



Public Health  
England

Protecting and improving the nation's health

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

## Report 2014

# About Public Health England

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# Contents

<b>Key messages</b>	<b>1</b>
<b>Information for the public</b>	<b>2</b>
Introduction	2
Antimicrobial resistance	2
Antimicrobial consumption	3
Antimicrobial stewardship	4
Future plans	5
<b>Executive summary</b>	<b>6</b>
Antibiotic resistance	6
Antibiotic consumption	9
Antimicrobial stewardship	11
Future plans	12
<b>Chapter 1: Introduction</b>	<b>13</b>
The importance of reducing antibiotic resistance	13
The English Surveillance Programme for Antimicrobial Utilisation and Resistance	14
Use of the ESPAUR 2014 Report	15
International efforts analogous and pertinent to ESPAUR	15
<b>Chapter 2: Antibiotic resistance in England</b>	<b>18</b>
Drug-bug combinations	19
Antibiotic susceptibility test results	19
Trend analysis	20
Population denominators	20
Trends in resistance by pathogen	21
<i>Escherichia coli</i>	21
Incidence of <i>E. coli</i> bloodstream infections	21
National trends in susceptibility of <i>E. coli</i> from bloodstream infections	21
Regional trends in susceptibility of <i>E. coli</i> from bloodstream infections	25
Geographical variation in susceptibility of <i>E. coli</i> from bloodstream infections in 2013	27
<i>Klebsiella pneumoniae</i>	29
Incidence of <i>K. pneumoniae</i> bloodstream infections	29
National trends in susceptibility of <i>K. pneumoniae</i> from bloodstream infections	29
Regional trends in susceptibility of <i>K. pneumoniae</i> from bloodstream infections	32
Geographical variation in susceptibility of <i>K. pneumoniae</i> from bloodstream infections in 2013	34
<i>Pseudomonas</i> spp.	36
Incidence of bloodstream infections due to <i>Pseudomonas</i> spp.	36
National trends in susceptibility of <i>Pseudomonas</i> spp. from bloodstream infections	36

Regional trends in susceptibility of <i>Pseudomonas</i> spp. from bloodstream infections	38
Geographical variation in susceptibility of <i>Pseudomonas</i> spp. from bloodstream infections in 2013	40
<i>Streptococcus pneumoniae</i>	42
Incidence of <i>S. pneumoniae</i> bloodstream infections	42
National trends in susceptibility of <i>S. pneumoniae</i> from bloodstream infections	42
Regional trends in susceptibility of <i>S. pneumoniae</i> from bloodstream infections in 2013	44
Geographical variation in susceptibility of <i>S. pneumoniae</i> from bloodstream infections in 2013	46
<b>Chapter 3: Antibiotic consumption</b>	<b>53</b>
Data source – primary care	55
Data source – other community	55
Data source – secondary care	55
Classification of data	55
Data definitions	56
Population denominators	57
Trend analysis	57
Maps	57
Total consumption of antibiotics	58
Total prescribing by key agents	58
Prescribing in the community from sources other than general practice	58
Prescribing by area team in 2013	60
Trends in consumption by antibiotic group: penicillins	62
Trends in consumption by antibiotic group: cephalosporins	65
Trends in consumption by antibiotic group: carbapenems	69
Trends in consumption by antibiotic group: tetracyclines	72
Trends in consumption by antibiotic group: quinolones	75
Trends in consumption by antibiotic group: macrolides	78
Trends in consumption by antibiotic group: sulfonamides and trimethoprim	81
Trends in consumption in other agents: nitrofurantoin	82
Trends in consumption in other agents: aminoglycosides	83
Trends in consumption in other agents: glycopeptides and daptomycin	84
Trends in consumption in other agents: <i>Clostridium difficile</i> treatment agents	86
Community prescribing by items	87
Hospital sector	89
<b>Chapter 4: Antibiotic prescribing and stewardship survey in secondary care</b>	<b>98</b>
Antibiotic policy and stewardship activities	101
The role of antimicrobial pharmacists	103
Start Smart then Focus Evaluation	103
Education and training	108
Empiric guidelines	109
Respiratory tract infections	110
Treatment of urinary tract infections	111
Clinical sepsis and cellulitis	112
Electronic prescribing	114

<b>Chapter 5: Future plans</b>	<b>117</b>
Development of an integrated system for antimicrobial resistance and consumption data	117
Reporting of antibiotic resistance in pathogens from other clinical specimens	118
Expansion of drug-bug combinations included in surveillance of antimicrobial resistance	118
Linkage of antibiotic resistance data with other data sets	118
Enhancement of community antibiotic consumption datasets	119
Understand prescribing in private practice in England	119
Validation of hospital antibiotic consumption datasets	119
Piloting and reporting of antimicrobial prescribing quality measures	119
Ecological analysis of associations between resistance and consumption	120
Measurement of impact of behavioural interventions and antibiotic resistance awareness campaigns	120
Improving education and training regarding antibiotic resistance.	120
Antimicrobial stewardship toolkits	120
Working with veterinary partners	120
Working with European initiatives	121
<b>Appendix A</b>	<b>122</b>
ESPAUR oversight group –terms of reference	
<b>Appendix B</b>	<b>125</b>
NHS regions	
NHS local area teams	
<b>Appendix C</b>	<b>127</b>
Defined daily doses of commonly used antibiotics	
<b>Appendix D</b>	<b>128</b>
ESPAUR clinical guidelines survey for secondary care	
<b>Appendix E</b>	<b>130</b>
ESPAUR SSTF implementation terms of reference and membership	
<b>Appendix F</b>	<b>131</b>
NHS England acute trust hospitals consented to antimicrobial consumption data release to PHE	
<b>Appendix G</b>	<b>135</b>
English NHS laboratories reporting to AmSurv	
English NHS laboratories requiring further work to report to AmSurv	
<b>Appendix H</b>	<b>137</b>
Glossary	

# List of Tables and Figures

## Tables

<b>ES.1</b>	Summary of key antibiotic resistance in bacteraemia in England	8
<b>ES.2</b>	Summary of total antibiotic use in England and comparisons with Europe	10
<b>2.1</b>	Drug-bug combinations	19
<b>2.2</b>	Incidence of <i>E. coli</i> bacteraemia by NHS Region, 2010 to 2013, based on voluntary reporting to LabBase2	21
<b>2.3</b>	Incidence of <i>K. pneumoniae</i> bloodstream infections by NHS Region, 2010 to 2013, based on voluntary reporting to LabBase2	29
<b>2.4</b>	Incidence of <i>Pseudomonas</i> spp. bloodstream infections by NHS Region, 2010 to 2013, based on voluntary reporting to LabBase2	36
<b>2.5</b>	Incidence of <i>S. pneumoniae</i> bloodstream infections by NHS Region, 2010 to 2013, based on voluntary reporting to LabBase2	42
<b>3.1</b>	Antibiotic consumption by group for hospital inpatients at the level of ATs, expressed as DDD per 100 admissions per day, England, 2013	91
<b>3.2</b>	Table demonstrating the most prevalent antibiotics used in acute trusts in the national Point Prevalence survey in 2011 and comparison with the most frequently consumed antibiotics (DDD per 100 admission) in 2011 and 2013	92
<b>3.3</b>	Ranks and relative consumption of the top 15 consumed agents in general practice and hospitals in England, 2013	93
<b>3.4</b>	Number of DDD per item of the top 15 drugs consumed in England, 2010-2013, for common antibiotics recommended in guidelines	95
<b>4.1</b>	Antimicrobial Policy key elements, 2011 and 2014 surveys, n=99	102
<b>4.2</b>	Reported good examples of SSTF Implementation within trusts	106
<b>4.3</b>	Trust feedback regarding the usefulness of SSTF and improvements required	107
<b>4.4</b>	Reported education and training initiatives from Acute trusts, n=99	108
<b>4.5</b>	First line and alternative antibiotics recommended in empiric guidelines in English acute NHS trusts for ten indications in 74 Acute trusts, n=1024	109
<b>4.6</b>	Reported number of antibiotics used for the treatment of pneumonias in empiric guidelines	110
<b>4.7</b>	Reported number of antibiotics used for the treatment of UTIs in empiric guidelines	111
<b>4.8</b>	reported number of antibiotics used for the treatment of sepsis and cellulitis in empiric guidelines	112
<b>4.9</b>	Availability of electronic prescribing in patient areas in Acute NHS trusts, n=76	114

## Figures

### Antibiotic Resistance in England

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<b>2.1</b>	Quarterly counts of <i>E. coli</i> bloodstream infections in England between 2010 and 2013 and proportions non-susceptible to a) ciprofloxacin, b) third-generation cephalosporins, c) gentamicin and d) carbapenems	<b>23</b>
<b>2.2</b>	Counts of <i>E. coli</i> isolates non-susceptible to ciprofloxacin, third-generation cephalosporins and gentamicin, based on voluntary reporting to LabBase2	<b>25</b>
<b>2.3</b>	Proportion of <i>E. coli</i> isolates from bloodstream infections non-susceptible to indicated antibiotics at the level of NHS Regions, 2010 and 2013 a) ciprofloxacin, b) third-generation cephalosporins, c) gentamicin and d) carbapenems	<b>26</b>
<b>2.4</b>	Proportions of <i>E. coli</i> bloodstream infection isolates in England between 2010 and 2013 non-susceptible to indicated antibiotics at the level of NHS area team in 2013	<b>28</b>
<b>2.5</b>	Quarterly counts of <i>K. pneumoniae</i> bloodstream infections and proportions non-susceptible to a) ciprofloxacin, b) third-generation cephalosporins, c) gentamicin and d) carbapenems	<b>30</b>
<b>2.6</b>	Counts of <i>K. pneumoniae</i> isolates non-susceptible to ciprofloxacin, third-generation cephalosporins and gentamicin, based on voluntary reporting to LabBase2	<b>32</b>
<b>2.7</b>	Proportion of <i>K. pneumoniae</i> from bloodstream infections non-susceptible to indicated antibiotics at the level of NHS Regions; a) ciprofloxacin, b) third-generation cephalosporins, c) gentamicin and d) carbapenems in England between 2010 and 2013	<b>33</b>
<b>2.8</b>	Proportions of <i>K. pneumoniae</i> bloodstream infection isolates non-susceptible to indicated antibiotics at the level of NHS area team in 2013. Grey areas represent ATs where <70% of isolates had susceptibility data available.	<b>35</b>
<b>2.9</b>	Quarterly counts of <i>Pseudomonas</i> spp. bloodstream infections and proportions non-susceptible to a) ciprofloxacin, b) ceftazidime, c) gentamicin and d) carbapenems in England between 2010 and 2013	<b>37</b>
<b>2.10</b>	Proportion of <i>Pseudomonas</i> spp. from bloodstream infections non-susceptible to indicated antibiotics at the level of NHS Regions; a) ciprofloxacin, b) ceftazidime, c) gentamicin and d) carbapenems in England between 2010 and 2013	<b>39</b>
<b>2.11</b>	Proportions of <i>Pseudomonas</i> spp. bloodstream infection isolates non-susceptible to indicated antibiotics at the level of NHS area team in 2013	<b>41</b>
<b>2.12</b>	Quarterly counts of <i>S. pneumoniae</i> bloodstream infections and proportions non-susceptible to a) penicillin, b) macrolide, and c) tetracycline in England between 2010 and 2013	<b>43</b>
<b>2.13</b>	Proportion of <i>S. pneumoniae</i> isolates from bloodstream infections non-susceptible to indicated antibiotics at the level of NHS Regions; a) penicillin, b) macrolide, c) tetracycline in England between 2010 and 2013	<b>44</b>
<b>2.14</b>	Proportions of <i>S. pneumoniae</i> bloodstream infection isolates non-susceptible to indicated antibiotics at the level of NHS area team in 2013. Grey areas represent ATs where <70% of isolates had susceptibility data available.	<b>46</b>

<b>2.15</b>	Annual combined counts of <i>E. coli</i> and <i>K. pneumoniae</i> non-susceptible to indicated antibiotics, based on voluntary reporting to LabBase2 a) ciprofloxacin, b) third-generation cephalosporins, c) gentamicin and d) carbapenems	<b>47</b>
<b>2.16</b>	Carbapenemase-producing Enterobacteriaceae referred from UK hospital microbiology laboratories and confirmed by PHE's Antimicrobial Resistance and Healthcare Associated Infections (AMRHA) Reference Unit.*	<b>50</b>
<b>2.17</b>	Proportion of carbapenem-non-susceptibility among isolates of <i>K. pneumoniae</i> in Europe a) 2009 b) 2012	<b>51</b>

## Antibiotic Consumption

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<b>3.1</b>	Antibiotic items dispensed in the community (HSCIC report) for a) Penicillins b) Other antibiotic groups with more than 100,000 items dispensed in 2013 across England, 2003-2013.	<b>54</b>
<b>3.2</b>	Consumption of total antibiotics, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	<b>59</b>
<b>3.3</b>	Total antibiotic consumption by group, expressed as DDD per 1000 inhabitants per day, across England, 2010-2013	<b>59</b>
<b>3.4</b>	Map of consumption by a) general practice and Hospital and b) general practice, expressed as DDD per 1000 inhabitants per day, by ATs, England, 2013	<b>61</b>
<b>3.5</b>	Map of consumption of a) Hospital inpatient and outpatient (total) b) Hospital inpatient, expressed as DDD per 1000 inhabitants per day, by ATs, England, 2013	<b>61</b>
<b>3.6</b>	Consumption of penicillins by general practice and Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	<b>63</b>
<b>3.7</b>	Consumption of most commonly utilised penicillins, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	<b>63</b>
<b>3.8</b>	Consumption of broad and narrow-spectrum penicillins at the level of ATs, expressed as DDD per 1000 inhabitants per day, England, 2013	<b>64</b>
<b>3.9</b>	Change in total penicillin consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013	<b>64</b>
<b>3.10</b>	Map of consumption of a) all penicillins b) penicillin/inhibitor combinations, expressed as DDD per 1000 inhabitants per day, by ATs, England, 2013	<b>65</b>
<b>3.11</b>	Consumption of cephalosporins prescribed by general practice and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	<b>66</b>
<b>3.12</b>	Consumption of different cephalosporins, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	<b>67</b>
<b>3.13</b>	Change in cephalosporin consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013	<b>67</b>
<b>3.14</b>	Change in third-generation cephalosporin consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013	<b>68</b>
<b>3.15</b>	Map of consumption of cephalosporins, expressed as DDD per 1000 inhabitants per day, by ATs, England, 2013	<b>68</b>
<b>3.16</b>	Consumption of carbapenems prescribed by general practice and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	<b>70</b>
<b>3.17</b>	Consumption of different carbapenems, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	<b>70</b>
<b>3.18</b>	Change in carbapenem consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013	<b>71</b>



<b>3.19</b>	Map of consumption of carbapenems at the level of ATs, England, 2013, expressed as DDD per 1000 inhabitants per day	71
<b>3.20</b>	Consumption of carbapenems prescribed by general practice and in Hospitals at the level of ATs, expressed as DDD per 1000 inhabitants per day, England, 2013	72
<b>3.21</b>	Consumption of tetracyclines prescribed by general practice and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	73
<b>3.22</b>	Consumption of different tetracyclines, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	73
<b>3.23</b>	Change in tetracycline consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013	74
<b>3.24</b>	Map of consumption of tetracyclines at the level of ATs, expressed as DDD per 1000 inhabitants per day, England, 2013	74
<b>3.25</b>	Consumption of quinolones prescribed by general practice and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	76
<b>3.26</b>	Consumption of different quinolones, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	76
<b>3.27</b>	Change in quinolone consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013	77
<b>3.28</b>	Map of consumption of quinolones at the level of ATs, expressed as DDD per 1000 inhabitants per day, England, 2013	77
<b>3.29</b>	Consumption of macrolides prescribed by general practices and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	79
<b>3.30</b>	Consumption of different macrolides, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	79
<b>3.31</b>	Change in macrolide consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013	80
<b>3.32</b>	Map of consumption of macrolides at the level of ATs, England, 2013, expressed as DDD per 1000 inhabitants per day	80
<b>3.33</b>	Consumption of sulfonamides and trimethoprim prescribed by general practices and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	81
<b>3.34</b>	Consumption of nitrofurantoin prescribed by general practices and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	82
<b>3.35</b>	Change in nitrofurantoin consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013	83
<b>3.36</b>	Consumption of nitrofurantoin prescribed by general practices and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	84
<b>3.37</b>	Consumption of glycopeptides prescribed by general practices and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	84
<b>3.38</b>	Consumption of daptomycin prescribed by general practices and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	85
<b>3.39</b>	Consumption of different glycopeptides, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	85
<b>3.40</b>	Consumption of oral vancomycin and oral metronidazole prescribed by general practices and in hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013	86
<b>3.41</b>	Consumption of packages of antibiotics, expressed as items per 1000 inhabitants per day, England, 2010-2013	87
<b>3.42</b>	Consumption of packages of antibiotics for systemic use in the community	88

	(general practice and other community prescribing) expressed as items per 1000 inhabitants per day, England, 2010-2013	
<b>3.43</b>	Map of consumption of packages of antibiotics, expressed as items per 1000 inhabitants per day, by ATs, England, 2013	88
<b>3.44</b>	Consumption of antibiotics in hospital inpatients, expressed as DDD per 100 admissions, by area teams, England, 2010-2013	90
<b>3.45</b>	Antibiotic consumption by group* for hospital inpatients, expressed as DDD per 100 admissions per day, England, 2010-2013	90

### Antibiotic Prescribing and Stewardship survey in Secondary Care

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<b>4.1</b>	Proportion of Acute Trust survey responses by area team, England 2014	100
<b>4.2</b>	Sizes of Acute trusts by teaching and non-teaching	101
<b>4.3</b>	Frequency of review of Antimicrobial Policy in Acute trusts	101
<b>4.4</b>	Proportion of trusts who reported separate antimicrobial drug charts/section,	102
<b>4.5</b>	Proportion of trusts who have implemented key antimicrobial stewardship activities recommended in SSTF guidance	103
<b>4.6</b>	Proportion of trusts with implemented SSTF action plan	104
<b>4.7</b>	Proportion of Trusts who have implemented audits recommended by SSTF, 2014	105
<b>4.8</b>	Differences in empiric guideline recommendations for first line treatment duration for pneumonias	110
<b>4.9</b>	Differences in empiric guideline first line antibiotics recommended for treatment of symptomatic upper UTIs and catheter associated upper UTIs	111
<b>4.10</b>	Differences in empiric guideline recommendations for first line treatment duration for upper UTIs versus lower UTIs	112
<b>4.11</b>	Differences in empiric guideline first line antibiotics recommended for treatment of clinical sepsis and intra-abdominal sepsis	113
<b>4.12</b>	Differences in empiric guideline recommendations for first line treatment duration for sepsis	113
<b>4.13</b>	Differences in empiric guideline recommendations for first line treatment duration for cellulitis UTIs	114

## Key Messages

- the number of patients with bloodstream infections has increased each year from 2010 to 2013
- there were an increased number of bloodstream infections where antibiotic resistance was identified
- antibiotic prescribing has increased in England year on year
- the majority of antibiotic prescribing takes place in the community (ie general practice)
- there is considerable variability in both antibiotic resistance and antibiotic prescribing across England; frequently areas with high prescribing also have high resistance
- individual healthcare organisations should use this data to benchmark their organisation

# Information for the public

## Introduction

The spread of bacteria resistant to antibiotics is an important health threat, as it means that antibiotics may no longer work when needed to treat infections. Antibiotics are unlike other drugs used in medicine, as the more we use them the less effective they become. This is because overuse gives resistant bacteria a greater chance to survive and spread. Antibiotic resistance is not a new challenge, but has been around for many decades. In the past, it was not regarded as a major problem as new antibiotics were regularly developed and could be used to treat infections caused by bacteria resistant to drugs already widely in use. What is different at the present time is that there are hardly any new antibiotics being developed, so we are unable to rely on new treatments becoming available to treat these resistant bacteria.

Many patients are at increased risk of getting infections as a consequence of the treatment they receive for other medical conditions. Medical care may allow bacteria to enter the body ( eg during surgery) or it may deplete their immune system, which reduces their ability to fight off infection ( eg during cancer treatment). Thus antibiotic resistance may have an adverse effect on our ability to deliver modern healthcare safely. Therefore efforts must be made to ensure we use currently available antibiotics as wisely as possible so that their effectiveness is preserved for as long as possible. We also must undertake surveillance of infections caused by antibiotic resistant bacteria to understand the extent of the problem and develop solutions.

As part of the response to the problem of antibiotic resistance, the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) is developing and improving surveillance systems to measure antibiotic use and antibiotic resistance as well as measuring the impact of resistance on the safety of patients and the general public. This is the first report from ESPAUR. The programme was established by Public Health England in 2013 in response to the strategic plan for controlling antibiotic resistance in the UK published by the Government in 2013. The data in this report provides, for the first time, national and regional surveillance of antibiotic resistance and antibiotic use trends from 2010 to 2013. This will enable general practices and hospitals to compare their data with regional and national trends. It will provide a baseline measure from which we can track changes in both prescribing and resistance in England.

## Antimicrobial resistance

Chapter 2 of the report highlights some common microbes (bacteria) that cause septicaemia, through bloodstream infections, and their sensitivity to commonly used antibiotics. These bacteria were chosen as they cause more than half of all bloodstream infections in England. A recent European report suggested that patients with bloodstream infections from multi-resistant bacteria were twice as likely to die compared to those with sensitive bacterial infections. They include: *Escherichia coli* (*E. coli*) which is the most common cause of bloodstream infection (sometimes known as blood poisoning); *Klebsiella pneumoniae* (*K. pneumoniae*), bacteria which cause outbreaks of infection in healthcare settings; *Pseudomonas* species, bacteria which particularly affects patients with weakened immune systems; and *Streptococcus*

*pneumoniae* (*S. pneumoniae*), the commonest bacteria causing pneumonia and a frequent cause of sinusitis, middle ear infections and meningitis.

Between 2010 and 2013 in England, bloodstream infections caused by *E. coli* and *K. pneumoniae* increased by 12% and 10% respectively. Although the percentage of these bacteria that were resistant to key antibiotics remained broadly stable over the 4-year period, the numbers of infections caused by resistant strains increased, due to an increased number of bloodstream infections. Similarly, although the number of bloodstream infections caused by *S. pneumoniae* declined by 25%, most probably related to the introduction of a new pneumococcal vaccine in 2010, there was still an increase in the number of isolates resistant to a key antibiotic.

### Antimicrobial consumption

It is important to know how widely antibiotics are being used, as their use is a major driver for the spread of antibiotic resistance. Chapter 3 of this report describes for the first time antibiotic use across the NHS in England, both in the community and in hospitals. From 2010 to 2013, the total use of antibiotics increased by 6%: within general practice use increased by 4%, while prescribing to hospital inpatients increased by 12% and other community prescriptions (eg those issued by dentists) increased by 32%. Throughout the four years, the vast majority of prescribing occurred in general practice. In 2013, 79% of prescribing was from general practice, 15% from hospital and 6.2% related to other community prescribers (predominantly dentists). The reasons for these increases are unknown at present but may represent changes in the number of patients presenting with infections requiring antibiotics or overprescribing of antibiotics by clinicians.

The most common antibiotics (penicillins) prescribed are predominantly indicated for use for sore throats, ear infections and chest infections. The largest increase in antibiotic use from 2010 to 2013 was seen with nitrofurantoin, which is used for cystitis and lower urinary tract infections. General practices and hospitals have decreased antibiotics that are known to predispose to *Clostridium difficile* infection but have replaced these with other broad spectrum antibiotics. Broad spectrum antibiotics are used to treat a wide range of infections and bacteria compared to narrow spectrum antibiotics which are targeted at a single infection or specific bacterial group. Increased use of broad spectrum agents is likely to drive more resistance than narrow spectrum agents.

There was significant variability in antibiotic use across the country. The highest combined general practice and hospital usage was in Merseyside, where levels of use were similar to those reported from Southern Europe, and over 30% higher than in the Thames Valley, which had the lowest usage. The highest prescribing from general practice was in Durham, Darlington and Tees, which was over 40% higher than in London. This may reflect healthcare access and delivery in London, where there may be shift from general practice prescribing to local hospitals and private healthcare. We should aim to reduce the variability in total prescribing across the country, to the safest level possible.

There is no doubt that national prescribing guidelines influence both primary care and secondary care use of antibiotics. This is evidenced by the marked decline in cephalosporin and quinolone use in the UK over the last decade, which was prioritised by both general practice and hospitals to reduce *C. difficile* infection. In addition, the marked increase in nitrofurantoin use over the last four years, demonstrates that national infection guidelines

promoting this antibiotic for the treatment of urinary tract infections have had an important impact.

The most recently published information comparing antibiotic use across different countries in Europe is for 2011. In the ESAC-net report, information on prescribing of antibiotics in England, Northern Ireland, Scotland and Wales were reported together; the UK was mid-range in the use of antibiotics in the community compared with other EU countries. However, all four countries in the UK were higher than the majority of other EU countries for antibiotic use in hospitals. This may relate, at least in part, to the different practices for prescribing and recording of prescriptions in UK hospitals, where prescriptions of antibiotics are dispensed by hospital pharmacies rather than community pharmacies. The Northern European countries (Denmark, Sweden), who have had surveillance programmes such as ESPAUR for nearly 20 years, have the lowest use of antibiotics. England should aim to become one of the low antibiotic use countries in Europe, which will require every prescriber to use antibiotics only when clinical symptoms meet criteria, at the shortest duration that is needed and using delayed or back-up prescriptions where possible.

The ESPAUR Report provides maps of England that show the levels of antibiotic use and resistance in different parts of the country. The findings confirm that areas with high prescribing of antibiotics commonly have higher antibiotic resistance. It should be noted that this finding is based on a single year snapshot and more research is needed to investigate this in more detail.

It is essential that all prescribers across England have access to, and can review, their own antibiotic use data. This will enable them to determine the reasons for prescribing, especially where their use is different to national trends. These reviews can inform the appropriate deployment of local strategies, aimed at improving the quality of antibiotic prescribing.

### Antimicrobial stewardship

Antimicrobial stewardship describes a bundle of measures that can be used to promote better use of antibiotics. National antimicrobial stewardship guidelines are available for general practice and hospitals. However these organisations are free to implement their own local antimicrobial stewardship policies.

Within the first year of ESPAUR, we have assessed hospital antimicrobial stewardship. In 2014, a survey of NHS trusts reported that the majority of respondents reviewed the national guidance on antimicrobial stewardship in secondary care known as Start Smart Then Focus (SSTF) but less than half had instituted an action plan to improve stewardship. Almost 80% of acute trusts collated data on at least one of the recommended audits in SSTF; however, specific audits that can be correlated to patient outcomes were rarely conducted. While more than 90% of responding NHS trusts had an antimicrobial stewardship committee, the survey showed that representation from hospital general physicians, surgeons, nurses and pharmacists was low. Two-thirds of trusts provided training in stewardship and antibiotics but only a minority performed prescribing competency assessments.

In order to embed antimicrobial stewardship recommendations within hospitals, engagement with a broad range of professional groups, including doctors (both senior and junior), surgeons, nurses and pharmacists is essential. The development of standardised training material and competency assessments is also required. ESPAUR has endorsed a proposal to establish a

Start Smart then Focus Implementation subgroup to consider options and recommendations for further embedding of SSTF into hospitals in England.

## Future Plans

Data from the first year of ESPAUR provides a baseline measure of antimicrobial resistance and use. This will allow us to determine the impact of future behaviour and educational strategies developed with both the public and healthcare professionals. Future work will focus on improving feedback of antibiotic resistance and antibiotic use data to prescribers and organisations, integrating data from the human and animal sector in England and antibiotic resistance and use comparisons across the UK and Europe.

## Executive summary

Antimicrobial resistance (AMR) is resistance of a microorganism to an antimicrobial drug that was originally effective for treatment of infections caused by it. Antimicrobial drugs encompass antibiotics (active against bacteria), antifungals, antivirals and antiparasitic agents. The consequences of AMR include increasing treatment failure for the most commonplace infections for example, urinary tract infections and decreasing the treatment options available where antibiotics are vital, such as during cancer treatment when patients are prone to infection. The Chief Medical Officer for England highlighted the problem of antimicrobial resistance in her 2013 annual report and this subsequently led to the UK cross-government five-year (2013-2018) antimicrobial resistance strategy (“the strategy”).

As part of the response to the problem of antibiotic resistance, the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) is developing and improving surveillance systems to measure antibiotic use and antibiotic resistance as well as measuring the impact of resistance of the safety of patients and the general public. The programme was established by Public Health England in 2013 in response to the strategy. This is the first report from the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR). This report concentrates on antibiotics and antibiotic resistance as the development of new antibiotics is severely limited and action is required to avoid a post-antibiotic future. Antibiotic prescribing and antibiotic resistance are inextricably linked. Overuse and incorrect use of antibiotics are major drivers of resistance.

The key aims of ESPAUR are to develop surveillance systems to measure both antimicrobial utilisation and resistance and to measure the impact of antimicrobial utilisation on antimicrobial resistance and patient/public safety. The data in this report provides, for the first time, national and regional surveillance of antibiotic resistance and antibiotic use trends from 2010 to 2013. This will enable general practices and hospitals to compare their data with regional and national trends. It will provide a baseline measure from which we can track changes in both prescribing and resistance in England.

### Antibiotic resistance

This report highlights some common microbes (bacteria) that cause septicaemia, through bloodstream infections, and their sensitivity to commonly used antibiotics. These bacteria were chosen as they are a common cause of bloodstream infection in England and have a known propensity to develop resistance. A recent European report suggested that patients with bloodstream infections from multi-resistant bacteria were twice as likely to die compared to those with sensitive bacterial infections.

Between 2010 and 2013, the overall incidence of *E. coli* bloodstream infections in England, based on voluntary reporting to LabBase2, increased by 12%.

Previous national surveillance had shown an increase in the proportions of isolates of *E. coli* resistant to ciprofloxacin, third-generation cephalosporins and gentamicin between 2001 and 2006/07, with a decline in resistance thereafter. However, this decline appeared to cease from 2010, with the proportions of isolates resistant to each antibiotic group remaining broadly stable between 2010 and 2013. Nationally, the proportions of isolates that were resistant each quarter



were in the range of 17-19% for ciprofloxacin, 10-12% for third-generation cephalosporins, 9-10% for gentamicin and 0.03-0.2% for imipenem/meropenem. This has nonetheless resulted in an increase in the burden of resistance in *E. coli*. For example, the numbers of isolates resistant to ciprofloxacin increased by 18% between 2010 and 2013. The corresponding increases in resistance to third-generation cephalosporins and gentamicin were 28% and 27%, respectively. The numbers of isolates resistant to imipenem/meropenem in each of the consecutive four years were too small to allow robust statistical analysis. There was significant geographical variability in the proportions of *E. coli* resistant to key agents: ciprofloxacin resistance ranged from 25% in London to 12% in Cumbria, Northumberland and Tyne and Wear while cephalosporin resistance ranged from 15% in London to 6% in Devon, Cornwall and the Isles of Scilly and gentamicin resistance ranged from 15% in London to 5% in Durham, Darlington and Tees.

Between 2010 and 2013, the overall incidence of *K. pneumoniae* bloodstream infections in England, based on voluntary reporting to LabBase2, increased by 10%. As with *E. coli*, similar trends in resistance were noted in *K. pneumoniae* between 2001 and 2009. However, the proportions of isolates resistant to each antibiotic group were broadly stable between 2010 and 2013, being in the ranges of 8-13% for ciprofloxacin, 9-13% for third-generation cephalosporins, 6-10% for gentamicin and 0.1-2% for imipenem/meropenem. The burden of resistance has also increased with the numbers of isolates resistant to ciprofloxacin increasing by 29% between 2010 and 2013. The corresponding increases in resistance to third-generation cephalosporins and gentamicin were 26% and 46%, respectively.

Considerable geographical variation was noted for *K. pneumoniae* resistant to ciprofloxacin, ranging from 17% in Durham, Darlington and North Tees to 3% in North Yorkshire and Humber. The highest rate of cephalosporin resistance (19%) was seen in Greater Manchester with the lowest rate (4%) being seen in Merseyside and in Shropshire and Staffordshire. This compares to an overall national rate of cephalosporin resistance of 11% in 2013. The highest rate of resistance to gentamicin (15%) was reported from Greater Manchester; this compares to an overall national rate of 8.5%.

Between 2010 and 2013, the overall incidence of bloodstream infections due to *Pseudomonas* spp. in England decreased by 9%. Nationally, the trends for the proportion of isolates non-susceptible to each antibiotic group were broadly stable between 2010 and 2013, being in the ranges of 8-12% for ciprofloxacin, 6-9% for ceftazidime, 4-7% for gentamicin and 8-13% for carbapenems. However, resistance to ciprofloxacin varied geographically, and ranged from 15% to 3% in 2013; for comparison, the overall national rate of ciprofloxacin resistance that year was 10%. Ceftazidime resistance ranged from 11% in Greater Manchester to 2% in Derbyshire and Nottingham, compared with overall national rate of 7%, while resistance to gentamicin (overall national rate of 4%) ranged from 0 to 8%. Rates of resistance to imipenem/meropenem ranged from 2% in Durham, Darlington and Tees to 17% in Greater Manchester, compared to the national rate of 10%.

Between 2010 and 2013, the overall incidence of *S. pneumoniae* bloodstream infections in England, decreased by 25%. The declining incidence of pneumococcal bacteraemia probably reflects the impact of the introduction of the 13-valent pneumococcal conjugate vaccine in 2010. Overall decreases were seen in all regions although the extent varied from 31% in the North to 15% in London. The trends for the proportion of isolates resistant to penicillin were broadly stable between 2010 and 2013, being in the ranges of 2-5%. For macrolides there was a small but significant increase in the annual rate of macrolide resistance from 4.8% in 2010 to

7.4% in 2013, which was reflected in a 12% increase in the number of macrolide-resistant isolates between 2010 and 2013. By the same token there was also a 22% increase in the number of isolates resistant to tetracycline. By contrast, the burden of resistance, as measured by total numbers of resistant isolates decreased by 14% for penicillin.

A particular focus of interest at the current time is resistance to carbapenems. These are widely regarded as our antibiotics “of last resort” for the treatment of severe infections, particularly those caused by Gram-negative bacteria. While the data indicate that carbapenems remain active for the treatment of bloodstream infections caused by *E. coli* or *K. pneumoniae* at the present time, with ≥98% of isolates still susceptible, this should not engender an aura of complacency for several reasons. Firstly, analysis of Enterobacteriaceae referred to PHE’s Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit shows a dramatic year-on-year increase in the number of isolates shown to be carbapenem-resistant due to production of carbapenemases ( $\beta$ -lactamases capable of degrading carbapenems and hence abolishing their antibacterial activity). Referred isolates were from a range of clinical sources including blood, urine, respiratory specimens, faeces and rectal screening swabs, and it is probably only a matter of time before this increased reservoir of resistant strains translates into increased numbers of systemic infections, either as a result of endogenous infection or transmission of the resistant pathogens to other vulnerable patients.

The key drug-bug combinations (proportion resistant bacteria to the key antibiotics) in 2013 are summarised in Table 1. This table also compares the proportion with antibiotic resistance in these key bacteria in England to European data from 2012. It demonstrates that *E. coli* and *S. pneumoniae* resistance is very similar; and *K. pneumoniae* and *Pseudomonas* spp. resistance is lower when compared to the European population weighted mean.

**Table ES.1. Summary of key antibiotic resistance in bacteraemia in England**

Pathogen	Rate per 100,000, 2013 (compared to 2010)	Antibiotic or antibiotic class	% resistant 2013 (compared to 2010)	Change in number of resistant bacteria 2010 to 2013	% resistant Europe 2012
<i>Escherichia coli</i>	52.6 (↑)	Ciprofloxacin	18.2 (↔)	↑	22.3
		Third-generation cephalosporins	10.9 (↔)	↑	11.8
		Gentamicin	9.7 (↔)	↑	10.3
		Imipenem/meropenem	0.1 (↔)	↑	<0.1
<i>Klebsiella pneumoniae</i>	8.8 (↑)	Ciprofloxacin	11.1 (↔)	↑	25.3
		Third-generation cephalosporins	11.4 (↔)	↑	25.7
		Gentamicin	8.5 (↑)	↑	22.2
		Imipenem/meropenem	1.0 (↑)	↑	6.2
<i>Pseudomonas</i> spp.	6.3 (↓)	Ciprofloxacin	10.4 (↔)	↑	21.0
		Ceftazidime	6.7 (↔)	↓	13.5
		Gentamicin	3.6 (↓)	↓	18.4
		Imipenem/meropenem	9.5 (↔)	↓	17.1
<i>Streptococcus pneumoniae</i>	6.1 (↓)	Penicillin	3.1 (↔)	↓	4.6
		Macrolides	8.1 (↑)	↑	8.5
		Tetracycline	6.1 (↑)	↑	-

## Antibiotic consumption

The consumption of antibiotics is a major driver for the development of antibiotic resistance in bacteria. This report brings together for the first time antibiotic consumption data from the NHS community and hospital pharmacies across England, to encourage a whole healthcare economy approach to antibiotic prescribing. Information on the consumption of antibiotics is essential if we are to reduce unnecessary prescribing.

From 2010 to 2013, total antibiotic consumption increased by 6%: general practice consumption increased 4%, prescribing to hospital inpatients increased by 12% and other community prescriptions ( eg dentists) increased by 32%. In 2013, the total measured consumption of antibiotics in England was 27.4 DDD per 1000 inhabitants per day (general practice 79%, Hospital 15% and other community consumption (predominantly dentists) 6%). This is an under-estimate of total consumption as it does not include private prescriptions, from private general practitioners, hospitals or dentists, which are not recorded centrally at present. The reasons for the increase in consumption are unknown but may represent changes in the number of patients presenting with infections requiring antibiotics or overprescribing of antibiotics by clinicians. The increase in other community prescriptions needs to be explored to assess whether general practice prescribing is being displaced to out-of-hours treatment centres.

In 2013, 66 different antibiotics were prescribed in both general practice and hospital settings. The top 15 antibiotics in general practice and hospitals accounted for 98% and 88% of consumption respectively. Throughout the period, the predominant antibiotics consumed in England were penicillins, tetracyclines and macrolides. Penicillin and macrolide consumption increased up to 2012 but subsequently decreased in 2013; in the four years, penicillin and macrolide consumption increased 3% and 6% respectively. Nitrofurantoin consumption increased 41% between 2010 and 2013, the largest increase observed. Within general practice, consumption of broad-spectrum antibiotics such as ciprofloxacin and cefalexin decreased, though co-amoxiclav demonstrated a significant increase. Within hospitals, the use of narrow-spectrum antibiotics decreased (phenoxymethylpenicillin, flucloxacillin and erythromycin) and the consumption of broad-spectrum antibiotics such as co-amoxiclav, piperacillin-tazobactam and meropenem significantly increased.

The highest combined general practice and hospital antibiotic consumption was in Merseyside, with similar levels reported as Southern Europe with 30.4 DDD per 1,000 inhabitants per day, over 30% higher than Thames Valley with the lowest consumption, (22.8 DDD per 1,000 inhabitants per day). The highest consumption from general practice was Durham, Darlington and Tees over 40% higher than London (26.5 versus 18.9 DDD per 1,000 inhabitants). This may reflect healthcare access and delivery in London, where there may be shift from general practice prescribing to local hospitals and private healthcare. In ATs, where there are large cities with many hospitals, more consumption of antibiotics occurs in hospital settings, particularly in outpatient departments. This may be related to more transient population and patients who are not registered with general practices or the geographical ease of access to secondary care departments in urban areas. In addition, the tertiary level hospitals with a large number of sub-specialties predominantly are present in large cities. These hospitals often have admissions from outside their geographical AT from across their region. However, it should be a national ambition to reduce the variability in total prescribing across the country, to the safest level possible, ideally by developing a case-mix adjustment of antibiotic use for hospitals alongside the current adjustment for primary care (STAR-PU).

In 2013, the ratio of broad and extended-spectrum penicillins ( eg amoxicillin and combinations of penicillins with inhibitors) to narrow-spectrum penicillins ( eg phenoxymethylpenicillin and flucloxacillin) varied across the country. For example, although Merseyside had the highest prescription of penicillins, it had the second lowest prescription of penicillin and inhibitor combinations. This demonstrates the complexity of consumption data, where high dose amoxicillin may be increasing the total DDD consumption measurement in a particular AT, but nonetheless reflect appropriate prescribing.

There is no doubt that national prescribing guidelines influence both primary care and secondary care consumption of antimicrobials. This is evidenced by the marked decline in cephalosporin and quinolones consumption in the UK over the last decade, which was prioritised by both primary and secondary care to reduce *C. difficile* infection. In addition, the marked increase in nitrofurantoin use over the last four years, demonstrates that national infection guidelines promoting this antibiotic for the treatment of urinary tract infections have had an important impact.

The most recent data published from the European Centre for Disease Control (ECDC), comparing antibiotic consumption in Europe, were for 2011. In that report England and the devolved administrations were reported together as the UK and were mid-range in the consumption of antimicrobials for community prescribing compared with other EU countries. The UK was a high outlier (more than twice the EU median) for antibiotic consumption assigned to the hospital sector. This may relate, at least in part, to differential prescribing and recording of prescription practices in UK hospitals. In the UK, hospital prescriptions of antibiotics are dispensed by hospital pharmacies, while in many other European countries, both outpatient and medication prescribed on discharge is dispensed in community pharmacies, thereby inflating general practice/community consumption and reducing hospital consumption. Further work will need to be undertaken with ECDC to understand these differences.

**Table ES.2. Summary of total antibiotic use in England and comparisons with Europe**

Antibiotic group	England 2013 (DDD per 1000 inhabitants per day)	England 2013 compared to England 2010	Europe 2011 (Median DDD per 1000 inhabitants per day)
Penicillins	13.7	↑	10.4
Other β-lactam antibacterials	0.6	↓	2
Tetracyclines	4.9	↑	2.2
Sulfonamides and trimethoprim	1.9	↑	0.5
Macrolides & similar	4.1	↑	3
Quinolones	0.6	↓	1.5
Other	1.7	↑	1.7
<b>Total</b>	<b>27.4</b>	↑	<b>21.3</b>

The Advisory Committee for Antimicrobial Resistance and Healthcare Associated Infection (ARHAI) in consultation with NHS England and Public Health England (PHE) has published antimicrobial prescribing quality measures for primary and secondary care.<sup>1</sup> The quality measures for primary care are reduction in total antibiotic consumption and the proportion of cephalosporin, quinolone and co-amoxiclav antibiotics used. The quality measures for secondary care are reductions in total antibiotic consumption and carbapenem consumption. The data in this report will act as a baseline for area teams to review the prescribing within their populations and develop action plans to meet these quality measures.

It is essential, as part of the next stage, that further validation and exploration of the data occurs. In comparing the maps of antibiotic consumption and resistance at a regional and sub-regional level it was noted that commonly areas with high prescribing have in general higher resistance. As these are just single snapshots of the data, this will require further investigation. It is also essential that English healthcare organisations, across primary and secondary care, have access to and review their own consumption data and determine the reasons for prescribing, through local audits, especially where their consumption is different to national trends ensuring that they have an appropriate stewardship strategy in place.

### Antimicrobial stewardship

Antimicrobial stewardship describes a bundle of measures that can be adopted to promote the appropriate use of antimicrobials, including evidence-based optimal standards for routine antibiotic use, ensuring competency and educational programmes for all staff that use antibiotics, communication of antibiotic issues to stakeholders, auditing the impact and outcome of the stewardship processes and most importantly optimising outcomes for patients who receive antibiotics.

National antimicrobial stewardship guidelines are available for primary and secondary care institutions. However hospitals and general practice are free to implement their own local antimicrobial stewardship policies. Within the first year of ESPAUR, an assessment of hospital antimicrobial stewardship showed a number of activities had been implemented. An increased number of trusts reported using a separate antimicrobial section on the drug chart to aid prescribing. The role of specialist antimicrobial pharmacists continues to remain embedded within Acute NHS Trusts. In addition, the antimicrobial pharmacist role spans a broad range of specialist activities. There was also evidence of collaboration between primary and secondary care colleagues on development of antimicrobial guidelines and stewardship activities across both sectors with 37% of respondents have a working relationship with primary care pharmacy colleagues in their area.

Between the 2012 and 2014 surveys, an additional 12% of respondents had formally reviewed national guidance on antimicrobial stewardship in secondary care (Start Smart Then Focus) with 48% having implemented formal action plans. While 79% of Acute Trusts collate data on at least one of the recommended audits in SSTF, audits that can be correlated to patient outcomes, for example, time to first dose in sepsis, were rarely performed.

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<sup>1</sup> Advisory 1/2152374732/18606265032/Committee on Antimicrobial Resistance and Hospital Acquired Infections (ARHAI) Recommended Antimicrobial Prescribing Quality Measures. 2014. <https://app.box.com/ARHAI-Minutes-Papers/1>

While more than 90% of responding NHS Trusts had an antimicrobial stewardship committee as recommended by the SSTF guidance, the survey showed that representation from outside the specialist antimicrobial stewardship area (ie infection or pharmacy specialists) on antimicrobial committees was low. In order to embed antimicrobial stewardship recommendations within organisations, engagement with the development and implementation of guidelines and audits from a broad range of professional groups ( eg nursing, general and specialist surgeons and physicians, junior doctors, general pharmacists) is essential.

ESPAUR has established a Start Smart then Focus Implementation subgroup to update the SSTF guidance and to consider options and recommendations for further embedding of SSTF into secondary care in England. Updated guidance will be launched for user testing in November 2014 taking into account current evidence and recommendations from this survey.

In 2015, the National Institute for Health and Care Excellence (NICE) will publish the national guidance “Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use for primary and secondary care”. This will become the guidance for NHS primary and secondary care organisations to implement and assess themselves against in this key area.

### Future plans

This report brings together antibiotic resistance, consumption and stewardship data across England for the first time. PHE is committed to developing a platform where organisations can interrogate the key resistance and consumption measures in one platform. Validation of individual hospital data is an essential step in this process and will be rolled out to all acute care organisations over the coming year. Once the validation of hospital pharmacy data is complete, PHE will publish data on the antimicrobial prescribing quality measures from NHS hospitals.

PHE has improved the laboratory surveillance systems to generate all antimicrobial resistance data from all clinical specimens and this will allow the expansion of drug-bug combinations reported. This is essential to guide appropriate antibiotic policies and improve stewardship in primary and secondary care.

PHE, with the other devolved UK health administrations, and veterinary partners will also produce a one health report encompassing antibiotic resistance and consumption data across the human and animal sectors in 2015.

# Chapter 1: Introduction

## The importance of reducing antibiotic resistance

Antimicrobial drugs encompass antibiotics (active against bacteria), antifungals, antivirals and antiparasitic agents. The focus of this first ESPAUR report is on resistance to antibiotics, which is a serious and increasing public health problem, as highlighted by the Chief Medical Officer for England in her 2013 annual report.<sup>2</sup> The consequences of antibiotic resistance include increasing treatment failure for the most commonplace infections for example, urinary tract infections and decreasing the treatment options available where antibiotics are vital, such as during cancer treatment when patients are prone to infection. As highlighted by the Prime Minister in July 2014, there is a striking lack of new antibiotics currently under development. If we are to avoid a post-antibiotic future, decisive action must be taken in the present to ensure we use the antibiotics we have effectively, and thus preserve their efficacy.

Antibiotic prescribing and antibiotic resistance are inextricably linked. Overuse and incorrect use of antibiotics are major drivers of resistance.<sup>3</sup> It is therefore important to understand the true nature of antibiotic use across both human and animal health and the burden of antibiotic resistance. Only once we understand these issues can we undertake informed actions to preserve antibiotics for future generations.

The UK published a cross-government five-year antimicrobial resistance strategy (encompassing antibiotics) in 2013.<sup>4,5</sup> The seven key aims of the strategy are 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 antimicrobial resistance research needs
- strengthened international collaboration

In July 2014 the government recognised that in addition to the UK 5 year antimicrobial resistance strategy work plan, there is a need for strong antimicrobial prescribing stewardship,

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<sup>2</sup> Davies S. Annual Report of the Chief Medical Officer 2011: Volume Two. Infections and the Rise of Antimicrobial Resistance. <http://www.dh.gov.uk/health/2013/03/cmo-vol2/> (27 June 2014, date last accessed).

<sup>3</sup> Hillier S, Roberts Z, Dunstan F, Butler C, Howard A, Palmer S. Prior antibiotics and risk of antibiotic-resistant community-acquired urinary tract infection: a case-control study. *J Antimicrob Chemother.* 2007 Jul;60(1):92-9.

<sup>4</sup> Department of Health and Defra. UK five year antimicrobial resistance strategy 2013-2018. [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/244058/20130902\\_UK\\_5\\_year\\_AMR\\_strategy.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/244058/20130902_UK_5_year_AMR_strategy.pdf)

<sup>5</sup> Ashiru-Oredope D, Hopkins S; English Surveillance Programme for Antimicrobial Utilization and Resistance Oversight Group. Antimicrobial stewardship: English Surveillance Programme for Antimicrobial Utilization and Resistance (ESPAUR). *J Antimicrob Chemother.* 2013 Nov;68(11):2421-3.

with the Science and Technology Committee recommending the following to ensure continuing access to working antimicrobials:<sup>6</sup>

- that the Government, as a matter of urgency, puts measures in place to drastically reduce the unnecessary prescription of antibiotics
- that the Government drives the development of clinically proven alternative, safe and effective strategies for use by General Practitioners when dealing with patients with acute infections which don't require antibiotics
- better education of medical students and greater focus on resistance during clinical career development
- that the Department of Health (DH) develops a system for monitoring post-prescription behaviour of patients who have been prescribed a course of antibiotics

## The English Surveillance Programme for Antimicrobial Utilisation and Resistance

The English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR) was established by Public Health England (PHE) in 2013 in response to the strategy.

ESPAUR's key aims are to develop surveillance systems to measure both antimicrobial utilisation and resistance and to measure the impact of antimicrobial utilisation on resistance and patient/public safety.

The programme also includes within its remit the development, with the DH expert advisory committee on Antimicrobial Resistance and Healthcare associated infections (ARHAI), of quality measures for optimal prescribing and markers for the consequences of these quality measures within primary and secondary care; and the development of initiatives with key partners for both public and professional behaviour change, including education, around antimicrobial prescribing and consumption.

National antimicrobial stewardship guidelines are available for primary and secondary care institutions.<sup>7,8</sup> However, hospitals and general practices are free to implement their own local antimicrobial stewardship policies. Enhanced open surveillance data for both antimicrobial consumption and resistance will strengthen the evidence base that informs these policies. Prior to the establishment of ESPAUR, national summaries of antimicrobial consumption in Primary care were published annually by the Health and Social Care Information Centre (HSCIC). No antimicrobial consumption data was routinely available for secondary care. This is the first presentation of prescribing data with a geographical breakdown across England. The antimicrobial consumption data in hospitals builds on the work programme of the Antimicrobial Stewardship Sub-Group of the Department of Health's Advisory Committee for Antimicrobial Resistance and Healthcare Associated Infection.

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<sup>6</sup> Ensuring access to working antimicrobials. First Report of the House of Commons Science and Technology Select Committee. July 2014. <http://www.parliament.uk/business/committees/committees-a-z/commons-select/science-and-technology-committee/news/report-amr/>

<sup>7</sup> Moore M, McNulty C. European Antibiotic Awareness Day 2012: TARGET antibiotics through guidance, education, and tools. *Br J Gen Pract.* 2012 Dec;62(605):621-2. doi: 10.3399/bjgp12X659132.

<sup>8</sup> Ashiru-Oredope D, Sharland M, Charani E, McNulty C, Cooke J; ARHAI Antimicrobial Stewardship Group. Improving the quality of antibiotic prescribing in the NHS by developing a new Antimicrobial Stewardship Programme: Start Smart--Then Focus. *J Antimicrob Chemother.* 2012 Jul;67 Suppl 1:i51-63.



PHE has developed voluntary laboratory surveillance of organisms causing bacteraemia. This report uses these sources of laboratory data to present the key drug-bug combinations that are critical in antimicrobial resistance and presents this data with the same geographical breakdown as the antimicrobial consumption dataset.

This report also describes the initial results of a survey in secondary care to determine the uptake of the antimicrobial stewardship initiative “Start Smart and Then Focus” and to understand the current policies for the major indications of antibiotic use in NHS acute hospitals.

## Use of the ESPAUR 2014 Report

In future reports ESPAUR intends to encompass work on other classes of antimicrobials. However, the focus of this first report is solely on prescribing of and bacterial resistance to antibiotics. These data are presented for the years 2010-2013 at national, regional and sub-regional level, across primary and secondary care. The report will enable commissioners and practitioners to examine the antibiotic consumption and resistance data within their area teams (ATs) to inform commissioning of resources and antibiotic stewardship policies. It will also allow individual primary and secondary care organisations to benchmark their own local data to AT, regional and national levels.

These data will form a standard against which antibiotic use and resistance can be compared in successive years, therefore providing an indication of the effectiveness of the UK five year antimicrobial resistance strategy.

In addition the report will describe the future plans for enhanced surveillance of antimicrobial consumption and resistance.

## International efforts analogous and pertinent to ESPAUR

Antimicrobial resistance knows no boundaries and is a global health problem. The UK devolved administrations are represented on the ESPAUR oversight group. The Scottish Management of Antimicrobial Resistance Action Plan (ScotMARAP) was published in 2008 and updated in 2014.<sup>9</sup> The Scottish Antimicrobial prescribing group is responsible for leading antimicrobial stewardship and surveillance aspects of this plan and, since its establishment in 2008, has successfully implemented data management systems for antimicrobial prescribing, surveillance and clinical audits.<sup>10</sup> The Antimicrobial Resistance Programme Surveillance Unit of Public Health Wales has also produced reports depicting antimicrobial consumption and resistance in Wales.<sup>11</sup> Colleagues in Northern Ireland are developing similar programmes. In future years, comparisons with other countries within the UK will be possible. ESPAUR and the devolved administrations will also work on a “One Health” report with our veterinary colleagues, detailing antimicrobial consumption and resistance in humans and animals across the UK.

