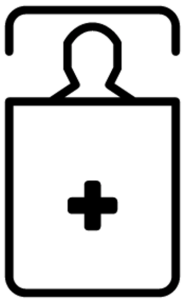
HSC Public Health Agency

Surveillance of Antimicrobial Use and Resistance in Northern Ireland, Annual Report, 2017

Contents

Executive summary

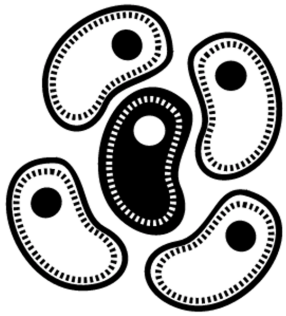


E. coli
Bloodstream Infection
980 in 2009
1487 in 2016

K. pneumoniae
Bloodstream Infection
143 in 2009
208 in 2016

E. coli resistance to
Piperacilin-tazobactam
8.8% in 2009
15.6% in 2016

K. pneumoniae resistance to
Piperacillin-tazobactam
8.6% in 2009
19% in 2016



Antibiotic Prescribing:
Primary care: 85%
Secondary care: 15%

2014 2015 2016

No change in total antibiotic use from 2014 to 2016 @ 32 DDD / 1000 inhabitants / day

Authors

Lynsey Patterson, MSc, PhD, MFPH
Declan Bradley, MB ChB, MA, MPH, PhD, MRCP(UK), FFPH

Acknowledgements

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We also thank the members of the Epidemiology Subgroup of the Healthcare-associated Infection and Antimicrobial Stewardship Improvement Board for their advice on the development of the report, noting in particular the assistance of David Farren, Derek Fairley and Sara Hedderwick.

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Background

Antibiotics have been one of the most important life-saving medical developments of the last century. When a course of antibiotics is prescribed, they will only work against certain types of bacteria and not others (so-called intrinsic resistance). In addition, some bacteria can develop tolerance to certain antibiotics or develop ways to break them down (so-called extrinsic resistance). In either case, if these go on to cause an infection it can be much more difficult to treat. This is called “antimicrobial resistance”. There is a risk of selecting for the survival of antimicrobial resistant organisms any time that antibiotics are used. Being prescribed a single course of antibiotics increases a person’s chance of acquiring resistant bacteria[1]. If the use of antibiotics remains unchecked, common infections will become more dangerous, and surgical procedures that require antibiotics will become more difficult to perform safely. Antimicrobial-resistant infections already cause illness and death for patients, and also disrupt care in hospitals. Reducing the use of antibiotics where they are not necessary now will help keep antibiotics working in the future. In recognition of this, the Department of Health (then the Department of Health, Social Services and Public Safety) published a five year Strategy for Tackling Antimicrobial Resistance (STAR 2012-2017) in 2012[2]. One of the key objectives of STAR was “to establish and maintain systems to monitor antimicrobial usage and surveillance of resistance”. This report is a product of the systems that have been established in response to this goal.

The tasks of preventing and reducing antimicrobial resistant infections, and reducing antimicrobial consumption are led at a policy level in Northern Ireland by the Department of Health-chaired Strategic Antimicrobial Resistance and Healthcare-associated Infection (SAMRHAI) group, which includes representatives responsible for animal and environmental as well as human health. For translating policy and strategy into action for human health, the Public Health Agency leads a multi-agency group, the Healthcare-associated Infection and Antimicrobial Stewardship Improvement Board, which has a number of themed subgroups that are responsible for regional efforts to reduce harm from antimicrobial use and resistance in different settings. This report is issued under the auspices of the Improvement Board. The report is divided into two major sections. The first describes trends in antibiotic resistance in Northern Ireland. We selected combinations of bacteria and antibiotics in line with those identified as key indicators as part of the UK Antimicrobial Resistance strategy[3]. In addition, we have made reference to additional bacteria-antibiotic combinations included in the English surveillance programme for antimicrobial utilisation and resistance (ESPAUR) report[4].

The second section describes the trends in antibiotic consumption in Northern Ireland. Antibiotic consumption is the key driver for the emergence of resistance. Antibiotics are prescribed across a range of settings including primary care (GP), secondary care (hospitals) and by dentists. In this inaugural report, we provide information for primary and secondary care. We aim to provide more detailed information about different healthcare settings and clinical specialities in future reports.

The aim of the report is to describe trends in antimicrobial resistance and antibiotic consumption in Northern Ireland. As surveillance data is information for action this report will inform and drive best practice in antimicrobial prescribing.

Method

Antibiotic resistance

Data sources

Testing for bacteria in human biological specimens and their susceptibility to antibiotics is conducted in laboratories in five Health and Social Care Trusts in Northern Ireland. Infections that meet certain criteria, usually the most severe that occur in the blood (bacteraemias), are reported voluntarily to the Public Health Agency's CoSurv Information System from each Trust's microbiology and/or virology laboratories. The resistance data included in this report includes selected bacteraemias that were reported to the PHA during 2009 - 2016 (presented by calendar year).

The data for carbapenemase producing organisms (CPO) has been collected as part of a voluntary reporting service. In cases where a microbiology laboratory suspects a CPO, the specimen is submitted to Public Health England's (PHE) Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) reference unit for investigation. The reference lab then notifies the PHA of positive results. Confirmed isolates include both colonisations and infections.

Definitions

Hospital microbiology laboratories report antimicrobial susceptibility test results "susceptible", "intermediate" or "resistant". For the purpose of this report, antibiotic susceptibility test results reported as "intermediate" or "resistant" were combined and presented as "non-susceptible". For analysis of resistance to more than one antibiotic, multidrug resistance (MDR) was defined as acquired non-susceptibility to at least one agent in three or more antimicrobial classes.

Antibiotic consumption

Data sources

Consumption data for primary and secondary care was obtained using the data submitted to the European Antimicrobial Consumption Surveillance Network (ESAC-Net). The primary care antimicrobial consumption data were extracted from the Electronic Prescribing Database by the Health and Social Care Board. The data includes all Health and Social Care (HSC; equivalent to National Health Service) general practitioner prescribing in practices and out-of-hours centres; all nurse, pharmacy and allied health professional HSC prescribing; and all HSC dental prescribing. The secondary care antimicrobial consumption data were extracted by each Trust's JAC Medicines Management System and aggregated for all five Trusts to give Northern Ireland totals. It was not possible to analyse at the level of hospital departments or systems, such as inpatient or outpatient. The data for both settings are available from 2014 - 2016 and are presented by calendar year.

Definitions

The classification of antibiotic used is based on the anatomical therapeutic chemical (ATC) classification system, using the WHO defined daily doses (DDD) for each drug and where grouped, this has been done according to Kucer's "The Use of Antibiotics" (6th edition)[5]. It is important to note that in England, hospitals usually dispense outpatient medications, whereas in Northern Ireland these are usually prescribed by general practitioners at the request of secondary care specialists. A significant proportion of outpatient prescribing is therefore counted under primary care in Northern Ireland and secondary care in England. There is currently no way of separating these prescriptions from the rest of primary care prescribing in Northern Ireland. In England, outpatient prescribing accounts for 6% of secondary care antimicrobial prescribing [4].

Denominator

Mid-year population estimates for 2014-2016 were obtained from the Northern Ireland Statistics and Research Agency (NISRA) and used to express DDD's per 1,000 inhabitants per day. Hospital activity and occupancy statistics were obtained from the Department of Health published data.

Results

Antibiotic resistance

E. coli bacteraemia

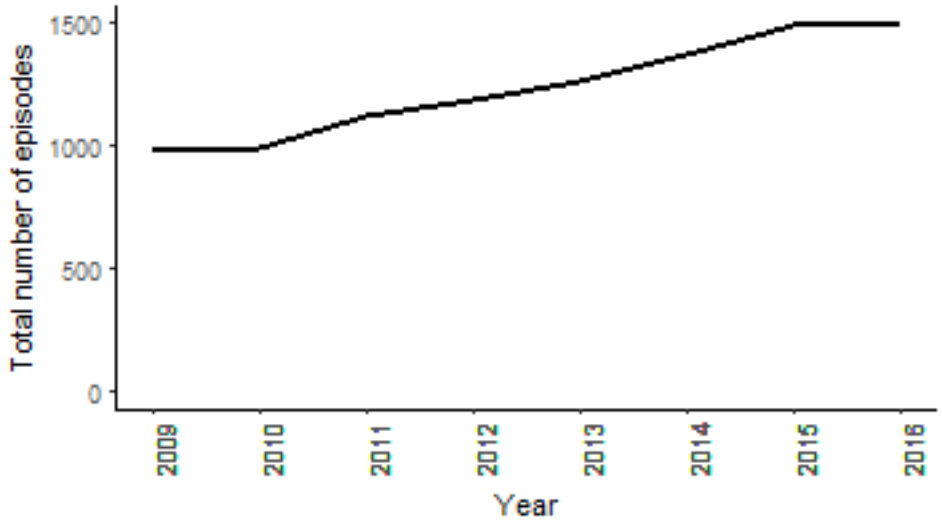

Figure 1: The total number of *E. coli* bacteraemias reported to the Public Health Agency, 2009 - 2016

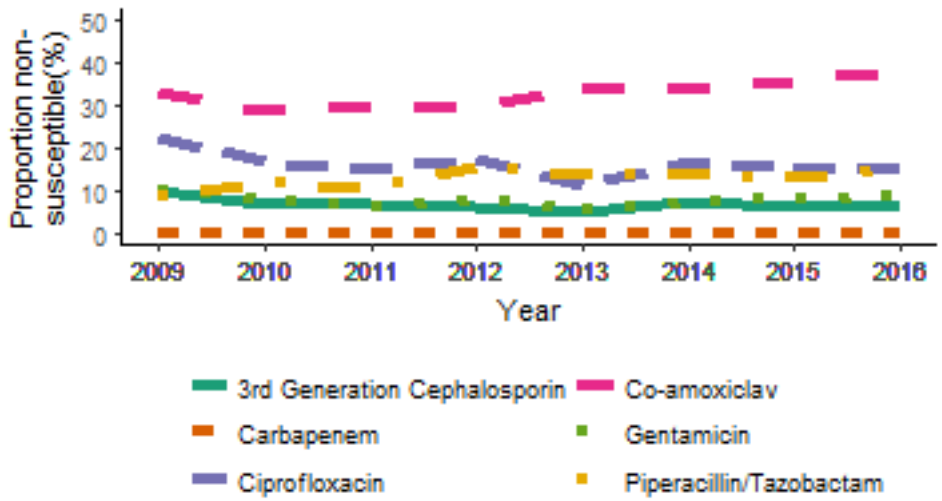

Figure 2: The proportion of *E. coli* bacteraemias resistant to selected antibiotics in NI, 2009 - 2016

The number of *E. coli* bacteraemias has increased between 2009 and 2016, from 980 cases to 1487 cases (Figure 1). The proportion of isolates tested against key antibiotics during 2016 is shown in Appendix 3.

Resistance to piperacillin/tazobactam and co-amoxiclav has increased over the time period (8.8% to 15.6% and 32.9% to 38.1% respectively). The proportion of isolates resistant to gentamicin has remained relatively stable during 2009 - 2016 (9.8% to 8.6%). Resistance among *E. coli* to carbapenems has remained negligible (no isolates detected in 2016). Resistance to third generation cephalosporins and ciprofloxacin has decreased (9.8% to 6.3% and 22.6% to 15.1% respectively (Figure 2).

Despite the reduction in the proportion of resisant isolates reported for the chosen antibioitics it should be noted that in absolute terms, the number of resistant isolates have increased. For example, while the proportion resistant to ciprofloxacin decreased during 2009 - 2016 (22.6% to 15.1%), the number of infections increased (182 to 190 episodes). The number of isolates resistant to three or more classes also increased (34 to 48 episodes)

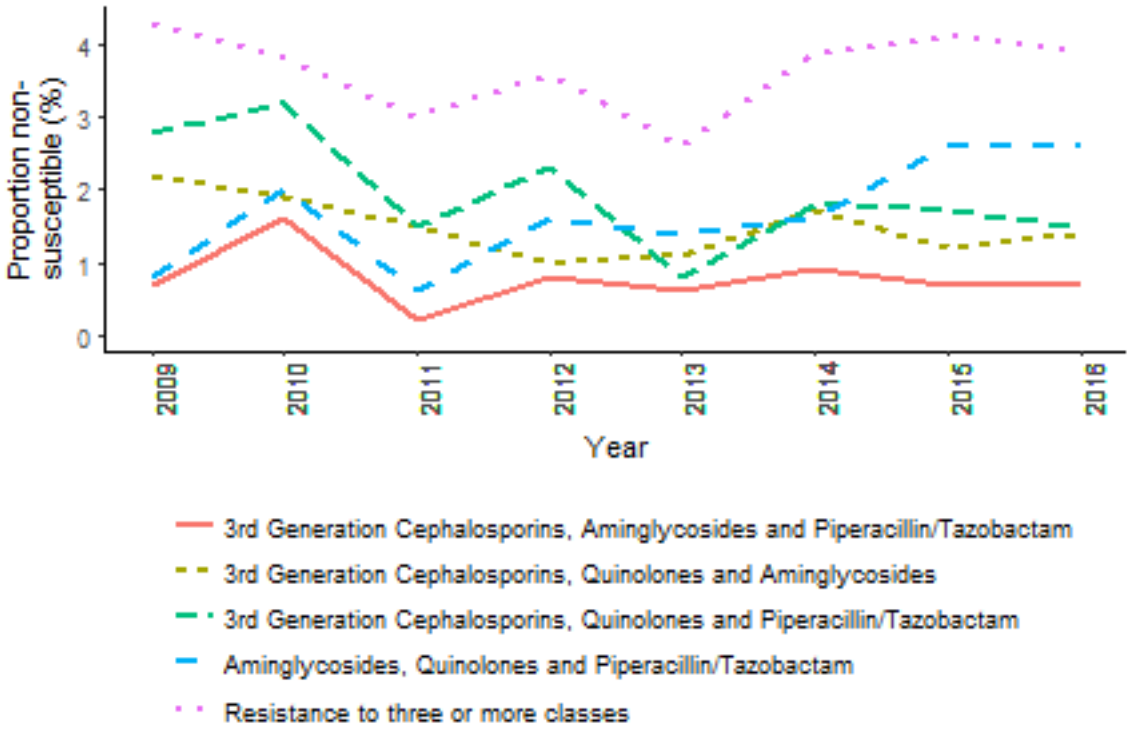

Figure 3: The proportion of *E. coli* bacteraemias reported to the Public Health Agency with multi-drug resistance, 2009 - 2016

The proportion of *E. coli* bacteraemias showing multi-resistance remained stable between

2009 and 2016 and varied in the range of 1-4%. Resistance to at least three or more classes has fluctuated around 4%. Within the named combination of antibiotic classes, the highest proportion of resistance was seen for combinations of aminoglycosides, quinolones and piperacillin/tazobactam and the lowest for third-generation cephalosporins, aminoglycosides and piperacillin/tazobactam (Figure 3).

