotics responsibly, guidance and education tools (a toolkit)
TATFAR	Transatlantic Taskforce on AMR
UTI	Urinary tract infection
WHO	World Health Organisation

Appendix E: Writing committee and acknowledgements

Executive Summary

Susan Hopkins, Alan Johnson

Chapter 1

Susan Hopkins, Berit Muller-Pebody, Alan Johnson

Chapter 2

Rebecca Guy, Sarah Gerver, Dean Ironmonger, Richard Puleston, Alan Johnson
TB: Miranda G. Loutet, Maeve K. Lalor, Jennifer A. Davidson, Tehreem Mohiyuddin and H. Lucy Thomas.
Gonorrhoea: Hikaru Bolt, Antara Kundu, Katy Town, Martina Furegato, Hamish Mohammed, Michelle Cole, Aura Andreason, Helen Fifer, Stephanie Chisholm, and Gwenda Hughes
CPE: Katie Hopkins, Rachel Freeman, Neil Woodford

Chapter 3

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