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<sup>9</sup> Scottish Management of Antimicrobial Resistance Action Plan 2014-18 (ScotMARAP2). July 2014. <http://www.scotland.gov.uk/Resource/0045/00456736.pdf>

<sup>10</sup> Scottish Antimicrobial Prescribing Group. Progress Report for 2008–2011. March 2011 [https://www.scottishmedicines.org.uk/files/sapg/SAPG\\_Progress\\_Report\\_2008-11.pdf](https://www.scottishmedicines.org.uk/files/sapg/SAPG_Progress_Report_2008-11.pdf)

<sup>11</sup> A Report from Public Health Wales Antimicrobial Resistance Programme Surveillance Unit: Antibacterial Resistance and Usage In Wales 2005-2011. November 2012. <http://www.wales.nhs.uk/sites3/page.cfm?orgId=457&pid=28906>

Across Europe antimicrobial resistance and usage data is collated and reported separately by the European Centre for Disease Prevention and Control (ECDC) through two systems – the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) and the European Antimicrobial Resistance Surveillance Network (EARS-Net). Community prescribing data has been shared with ECDC and previously with ESAC-Net by the British Society for Antimicrobial Chemotherapy (BSAC) and Health and Social Care Information Centre (HSCIC). With the agreement of all the UK countries, we have shared the hospital data this year for the first time with ECDC via ESAC-Net. PHE has also co-ordinated the UK submission to EARS-Net from sentinel laboratories since the inception of the EARS-Net programme.

The Swedish Strategic Programme for the Rational use of Antimicrobial Agents and Surveillance of Resistance (STRAMA) was established in 1994 and has contributed to a marked reduction in antimicrobial consumption in Sweden without measurable adverse consequences for patient safety.<sup>12</sup> The Belgian Antibiotic Policy Coordination Committee (BAPCOC) has also reported that their recommended interventions have contributed to a measurable decrease in antibiotic consumption and resistance within Belgian healthcare institutions.<sup>13</sup> Since 1996, DANMAP (the Danish Integrated Antimicrobial Resistance Monitoring and Research Programme) has published an annual report on the occurrence of antimicrobial resistance in zoonotic, indicator, and pathogenic bacteria from animals, food, and humans in Denmark.<sup>14</sup>

The Transatlantic Taskforce on Antimicrobial Resistance (TATFAR) was established in 2009 to improve co-operation between the USA and EU regarding appropriate therapeutic use of antimicrobial drugs in medical and veterinary communities, prevention of healthcare and community-associated drug-resistant infections, and strategies for improving the pipeline of new antimicrobial drugs.<sup>15</sup>

Surveillance programmes analogous to ESPAUR exist globally.<sup>16,17</sup> In April 2014 the World Health Organisation (WHO) published a global report on Antimicrobial Resistance, which highlighted that global surveillance of resistance was not harmonised and required strengthening in order to inform antimicrobial stewardship strategies internationally, monitor the effectiveness of public health interventions and detect new resistance trends and threats.<sup>18</sup> In May 2014 the WHO World Health Assembly passed a resolution, which urged member states to strengthen drug management systems, support research to extend the lifespan of existing drugs, and to encourage the development of new diagnostics and treatment option. As part of

<sup>12</sup> Mölsted S, Erntell M, Hanberger H, et al. Sustained reduction of antibiotic use and low bacterial resistance: 10-year follow-up of the Swedish Strama programme. *Lancet Infect Dis* 2008;8:125-32.

<sup>13</sup> Goossens H, Coenen S, Costers M, De Corte S, De Sutter A, Gordts B, Laurier L, Struelens MJ. Achievements of the Belgian Antibiotic Policy Coordination Committee (BAPCOC). *Euro Surveill.* 2008;13(46):pii=19036. Available online: <http://www.eurosurveillance.org/ViewArticle.aspx?ArticleId=19036>

<sup>14</sup> DANMAP. <http://www.danmap.org/About%20Danmap.aspx>

<sup>15</sup> Transatlantic Taskforce on Antimicrobial Resistance Progress Report. May 2014.

[http://www.cdc.gov/drugresistance/pdf/TATFAR-Progress\\_report\\_2014.pdf](http://www.cdc.gov/drugresistance/pdf/TATFAR-Progress_report_2014.pdf)

<sup>16</sup> Lesho EP, Waterman PE, Chukwuma U, McAuliffe K, Neumann C, Julius MD et al. The Antimicrobial Resistance Monitoring and Research (ARMoR) Program: The US Department of Defense Response to Escalating Antimicrobial Resistance. *Clin Infect Dis.* 2014 May 1. pii: ciu319. [Epub ahead of print]

<sup>17</sup> Australian Commission on Safety and Quality in Helathcare. National surveillance and reporting of antimicrobial resistance and antibiotic usage for human health in Australia. June 2013. <http://www.safetyandquality.gov.au/wp-content/uploads/2014/02/National-surveillance-and-reporting-of-antimicrobial-resistance-and-antibiotic-usage-for-human-health-in-Australia.pdf>

<sup>18</sup> World Health Organisation. Antimicrobial Resistance: Global report on surveillance. June 2014. [http://apps.who.int/iris/bitstream/10665/112642/1/9789241564748\\_eng.pdf?ua=1](http://apps.who.int/iris/bitstream/10665/112642/1/9789241564748_eng.pdf?ua=1)

the resolution the WHO will also develop a draft global action plan to combat antimicrobial resistance for approval in 2015.

The Commonwealth also provides a valuable network for international collaboration to combat AMR. PHE is leading the development of a Commonwealth microbiology laboratory twinning initiative to combat AMR, in which high income Commonwealth countries can twin with low and middle income Commonwealth countries. This will support Commonwealth countries' responses to AMR for their own populations and contribute to wider regional and international efforts. Twinning may be extended from laboratory capacity building to epidemiological partnering, strengthening disease surveillance and sharing wider expertise.

This report demonstrates England's current and growing capacity in the surveillance of antibiotic consumption and resistance and will assist WHO and other countries in developing and strengthening surveillance systems to monitor this public health threat.

# Chapter 2: Antibiotic resistance in England

## Introduction

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The burgeoning problem of antibiotic resistance poses a major threat to public health, not only in the UK but across the world.<sup>2,19,17</sup> Antibiotics are not only essential for the treatment of common bacterial infections that present in the community, such as skin, urinary tract or sexually-transmitted infections, but also for the management of healthcare-associated infections that occur in vulnerable patients predisposed to infection by invasive or immunosuppressive procedures that are part of their medical care. Thus the occurrence of resistance, which can result in failure to treat infection effectively, can adversely impact on the management of patients in diverse clinical settings.

Clinical decisions regarding choice of empiric antibiotic therapy for infection require knowledge of the likely pathogen(s), the site of infection and the likely susceptibility of these pathogens to antibiotic agents. While insight can be gained from clinical experience, optimal decision making is dependent on surveillance data to inform both the changing aetiology of infections and the changing antibiotic susceptibility of the causative pathogens in different settings and over time. This report presents data from England on the susceptibility of four pathogens to key antibiotics (so called “drug-bug” combinations). The four pathogens (*Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas* spp. and *Streptococcus pneumoniae*) are common causes of bloodstream infections and are highlighted in the recently published UK 5-year Antimicrobial Resistance Strategy<sup>4</sup> as the focus of current surveillance.

The data in this report are based on monitoring the susceptibility of isolates from bloodstream infections. In contrast to previous surveillance reports, which have focussed on trends at the national level, data are also presented at regional and sub-regional (area team) level. This will allow investigation of potential associations between national, regional and local levels of antibiotic resistance and corresponding data on antibiotic use.

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<sup>2</sup> Chief Medical Officer. Annual Report of the Chief Medical Officer, Volume Two, 2011: Infections and the rise of antimicrobial resistance. Online: Department of Health; 2013 Mar.

<sup>19</sup> Centers for Disease Control and Prevention. Antibiotic Resistance Threats in the United States, 2013. <http://www.cdc.gov/drugresistance/threat-report-2013/index.html>: CDC; 2013.

<sup>17</sup> World Health Organisation. Antimicrobial resistance: global report on surveillance 2014. <http://www.who.int/drugresistance/documents/surveillance-report/en/>.

<sup>4</sup> Department of Health. UK 5 Year Antimicrobial Resistance (AMR) Strategy 2013-2018

# Methods

## Drug-bug combinations

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

**Table 2.1 Drug-bug combinations**

Pathogen	Antibiotic or antibiotic class
<i>Escherichia coli</i>	Ciprofloxacin
	Third-generation cephalosporins
	Gentamicin
	Imipenem/meropenem
<i>Klebsiella pneumoniae</i>	Ciprofloxacin
	Third-generation cephalosporins
	Gentamicin
	Imipenem/meropenem
<i>Pseudomonas spp.</i>	Ciprofloxacin
	Ceftazidime
	Gentamicin
	Imipenem/meropenem
<i>Streptococcus pneumoniae</i>	Penicillin
	Macrolides
	Tetracycline

## Antibiotic susceptibility test results

Data on the susceptibility of each pathogen to key antibiotics were obtained from LabBase2, a national database maintained by Public Health England. Raw data are electronically submitted to LabBase2 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”.

As patients may have more than one positive blood culture taken, blood cultures taken from the same patient that yielded growth of the same pathogen with the same antibiotic susceptibility pattern during a 14-day period from the initial positive blood culture were regarded as comprising the same episode of infection and were de-duplicated.

There are some caveats regarding data quality that need to be considered, including: (i) incomplete data collection, as reporting is done on a voluntary basis; (ii) variation in laboratory testing methods and (iii) different laboratories may test and report on different antibiotic panels for the same pathogens. With regard to incomplete case ascertainment due to voluntary reporting, a comparison of trends in bloodstream infections derived using data from a sub-set of consistently reporting laboratories versus the totality of data from all laboratories showed similar findings.<sup>20</sup> Similarly, comparison of trends in antibiotic resistance in a range of pathogens assessed using data from LabBase2 and data from a sentinel surveillance scheme in which laboratories submitted isolates to Public Health England's Antimicrobial Resistance and Healthcare Associated Infections (AMRHA) Reference Unit for centralised susceptibility testing, again showed similar findings.<sup>21</sup> With regard to variation in testing methods, it is noteworthy that hospital microbiology laboratories in England are required to participate in the scheme run by the UK National External Quality Assessment Service.<sup>22</sup> In this scheme, pathogens with known resistance profiles are distributed to laboratories for blind testing and laboratories reporting incorrect results are notified so that they may take remedial action to improve the quality of their testing methodology). Taken together, these factors indicate that the surveillance data reported here are robust despite the caveats mentioned above.

## Trend analysis

Trends in resistance for the designated drug-bug combinations in England were assessed for the time period 2010 to 2013 at national, regional and sub-regional (area team) level. Details on NHS Regions and area teams (ATs) are given in Appendix B. Cases of bloodstream infections were assigned at sub-national level using the patient's residential postcode, or if not available, their General Practitioner's postcode; if neither were available, the postcode of the reporting laboratory was used. Postcodes were mapped to NHS ATs obtained from the Health and Social Care Information Centre.<sup>23</sup>

## Population denominators

Incidence rates for bloodstream infections were calculated using 2010, 2011 and 2012 mid-year resident population estimates, based on the 2011 census for England; 2013 estimates are based on 2012 mid-year estimates.<sup>24</sup>

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<sup>20</sup> Wilson J *et al.*, Elgohari S, Livermore DM, Cookson B, Johnson A, Lamagni T, Chronias A, Sheridan E. Trends among pathogens reported as causing bacteremia in England, 2004–2008. *Clin Microbiol Infect* **2011**; 451–458.]

<sup>21</sup> [British Society for Antimicrobial Chemotherapy Resistance Surveillance Project, 1999/2000–2006/7. *J Antimicrob Chemother* 2008; 62 (Supplement 2)].

<sup>22</sup> (<http://www.ukneqasmicro.org.uk/images/pdf/DOC.0398.pdf>).

<sup>23</sup> <http://systems.hscic.gov.uk/data/ods>

<sup>24</sup> <http://www.statistics.gov.uk/statbase/Product.asp?vlnk=15106>

# Results

## Trends in resistance by pathogen

### *Escherichia coli*

#### Incidence of *E. coli* bloodstream infections

Between 2010 and 2013, the overall incidence of *E. coli* bloodstream infections in England, based on voluntary reporting to LabBase2, increased by 12% from 47.0 to 52.6 cases per 100,000 population (Table 2.2). Some degree of seasonal variation was noted with more isolates reported each year in quarter 3 (Figure 2.1). Year-on-year increases were seen in the South of England (overall increase over 4 years of 17%), London (19%) and the Midlands and East of England (11%) while in the North, the incidence increased between 2010 and 2012 but decreased in 2013 to give an overall increase over the four-year period of 6%. Comparison with the numbers of *E. coli* bloodstream infections reported to the national mandatory reporting scheme (which started in June 2011)<sup>25</sup> showed 84% case ascertainment through voluntary reporting to LabBase2 in both 2012 and 2013. A comparison of both voluntary and mandatory reporting at regional level showed inter-regional variation in case ascertainment, ranging from 90% in London, 87% in the Midlands and East, 86% in the South to 78% in the North. Of the 25 ATs, five (three in the North and two in the South) reported <70% of cases in 2013.

**Table 2.2 Incidence of *E. coli* bacteraemia by NHS Region, 2010 to 2013, based on voluntary reporting to LabBase2**

NHS Region	Rate per 100, 000 population			
	2010	2011	2012	2013
South	40.6	44.8	45.7	47.7
London	42.3	46.7	47.9	50.2
Midlands and East	49.0	52.2	52.7	54.3
North	53.0	57.7	57.5	56.4
<b>England</b>	<b>47.0</b>	<b>51.0</b>	<b>51.5</b>	<b>52.6</b>

#### National trends in susceptibility of *E. coli* from bloodstream infections

The national trends in susceptibility of *E. coli* from blood to four antibiotic groups (ciprofloxacin, third-generation cephalosporins, gentamicin and imipenem/meropenem) are shown in Figure 2.1 (a-d). Susceptibility data were available for >70% of isolates tested against each antibiotic group each quarter, with the highest level of reporting seen for gentamicin (86-92% of isolates per quarter) and the lowest level for imipenem/meropenem (71-77% per quarter).

<sup>25</sup> [http://www.hpa.org.uk/webc/HPAwebFile/HPAweb\\_C/1317140907317](http://www.hpa.org.uk/webc/HPAwebFile/HPAweb_C/1317140907317)

Previous national surveillance had shown an increase in the proportions of isolates of *E. coli* non-susceptible to ciprofloxacin, third-generation cephalosporins and gentamicin between 2001 and 2006/07, with a decline in non-susceptibility thereafter.<sup>26</sup> However, as shown in Figure 2.1, the decline in non-susceptibility to these agents appeared to cease from 2010, with the proportion of isolates non-susceptible to each antibiotic group remaining broadly stable between 2010 and 2013. The proportion of isolates that were non-susceptible were in the range of 17-19% for ciprofloxacin, 10-12% for third-generation cephalosporins, 9-10% for gentamicin and 0.03-0.2% for imipenem/meropenem.

It is important to note, however, that although the proportion of isolates that were non-susceptible to the indicated antibiotics remained relatively stable between 2010 and 2013, the increasing incidence of *E. coli* during this time meant that the burden of antibiotic resistance, as measured by total numbers of resistant isolates, nonetheless increased. For example, the numbers of isolates non-susceptible to ciprofloxacin reported to LabBase2 rose from 3,654 in 2010 to 4,321 in 2013, an increase of 18.3% (Figure 2.2). The corresponding increases in non-susceptibility to third-generation cephalosporins and gentamicin were 28% and 27%, respectively. The numbers of isolates non-susceptible to imipenem/meropenem in each of the consecutive four years (9, 22, 30 and 14, respectively) were too small to allow robust statistical analysis.

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<sup>26</sup> Livermore DM *et al.* Declining cephalosporin and fluoroquinolone non-susceptibility among bloodstream Enterobacteriaceae from the UK: links to prescribing change? *J Antimicrob Chemother* 2013; 68: 2667-2674.

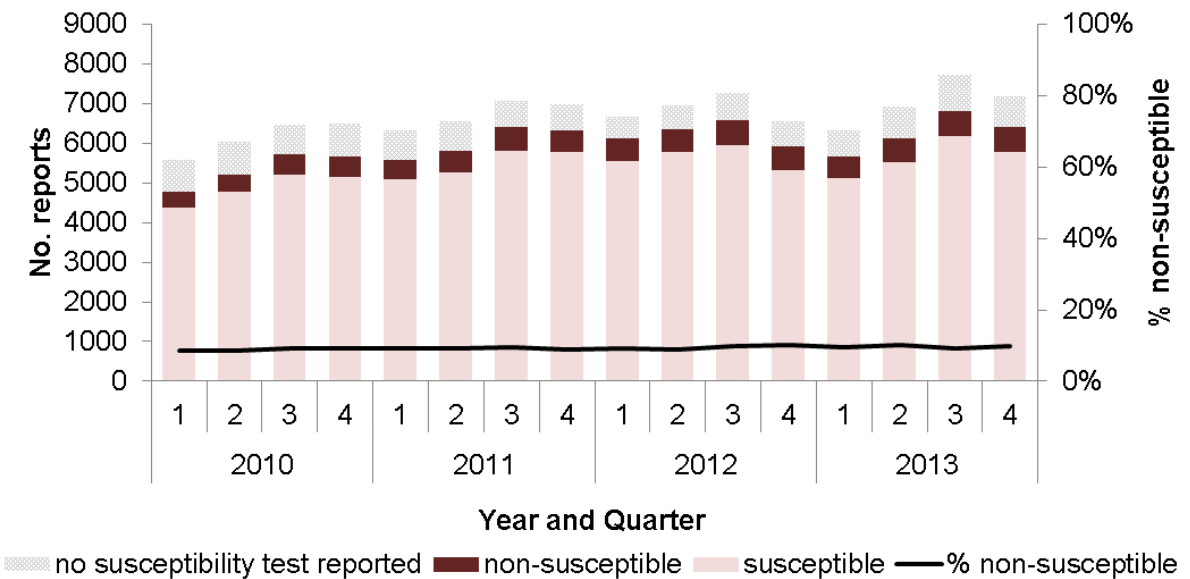


**Figure 2.1 Quarterly counts of *E. coli* bloodstream infections and proportions non-susceptible to a) ciprofloxacin, b) third generation cephalosporins, c) gentamicin and d) imipenem/meropenem in England between 2010 and 2013**

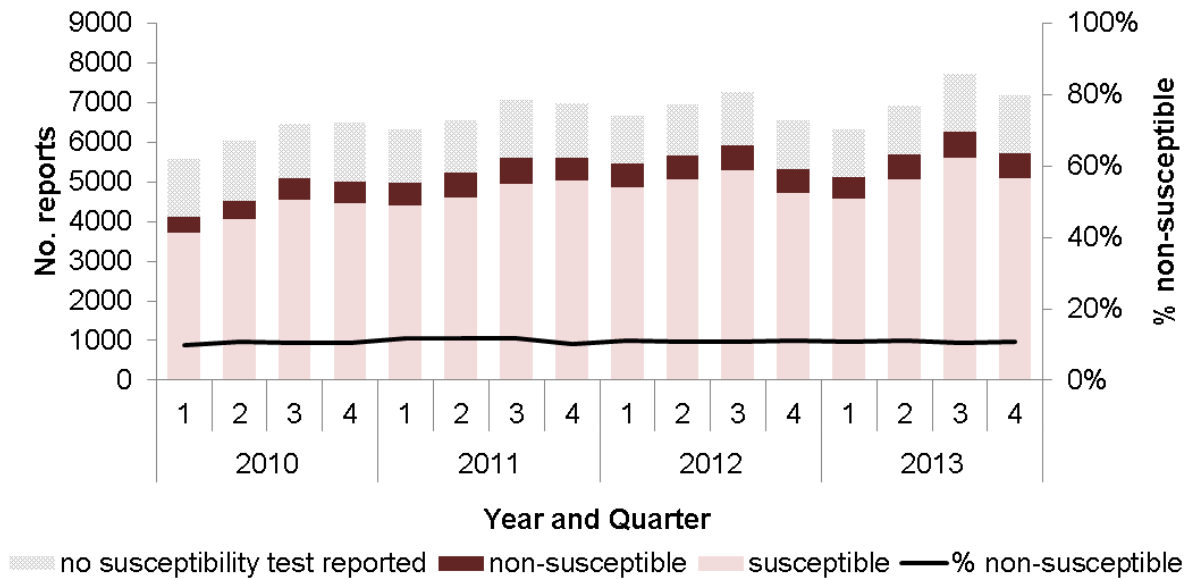
**a) Ciprofloxacin**



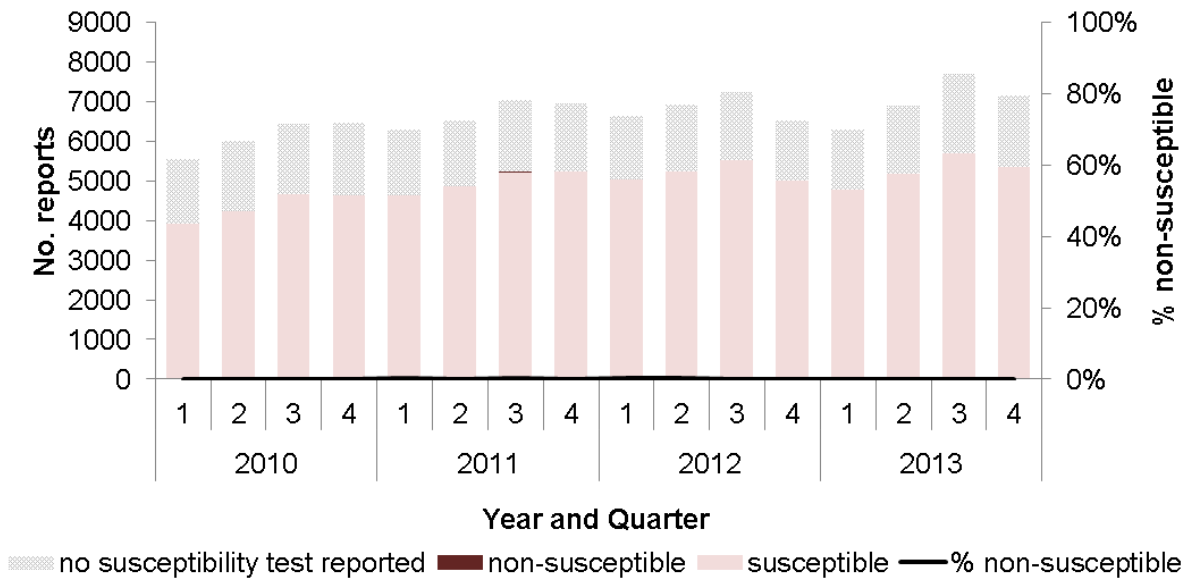
**b) Third-generation cephalosporins**



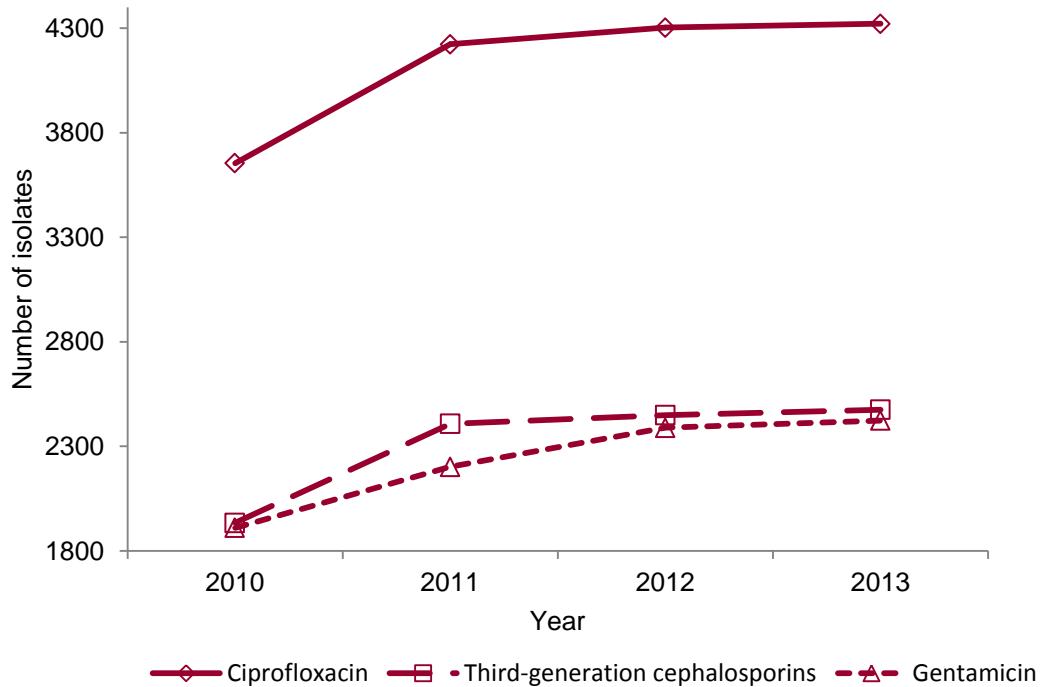
**c) Gentamicin**



**d) Imipenem/meropenem**



**Figure 2.2 Counts of *E. coli* isolates non-susceptible to ciprofloxacin, third-generation cephalosporins and gentamicin, based on voluntary reporting to LabBase2**



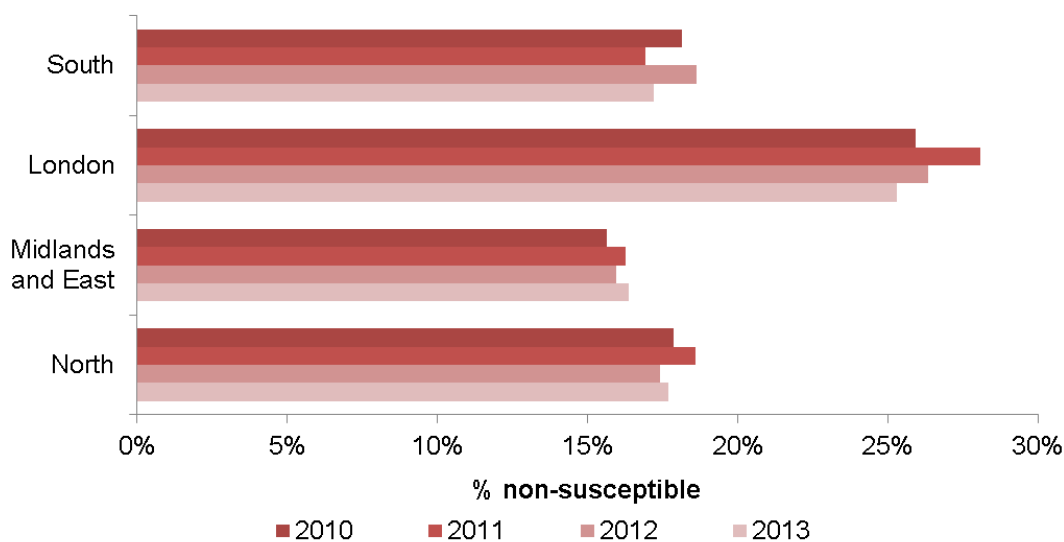
**Regional trends in susceptibility of *E. coli* from bloodstream infections**

The regional trends in susceptibility of *E. coli* from blood to ciprofloxacin, third-generation cephalosporins, gentamicin and imipenem/meropenem are shown in Figure 2.3 (a-d). For ciprofloxacin, third-generation cephalosporins and gentamicin, the proportions of non-susceptible isolates were significantly higher in London than in the other three regions for all years. Although the rates of non-susceptibility in each region showed year-to-year variation, the changes were not significant. Carbapenem non-susceptibility was seen in all regions in all years with the exception of London in 2010, but when seen, the proportion of non-susceptible isolates was very low (range 0.03% to 0.16%), with no consistent temporal trend.

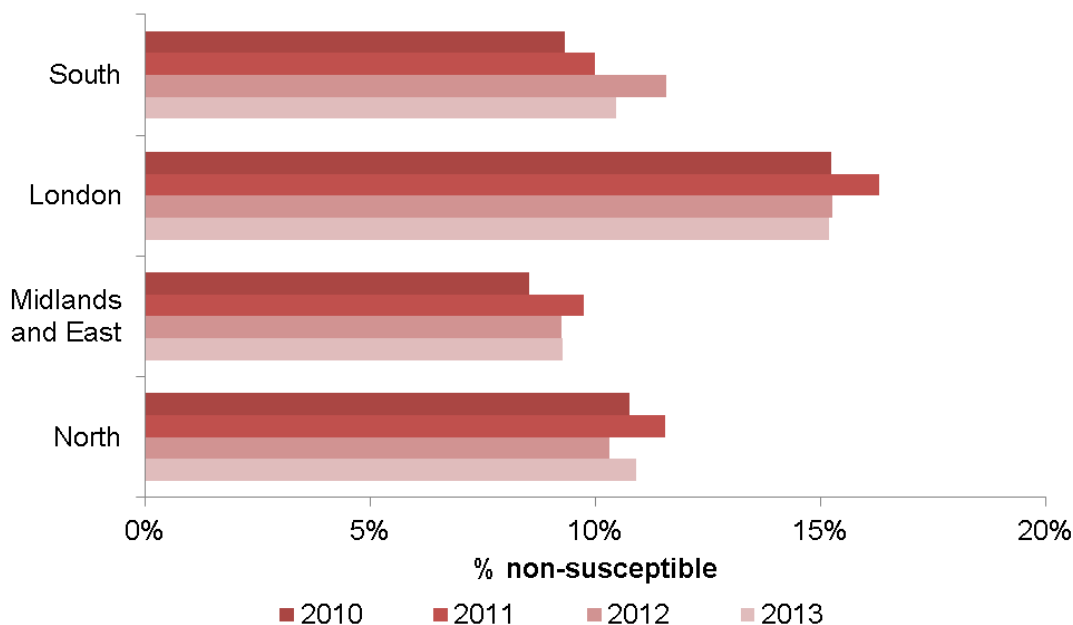
**Figure 2.3 Proportion of *E. coli* isolates from bloodstream infections non-susceptible to indicated antibiotics at the level of NHS Regions, 2010 and 2013.**

**a) ciprofloxacin, b) third-generation cephalosporins, c) gentamicin and d) carbapenems between 2010 and 2013**

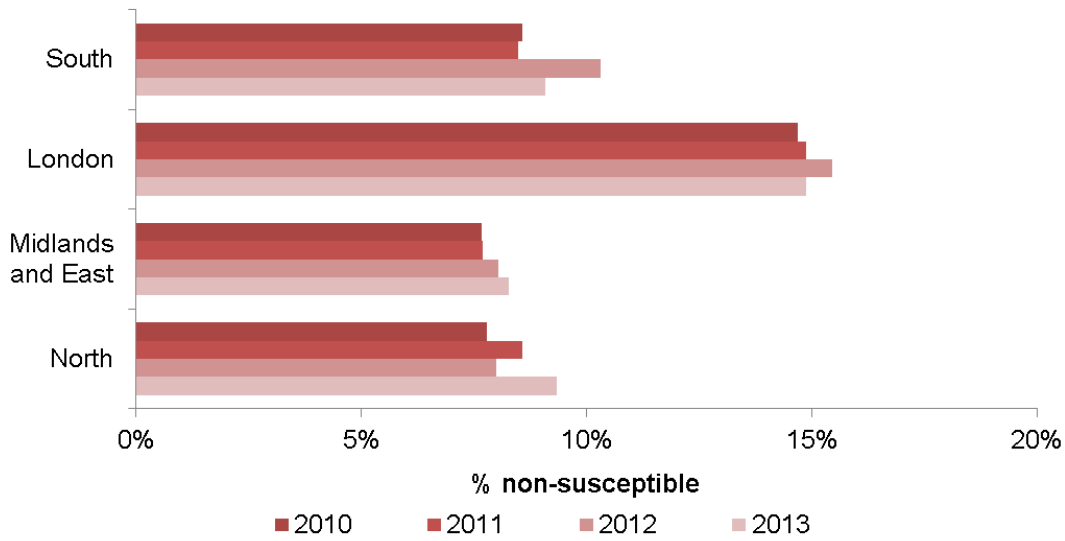
**a) Ciprofloxacin**



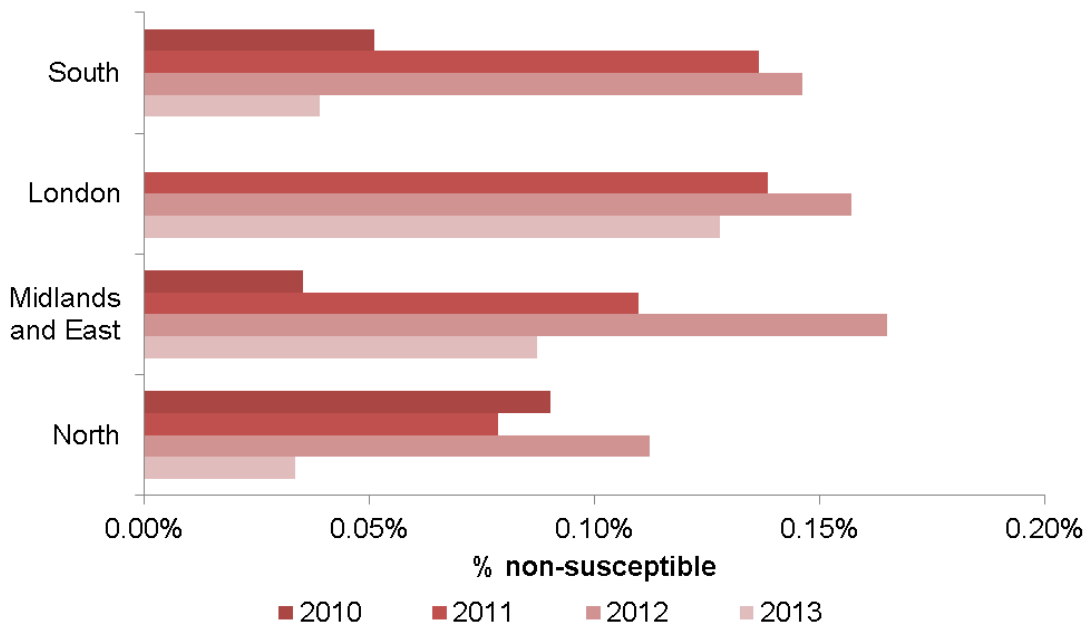
**b) Third-generation cephalosporins**



**c) Gentamicin**



**d) Imipenem/meropenem**



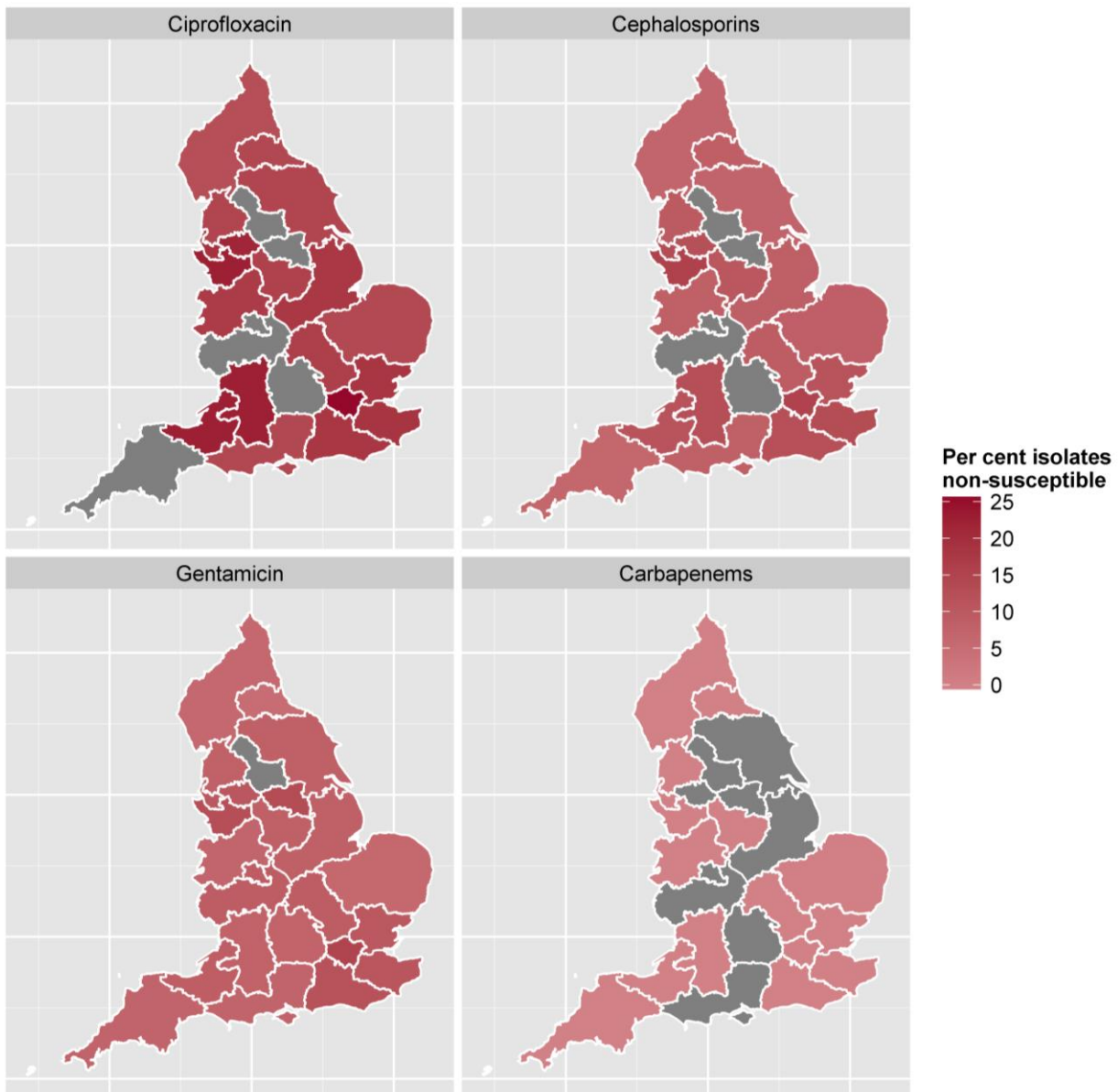
**Geographical variation in susceptibility of *E. coli* from bloodstream infections in 2013**

The proportion of *E. coli* non-susceptible to each antibiotic group at the level of ATs in 2013 is shown in Figure 2.4. Data are only shown for those ATs where susceptibility test results were available for  $\geq 70\%$  of isolates. The reasons why some ATs reported data for  $< 70\%$  of isolates may be due to lack of laboratory testing for susceptibility to particular antibiotics, but more commonly may reflect the fact that the susceptibility test results were suppressed at the time clinical reports were issued as a way of influencing which antibiotics were to be prescribed. Such suppressed results were not available for analysis in LabBase2.

Considerable variation was noted for non-susceptibility to ciprofloxacin, ranging from 25% in London to 12% in Cumbria, Northumberland and Tyne and Wear. This compares to the overall national rate of ciprofloxacin non-susceptibility in 2013 of 18.2%. Two ATs in the North of England and two in the South had non-susceptibility rates of >20% while two regions in the North, one in the Midlands and East and one in the South had <15% of isolates reported as non-susceptible.

The highest rate of cephalosporin non-susceptibility (15%) was seen in London and in Cheshire, Warrington and Wirral, with the lowest rate (6%) seen in Devon, Cornwall and the Isles of Scilly. This compares to the overall rate of cephalosporin non-susceptibility of 10.9%. London also had the highest rate of non-susceptibility to gentamicin (15%), with the lowest rate (5%) seen in Durham, Darlington and Tees (in comparison with overall national rate of 9.7%). Rates of non-susceptibility to carbapenems were uniformly low (0.0-0.2%) across all ATs (c.f. overall national rate of 0.07% in 2013).

**Figure 2.4 Proportions of *E. coli* bloodstream infection isolates non-susceptible to indicated antibiotics at the level of NHS area team in 2013. Grey areas represent ATs where <70% of isolates had susceptibility data available**



## *Klebsiella pneumoniae*

### Incidence of *K. pneumoniae* bloodstream infections

Between 2010 and 2013, the overall incidence of *K. pneumoniae* bloodstream infections in England, based on voluntary reporting to LabBase2, increased by 10% from 8.0 to 8.8 cases per 100,000 population (Table 2.3). Some degree of seasonal variation was noted with more isolates reported each year in quarters 3 and 4 (Figure 2.4). At regional level, the largest increase was observed in London (39%) with increases also observed in the South (12%) and the Midlands and East of England (7.3%). The incidence of reported cases in the North increased between 2010 and 2012, but then declined to give an overall decrease of 2% over the entire four year period.

**Table 2.3 Incidence of *K. pneumoniae* bloodstream infections by NHS Region, 2010 to 2013, based on voluntary reporting to LabBase2**

NHS Region	Rate per 100, 000 population			
	2010	2011	2012	2013
South	7.2	7.7	7.8	8.1
London	8.0	9.9	10.3	11.2
Midlands and East	7.8	8.5	8.6	8.4
North	8.9	9.1	9.5	8.7
<b>England</b>	<b>8.0</b>	<b>8.7</b>	<b>8.9</b>	<b>8.8</b>

### National trends in susceptibility of *K. pneumoniae* from bloodstream infections

The temporal trends in susceptibility of *K. pneumoniae* from blood to four antibiotic groups (ciprofloxacin, third-generation cephalosporins, gentamicin and imipenem/meropenem) are shown in Figure 2.5 (a-d). Susceptibility data were available for ≥70% of isolates tested against each antibiotic group each quarter, with the highest level of reporting seen for gentamicin (82-91% of isolates per quarter) and the lowest level for imipenem/meropenem (70-77% per quarter).

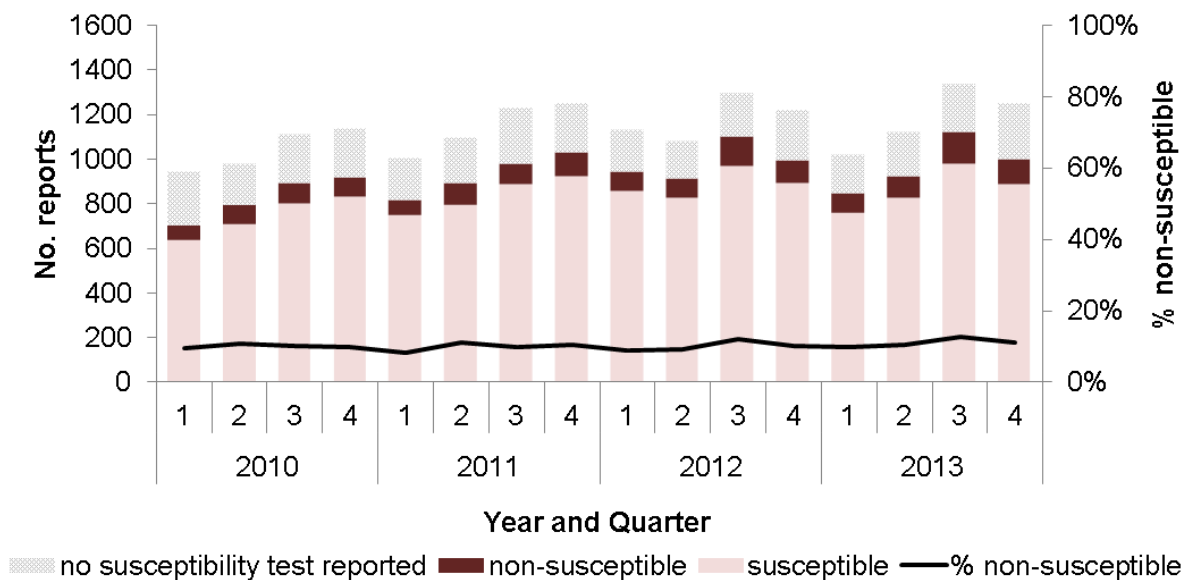
As with *E. coli*, previous national surveillance had shown an increase in the proportions of isolates of *K. pneumoniae* non-susceptible to ciprofloxacin, third-generation cephalosporins and gentamicin between 2001 and 2006, with a decline in non-susceptibility thereafter.<sup>25</sup> As shown in Figure 2.5, the decline in non-susceptibility to these agents appeared to cease from 2010, with the proportion of isolates non-susceptible to each antibiotic group being broadly stable between 2010 and 2013, being in the ranges of 8-13% for ciprofloxacin, 9-13% for third-generation cephalosporins, 6-10% for gentamicin and 0.1-2% for imipenem/meropenem.

<sup>25</sup> Livermore DM *et al.* Declining cephalosporin and fluoroquinolone non-susceptibility among bloodstream Enterobacteriaceae from the UK: links to prescribing change? J Antimicrob Chemother 2013; 68: 2667-2674.

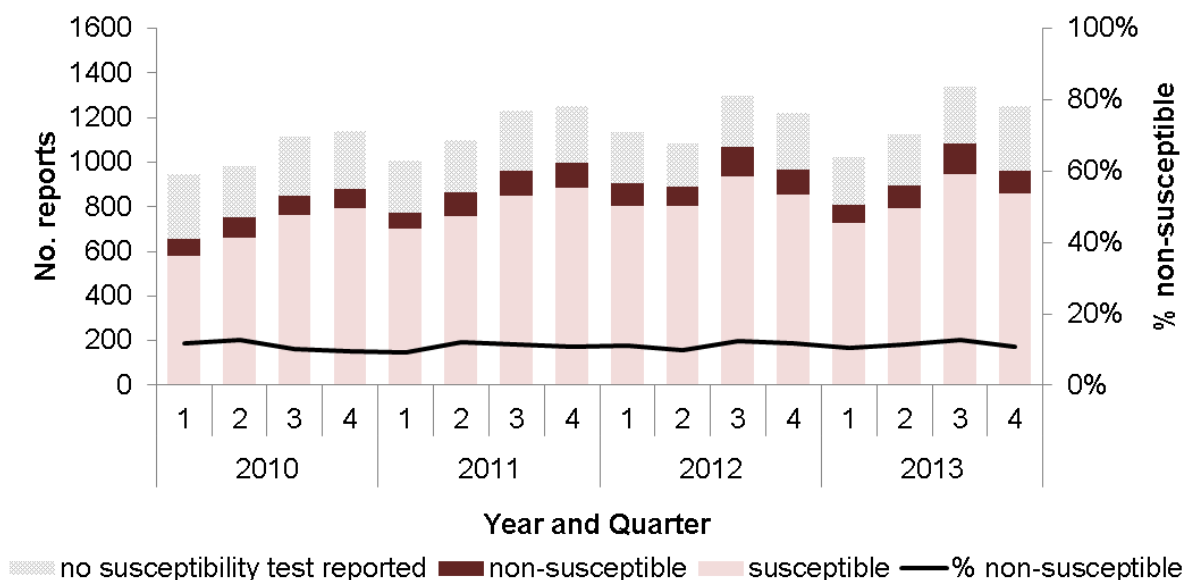
As with *E. coli*, although the proportion of isolates that were non-susceptible to the indicated antibiotics remained relatively stable between 2010 and 2013, the increasing incidence of *K. pneumoniae* during this time meant that the burden of antibiotic resistance, as measured by total numbers of resistant isolates, nonetheless increased. For example, the numbers of isolates non-susceptible to ciprofloxacin reported to LabBase2 rose from 333 in 2010 to 431 in 2013, an increase of 29% (Figure 2.6). The corresponding increases in non-susceptibility to third-generation cephalosporins and gentamicin were 26% and 46%, respectively. The numbers of isolates non-susceptible to imipenem/meropenem in each of the consecutive four years (14, 32, 34 and 34, respectively) were too small to allow robust statistical analysis.

**Figure 2.5 Quarterly counts of *K. pneumoniae* bloodstream infections and proportions non-susceptible to a) ciprofloxacin, b) third-generation cephalosporins, c) gentamicin and d) carbapenems in England between 2010 and 2013**

**a) Ciprofloxacin**

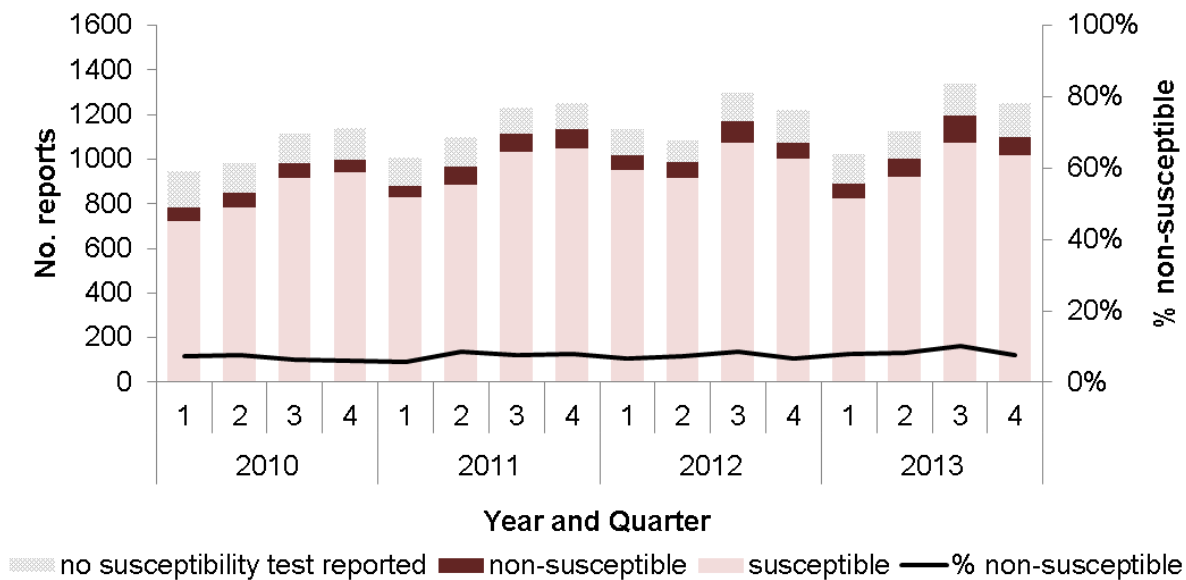


**b) Third-generation cephalosporins**

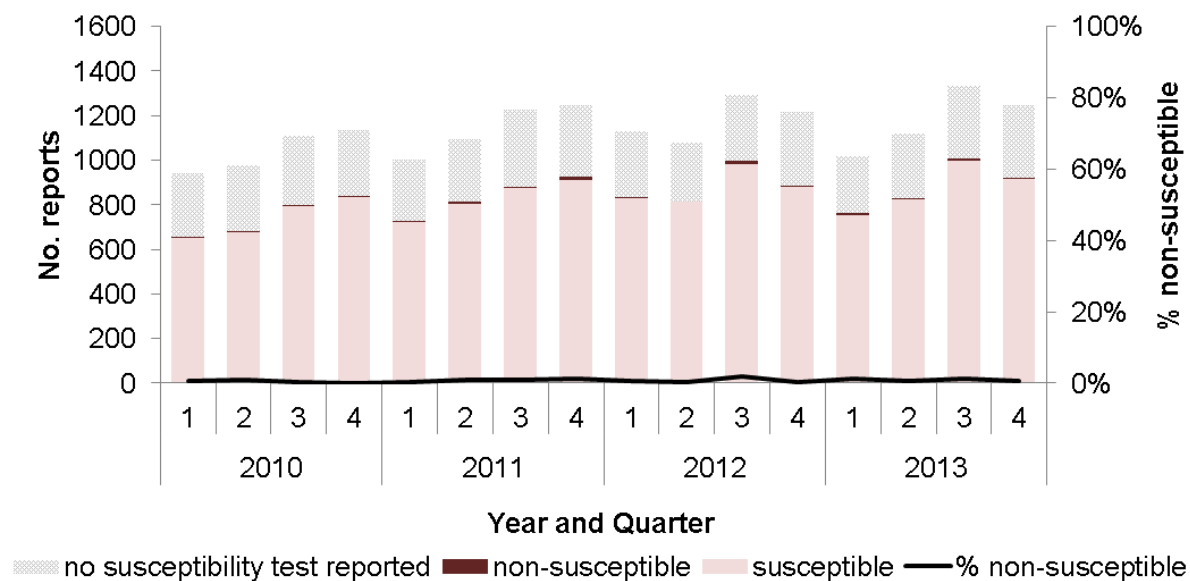




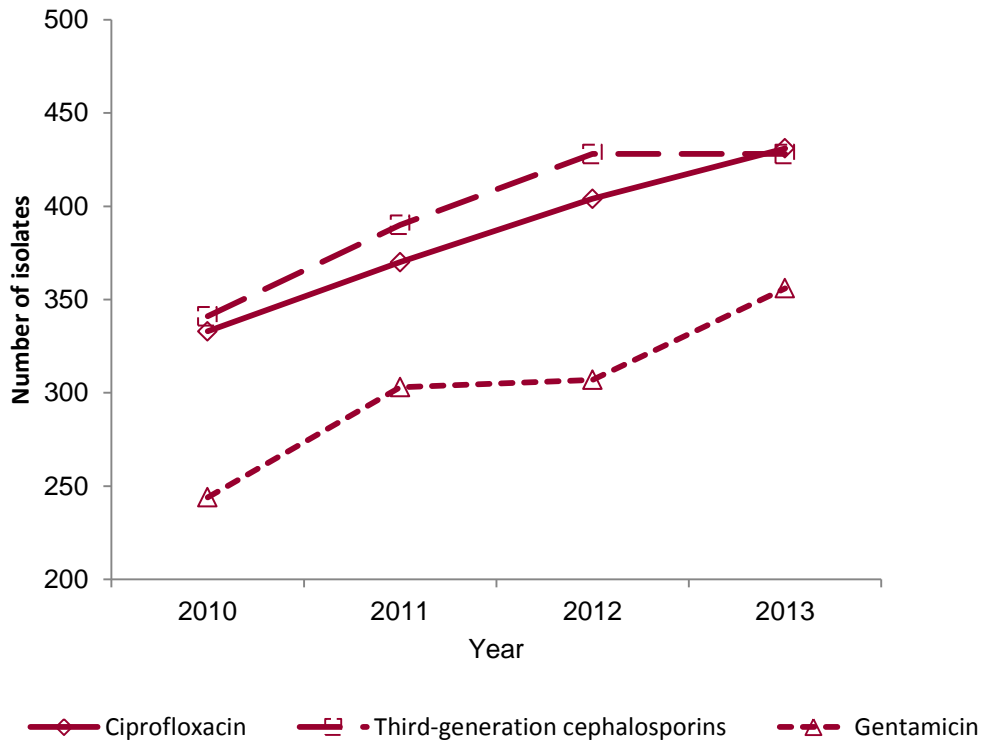
**c) Gentamicin**



**d) Imipenem/meropenem**



**Figure 2.6 Counts of *K. pneumoniae* isolates non-susceptible to ciprofloxacin, third-generation cephalosporins and gentamicin, based on voluntary reporting to LabBase2**

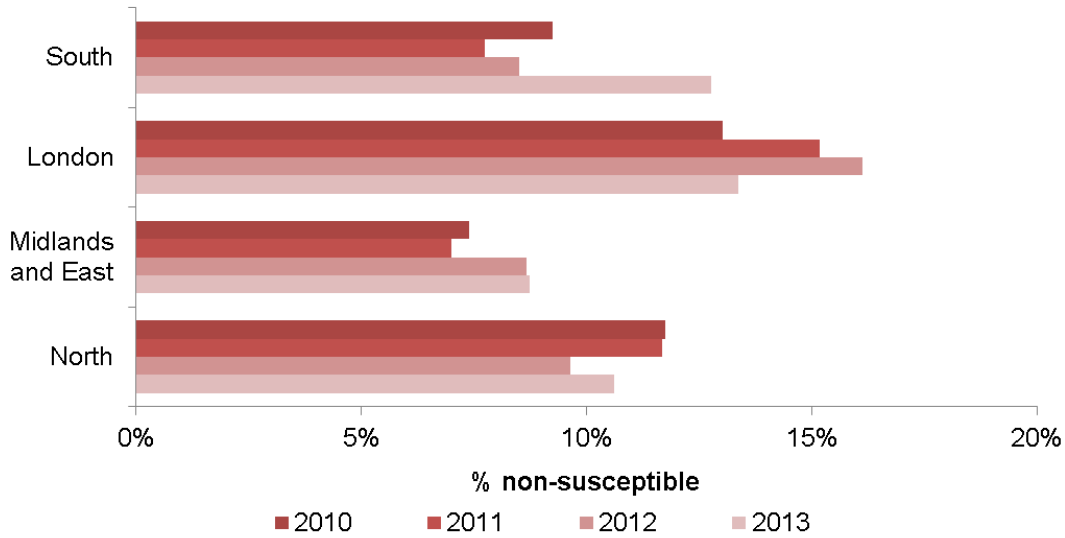


**Regional trends in susceptibility of *K. pneumoniae* from bloodstream infections**

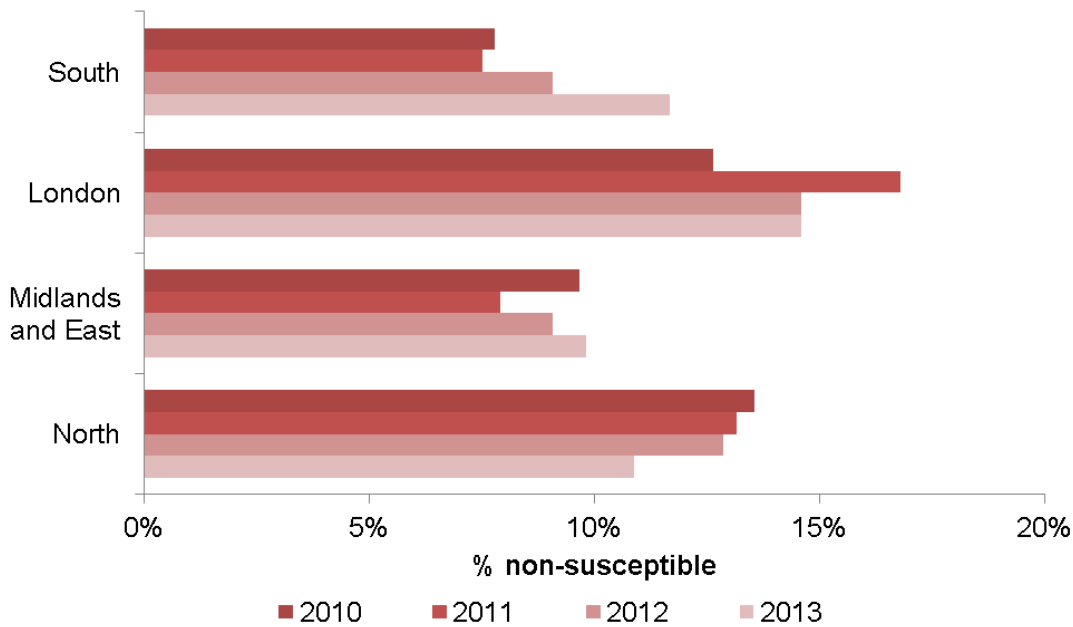
The regional trends in susceptibility of *K. pneumoniae* from bloodstream infections to ciprofloxacin, third-generation cephalosporins, gentamicin and imipenem/meropenem are shown in Figure 2.7 (a-d). The rates of non-susceptibility to ciprofloxacin, cephalosporins and gentamicin were generally highest in London and lowest in the Midlands and East of England; other inter-regional variation was not significant. The proportions of isolates of *K. pneumoniae* non-susceptible to carbapenems was highest in the North in 2010 and 2011, but by 2013, the proportions of non-susceptible isolates in the North, London and the South were comparable at 1.1-1.3%, compared with 0.4% in the Midlands and East.