K. pneumoniae bacteraemia

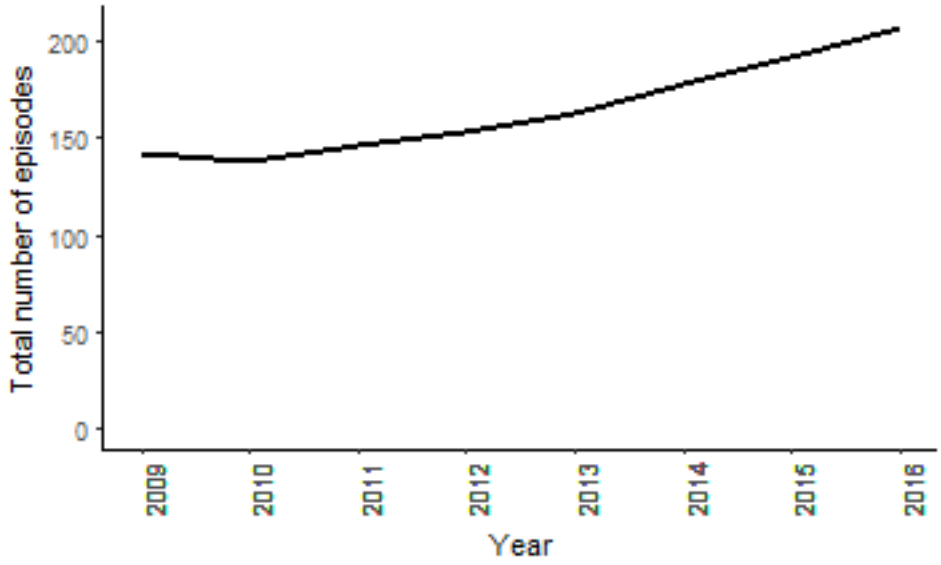

Figure 4: The total number of *K. pneumoniae* bacteraemias reported to the Public Health Agency, 2009 - 2016

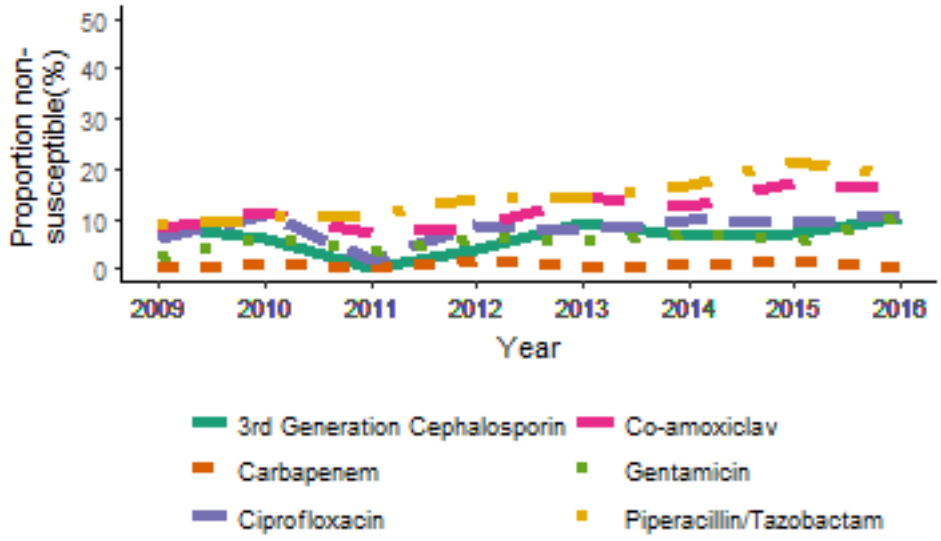

Figure 5: The proportion of *K. pneumoniae* bacteraemias resistant to selected antibiotics in NI, 2009 - 2016

In 2016, the two most common species among blood culture isolates of the genus *Klebsiella* were *K. pneumoniae* (208/269; 77%) and *K. oxytoca* (60/269; 22%). The following

describes trends and resistance for *K. pneumoniae*.

The number of *K. pneumoniae* bacteraemias has increased between 2009 and 2016, from 143 cases to 208 cases (Figure 4). The proportion of isolates tested against key antibiotics during 2016 is shown in Appendix 3.

There has been an increase in the proportion of *K. pneumoniae* bacteraemias resistant to selected antibiotics over the 5 year period: ciprofloxacin (6.3% to 10.7%); gentamicin (2.2% to 10.9%); co-amoxiclav (8.1% to 15.6%) and piperacillin/tazobactam (8.6% to 19%). There was a smaller increase in the proportion of isolates resistant to third generation cephalosporins (8.7% to 10.4%). Resistance to carbapenems remained relatively stable over the period 2009 - 2016 (0% in 2016; Figure 5).

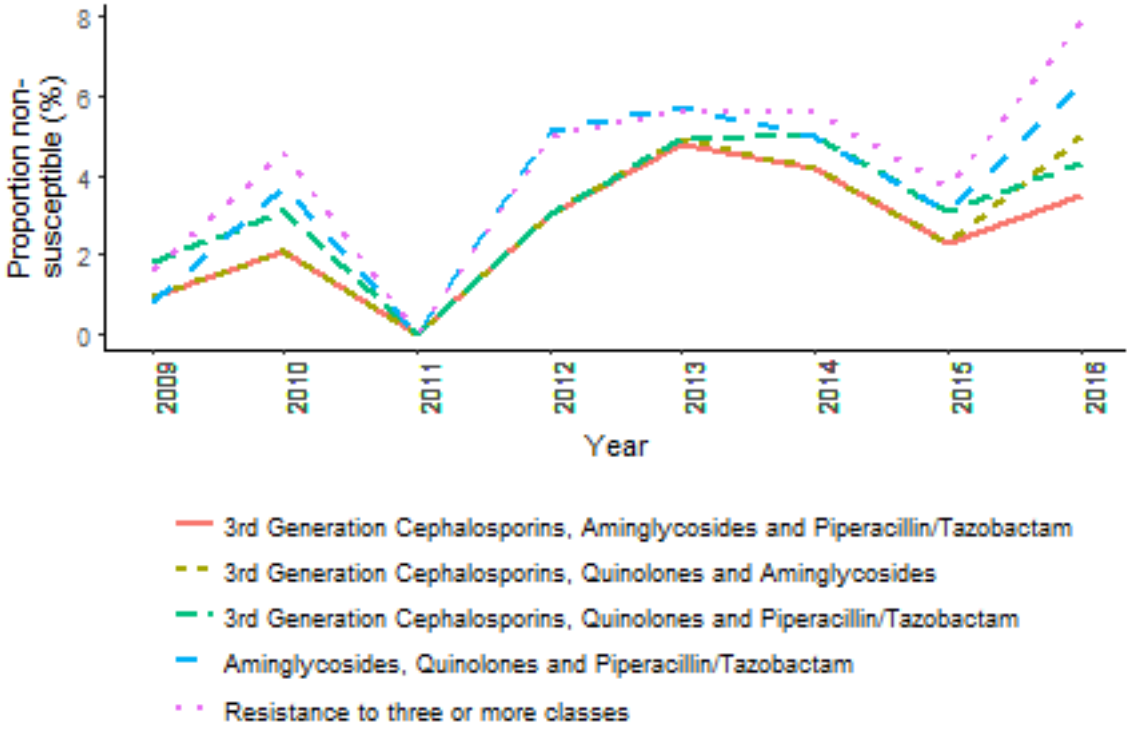

Figure 6: The proportion of *K.pneumoniae* bacteraemias reported to the Public Health Agency with multi-drug resistance, 2009 - 2016

The proportion of *K. pneumoniae* bacteraemias showing multi-resistance has increased slightly between 2009 and 2016 across all antibiotic combinations. Multi-resistance varied between 0 - 8%. The proportion of *K. pneumoniae* bacteraemias exhibiting resistance to three or more classes has increased over time. Within the named combinations of antibiotic classes, the highest proportions were seen for combinations of aminoglycosides,

quinolones and piperacillin/tazobactam and the lowest for third generation cephalosporins, aminoglycosides and piperacillin/tazobactam (Figure 6).

Unlike *E. coli* both the proportion and absolute numbers of *K. pneumoniae* bacteraemias have increased. For example, the proportion of *K. pneumoniae* resistant to ciprofloxacin increased by 4% during 2009 - 2016 (6.3% to 10.7%), the number of infections doubled (8 to 19 episodes). The number of isolates resistant to three or more classes also increased (2 to 14 episodes).

Pseudomonas species bacteraemia

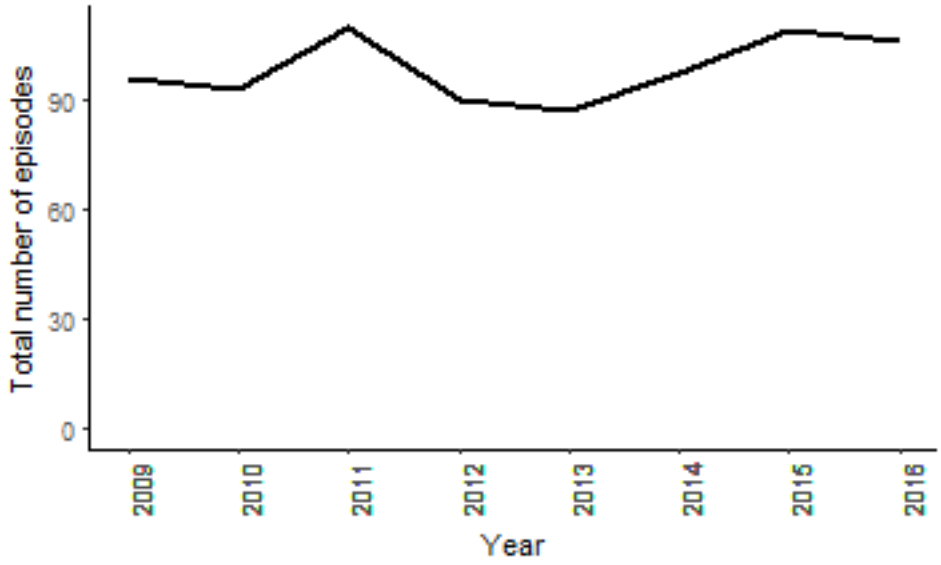

Figure 7: The total number of Pseudomonas species bacteraemias reported to the Public Health Agency, 2009 - 2016

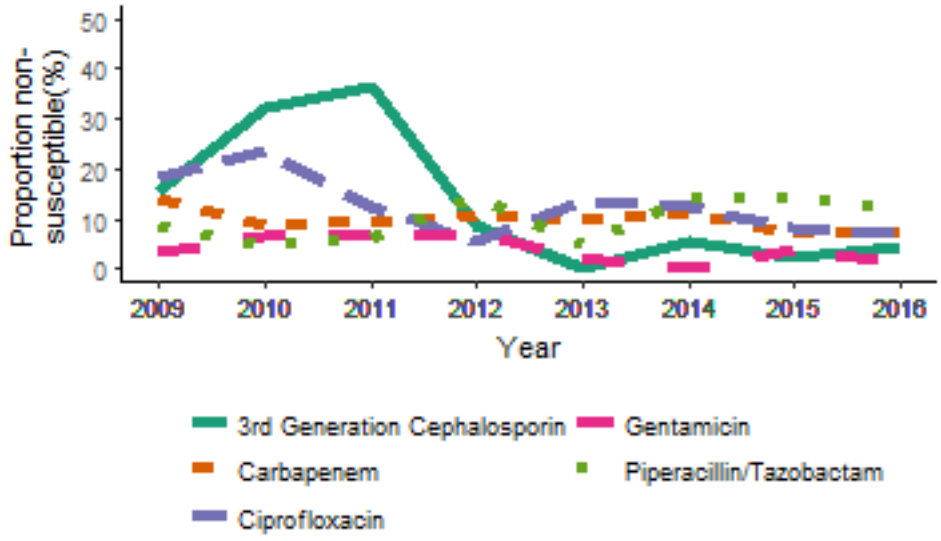

Figure 8: The proportion of Pseudomonas species bacteraemias resistant to selected antibiotics in NI, 2009 - 2016

The number of *Pseudomonas species* bacteraemias has remained relatively stable over the last 5 years, with a slight decrease from 2015 to 2016 (109 cases to 106 cases;

Figure 7). The proportion of isolates tested against key antibiotics during 2016 is shown in Appendix 3.

There has been a slight increase in the proportion of *Pseudomonas species* bacteraemias resistant to piperacillin/tazobactam over the 5 year period (8.5% to 12.1%). Resistance among selected antibiotics has decreased: ciprofloxacin (18.2% to 7.1%); third generation cephalosporins (15.7% to 4.3%); gentamicin (3.2% to 1%) and; carbapenems (14.3% to 7.1%; Figure 8).