**Figure 2.7 Proportion of *K. pneumoniae* from bloodstream infections non-susceptible to indicated antibiotics at the level of NHS Regions; a) ciprofloxacin, b) third-generation cephalosporins, c) gentamicin and d) carbapenems in England between 2010 and 2013**

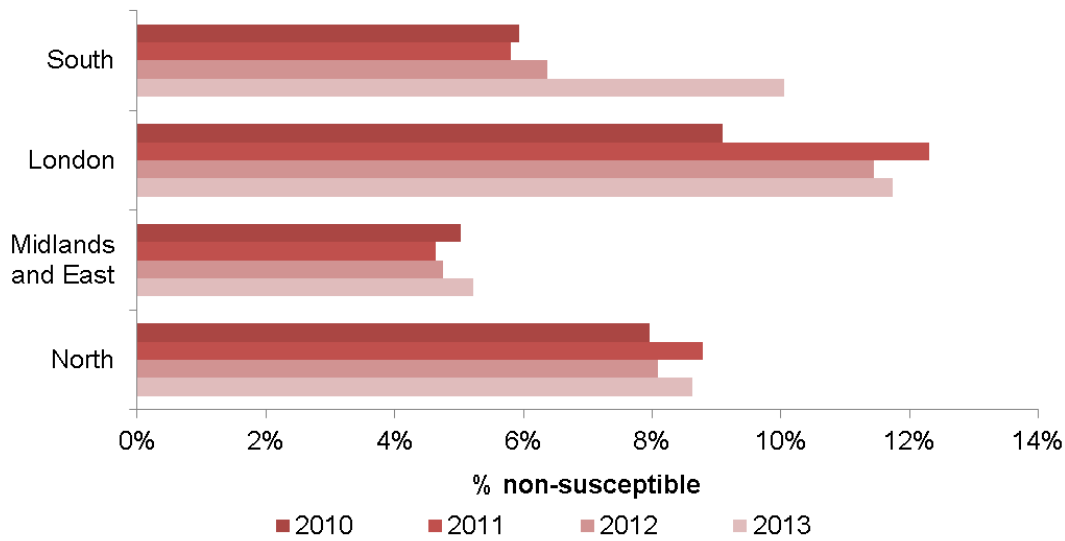
**a) Ciprofloxacin**



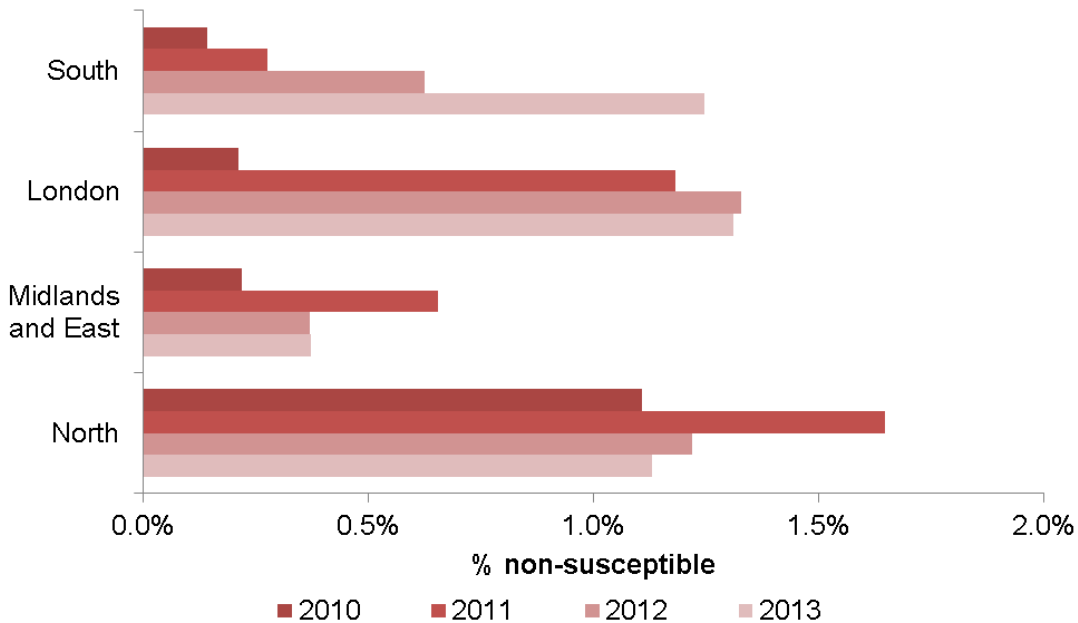
**b) Third-generation cephalosporins**



**c) Gentamicin**



**d) Imipenem/meropenem**



**Geographical variation in susceptibility of *K. pneumoniae* from bloodstream infections in 2013**

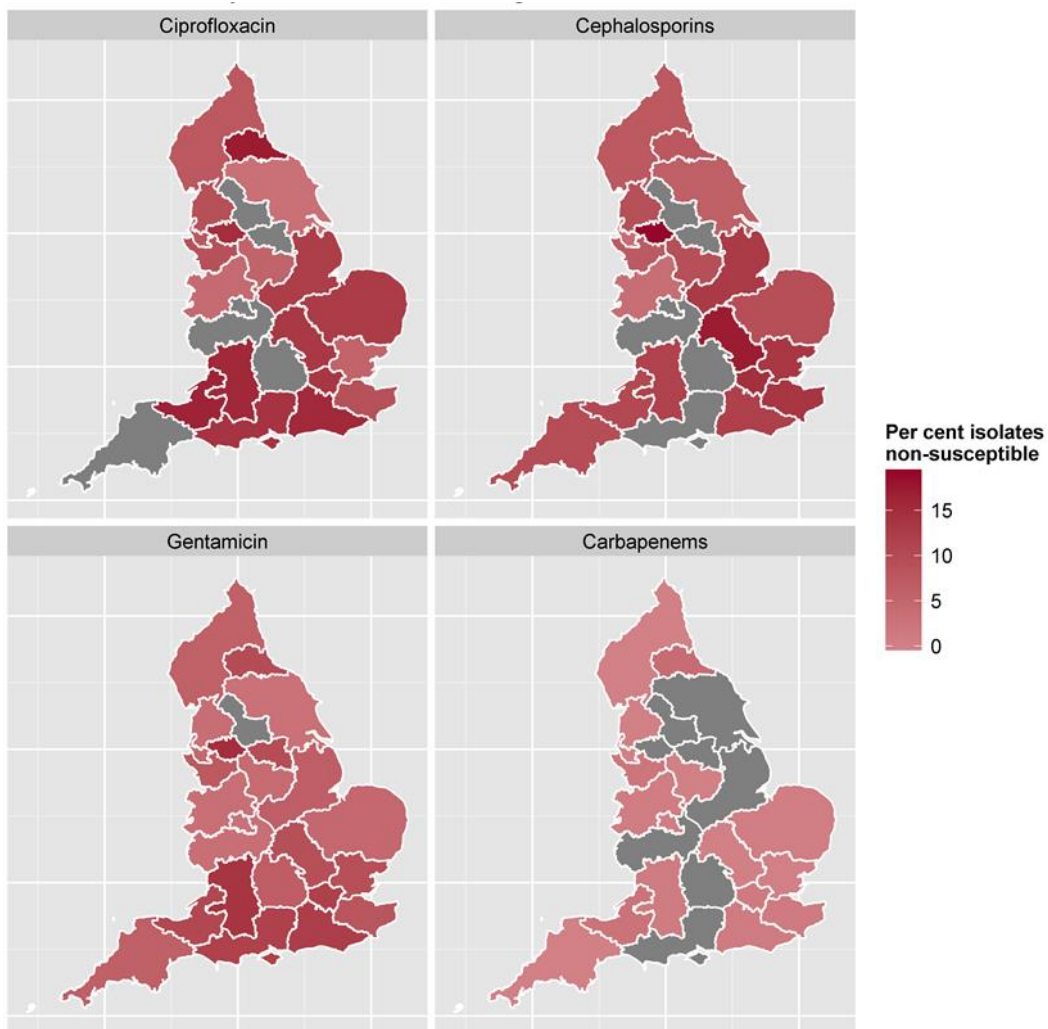
The proportion of *K. pneumoniae* non-susceptible to each antibiotic group at the level of ATs is shown in Figure 2.8. Data are only shown for those ATs where susceptibility test results were available for ≥70% of isolates.

Considerable variation was noted for non-susceptibility to ciprofloxacin, ranging from 17% in Durham, Darlington and North Tees to 3% in North Yorkshire and Humber. This compares to the overall national rate of ciprofloxacin non-susceptibility in 2013 of 11%. One AT in the North of England and three in the South had non-susceptibility rates of >15% while one region in the North and three in the Midlands had <8% of isolates reported as non-susceptible.

The highest rate of cephalosporin non-susceptibility (19%) was seen in Greater Manchester with the lowest rate (4%) being seen in Merseyside and in Shropshire and Staffordshire. This compares to an overall national rate of cephalosporin non-susceptibility of 11.4% in 2013. The highest rate of non-susceptibility to gentamicin (15%) was reported from Greater Manchester; this compares to an overall national rate of 8.5%. Two ATs in the North and four in the Midlands and East of England had gentamicin non-susceptibility rates of <5%.

Rates of non-susceptibility to carbapenems ranged from 0% to 3.8%. However, this should be interpreted with caution due to the low numbers of non-susceptible isolates (range 0-9) reported by individual ATs.

**Figure 2.8 Proportions of *K. pneumoniae* bloodstream infection isolates non-susceptible to indicated antibiotics at the level of NHS area team in 2013. Grey areas represent ATs where <70% of isolates had susceptibility data available.**



*Pseudomonas* spp.**Incidence of bloodstream infections due to *Pseudomonas* spp.**

Between 2010 and 2013, the overall incidence of bacteraemia due to *Pseudomonas* spp. in England, based on voluntary reporting to LabBase2, decreased by 9% from 6.9 to 6.3 cases per 100,000 population (Table 2.4). Some degree of seasonal variation was noted with more isolates reported each year in quarters 3 and 4 (Figure 2.7). At regional level, the largest decrease was seen in the North (15%) with the smallest decreases being seen in the South and the Midlands and East of England (4% and 5%, respectively).

**Table 2.4 Incidence of *Pseudomonas* spp. bloodstream infections by NHS Region, 2010 to 2013, based on voluntary reporting to LabBase2**

NHS Region	Rate per 100, 000 population			
	2010	2011	2012	2013
South	6.9	6.3	6.7	6.5
London	7.9	7.7	7.4	7.0
Midlands and East	6.9	6.4	6.8	6.6
North	6.2	6.0	5.8	5.3
<b>England</b>	<b>6.9</b>	<b>6.5</b>	<b>6.6</b>	<b>6.3</b>

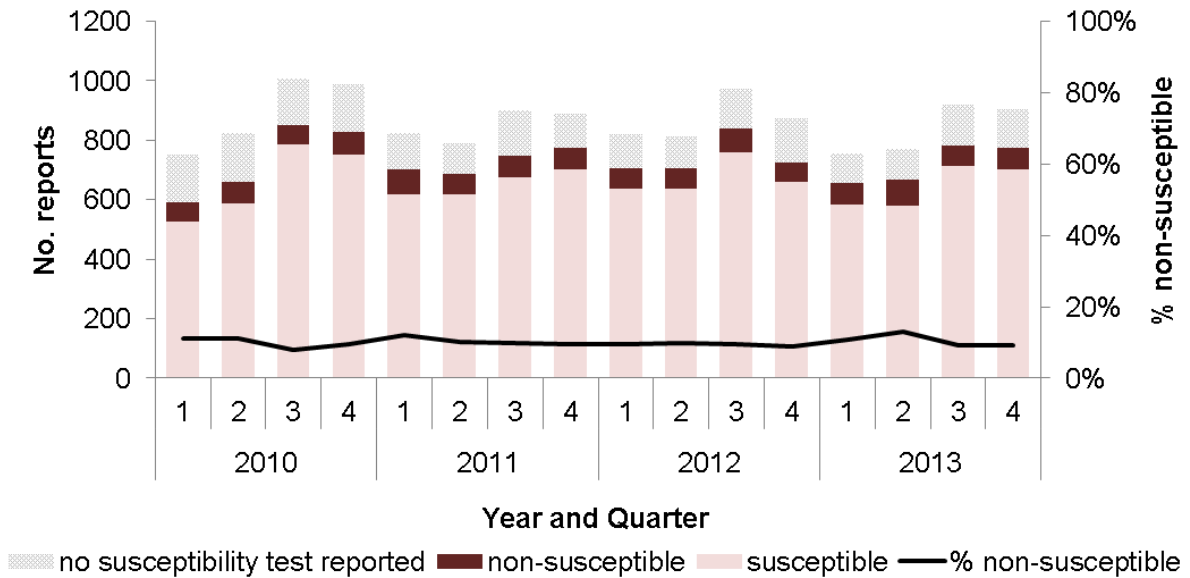
**National trends in susceptibility of *Pseudomonas* spp. from bloodstream infections**

The temporal trends in susceptibility of *Pseudomonas* spp. from bloodstream infections to ciprofloxacin, ceftazidime, gentamicin and imipenem/meropenem are shown in Figure 2.9 (a-d). Susceptibility data were available for >70% of isolates for each antibiotic group each quarter, with the highest level of reporting seen for gentamicin (84-91% of isolates per quarter) and the lowest levels for ceftazidime and imipenem/meropenem (73-84% and 75-83%, respectively).

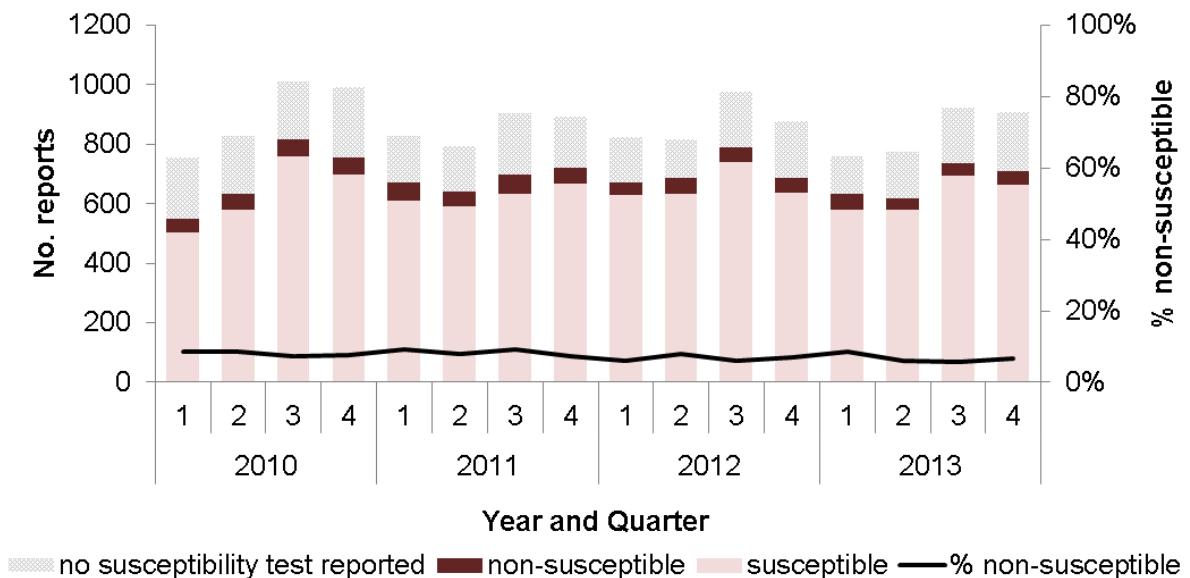
As shown in Figure 2.9, the trends for the proportion of isolates non-susceptible to each antibiotic group were broadly stable between 2010 and 2013, being in the ranges of 8-12% for ciprofloxacin, 6-9% for ceftazidime, 4-7% for gentamicin and 8-13% for carbapenems.

**Figure 2.9 Quarterly counts of *Pseudomonas* spp. bloodstream infections and proportions non-susceptible to a) ciprofloxacin, b) ceftazidime, c) gentamicin and d) carbapenems in England between 2010 and 2013**

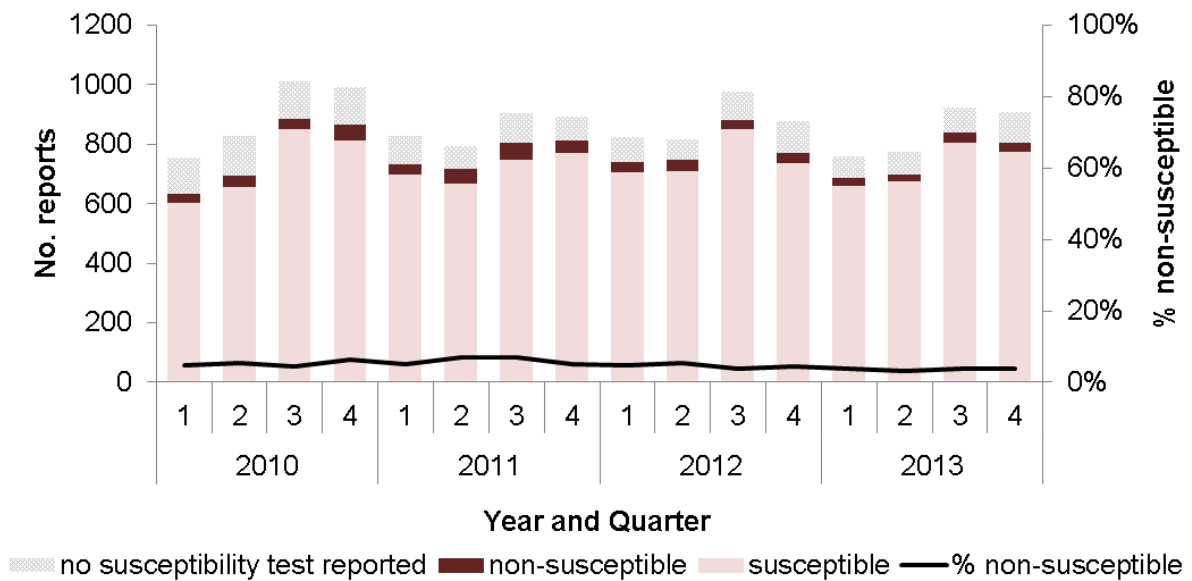
**a) Ciprofloxacin**



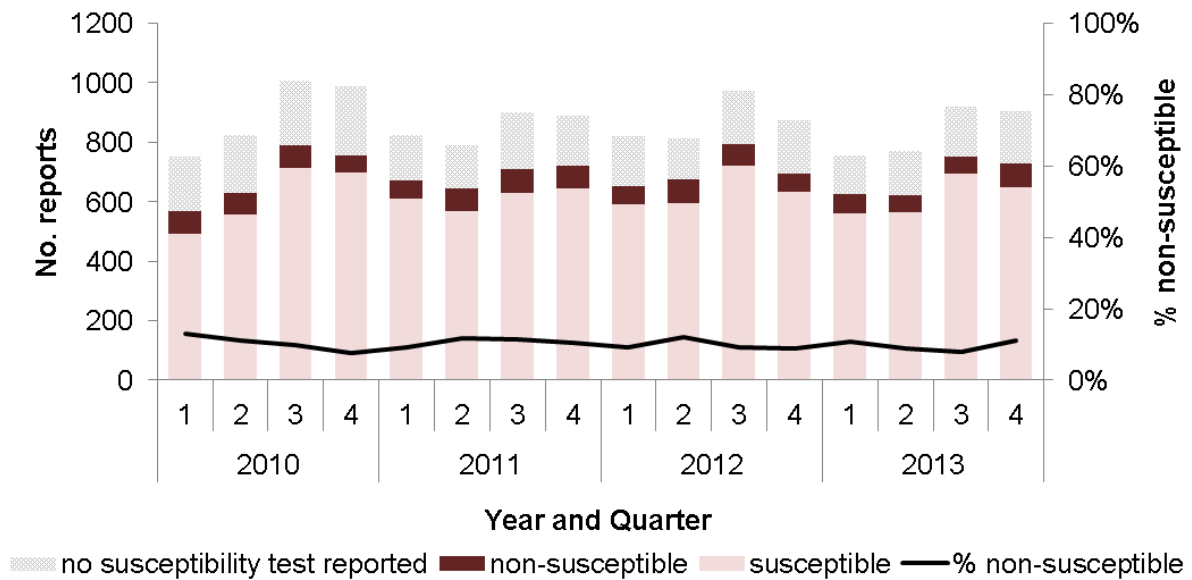
**b) Ceftazidime**



**c) Gentamicin**



**d) Imipenem/meropenem**



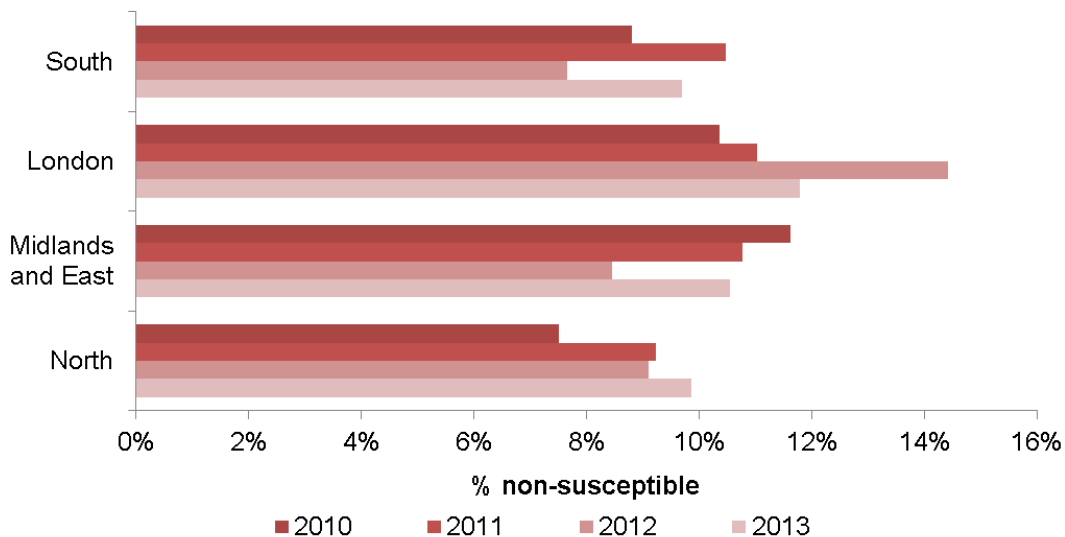
**Regional trends in susceptibility of *Pseudomonas* spp. from bloodstream infections**

The regional trends in susceptibility of *Pseudomonas* spp. from bloodstream infections to ciprofloxacin, ceftazidime, gentamicin and imipenem/meropenem are shown in Figure 2.10 (a-d). Although year-on-year decreases in non-susceptibility to ceftazidime and gentamicin were noted in the Midlands and East, these changes were not significant. Apart from the rate of non-susceptibility to ciprofloxacin being significantly higher in London compared with other regions in 2012, no other clear trends were evident.

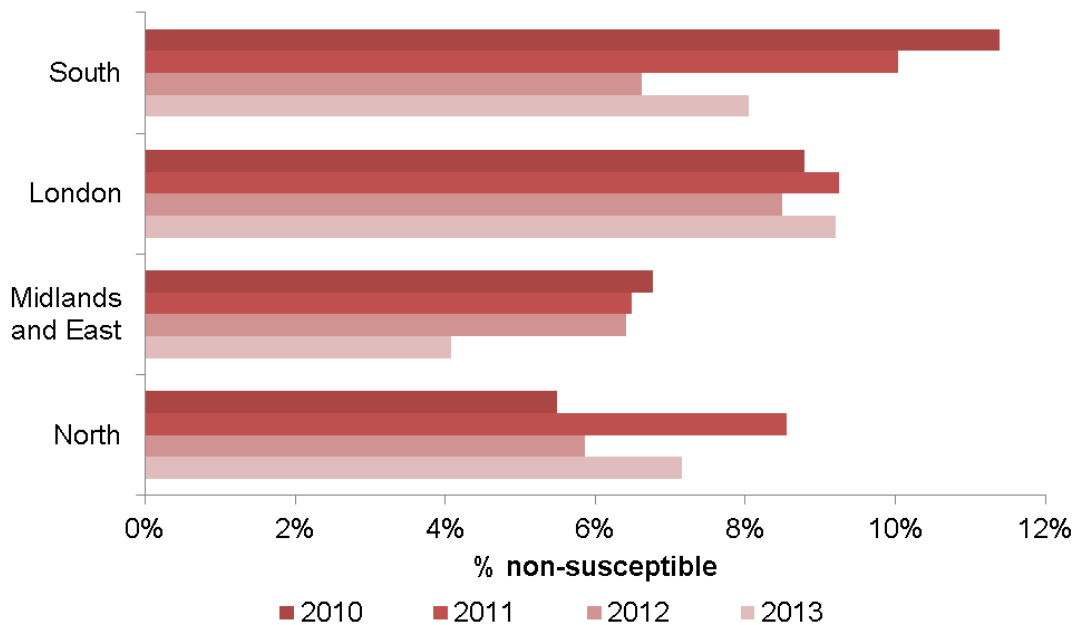


**Figure 2.10 Proportion of *Pseudomonas* spp. from bloodstream infections non-susceptible to indicated antibiotics at the level of NHS Regions; a) ciprofloxacin, b) ceftazidime, c) gentamicin and d) carbapenems in England between 2010 and 2013**

**a) Ciprofloxacin**



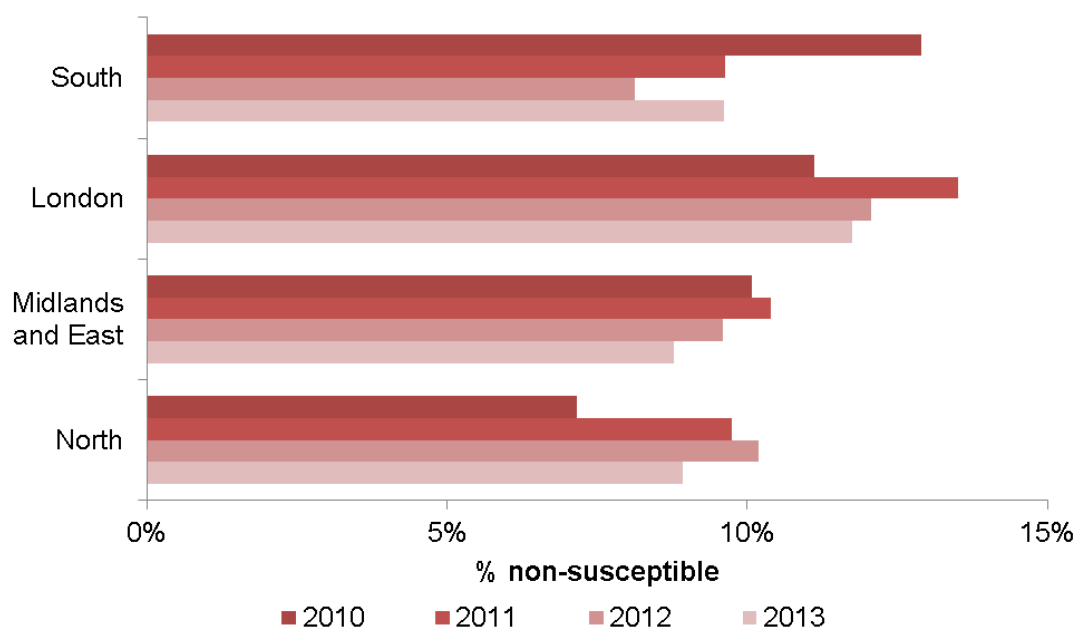
**b) Ceftazidime**



**c) Gentamicin**



**d) Imipenem/meropenem**



**Geographical variation in susceptibility of *Pseudomonas* spp. from bloodstream infections in 2013**

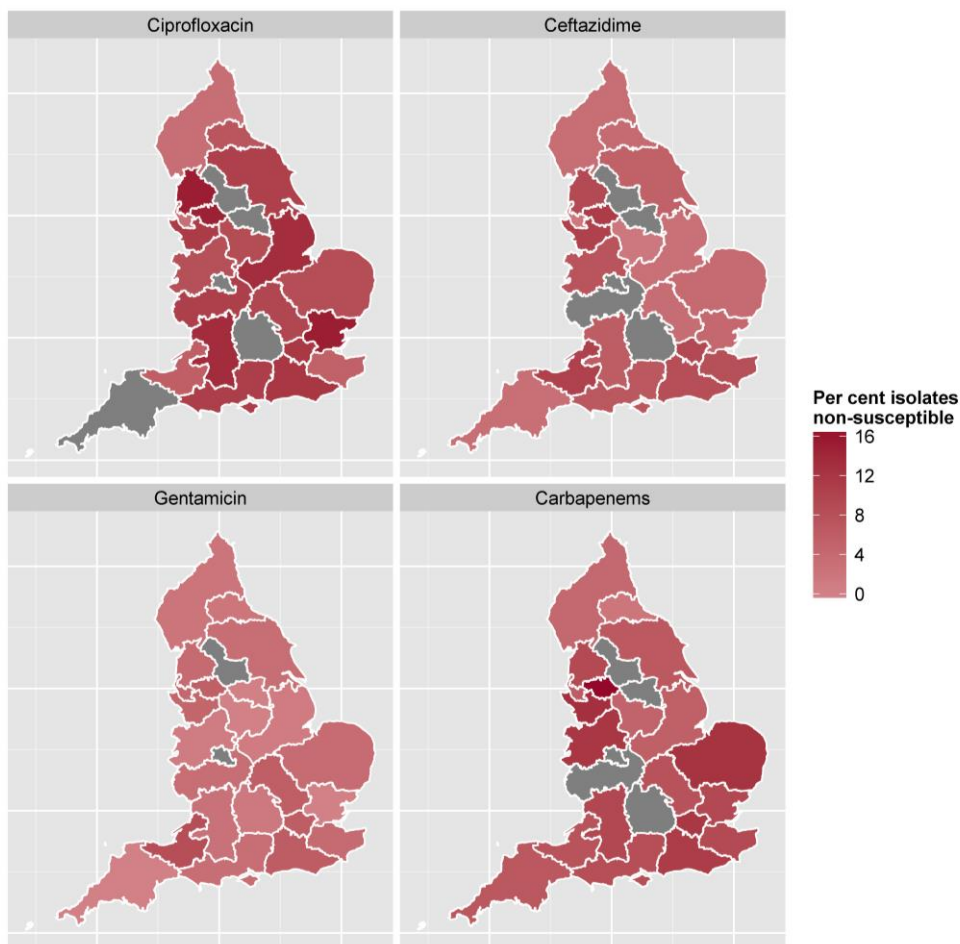
The proportion of *Pseudomonas* spp. non-susceptible to each antibiotic group at the level of ATs is shown in Figure 2.11. Data are only shown for those ATs where susceptibility test results were available for  $\geq 70\%$  of isolates.

Non-susceptibility to ciprofloxacin ranged from 15% (reported by two ATs in the North and one in the Midlands and East) to 3% (reported by two ATs also in the North). For comparison, the overall national rate of ciprofloxacin non-susceptibility in 2013 was 10%. Ceftazidime non-

susceptibility ranged from 11% in Greater Manchester to 2% in Derbyshire and Nottingham (compared with overall national rate of 7%). Non-susceptibility to gentamicin (overall national rate of 4%) ranged from 0 to 8%.

Rates of non-susceptibility to imipenem/meropenem ranged from 2% (Durham, Darlington and Tees) to 17% in Greater Manchester, both ATs being in the North of England. This compared to the national rate of 10%.

**Figure 2.11 Proportions of *Pseudomonas* spp. bloodstream infection isolates non-susceptible to indicated antibiotics at the level of NHS area team in 2013. Grey areas represent ATs where <70% of isolates had susceptibility data available**



## *Streptococcus pneumoniae*

### Incidence of *S. pneumoniae* bloodstream infections

Between 2010 and 2013, the overall incidence of *S. pneumoniae* bloodstream infections in England, based on voluntary reporting to LabBase2, decreased by 25% from 8.1 to 6.1 cases per 100,000 population (Table 2.5). The declining incidence of pneumococcal bacteraemia probably reflects the impact of the introduction of the 13-valent pneumococcal conjugate vaccine in 2010.<sup>27</sup> Overall decreases were seen in all regions although the extent varied from 31% in the North to 15% in London. As shown in Figure 2.12, the incidence of pneumococcal bacteraemia showed seasonal variation with the highest rates seen in the first and fourth quarters of each calendar year.

**Table 2.5 Incidence of *S. pneumoniae* bloodstream infections by NHS Region, 2010 to 2013, based on voluntary reporting to LabBase2**

NHS Region	Rate per 100, 000 population			
	2010	2011	2012	2013
South	7.9	6.9	6.7	6.3
London	6.7	5.2	5.8	5.7
Midlands and East	7.9	7.2	6.3	5.7
North	9.3	8.5	7.6	6.4
<b>England</b>	<b>8.1</b>	<b>7.2</b>	<b>6.7</b>	<b>6.1</b>

### National trends in susceptibility of *S. pneumoniae* from bloodstream infections

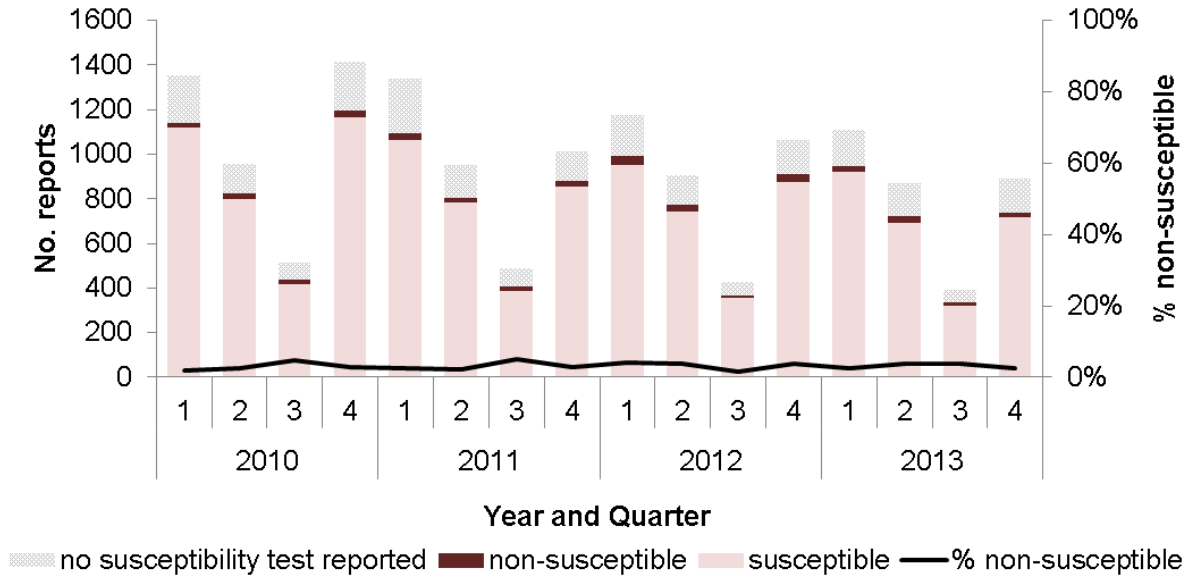
The temporal trends in susceptibility of *S. pneumoniae* from bloodstream infections to penicillin, macrolides (erythromycin, clarithromycin or azithromycin) and tetracycline are shown in Figure 2.12 (a-c). Susceptibility data for penicillin and macrolides were available for >80% of isolates each quarter (ranges 82-87% and 81-84%, respectively) but for tetracycline the proportion of isolates for which susceptibility data were reported was within the range of 66-72%.

As shown in Figure 2.12, the trends for the proportion of isolates non-susceptible to penicillin were broadly stable between 2010 and 2013, being in the ranges of 2-5%. For macrolides there was a small but significant increase in the annual rate of macrolide non-susceptibility from 4.8% (95% CI 4.0-5.6%) in 2010 to 7.4% (95% CI 6.3-8.6%) in 2013, which was reflected in a 12% increase in the number of macrolide-non-susceptible isolates from 193 in 2010 to 217 in 2013. By the same token there was also a 22% increase in the number of isolates non-susceptible to tetracycline (116 in 2010 rising to 141 in 2013). By contrast, the burden of resistance, as measured by the total numbers of non-susceptible isolates to penicillin, decreased by 14%.

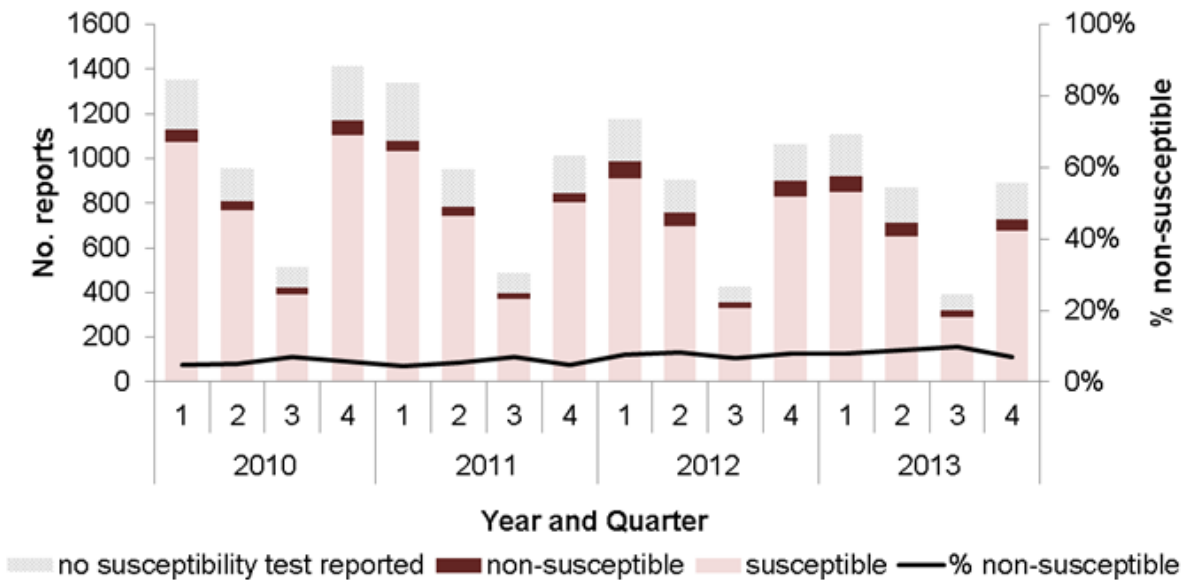
<sup>27</sup> <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/Pneumococcal/>

**Figure 2.12 Quarterly counts of *S. pneumoniae* bloodstream infections and proportions non-susceptible to a) penicillin, b) macrolides, and c) tetracycline in England between 2010 and 2013**

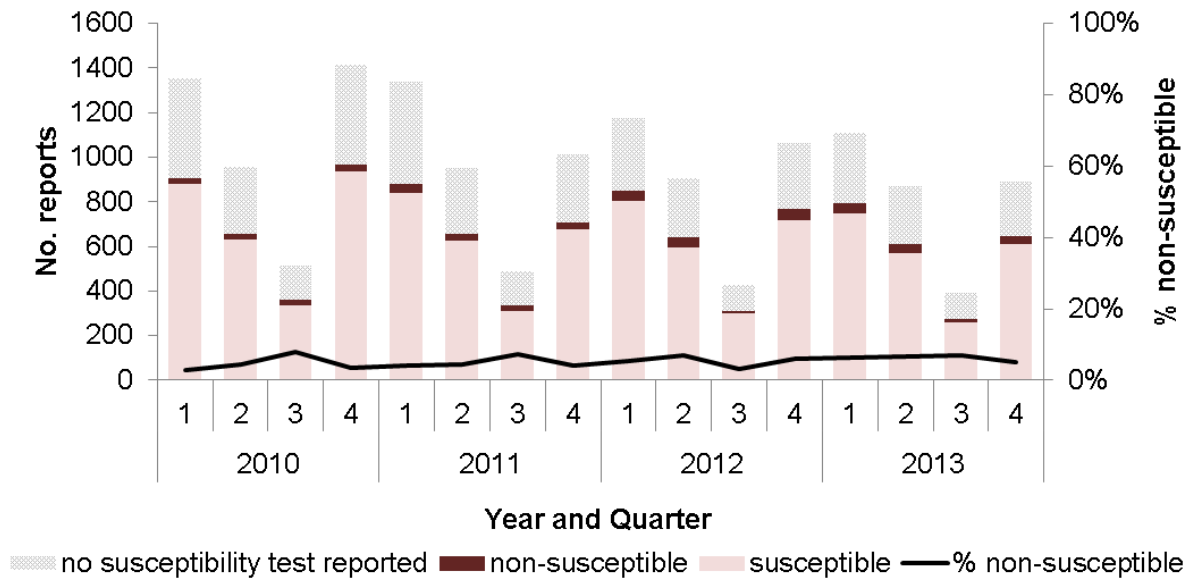
**a) Penicillin**



**b) Macrolides**



**c) Tetracycline**

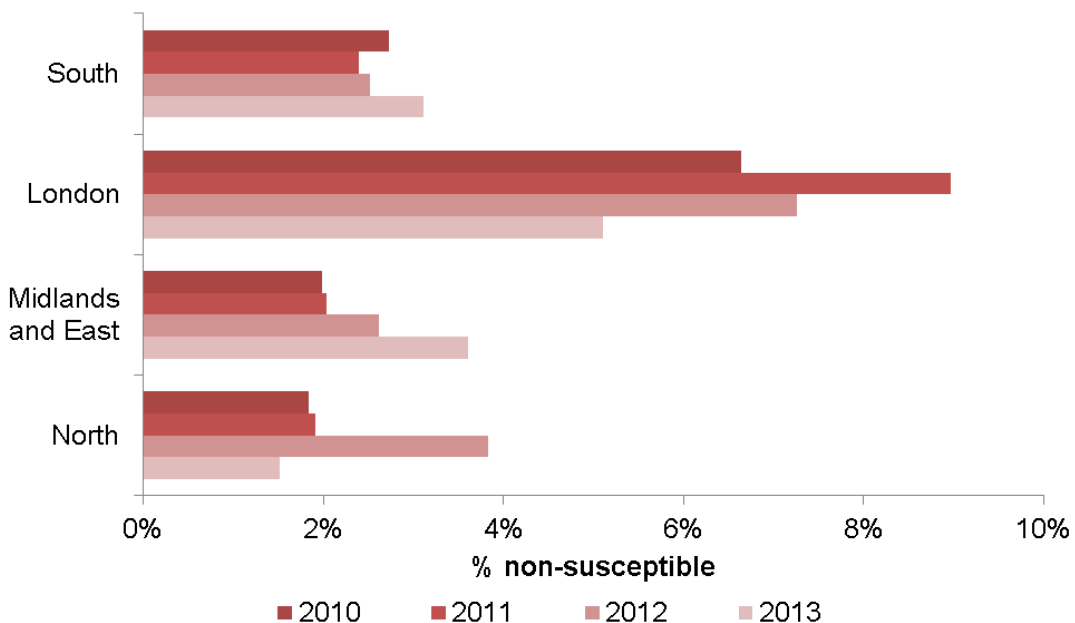


**Regional trends in susceptibility of *S. pneumoniae* from bloodstream infections in 2013**

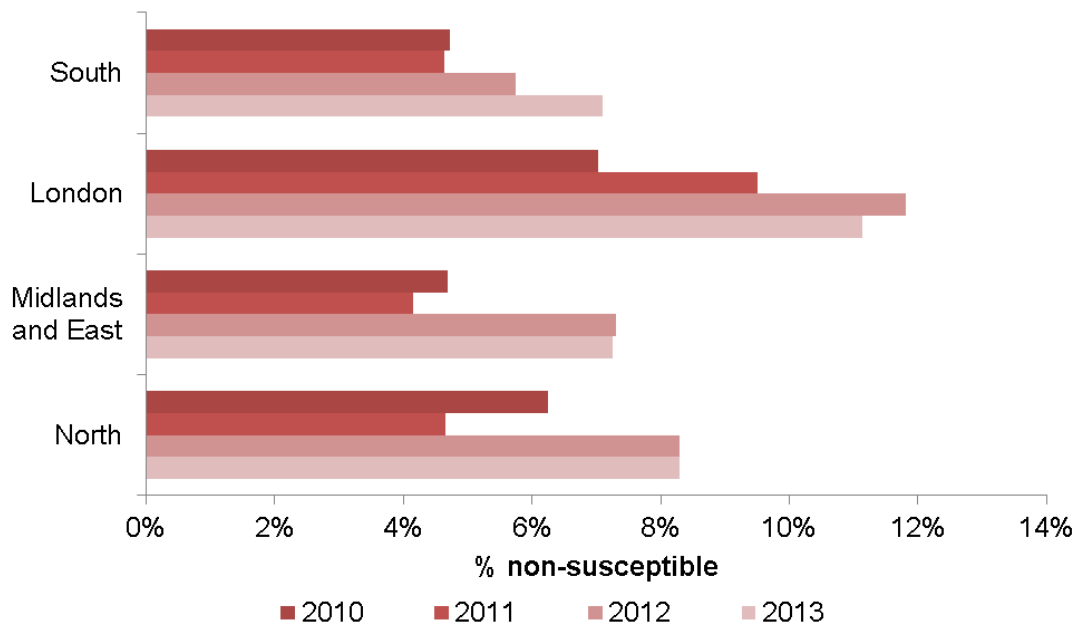
The regional trends in susceptibility of *S. pneumoniae* from bloodstream infections to penicillin, macrolides and tetracycline are shown in Figure 2.13 (a-c). The highest rates of resistance for all three antibiotic classes were seen in London, but there were no other clear temporal or regional trends.

**Figure 2.13 Proportion of *S. pneumoniae* isolates from bloodstream infections non-susceptible to indicated antibiotics at the level of NHS Regions; a) penicillin, b) macrolides, c) tetracycline in England between 2010 and 2013**

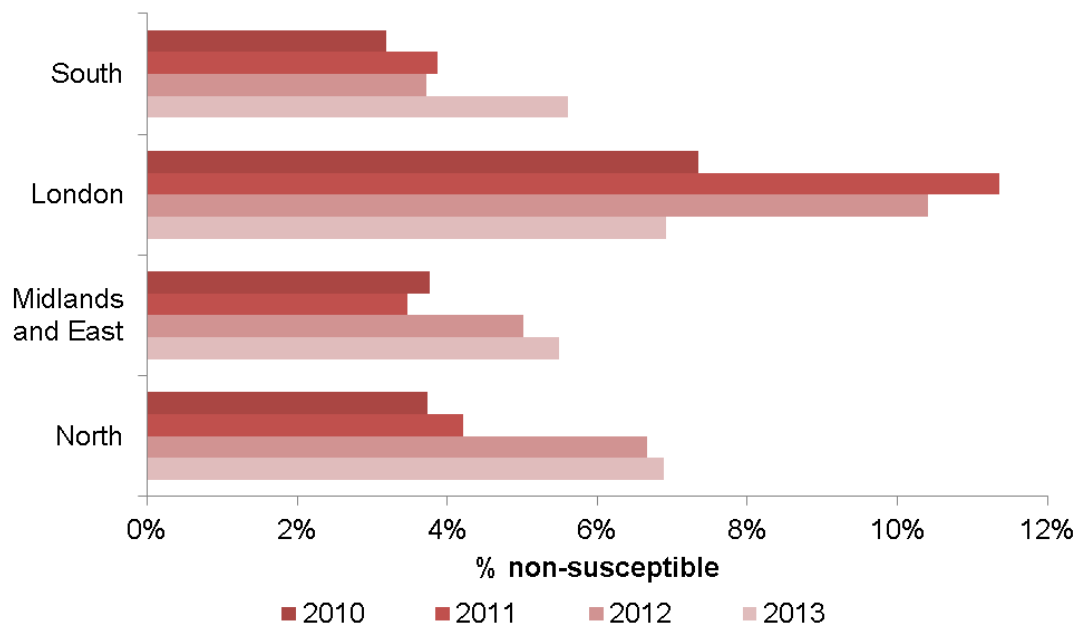
**a) Penicillin**



**b) Macrolides**



**c) Tetracycline**



**Geographical variation in susceptibility of *S. pneumoniae* from bloodstream infections in 2013**

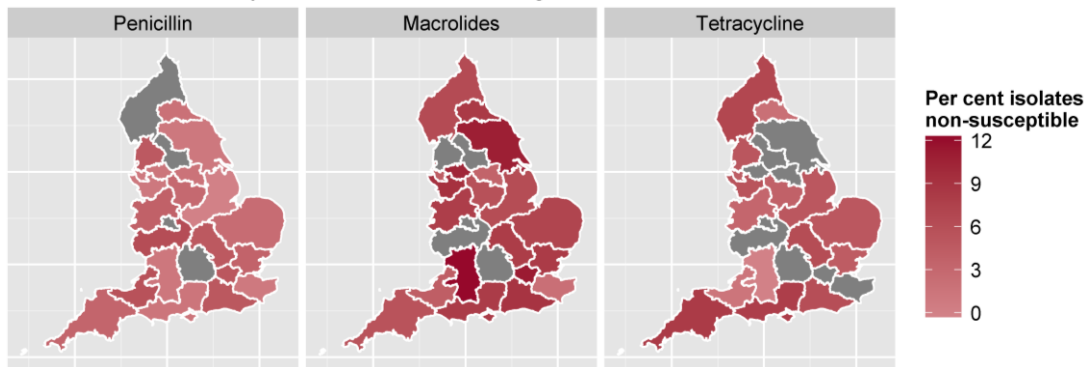
The proportion of *S. pneumoniae* non-susceptible to each antibiotic group at the level of ATs in 2013 is shown in Figure 2.14. Data are only shown for those ATs where susceptibility test results were available for ≥70% of isolates.

Variation was noted for non-susceptibility to penicillin, ranging from 1% to 6%. This compares to the overall national rate of penicillin non-susceptibility in 2013 of 3.1%. The distribution appeared heterogeneous with penicillin non-susceptibility rates of 5-6% being seen in London, two ATs in the South, two AT in the Midlands and East of England and one AT in the North.

Variation was also noted for non-susceptibility to macrolides, ranging from 2% to 12% (c.f. overall national non-susceptibility rate of 6.7% in 2013). The highest rates of resistance were seen in the South (12%, Bath, Gloucester, Swindon and Wiltshire) and North (11%, North Yorkshire and Humber), with the South also having the AT with the lowest rate of non-susceptibility (2%, Kent and Medway).

Non-susceptibility to tetracycline varied from 0% to 8%, with the two ATs with the highest rate of non-susceptibility (8%, Wessex; Devon, Cornwall and the Isles of Scilly) and the AT with the lowest rate (0%, Bath, Gloucestershire, Swindon and Wiltshire) all being in the South. For comparison, the overall national rate of non-susceptibility to tetracycline in 2013 was 6.1%.

**Figure 2.14 Proportions of *S. pneumoniae* bloodstream infection isolates non-susceptible to indicated antibiotics at the level of NHS area team in 2013. Grey areas represent ATs where <70% of isolates had susceptibility data available.**





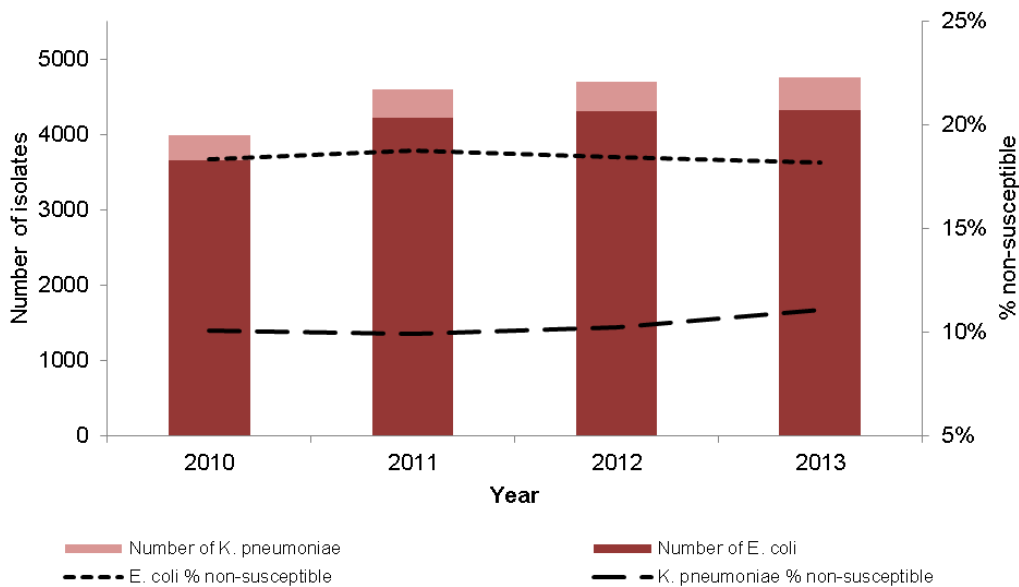
# Discussion

While previously published data on antimicrobial resistance in the UK have focussed on the national picture, this report also collates for the first time data on resistance at both regional and sub-regional levels. Such data will hopefully inform end users as regards the local epidemiology and burden of antibiotic resistance and allow bench marking against regional and national trends. The data presented have focussed on four pathogens highlighted in the UK 5-year Antimicrobial Resistance Strategy. Data are presented for the period 2010 to 2013 and thus establish the baseline level of resistance in these pathogens in the four years prior to implementation of the strategic plan.

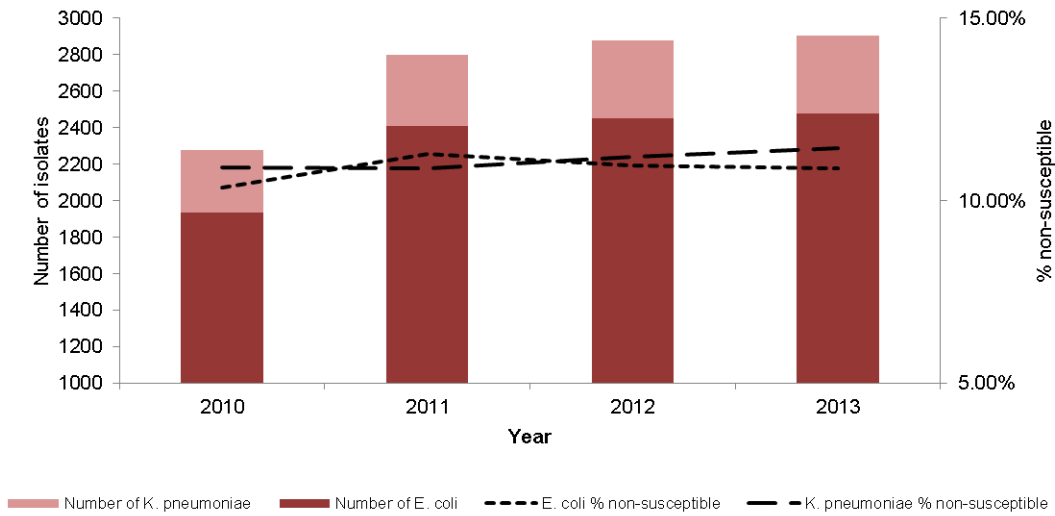
Of particular note is that although the proportions of isolates of *E. coli* and *K. pneumoniae* from blood culture resistant to ciprofloxacin, third-generation cephalosporins and gentamicin remained broadly stable over the 4-year period, the burden of resistance, as measured by total numbers of isolates non-susceptible to each antibiotic class nonetheless increased, due to the increased incidence of bloodstream infections due to these pathogens. The total numbers of non-susceptible *E. coli* and *K. pneumoniae* reported to LabBase2 are shown in Figure 2.15, the percentage increase between 2010 and 2013 being 19% for ciprofloxacin, 28% for third-generation cephalosporins and 29% for gentamicin.

**Figure 2.15 Annual combined counts of *E. coli* and *K. pneumoniae* non-susceptible to indicated antibiotics, based on voluntary reporting to LabBase2.**

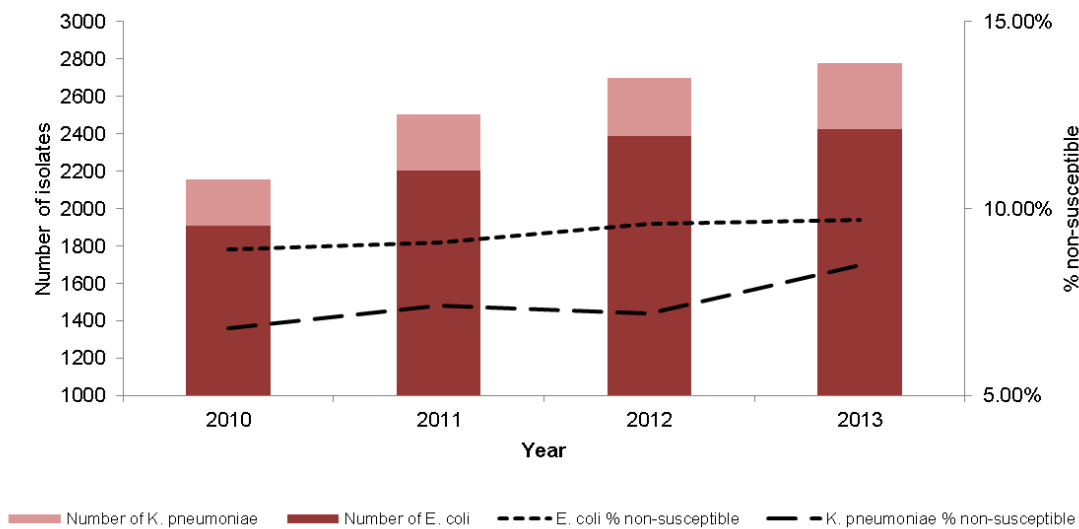
## a) Ciprofloxacin



**b) Third-generation cephalosporins**



**c) Gentamicin**



Although the incidence of bacteraemia due to *S. pneumoniae* declined by 25%, a small but significant increase in the proportion of isolates non-susceptible to macrolides also resulted in an overall slight increase in the total numbers of such isolates over the 4-year period. In contrast to the above pathogens, there was no increase in the burden of *Pseudomonas* spp. non-susceptible to the antibiotics studied.

Another pathogen where resistance to ciprofloxacin and third-generation cephalosporins is a concern is *Neisseria gonorrhoeae*, which was also highlighted as a focus for national

surveillance in the UK 5-year Antimicrobial Resistance Strategy.<sup>4</sup> National surveillance of gonorrhoea is undertaken via a network of sentinel genitourinary medicine clinics under the auspices of the Gonococcal Resistance to Antimicrobials Surveillance Programme (GRASP). Previous national guidance had recommended ciprofloxacin as first-line treatment for gonorrhoea, but rising levels of ciprofloxacin resistance noted from 2002 resulted in a change to the guidance in 2005, with ciprofloxacin being replaced by the extended-spectrum cephalosporins cefixime or ceftriaxone as recommended therapy. However, data from GRASP showed a subsequent increase in isolates of *N. gonorrhoeae* showing reduced susceptibility to cefixime. As a consequence, the national guidance was again amended in 2011, with current recommended treatment now comprising an increased dose of ceftriaxone (500 mg) combined with azithromycin.<sup>28</sup> This change was introduced to help prolong the use of cephalosporins for treating gonorrhoea following the emergence of decreased susceptibility to cefixime. Subsequent data from GRASP have shown a decline in the proportion of isolates exhibiting decreased susceptibility to cefixime, particularly in isolates infecting MSM and women. However, in 2012, decreased susceptibility to ceftriaxone was seen for the first time since it was last reported in 2009.<sup>29</sup> Clearly on-going surveillance via GRASP will be essential for monitoring further trends in gonococcal resistance.

A particular focus of interest at the current time is resistance to carbapenems. These are widely regarded as our antibiotics “of last resort” for the treatment of severe infections, particularly those caused by Gram-negative bacteria. While the data indicate that carbapenems remain active for the treatment of bloodstream infections caused by *E. coli* or *K. pneumoniae* at the present time, with  $\geq 98\%$  of isolates still susceptible, this should not engender an aura of complacency for several reasons. Firstly, as shown in Figure 2.16, analysis of Enterobacteriaceae referred to PHE’s Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit shows a dramatic year-on-year increase in the number of isolates shown to be carbapenem-resistant due to production of carbapenemases ( $\beta$ -lactamases capable of degrading carbapenems and hence abolishing their antibacterial activity). Referred isolates were from a range of clinical sources including blood, urine, respiratory specimens, faeces and rectal screening swabs, and it is probably only a matter of time before this increased reservoir of resistant strains translates into increased numbers of systemic infections, either as a result of endogenous infection or transmission of the resistant pathogens to other vulnerable patients.

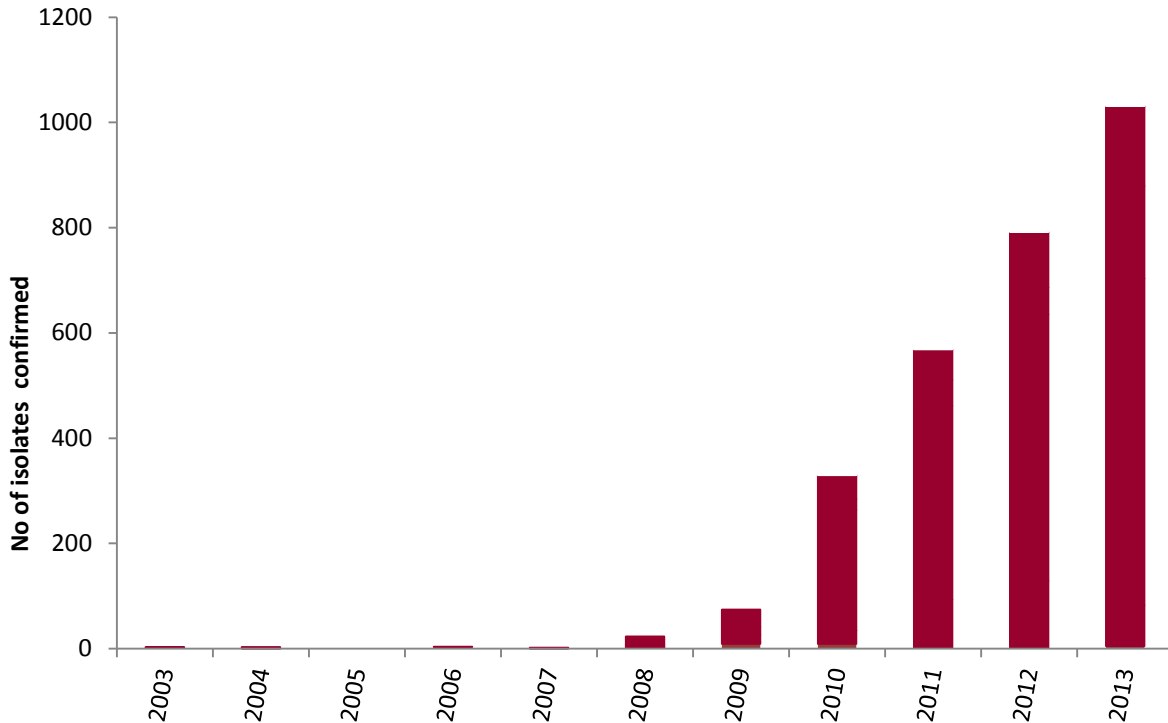
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<sup>4</sup> Department of Health. UK 5 Year Antimicrobial Resistance (AMR) Strategy 2013-2018

<sup>28</sup> British Society for Sexual Health and HIV. UK national guideline for the management of gonorrhoea in adults, 2011. <http://www.bashh.org/documents/3920.pdf>

<sup>29</sup> GRASP 2012 Report. [http://www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb\\_C/1317140152044](http://www.hpa.org.uk/webw/HPAweb&HPAwebStandard/HPAweb_C/1317140152044)

**Figure 2.16 Carbapenemase-producing Enterobacteriaceae referred from UK hospital microbiology laboratories and confirmed by PHE’s Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit.\***

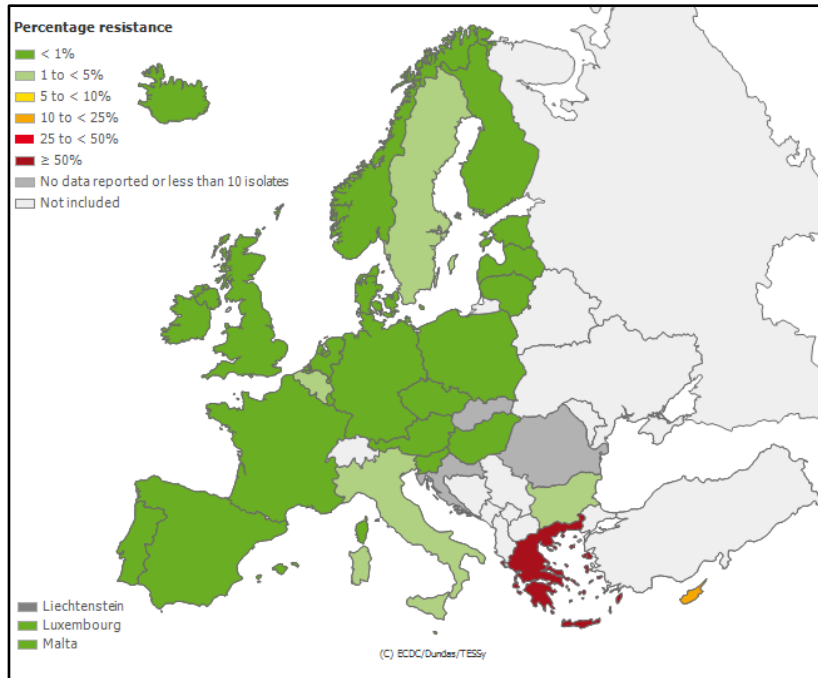


\*This reports all confirmed isolates of CPE sent to AMRHAI Reference Unit voluntarily by clinical laboratories in the UK, and includes screening and clinical isolates. An individual patient may be counted more than once if multiple samples were sent. This is not structured surveillance data.

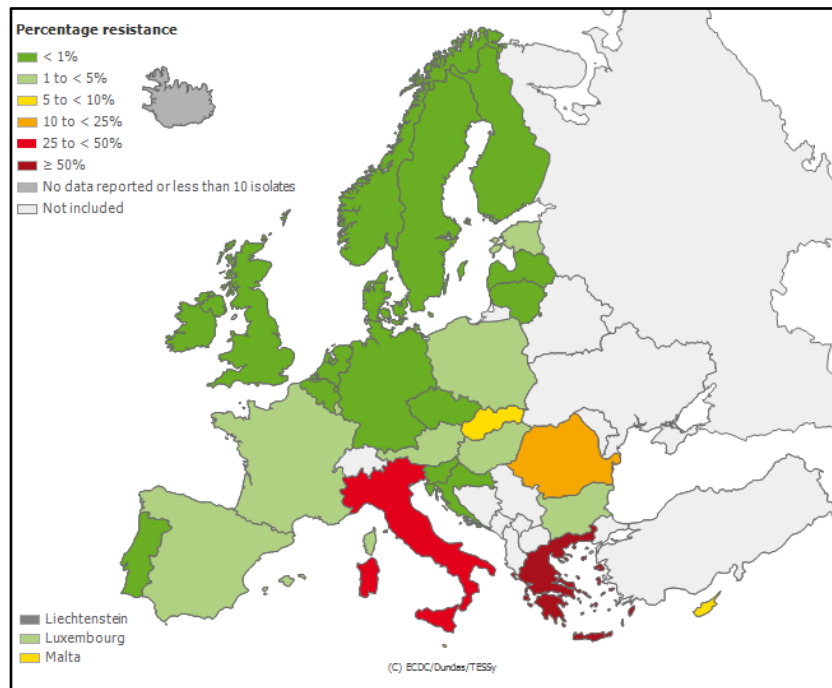
Furthermore, surveillance in other countries has shown that the prevalence of carbapenem resistance in Enterobacteriaceae can increase markedly over a short period of time. For example, data from EARS-net, a pan-European surveillance network, shows a dramatic increase in the proportion of isolates of *K. pneumoniae* from blood in Italy, from 1.3% in 2009 to 29% in 2012 (Figure 2.17).

**Figure 2.17 Proportion of carbapenem-non-susceptibility among isolates of *K. pneumoniae* in Europe**

**a) 2009**



**b) 2012**



While a considerable body of useful information is presented in this report, there are some limitations. In particular, the level of reporting of antibiotic susceptibility test results in some areas of England offers scope for improvement. Sub-optimal levels of reporting may have occurred for a variety of reasons, including non-participation of laboratories in surveillance, failure to test or report particular drug-bug combinations or suppression of laboratory susceptibility results for clinical reasons (mainly to influence prescribing behaviour) with an associated failure of the suppressed results to be captured in the surveillance database. The forthcoming implementation of PHE's new second generation surveillance system (SGSS), which has incorporated the AmSurv Surveillance System, is likely to help address this issue, as AmSurv collects all antimicrobial susceptibility test results, including suppressed results, from participating laboratories.<sup>30,31</sup>

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<sup>30</sup> Ironmonger D *et al.* AmWeb: a novel interactive web tool for antimicrobial resistance surveillance, applicable to both community and hospital patients. *J Antimicrob Chemother* 2013; 68: 2406-13.

<sup>31</sup> Johnson AP. Improving antimicrobial stewardship: AmWeb, a tool for helping microbiologists in England to 'Start Smart' when advising on antibiotic treatment. *J Antimicrob Chemother* 2013; 68: 2181-2.

## Chapter 3: Antibiotic consumption

### Introduction

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The consumption of antibiotics is a major driver for the development of antibiotic resistance in bacteria. Information on the consumption of antibiotics is therefore essential if we are to reduce unnecessary prescribing and reduce the pressure for bacteria to become resistant to these drugs. This report brings together for the first time antibiotic consumption data from community and hospital settings across England.

Two multinational European studies have demonstrated that antibiotic prescribing of penicillins, cephalosporins and macrolides in primary care is significantly correlated with resistance in *Streptococcus pneumoniae*.<sup>32,33</sup> In addition, a pooled meta-analysis demonstrated that for both urinary tract and respiratory tract infections, the odds of patients being colonized with antibiotic-resistant bacteria within two months of receiving an antibiotic were more than doubled.<sup>34</sup> Similarly, within hospitals, antibiotic prescribing is known to select for resistant organisms.<sup>35</sup>

Most prescriptions for antibiotics are written by medical, nursing and non-medical prescribers in general practice. Additional prescriptions dispensed in the community are written by community nurses outside general practice, dentists and other non-medical prescribers and occasionally hospital prescribers. Community prescriptions have been available through the NHS Business Services Authority (NHSBSA) since 1991, and are published annually as items dispensed and cost of items. The Health and Social Care Information Centre (HSCIC), noted in their most recent report that since 2003, the number of antibiotic items prescribed has increased, with one class exception, namely cephalosporins (Figure 3.1).<sup>36</sup>

In England, hospital practitioners also prescribe a number of antibiotics that are subsequently consumed in the community. These include antibiotics prescribed in Accident & Emergency departments, Urgent Care centres in acute hospitals, outpatient, day surgery or medical departments (ie not overnight admissions). In addition, many patients who receive antibiotics as hospital inpatients complete the course at home.

This chapter presents the total prescribing data across England and highlights the key prescribing across NHS geographies. In addition, general practice and Hospital prescribing is presented at sub-regional level (ATs) to ascertain if there were key differences in prescribing across the country. This report will predominantly utilise defined daily doses (DDD), which allows comparisons between countries. The DDD for the most common antibiotics prescribed in

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<sup>32</sup> Bronzwaer SL, Cars O, Buchholz U, Molstad S, Goettsch W, Veldhuijzen IK et al. A European study on the relationship between antimicrobial use and antimicrobial resistance. *Emerg Infect Dis* 2002; 8(3):278-282.

<sup>33</sup> Goossens H, Ferech M, Vander SR, Elseviers M. Outpatient antibiotic use in Europe and association with resistance: a cross-national database study. *Lancet* 2005; 365(9459):579-587

<sup>34</sup> Costelloe C, Metcalfe C, Lovering A, Mant D, Hay AD. Effect of antibiotic prescribing in primary care on antimicrobial resistance in individual patients: systematic review and meta-analysis. *BMJ* 2010; 340:c2096.

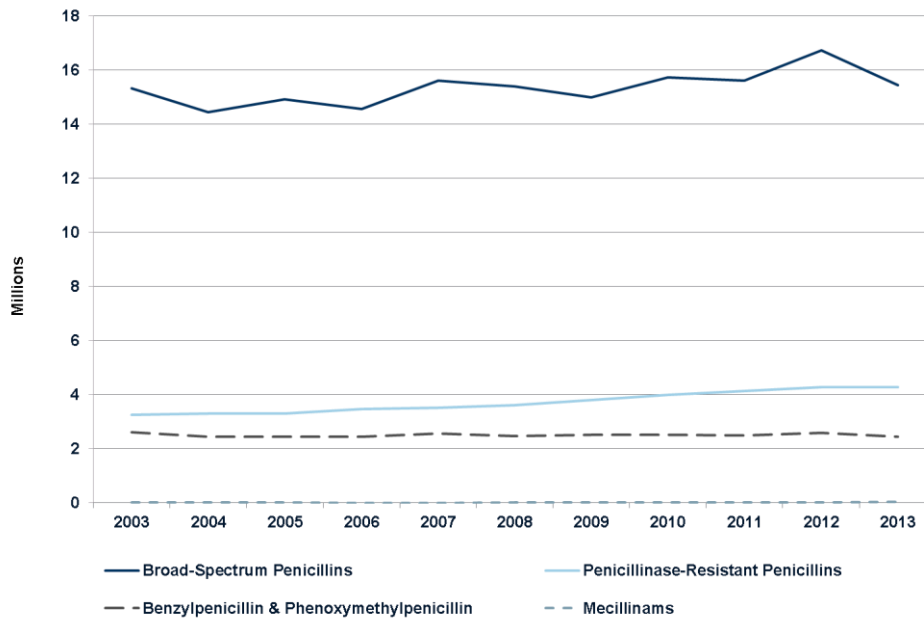
<sup>35</sup> Tacconelli E, De AG, Cataldo MA, Mantengoli E, Spanu T, Pan A et al. Antibiotic usage and risk of colonization and infection with antibiotic-resistant bacteria: a hospital population-based study. *Antimicrob Agents Chemother* 2009; 53(10):4264-4269.

<sup>36</sup> Prescriptions Dispensed in the Community, England 2003-2013. Prescribing and Primary Care, Health and Social Care Information Centre. 9 July 2014

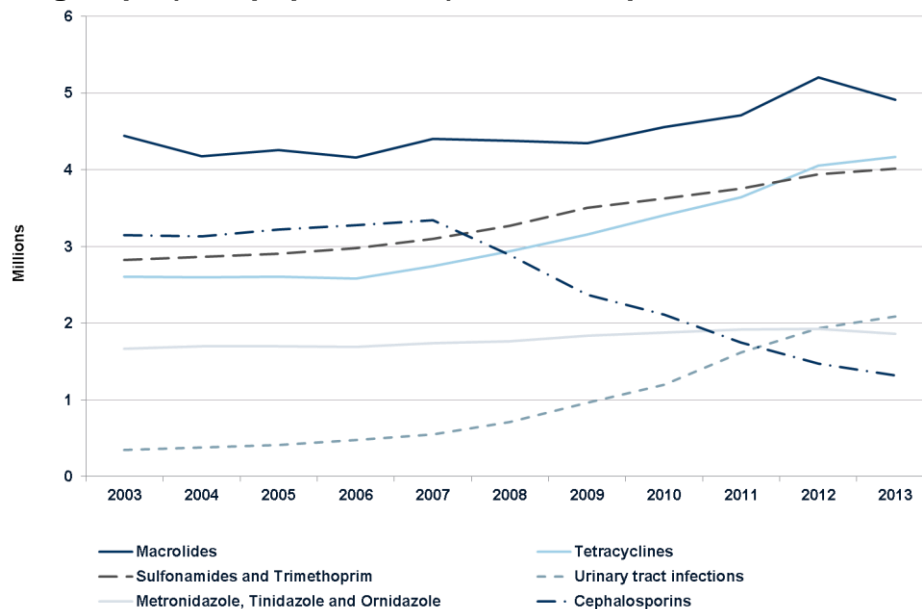
England are outlined in Appendix C. In particular the population rates of prescribing are compared those published by the European Centre for Disease Prevention and Control (ECDC).<sup>37</sup>

**Figure 3.1 Antibiotic items dispensed in the community (HSCIC report) for a) Penicillins b) Other antibiotic groups with more than 100,000 items dispensed in 2013 across England, 2003-2013.<sup>33</sup>**

**a) Penicillins, by group, items dispensed**



**b) Antibiotic groups (except penicillins)\*, items dispensed**



\* Nitrofurantoin used predominantly for urinary tract infections

<sup>37</sup> European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe 2011. Stockholm, ECDC; 2014

<sup>33</sup> Prescriptions Dispensed in the Community, England 2003-2013. Prescribing and Primary Care, Health and Social Care Information Centre. 9 July 2014



# Methods

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All data in this report are presented by calendar year from 2010 to 2013.

## Data source – primary care

Information on the use of antibiotics prescribed in general practice was obtained from the NHSBSA database. NHS Prescription services internally audit the prescription data as 97.5% accurate.

## Data source – other community

Information on the use of additional prescriptions dispensed in the community written by out-of-hours prescribers, nurses, dentists and other non-medical prescribers and occasionally hospital prescribers was obtained using the national Prescription Cost Analysis dataset and removing the items dispensed from general practice. This data set is only available at national level.

## Data source – secondary care

Information on the use of antibiotics in secondary care was obtained from the IMS Health. The database held by IMS Health collects information from hospital pharmacy systems, for drugs dispensed to individual patients and wards. All NHS trusts except Great Ormond Street (current contract with IMS Health excludes the inclusion of their data in sub-regional reports) and Weston Area Health Trust (data quality issues) were included. Individual hospital data are not shown as this forms part of the current confidentiality agreement with IMS Health. Ninety nine percent of trusts contribute to this dataset. Data for individual organisations were categorised by inpatient or outpatient (including day-case, regular day attenders and A&E), where possible, for individual organisations, and then grouped to AT level. This data was not validated at an individual organisation level and 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. 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). More detailed consumption data is provided for the antibiotics that are most frequently consumed or are important in the treatment of multi-drug resistant infections.

## Data definitions

Data on primary and secondary care use were presented using defined daily dose (DDD) to enable international comparisons. The DDD is the internationally recognised unit of measurement of medicine consumption, recommended by the World Health Organisation (WHO), which allows comparison of use of medicines over time and between different countries (or locations). 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 are based on their use in infections of moderate severity. 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/](http://www.whocc.no/atc_ddd_index/)

Data on antibiotic use in primary care were 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. Item figures do not provide any indication of the length of treatment or the dose prescribed. Items are not as 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.

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 and in each AT. Additionally, general practice and other community prescriptions were also presented as number of items per 1000 inhabitants per day.

Secondary care data is also presented per 100 admissions and per 100 bed-days.

Data are 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; predominantly dental but also includes community nurse, other non-medical prescribers or hospital prescriptions dispensed in the community
- Community - Combined general practice and Other Community prescriptions
- 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 for a patient attending the hospital outpatient, day unit, A&E, urgent care centre etc
- Hospital – combined hospital inpatient and outpatient prescriptions

## Population denominators

Consumption rates at national and AT level were calculated using 2010, 2011 and 2012 mid-year resident population estimates, based on the 2011 census for England; 2013 consumption rates are based on 2012 mid-year population estimates.<sup>38</sup>

From 2010 to 2013, admissions to hospital rose by 2.4% and bed-days declined by 1.3%. This suggests that there was increased activity and earlier discharges from hospitals. One-stop dispensing refers to the practice of combining inpatient and discharge dispensing into a single 28-day supply, labelled for discharge. This means that when a patient is discharged, not all of their medicines will need re-dispensing from the pharmacy as they will have sufficient supply on the ward, labelled appropriately. Discharge medication (excluding one-stop) where a patient continues their antibiotic at home on discharge (take away) is dispensed on their last inpatient day. All one-stop and discharge dispensing were included as part of inpatient consumption in the IMS Health dataset. The admission rather than bed-day denominator was therefore favoured in this report, as the consumption of antibiotics reflects hospital activity for admissions rather than those who are in hospital only. The presentation of DDD per admissions rather than bed-days builds on previous work from ARHAI sub-committees.<sup>39</sup>

Aggregate denominator admission data, by 3-digit provider code for the calendar years 2010-2013, were extracted from the HES in-patient database using the HES Data Interrogation System (HDIS). Data for individual trusts were then merged to provide an admission denominator by AT.

## Trend analysis

National and AT trends in the consumption of antibiotics were assessed for the last 4 years (2010-2013). A linear regression was applied with the dependent variable being antibiotic consumption in DDD per 1000 inhabitants per day and the explanatory variable being year. Statistical significance was  $p < 0.05$ .

## Maps

The maps in this section present the consumption data across AT. The ranges on the maps are presented from zero to the highest consumption for that particular antibiotic/ group of agents in the latest available ECDC report.<sup>34</sup> This demonstrates the variability across ATs and also demonstrates where the Area Team is compared to the highest and lowest consumption in Europe; where graphs are of paler blue this demonstrates that prescribing in England in this group is lower than the European median.

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<sup>38</sup> <http://www.statistics.gov.uk/statbase/Product.asp?vlnk=15106>

<sup>39</sup> Cooke J et al. Longitudinal trends and cross-sectional analysis of English national hospital antibacterial use over 5 years (2008-2013): working towards hospital prescribing quality measures. *J Antimicrob Chemother* 2014 (in press).

<sup>34</sup> European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe 2011. Stockholm, ECDC; 2014

# Results

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## Total consumption of antibiotics

From 2010 to 2013, the combined community and hospital prescriptions increased by 6%, from 25.9 to 27.4 DDD per 1,000 inhabitants per day. This increase in prescribing predominantly took place between 2011 and 2012, where there was a 7.8% increase in consumption; 2012 to 2013 reversed this trend with a 1.4% decline in total consumption (Figure 3.2).

General practice consumption increased 4.1% between 2010 and 2013, from 20.6 to 21.5 DDD per 1000 inhabitants per day. There was a 7.8% increase from 2011 to 2012 and subsequently a 3.5% decline from 2012 to 2013 in GP prescribing. Prescribing to hospital inpatients increased year-on-year by an average of 3.5%, with a total increase of 11.9% from 2010 to 2013 (2.3 to 2.5 DDD per 1000 inhabitants per day). Prescribing to hospital outpatients remained stable from 2010 to 2013 at 1.7 DDD per 1000 inhabitants per day. The largest percentage increase occurred in other community prescribing with consumption increasing by 32% from 1.3 to 1.7 DDD per 1000 inhabitants per day.

Throughout the four years, the vast majority of prescribing occurred in general practice. In 2013, 78.5% of prescribing was from general practice, with 9.1% and 6.2% for hospital inpatients and outpatients respectively, and 6.2% related to other community prescribers (predominantly dentists).

## Total prescribing by key agents

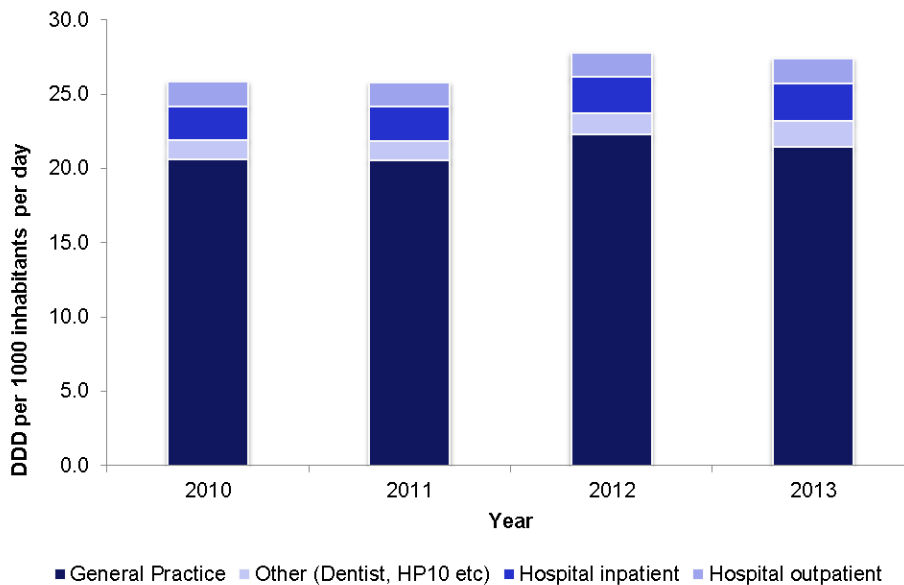
From 2010 to 2013, the predominant antibiotics in use in England were penicillins, tetracyclines and macrolides (Figure 3.3). Penicillin and macrolide consumption increased in 2012 but subsequently decreased in 2013; overall increases in penicillin and macrolide consumption between 2010 and 2013 were 3.4% and 6%, respectively. Nitrofurantoin consumption increased the most, a 41% rise, between 2010 and 2013.

In terms of the totality of prescribing in 2013, 66 different antibiotics were prescribed, with the top 15 agents accounting for 98% and 88% of general practice and hospital consumption, respectively. The proportions of total consumption accounted for by penicillins, tetracyclines and macrolides were 49.8%, 18% and 14.9%, respectively.

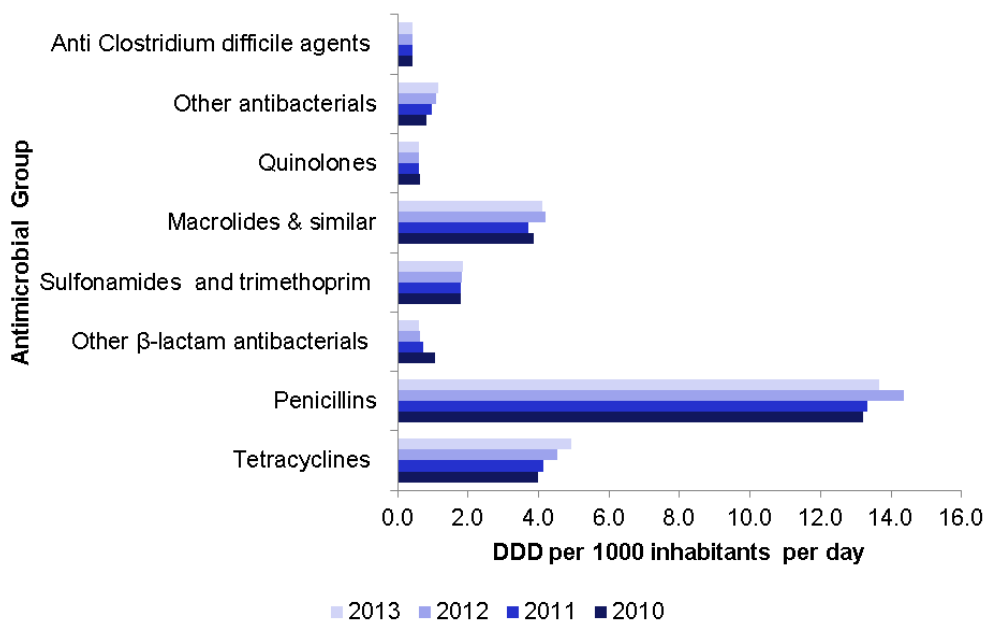
## Prescribing in the community from sources other than general practice

In 2013, the largest antibiotic group prescribed by this sector were the penicillins (75%), followed by metronidazole (8.3%), macrolides (8.2%) and tetracyclines (3.9%). This largely reflects prescribing from dental practices where guidelines recommend these agents for the treatment of dental abscesses and gingivitis.

**Figure 3.2 Consumption of total antibiotics, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**



**Figure 3.3 Total antibiotic consumption by group\*, expressed as DDD per 1000 inhabitants per day, across England, 2010-2013**



\*Other  $\beta$ -lactam antibacterials include cephalosporins and carbapenems.

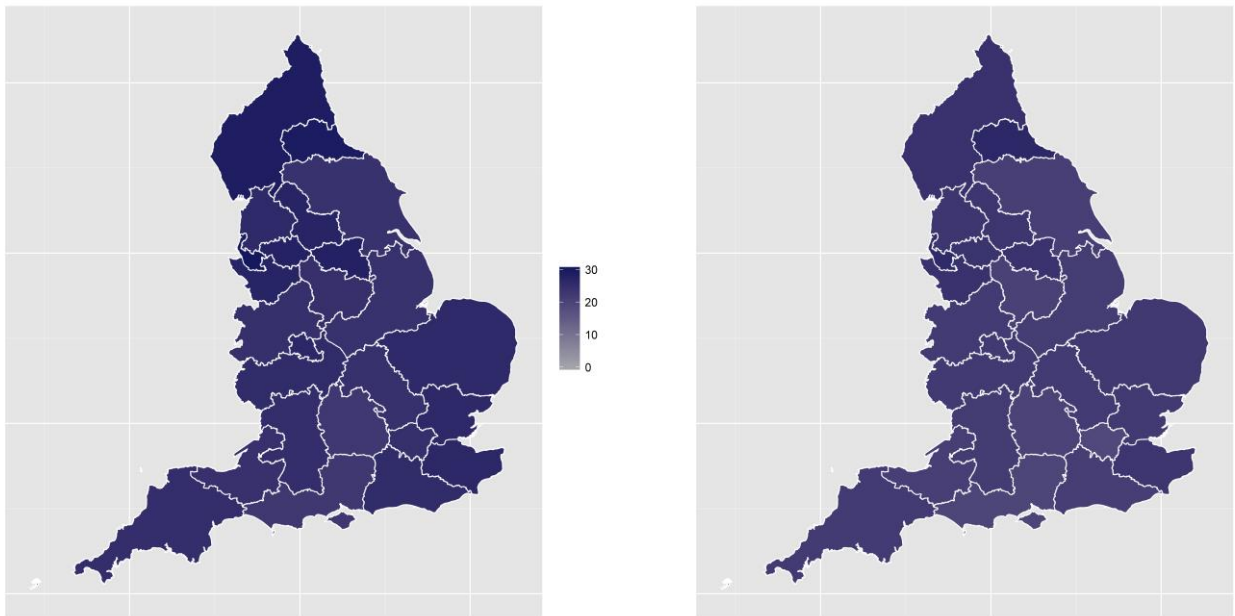
## Prescribing by area team in 2013

Area teams in the North of England had consistently higher general practice and combined general practice and hospital consumption than the South of England. The highest combined antibiotic consumption was in Merseyside, which had similar levels to those reported in Southern Europe, with 30.4 DDD per 1,000 inhabitants per day, over 30% higher than the AT with the lowest consumption (Thames Valley, 22.8 DDD per 1,000 inhabitants per day).

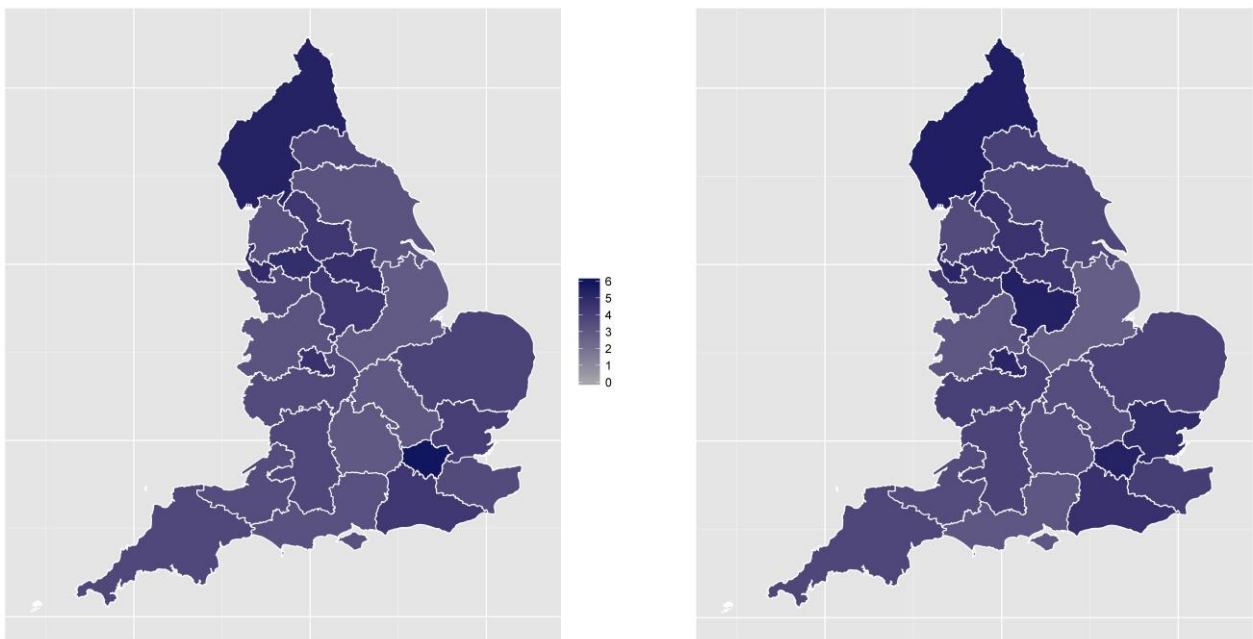
The highest consumption in general practice was Durham, Darlington and Tees, which was over 40% higher than London (26.5 versus 18.9 DDD per 1,000 inhabitants); this however may reflect healthcare access and delivery in London (Figure 3.4).

The ATs with the largest urban populations had the highest hospital consumption. Rates of hospital prescribing in London (6.0 DDD per 1000 inhabitants per day) and Cumbria, Northumberland and Tyne (5.4 DDD per 1000 inhabitants per day) were significantly higher than for England as a whole (4.2 DDD per 1000 inhabitants per day) and approximately twice the rate seen in the AT with the lowest total hospital consumption (Leicestershire and Lincolnshire, 2.9 DDD per 1000 inhabitants per day). The ATs with the highest total hospital consumption also had the highest inpatient consumption, though there was less variability across the ATs (Figure 3.5).

**Figure 3.4 Map of consumption by a) general practice and hospital and b) general practice, expressed as DDD per 1000 inhabitants per day, by ATs, England, 2013**  
a) General practice and hospital                      b) General practice



**Figure 3.5 Map of consumption of a) Hospital inpatient and outpatient (total) b) Hospital inpatient, expressed as DDD per 1000 inhabitants per day, by ATs, England, 2013**  
a) Hospital inpatient and outpatient                      b) Hospital inpatient



## 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.  $\beta$ -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.<sup>40</sup>

The  $\beta$ -lactam/ $\beta$ -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 or sepsis without a defined source. With the reductions in cephalosporin and quinolones use in England in the last decade, these combination agents have become key agents in many hospital empiric policies.

Penicillins accounted for almost 50% of total antibiotic consumption in England over the last four years. Between 2010 and 2013 there was a 3.2% increase in total consumption of this group from 12.0 to 12.4 DDD per 1000 inhabitants per day; which for the most part occurred between 2011 and 2012 (an 8.1% increase), although this subsequently declined by 5.1% from 2012 to 2013. Hospital inpatient consumption of these agents has increased by approximately 3% per year in the last 4 years, from 1.2 to 1.4 DDD per 1000 inhabitants per day. This increase was statistically significant for hospital inpatients (Figure 3.6).

The top five most commonly used antibiotics in this class are presented in Figure 3.7. Amoxicillin was the most frequent penicillin used (54% of all penicillins), which increased between 2011 and 2012, but returned to 2010 levels in 2013 (6.7 DDD per 1000 inhabitants per day). In 2013, 94% of amoxicillin consumption was in general practice. In the last four years, co-amoxiclav use increased from 1.9 to 2.2 DDD per 1000 inhabitants per day (13% increase). In 2013, 59% of co-amoxiclav was from general practice prescriptions. Piperacillin-tazobactam consumption, while low overall increased from 0.06 to 0.09 DDD per inhabitants per day (46% increase); this predominantly reflected hospital consumption (>99%) as this parenteral agent is rarely used in primary care.

There was increased consumption of penicillins across the majority of ATs over the last 4 years. In addition, the year to year trend of consumption over the four years was remarkably similar, with all ATs increasing their consumption in 2012, followed by a reduction in 2013, although there was an overall net increase in usage over the last four years (Figure 3.9).

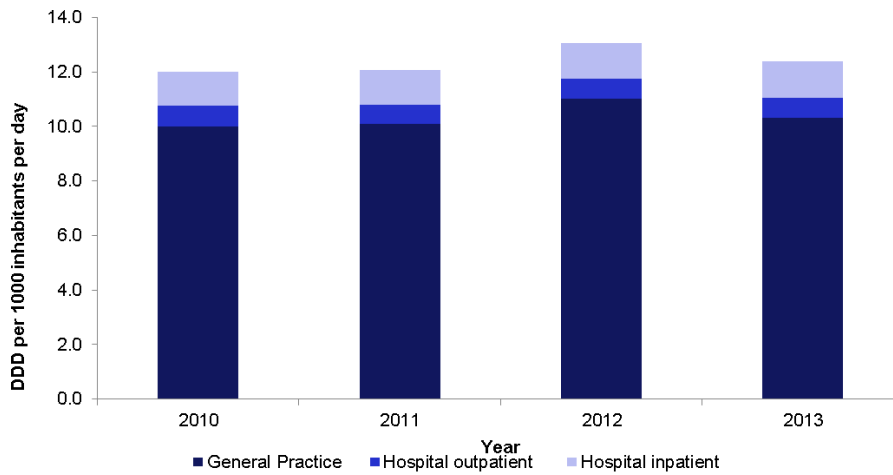
In 2013, the ratio of broad and extended-spectrum penicillins ( eg amoxicillin and combinations of penicillins with inhibitors) to narrow-spectrum penicillins ( eg phenoxymethylpenicillin and flucloxacillin) varied across ATs (Figure 3.8). In 2013, total penicillin consumption varied significantly, with the highest consumption occurring in Merseyside and the lowest in Wessex

<sup>40</sup> Management of Infection Guidance for Primary Care. British Infection Association, RCGP General Practice and PHE. 2012 available at <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/PrimaryCareGuidance/>

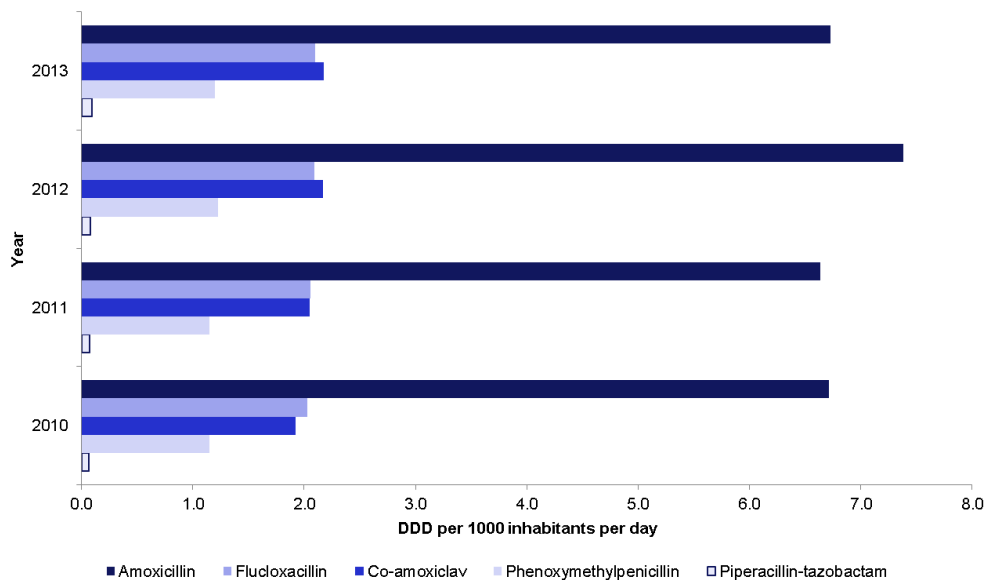


(14.2 compared with 9.5 DDD per 1,000 inhabitants per day). However, although Merseyside had the highest level of prescribing for penicillins, it had the second lowest level of penicillin and inhibitor combinations, at 1.4 DDD per 1000 inhabitants per day, which was less than half the consumption of East Anglia (2.9 DDD per 1000 inhabitants per day) (Figure 3.10). The consumption of penicillin/ inhibitor combinations was lower than the majority of other EU countries.<sup>34</sup>

**Figure 3.6 Consumption of penicillins by general practice and Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**

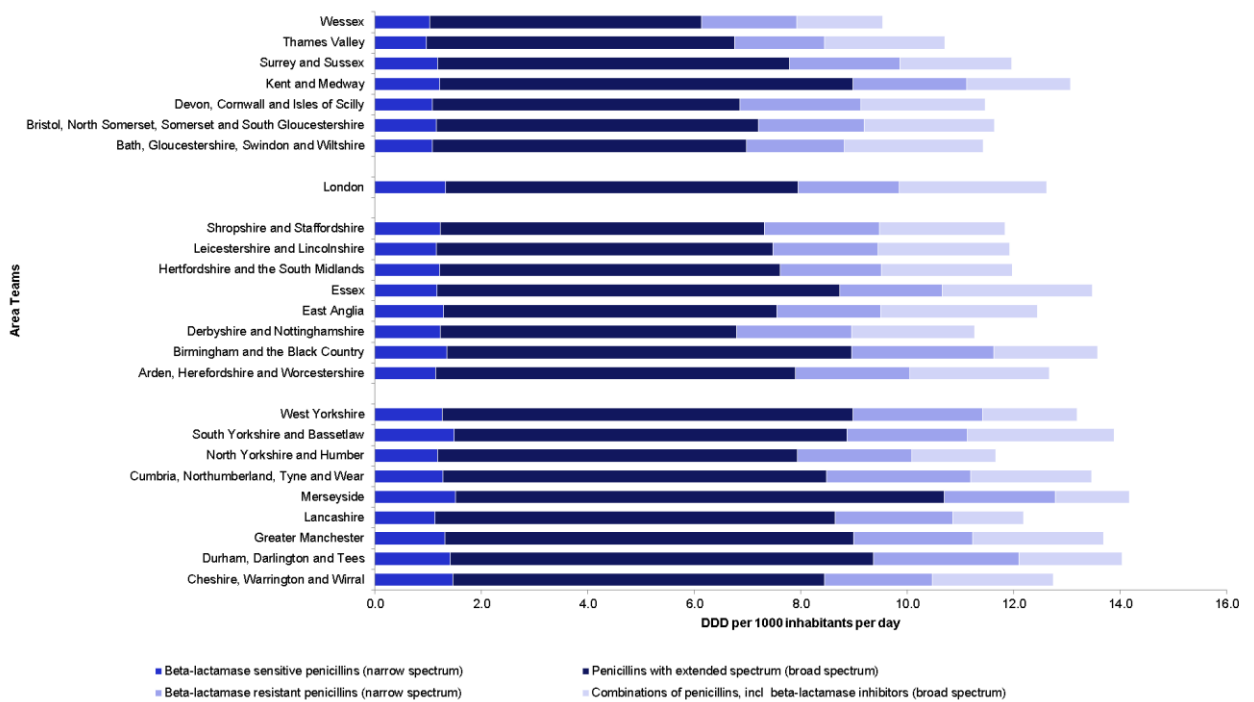


**Figure 3.7 Consumption of most commonly utilised penicillins, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**

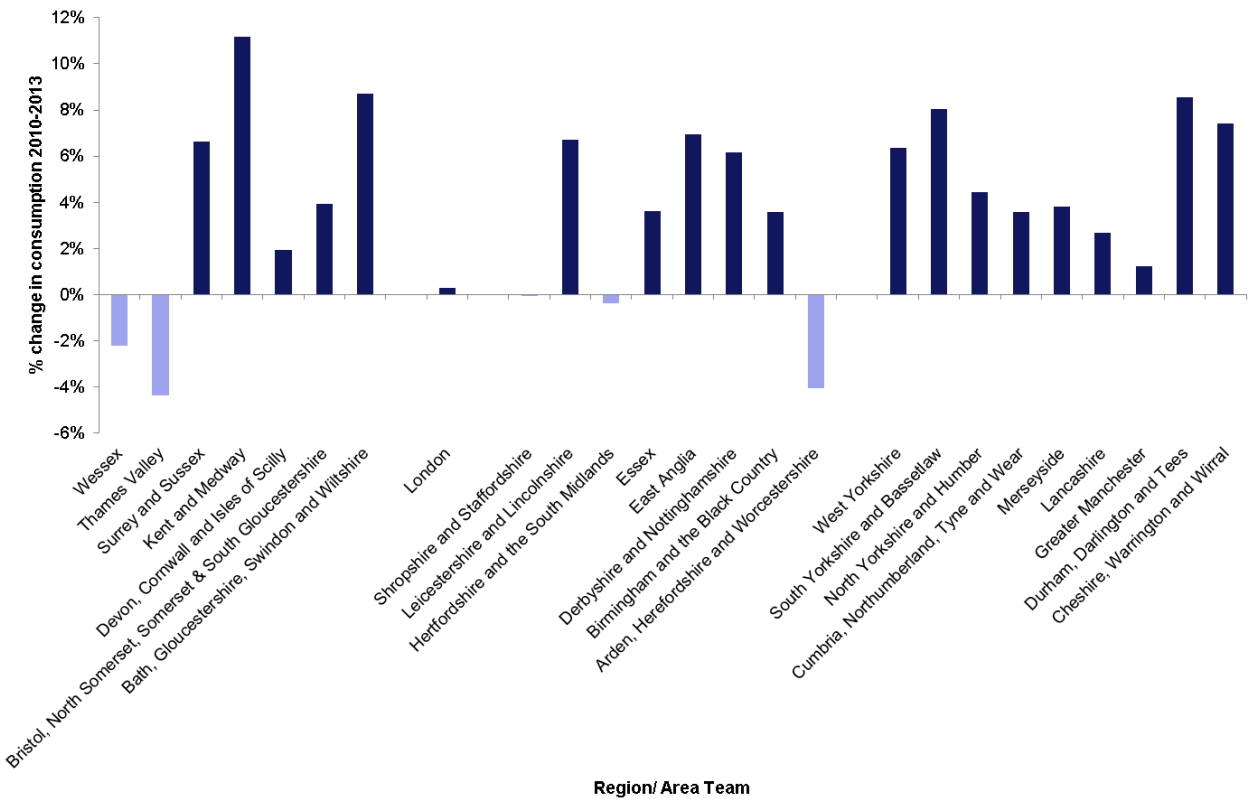


<sup>34</sup> European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe 2011. Stockholm, ECDC; 2014

**Figure 3.8 Consumption of broad and narrow-spectrum penicillins at the level of ATs, expressed as DDD per 1000 inhabitants per day, England, 2013**



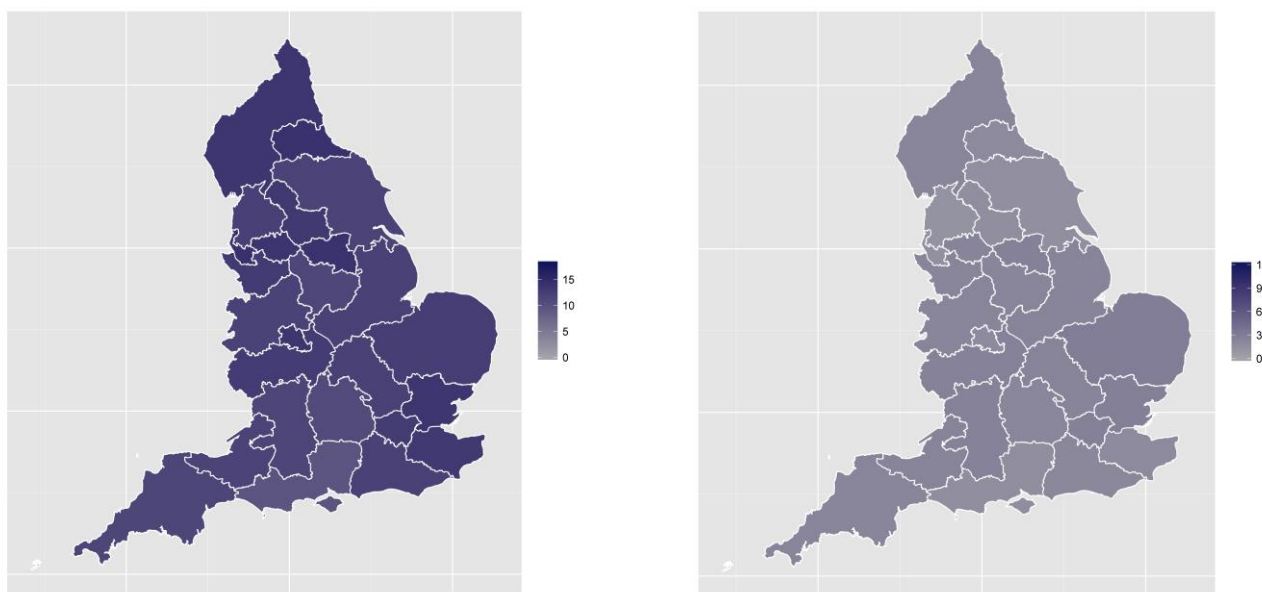
**Figure 3.9 Change in total penicillin consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013**



**Figure 3.10 Map of consumption of a) all penicillins b) penicillin/inhibitor combinations, expressed as DDD per 1000 inhabitants per day, by ATs, England, 2013**

a) All penicillins

b) Penicillin/inhibitor combinations



### Trends in consumption by antibiotic group: cephalosporins

Cephalosporins were first developed in the 1960s and were initially most active against Gram-positive organisms such as staphylococci and streptococci. 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.<sup>36</sup> More recently, cephalosporin resistance in gonorrhoea has emerged and the recommended treatment is now combination treatment of ceftriaxone and azithromycin.<sup>41</sup>

Between 2010 and 2013 there was a continued decline in cephalosporin use with an overall reduction of 48% across all sectors; in 2013 the consumption of cephalosporins was 0.5 DDD per 1000 inhabitants per day (Figure 3.11). However this trend was predominantly accounted for by general practice prescribing, which saw a 55% reduction in consumption from 2010 to 2013, from 0.8 to 0.4 DDD per 1000 inhabitants per day. Hospital outpatient consumption decreased by 10%, to 0.04 DDD per 1000 inhabitants per day and hospital inpatient consumption remained unchanged at 1.0 DDD per 1000 inhabitants per day. This probably

<sup>36</sup> 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/>

<sup>41</sup> 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

reflects the large reductions seen in the last decade and the use of these agents now is predominantly under the guidance of infection specialists for specific indications. In 2011, England and the devolved UK healthcare administrations had the lowest consumption of third-generation cephalosporins in the EU.<sup>34</sup>

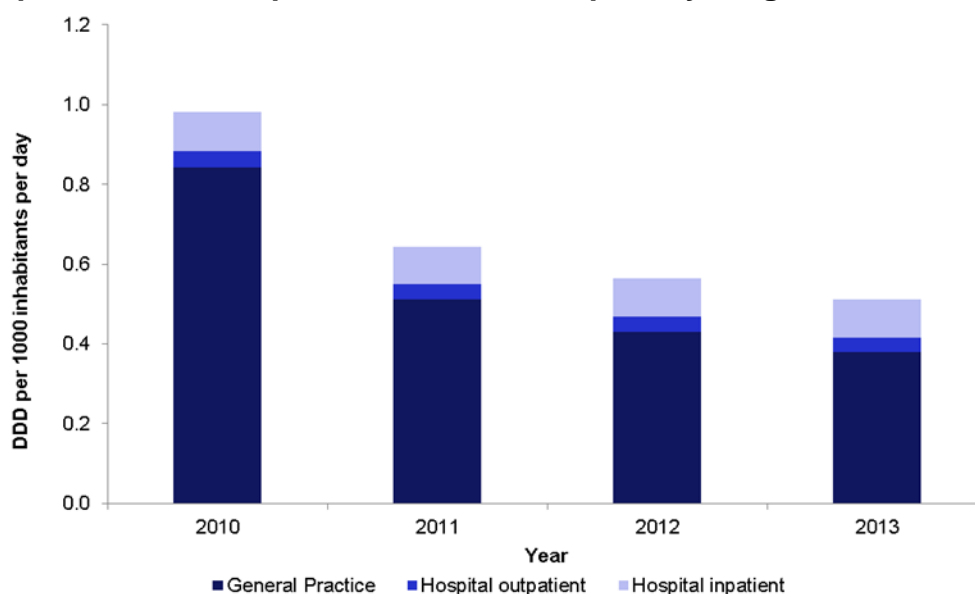
The top six agents used in this class are presented in Figure 3.12. Oral cephalosporins (cefalexin, cefaclor and cefuroxime) were the predominant cephalosporins consumed, and decreased by 30%, 91% and 26% respectively, between 2010 and 2013. Third-generation cephalosporins (ceftriaxone and cefotaxime) have increased by 56% and 14% respectively, though they account for less than 10% of total cephalosporin consumption and the lowest in Europe. Ceftriaxone consumption in particular may be increasing due to the 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.