S. aureus bacteraemia

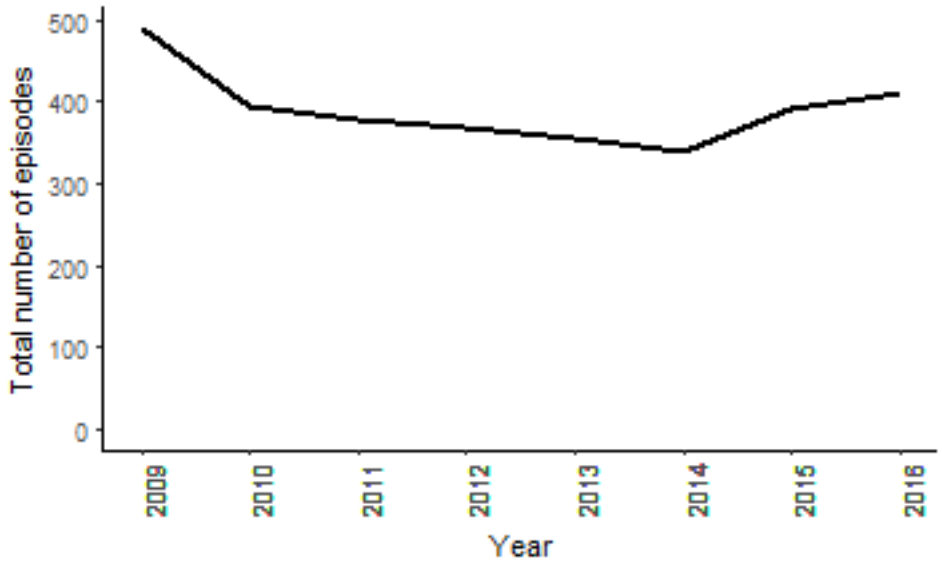

Figure 9: The total number of *S. aureus* bacteraemias reported to the Public Health Agency, 2009 - 2016

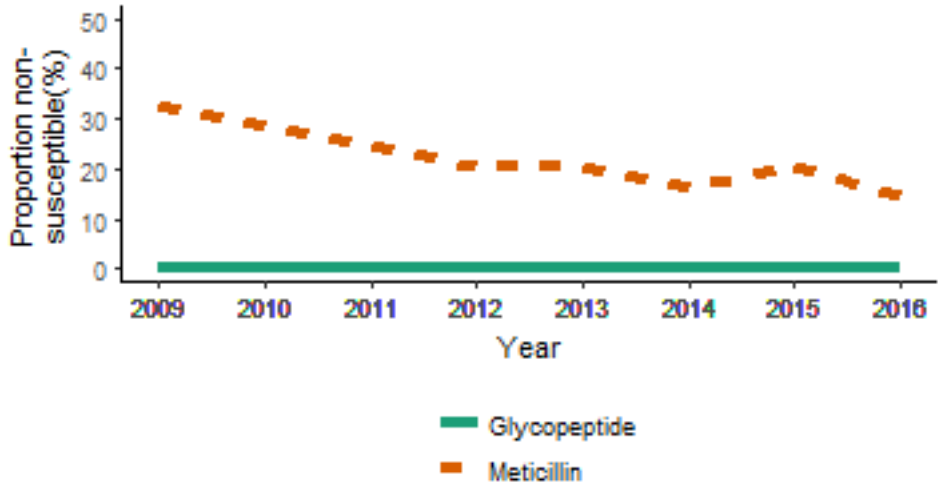

Figure 10: The proportion of *S. aureus* bacteraemias resistant to selected antibiotics in NI, 2009 - 2016

During the last five years, the number of *S. aureus* bacteraemias had been decreasing but has increased year on year from 2014 to 2016 (338, 393 and 411 cases respectively;

Figure 9). The proportion of isolates tested against key antibiotics during 2016 is shown in Appendix 2. The proportion of *S. aureus* that are resistant to meticillin (MRSA) has been decreasing over the last 5 years, with a low of 14.6% in 2016. The proportion of *S. aureus* that are resistant to glycopeptides has remained low (Figure 10).

Enterococcus species bacteraemia

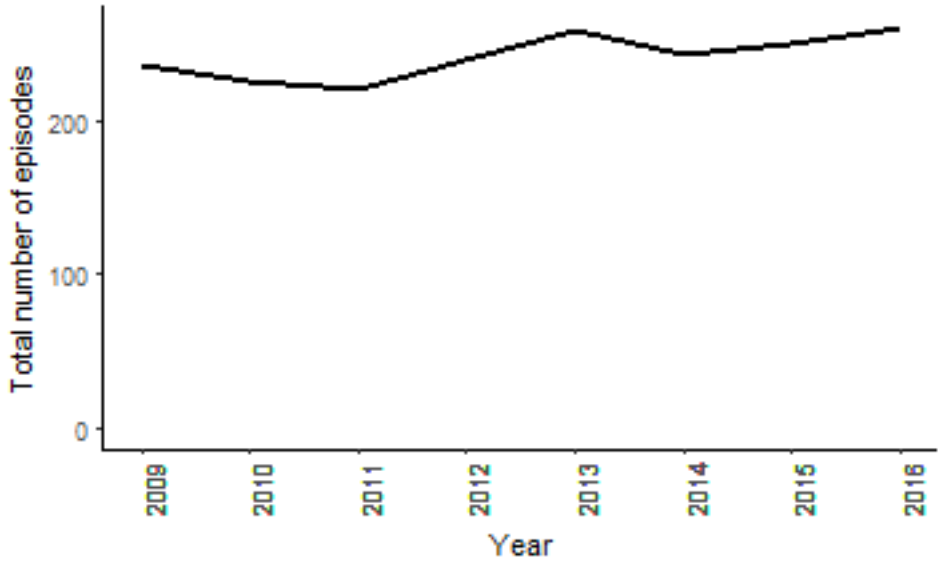

Figure 11: The total number of Enterococcus species bacteraemias reported to the Public Health Agency, 2009 - 2016

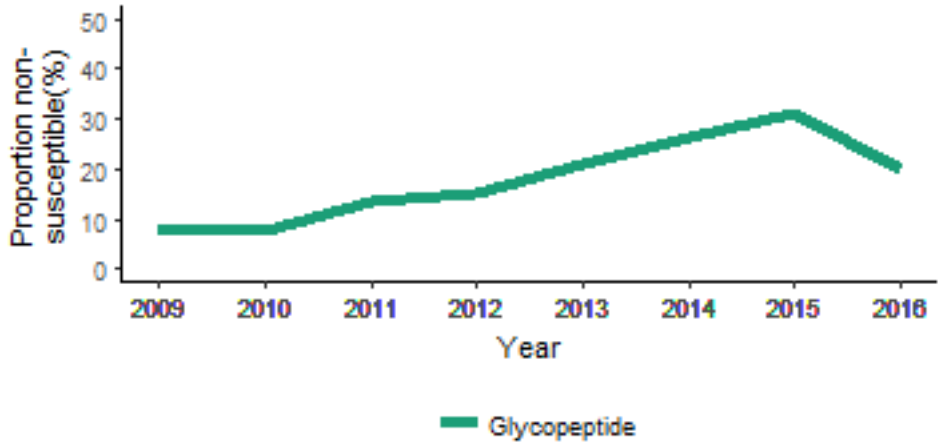

Figure 12: The proportion of Enterococcus species bacteraemias resistant to selected antibiotics in NI, 2009 - 2016

The number of *Enterococcus species* bacteraemias has fluctuated over the last 5 years, with a slight increase from 2015 to 2016 (250 cases to 261 cases; Figure 11). During

2016, 90.8% were tested against glycopeptides. Resistance to glycopeptides has been increasing over the last 5 years, but decreased from 2015 to 2016 where 19.8% were resistant (Figure 12).

S. pneumoniae bacteraemia

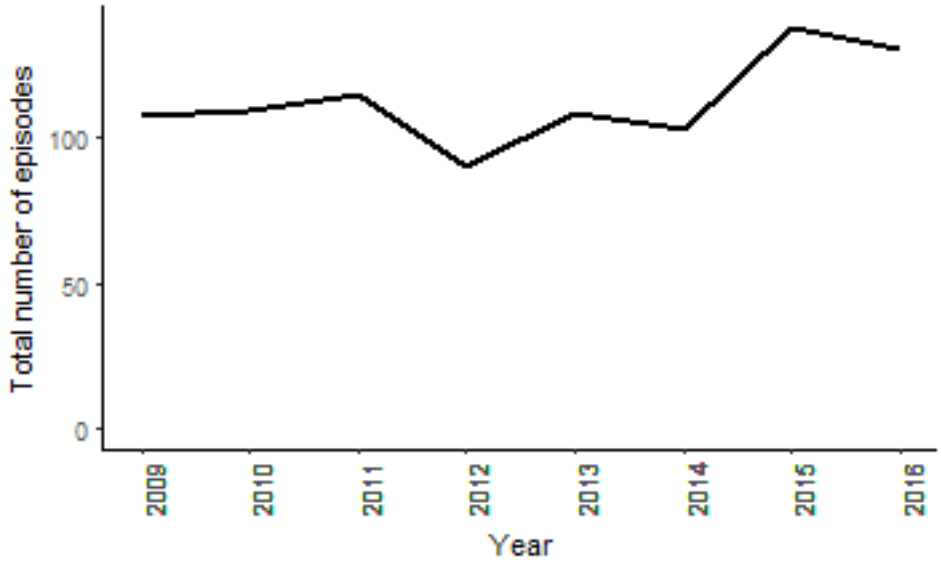

Figure 13: The total number of *S. pneumoniae* bacteraemias reported to the Public Health Agency, 2009 - 2016

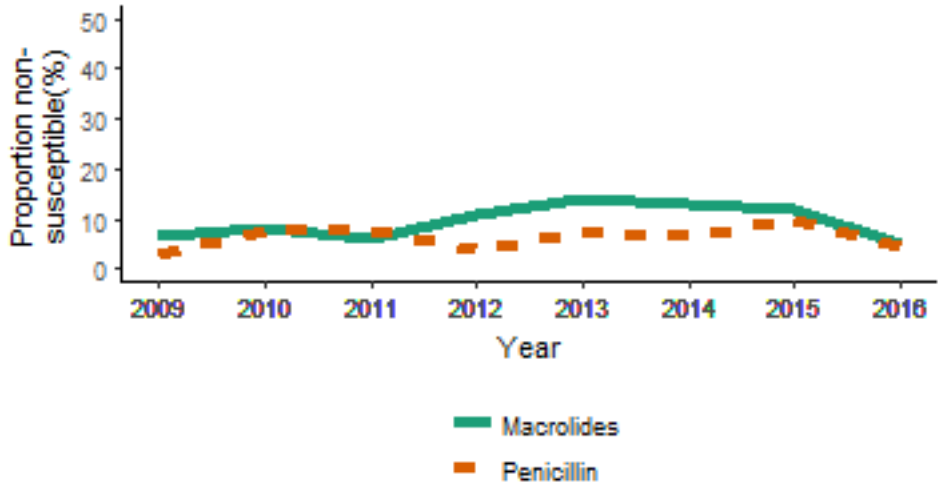

Figure 14: The proportion of *S. pneumoniae* bacteraemias resistant to selected antibiotics in NI, 2009 - 2016

There has been a general increase in the number of *S. pneumoniae* bacteraemias during the time period, with a slight decrease reported from 2015 to 2016 (138 cases to 130 cases;

Figure 13). The proportion of isolates tested against key antibiotics during 2016 is shown in Appendix 3. While the proportion of *S. pneumoniae* that are resistant to macrolides increased between 2009-2013, it has been decreasing since (6.7% to 5.1% during 2009 - 2016) while resistance to penicillin has increased slightly (2.9% to 4.5%; Figure 14).

Acinetobacter species bacteraemia

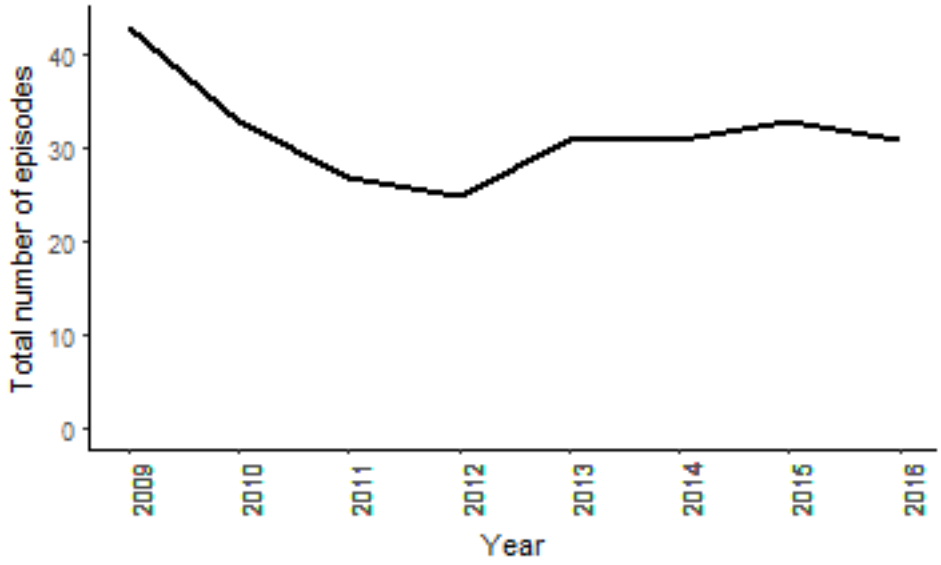

Figure 15: The total number of Acinetobacter species bacteraemias reported to the Public Health Agency, 2009 - 2016

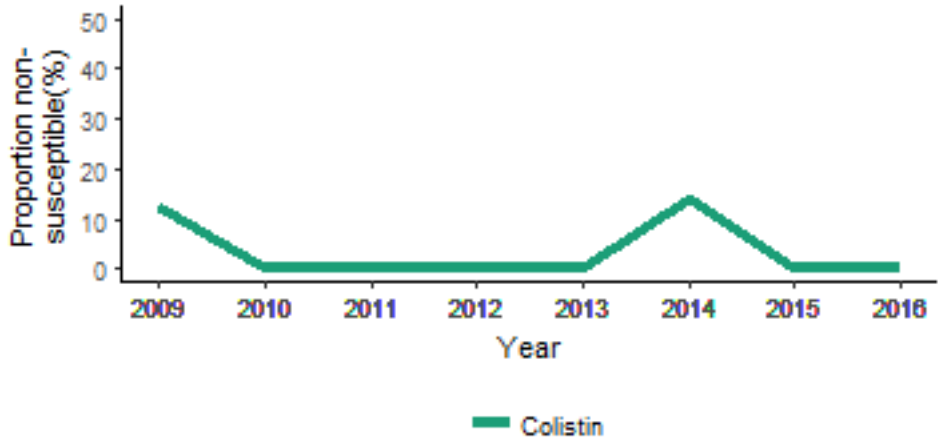

Figure 16: The proportion of Acinetobacter species bacteraemias resistant to selected antibiotics in NI, 2009 - 2016

The total number of *Acinetobacter species* bacteraemias has decreased during 2015 to 2016 from 33 cases to 31 cases (Figure 15). During 2016, 29 were tested against colistin.

Resistance to colistin among *Acinetobacter species* has remained at zero (Figure 16).