All ATs have decreased their total cephalosporin consumption over the last four years; the ATs with the highest consumption in 2010 decreased the most, for example, Merseyside decreased consumption to 1.2 from 2.7 DDD per 1000 inhabitants per day (Figure 3.13).

However, third-generation cephalosporins have increased in 19 ATs over the last four years with Kent and Medway consumption increasing by 85% (Figure 3.14).

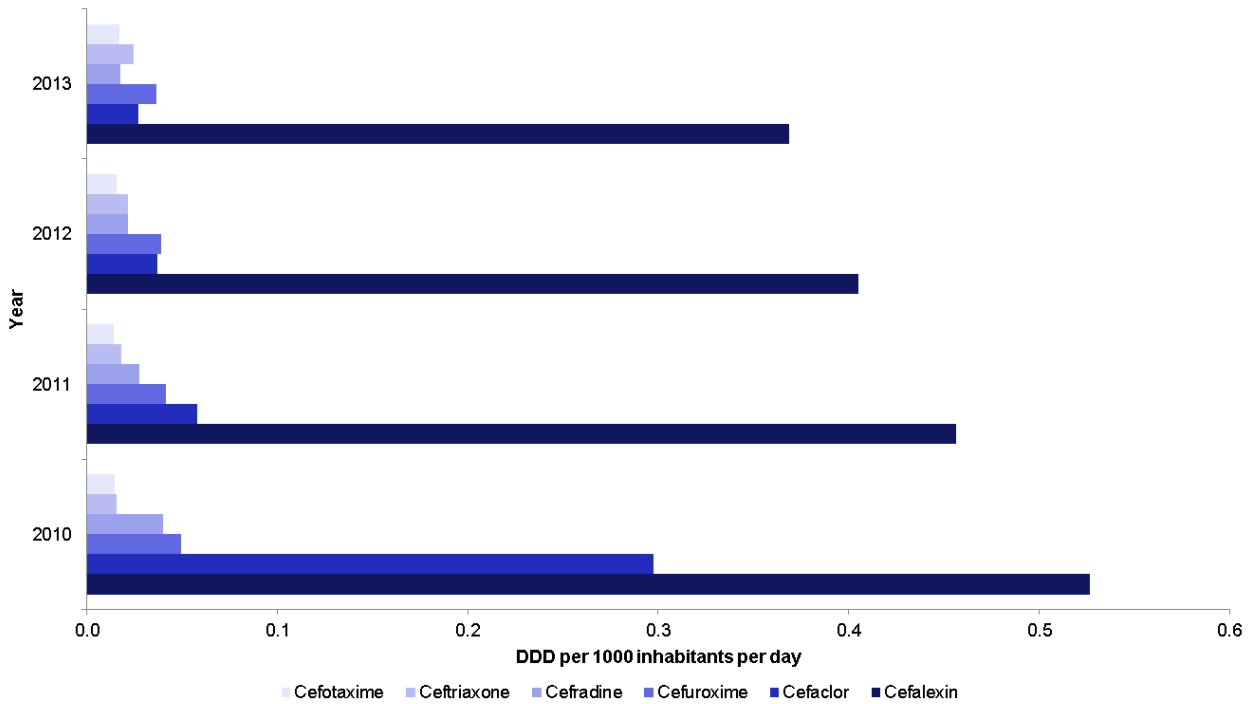
There was still more than a five-fold difference in consumption between the highest AT (Merseyside 2.7 DDD per 1000 inhabitants per day) and the lowest (Bristol, North Somerset, Somerset and South Gloucestershire at 0.5 DDD per 1,000 inhabitants per day), and in general ATs in the North region have the highest consumption (Figure 3.15). All ATs remain in the lowest consumption group compared to other EU countries.

**Figure 3.11 Consumption of cephalosporins prescribed by general practice and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**

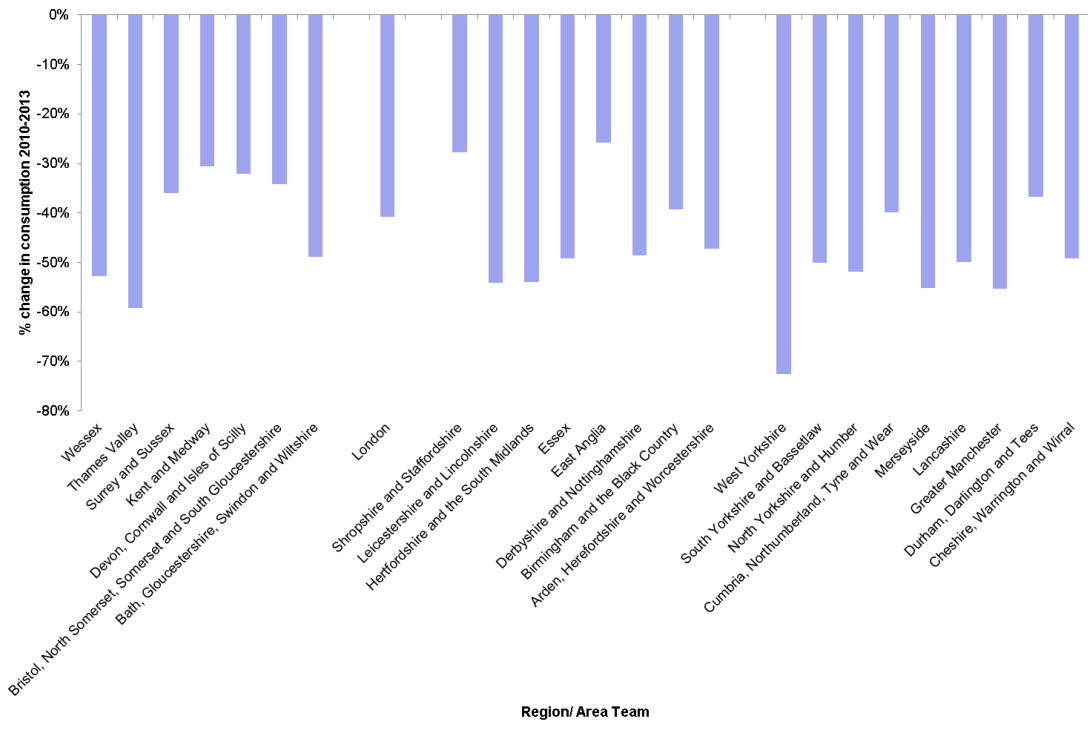


<sup>34</sup> European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe 2011. Stockholm, ECDC; 2014

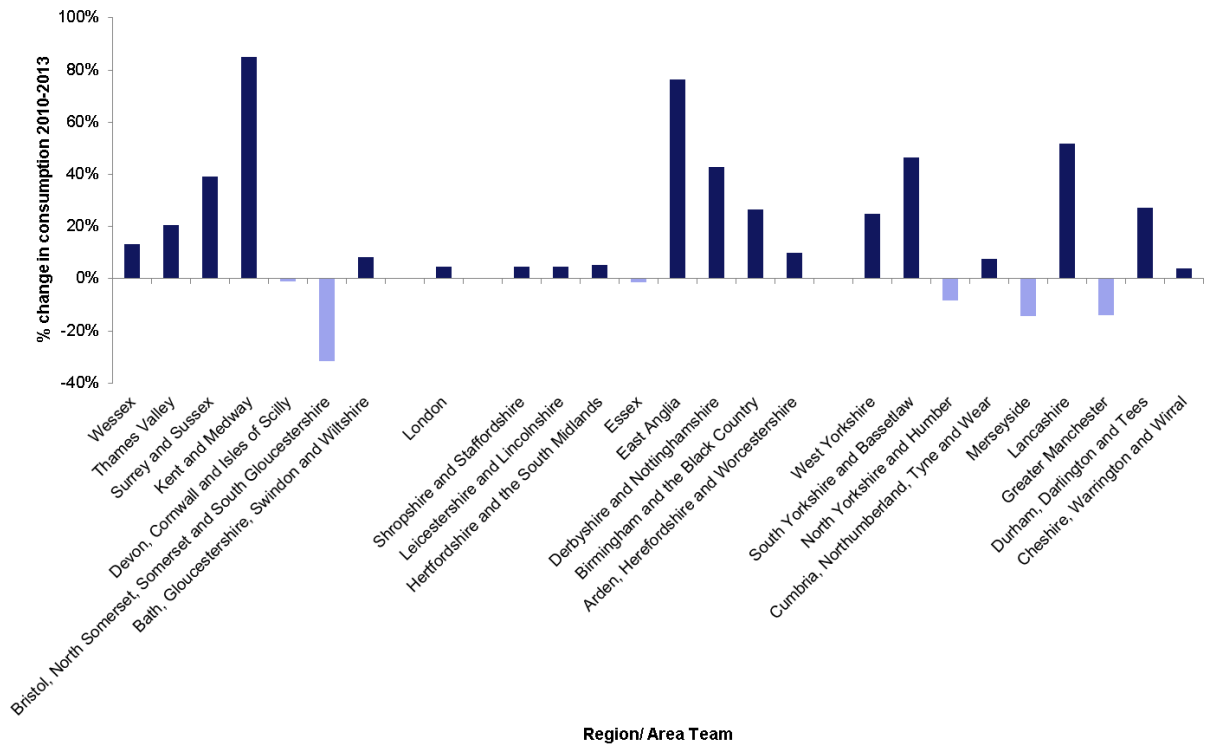
**Figure 3.12 Consumption of different cephalosporins, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**



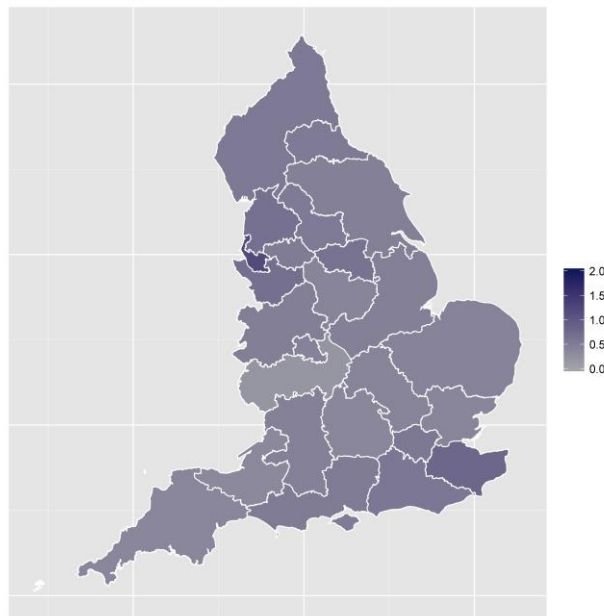
**Figure 3.13 Change in cephalosporin consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013**



**Figure 3.14 Change in third-generation cephalosporin consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013**



**Figure 3.15 Map of consumption of cephalosporins, expressed as DDD per 1000 inhabitants per day, by ATs, England, 2013**



## Trends in consumption by antibiotic group: 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  $\beta$ -lactamase enzymes (the enzymes that breakdown other  $\beta$ -lactam penicillins and cephalosporins). However, in recent years, resistance to this antibiotic class has emerged (due to the production of carbapenemases) and is now spreading rapidly worldwide. A major cause of concern is that there are no new antibiotics in development that effectively work 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, where OPAT is available.

### Carbapenem consumption

Although carbapenems account for only 0.3% of total antibiotic consumption in 2013, their use increased by 31.3% in England between 2010 and 2013 (0.06 to 0.08 DDD per 1000 inhabitants per day); this trend is statistically significant. 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 3.16).

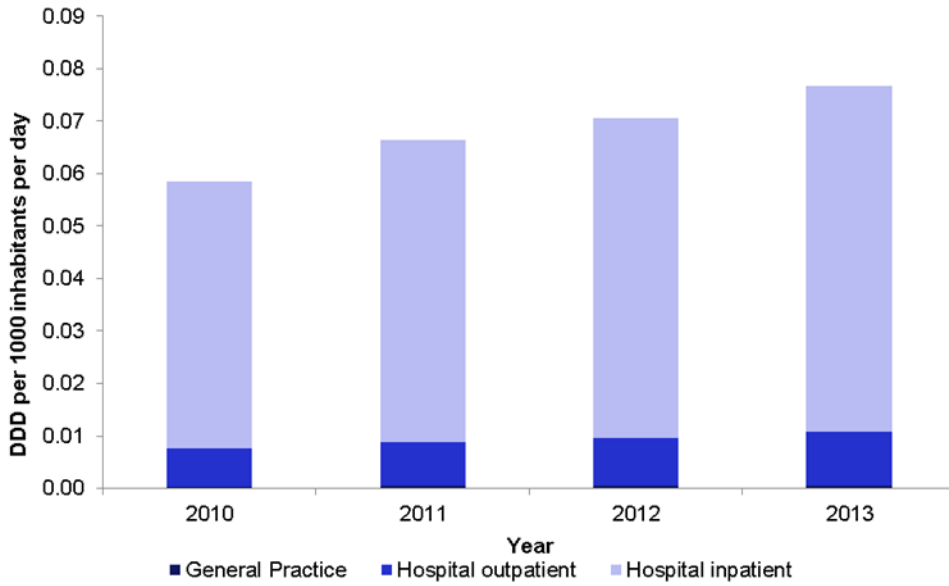
Meropenem was the predominant carbapenem in use over the last four years accounting for approximately 89% of use; ertapenem and imipenem were used less frequently at 10% and 1% respectively. Consumption of both meropenem and ertapenem increased in a similar manner at 37% and 36% respectively, while use of imipenem reduced by 76% over this period (Figure 3.17).

Twenty three ATs increased their carbapenem consumption over this period and only two ATs have decreased (Figure 3.18). The largest increase, between 2010 and 2013, occurred in North Yorkshire and Humber (120%), though this AT had the lowest use in 2010 and in 2013 remained statistically below the national average (0.02 to 0.41 DDD per 1,000 inhabitants per day). Greater Manchester was one of two ATs to reduce their carbapenem consumption over the last 4 years; a decrease of 7% allowed them to fall from the highest consumers in 2010 to the fourth highest in 2013.

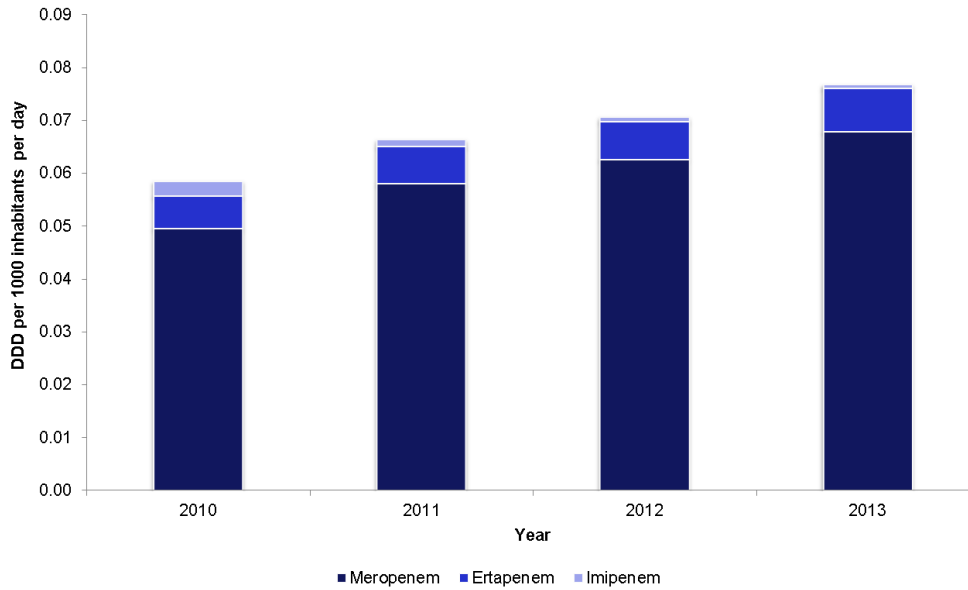
In 2013, as with all antibiotic consumption there was significant North/South divide in the consumption of carbapenems (Figure 3.19).

In 2013, hospital outpatient consumption varied across all ATs with the ratio of hospital outpatient to inpatient prescribing ranging from 3.5% in Cheshire, Warrington and Wirral to 31% in Derbyshire and Nottinghamshire. This most probably reflects access to OPAT as part of continuing care after an inpatient stay though may also represent miscoding at hospital pharmacies (Figure 3.20).

**Figure 3.16 Consumption of carbapenems prescribed by general practice and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**

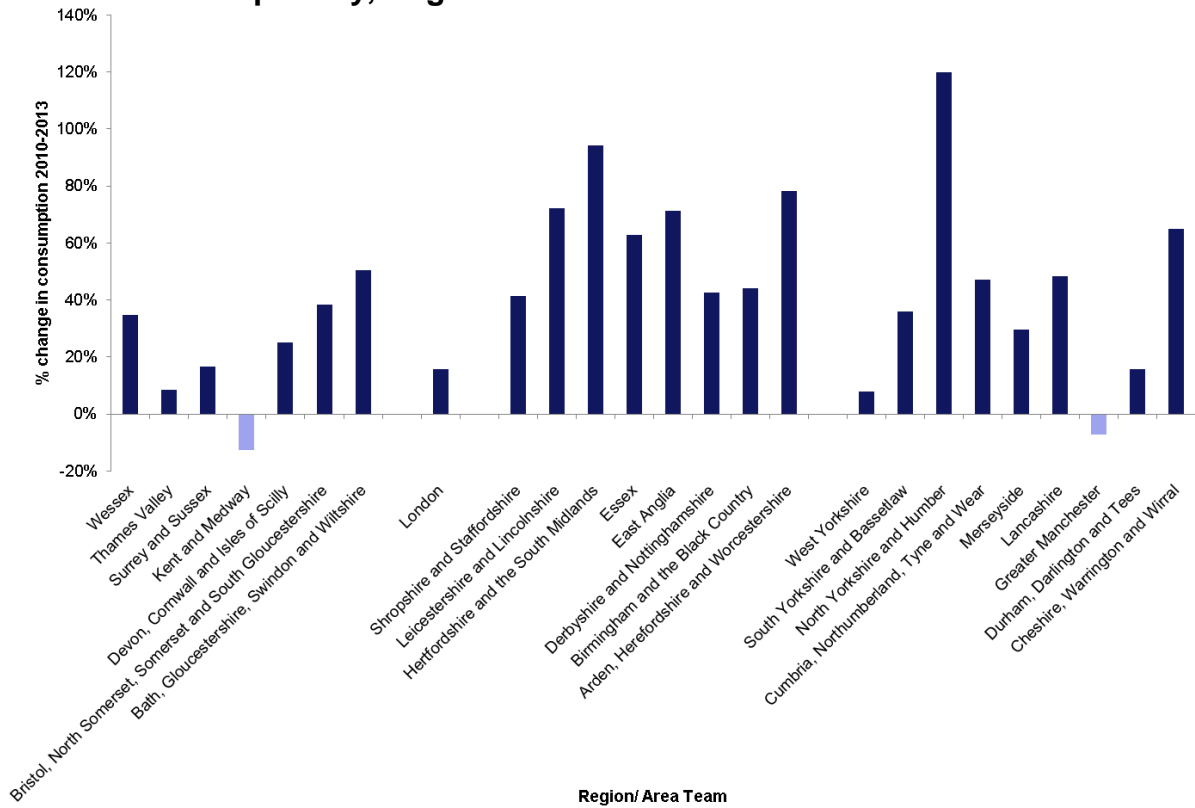


**Figure 3.17 Consumption of different carbapenems, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**

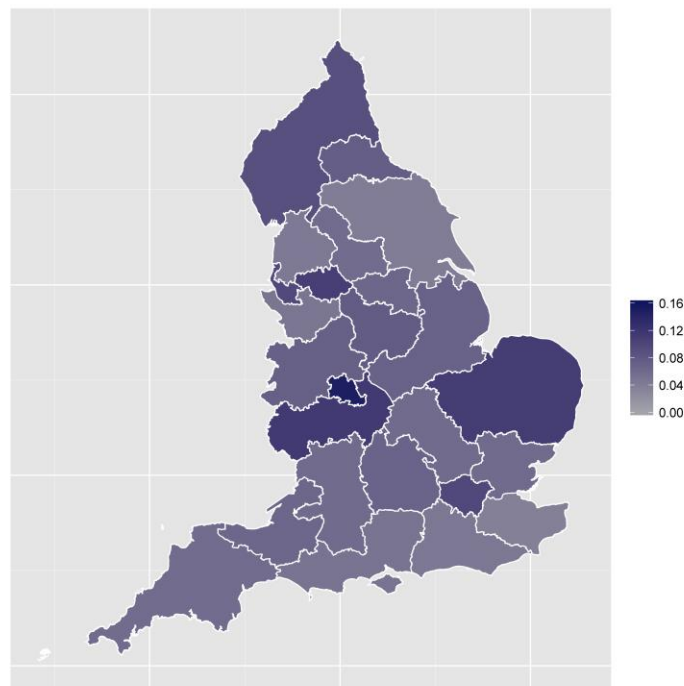




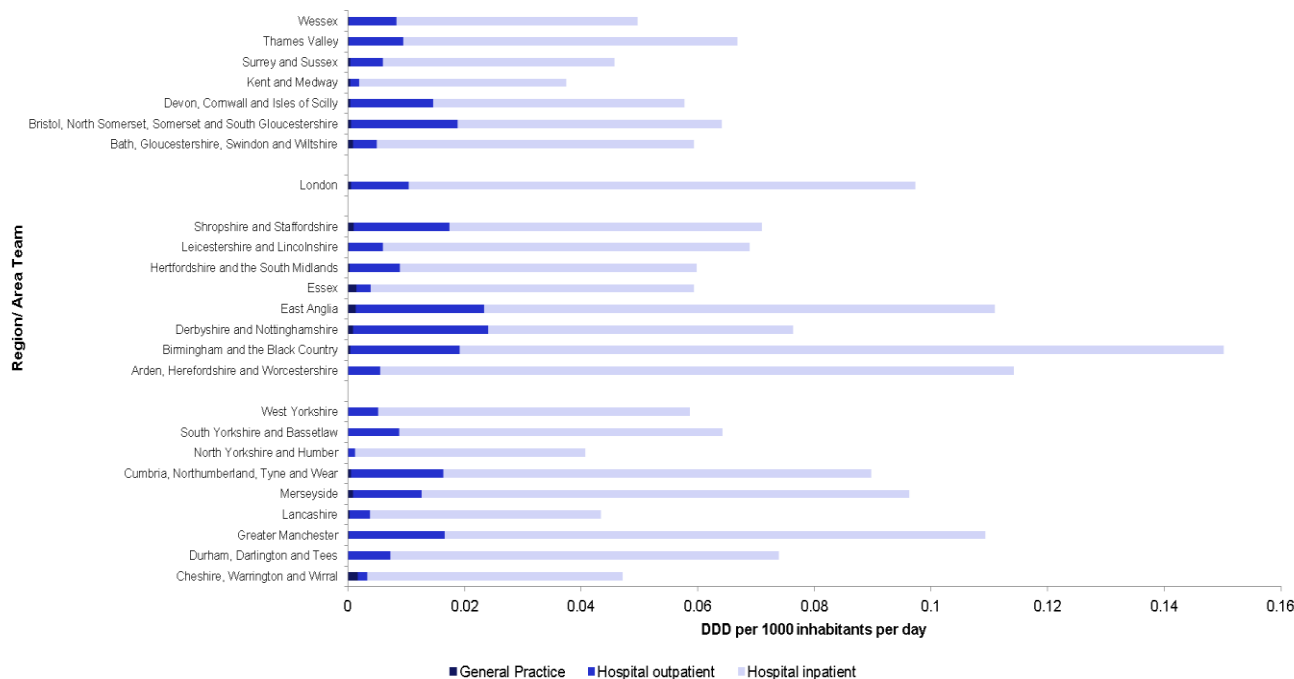
**Figure 3.18 Change in carbapenem consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013**



**Figure 3.19 Map of consumption of carbapenems at the level of ATs, England, 2013, expressed as DDD per 1000 inhabitants per day**



**Figure 3.20 Consumption of carbapenems prescribed by general practice and in Hospitals at the level of ATs, expressed as DDD per 1000 inhabitants per day, England, 2013**



### Trends in consumption by antibiotic group: 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.<sup>36</sup> The other predominant uses of tetracyclines are in moderately severe acne and rosacea, predominantly lymecycline, oxytetracycline and minocycline.

Tetracyclines comprised almost 18% of total consumption of antibiotics and 92% of consumption was in general practice throughout the four year period. From 2010 to 2013 there was a statistically significant increase in prescribing in both general practice (3.9 to 4.5 DDD per 1000 inhabitants per day) and hospital inpatient consumption (0.18 to 0.21 DDD per 1000 inhabitants per day) (Figure 3.21).

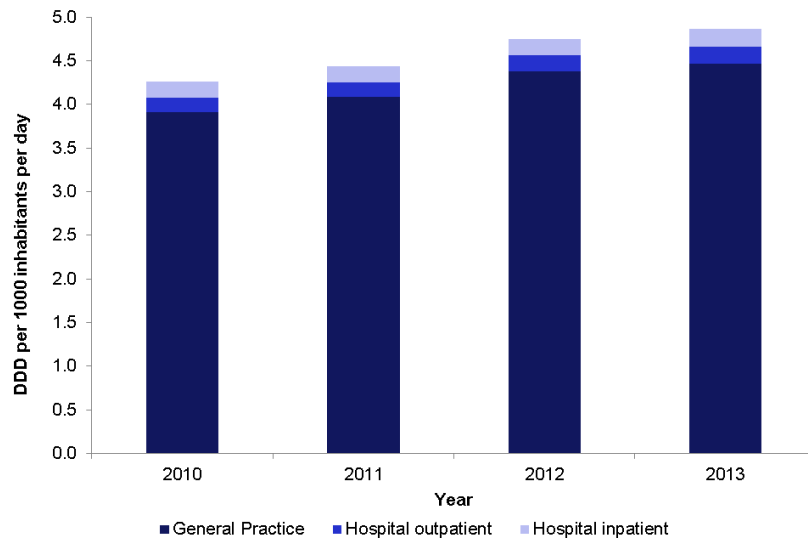
The top five agents prescribed in this class are presented in Figure 3.22. Over the four years, the predominant agents consumed were doxycycline and lymecycline (42.6% and 35.4%).

Over the four years, all ATs have increased consumption. The AT with the largest increase in consumption occurred in Leicester and Lincolnshire (from 4.2 to 5.2 DDD per 1,000 inhabitants per day, 25% increase) (Figure 3.23).

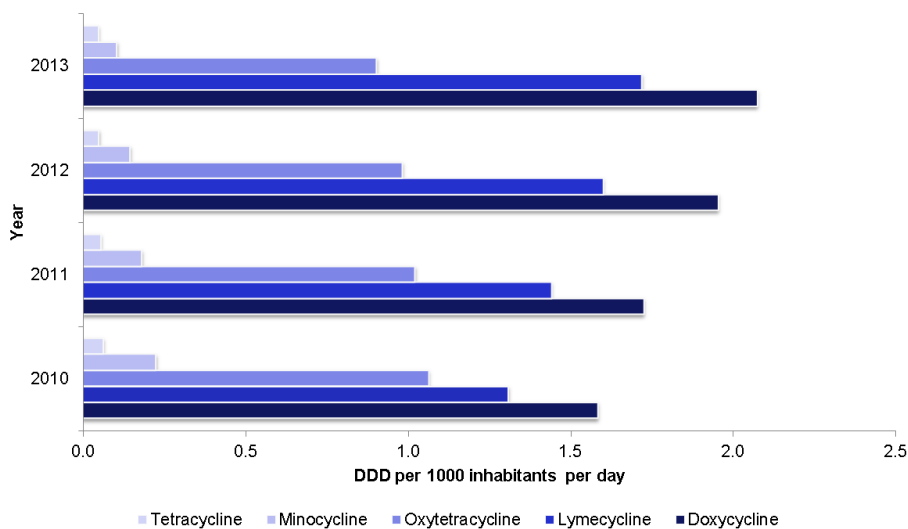
<sup>36</sup> Management of Infection Guidance for Primary Care. British Infection Association, RCGP and PHE. 2012 available at <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/PrimaryCareGuidance/>

In 2013, there was marked variation in consumption across the ATs: London had the lowest consumption (4.1 DDD per 1,000 inhabitants per day) compared to highest in Cumbria, Northumberland and Tyne and Wear (6.4 DDD per 1,000 inhabitants per day). Again, the North region had generally higher consumption than the South (Figure 3.24). However, all ATs, were in the highest quintile compared with Europe. Although this most likely reflects our primary care antibiotic guidance, it may also be that this is an important area of prescribing to explore further to assess appropriateness of these prescriptions.

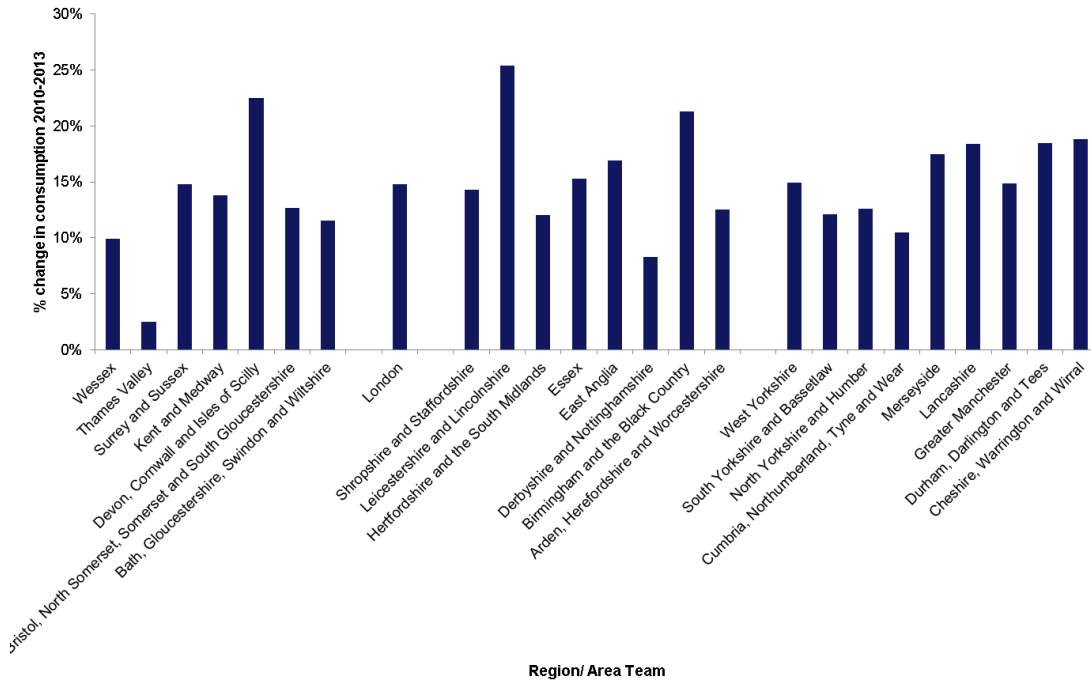
**Figure 3.21 Consumption of tetracyclines prescribed by general practice and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**



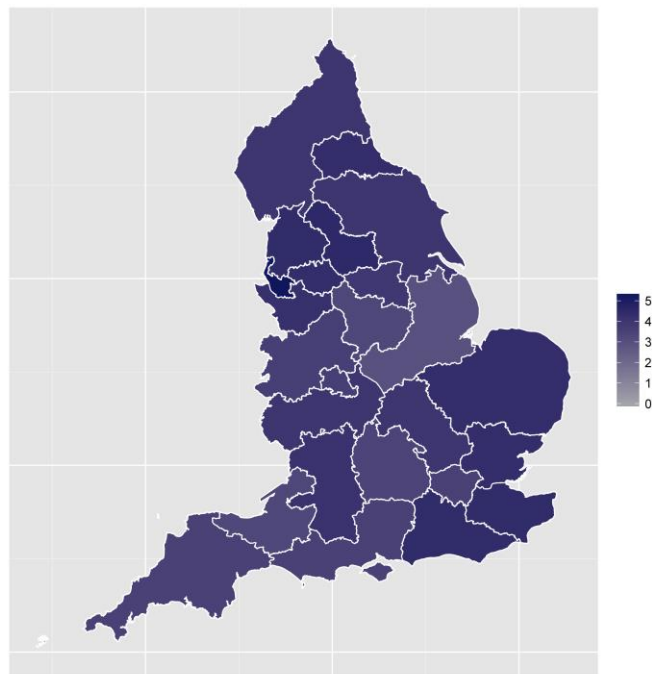
**Figure 3.22 Consumption of different tetracyclines, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**



**Figure 3.23 Change in tetracycline consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013**



**Figure 3.24 Map of consumption of tetracyclines at the level of ATs, expressed as DDD per 1000 inhabitants per day, England, 2013**



## Trends in consumption by antibiotic group: 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. It is thought by many 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 methicillin-resistant *Staphylococcus aureus* (MRSA) infections. In national infection guidelines, ciprofloxacin is recommended only for the treatment of acute prostatitis or pyelonephritis.<sup>36</sup>

### Consumption

Overall, quinolone use significantly declined from 2010 to 2013 from 0.61 to 0.58 DDD per 1000 population per day. However, this decrease has all taken place in general practice where there has been a 6% decrease; hospital inpatients and hospital outpatient consumptions have increased 10% and 5% respectively in this period (Figure 3.25).

The main quinolone prescribed across the four years was ciprofloxacin; consumption has decreased very slightly over the last four years. Use of respiratory fluoroquinolones, for example, levofloxacin and moxifloxacin, increased 21% and 17% respectively, though use still remained very low compared with other EU countries (Figure 3.26).

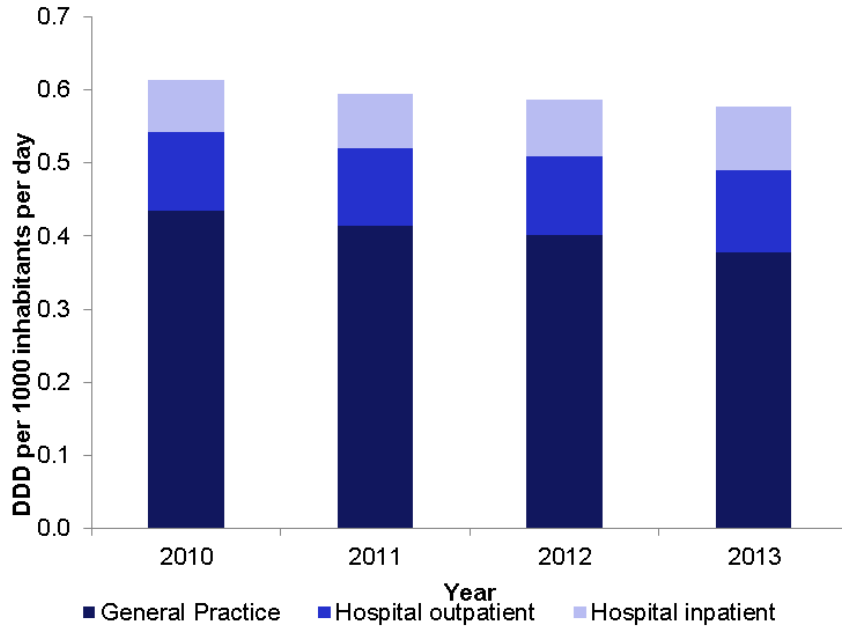
Across ATs, the majority have decreased their use of quinolones from 2010 to 2013 (Figure 3.27). In 2013 the AT with the highest consumption was Bath, Gloucestershire, Swindon and Wiltshire AT (0.8 DDD per 1000 inhabitants per day) (Figure 3.28). All ATs remain in the lowest quintile in comparison with other EU countries.<sup>34</sup>

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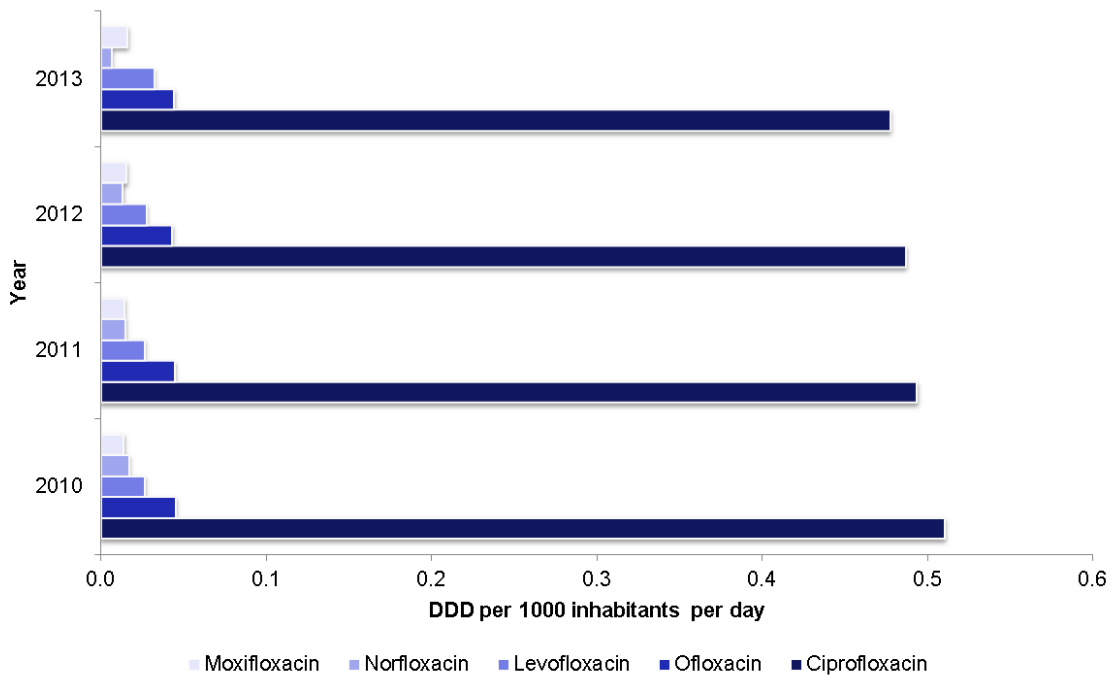
<sup>36</sup> Management of Infection Guidance for Primary Care. British Infection Association, RCGP and PHE. 2012 available at <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/PrimaryCareGuidance/>

<sup>34</sup> European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe 2011. Stockholm, ECDC; 2014

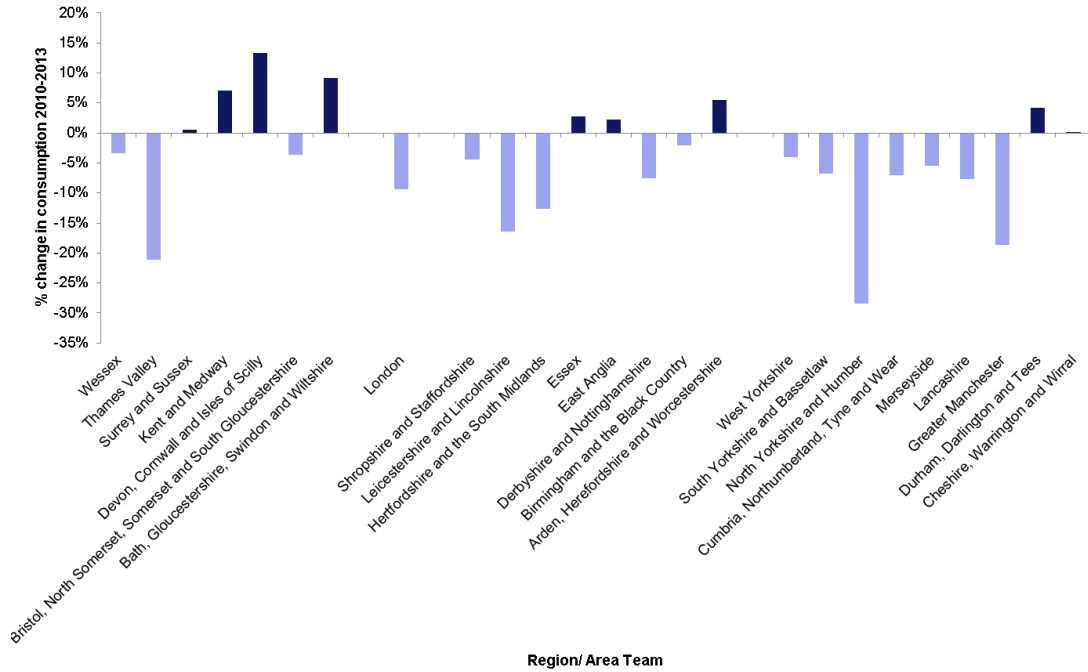
**Figure 3.25 Consumption of quinolones prescribed by general practice and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**



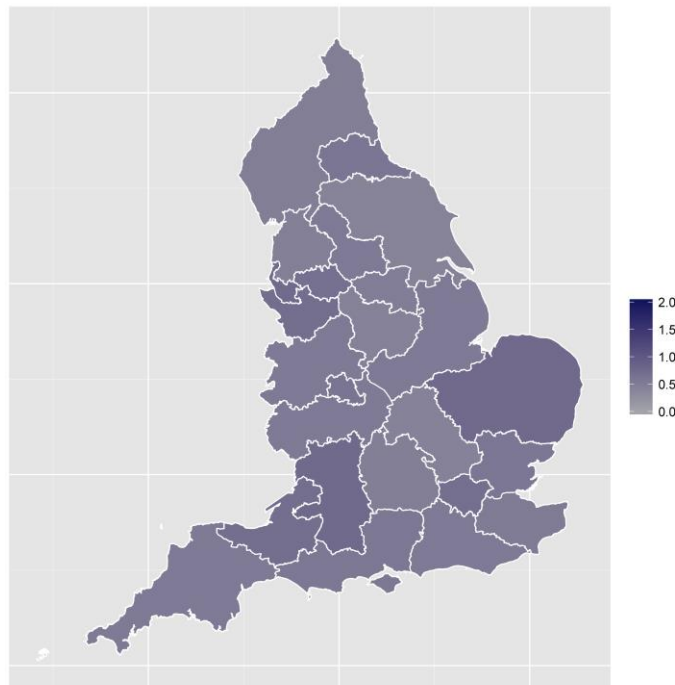
**Figure 3.26 Consumption of different quinolones, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**



**Figure 3.27 Change in quinolone consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013**



**Figure 3.28 Map of consumption of quinolones at the level of ATs, expressed as DDD per 1000 inhabitants per day, England, 2013**



## Trends in consumption by antibiotic group: macrolides

Macrolides are bacterial protein synthesis inhibitors that are active against most Gram-positive species and respiratory Gram-negative pathogens including *Haemophilus* spp., *Bordetella 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 are also recommended as part of the triple therapy for the eradication of *Helicobacter pylori* and for treatment of *Chlamydia trachomatis* genital tract infections.<sup>36</sup>

Between 2010 and 2013 macrolide consumption increased by 5.8%. The increase was most marked between 2011 and 2012 in general practice (13.8% increase) and subsequently declined by 3.2% between 2012 and 2013 (3.2 to 3.4 DDD per 1000 inhabitants per day between 2010 and 2013). Hospital inpatient consumption increased the most over the four years (19.8%; 0.21 to 0.25 DDD per 1000 inhabitants per day) though still remains a very small proportion of overall use, while hospital outpatient consumption changed minimally over the four years. In 2013, 88% of macrolide consumption related to general practice prescriptions (Figure 3.29).

The most frequently used macrolide was clarithromycin and consumption has increased by 20% from 1.7 to 2.9 DDD per 1000 inhabitants per day over the last four years. Consumption of erythromycin decreased by 18% and azithromycin, while used the least, increased by 55% in the same period (Figure 3.30).

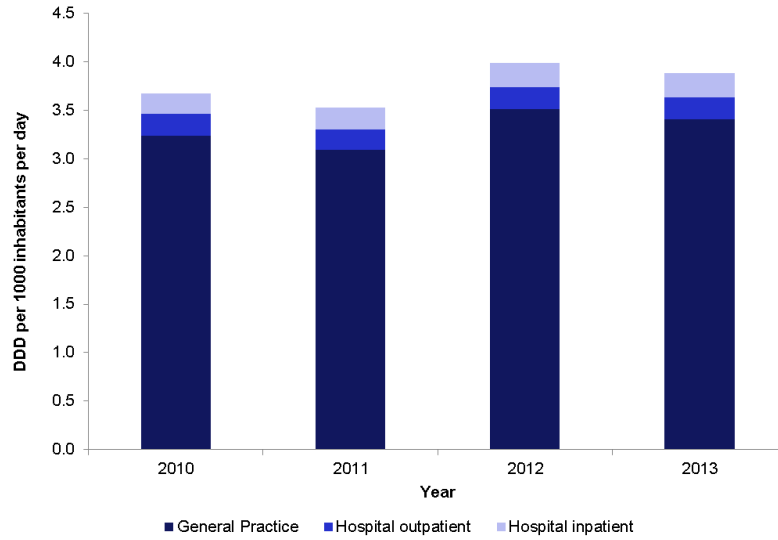
More than 80% of ATs increased their consumption of macrolides in the last four years (Figure 3.31). In 2013, Merseyside has increased its consumption by 25% and is now the highest at 5.3 DDD per 1000 inhabitants per day; almost twice as high as the lowest consumer, Leicester and Lincolnshire at 2.9 DDD per 1000 inhabitants per day who decreased consumption by 7% over the last 4 years (Figure 3.32)

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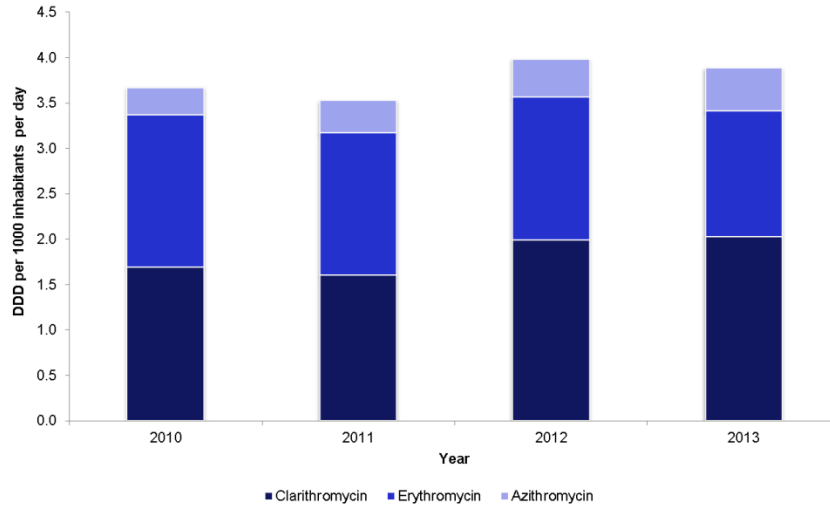
<sup>36</sup> Management of Infection Guidance for Primary Care. British Infection Association, RCGP and PHE. 2012 available at <http://www.hpa.org.uk/Topics/InfectiousDiseases/InfectionsAZ/PrimaryCareGuidance/>



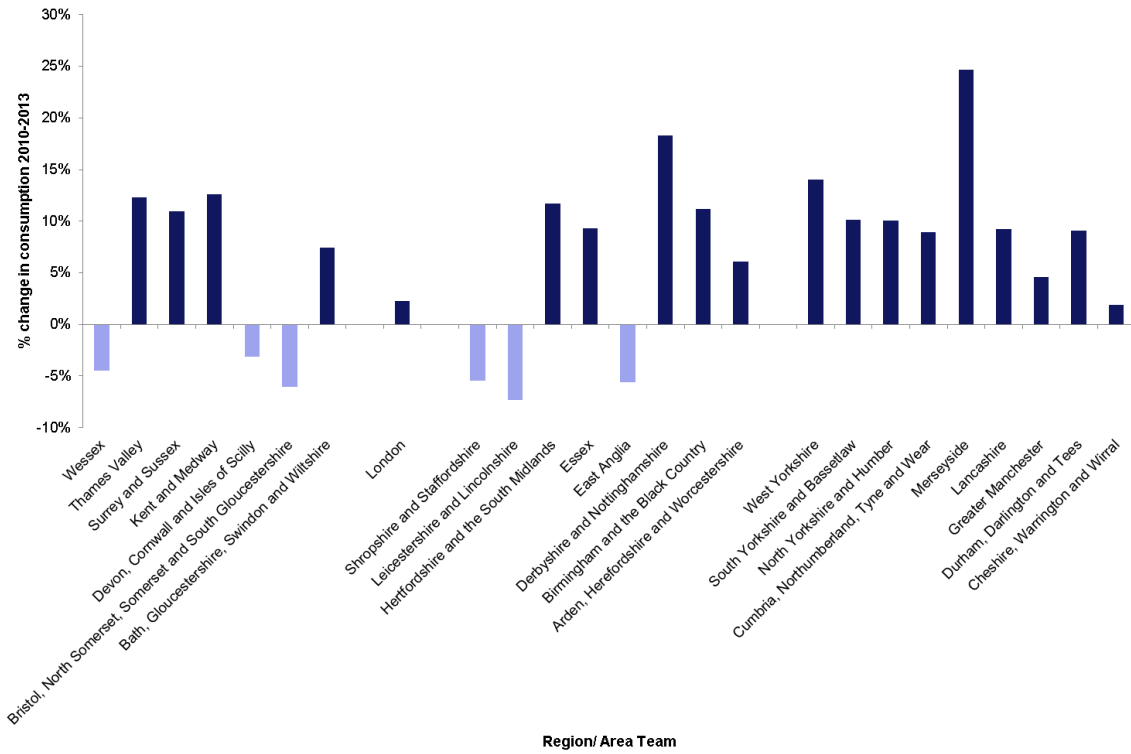
**Figure 3.29 Consumption of macrolides prescribed by general practices and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**



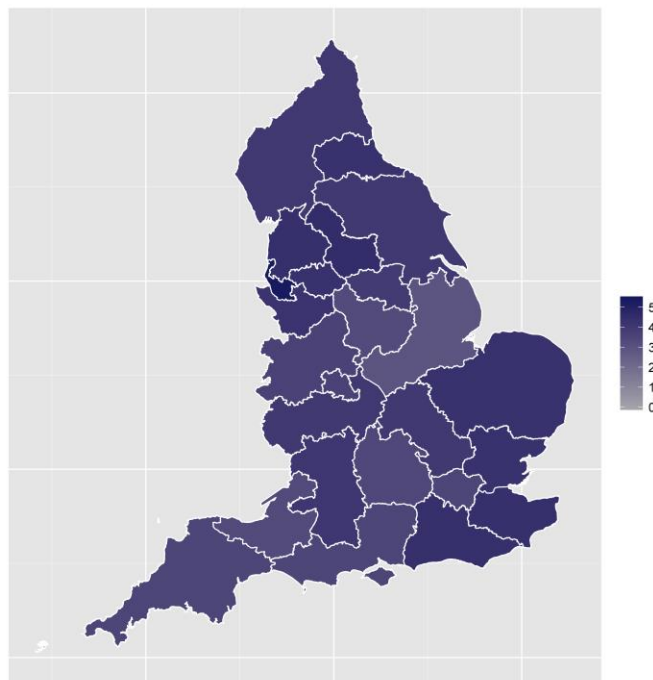
**Figure 3.30 Consumption of different macrolides, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**



**Figure 3.31 Change in macrolide consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013**



**Figure 3.32 Map of consumption of macrolides at the level of ATs, England, 2013, expressed as DDD per 1000 inhabitants per day**



## Trends in consumption by antibiotic group: sulfonamides and trimethoprim

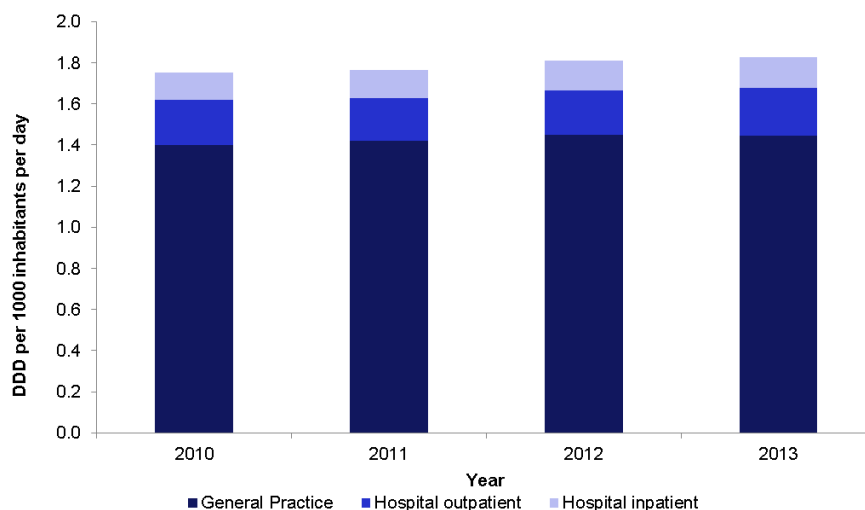
Sulfonamides and trimethoprim can either be used individually or co-formulated. Both antibiotics are bacteriostatic and act by inhibiting enzymes that are involved in the biosynthesis of folic acid in microbes. They have a wide spectrum of activity against bacteria, fungi and protozoa. In national infection guidelines, trimethoprim is recommended for the treatment of urinary tract infections.<sup>36</sup>

Between 2010 and 2013 total consumption of this antibiotic group increased by 4.2%, ranging from 3.2% in general practice (1.40 to 1.45 DDD per 1000 inhabitants per day) to 12.6% in hospital inpatients (0.13 to 0.15 DDD per 1000 inhabitants per day) (Figure 3.33). England has one of the highest consumption of sulfonamides and trimethoprim in the EU. Eighty five percent of consumption was trimethoprim with the remainder being either sulfonamide or sulfonamide/trimethoprim combination therapy.

The majority of ATs increased consumption over the last 4 years. Shropshire and Staffordshire increased the most from 1.5 to 1.9 DDD per 1000 inhabitants per day (a 20% increase) to higher than the national average. Bristol, North Somerset, Somerset and South Gloucestershire decreased the most, 11% from 2.2 to 1.9 DDD per 1000 inhabitants per day.

In 2013, consumption varied across ATs from 1.5 to 2.3 DDD per 1,000 inhabitants per day (lowest in Thames Valley; highest in Durham, Darlington and Tees). All ATs remained in the highest quintile of consumption compared to other EU countries.

**Figure 3.33 Consumption of sulfonamides and trimethoprim prescribed by general practices and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**



<sup>36</sup> 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/>

## Trends in consumption in other agents: nitrofurantoin

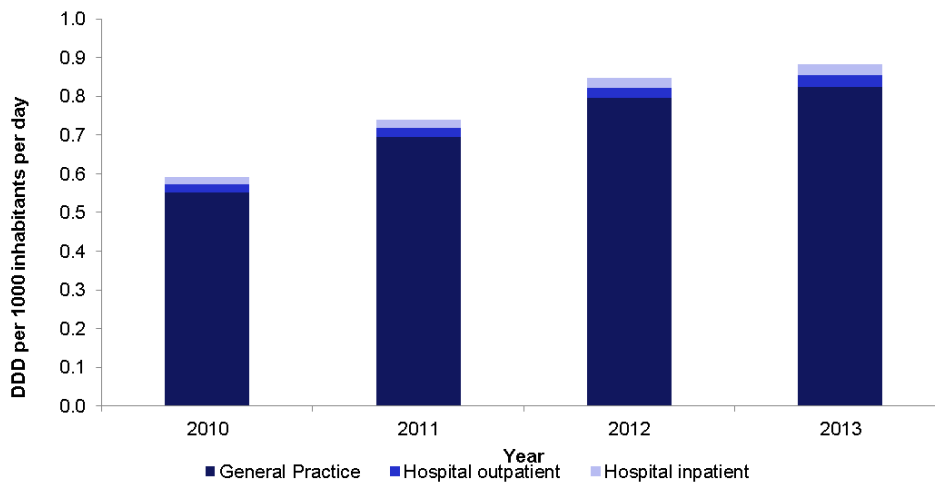
Nitrofurantoin is a key agent in the treatment of community urinary tract infection (UTI) infections. It is recommended for this indication in the national infection guidelines.<sup>36</sup>

Nitrofurantoin consumption increased by approximately 50% over the last 4 years from 0.6 to 0.9 DDD per 1000 inhabitants per day. Use increased in a similar trend across general practice and hospital prescribing; though more than 90% of consumption originates from General Practice prescriptions (Figure 3.34)

All ATs have increased consumption: Wessex had the lowest increase at 5.3%, though started with the highest consumption in 2010 (0.8 DDD per 1000 inhabitants per day). West Yorkshire increased the most, doubling consumption in the four years from 0.4 to 0.9 DDD per 1000 inhabitants per day (Figure 3.35).

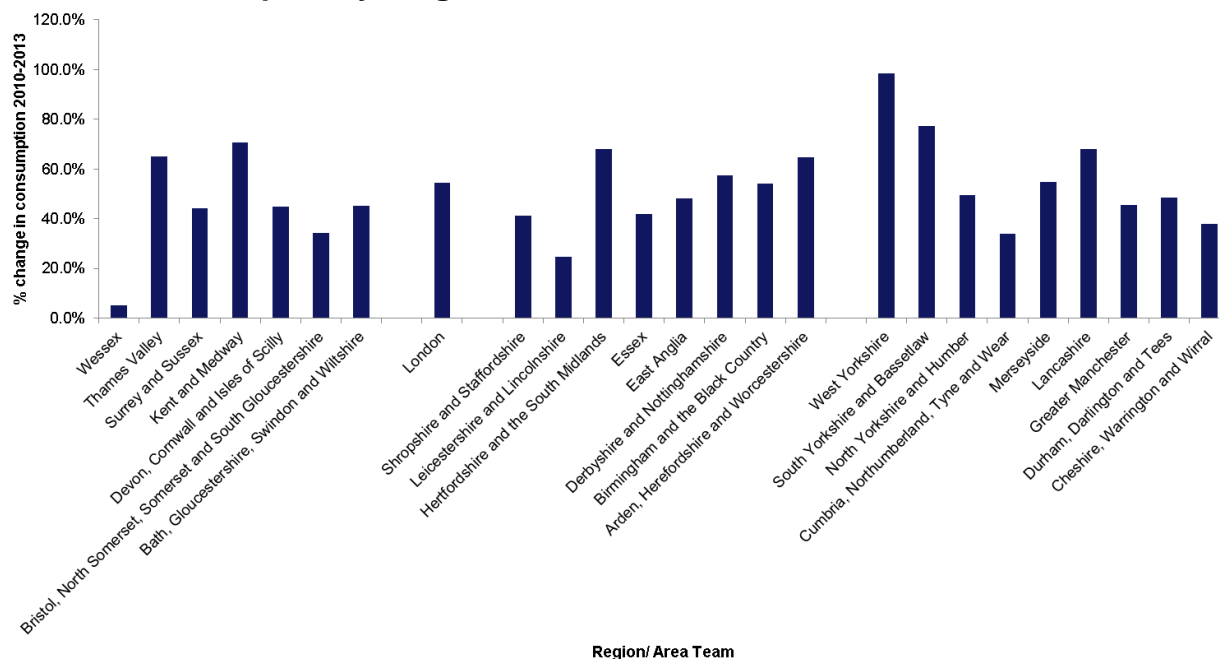
There remains substantial variation in consumption with London the lowest (0.7 DDD per 1000 inhabitants per day), and Hertfordshire and South Midlands the highest (1.1 DDD per 1000 inhabitants per day).

**Figure 3.34 Consumption of nitrofurantoin prescribed by General Practices and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**



<sup>36</sup> 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/>

**Figure 3.35 Change in nitrofurantoin consumption at the level of ATs, expressed as DDD per 1000 inhabitants per day, England 2010-2013**



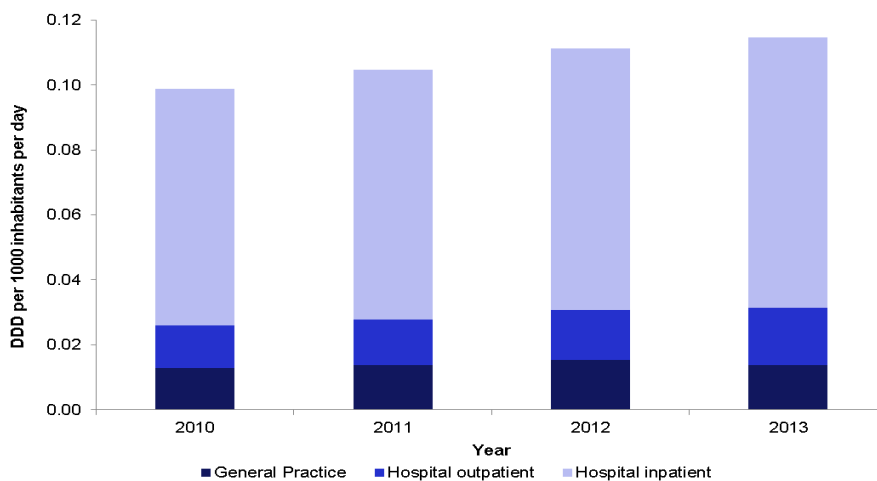
### Trends in consumption in other agents: aminoglycosides

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 of these developed, 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 increased 3.1% from 2010 to 2013. Unlike many other antibiotics more than 90% of the consumption occurred in hospital inpatients or outpatients. The most frequent aminoglycoside used was gentamicin, with 70% of DDD consumption. General Practice consumption is almost entirely limited to inhaled tobramycin, which was most likely being used as a prophylactic or treatment agent in individuals with bronchiectasis (Figure 3.36).

The AT with the highest consumption in 2013, was Devon, Cornwall and Isles of Scilly at 0.17 DDD per 1000 inhabitants per day and the lowest was Derbyshire and Nottinghamshire at 0.06 DDD inhabitants per day.

**Figure 3.36 Consumption of aminoglycosides prescribed by General Practices and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**

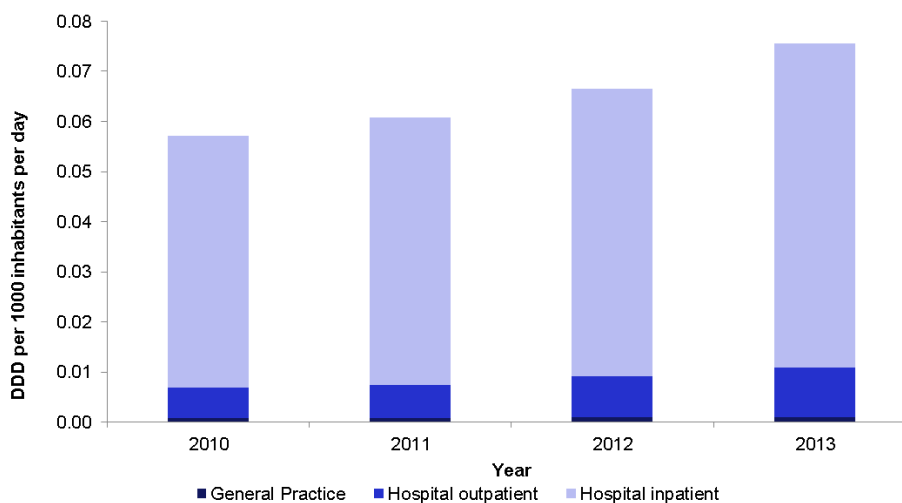


### Trends in consumption in other agents: glycopeptides and daptomycin

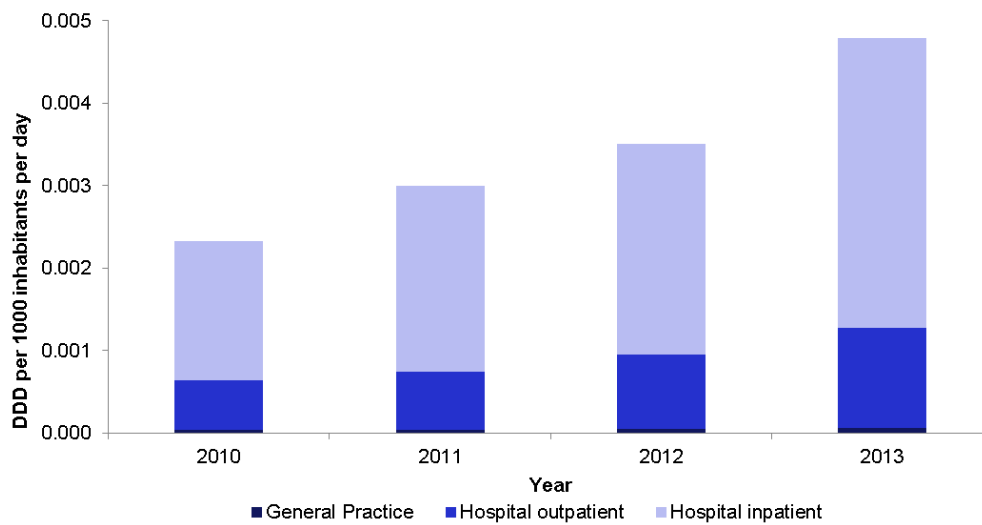
The parenteral (intravenous) form of these antibiotics is almost exclusively used to treat infections due to resistant Gram-positive bacteria, such as MRSA, enterococci or coagulase-negative staphylococci.

Despite a significant reduction in MRSA bacteraemia and other infections, the use of parenteral glycopeptides continued to increase in the last four years (Figure 3.37). From 2010 to 2013 the consumption of daptomycin has doubled, though still remains very low at less than 0.005 DDD per 1000 inhabitants per day (Figure 3.38). Teicoplanin consumption has increased from 0.04 to 0.05 DDD per 1000 inhabitant per day. Parenteral vancomycin use has remained static. This may be related to higher doses of Teicoplanin prescribed per day compared to dose as defined in the DDD (Figure 3.39).

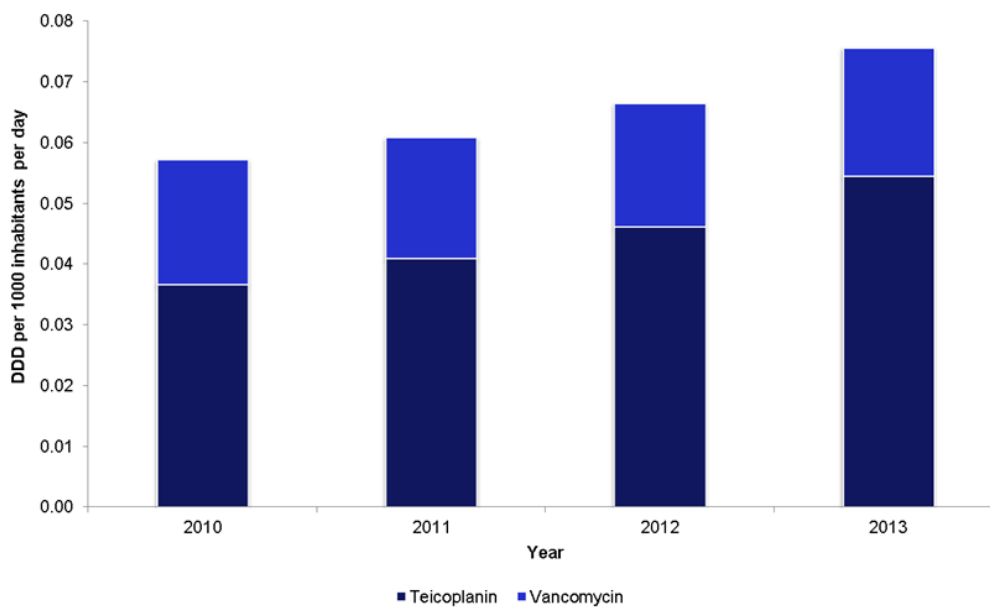
**Figure 3.37 Consumption of glycopeptides prescribed by General Practices and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**



**Figure 3.38 Consumption of daptomycin prescribed by General Practices and in Hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**



**Figure 3.39 Consumption of different glycopeptides, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**

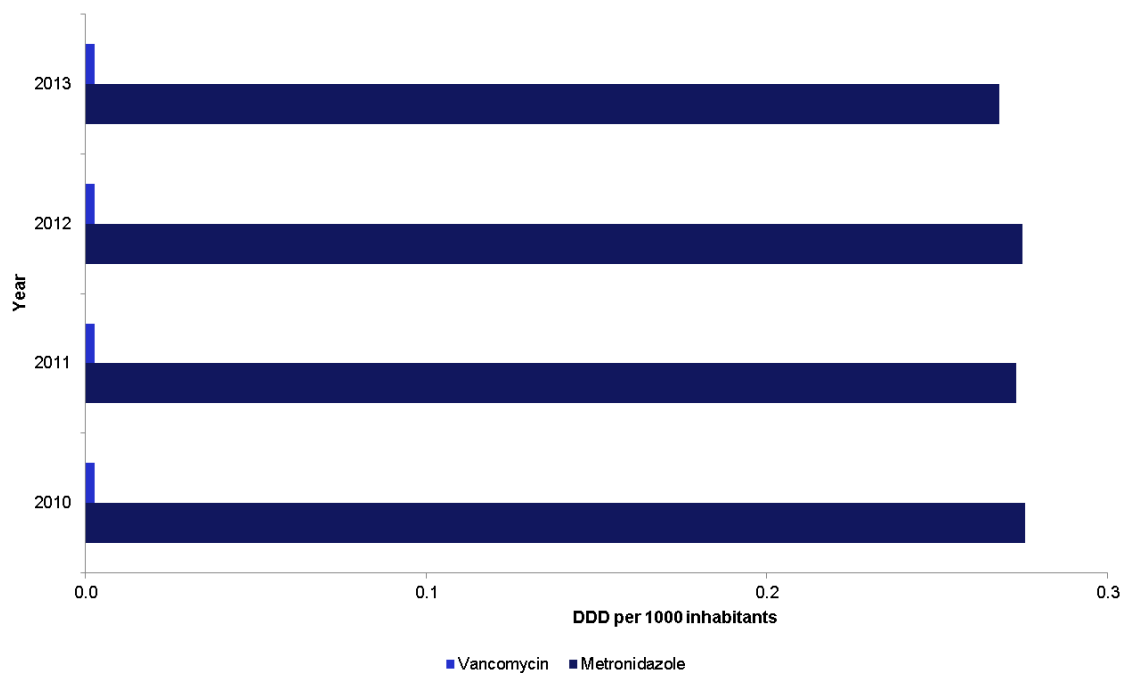


## Trends in consumption in other agents: *Clostridium difficile* treatment agents

Three agents constitute the predominant treatment for this infection. In England, oral vancomycin and fidaxomicin are not used for other conditions. However, in the community infection guidelines oral metronidazole is used to treat *H. pylori* infection and also as a second line agent for animal bites; so consumption cannot be clearly related to *C. difficile* infection. In hospitals, metronidazole is also used to treat anaerobic infections, especially related to intra-abdominal sepsis.

Consumption of these three agents has declined by 3% over the last 4 years, as *C. difficile* rates continue to fall, with a 3% and 5% reduction in metronidazole and vancomycin consumption respectively (Figure 3.40). Fidaxomicin was licensed in 2011 and consumption has remained very low (<0.001 DDD per 1000 inhabitants).

**Figure 3.40 Consumption of oral vancomycin and oral metronidazole prescribed by General Practices and in hospitals, expressed as DDD per 1000 inhabitants per day, England, 2010-2013**





## Community prescribing by items

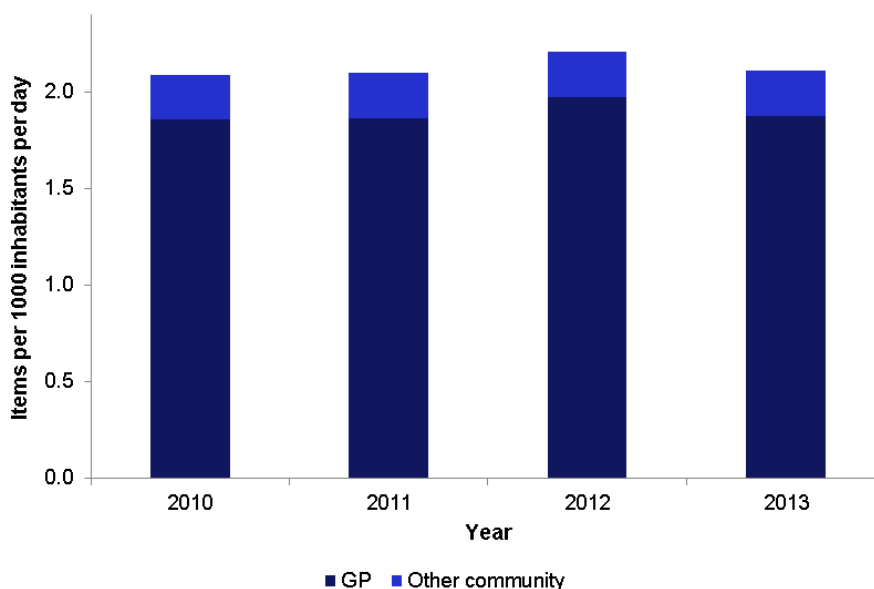
Prescribing of antibiotics is frequently described in terms of prescription items dispensed where each antibiotic prescription is one item. Between 2010 and 2013, items prescribed in the community remained stable at 2.1 per 1000 inhabitants per day; with 89% related to General Practice prescriptions. However, there was a 5.3% increase between 2011 and 2012 and a subsequent 4.5% decrease between 2012 and 2013 (Figure 3.41).

Translating this into proportion of English inhabitants receiving antibiotics each year, suggests that this could be as high as 77%. However, a significant proportion of these prescriptions will be repeat prescriptions, especially those patients with recurrent UTIs, chronic bronchitis, other chronic infections or receiving long term prophylactic treatment. In Scotland, where individual patient prescribing data were available, one-third of the Scottish population had received at least one antibiotic, 8.3% at least 3 and 2.1% at least 6 antibiotic prescriptions in 2012.<sup>38</sup>

In England, the most common prescriptions were penicillins (54%), followed by macrolides (12%), tetracyclines (10%) and sulfonamides and trimethoprim (10%). Cephalosporins accounted for 3% and quinolones 2% of total prescribing (Figure 3.42).

Similar trends were also seen in the items prescribed compared with DDD consumption per 1000 inhabitants per day across ATs (Figure 3.43). London remained the lowest and Durham, Darlington and Tees the highest with 1.6 and 2.2 items prescribed per 1000 inhabitants per day, which remained lower than the European population weighted mean of 3.1 DDD per 1000 inhabitants per day.<sup>34</sup>

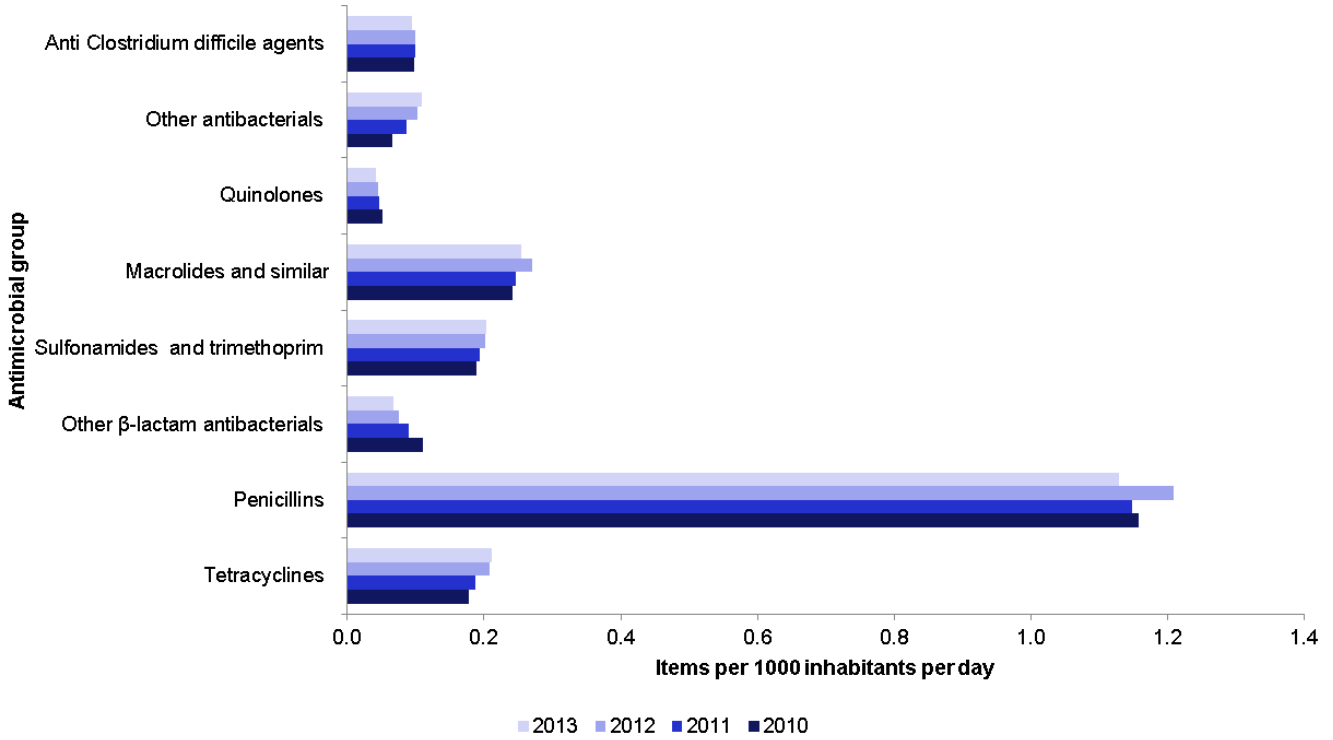
**Figure 3.41 Consumption of packages of antibiotics, expressed as items per 1000 inhabitants per day, England, 2010-2013**



<sup>38</sup> Report on Antimicrobial Use and Resistance in Humans in 2012. Health Protection Scotland and Information Services Division. 2014

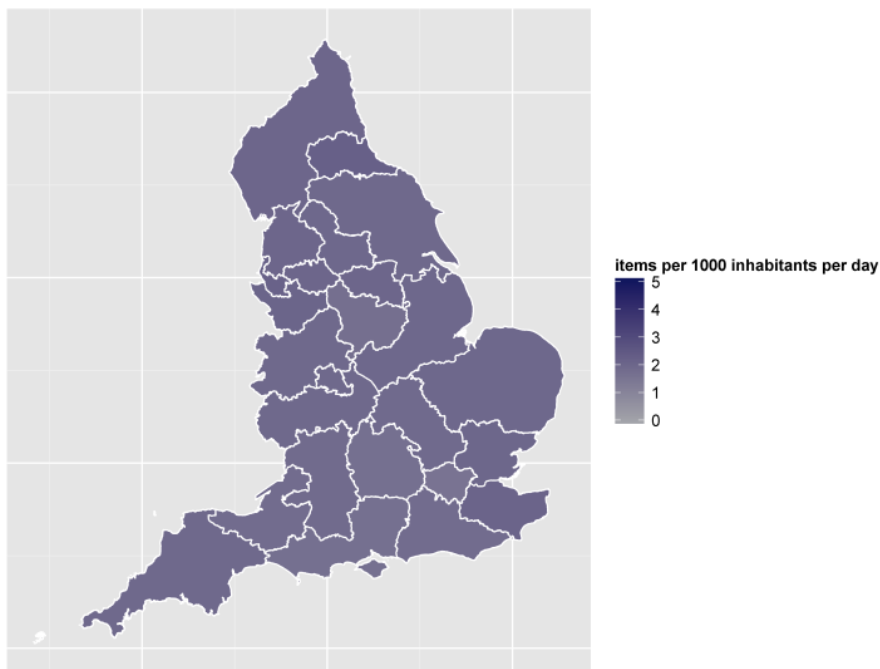
<sup>34</sup> European Centre for Disease Prevention and Control. Surveillance of antimicrobial consumption in Europe 2011. Stockholm, ECDC; 2014

**Figure 3.42 Consumption of packages of antibiotics\* for systemic use in the community (General Practice and other community prescribing) expressed as items per 1000 inhabitants per day, England, 2010-2013**



\*Other  $\beta$ -lactam antibacterials includes cephalosporins and carbapenems.

**Figure 3.43 Map of consumption of packages of antibiotics, expressed as items per 1000 inhabitants per day, by ATs, England, 2013**



## Hospital sector

Between 2010 and 2013, total hospital prescribing has increased by 7.5% per 1000 inhabitants per day. This prescribing is predominantly related to increased inpatient prescribing which has increased by 11.9% compared to outpatient prescribing which has increased only 1.3% in the same time interval.

In the main section of this report, population denominators were used and included all hospital prescribing, as data were reported at an AT level. This section in particular, is to allow hospitals to benchmark themselves compared with other hospitals, using a specific hospital activity denominator.

Consumption of antibiotics in hospital inpatients, expressed as DDD per 100 admissions has increased by 11% between 2010 and 2013 (Figure 3.44).

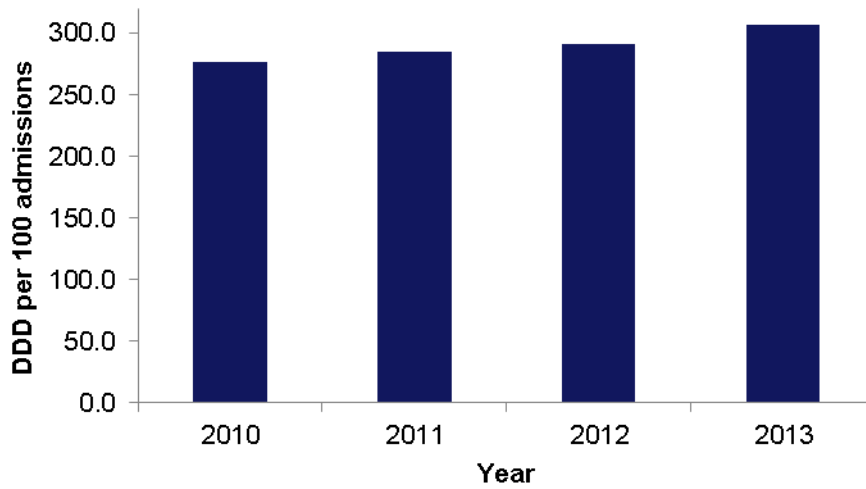
This increase occurred over all antibiotic groups, as demonstrated in Figure 3.45. The smallest increase occurred in penicillins, though in this group there was a switch from amoxicillin and flucloxacillin to increased use of co-amoxiclav and piperacillin-tazobactam.

There was significant variability with respect to the consumption of agents utilised by hospitals across the ATs. This pattern is similar to the pattern described by each of the agents. A detailed breakdown of each antibiotic group which can be used to further explore individual hospital inpatient consumption is presented in Table 3.1

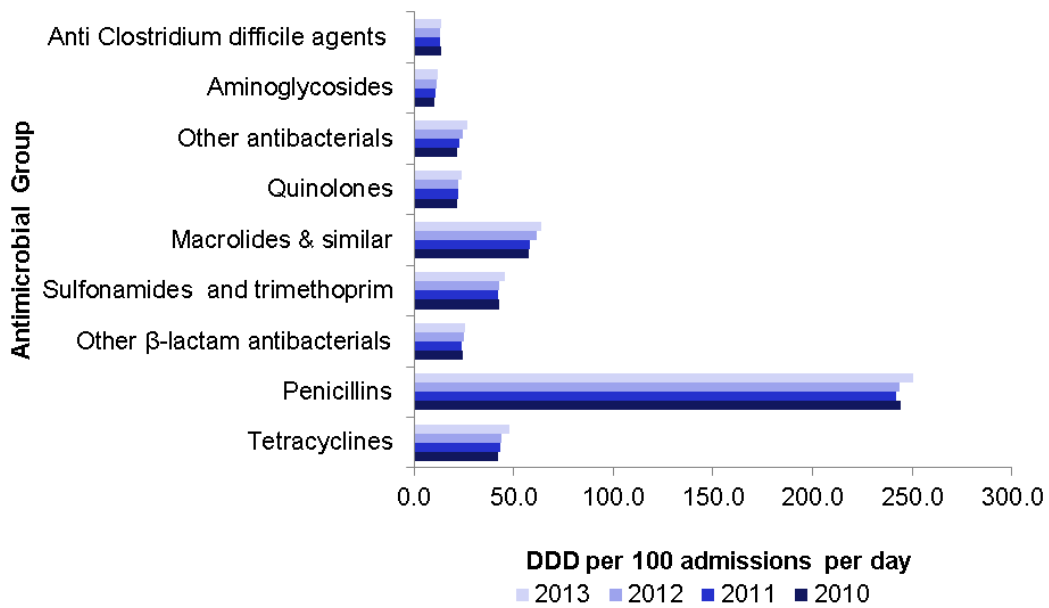
In 2013, the commonest agent prescribed in hospitals was co-amoxiclav at 108 DDD per 100 admissions, 21% of total consumption in inpatients. The consumption of co-amoxiclav increased 12.1% between 2010 and 2013. The most frequently prescribed agents are outlined in Table 3.2. The two agents that have increased the most within this table are meropenem (6.0 to 9.2 DDD per 100 admissions) and piperacillin-tazobactam (7.9 and 11.4 DDD per 100 admissions) at 36% and 49% respectively.

In addition, the data for hospital inpatients were compared to the point prevalence survey (Table 3.2). In this table, we demonstrate that there is a similar pattern across the most frequent agents prescribed. The antibiotics used most frequently for community acquired infections (penicillins and macrolides) demonstrated much higher consumption than the prevalence survey suggested and the inverse for those antibiotics used to more commonly treat healthcare associated infections. This most likely relates to one-stop or discharge dispensing (where patients are dispensed antibiotics when they are hospital inpatients to continue to take when they have been discharged). Many of these patients may have short inpatient stays be under-represented in prevalence surveys.

**Figure 3.44 Consumption of antibiotics in hospital inpatients, expressed as DDD per 100 admissions, by area teams, England, 2010-2013**



**Figure 3.45 Antibiotic consumption by group\* for hospital inpatients, expressed as DDD per 100 admissions per day, England, 2010-2013**



\*Other  $\beta$ -lactam antibacterials includes cephalosporins and carbapenems.

**Table 3.1 Antibiotic consumption by group for hospital inpatients at the level of ATs, expressed as DDD per 100 admissions per day, England, 2013**

Area team	Penicillins	Macrolides & similar	Tetracycline	Other $\beta$ -lactam	Other groups	Sulfonamide and trimethoprim	Amino-glycoside	Quinolone
Cheshire, Warrington and Wirral	138.5	29.0	21.6	13.2	31.2	14.7	10.5	17.4
Durham, Darlington and Tees	158.4	27.3	13.6	15.7	17.7	14.8	4.0	14.0
Greater Manchester	138.6	29.8	20.4	18.3	16.3	21.8	7.9	12.0
Lancashire	118.4	42.2	14.5	14.8	12.7	15.4	10.7	5.8
Merseyside	126.4	33.7	23.1	32.4	21.2	14.6	6.8	13.2
Cumbria, Northumberland, Tyne and Wear	174.1	31.8	24.5	16.9	17.4	23.8	12.2	8.4
North Yorkshire and Humber	168.5	33.2	13.4	13.2	17.2	21.6	10.2	9.9
South Yorkshire and Bassetlaw	148.0	31.1	17.2	23.7	16.6	12.2	6.5	6.4
West Yorkshire	185.0	43.6	17.4	20.4	19.5	17.4	9.2	11.2
Arden, Herefordshire and Worcestershire	195.0	38.3	15.8	20.6	17.3	18.3	13.1	9.3
Birmingham and the Black Country	138.5	27.1	15.8	17.9	13.3	12.8	6.7	10.1
Derbyshire and Nottinghamshire	193.6	45.8	138.8	22.2	17.4	19.6	6.7	8.8
East Anglia	131.3	30.4	12.5	20.7	13.3	12.3	9.4	9.6
Essex	248.3	55.4	19.2	19.3	25.1	24.2	14.1	10.2
Hertfordshire and the South Midlands	198.9	39.7	24.3	20.7	24.9	23.2	8.5	8.0
Leicestershire and Lincolnshire	154.9	21.1	23.8	23.4	14.3	17.2	8.0	10.0
Shropshire and Staffordshire	99.5	21.2	10.4	12.6	12.8	11.0	7.0	5.0
London	196.2	37.7	29.0	25.6	24.6	19.0	11.8	13.9
Bath, Gloucestershire, Swindon and Wiltshire	172.3	37.4	22.8	15.7	22.1	17.8	13.6	15.0
Bristol, North Somerset, Somerset and South Gloucestershire	127.9	16.9	11.0	11.9	14.9	21.9	11.9	8.5
Devon, Cornwall and Isles of Scilly	130.1	22.0	33.9	12.9	16.6	18.4	12.6	9.5
Kent and Medway	199.7	37.7	14.5	17.4	16.0	22.0	11.0	8.2
Surrey and Sussex	214.2	43.7	26.1	22.6	30.8	23.7	15.9	9.9
Thames Valley	138.1	28.4	21.6	23.8	23.7	15.7	10.1	9.5
Wessex	111.8	21.3	40.2	20.3	15.5	14.3	10.6	7.8
England	160.2	33.0	25.0	19.1	18.9	17.9	10.0	10.1

**Table 3.2. Table demonstrating the most prevalent antibiotics used in acute trusts in the national Point Prevalence survey in 2011 and comparison with the most frequently consumed antibiotics (DDD per 100 admission) in 2011 and 2013**

Antibiotics	PPS	DDD	
	2011	2011	2013
Co-amoxiclav	13.0%	21.8%	21.6%
Flucloxacillin	7.3%	17.0%	15.1%
Amoxicillin	4.5%	9.4%	10.0%
Doxycycline	2.4%	7.7%	7.9%
Clarithromycin	4.8%	6.3%	7.2%
Metronidazole	7.7%	4.6%	4.3%
Trimethoprim	4.2%	4.0%	3.7%
Piperacillin-Tazobactam	8.7%	3.0%	3.5%
Gentamicin	6.0%	2.7%	2.8%
Ciprofloxacin	2.7%	2.4%	2.4%
Meropenem	3.9%	2.2%	2.4%

## Discussion

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This report collates together, for the first time, prescribing across primary and secondary care in England. We have focussed on the NHS geographical boundaries, to encourage a whole healthcare economy approach to antibiotic prescribing. In 2013, the total measured consumption of antibiotics in England was 27.4 DDD per 1000 inhabitants per day (general practice 79%, Hospital 15% and other community consumption (predominantly dentists) 6%). This is an under-estimate of total consumption as it does not include private prescriptions, from private general practitioners, hospitals or dentists, which are not recorded centrally at present. From 2010 to 2013, the total use of antibiotics increased by 6%: within general practice use increased by 4%, while prescribing to hospital inpatients increased by 12% and other community prescriptions ( eg dentists and out-of-hours) increased by 32%. The reasons for the increase in consumption are unknown but may represent changes in the number of patients presenting with infections requiring antibiotics or overprescribing of antibiotics by clinicians. The increase in other community prescriptions needs to be explored to assess whether general practice prescribing is being displaced to out-of hours treatment centres.

Individual prescription items of antibiotics can only be measured for community prescriptions, as hospitals may dispense in bulk to wards, and each individual dispensing may not be to an individual patient. In 2013, total items of antibiotics prescribed were 2.1 items per 1000 inhabitants per day (general practice 1.9 and other community 0.2 items per 1000 inhabitants per day). The other community prescribing, largely reflects dental prescriptions, which cannot be broken down by AT. It is likely to be a gross underestimation of dental prescribing as up to 50% of dental treatments are performed privately and private prescriptions are not captured in this data.<sup>40</sup>

There was significant variability in total antibiotic use and the use of different antibiotics across the country, in both primary and secondary care. The highest combined general practice and hospital usage was in Merseyside, where levels of use were similar to those reported from Southern Europe, and over 30% higher than in the Thames Valley, which had the lowest usage. The highest prescribing from general practice was in Durham, Darlington and Tees, which was over 40% higher than in London. This may reflect healthcare access and delivery in London, where there is greater access to local hospitals and private healthcare. In ATs, where there are large cities with many hospitals, more consumption of antibiotics occurs in hospital settings, particularly in outpatient departments. This may be related to more transient population and patients who are not registered with general practices or the geographical ease of access to secondary care departments in urban areas. In addition, the tertiary level hospitals with a large number of sub-specialties predominantly are present in large cities. These hospitals often have admissions from outside their geographical AT from across their region. However, it should be a national ambition to reduce the variability in total prescribing across the country, to the safest level possible, ideally by developing a case-mix adjustment of antibiotic use for hospitals alongside the current adjustment for primary care (STAR-PU).

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<sup>40</sup> The privatisation of NHS dentistry? A national snapshot of general dental practitioners. D Buck, JT Newton. *British Dental Journal* (2001); 190: 115 - 118 (2001)

In 2013, 66 different antibiotics were prescribed in both general practice and hospital. The top 15 antibiotics in general practice and hospitals accounted for 98% and 88% of consumption respectively. These antibiotics are summarised in Table 3.3. Over the last four years, consumption of the majority of antibiotics in the top 15 in both general practice and hospital increased. Within general practice prescribing, broad-spectrum antibiotics ciprofloxacin and cefalexin decreased, though co-amoxiclav demonstrated a significant increase. Within hospitals, narrow-spectrum agents decreased (phenoxymethylpenicillin, flucloxacillin and erythromycin) with increases noted across broad-spectrum agents such as co-amoxiclav, piperacillin-tazobactam and meropenem. Further work is required to determine whether heterogeneous antibiotic use reduces antibiotic resistance and how this approach could be developed across primary and secondary care in England.

**Table 3.3 Ranks and relative consumption of the top 15 consumed agents in general practice and hospitals in England, 2013.**

Community consumption in 2013				Hospital Consumption in 2013			
	Rank	Proportion of all antibiotics	Relative to 2010		Rank	Proportion of all antibiotics	Relative to 2010
Amoxicillin	1	29.3%	no change	Co-amoxiclav	1	21.1%	increased
Clarithromycin	2	7.9%	increased	Flucloxacillin	2	12.9%	decreased
Doxycycline	3	7.9%	increased	Amoxicillin	3	10.1%	no change
Lymecycline	4	7.9%	increased	Doxycycline	4	8.7%	increased
Flucloxacillin	5	7.2%	increased	Clarithromycin	5	7.7%	increased
Trimethoprim	6	6.4%	increased	Co-trimoxazole	6	4.9%	increased
Erythromycin	7	6.1%	increased	Trimethoprim	7	3.9%	no change
Co-amoxiclav	8	6.0%	increased	Metronidazole	8	3.8%	no change
Phenoxymethylpenicillin	9	5.3%	increased	Ciprofloxacin	9	3.5%	no change
Oxytetracycline	10	4.2%	decreased	Azithromycin	10	2.3%	increased
Nitrofurantoin	11	3.8%	increased	Piperacillin-tazobactam	11	2.2%	increased
Azithromycin	12	1.8%	increased	Gentamicin	12	1.8%	increased
Ciprofloxacin	13	1.5%	decreased	Meropenem	13	1.6%	increased
Cephalexin	14	1.5%	decreased	Phenoxymethylpenicillin	14	1.6%	decreased
Metronidazole	15	0.7%	no change	Erythromycin	15	1.4%	decreased

The relative changes of each agent need to be interpreted with caution as an increase in one group may cause a reduction in another, where an alternative agent is used for the same clinical indication. For example, although Merseyside had the highest prescription of penicillins, it had the second lowest prescription of penicillin and inhibitor combinations. This demonstrates the complexity of consumption data, where high dose amoxicillin may increase the total DDD



consumption measurement in a particular AT, but yet be more appropriate narrower spectrum prescribing.

There are some key differences in recommended doses compared to defined daily doses to highlight. The standard dose now recommended for amoxicillin is 500mg three times per day where the DDD is 1g per day; with similar recommendations on the dose for co-amoxiclav. Clarithromycin likewise is commonly recommended as 500mg twice per day, where the DDD is 500mg per day. Other antibiotics where the recommended dose is equal to the DDD, such as nitrofurantoin and trimethoprim, mean that changes in DDD per item of these drugs is more likely to reflect a change in the duration prescribed.

**Table 3.4 Number of DDD per item of the top 15 drugs consumed in England, 2010-2013, for common antibiotics recommended in guidelines**

Drug Name	DDD			
	2010	2011	2012	2013
Amoxicillin	11.1	11.3	11.6	11.7
Co-amoxiclav	10.8	11.3	11.8	12.1
Azithromycin	15.9	16.2	16.0	16.0
Cefuroxime	13.1	13.1	12.9	12.7
Ceftriaxone	4.8	5.2	5.2	4.6
Ciprofloxacin	8.5	8.7	8.9	9.1
Clarithromycin	18.1	14.4	14.9	15.2
Doxycycline	15.9	15.5	15.0	15.0
Erythromycin	12.1	12.3	12.6	13.1
Flucloxacillin	7.0	7.1	7.2	7.4
Levofloxacin	10.4	10.9	11.2	12.1
Lymecycline	32.3	32.1	31.9	31.8
Nitrofurantoin	9.0	8.5	8.2	8.0
Phenoxymethylpenicillin	8.5	8.7	9.1	9.5
Trimethoprim	7.3	7.2	7.2	7.1

Between 2010 and 2013, the DDD per item was remarkably similar across the majority of agents used in England. Key changes in DDD per items related to increased DDD per item for levofloxacin (17%), co-amoxiclav (12%), phenoxymethylpenicillin (12%) erythromycin (8%) ciprofloxacin (7%) and amoxicillin (6%); and decreased DDD per item for nitrofurantoin (12%) and doxycycline (5%). Nitrofurantoin in particular has reduced from 9 to 8 DDD per item, which given that the dose recommended has not changed may be the result of shorter prescription courses of this agent, in line with national guidelines (Table 3.4).

Between 2010 and 2013, total hospital prescribing has increased by 7.5% per 1000 inhabitants per day. This prescribing is predominantly related to increased inpatient prescribing which has increased by 11.9% compared to outpatient prescribing which has increased only 1.3% in the

same time interval. Compared to using a population denominator, the consumption of antibiotics in hospital inpatients, expressed as DDD per 100 admissions also increased by 11% between 2010 and 2013. In 2013, the commonest agent prescribed in hospitals was co-amoxiclav at 108 DDD per 100 admissions, 21% of total consumption in inpatients. The consumption of co-amoxiclav increased 12.1% between 2010 and 2013. However between 2008/9 and 2010/11, total inpatient consumption of co-amoxiclav increased by 37%, corresponding to the period when the greatest reductions in first and second generation cephalosporins occurred, suggesting a switch from one antibiotic class to another.<sup>39</sup> The two agents that have increased the most within this table are meropenem (6.0 to 9.2 DDD per 100 admissions) and piperacillin-tazobactam (7.9 and 11.4 DDD per 100 admissions) at 36% and 49% respectively.

There is no doubt that national prescribing guidelines influence both primary and secondary care consumption of antibiotics. This is evidenced by the marked decline in cephalosporin and quinolones consumption in the UK over the last decade, which was prioritised across the healthcare economy to reduce *Clostridium difficile* infection. Between 2007/8 and 2011/12, there was a decline in hospital use of first and second generation cephalosporins by 41% and 55% respectively; third generation cephalosporins only declined by 4%.<sup>42</sup> The use of quinolones, (particularly oral ciprofloxacin) reduced by 24% in this 5 year period. In addition, the marked increase in nitrofurantoin use over the last four years, demonstrates that national infection guidelines promoting this agent for the treatment of urinary tract infections have had an important impact.

In 2012, the most recent year General Practise data was available from Scotland, the consumption of antibiotics was very similar to England (22.1 in Scotland compared with 22.3 DDD per 1000 inhabitants per day in England). However, hospital prescribing was 10% higher in English compared to Scottish hospitals (4.1 compared with 3.7 DDD per 1000 inhabitants per day).<sup>43</sup> The number of general practice prescription items for antibiotics was lower in England (2.1 items per 1000 inhabitants per day) than other UK devolved administrations and the EU median (3.1 items per 1000 inhabitants per day). In England, general practice prescribed 10% fewer items than Scotland, 22% fewer than Wales and 52% fewer than Northern Ireland.<sup>7</sup>

The most recent data published from ECDC, comparing other European countries, was for 2011. In that report the four health administrations in the UK were reported together and were mid-range in the consumption of antibiotics for community prescribing compared with other EU countries. However, England (along with other devolved administrations) was a high outlier, more than twice the EU median, for antibiotic consumption assigned to the hospital sector. This may relate, at least in part, to differential prescribing and recording of prescription practices in UK hospitals. In the UK, hospital prescriptions of antibiotics are dispensed by hospital pharmacies. In many other European countries, both outpatient and medication prescribed on discharge is dispensed in community pharmacies, thereby inflating general practice/ community

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<sup>39</sup> Cooke J et al. Longitudinal trends and cross-sectional analysis of English national hospital antibacterial use over 5 years (2008-2013): working towards hospital prescribing quality measures. *J Antimicrob Chemother* 2014 (in press).

<sup>42</sup> Cooke J, Stephens P, Ashiru-Oredope D, Johnson AP, Livermore DM, Sharland M, on behalf of the Antimicrobial Stewardship Sub-Group of the Department of Health's Advisory Committee for Antimicrobial Resistance and Healthcare Associated Infection. *Public Health* 2014 (in press)

<sup>43</sup> Report on Antimicrobial Use and Resistance in Humans in 2012. Health Protection Scotland and Information Services Division. 2014

consumption and reducing hospital consumption. Further work will need to be undertaken with ECDC and ESAC-net to understand these differences.