Voluntary Carbapenamse Producing Organisms surveillance

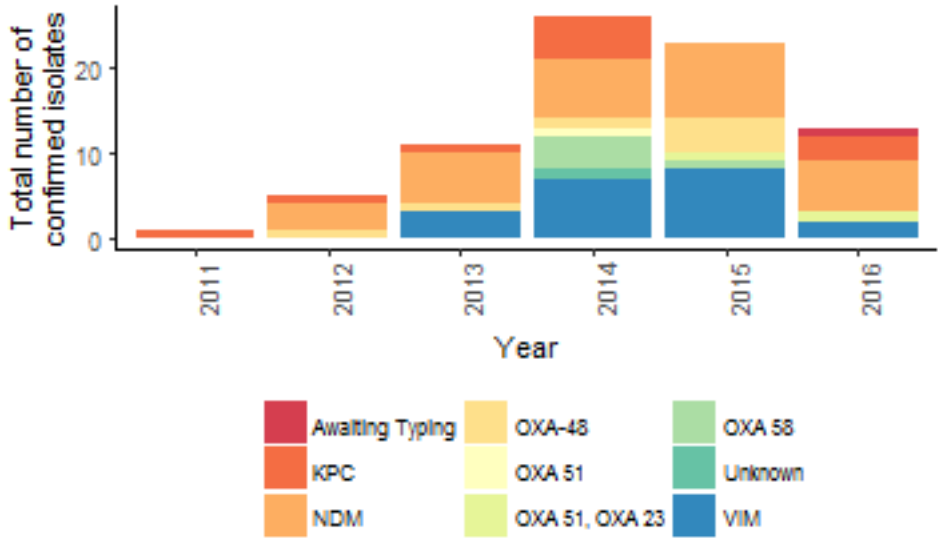

Figure 17: Carbapenamase activity among CPO confirmed isolates that have been sent to Public Health England's AMRHAI Reference unit, 2011 - 2016

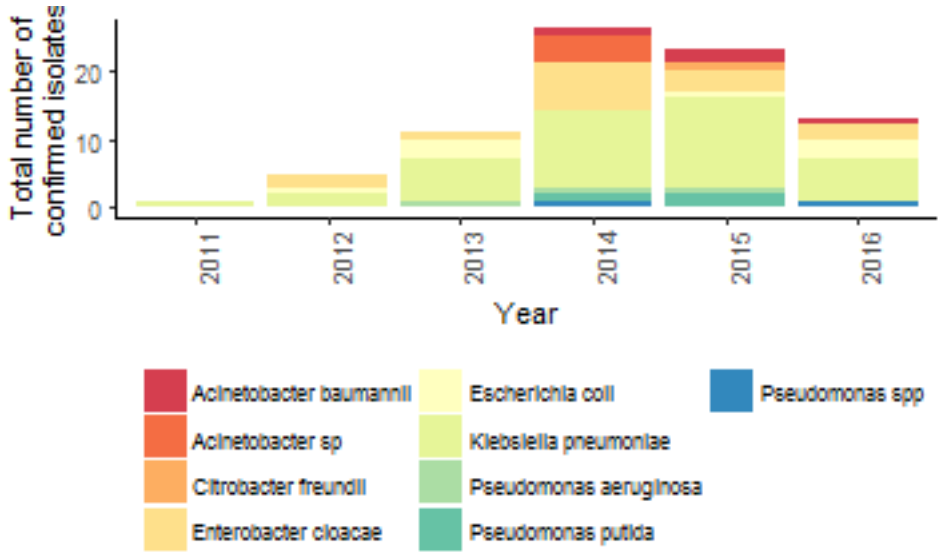

Figure 18: Organisms with confirmed carbapenamase production among isolates that have been sent to Public Health England's AMRHAI Reference unit, 2011 - 2016

The number of CPO reported to the PHA increased between 2011 and 2014 but has decreased year on year thereafter (13 episodes reported during 2016). This likely reflects

the voluntary nature of reporting (case ascertainment) as well as local developments in the ability to test for CPO. The most common reported resistance mechanism is New Delhi Metallo-Beta-lactamase (NDM) (31 episodes during 2011-2016; Figure 17). The most commonly reported CPO over the time period was *K. pneumoniae* (Figure 18).

Antibiotic resistance in *Neisseria gonorrhoeae*

Gonorrhoea has been identified as at risk of becoming an untreatable disease due to the emergence of antimicrobial resistance to successive standard treatments. This has necessitated changes to recommended antibiotic prescribing. In the UK, current recommended treatment guidelines include ceftriaxone with azithromycin, along with routine test of cure[6]. Third-generation cephalosporins are the last remaining effective antibiotics but reports of treatment failures and increasing minimum inhibitory concentrations (MIC) levels have raised concerns that they will no longer be a suitable treatment option[7]. Since 2015, NI has participated in the European Gonococcal Antimicrobial Surveillance Programme(Euro-GASP)[8] through the Royal Victoria Hospital, Belfast. This GUM clinic captured 62% of all gonorrhoea diagnoses made during 2016.

In 2016, gonorrhoea diagnoses accounted for 10% (592/5,719) of all new STI diagnoses made in NI GUM clinics. During the study period, 20 isolates were cultured and sent to Public Health England for inclusion in EuroGASP. Of these, *N. gonorrhoeae* was successfully retrieved from 13 isolates (65%).

During 2015 and 2016, 49 isolates were tested within the EuroGASP programme and showed similar resistance pattern to the UK overall with 12% resistant to azithromycin and 0% resistant to ceftriaxone.

The full report for this surveillance programme will be published on the PHA website.

Antibiotic consumption

Rates of antibiotic consumption by healthcare setting

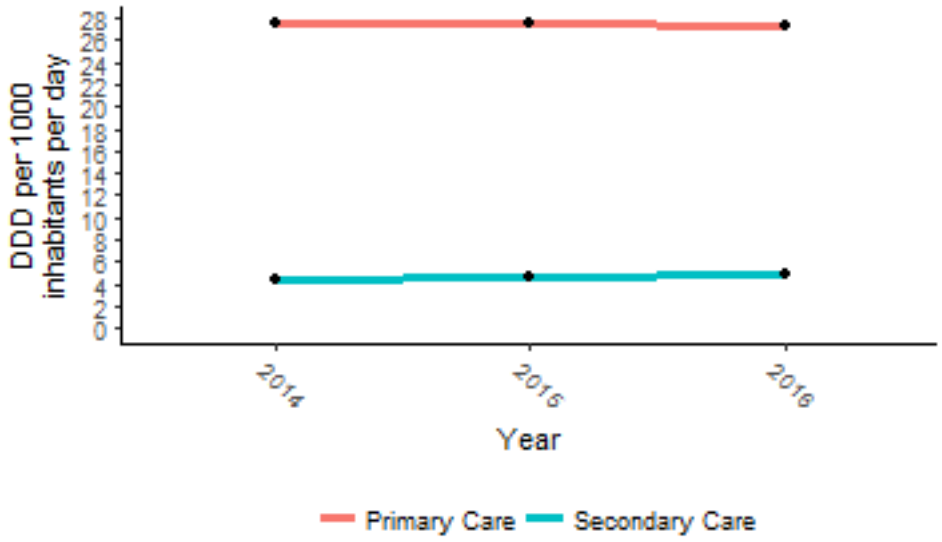

Figure 19: Total antibiotic consumption, expressed as DDD per 1000 inhabitants per day, NI, 2014-2016

In 2016, the total consumption of antibiotics in primary and secondary care was 32 per 1000 inhabitants per day (32.12 and 32.21 per 1000 inhabitants per day in 2014 and 2015 respectively).

The majority of antibiotic prescribing took place in primary care (85% during 2016; Figure 19). In primary care, rates have been stable since 2014 (during 2016 the overall rate of prescribing in primary care was 27.22 per 1000 inhabitants per day). There has also been no change in the overall rate of antibiotic prescribing in secondary care (4.79 per 1000 inhabitants per day during 2016; Figure 19).

Rates of antibiotic consumption in Secondary care

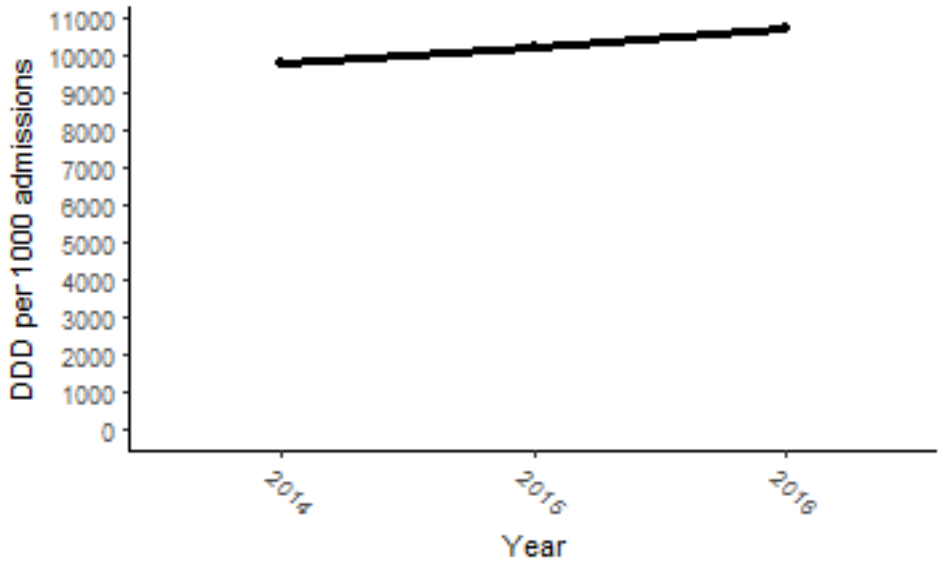

Figure 20: Total antibiotic consumption, expressed as DDD per 1000 admissions, NI, 2014-2016

There has been a year on year increase in the rate of antibiotic consumption expressed as DDD per 1000 admissions: 9772 in 2014 to 10728 DDD per 1000 admissions in 2016 (Figure 20).

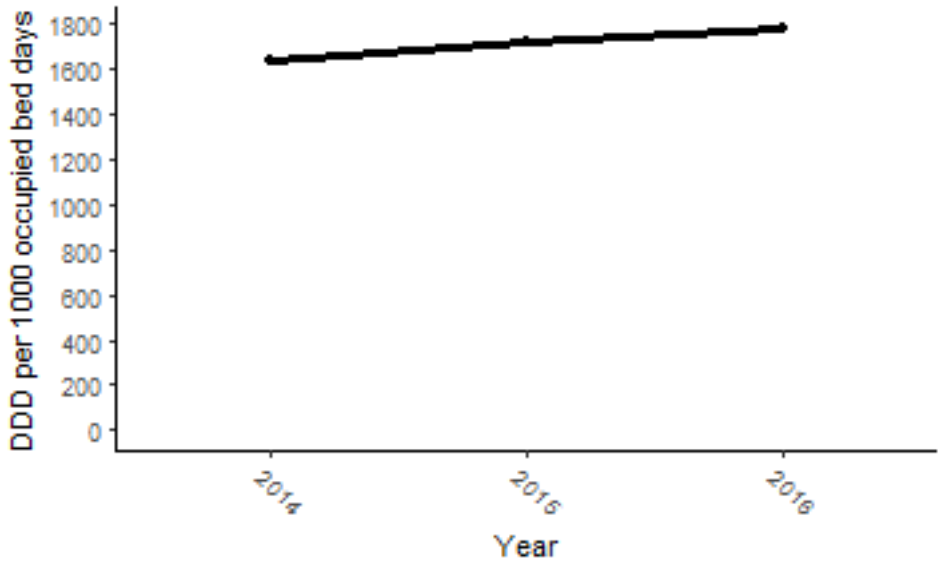

Figure 21: Total antibiotic consumption, expressed as DDD per 1000 occupied bed days, NI, 2014-2016

Like the admissions data, the rate of antibiotic consumption per 1000 occupied bed days has been increasing year on year: 1643 in 2014 to 1787 DDD per 1000 occupied beddays in 2016 (Figure 21).

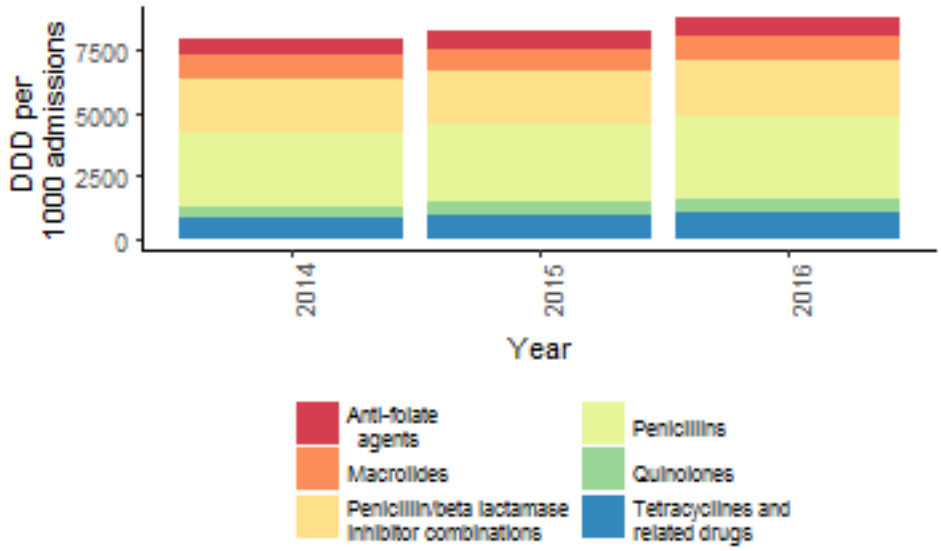

Figure 22: Total antibiotic consumption by key agents in secondary care, expressed as DDD per 1000 admissions, NI, 2014-2016

This figure shows the top 6 key agents prescribed in secondary care. During 2016, the highest rates for antibiotic consumption were penicillins (3331 DDD per 1000 admissions), Penicillin/beta lactamase inhibitor combinations (2247 DDD per 1000 admissions) and tetracyclines and related drugs (1058 DDD per 1000 admissions; Figure 22).

Antibiotic consumption by key agents

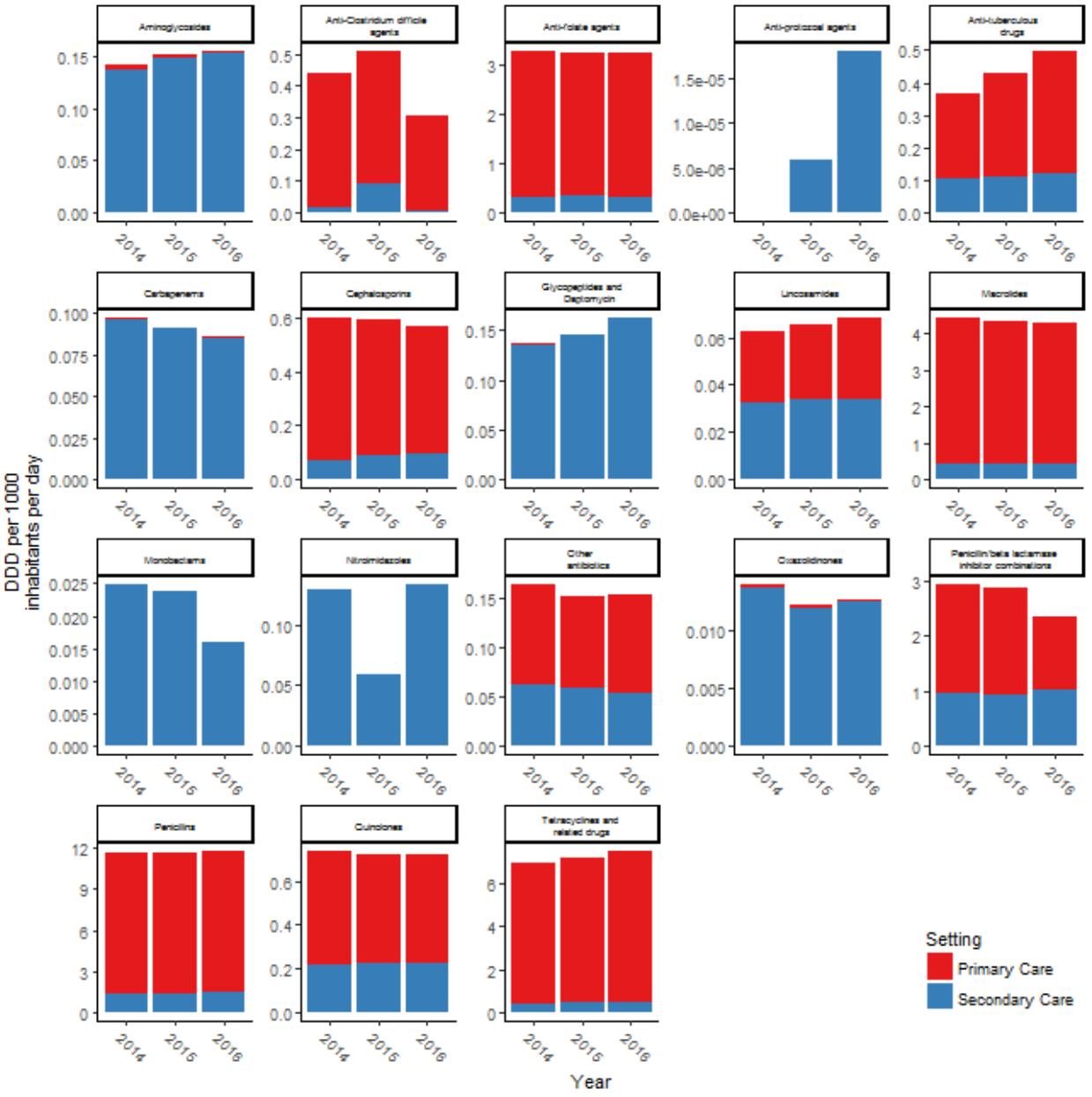

Figure 23: Total antibiotic consumption by key antibiotic groups[2], expressed as DDD per 1000 inhabitants per day, NI, 2014-2016

[2]Oral/rectal prepations for metronidazole(ATC P01AB01) and vancomycin (ATC A07AA09) are included in the anti-*Clostridium difficile* agents and do not appear in the nitroimidazoles or glycopeptides category respectively.

Note: differing scales on y-axis

During 2016, the most frequently used antibiotics in both primary and secondary care in NI were Penicillins (37.7% and 31.1% respectively), tetracyclines and related drugs (25.8% and 9.9% respectively) and macrolides (14.3% and 8.5% respectively). Overall, the rate of antibiotic prescribing has remained relatively stable across all groups (Figure 23).

Antibiotic consumption by class and individual antibiotics

Penicillins

Table 1: Total rate of Penicillins DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Class	DDD	Population	rate
2014	Penicillins	7839445	1840500	11.67
2015	Penicillins	7865333	1851600	11.64
2016	Penicillins	7986684	1862100	11.75

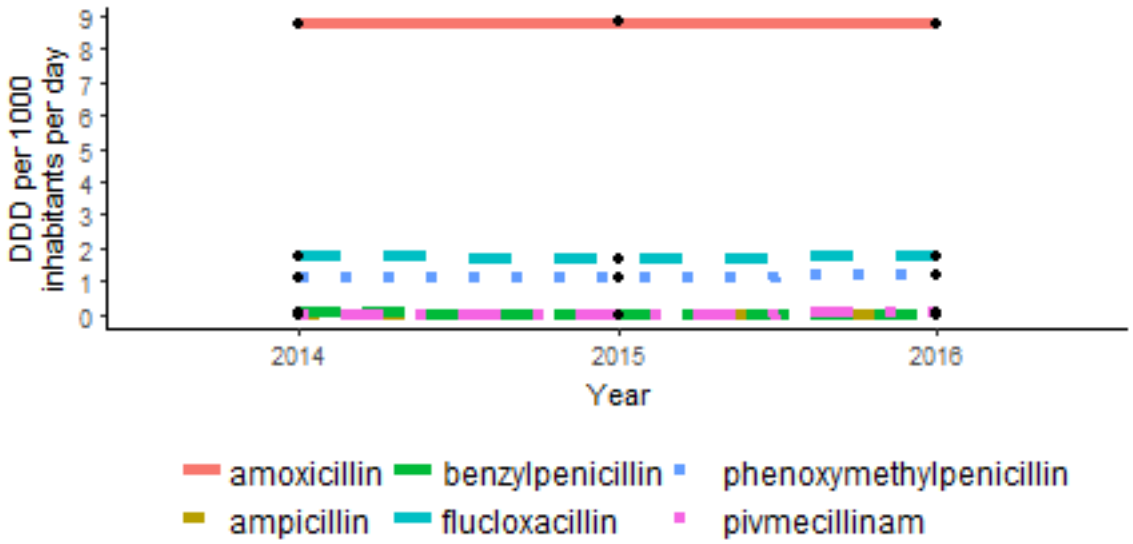

Figure 24: Consumption of most commonly used penicillins expressed per 1000 inhabitants per day, NI, 2014 - 2016

The figure represents the top six antimicrobial agents used in the Penicillins class. Penicillins accounted for 36.7% of antibiotic consumption in 2016. The rate of penicillin consumption has remained relatively stable with a rate of 11.75 per 1000 inhabitants per day during 2016. The highest rate was for amoxicillin (8.74 DDD per 1000 inhabitants per day in 2016; Figure 24).

Cephalosporins

Table 2: Total rate of Cephalosporins DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Class	DDD	Population	rate
2014	Cephalosporins	403786	1840500	0.60
2015	Cephalosporins	403585	1851600	0.60
2016	Cephalosporins	386092	1862100	0.57

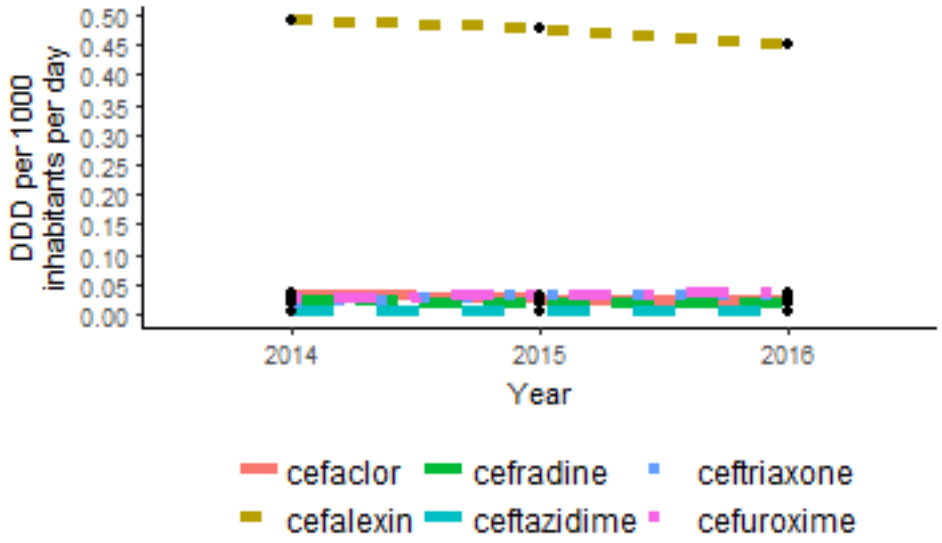

Figure 25: Consumption of most commonly used cephalosporins expressed per 1000 inhabitants per day, NI, 2014 - 2016

The figure represents the top six agents used in the Cephalosporins class. The rate of cephalosporin consumption has remained relatively stable with a rate of 0.57 DDD per 1000 inhabitants per day during 2016. The highest rate was for cefalexin, the rate of which has decreased over time (0.45 DDD per 1000 inhabitants per day during 2016; Figure 25).

Tetracyclines and related drugs

Table 3: Total rate of tetracyclines and related drugs consumption expressed as DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Class	DDD	Population	rate
2014	Tetracyclines and related drugs	4657539	1840500	6.93
2015	Tetracyclines and related drugs	4850875	1851600	7.18
2016	Tetracyclines and related drugs	5091340	1862100	7.49

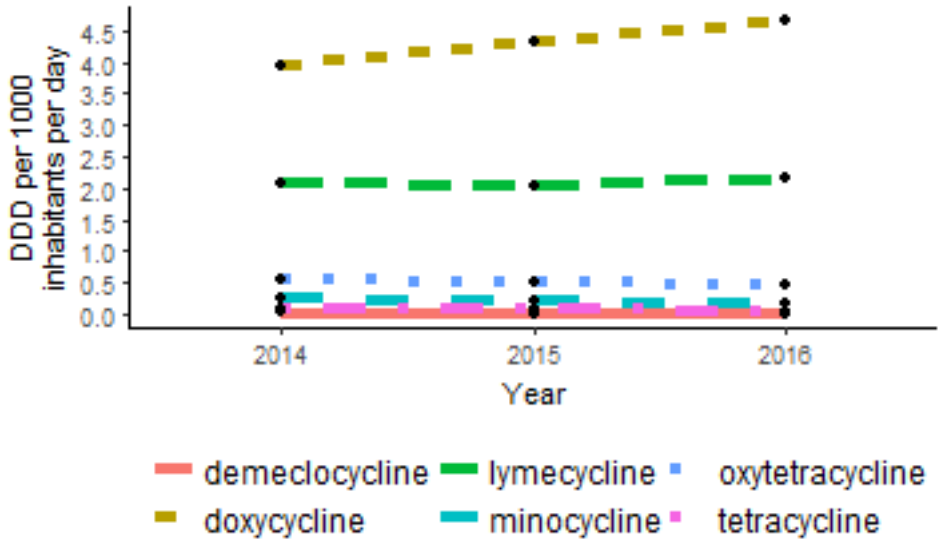

Figure 26: Consumption of most commonly used tetracyclines and related drugs[4] expressed per 1000 inhabitants per day, NI, 2014 - 2016

The figure represents the top six agents used in the tetracyclines and related drugs class. Tetracyclines and related drugs accounted for 23.4% of all antibiotic consumption in 2016. The rate of tetracyclines and related drugs consumption has increased during 2014 - 2016 with a rate of 7.49 DDD per 1000 inhabitants per day during 2016. The highest rate was for doxycycline, the rate of which has increased over time (3.95 to 4.64 DDD per 1000 inhabitants per day from 2014 to 2016; Figure 26).

[4]While demeclocycline and lymecycline are not primarily used for their antimicrobial effects they have been included as they can still be considered drivers of resistance.

Quinolones

Table 4: Total rate of Quinolones consumption expressed as DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Class	DDD	Population	rate
2014	Quinolones	493831	1840500	0.74
2015	Quinolones	488642	1851600	0.72
2016	Quinolones	490773	1862100	0.72

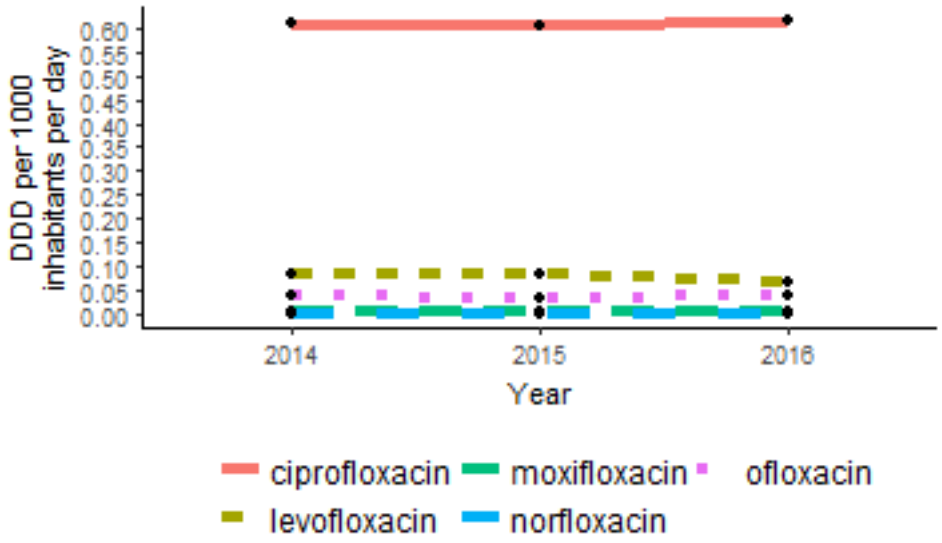

Figure 27: Consumption of most commonly used quinolones expressed per 1000 inhabitants per day, NI, 2014 - 2016

The rate of Quinolones consumption has remained stable during 2014 - 2016 with a rate of 0.72 DDD per 1000 inhabitants per day during 2016. The highest rate was for ciprofloxacin which has been stable over time (0.61 DDD per 1000 inhabitants per day in 2016; Figure 27).