ARHAI in consultation with NHS England and PHE have published antimicrobial prescribing quality measures for primary and secondary care.<sup>1</sup> The quality measures for primary care are reduction in total antibiotic consumption and the proportion of cephalosporin, quinolone and co-amoxiclav antibiotics used. The quality measures for secondary care are reductions in total antibiotic consumption and carbapenem consumption. The data in this report will act as a baseline for area teams to review the prescribing within their populations and develop action plans to meet these quality measures.

It is essential, as part of the next stage, that further validation and exploration of the data occurs. In comparing the maps of antibiotic consumption and resistance at a regional and sub-regional level it was noted that commonly areas with high prescribing have in general higher resistance. As these are just single snapshots of the data, this will require further investigation. It is also essential that English healthcare organisations, across primary and secondary care, have access to and review their own consumption data and determine the reasons for prescribing, through local audits, especially where their consumption is different to national trends ensuring that they have an appropriate stewardship strategy in place. Current hospital stewardship and infection guidelines are discussed in Chapter 4.

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<sup>1</sup> Advisory Committee on Antimicrobial Resistance and Hospital Acquired Infections (ARHAI) Recommended Antimicrobial Prescribing Quality Measures. 2014. <https://app.box.com/ARHAI-Minutes-Papers/1/2152374732/18606265032/1>

## Chapter 4: Antibiotic prescribing and stewardship survey in secondary care

### Introduction

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Key area two of the UK five year Antimicrobial resistance strategy highlights the need for optimising prescribing practice through implementation of antibiotic stewardship programmes that promote rational prescribing and better use of existing and new rapid diagnostics.

Controlling antibiotic resistance and ensuring appropriate use of antibiotics requires a multifaceted approach. An antimicrobial stewardship programme (ASP) is an approach that can be used to improve antibiotic prescribing and control antibiotic resistance.

An ASP describes a bundle of measures that can be adopted to promote the appropriate use of antibiotics, including:

- evidence-based optimal standards for routine antibiotic use, eg correct selection of agent, dose, route of administration and duration of therapy
- ensuring competency and educational programmes for all staff that use antibiotics
- communicating antibiotic issues to all stakeholders
- auditing the impact and uptake of these processes
- optimizing outcomes for patients who receive antibiotics

Antimicrobial stewardship has been part of formal guidance by the Department of Health (DH) since 2009. In 2011, the first national dedicated antimicrobial stewardship guidance for secondary care – Start Smart then Focus (SSTF) – was published and recommended for all hospital initiated antibiotic prescriptions.<sup>8</sup> SSTF aims to encourage clinicians to:

- initiate prompt effective antibiotic treatment within 1 hour (or as soon as possible) in patients with life-threatening infections
- document on drug chart and in medical notes: route, indication, dose, duration (RIDD)
- make a clinical review and document antimicrobial prescribing decision at 48 hours

Additionally, the Start Smart then Focus guidance recommended that a multidisciplinary Antimicrobial Stewardship Committee should be set up to develop and implement the organisation's ASP for all adults and children admitted to hospital. This committee/management team were recommended to report to at least one of the following:

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<sup>8</sup> Ashiru-Oredope, D., Sharland, M., Charani, E., McNulty, C. & Cooke, J. Improving the quality of antibiotic prescribing in the NHS by developing a new Antimicrobial Stewardship Programme: Start Smart—Then Focus. *Journal of Antimicrobial Chemotherapy*. 2012. 67 (suppl 1), i51-i63

- Director of Infection Prevention and Control (DIPC)
- Infection Prevention Control Committee (IPCC)
- Drugs and Therapeutic Committee or equivalent

The 2011 national point prevalence survey (PPS) in secondary care of healthcare associated infections and antimicrobial use (AMU) highlighted that the overall prevalence of antimicrobial use in England was 34.7%; with higher prevalence of AMU in adults 35.3% compared with paediatrics 28.7%.<sup>40</sup> AMU prevalence was greatest in intensive care units at 60.8%. The PPS found that when reviewing hospital inpatient prescriptions, the most common reason for prevalent prescriptions related to community acquired infections (53%); most frequently respiratory tract infections (30.9%) then skin, soft tissue, bone and joint infections (19.0%).

Aspects of Antimicrobial Stewardship activities detailed in DH guidance were assessed in acute hospitals in England in 2011 (published 2013).<sup>41,42,43</sup> Following the publication of SSTF in 2011, an initial assessment of its implementation was carried out in 2012.<sup>44</sup>

This chapter will present the results of a survey coordinated by ESPAUR which aims to understand and interpret data on antibiotic consumption and resistance in the context of:

- antimicrobial policy
- antimicrobial stewardship
- SSTF uptake and implementation
- education and training: frequency and format
- clinical guidelines for antibiotic choice and duration
- electronic-prescribing uptake and secondary use of data

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<sup>40</sup> English National Point Prevalence Survey on Healthcare-associated Infections and Antimicrobial Use, 2011. Available at: [http://www.hpa.org.uk/webc/hpawebfile/hpaweb\\_c/1317134304594](http://www.hpa.org.uk/webc/hpawebfile/hpaweb_c/1317134304594)

<sup>41</sup> Department of Health. The Health and Social Care Act 2008: Code of Practice for Health and Adult Social Care on the Prevention and Control of Infections and Related Guidance. 2008. [http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH\\_110288](http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/en/Publicationsandstatistics/Publications/PublicationsPolicyAndGuidance/DH_110288) (18 July 2014, date last accessed).

<sup>42</sup> Wickens H, Farrell S, Ashiru-Oredope D, Jacklin A, Holmes A. The increasing role of pharmacists in antimicrobial stewardship in English hospitals. *Journal of Antimicrobial Chemotherapy*. 2013.

<sup>43</sup> Department of Health and the Health Protection Agency. Clostridium difficile infection: How to deal with the problem. 2008 [http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod\\_consum\\_dh/groups/dh\\_digitalassets/documents/digitalasset/dh\\_093218.pdf](http://webarchive.nationalarchives.gov.uk/20130107105354/http://www.dh.gov.uk/prod_consum_dh/groups/dh_digitalassets/documents/digitalasset/dh_093218.pdf) (18 July 2014, date last accessed).

<sup>44</sup> Start Smart then Focus: a survey of implementation [https://www.gov.uk/government/uploads/system/uploads/attachment\\_data/file/245884/Poster\\_Start\\_Smart\\_Then\\_Focus.pdf](https://www.gov.uk/government/uploads/system/uploads/attachment_data/file/245884/Poster_Start_Smart_Then_Focus.pdf) (18 July 2014, date last accessed).

# Methods

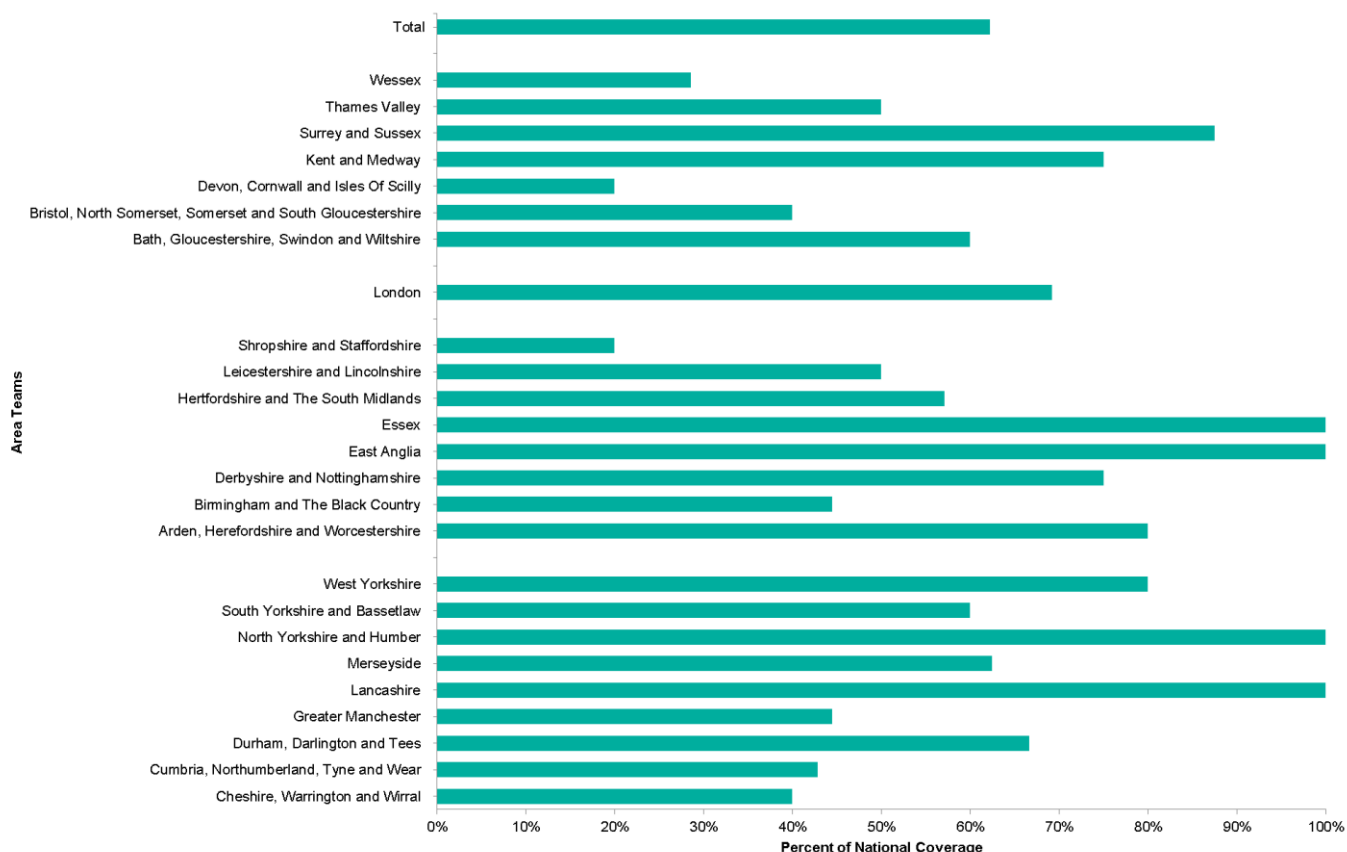
A web-based survey on clinical guidelines and antibiotic stewardship in secondary care was distributed nationally to 91% of Acute Trusts in England (146/159). The survey was piloted by 18 Acute Trusts in the East of England. Following amendments to the survey as suggested by the pilot, it was distributed nationally via email to a further 128 Acute NHS Trusts. The survey was estimated to take 15-20 minutes to complete and the responses were analysed using STATA (version 13) and Microsoft Excel. As this was a voluntary audit activity completed by healthcare professionals, ethics approval was not required.

The survey can be found in Appendix D.

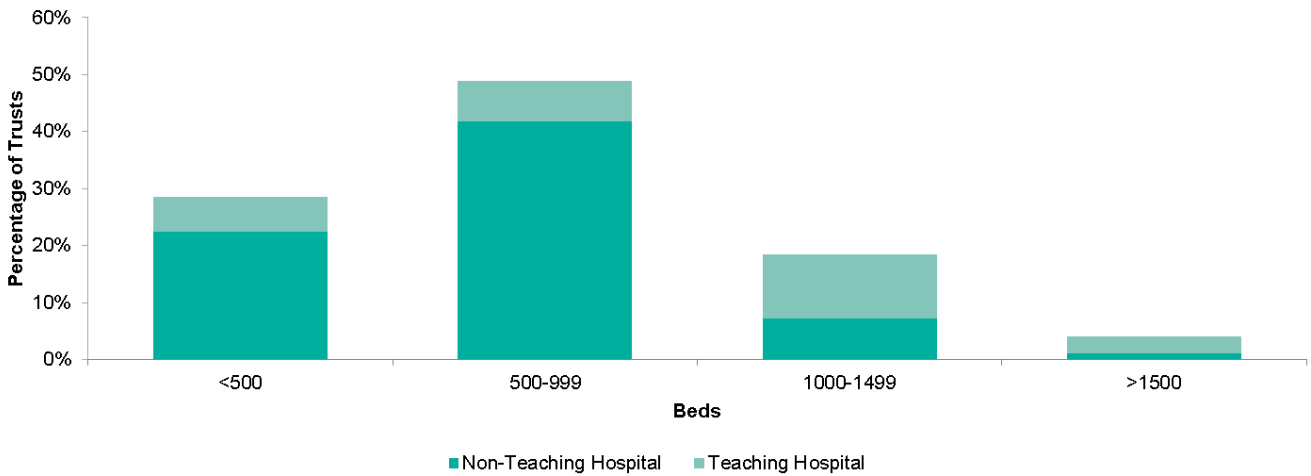
# Results

In 2014 there were 159 Acute NHS Trusts in England; 146 were contacted, of which 99 responded (response rate of 67.8%). There were representatives from all area teams (ATs) in England (Figure 4.1). Twenty-eight of responding Trusts were teaching hospitals and 71 non-teaching hospitals. The average number of hospitals sites per trust was 2.2 (range 1 – 5), with half of the hospitals having 500-999 beds (Figure 4.2).

**Figure 4.1 Proportion of Acute Trust survey responses by area team, England 2014 n=99/159**



**Figure 4.2 Sizes of Acute trusts by teaching and non-teaching, n=99**

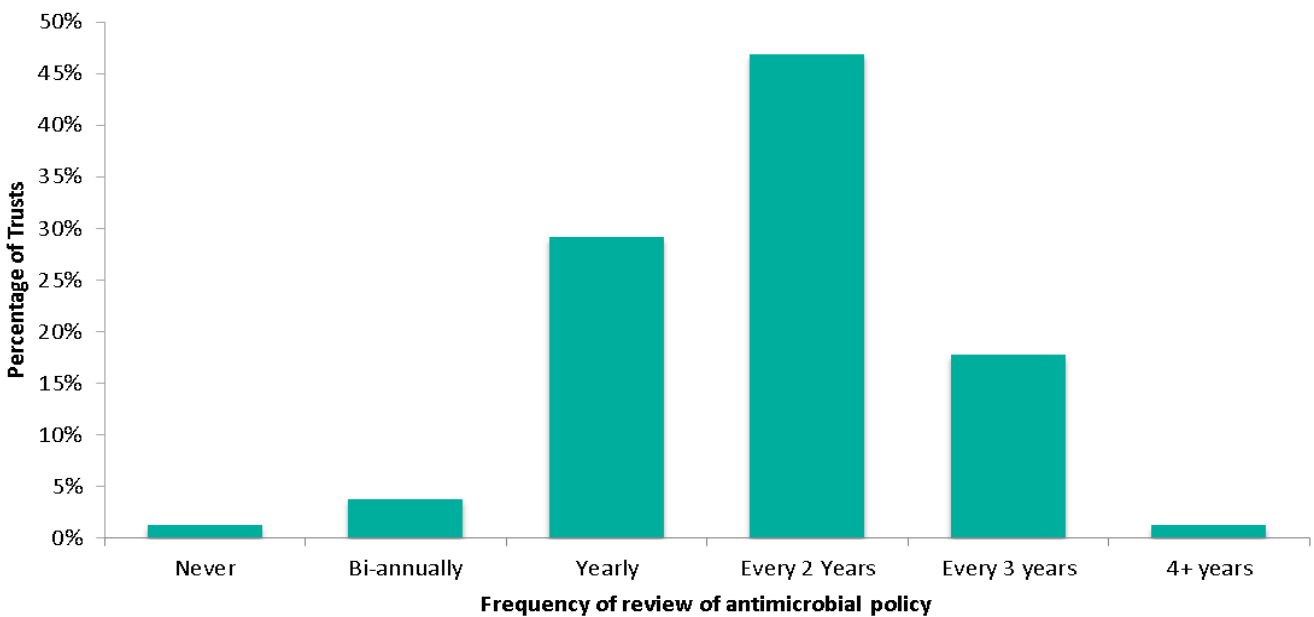


### Antibiotic policy and stewardship activities

Over 94% of responding trusts reported having an antimicrobial formulary and empiric guidance in place. Approximately 37% of trusts update their antimicrobial policies every 2 years with 23% and 14% updating yearly or every three years respectively (Figure 4.3). Nine percent did not provide answers for frequency of antimicrobial policy updates.

Reserved/restricted antibiotics lists were present in 86% of trusts and 82% utilised an intravenous to oral switch policy; unchanged from 2011. Compared to the 2011 audit, fewer trusts reported using an automatic stop policy, 21% compared to 36%, and the number of trusts with a separate antimicrobial drug chart/section increased from 32% to 58% (Table 4.1). The proportion of trusts with separate antimicrobial drug charts/sections varies across ATs (Figure 4.4). All trusts without an automatic stop policy had a separate antimicrobial drug chart/section.

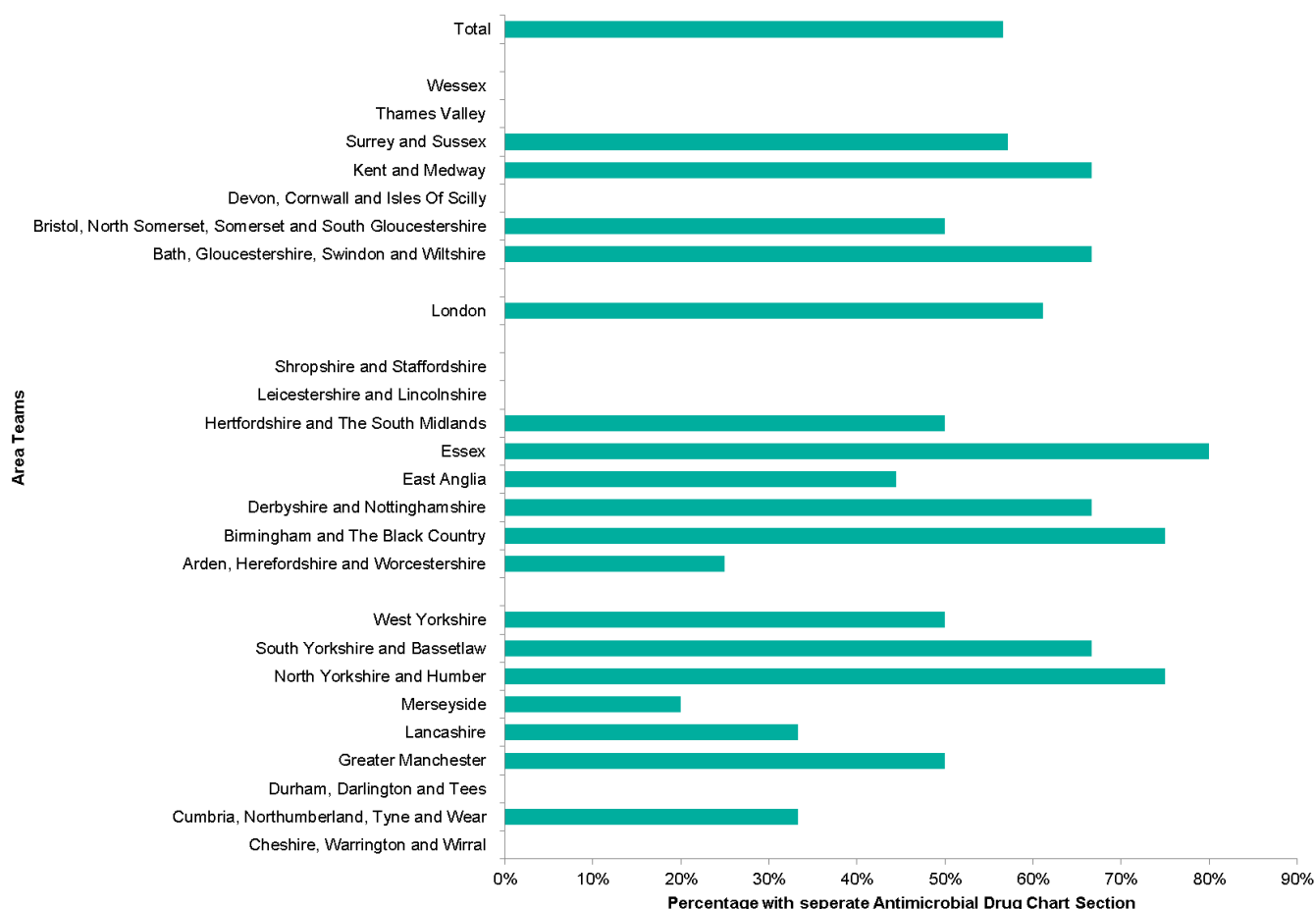
**Figure 4.3 Frequency of review of Antimicrobial Policy in Acute trusts, n=79**



**Table 4.1 Antimicrobial Policy key elements, 2011 and 2014 surveys, n=99**

Antimicrobial Policy: key elements reported by Trusts	2011	2014	Change
Antimicrobial formulary	96%	93%	-3%
Empiric usage guidance	99%	93%	-6%
Reserved antibiotic list	91%	85%	-6%
IV-Oral switch	87%	81%	-6%
Surgical antibiotic prophylaxis	100%	98%	-2%
Automatic stop policy	36%	21%	-14%
Separate antibiotic drug chart/section	32%	58%	+26%
Restricted antibiotics list	90%	90%	0%

**Figure 4.4 Proportion of trusts who reported separate antimicrobial drug charts/section, n=99**





## The role of antimicrobial pharmacists

Of the responding trusts 96% had at least one substantial antimicrobial specialist in post (average 1.5 specialist antimicrobial pharmacist/pharmacy technician per trust). A vast majority (90%) of all responding trusts had a specialist pharmacist at band 8a and above as the main post holder; five trusts had a consultant antimicrobial/infectious diseases pharmacist in post and only one trust had a pharmacy technician (band 5) as the main post holder.

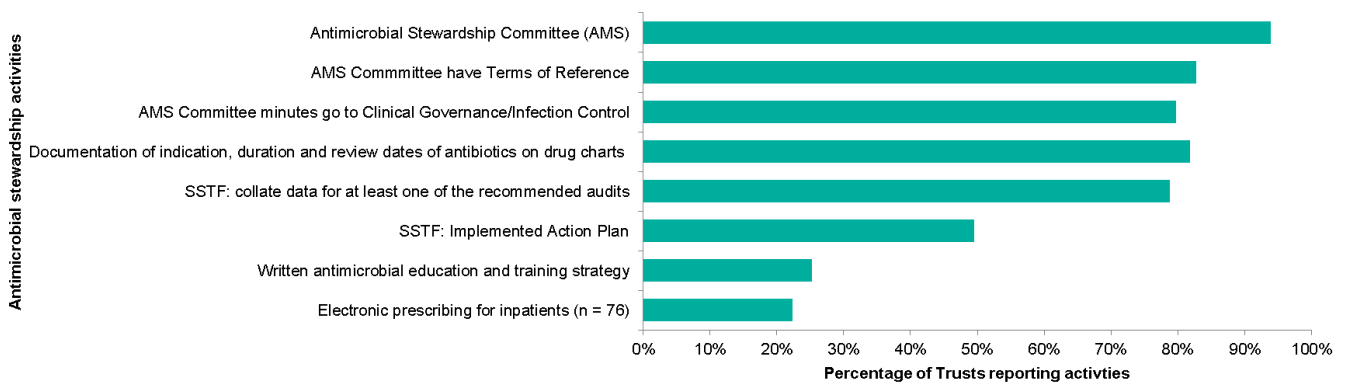
The survey responses demonstrated that the antimicrobial pharmacist had an extensive role which included: writing antimicrobial guidelines and policies (97%); making anti-infective formulary decisions (choosing which antimicrobials should be available on the trust formulary) (94%); being available by phone or pager for referrals (93%) performing multi-disciplinary antibiotic review rounds (88%), as well as attending Trust infection prevention and control committee meetings (90%). Maintaining awareness of local resistance patterns (56%), horizon scanning (71%) and attending ward rounds on specialities with high antibiotic use (65%) were less common activities.

For the first time we captured collaboration between primary and secondary care colleagues on development of antimicrobial guidelines and stewardship activities across both sectors; 37% of respondents had a working relationship with primary care pharmacy colleagues in their area and were able to provide a named contact.

## Start smart then focus evaluation

The survey demonstrated that 94% of trusts had a dedicated AMS committee. Of these trusts, 88% responded that the AMS committee had terms of reference, 97% minutes and actions list and 85% had the recommended governance structure reporting to the IPCC or equivalent (Figure 4.5).

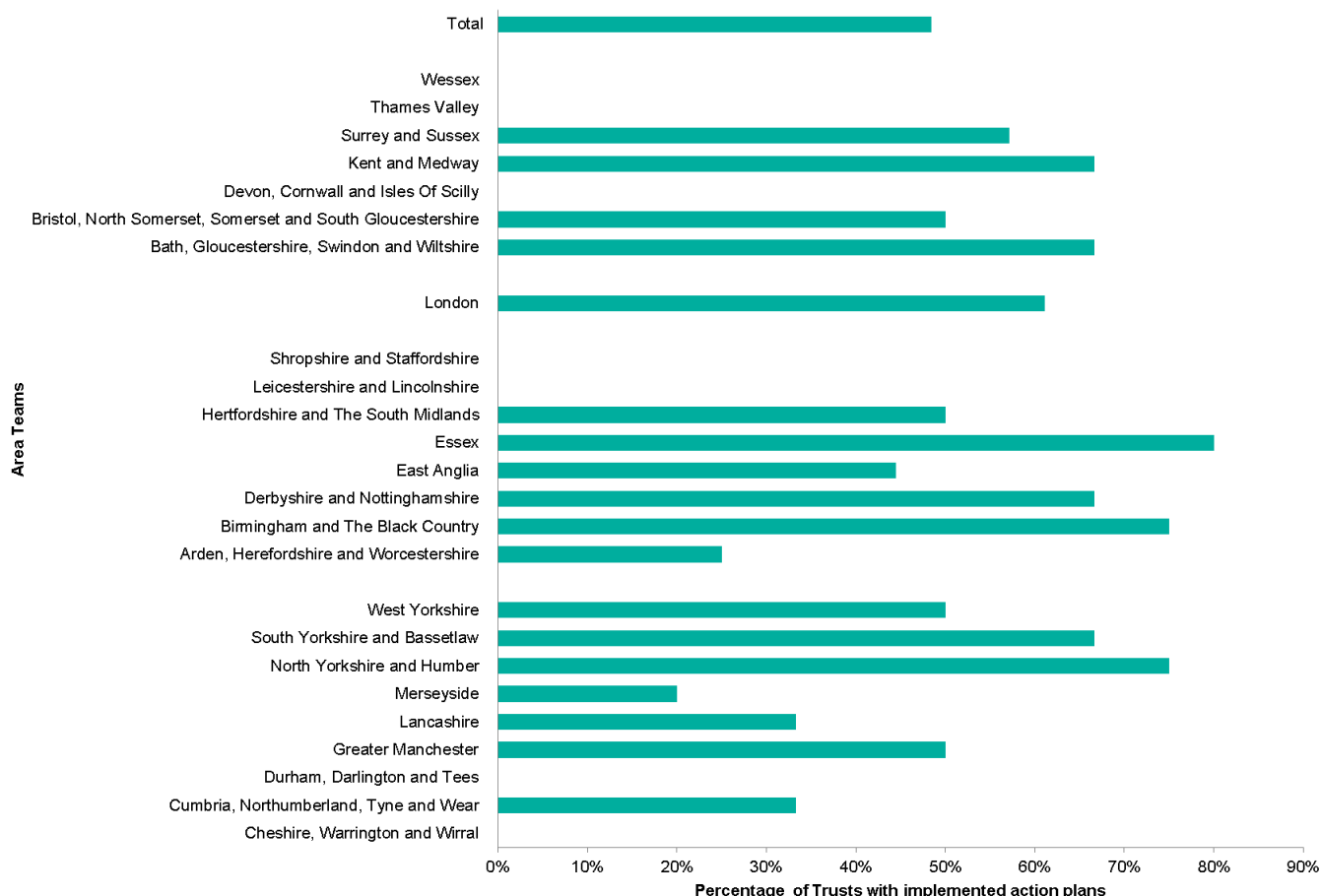
**Figure 4.5 Proportion of trusts who have implemented key antimicrobial stewardship activities recommended in SSTF guidance, n=99**



The membership of the committees varied across respondents. Microbiologists (92%) and specialist antimicrobial pharmacists (87%) were the most common members. Representation from nursing (43%), physicians (47%), general pharmacists (7%), junior doctors (21%) and surgeons (36%) were low.

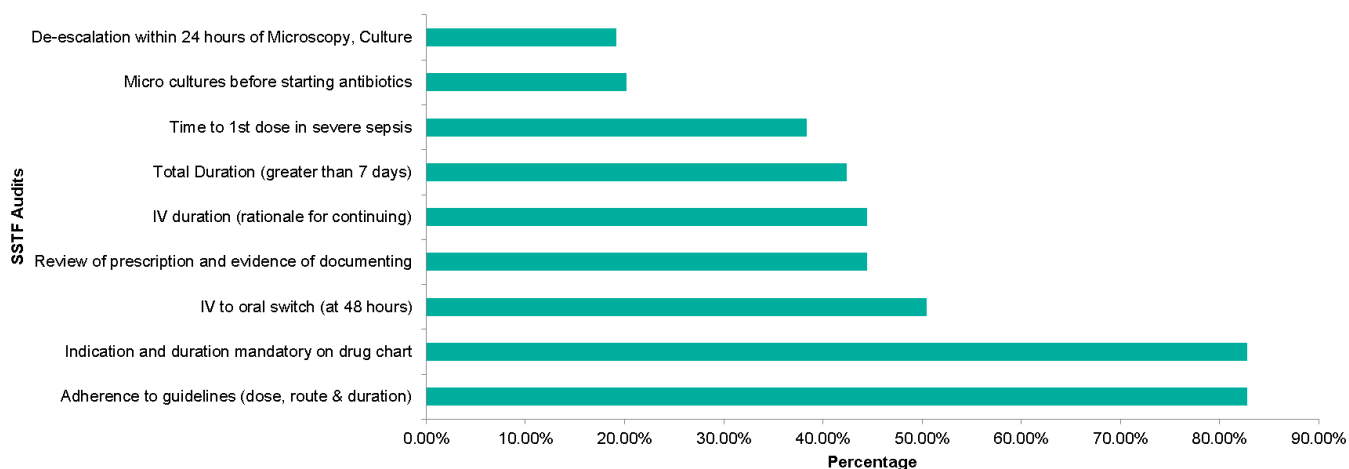
A large majority (87.9%) of trusts reported reviewing the SSTF guidance formally or informally; only 48% of trusts reported implementing a SSTF action plan after the guidance review (p=0.02). There was variation across the Area Teams for the implementation of these actions plans (Figure 4.6).

**Figure 4.6 Proportion of trusts with implemented SSTF action plan, n=99**



Thirty-nine percent (39%) of trusts conducted a Trust-wide point prevalence survey quarterly, whereas 85% conducted their PPS at least annually; only 3% of Trusts reported never conducting a PPS (n=80). Seventy-nine percent of all respondents collate data for at least one or more of the suggested audits within Trust audit plan or as part of Trust wide antimicrobial PPS The most frequent recommended SSTF audits included: adherence to guidelines of dose, route and duration (84%), indication and duration documented on drug chart (82%) and IV to oral switch at 48 hours (51%). Other audits were performed by fewer Trusts (19-44%) (Figure 4.7).

**Figure 4.7 Proportion of Trusts who have implemented audits recommended by SSTF, 2014, n=99**



Survey respondents were asked to provide examples of local initiatives of implementing Start Smart Then Focus that would be useful to others (a selection is highlighted in Table 4.2). Additionally respondents were also asked to provide feedback regarding the usefulness of SSTF and improvements required as well as provide practical examples of how they had implemented SSTF (Table 4.3).

**Table 4.2 Reported good examples of SSTF Implementation within trusts**

### EXAMPLES OF SSTF IMPLEMENTATION

#### **Training and Education:**

*Included in the mandatory infection control training for all Doctors. Electronic prescribing has enable us to force the addition of a stop date on oral treatment and addition of an indication.*

Derby Hospitals NHS Foundation Trust

*Antimicrobial guidelines being accessed from mobile phones and desktops from a new app. [We are] producing an e-learning package for medics and pharmacists to improve their understanding of antibiotic prescribing.*

Portsmouth Hospitals NHS Trust

#### **Many Trusts are performing audits, some examples of good practice are listed below:**

*Prescribers [perform] audits themselves, [this] creates ownership within medical teams...; the data is validated by an antimicrobial pharmacist.*

University Hospitals of Leicester

*Monthly prudent prescribing indicator audits completed by doctors on consultant led ward rounds. F1 doctors allocated as antibiotic 'champions' on each ward.*

Kingston Hospital NHS Foundation Trust

*Implemented antimicrobial stewardship audits led by a group of antimicrobial consultant champions (one per specialty).*

Nottingham University Hospitals NHS Trust

*[We conduct] monthly point prevalence 'antibiotic performance reports' where we document Trust-wide documentation of indication and stop/review dates. This is fed back to the [Infection Prevention and Control] Committee and discussed at various clinical governance meetings; this has led to improvements in documentation rates*

Cambridge University Hospitals NHS Foundation Trust

*Regular audits of quality measures (5 patients per ward per month).*

- 1. Indication documented in medical notes*
- 2. Choice of antibiotic(s) according to guideline or justification for off-guideline*
- 3. Prescribed dose appropriate for age, weight, organ function, disease severity*
- 4. Documented evidence of review of prescription at 48-72 hours*
- 5. Total course length not exceeding 7 days or justified*

University Hospital Southampton NHS Foundation Trust

*Changing Environment: We have audited whether antibiotics are reviewed at 48 hours.*

The Great Western Hospitals NHS trust

**Table 4.3 Trust feedback regarding the usefulness of SSTF and improvements required**

### IMPROVEMENTS FEEDBACK

*Structure/order of content is not as easy to follow as it might be; sometimes seems to refer to the same points at more than one place in the document, making it difficult to concisely understand what the document requires of Trusts and their employees.*

*The audit programme is perhaps too extensive/difficult to implement comprehensively and it may have been better to pick one or two appropriate outcome measures & suggest that they are completed as mandatory measures to give some element of comparative data & potential for benchmarking.*

*It would be nice if these could be 'badged' and adapted nationally (e.g PHE, UKCPA) so that there is a definitive set of resources we could all use.*

*Shared examples of good practice are essential.*

*It would be useful to have recommendations on what to measure and report in terms of antibiotic usage, and what [key performance indicators] to report on for antibiotic use.*

*Guidelines are not that helpful as there is no push to actually use them. A lot of the work on this needs to be done nationally (especially the education aspects) rather than everyone working locally on the same things and duplicating work.*

*Needs a national data collection for audits to allow benchmarking.*

*Microbiology results are not available at 48 hours so treatment related decisions based on these tend to be made at 72 hours. This is a more realistic standard for implementation and audit against. Recommendations could have been prioritised to ease implementation.*

*Useful but would suggest some of the audit criteria are made mandatory eg annual submission of DDD data. The audits need to be practical and focussed. For example time to 1st dose + review of micro cultures prior to starting antibiotics are a challenge to audit.*

*Having locally agreed antimicrobial CQUINs targets in 2012/13 really helped us get antimicrobial stewardship on the agenda - very helpful (and resulted in improved compliance with prescribing indicators)!*

## Education and training

Only 24% of all respondents had a written antimicrobial education and training strategy. Although 66% of responding trusts provide in person training on antimicrobial stewardship and prescribing and provide antibiotic guidelines for doctors on induction; only 22% performed competency assessments for prescribers. Seven trusts who did not provide in person training provided mandatory e-learning training for junior doctors. Seventy-two percent of trusts provide teaching on induction for all pharmacists. Training for nurses and non-medical prescribers however was low at 28% and 20% respectively (Table 4.4).

**Table 4.4 Reported education and training initiatives from Acute trusts, n=99**

Education and Training Initiatives	Percent
Trust has a written Antimicrobial Education and Training Strategy	24%
Competency assessments	
carried out for prescriber	22%
are mandatory	20%
All doctors on induction receive	
antibiotic guidelines	63%
antibiotic guidelines and a lecture/in person training on antimicrobial prescribing	66%
antibiotic guidelines and need to do an e-learning module on antimicrobial prescribing	21%
Teaching on induction for	
all nurses	28%
all pharmacists	72%
non-medical prescribers	20%
Mandatory e-learning for	
senior doctors (registrar and higher)	16%
junior doctors	21%

## Empiric guidelines

Tables 4.5-4.8 and Figures 4.8-4.13 highlight the recommended first line antibiotics and combination therapies within NHS Acute Trust empiric guidelines for ten infections: (community acquired pneumonia CURB 0-1, 2, 3-4; hospital acquired pneumonia, lower, upper and catheter associated urinary tract infections, cellulitis, clinical sepsis with no defined source and intra-abdominal sepsis including hepatobiliary).<sup>40</sup> The response rate to the guidelines section was lower than the stewardship questions (~50%).

Eighteen different antibiotics were recommended alone or as part of a combination in empiric antibiotic guidelines. Penicillins in particular amoxicillin (17.3%); co-amoxiclav (12.8%) and piperacillin-tazobactam (9.4%) were three of the five most frequently recommended antibiotics in guidelines. The other two were clarithromycin (12.9%) and gentamicin (12.8%). Cephalosporins, quinolones and carbapenems were in bottom five recommended 1<sup>st</sup> line antibiotics (Table 4.5). For alternative antibiotic treatments eg penicillin allergy the most common recommendations in empiric guidelines were clarithromycin, doxycycline, nitrofurantoin, ciprofloxacin and meropenem (Table 4.6-4.9).

Trusts were asked to provide the duration of treatment for the first line therapies discussed above. In addition to the categories presented, some trusts reported unspecified "other" durations or did not report treatment durations. It may be that empiric guidelines for some trusts did not specify treatment duration; these differences are reflected in the sample sizes reported (Figures 4.8, 4.10, 4.12).

**Table 4.5 First line and alternative antibiotics recommended in empiric guidelines in English acute NHS trusts for ten indications in 74 Acute trusts, n=1024**

Antibiotics	Percent	
	First Line	Alternate to first line
Amoxicillin	17.3	1.0
Clarithromycin	12.9	14.5
Co-Amoxiclav	12.8	2.7
Gentamicin	12.8	5.4
Piperacillin-Tazobactam	9.4	2.7
Flucloxacillin	7.6	0.9
Benzylpenicillin	5.0	0.3
Trimethoprim	4.9	2.6
Nitrofurantoin	3.0	0.7
Metronidazole	4.3	7.7
Doxycycline	2.7	10.5
Vancomycin	2.3	4.3
Teicoplanin	0.9	6.1
Cefuroxime	0.8	6.1
Meropenem	0.7	6.3
Ciprofloxacin	0.6	6.3
Levofloxacin	0.1	5.8
Other antibiotics	2.0	16.2

<sup>40</sup> English National Point Prevalence Survey on Healthcare-associated Infections and Antimicrobial Use, 2011. Available at: [http://www.hpa.org.uk/webc/hpawebfile/hpaweb\\_c/1317134304594](http://www.hpa.org.uk/webc/hpawebfile/hpaweb_c/1317134304594)

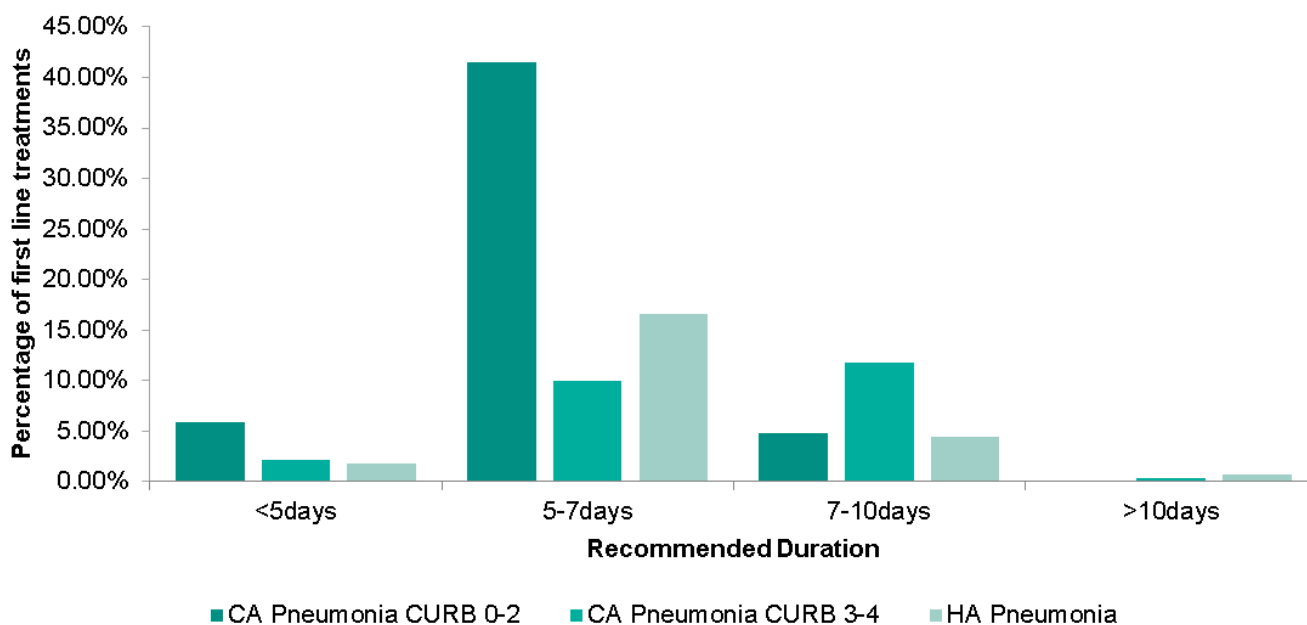
## Respiratory tract infections

**Table 4.6 Reported number of antibiotics used for the treatment of pneumonias in empiric guidelines**

Indication	n	Number of antibiotic agents used in treatment		
		One	Two	Three
Community acquired pneumonia (CURB-65) 0-1	74	78.4%	21.6%	0.0%
Community acquired pneumonia CURB-65 2	74	14.9%	85.1%	0.0%
Community acquired pneumonia CURB-65 3-4	73	2.7%	95.9%	1.4%
Hospital acquired Pneumonia	72	73.6%	25.0%	1.4%

Penicillins (in particular amoxicillin) are recommended in all of the empiric guidelines for community acquired pneumonia either as monotherapy (CURB 1) or in combination with a second agent (CURB 2 and 3-4) (Table 4.6). For hospital acquired pneumonia (n=72), 73% recommend monotherapy with penicillins, most commonly piperacillin-tazobactam (31.9%) or co-amoxiclav (22.2%); alternatively, 16.7% of Trusts recommend gentamicin in combination therapy with benzylpenicillin (6.9%) or co-amoxiclav (5.5%) (p=0.01). The most common duration recommended in empiric guidelines for community acquired pneumonia CURB 0-2 and hospital acquired pneumonia was 5-7days, compared with 7-10 days for CA pneumonia CURB 3-4 (Figure 4.8).

**Figure 4.8 Differences in empiric guideline recommendations for first line treatment duration for pneumonias, n=272**





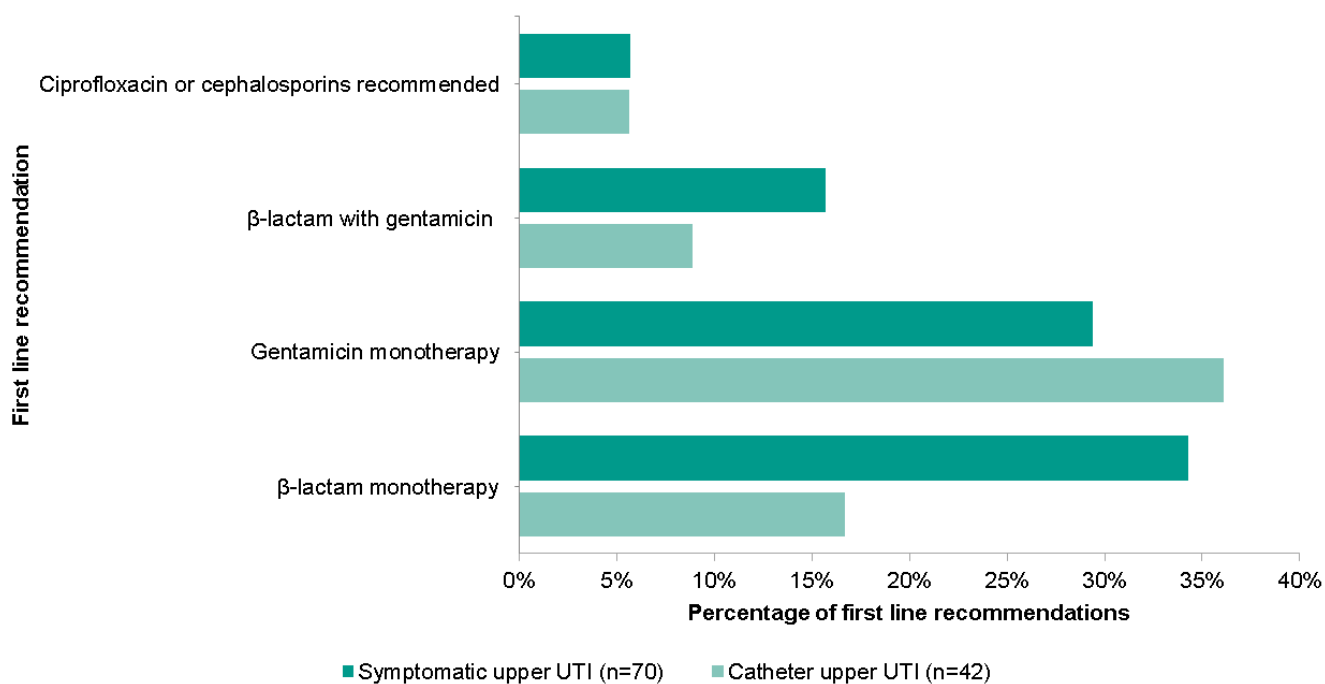
## Treatment of urinary tract infections

**Table 4.7 Reported number of antibiotics used for the treatment of UTIs in empiric guidelines**

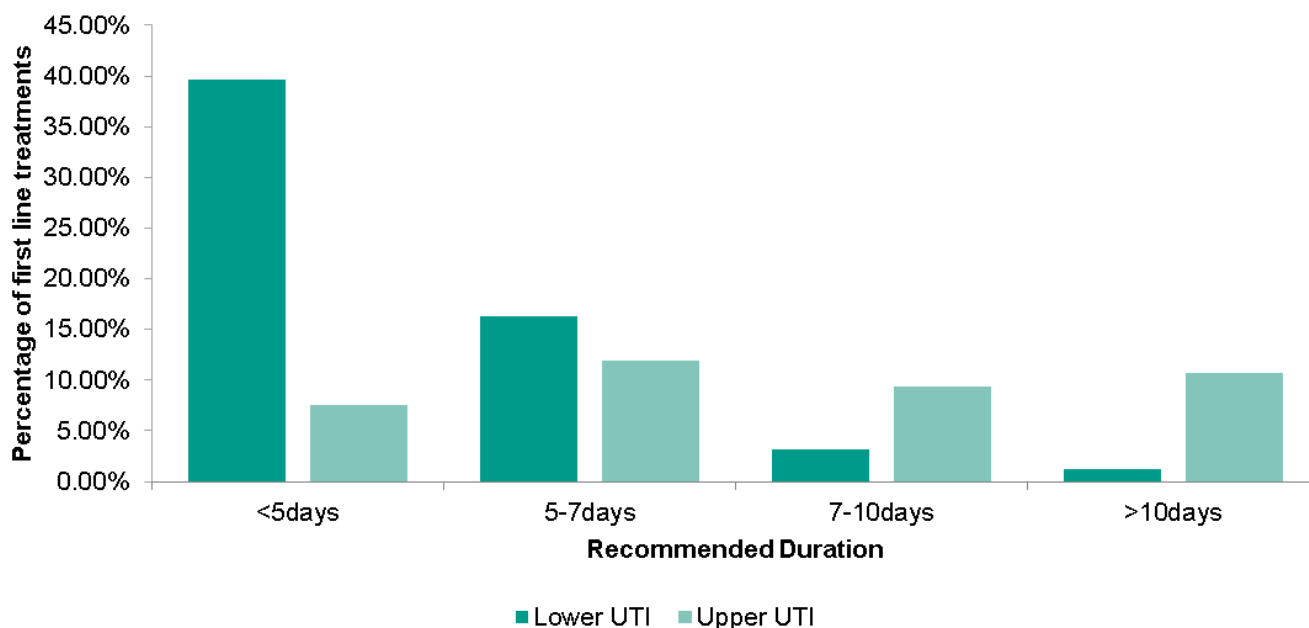
Indication	n	Number of antibiotic agents used in treatment		
		One	Two	Three
Symptomatic lower UTI	72	98.6%	1.4%	0.0%
Symptomatic upper UTI	70	72.9%	25.7%	0.3%
Catheter Associated UTI	42	85.7%	16.7%	0.0%

There were differences between treatment in lower UTI, upper UTI and catheter associated UTIs. A single antibacterial was recommended for the majority (>72%) of urinary tract infections. For lower UTIs, the predominant antibiotics recommended in empiric guidelines were trimethoprim (54.2%) or nitrofurantoin (20.8%) monotherapy; the remaining 23% recommended penicillins and glycopeptides. First line antibiotics recommended for treatment of symptomatic upper UTI and catheter associated upper UTI varied significantly across the county, the first line treatments presented in Figure 4.9 account for 85% and 67% of the recommended treatments for symptomatic upper and catheter associated UTIs respectively. The recommended duration for treatment of UTIs varied across the organisations, 40% recommended <5 days treatment duration for lower UTI and 15% recommended 5-7 days. There was greater variability in duration recommended for upper UTI (Figure 4.10).

**Figure 4.9 Differences in empiric guideline first line antibiotics recommended for treatment of symptomatic upper UTIs (n=70) and catheter associated upper UTIs (n=42)**



**Figure 4.10 Differences in empiric guideline recommendations for first line treatment duration for upper UTIs versus lower UTIs, n=159**



### Clinical sepsis and cellulitis

**Table 4.8 reported number of antibiotics used for the treatment of sepsis and cellulitis in empiric guidelines**

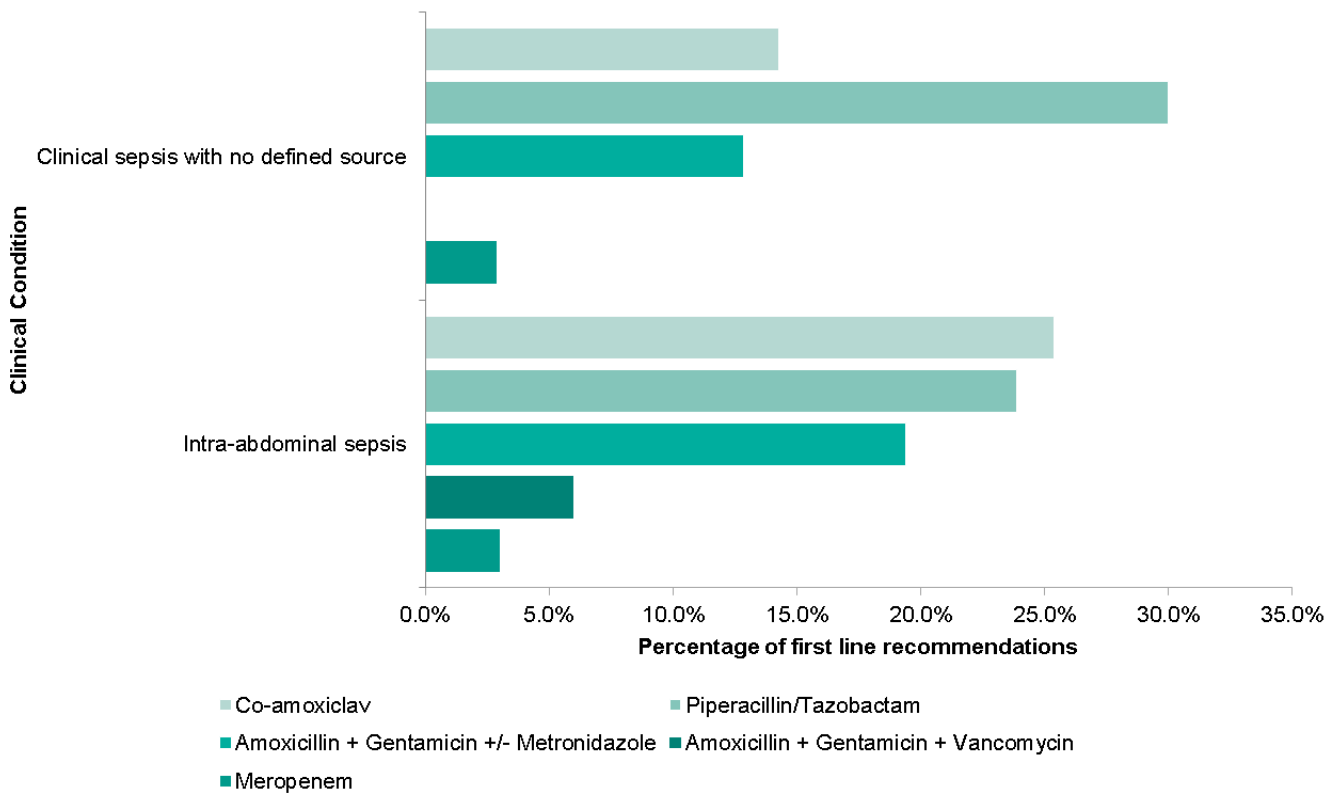
Indication	n	Number of antibiotic agents used in treatment		
		One	Two	Three
Clinical Sepsis with no defined source	70	35.7%	42.9%	21.4%
Intra-abdominal sepsis including hepatobiliary	67	43.2%	28.4%	28.4%
Cellulitis	72	70.8%	29.2%	0.0%

A majority of trusts recommend the combination of two or more agents in the treatment of clinical sepsis with no defined source (63.1%) and intra-abdominal sepsis (56.7%) (Table 4.8). All guidelines include the use of penicillins either as monotherapy or in the combination of therapy.