Macrolides

Table 5: Total rate of Macrolides consumption expressed as DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Class	DDD	Population	rate
2014	Macrolides	2967557	1840500	4.42
2015	Macrolides	2920673	1851600	4.32
2016	Macrolides	2916764	1862100	4.29

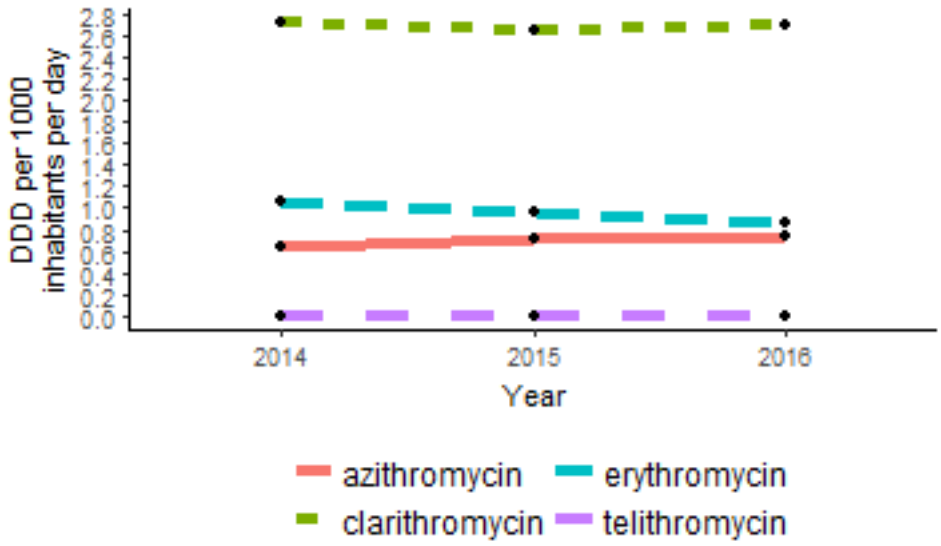

Figure 28: Consumption of most commonly used macrolides expressed per 1000 inhabitants per day, NI, 2014 - 2016

Macrolides accounted for 13.4% of all antibiotic consumption in 2016. The rate of Macrolides consumption has remained stable during 2014 - 2016 with a rate of 4.29 DDD per 1000 inhabitants per day in 2016. The highest rate was for clarithromycin which has been stable over time (2.7 DDD per 1000 inhabitants per day in 2016; Figure 28).

Carbapenems

Table 6: Total rate of Carbapenems consumption expressed as DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Class	DDD	Population	rate
2014	Carbapenems	65191	1840500	0.10
2015	Carbapenems	61799	1851600	0.09
2016	Carbapenems	58255	1862100	0.09

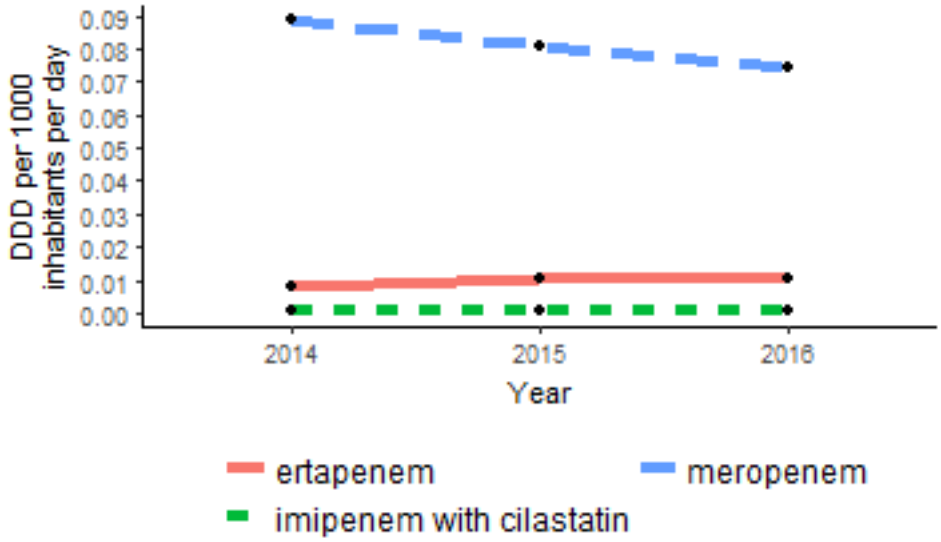

Figure 29: Consumption of most commonly used carbapenems expressed per 1000 inhabitants per day, NI, 2014 - 2016

The rate of Carbapenems consumption has remained stable during 2014 - 2016 with a rate of 0.09 DDD per 1000 inhabitants per day in 2016. The highest rate was for meropenem which has decreased slightly over time (0.09 in 2014 to 0.07 DDD per 1000 inhabitants per day in 2016; Figure 29).

Penicillin/beta lactamase inhibitor combinations

Table 7: Total rate of Penicillin/beta lactamase inhibitor combinations consumption expressed as DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Class	DDD	Population	rate
2014	Penicillin/beta lactamase inhibitor combinations	1961833	1840500	2.92
2015	Penicillin/beta lactamase inhibitor combinations	1932974	1851600	2.86
2016	Penicillin/beta lactamase inhibitor combinations	1594932	1862100	2.35

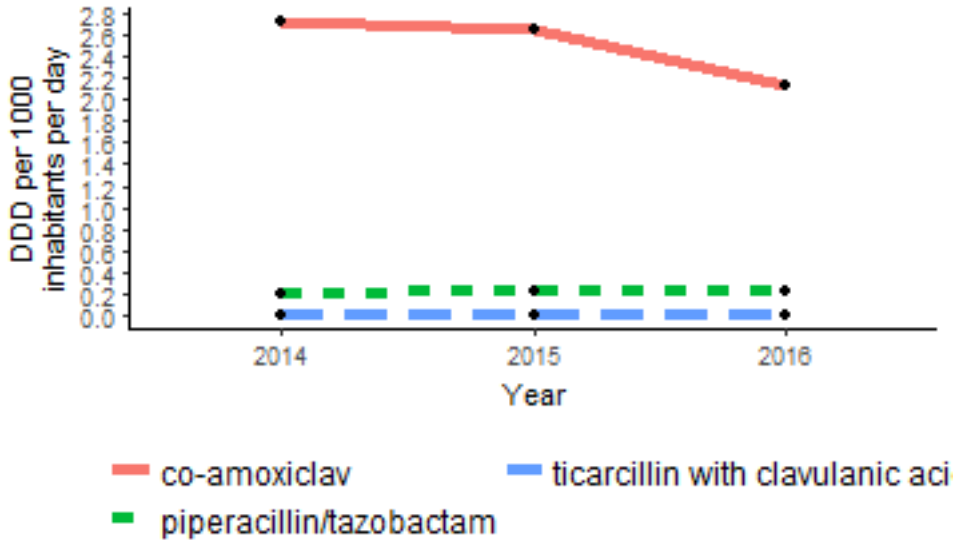

Figure 30: Consumption of most commonly used Penicillin/beta lactamase inhibitor combinations expressed per 1000 inhabitants per day, NI, 2014 - 2016

The rate of Penicillin/beta lactamase inhibitor combinations consumption has decreased during 2014 - 2016 with a rate of 2.35 DDD per 1000 inhabitants per day in 2016. The highest rate was for co-amoxiclav which has decreased over time (2.72 to 2.13 DDD per 1000 inhabitants per day from 2014 to 2016). The use of piperacillin/tazobactam has been stable over time (0.21 DDD per 1000 inhabitants per day in 2016; Figure 30).

Glycopeptides and daptomycin

Table 8: Total rate of glycopeptides and daptomycin consumption expressed as DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Class	DDD	Population	rate
2014	Glycopeptides and Daptomycin	91354	1840500	0.14
2015	Glycopeptides and Daptomycin	98695	1851600	0.15
2016	Glycopeptides and Daptomycin	110211	1862100	0.16

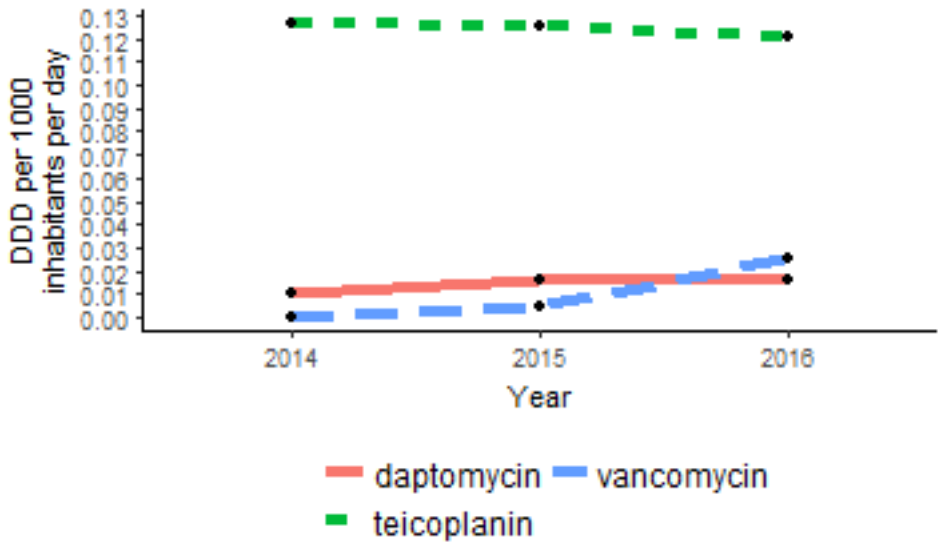

Figure 31: Consumption of most commonly used glycopeptides and daptomycin expressed per 1000 inhabitants per day, NI, 2014 - 2016

The rate of glycopeptide and daptomycin consumption has remained stable during 2014 - 2016 with a rate of 0.16 DDD per 1000 inhabitants per day in 2016. The highest rate was for teicoplanin which has been stable over time (0.12 DDD per 1000 inhabitants per day in 2016; Figure 31).

Anti-folate agents

Table 9: Total rate of Anti-folate agents consumption expressed as DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Class	DDD	Population	rate
2014	Anti-folate agents	2198383	1840500	3.27
2015	Anti-folate agents	2202642	1851600	3.26
2016	Anti-folate agents	2203877	1862100	3.24

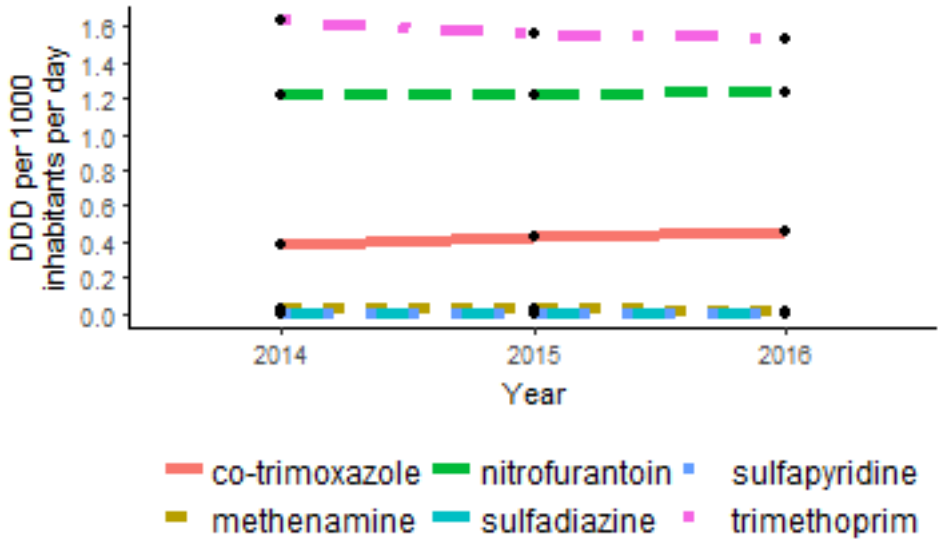

Figure 32: Consumption of most commonly used anti-folate agents expressed per 1000 inhabitants per day, NI, 2014 - 2016

Anti-folate agents accounted for 10.1% of all antibiotic consumption in 2016. The rate of Anti-folate agents consumption has remained stable during 2014 - 2016 with a rate of 3.24 DDD per 1000 inhabitants per day in 2016. The highest rate was for trimethoprim which has decreased slightly over time (1.62 to 1.53 DDD per 1000 inhabitants per day from 2014 to 2016; Figure 32).

Antibiotic consumption of key agents by healthcare setting

Trimethoprim

Table 10: Total rate of trimethoprim consumption expressed as DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Antibiotic	DDD	Population	rate
2014	trimethoprim	1090980	1840500	1.62
2015	trimethoprim	1053447	1851600	1.56
2016	trimethoprim	1038717	1862100	1.53

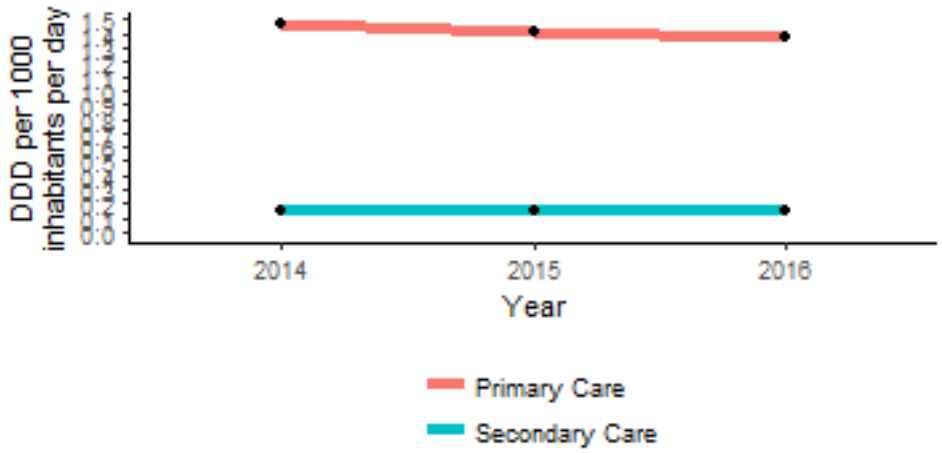

Figure 33: Consumption of trimethoprim by prescriber location expressed per 1000 inhabitants per day, NI, 2014 - 2016

Overall, the rate of trimethoprim consumption has decreased slightly during 2014 - 2016 with a rate of 1.53 DDD per 1000 inhabitants per day during 2016. This trend is influenced by stable rates of trimethopim consumption in primary care during 2014 - 2016 (1.47 to 1.37 DDD per 1000 inhabitants per day) with no change in secondary care during 2014-2016 (0.15 to 0.15 DDD per 1000 inhabitants per day; Figure 33).

Nitrofurantoin

Table 11: Total rate of nitrofurantoin consumption expressed as DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Antibiotic	DDD	Population	rate
2014	nitrofurantoin	812684	1840500	1.21
2015	nitrofurantoin	817469	1851600	1.21
2016	nitrofurantoin	840255	1862100	1.24

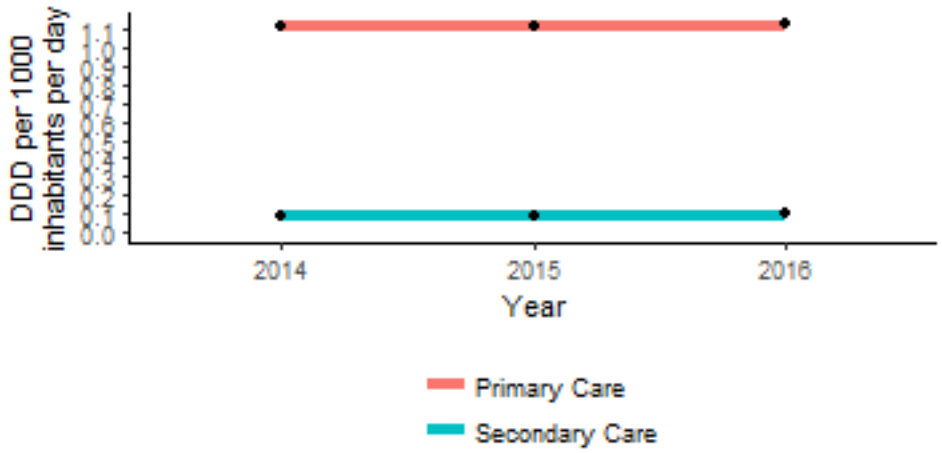

Figure 34: Consumption of nitrofurantoin by prescriber location expressed per 1000 inhabitants per day, NI, 2014 - 2016

Overall, the rate of nitrofurantoin consumption has remained stable during 2014 - 2016 with a rate of 1.24 DDD per 1000 inhabitants per day in 2016. Rates in both primary and secondary care have not changed during 2014 - 2016 (1.13 to 1.14 DDD per 1000 inhabitants per day in primary care and 0.08 to 0.1 DDD per 1000 inhabitants per day in secondary care; Figure 34).

Aminoglycosides

Table 12: Total rate of Aminoglycosides consumption expressed as DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Class	DDD	Population	rate
2014	Aminoglycosides	95301	1840500	0.14
2015	Aminoglycosides	102535	1851600	0.15
2016	Aminoglycosides	105419	1862100	0.16

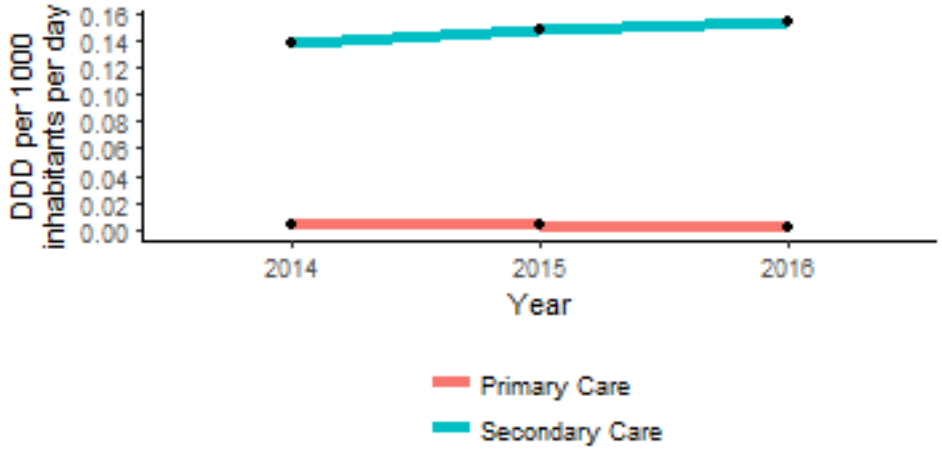

Figure 35: Consumption of aminoglycosides by prescriber location expressed per 1000 inhabitants per day, NI, 2014 - 2016

Overall, the rate of Aminoglycosides consumption has remained stable during 2014 - 2016 with a rate of 0.16 DDD per 1000 inhabitants per day in 2016. This trend is influenced by stable rates in primary care during 2014 - 2016 (0 DDD per 1000 inhabitants per day during 2016) and a slight increase in secondary care (0.14 to 0.15 DDD per 1000 inhabitants per day; Figure 35).

Glycopeptides and daptomycin

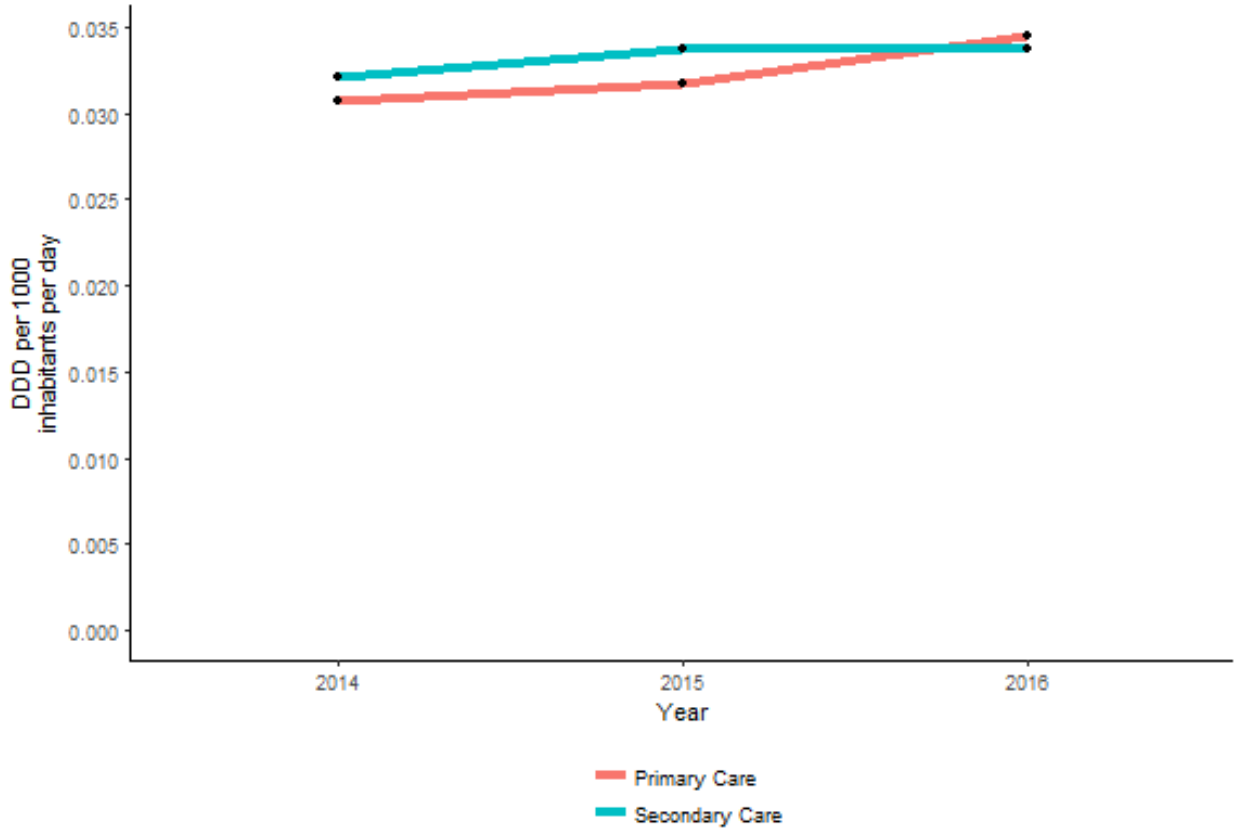

Figure 36: Consumption of glycopeptide and daptomycin by prescriber location expressed per 1000 inhabitants per day, NI, 2014 - 2016

The consumption rates of glycopeptides and daptomycin have been stable in primary care during 2014 - 2016 (0 DDD per 1000 inhabitants per day during 2016) and in secondary care (0.16 DDD per 1000 inhabitants per day; Figure 36).

Colistin

Table 13: Total rate of colistin consumption expressed as DDD per 1000 inhabitants per day, NI, 2014-2016.

Year	Antibiotic	DDD	Population	rate
2014	colistin	87099	1840500	0.13
2015	colistin	81284	1851600	0.12
2016	colistin	86434	1862100	0.13

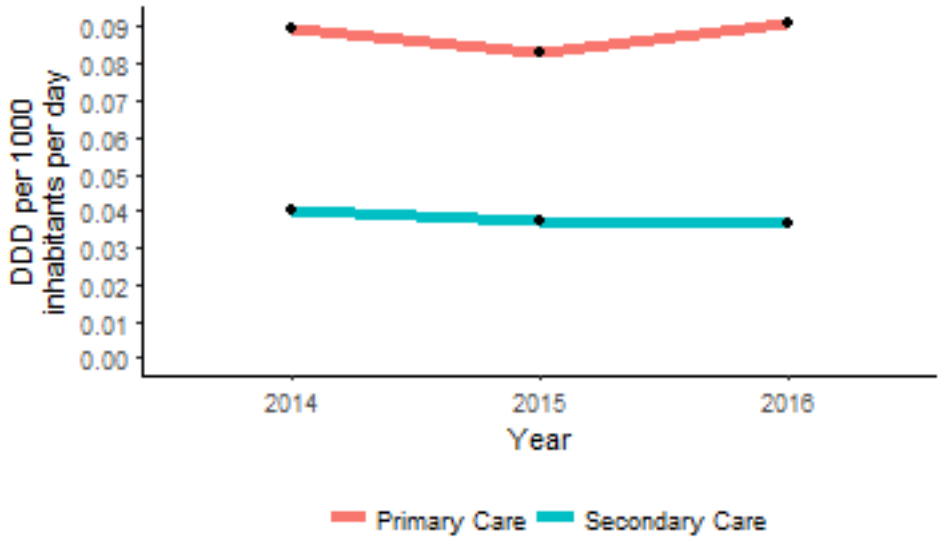

Figure 37: Consumption of colistin by prescriber location expressed per 1000 inhabitants per day, NI, 2014 - 2016

Overall, the rate of colistin consumption has remained stable during 2014 - 2016 with a rate of 0.13 DDD per 1000 inhabitants per day in 2016. This trend is influenced by stable rates in primary care during 2014 - 2016 (0.09 in 2014 to 0.09 DDD per 1000 inhabitants per day during 2016) and in secondary care (0.04DDD per 1000 inhabitants per day during 2016; Figure 37).

Antibiotic guardians

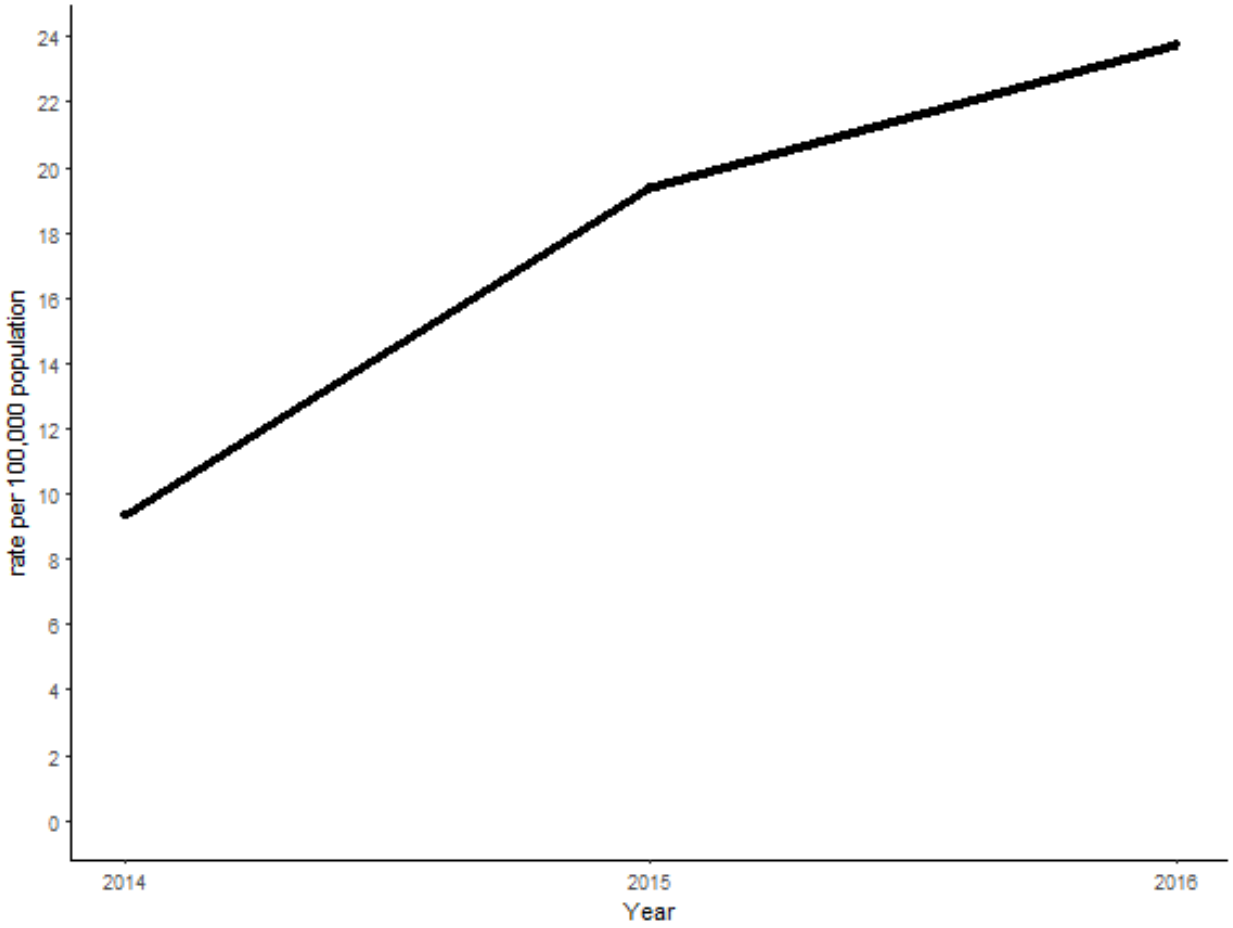

Figure 38: Cumulative rate of antibiotic guardians per 100,000 population, NI, 2014 - 2016

There has been a year on year increase in the cumulative rate of antibiotic guardians in Northern Ireland. During 2016, there were 440 individuals registered (24 individuals per 100,000 population; Figure 38).