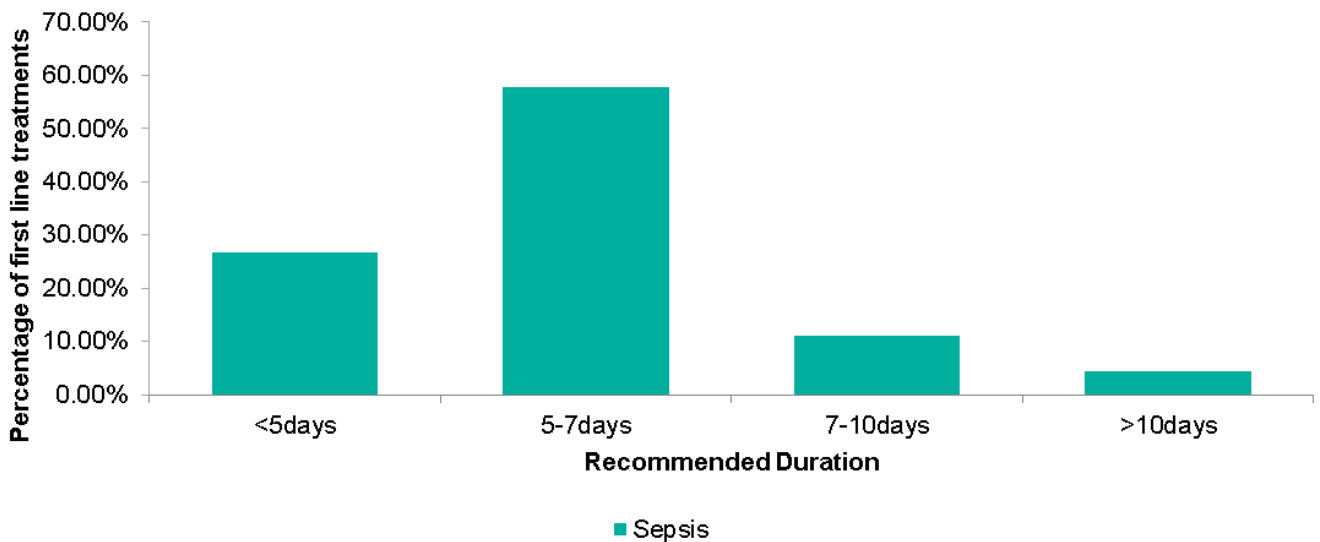
The recommended treatments highlighted in Figure 4.11 account for 60% and 77.6% of first line empiric guidelines demonstrating the variance in empiric guidelines for the treatment of clinical sepsis with no defined source and intra-abdominal sepsis respectively. More than 50% of Trusts that responded recommended treating for 5-7 days (Figure 4.12).

For the treatment of cellulitis, 68% of Trusts recommended flucloxacillin monotherapy and 22% recommend the use of a combination of penicillins (benzylpenicillin) and flucloxacillin. The most common duration recommendations were 5-7 days (45%) and 7-10 days (38%).

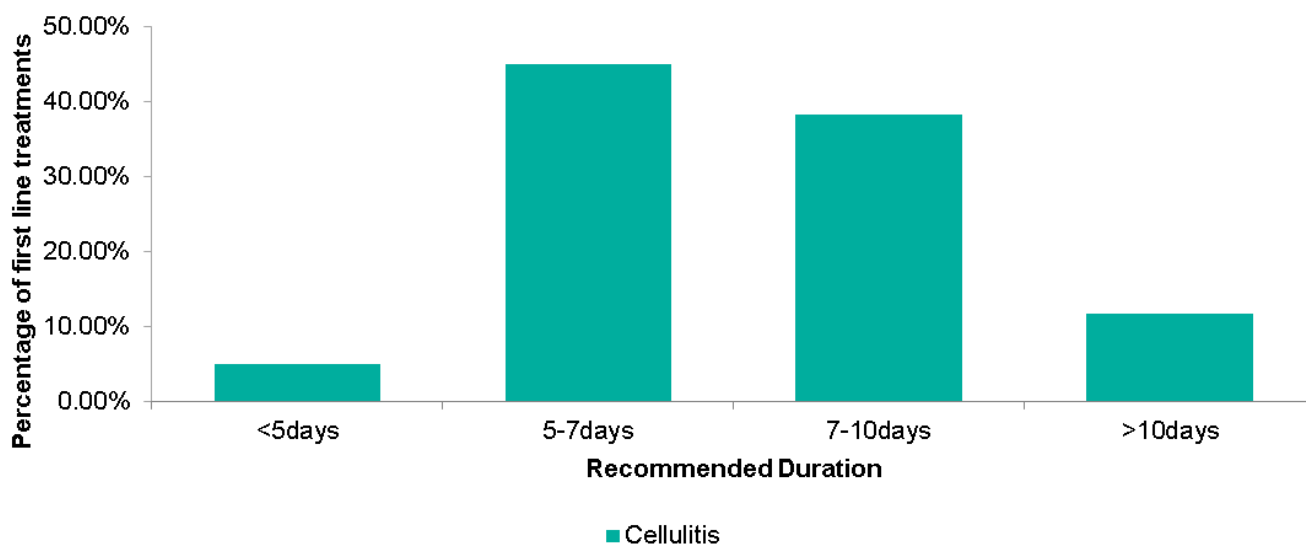
**Figure 4.11 Differences in empiric guideline first line antibiotics recommended for treatment of clinical sepsis, n=70, and intra-abdominal sepsis, n=67**



**Figure 4.12 Differences in empiric guideline recommendations for first line treatment duration for sepsis, n=90**



**Figure 4.13 Differences in empiric guideline recommendations for first line treatment duration for cellulitis UTIs, n=60**



### Electronic prescribing

Of the 76 respondents for this question, 17 (22.4%) trusts had electronic prescribing for at least one in-patient area, only six trusts (7.9%) had e-electronic prescribing for 90% of all prescriptions in all in inpatient areas (Table 4.7). A further 11 trusts stated that electronic prescribing will be in place for all in patient areas by April 2015.

**Table 4.9 Availability of electronic prescribing in patient areas in Acute NHS trusts, n=76**

E-prescribing	Percentage
Trust has electronic-prescribing for inpatients	22.4
e-prescribing for >90% inpatients in:	
Adult ICU	7.9
Paediatric/neonatal ICU	3.9
Neonatal/paediatrics	7.9
Adult medicine	15.8
Adult surgery	14.5
Geriatrics	15.8
All Areas	7.9
Other	5.3

## Discussion

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Components of antimicrobial policies have remained consistent from 2011 to 2014. However, two significant changes are important to highlight; fewer Trusts reported utilising an automatic stop policy and the number of Trusts with a separate antimicrobial drug chart/section had increased. It is likely that separate antimicrobial sections/drug charts for antimicrobials reduced the need for automatic stop policies. The survey results show that all Trusts without an automatic stop policy had a separate antimicrobial section/drug chart.

The role of specialist antimicrobial pharmacists continues to remain embedded within Acute NHS Trusts with most having a specialist pharmacist at band 8a and above in post. In addition the antimicrobial pharmacist role spanned a broad range of specialist activities.

For the first time we captured collaboration between primary and secondary care colleagues on development of antimicrobial guidelines and stewardship activities across both sectors; 37% of respondents had a working relationship with primary care pharmacy colleagues in their area and were able to provide a named contact. Cross-sector Antimicrobial Stewardship is important; feasibility and standardisation should be explored.

Effective implementation of the SSTF guidance in particular interventions to increase the frequency and effectiveness of post prescription reviews could reduce unnecessarily broad-spectrum and prolonged antibiotic therapy.

The 2012 SSTF survey found that of the acute trusts that responded to the survey 43% had completed a formal review of SSTF. Between the 2012 and 2014 surveys, an additional 12% of respondents had formally reviewed SSTF. There has been no change in the proportion of Trusts that have implemented an action plan. While 79% of acute trusts collated data on at least one of the recommended audits in SSTF, areas correlated to patient outcomes ( eg time to first dose in severe sepsis) were rarely performed (Figure 4.5).

Comments from respondents highlighted that the NHS has found SSTF to be very useful in focusing attention on improving antimicrobial stewardship within the NHS; they also provided useful feedback for further improvements in the SSTF guidance as well as practical examples of how SSTF has been implemented. It is important that more Trusts within the NHS formally review and have an action plan in place to implement the SSTF guidance.

Whilst more than 90% of responding NHS Trusts had an antimicrobial stewardship committee as recommended by the SSTF guidance, the survey showed that representation from outside the specialist antimicrobial stewardship area (ie infection or pharmacy specialists) on antimicrobial committees remained low. In order to embed antimicrobial stewardship recommendations within organisations, engagement with the development and implementation of guidelines and audits from a broad range of professional groups ( eg nursing, general and specialist surgeons and physicians, junior doctors and general pharmacists) is essential.

Extrapolation of the empiric guidelines data may be limited due to 74% of respondents completing the guidelines questions in the survey. For some conditions, symptomatic upper UTI and catheter associated UTI, the response rates were particularly low. It is unclear why the responses were much lower for symptomatic upper UTI and catheter associated UTI for example, it may be that these Trusts did not have specific guidelines for these infections.

In 2013, a survey of post prescription reviews recommended by SSTF determined that trust antibiotic policies relied heavily on broad-spectrum penicillins (particularly penicillin/inhibitor combinations) and prolonged courses (7 days or more).<sup>45</sup>

The top five antibiotics recommended in empiric guidelines for 10 common infections were amoxicillin, clarithromycin, co-amoxiclav, gentamicin, and piperacillin-tazobactam.<sup>40</sup> Although meropenem did not feature in the top 10 of recommended antibiotics recommended as first line in empiric guidelines, meropenem was in the top 10 most commonly prescribed antibiotics in the 2011 PPS. The recommendation by the Department of Health guidance limiting the use of fluoroquinolone and cephalosporin to minimise the risk of *Clostridium difficile* infection (CDI) were also reflected by the results of this survey; cephalosporins and quinolones were recommended in less than 6% of empiric guidelines and only for upper and catheter associated urinary tract infections. However co-amoxiclav, potentially a high risk antibiotic for CDI from observational data, was commonly prescribed.

Only 8% of the 76 responding NHS Trusts had electronic prescribing in all in patient areas. Monitoring of key elements recommended by the start smart then focus guidance and antibiotic consumption will potentially be improved with further embedding of electronic prescribing. A common barrier to implementation of auditing recommendations is time constraints on staff to collect the data required.<sup>8</sup>

ESPAUR has endorsed a proposal to establish a Start Smart then Focus Implementation subgroup to consider options and recommendations for further embedding of SSTF into secondary care in England. The Terms of reference and membership of the subgroup may be found in Appendix E. The subgroup first met in June 2014 and updated guidance will be launched for user testing in November 2014 taking into account current evidence and recommendations from this survey.

In 2015, the National Institute for Health and Care Excellence (NICE) will publish the national guidance; Antimicrobial stewardship: systems and processes for effective antimicrobial medicine use for primary and secondary care. This will become the guidance for NHS primary and secondary care organisations to implement and assess themselves against in this key area.<sup>44</sup>

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<sup>45</sup> Hand K, Walker S and Llewelyn M Review of antimicrobial prescriptions at 24-48 hours; a survey of current NHS hospital practice. ECCMID 2014

<sup>40</sup> English National Point Prevalence Survey on Healthcare-associated Infections and Antimicrobial Use, 2011. Available at: [http://www.hpa.org.uk/webc/hpawebfile/hpaweb\\_c/1317134304594](http://www.hpa.org.uk/webc/hpawebfile/hpaweb_c/1317134304594)

<sup>8</sup> Ashiru-Oredope, D., Sharland, M., Charani, E., McNulty, C. & Cooke, J. Improving the quality of antibiotic prescribing in the NHS by developing a new Antimicrobial Stewardship Programme: Start Smart—Then Focus. *Journal of Antimicrobial Chemotherapy*. 2012. 67 (suppl 1), i51-i63

<sup>44</sup> NICE. Antimicrobial Stewardship <https://www.nice.org.uk/Guidance/InDevelopment/GID-ANTIMICROBIALSTEWARDSHIP/Documents>

## Chapter 5: Future plans

This report brings together for the first time antibiotic resistance and antibiotic consumption surveillance data across England. In addition, it reports on current antimicrobial stewardship and guidelines in secondary care.

In this section, we describe the future plans for this programme.

### Development of an integrated system for antimicrobial resistance and consumption data

The PHE Information Strategy aims to amalgamate surveillance systems and provide PHE and partner organisations with a standardised set of tools to access and analyse information. The second generation surveillance system (SGSS) is a web-enabled surveillance database application. It replaces the PHE laboratory infectious disease notification system (CoSurv) and the antimicrobial reporting system (AmSurv) with a single data repository. This system 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. This system will be launched for healthcare professionals in October 2014.

One of the key objectives of ESPAUR is to provide improved access to antimicrobial utilisation surveillance data for both primary and secondary care. Currently, PHE, primary care providers and commissioners have access to primary care prescribing data at an individual general practice level; and IMS Health have given PHE access to secondary care data to area team level. PHE and NHS-England wrote to all Chief Executives of NHS Trusts in England requesting access to organisation level data held by IMS Health in March 2014. As of September 2014, 100% of NHS Acute Trusts have given permission for PHE to access their data held by IMS Health and Rx Info (Appendix F).

An outline specification and business case for a change to SGSS to incorporate this prescribing data, which can then be viewed by public health or NHS geographies, was approved in June 2014.

The development of an antimicrobial prescribing surveillance system within SGSS will provide a single web portal to access laboratory reports and antimicrobial consumption data, to allow NHS organisations to benchmark their antimicrobial consumption data, with user access restricted to the NHS and PHE, unless by specific agreement with PHE. It will include graphical reporting tools that will enable the direct comparison of antimicrobial consumption and observed antimicrobial resistance for the same organisations or geographical areas, meeting a key objective of ESPAUR. Although initially only aggregate prescribing data will be incorporated in the SGSS data model, the system will be capable of including patient-level antimicrobial prescribing information when this is available.

This system will go live with the data in this report in March 2015 and will then be updated with prescribing data on a quarterly basis to allow interrogation by healthcare professionals from primary, secondary care and public health.

## Reporting of antibiotic resistance in pathogens from other clinical specimens

The antibiotic resistance data included in this report has focussed on surveillance of isolates from cases of bacteraemia. The rationale for this is that surveillance systems were in place for the time period reported. In addition, Europe-wide surveillance of antibiotic resistance is also based on surveillance of bloodstream infections.<sup>46</sup> However, the implementation of SGSS/AmSurv, which will capture all antibiotic susceptibility test results from participating laboratories. This will allow analysis of trends in resistance from a much wider range of clinical sources ( eg urinary tract or respiratory isolates). Moreover, in contrast to LabBase, where suppression of results for clinical reasons renders such results unavailable for surveillance purposes, all validated results in AmSurv will be available for analysis irrespective of suppression in the source laboratory. Greater completeness of reporting of test results for isolates will also facilitate analysis of patterns of multi-resistance, which is currently problematic using LabBase data. It should however, be noted that reporting to AmSurv is done on a voluntary basis and that the ability to submit data electronically requires that hospital microbiology computer systems be interfaced AmSurv. As of September 2014, 82% of laboratories in England have started reporting (Appendix G). Laboratories not yet reporting may require investment in their laboratory information systems to allow this data to be submitted to PHE, and this has must be a priority if surveillance is to be sufficiently robust to determine the total burden of resistant pathogens in England.

## Expansion of drug-bug combinations included in surveillance of antimicrobial resistance

The antibiotic consumption and stewardship chapters highlighted increased prescribing of antibiotics not currently included in the core list of drug-bug combinations recommended for surveillance of resistance. Future developments are likely to include expansion of this core list to include additional antibiotics, particularly  $\beta$ -lactam/ $\beta$ -lactamase inhibitor combinations such as piperacillin/tazobactam. However, there are technical difficulties in accurately determining the susceptibility of pathogens to some of these agents and the quality of routinely generated data provided by hospital microbiology laboratories will need to be validated by, for example, comparison with bacteraemia surveillance data available from the PHE AMRHA1 reference unit.

## Linkage of antibiotic resistance data with other data sets

A further limitation of current surveillance based on collection and collation of routinely generated hospital microbiology laboratory data is that some clinical and epidemiological data may not be available, in particular dates of hospital admission and discharge. One approach to addressing this limitation is integration of microbiology laboratory data with hospital episode statistics (HES) data. HES is a data warehouse containing details of all admissions, outpatient appointments and A&E attendances at NHS hospitals in England, as well as a range of clinical data. Integration of these data sets will allow determination of the location of onset of infection and application of algorithm rules to determine whether the infection was healthcare-associated

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<sup>46</sup> Antimicrobial resistance surveillance in Europe 2012.  
[http://ecdc.europa.eu/en/publications/\\_layouts/forms/Publication\\_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=963](http://ecdc.europa.eu/en/publications/_layouts/forms/Publication_DispForm.aspx?List=4f55ad51-4aed-4d32-b960-af70113dbb90&ID=963)



or a community infection, which will inform as to where to target resources for infection prevention and control. A pilot study using paediatric data successfully investigated the incidence and aetiology of hospital-acquired bloodstream infections in children and the antibiotic susceptibility of the causative pathogens.<sup>47</sup>

## Enhancement of community antibiotic consumption datasets

Within community prescribing, PHE will pursue with partners more granular reporting of antimicrobial consumption data with, as a minimum, age and sex stratified datasets with NHSBSA and HSCIC. It will also pursue the reporting of individual dental practice and out-of-hours prescribing.

## Understand prescribing in private practice in England

No national data on prescribing in private practice exists. This is a large complex area and includes prescribing in general practice, Dental Practice and Independent Healthcare Organisations. ESPAUR will pursue methods that can be used to assess antibiotic prescribing in private practice.

## Validation of hospital antibiotic consumption datasets

Analysis of antibiotic consumption data using hospital admissions as the denominator showed significant variability in antibiotic consumption between ATs. However until we understand the individual hospital mechanisms for recording the dispensing of antibiotics, particularly inpatient and outpatient dispensing and the management of ward-dispensed medication, we cannot fully understand or explain this variation. Ideally, hospital pharmacies would record the patient location (inpatient, outpatient), specialty and type of dispensing using a standardised method, allowing comparison across location, specialty and type of dispensing to occur. In order to understand variations in hospital prescribing, we need to validate individual hospital consumption of antibiotics and develop a standardised reporting output, for both specialties and inpatient and outpatient prescribing within hospitals, to allow case-mix adjusted consumption rates within hospitals. Patient level electronic prescribing data is available in less than 20% of organisations; this will be an essential information technology development in order to understand the individual and ecological impact of antibiotic use.

## Piloting and reporting of antimicrobial prescribing quality measures

The Department of Health's advisory committee on Antimicrobial Resistance and Healthcare Associated Infections, in association with NHS England and PHE have developed quality measures for general practice and Hospital antimicrobial prescribing in England.<sup>1</sup> These quality measures will be implemented as standard graphics and tables into the SGSS, and made available for healthcare providers and commissioners to review. However this annual report will

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<sup>47</sup> Blackburn RM et al. Exploring the Epidemiology of Hospital-Acquired Bloodstream Infections in Children in England (January 2009-March 2010) by Linkage of National Hospital Admissions and Microbiological Databases. *Pediatr Infect Dis J* 2012;1:284-94.

<sup>1</sup> Advisory Committee on Antimicrobial Resistance and Hospital Acquired Infections (ARHAI) Recommended Antimicrobial Prescribing Quality Measures. 2014. <https://app.box.com/ARHAI-Minutes-Papers/1/2152374732/18606265032/1>

continue to measure all antibiotic agents to allow us to determine the impact of these quality measures and any unintended consequences through changes in antimicrobial policies and prescriptions over time.

## Ecological analysis of associations between resistance and consumption

Future ecological analysis combining data on antibiotic resistance and consumption at AT and related general practice and Hospital level will be undertaken to further assess associations between these parameters. This would also allow the development of a better understanding of health inequalities that influence antibiotic prescribing and resistance.

In addition, as discussed above, laboratory data on infections will be integrated with HES data in order to determine the location of patients at the time of onset and apply algorithm rules to determine whether the infection was healthcare-associated or a community infection. This is essential in order to determine where resources in infection prevention should be delivered.

## Measurement of impact of behavioural interventions and antibiotic resistance awareness campaigns

The data generated through the surveillance systems will be used to measure the impact of future behavioural interventions delivered by the DH and PHE behavioural insights team with the aims of having caused ecological changes in prescribing and resistance through these interventions. English actions for European Antibiotic Awareness Day and future AMR campaigns will be captured.

## Improving education and training regarding antibiotic resistance.

ARHAI and PHE have developed competencies for antimicrobial prescribers. The ESPAUR Oversight Group has developed in partnership with Health Education England, a short-life working group, that will aim to assess and provide recommendations on methods to provide this training and embed these competencies into all relevant curricula

## Antimicrobial stewardship toolkits

There are two major toolkits in England: Start Smart Then Focus for secondary care and TARGET for primary care. This report has outlined how secondary care has embedded SSTF. A pilot survey to assess TARGET in primary care is currently in progress. A sub-group has been developed to improve the SSTF toolkit based on current feedback and provide methods for improved implementation. A similar process will be undertaken with TARGET.

## Working with veterinary partners

ESPAUR has commenced work with DEFRA and DARC to develop a one health report encompassing AMR and consumption data across the human and veterinary sectors in England. This report will be released in 2015.

## Working with European initiatives

ESPAUR has submitted both antimicrobial consumption data and resistance data to ECDC through ESAC-net and EARS-net respectively. We will continue to work with ECDC to understand the differences in healthcare delivery and methods of improving the data generated. In addition, we will continue to work with partner organisations across England to lead the response to European Antibiotic Awareness Day (EAAD). This year we have developed the Antibiotic Guardian campaign.<sup>48</sup> The main objective of the campaign is that by 30 November at least 10,000 healthcare professionals and members of the public will have committed to at least one pledge for prudent use of antimicrobials in support of EAAD 2014. The [AntibioticGuardian.com](http://AntibioticGuardian.com) pledge campaign will provide an outcome measure on both public and professional engagement and act as a driver to reduce both requests for antibiotics and antibiotic prescriptions. The pledge system will also help people feel that they have taken concrete personal and collective action to help keep antibiotics active. This may in turn act as a catalyst for behaviour change that will be measured through contact with the individuals who have pledged on the website.

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<sup>48</sup> AntibioticGuardian.com pledge campaign <http://antibioticguardian.com>

# Appendix A

## ESPAUR oversight group – terms of reference

### 1.0 Issue

1.1 The PHE Antimicrobial Resistance & Stewardship and Healthcare-Associated Infection, (AMRS & HCAI) Programme Board has considered how it could establish a national programme to develop and maintain robust information and surveillance systems to measure antimicrobial utilisation and its impact on resistance and patient safety in England – to be named the English Surveillance Programme for Antimicrobial Utilisation and Resistance (ESPAUR).

### 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, AMR, HCAI & AMRS Programme Board, Behavioural insight, Public Health Strategy, the 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 Antimicrobial Resistance (ARHAI).
5. Health & Social Care Information Centre.
6. IMS Health and Rx-Info Ltd (Define).
7. British Society for Antimicrobial Chemotherapy.
8. UK Clinical Pharmacy Association: Infection Management Group.
9. Care Quality Commission.
10. NICE Medicines and Prescribing Centre.
11. British National Formulary.
12. Pharmaceutical Advisers Group.
13. Royal Pharmaceutical Society - Frontline Chief Pharmacist & community pharmacist.
14. Royal College of Nursing, Physicians, General Practitioners and Surgeons.
15. Patient/lay representation.
16. Independent/private sector healthcare - [independenthealthcare.org.uk](http://independenthealthcare.org.uk).
17. NHS Trust Development.
18. Veterinary Medicines Directorate – DEFRA.

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

### **3.0 Aims and Objectives**

- 3.1 The aim of the ESPAUR is to develop and maintain robust data information and surveillance/monitoring systems to measure antimicrobial utilisation and resistance in England and its impact on antimicrobial resistance and patient/public safety.

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

- 3.3 Specifically, the oversight group will:

- I. Deliver the key components of the annual report from the ESPAUR.
- II. Participate in the integration and analysis of varying antimicrobial usage datasets across primary and secondary care.
- III. Contribute to the real-time monitoring and measurement systems for antibiotic consumption in hospitals with a view to supporting antimicrobial stewardship in the NHS and the independent sector.
- IV. Review the systems developed to ensure that the antimicrobial usage data can be linked with *C. difficile* rates and other bacterial resistance surveillance data.
- V. 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).
- VI. Enhance data analysis and advice on use of carbapenems and other Critically Important Antibiotics in the NHS and the independent sector.
- VII. Develop quality measures for optimal antimicrobial prescribing in primary and secondary care.
- VIII. Advise on the development and implementation of methods to monitor the clinical outcomes including any unintended consequences; for example increased prescribing of particular antibiotics.
- IX. Work with other stakeholders and PHE behavioural insights/social marketing teams to agree approaches and initiatives to change public and professional behaviour around antimicrobial consumption, prescribing and management of antibiotic allergies.
- X. Ensure that the outputs inform the national research agenda in this area.
- XI. Evaluate and assess the impact of initiatives developed.

### **4.0 Governance**

- 4.1 The Chair of the HCAI & AMRS Programme 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 nominated and voted in by members during the first meeting.

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.

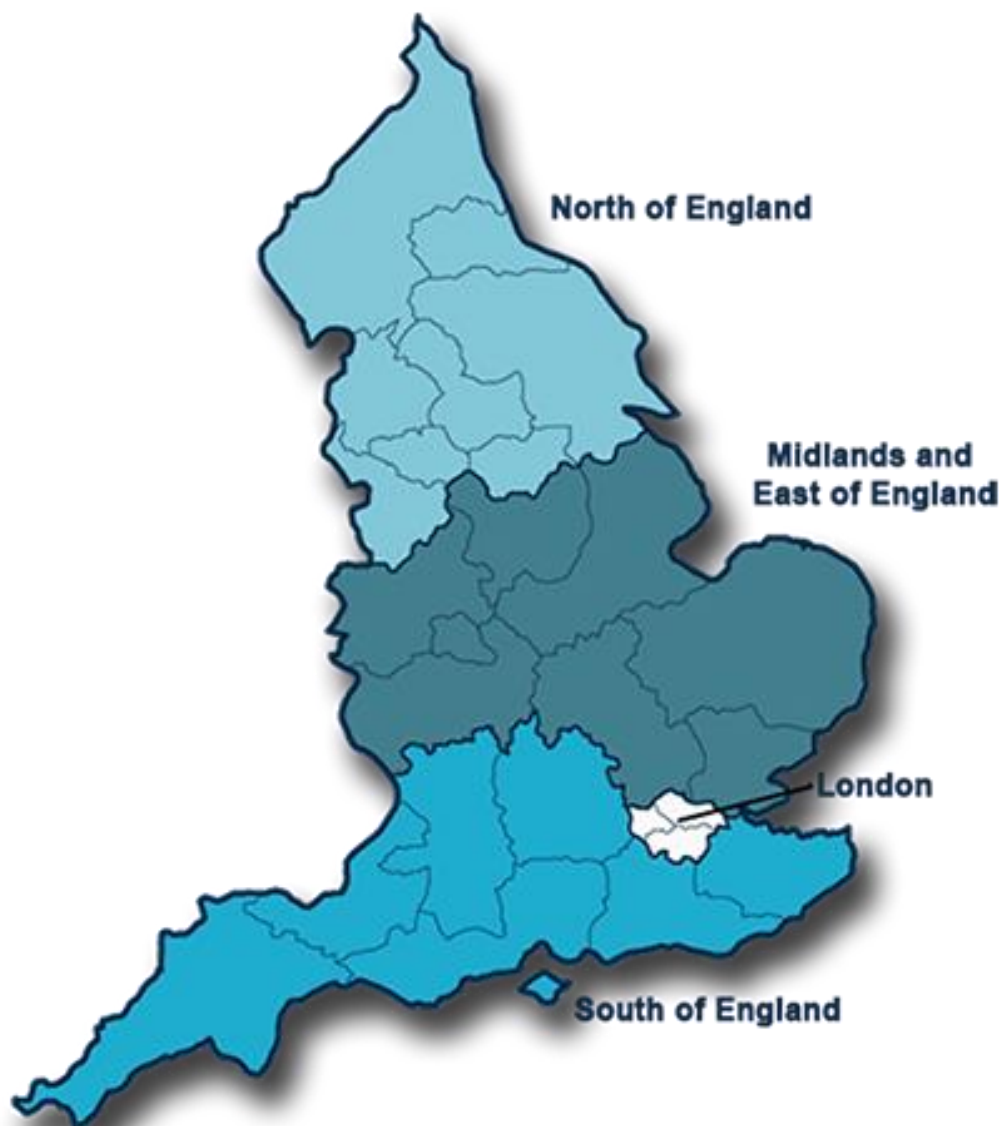
5.2 In addition to the above topics, the ESPAUR will consider matters it deems appropriate to fulfil its responsibilities. The ESPAUR may invite assistance from independent experts and advisors to assist them on matters.

## **6.0 Reporting Structure/Outputs and communications**

6.1 The ESPAUR will provide quarterly updates to the HCAI & AMRS Programme 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

## NHS regions



## NHS local area teams



<b>Q44</b>	Cheshire, Warrington and Wirral	<b>Q57</b>	Essex
<b>Q45</b>	Durham, Darlington and Tees	<b>Q58</b>	Hertfordshire and the South Midlands
<b>Q46</b>	Greater Manchester	<b>Q59</b>	Leicestershire and Lincolnshire
<b>Q47</b>	Lancashire	<b>Q60</b>	Shropshire and Staffordshire
<b>Q48</b>	Merseyside	<b>Q71</b>	London
<b>Q49</b>	Cumbria, Northumberland, Tyne and Wear	<b>Q64</b>	Bath, Gloucestershire, Swindon and Wiltshire
<b>Q50</b>	North Yorkshire and Humber	<b>Q65</b>	Bristol, North Somerset, Somerset and South Gloucestershire
<b>Q51</b>	South Yorkshire and Bassetlaw	<b>Q66</b>	Devon, Cornwall and Isles of Scilly
<b>Q52</b>	West Yorkshire	<b>Q67</b>	Kent and Medway
<b>Q53</b>	Arden, Herefordshire and Worcestershire	<b>Q68</b>	Surrey and Sussex
<b>Q54</b>	Birmingham and the Black Country	<b>Q69</b>	Thames Valley
<b>Q55</b>	Derbyshire and Nottinghamshire	<b>Q70</b>	Wessex
<b>Q56</b>	East Anglia		



# Appendix C

## Defined daily doses of commonly used antibiotics

Antimicrobial Group	Antibiotic name	Route of administration	DDD	unit
Tetracyclines	Doxycycline	Oral	0.1	g
	Lymecycline	Oral	0.6	g
Penicillins	Amoxicillin	Oral	1	g
	Amoxicillin	Parenteral	1	g
	Benzylpenicillin	Parenteral	3.6	g
	Phenoxymethylpenicillin	Oral	2	g
	Flucloxacillin	Oral	2	g
	Flucloxacillin	Parenteral	2	g
	Co-amoxiclav	Oral	1	g
	Co-amoxiclav	Parenteral	3	g
	Piperacillin/tazobactam	Parenteral	14	g
	Cephalosporins	Cefalexin	Oral	2
Cefradine		Oral	2	g
Cefradine		Parenteral	2	g
Cefuroxime		Oral	0.5	g
Cefuroxime		Parenteral	3	g
Cefotaxime		Parenteral	4	g
Ceftazidime		Parenteral	4	g
Ceftriaxone		Parenteral	2	g
Cefixime		Oral	0.4	g
Carbapenems	Meropenem	Parenteral	2	g
	Ertapenem	Parenteral	1	g
Trimethoprim	Trimethoprim	Oral	0.4	g
	Trimethoprim	Parenteral	0.4	g
Macrolides	Erythromycin	Oral	1	g
	Erythromycin	Parenteral	1	g
	Erythromycin ethylsuccinate	Oral	2	g
	Clarithromycin	Oral	0.5	g
	Clarithromycin	Parenteral	1	g
	Azithromycin	Oral	0.3	g
	Azithromycin	Parenteral	0.5	g
Aminoglycosides	Gentamicin	Parenteral	0.24	g
	Amikacin	Parenteral	1	g
Quinolones	Ofloxacin	Oral	0.4	g
	Ofloxacin	Parenteral	0.4	g
	Ciprofloxacin	Oral	1	g
	Ciprofloxacin	Parenteral	0.5	g
	Levofloxacin	Oral	0.5	g
	Levofloxacin	Parenteral	0.5	g
Glycopeptides	Vancomycin	Parenteral	2	g
	Teicoplanin	Parenteral	0.4	g
Nitrofurantoin	Nitrofurantoin	Oral	0.2	g
Anti- <i>Clostridium difficile</i> agents	Metronidazole	Oral	2	g
	Vancomycin	Oral	2	g
	Fidaxomicin	Oral	0.4	g

## Appendix D

### ESPAUR clinical guidelines survey for secondary care

The clinical guidelines survey for Secondary care may be found by following the link; if you have not already completed the survey please do so here:

[https://surveys.phe.org.uk/TakeSurvey.aspx?SurveyID=ESPAUR\\_AMPSGSC](https://surveys.phe.org.uk/TakeSurvey.aspx?SurveyID=ESPAUR_AMPSGSC)

As an overview of the survey the questions have been given below:

1. Please provide your email address.
2. Please enter the name of the NHS Trust you are entering guidance for.
3. Approximately, how many beds are there in your Trust?
4. How many hospitals/sites are there within your Trust?
5. Please select which area team you belong to.
6. What is your role within the organisation?
7. How many pharmacists work in your Trust (whole time equivalents)?
8. How are the antimicrobial post(s) graded?
9. Does the Trust have a dedicated antimicrobial policy/management code, which details your overarching strategies for ensuring appropriate antimicrobial usage?\*
10. When was the antimicrobial policy last reviewed?
11. How often is the antimicrobial policy reviewed?
12. Does the Trust have an Antimicrobial Stewardship Committee/Group (separate to Infection Control Committee or Drugs and Therapeutics Committee)?
13. In my Trust, the following [antimicrobial] guidelines/policies are in place.
14. Which departments are consulted in order for antimicrobial clinical guidelines to be reviewed/updated?
15. The Trust pharmacy antimicrobial specialist(s) take an active role in [antimicrobial stewardship/policy actions and activities].
16. You have indicated that your Trust does not have a dedicated Antimicrobial Stewardship Committee/Group. Which committee has the written remit for antimicrobial stewardship in the Trust?\*
17. You have indicated that your Trust has an Antimicrobial Stewardship Committee/Group. What professional groups are represented by your committee, as defined in the Committee's Terms of Reference?
18. Does the Trust Antimicrobial Stewardship Committee/Group have: Terms of Reference, Minutes or Action Lists, Minutes go to Clinical Governance/Infection Control/DTC or a higher level?
19. Does the Trust have a restricted antibiotics list?
20. What actions have you taken with regards to the national guidance - Start Smart then Focus?
21. Do you have any examples of local initiatives of implementing Start Smart Then Focus that would be useful to others?

22. Do you have any feedback on the Start Smart Then Focus - usefulness, improvement required etc?
23. In your Trust, is it mandatory to document indication and duration/review dates of antibiotics on drug charts?
24. Which of the audits have been implemented within the audit plan or already collated as part of the Trust-wide PPS?
25. Please answer the following questions about the most recent survey/audits of 24-48 hour review of antimicrobial prescriptions and subsequent antimicrobial prescribing decisions in your trust.
26. How often are Trust-wide antimicrobial point prevalence studies conducted?
27. In your Trust is there a written Antimicrobial Education and Training Strategy? Is competency assessment carried out for prescribers? Is this assessment mandatory?
28. What antimicrobial prescribing and stewardship training takes place within the Trust?
29. How often do doctors, nurses, pharmacists and non-medical prescribers have to receive mandatory prescribing lectures and/or e-learning updates.
30. Please state the conditions against which meropenem, ertapenem and imipenem may be used as described in the Trust's antimicrobial formulary.
31. For each of colorectal, orthopaedic and vascular surgical procedures please tell us:
  - which antibiotic agent (or combination) you recommend for first line use for the prevention of surgical site infections
  - whether you recommend that this be given as a single dose or repeat doses
  - if repeat doses at what interval do you recommend for first and subsequent doses
  - when did these recommendations come into effect?
  - are there any exceptions to the recommendations ( eg based on age or BMI), how do they differ?
32. For each of the infections listed below please tell us:
  - what is recommended for first line treatment in the general adult empirical antimicrobial formulary
  - the dose and duration stated in the clinical guideline
33. Please upload a copy of the most current Trust documents below for: Common infections empiric treatment guideline and surgical prophylaxis guideline.
34. If you cannot upload the guidelines, please provide a link to download them
35. Does your Trust have electronic prescribing for inpatients?\*
36. Do the following inpatient areas have greater than 90% of prescriptions written electronically?
37. Do you have access to the data to review: whether allergy has been documented, whether the dose used is correct given the patients age and co-morbidities, whether the indication is documented, whether the duration is documented, whether the correct agent for the indication (according to local guidelines) is documented?
38. You've indicated that your Trust does not have electronic prescribing for inpatients. Will your Trust have electronic prescribing in the following areas by April 2015?

# Appendix E

## ESPAUR SSTF implementation terms of reference and membership

### 1.0 The remit of the implementation subgroup will be:

- to identify existing mechanisms for embedding the published Start Smart then Focus guidance into secondary care in England, including learning from the actions of other healthcare economies in implementing AMS programmes
- investigate mechanisms for ensuring a commitment from Trusts to implement SSTF and declare how they are implementing the guidance
- update the Start Smart then Focus guidance to ensure that recent evidence taken into account – For publication in November 2014
- identify and provide methods/ideas of systems through which secondary care Trusts can share learning and limit duplication of Take forward the results and recommendations from the National surveys to measure Trust compliance with the quality improvement measures and audits recommended in SSTF
- determine a system for monitoring AMS nationally using prevalence tools
- develop national benchmarking/quality measures around stewardship eg number of antimicrobial pharmacists, AMS activities
- identify if education and training available is sufficient and explore developing a national e-learning template for AMS for hospital teams
- identify particular research questions to inform the national research agenda
- identify methods to evaluate and assess the impact of initiatives developed

### 2.0 SSTF-I MEMBERSHIP

#### 2.1 Membership

- Dr Diane Ashiru-Oredope (PHE/ESPAUR/ARHAI Pharmacist Lead) – Chair SSTF-I Group
- Dr Gavin Barlow (Hull – developed BSAC NICHE project)
- Dr Oliver Dyer – Junior Doctor
- Dr Mark Gilchrist - UKCPA
- Dr Kieran Hand - ARHAI Member
- Dr James Hatcher – Registrar
- David Ladenheim (EoE Antimicrobial Pharmacists)
- Professor Alasdair MacGowan - Public Health Microbiologist South West and Consultant in Infection Public Health England & North Bristol Trust
- Dr Daryll Menezes – Registrar
- Dr Bharat Patel (PHE)
- Ms Laura Witney - UKCPA
- Dr Emma Budd (Secretariat)

#### 2.2 Together with representatives from:

- CQC – Brian Brown
- NHS England – Kate Morrow
- Royal College of Nursing – Rose Gallagher
- Royal Pharmaceutical Society – Philip Howard
- Royal College of Surgeons (RCS) – Tony Young
- Royal College of Physicians (RCP) – Druin Burch
- Infection Prevention Society (IPS) – Heather Loveday

## Appendix F

### NHS England acute trust hospitals consented to antimicrobial consumption data release to PHE

One-hundred percent of NHS Acute Trusts in England gave consent for the release of antimicrobial consumption data from IMS Health and Rx Info to PHE by 26/09/2014.

Aintree University Hospital NHS Foundation Trust  
Airedale NHS Foundation Trust  
Alder Hey Children's NHS Foundation Trust  
Ashford and St Peter's Hospitals NHS Foundation Trust  
Barking, Havering and Redbridge University Hospitals NHS Trust  
Barnet and Chase Farm Hospitals NHS Trust  
Barnsley Hospital NHS Foundation Trust  
Barts Health NHS Trust  
Basildon and Thurrock University Hospitals NHS Foundation Trust  
Bedford Hospital NHS Trust  
Birmingham Children's Hospital NHS Foundation Trust  
Birmingham Women's NHS Foundation Trust  
Blackpool Teaching Hospitals NHS Foundation Trust  
Bolton NHS Foundation Trust  
Bradford Teaching Hospitals NHS Foundation Trust  
Brighton and Sussex University Hospitals NHS Trust  
Buckinghamshire Healthcare NHS Trust  
Burton Hospitals NHS Foundation Trust  
Calderdale and Huddersfield NHS Foundation Trust  
Cambridge University Hospitals NHS Foundation Trust  
Central Manchester University Hospitals NHS Foundation Trust  
Chelsea and Westminster Hospital NHS Foundation Trust  
Chesterfield Royal Hospital NHS Foundation Trust  
City Hospitals Sunderland NHS Foundation Trust  
Colchester Hospital University NHS Foundation Trust  
Countess of Chester Hospital NHS Foundation Trust  
County Durham and Darlington NHS Foundation Trust  
Croydon Health Services NHS Trust  
Dartford and Gravesham NHS Trust  
Derby Hospitals NHS Foundation Trust  
Doncaster and Bassetlaw Hospitals NHS Foundation Trust  
Dorset County Hospital NHS Foundation Trust  
Ealing Hospital NHS Trust  
East and North Hertfordshire NHS Trust  
East Cheshire NHS Trust  
East Kent Hospitals University NHS Foundation Trust  
East Lancashire Hospitals NHS Trust  
East Sussex Healthcare NHS Trust

Epsom and St Helier University Hospitals NHS Trust  
Frimley Park Hospital NHS Foundation Trust  
Gateshead Health NHS Foundation Trust  
George Eliot Hospital NHS Trust  
Gloucestershire Hospitals NHS Foundation Trust  
Great Ormond Street Hospital For Children NHS Foundation Trust  
Great Western Hospitals NHS Foundation Trust  
Guy's and St Thomas' NHS Foundation Trust  
Hampshire Hospitals NHS Foundation Trust  
Harrogate and District NHS Foundation Trust  
Heart of England NHS Foundation Trust  
Heatherwood and Wexham Park Hospitals NHS Foundation Trust  
Hinchingsbrooke Health Care NHS Trust  
Homerton University Hospital NHS Foundation Trust  
Hull and East Yorkshire Hospitals NHS Trust  
Imperial College Healthcare NHS Trust  
Ipswich Hospital NHS Trust  
Isle of Wight NHS Trust  
James Paget University Hospitals NHS Foundation Trust  
Kettering General Hospital NHS Foundation Trust  
King's College Hospital NHS Foundation Trust  
Kingston Hospital NHS Foundation Trust  
Lancashire Teaching Hospitals NHS Foundation Trust  
Leeds Teaching Hospitals NHS Trust  
Lewisham and Greenwich NHS Trust\*  
Liverpool Heart and Chest Hospital NHS Foundation Trust  
Liverpool Women's NHS Foundation Trust  
Luton and Dunstable University Hospital NHS Foundation Trust  
Maidstone and Tunbridge Wells NHS Trust  
Medway NHS Foundation Trust  
Mid Cheshire Hospitals NHS Foundation Trust  
Mid Essex Hospital Services NHS Trust  
Mid Staffordshire NHS Foundation Trust  
Mid Yorkshire Hospitals NHS Trust  
Milton Keynes Hospital NHS Foundation Trust  
Moorfields Eye Hospital NHS Foundation Trust  
Norfolk and Norwich University Hospitals NHS Foundation Trust  
North Bristol NHS Trust  
North Cumbria University Hospitals NHS Trust  
North Middlesex University Hospital NHS Trust  
North Tees and Hartlepool NHS Foundation Trust  
North West London Hospitals NHS Trust  
Northampton General Hospital NHS Trust  
Northern Devon Healthcare NHS Trust  
Northern Lincolnshire and Goole NHS Foundation Trust  
Northumbria Healthcare NHS Foundation Trust  
Nottingham University Hospitals NHS Trust  
Oxford University Hospitals NHS Trust  
Papworth Hospital NHS Foundation Trust  
Pennine Acute Hospitals NHS Trust

Peterborough and Stamford Hospitals NHS Foundation Trust  
Plymouth Hospitals NHS Trust  
Poole Hospital NHS Foundation Trust  
Portsmouth Hospitals NHS Trust  
Queen Victoria Hospital NHS Foundation Trust  
Royal Berkshire NHS Foundation Trust  
Royal Brompton & Harefield NHS Foundation Trust  
Royal Cornwall Hospitals NHS Trust  
Royal Devon and Exeter NHS Foundation Trust  
Royal Free London NHS Foundation Trust  
Royal Liverpool and Broadgreen University Hospitals NHS Trust  
Royal National Hospital For Rheumatic Diseases NHS Foundation Trust  
Royal National Orthopaedic Hospital NHS Trust  
Royal Surrey County Hospital NHS Foundation Trust  
Royal United Hospital Bath NHS Trust  
Salford Royal NHS Foundation Trust  
Salisbury NHS Foundation Trust  
Sandwell and West Birmingham Hospitals NHS Trust  
Sheffield Children's NHS Foundation Trust  
Sheffield Teaching Hospitals NHS Foundation Trust  
Sherwood Forest Hospitals NHS Foundation Trust  
Shrewsbury and Telford Hospital NHS Trust  
South Devon Healthcare NHS Foundation Trust  
South Tees Hospitals NHS Foundation Trust  
South Tyneside NHS Foundation Trust  
South Warwickshire NHS Foundation Trust  
Southend University Hospital NHS Foundation Trust  
Southport and Ormskirk Hospital NHS Trust  
St George's Healthcare NHS Trust  
St Helens and Knowsley Hospitals NHS Trust  
Stockport NHS Foundation Trust  
Surrey and Sussex Healthcare NHS Trust  
Tameside Hospital NHS Foundation Trust  
Taunton and Somerset NHS Foundation Trust  
The Christie NHS Foundation Trust  
The Clatterbridge Cancer Centre NHS Foundation Trust  
The Dudley Group NHS Foundation Trust  
The Hillingdon Hospitals NHS Foundation Trust  
The Newcastle Upon Tyne Hospitals NHS Foundation Trust  
The Princess Alexandra Hospital NHS Trust  
The Queen Elizabeth Hospital, King's Lynn, NHS Foundation Trust  
The Robert Jones and Agnes Hunt Orthopaedic Hospital NHS Foundation Trust  
The Rotherham NHS Foundation Trust  
The Royal Bournemouth and Christchurch Hospitals NHS Foundation Trust  
The Royal Marsden NHS Foundation Trust  
The Royal Orthopaedic Hospital NHS Foundation Trust  
The Royal Wolverhampton NHS Trust  
The Walton Centre NHS Foundation Trust  
The Whittington Hospital NHS Trust  
United Lincolnshire Hospitals NHS Trust

University College London Hospitals NHS Foundation Trust  
University Hospital Of North Staffordshire NHS Trust  
University Hospital Of South Manchester NHS Foundation Trust  
University Hospital Southampton NHS Foundation Trust  
University Hospitals Birmingham NHS Foundation Trust  
University Hospitals Bristol NHS Foundation Trust  
University Hospitals Coventry and Warwickshire NHS Trust  
University Hospitals of Leicester NHS Trust  
University Hospitals of Morecambe Bay NHS Foundation Trust  
Walsall Healthcare NHS Trust  
Warrington and Halton Hospitals NHS Foundation Trust  
West Hertfordshire Hospitals NHS Trust  
West Middlesex University Hospital NHS Trust  
West Suffolk NHS Foundation Trust  
Western Sussex Hospitals NHS Foundation Trust  
Weston Area Health NHS Trust  
Wirral University Teaching Hospital NHS Foundation Trust  
Worcestershire Acute Hospitals NHS Trust  
Wrightington, Wigan and Leigh NHS Foundation Trust  
Wye Valley NHS Trust  
Yeovil District Hospital NHS Foundation Trust  
York Teaching Hospital NHS Foundation Trust

We thank all Chief Executives, Chief Pharmacists, Medical Directors and Antimicrobial Stewardship groups for their support in this initiative.



## Appendix G

### English NHS laboratories reporting to AmSurv

Addenbrooke's	Kingston
Ashford	Lancashire Teaching Hospitals NHS Trust
Barnet & Chase Farm	Leicester
Barnsley	Lewisham
Barnstaple	Lincoln
Barts Health NHS Trust	Lister, Stevenage
Bedford	Luton
Birmingham Children's Hospital	Maidstone Hospital
Birmingham PHE laboratory	Manchester MRI (HPA Laboratory)
Birmingham Women's Hospital	Medway Maritime
Blackpool Victoria Hospital	Mid Yorkshire Hospitals Trust
Boston NHS	Middlesbrough
Bournemouth	Milton Keynes Hospital
Brighton	North Tyneside
Bristol	New Cross Hospital
Calderdale & Huddersfield	Newcastle Freeman/RVI & PHE Lab
Carlisle	North Hampshire Hospital, Basingstoke
Chelmsford	North Middlesex
Colchester	Nottingham
Countess Of Chester Hospital	Oxford, John Radcliffe
Darent Valley Hospital	Peterborough
Darlington	Plymouth
Derbyshire Royal Infirmary NHS	Poole
Dryburn - Durham	Portsmouth
East Lancashire NHS Trust	Princess Alexandra Hospital Harlow
Eastbourne General, Eastbourne	Queen Elizabeth, Woolwich
Exeter	Queen's Hospital Burton
Frenchay/Southmead (North Bristol)	Queen's Romford
Frimley Park, Camberley	Reading PHL
Gateshead	Rotherham
Gloucestershire (Cheltenham & Gloucester)	Royal Bolton Hospital
Grantham NHS	Royal Brompton (Micro)
Grimsby NHS	Royal Free (Micro)
Harrogate	Royal Liverpool University Hospital
Hereford Hospital	Royal Oldham Hospital
Hillingdon	Russell's Hall Hospital
Homerton	Salisbury
Hope Hospital	Sandwell and West Birmingham Hospital
Hull	Scunthorpe NHS
Imperial, Chelsea & Westminster	Sheffield Teaching Hospitals Trust
Ipswich	Shrewsbury Hospital
Kettering General	Southampton
King's (Micro)	Southend
Kingsmill NHS	Southport & Formby DGH

St George's	University Hospital Birmingham (Queen Elizabeth)
St Helier	University Hospital North Staffordshire
St. Mary's, Isle of Wight	University Hospitals Coventry & Warwick
Stafford DGH	Walsall Manor Hospital
Stockport Acute Services NHS Trust	Watford
Stoke Mandeville, Aylesbury	West Suffolk, Bury St Edmunds
Swindon	Weston-super-Mare
Tameside General Hospital	Wexham Park, Slough
Taunton	Whiston Hospital
TDL (Ealing & Northwick Park) Micro	Whittington
Torquay/Torbay	Worcester Hospital
Truro	York (inc. Scarborough) NHS Trust
University Hospital Aintree	

### English NHS laboratories requiring further work to report to AmSurv

Basildon General	North Tees
Northampton General	Sunderland
Norwich	Bassetlaw NHS
Princess Alexandra Hospital Harlow	Chesterfield NHS
Airedale	Great Ormond St
Doncaster	Guys and St Thomas
Leeds Teaching Hospitals Trust	Royal Marsden
Furness General Hospital	UCLH (Micro)
Macclesfield DGH	Crawley Hospital
Royal Lancaster Infirmary	Dorchester
Royal Liverpool Children's Hospital	St Richards, Chichester
Warrington Hospital NHS Trust	Guernsey

Thank you to all of the microbiology laboratories and PHE regional information teams and Field Epidemiology Services for enabling this data to be reported.

# Appendix H

## Glossary

### Antibacterial

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

### Antimicrobial stewardship

Antimicrobial stewardship is a key component of a multifaceted approach to preventing emergence of antimicrobial resistance. Good antimicrobial stewardship 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.

### Antimicrobial resistance

Antimicrobial resistance (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  $\beta$ -lactam antibiotics, especially in members of Enterobacteriaceae family are increasing worldwide and an emerging threat.

### Carbapenems

Carbapenems are broad-spectrum  $\beta$ -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 HCAs 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 $\beta$ -Lactamases (ESBL)

Extended-Spectrum  $\beta$ -Lactamases (ESBL) are enzymes produced by bacteria making them resistant to penicillins and cephalosporins. Resistance to third- generation cephalosporins in *E. coli* (and other 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 I

## Abbreviations

<b>Acronym</b>	<b>Full Name</b>
AMC	Antimicrobial Consumption
AMR	Antimicrobial Resistance
AMRHAI	Antimicrobial Resistance and Healthcare Associated Infections Reference Unit (PHE)
ASP	Antimicrobial Stewardship Programme
AT	Area team
ARHAI	Antimicrobial Resistance 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 Antimicrobial Resistance Committee
DDD	Defined Daily Dose
DEFRA	Department for Environment, Food & Rural Affairs
DH	Department of Health
DIPC	Director of Infection Prevention and Control
EAAD	European Antibiotic Awareness Day
EARS-net	European Antimicrobial Resistance Surveillance Network
ECDC	European Centre of Disease Prevention and Control
ESAC-net	European Surveillance of Antimicrobial Consumption Network
ESBL	Extended-Spectrum $\beta$ -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 Antimicrobial Resistance 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 & education tools (a toolkit)
TATFAR	Transatlantic Taskforce on Antimicrobial Resistance
UTI	Urinary Tract Infection
WHO	World Health Organisation

## Appendix J

### Writing Committee and Acknowledgements

#### Writing Committee – Core membership

- Diane Ashiru-Oredope
- Alex Bhattacharya
- Emma Budd
- Rebecca Guy
- Susan Hopkins
- Alan Johnson
- Berit Muller-Pebody

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- Rose Gallagher
- David Livermore
- Julie Robotham
- Peter Stephens
- Jonathan Underhill
- Laura Whitney
- Mark Wilcox
- Neil Woodford

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- NHS Business Services Authority, Health and Social Care Information Centre and IMS Health for providing the raw antimicrobial consumption data
- NHS microbiology laboratories, PHE regional information managers and PHE field epidemiology services for providing the raw antimicrobial resistance data
- antimicrobial pharmacists across English NHS Trusts for responding to the antimicrobial stewardship survey
- East of England pharmacy network, especially Christianne Micallef and David Ladenheim for piloting the antimicrobial stewardship survey



Written on behalf of the ESPAUR Oversight Group

<b>Name</b>	<b>Organisation</b>
Diane Ashiru-Oredope	ESPAUR Project Lead, PHE - AMRS & HCAI Pharmacist Lead
Nicholas Brown	British Society for Antimicrobial Chemotherapy
Brian Brown	Care Quality Commission
Sue Carter	Pharmaceutical Advisors Group
Tim Chadborn	PHE - Behavioural Insights
Andre Charlett	PHE - Statistics, Modelling and Economics Dept
Anna Cichowska	PHE - Public Health Strategy
Stephen Dobra	DH - Analytics
Susan Eckford	Veterinary Medicines Directorate
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Richard Pinder	PHE - Behavioural Insights
Richard Puleston	PHE - Field Epidemiology Services
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