Discussion

This is the first report of antimicrobial resistance and antimicrobial consumption in Northern Ireland. We have aimed to make the content generally comparable with the ESPAUR report for England[4]. In future reports, we aim to be able to access, analyse and report more detailed information about antimicrobial use and resistance in specific healthcare settings.

Antimicrobial resistance

The focus for the antimicrobial resistance section was the organism-antibiotic combinations that were identified as part of the UK AMR strategy[3]. In NI, surveillance for these organisms is not mandatory and is based on the voluntary reporting by the microbiology laboratories to the PHA. Therefore, underreporting of the organisms is a possibility.

The information presented in this report demonstrates increasing incidence and increasing resistance of many bloodstream infections, particularly *E. coli* and *K. pneumoniae*. A steady increase in infections caused by glycopeptide-resistant enterococci was only broken by a decline in 2016.

E. coli and *K. pneumoniae* bloodstream infections have been targeted as part of the UK governments ambition to reduce healthcare-associated gram-negative bloodstream infections by 50% by 2020. In order to reduce the number of these infections, local teams will need timely information about the characteristics of the patients who are affected, the risk factors that contributed to the infection and which healthcare settings were responsible. We are working towards implementing a harmonised, enhanced healthcare-associated infection surveillance programme that will capture information on existing mandatory surveillance organisms (*Staphylococcus aureus*, *Clostridium difficile* and Pseudomonas species from augmented care settings) and extend this to include enhanced information about *E. coli*, *K. pneumoniae*, Pseudomonas species from all settings and carbapenamase-producing organisms (CPOs). These new data will be an important source of business intelligence for Health and Social Care Trusts as they aim to improve the quality and safety of the care that they provide. The success of this new programme will require Trusts to take steps to implement new data collection arrangements quickly for the benefit of their patients.

Antimicrobial resistance in most of the selected organisms has remained relatively stable since 2009. The resistance trends for the gram negative bacteraemias are similar to

that observed in England and, for the most part, the proportions resistant are lower in NI. There are higher proportions of *E. coli*, *K. pneumoniae* and Pseudomonas species resistant to piperacillin/tazobactam in NI compared to England (15.6%, 19% and 12% in NI during 2016 compared to 11.8%, 17.8% and 10.3% in England). For *K. pneumoniae*, the proportion resistant to gentamicin was also higher in NI than in England during 2016 (10.9% compared to 8.9% respectively). While the proportion of isolates that are resistant to key antibiotics has not changed very much over time, the absolute number of resistant infections has increased because of the overall rising number of infections.

As antimicrobial resistance is a transmissible global problem, PHA will collaborate with Public Health England and the Scottish, Welsh and Irish public health organisations, to contribute to the European Antimicrobial Resistance Surveillance Network (EARS-Net) and the World Health Organisation's Global Antimicrobial Resistance Surveillance System (GLASS). This will ensure standardised information on antimicrobial resistance is available to inform comparisons and drive improvement.

Antibiotic consumption

Total antibiotic consumption in Northern Ireland has remained unchanged for three years at 32 DDD per 1,000 inhabitants, with little overall change in primary or secondary care. Despite this, the rate of antimicrobial consumption in secondary care per admission or per occupied bed day has steadily increased over time, perhaps suggesting that the case-mix of hospital inpatients has become more severe over time. This stasis is in contrast with the situation in England, where antibiotic consumption has fallen, and is now measured at 21 DDD per 1,000 inhabitants per day. By this measure, Northern Ireland's total antibiotic consumption is 52% higher than that of England.

Penicillins, tetracyclines and macrolides were the most commonly prescribed antibiotics in both settings, and there has been little change in these in either setting. There were some welcome reductions in the use of specific antibiotics. The use of carbapenems, and meropenem in particular, declined over time in Northern Ireland, which is an encouraging trend. Use of co-amoxiclav also fell markedly in 2016, and trimethoprim use fell slightly. In general, however, comparison with antimicrobial use in England highlights substantially higher use in Northern Ireland. Piperacillin/tazobactam consumption remained unchanged in 2016 at 0.21 DDD per 1,000 inhabitants per day, which is more than twice the declining rate in England (0.1 DDD per 1,000 inhabitants per day). The rate of cephalosporin use was steady at 0.57 DDD per 1,000 inhabitants per day, which is nearly twice the declining English rate of 0.33 DDD per 1,000 inhabitants per day. The use of tetracyclines, particularly doxycycline, increased in Northern Ireland to 7.49 DDD per 1,000 inhabitants per day, which was much higher than the English rate of 4.7 DDD per 1,000 inhabitants per day. The use of quinolones and macrolides has remained unchanged over the last 3 years in Northern Ireland, during which time use has decreased in England.

Colistin is an antibiotic of last resort that is used for multidrug-resistant infections and also as an inhaled therapy for people with cystic fibrosis. Colistin consumption in Northern Ireland has been steady for the last three years, but rates are higher than in England (0.13 DDD per 1,000 inhabitants per day in 2016 in NI and 0.073 DDD per 1,000 inhabitants per day in 2016 in England).

The amount of antimicrobial use in Northern Ireland is markedly higher than England. Understanding the reasons for the difference is a complex task. Most antibiotics were prescribed in the primary care setting. In order to understand and address the factors that lead to antibiotic consumption, we need information about the characteristics of the people who are prescribed them. There is currently no publicly available information about the

factors that influence antibiotic prescribing in Northern Ireland. It is a priority for PHA to work with the Health and Social Care Board and other primary care stakeholders to fill this information gap. In the secondary care setting, investigating the reasons for differences is vastly more difficult because antimicrobial consumption is measured at ward level, not at patient level, and therefore there is no routine source of information that links antibiotic use to individual patient details. Health and Social Care Northern Ireland has committed to developing a new electronic health care record ("Encompass"), which will ultimately include electronic prescribing, which will provide a rich source of information about the factors influencing antimicrobial consumption. However, over-use of antibiotics is already causing harm to patients, and we cannot afford to wait years before addressing the challenges of inappropriate antimicrobial prescribing. Reducing antimicrobial consumption safely is the complex challenge that faces all of us. One way of engaging clinicians (as well as other professionals and the public) in this challenge, is to encourage them to sign up to an Antibiotic Guardian pledge. There were fewer new Antibiotic Guardians in 2016 than in previous years, and we have put in place new measures to promote this campaign, particularly to professionals.

Actions to reduce antimicrobial use and resistance

Public communication

The O'Neill report recommended a major global information campaign to raise awareness about the future harms likely to occur if antibiotic use was not reduced. PHA has developed a communications plan to communicate with people in Northern Ireland about the potential harms related to inappropriate antibiotic use. This will involve running engagement events, social media and news releases at key points. Highlights include:

- Significant press and social media activity planned around World Antibiotic Awareness Week (13-18 November 2017)
- A public engagement event about antimicrobial resistance on European Antibiotic Awareness Day in the W5 science education centre in Belfast (18 November 2017)
- PHA is working with Council for the Curriculum, Examinations and Assessment to map the learning outcomes from the PHE-produced e-Bug materials against the NI primary and secondary curricula and to promote the materials to schools
- PHA is working with the Northern Ireland STEM Ambassador Hub and Centre of Excellence in Public Health, QUB, to deliver classes about antimicrobial resistance to pupils in 2017 and 2018 using the e-Bug materials

Changing prescribing behaviour

Safely reducing antimicrobial use is a complex challenge that will require an understanding of the capacity, opportunity and motivation of prescribers to decide when not to prescribe antibiotics. PHA is working closely with behavioural scientists in the Innovation Lab (based in the Department of Finance) to learn more about prescribing behaviour and how to safely bring about circumstances that change it. Recent initiatives to reduce antimicrobial consumption include:

- Endorsement of the TARGET toolkit for GPs by the Improvement Board and promotion of this to GPs through the Royal College of General Practitioners. Workshops for GPs will be delivered in 2018.
- A survey of GPs about the factors that influence their antibiotic prescribing decisions was conducted by the Innovation lab in September and October 2017, with preliminary results due to be presented on 13 November 2017.

- A systematic review of behavioural science interventions for antimicrobial stewardship is underway between the Innovation Lab and PHA.
- A guest editorial was published in the Ulster Medical Journal in September 2017 aimed at promoting awareness of antibiotic stewardship, the Antibiotic Guardian pledge and events occurring around World Antibiotic Awareness Week[9].
- A letter using behaviour change techniques was written from the Chief Medical Officer, Dr Michael McBride, to GPs in the 20% highest antibiotic prescribing practices in October 2017, based on one that was shown to be effective in a randomised controlled trial[10].
- A pilot of point-of-care CRP testing for respiratory infections in primary care is underway in five general practices, with one in each LCG area. Evaluation of the pilot will be used to inform decisions about wider adoption.

Appendix 1: AMR surveillance categories

Table 14: Antibiotic names (trade and generic) and assigned surveillance group for the antimicrobial resistance data

Antibiotic surveillance group	Individual antibiotic name
3rd Generation Cephalosporin	cefotaxime
3rd Generation Cephalosporin	claforan
3rd Generation Cephalosporin	ceftazidime
3rd Generation Cephalosporin	fortum
3rd Generation Cephalosporin	cefpodoxime
3rd Generation Cephalosporin	ceftizoxime
3rd Generation Cephalosporin	ceftriaxone
Carbapenem	meronem
Carbapenem	meropenem
Carbapenem	imipenem
Carbapenem	ertapenem
Ciprofloxacin	ciprofloxacin
Ciprofloxacin	low level ciprofloxacin
Ciprofloxacin	ciproxin
Co-amoxiclav	co-amoxiclav
Co-amoxiclav	amoxicillin/clavulanate
Co-amoxiclav	augmentin
Colistin	colistin
Colistin	colomycin
Gentamicin	gentamicin
Gentamicin	lugacin
Gentamicin	cidomycin
Gentamicin	genticin
Gentamicin	garamycin
Gentamicin	high_level gentamicin
Glycopeptide	vancocin
Glycopeptide	vancomycin
Glycopeptide	teicoplanin
Macrolides	clarithromycin

Antibiotic surveillance group	Individual antibiotic name
Macrolides	erythromycin
Macrolides	azithromycin
Macrolides	erythrocin
Macrolides	erythromid
Methicillin	cefoxitin
Methicillin	flucloxacillin
Methicillin	floxapen
Methicillin	oxacillin
Methicillin	meticillin
Methicillin	celbenin
Methicillin	cloxacillin
Methicillin	orbenin
Penicillin	apsin
Penicillin	benzylpenicillin
Penicillin	phenoxymethylpenicillin
Penicillin	penicillin
Penicillin	penidural
Piperacillin/Tazobactam	tazocin
Piperacillin/Tazobactam	piperacillin/tazobactam

Appendix 2: AMC data categories

Table 15: Antibiotic names, ATC codes and assigned surveillance group for the antimicrobial consumption data

Antibiotic surveillance group	Individual antibiotic name	ATC codes
Aminoglycosides	amikacin	J01GB06
Aminoglycosides	gentamicin	J01GB03
Aminoglycosides	neomycin	A07AA01
Aminoglycosides	neomycin	J01GB05
Aminoglycosides	tobramycin	J01GB01
Anti-Clostridium difficile agents	fidaxomicin	A07AA12
Anti-Clostridium difficile agents	metronidazole	P01AB01
Anti-Clostridium difficile agents	vancomycin	A07AA09
Anti-folate agents	co-trimoxazole	J01EE01
Anti-folate agents	dapsone	J04BA02
Anti-folate agents	methenamine	J01XX05
Anti-folate agents	nitrofurantoin	J01XE01
Anti-folate agents	sulfadiazine	J01EC02
Anti-folate agents	sulfapyridine	J01EB04
Anti-folate agents	sulphamethoxypyridazine	J01ED05
Anti-folate agents	trimethoprim	J01EA01
Anti-protozoal agents	paromomycin	A07AA06
Anti-tuberculous drugs	capreomycin	J04AB30
Anti-tuberculous drugs	cycloserine	J04AB01
Anti-tuberculous drugs	ethambutol	J04AK02
Anti-tuberculous drugs	isoniazid	J04AC01
Anti-tuberculous drugs	prothionamide	J04AD01
Anti-tuberculous drugs	pyrazinamide	J04AK01
Anti-tuberculous drugs	rifabutin	J04AB04
Anti-tuberculous drugs	rifampicin	J04AB02
Anti-tuberculous drugs	rifampicin + isoniazid	J04AM02
Anti-tuberculous drugs	rifampicin+isoniazid+pyrazinamide	J04AM05
Anti-tuberculous drugs	rifaximin	A07AA11
Anti-tuberculous drugs	streptomycin	J01GA01

Antibiotic surveillance group	Individual antibiotic name	ATC codes
Carbapenems	ertapenem	J01DH03
Carbapenems	imipenem with cilastatin	J01DH51
Carbapenems	meropenem	J01DH02
Cephalosporins	cefaclor	J01DC04
Cephalosporins	cefadroxil	J01DB05
Cephalosporins	cefalexin	J01DB01
Cephalosporins	cefazolin	J01DB04
Cephalosporins	cefixime	J01DD08
Cephalosporins	cefotaxime	J01DD01
Cephalosporins	cefoxitin	J01DC01
Cephalosporins	cefpodoxime	J01DD13
Cephalosporins	cefradine	J01DB09
Cephalosporins	ceftaroline	J01DI02
Cephalosporins	ceftazidime	J01DD02
Cephalosporins	ceftriaxone	J01DD04
Cephalosporins	cefuroxime	J01DC02
Glycopeptides and Daptomycin	daptomycin	J01XX09
Glycopeptides and Daptomycin	teicoplanin	J01XA02
Glycopeptides and Daptomycin	vancomycin	J01XA01
Lincosamides	clindamycin	J01FF01
Macrolides	azithromycin	J01FA10
Macrolides	clarithromycin	J01FA09
Macrolides	erythromycin	J01FA01
Macrolides	telithromycin	J01FA15
Monobactams	aztreonam	J01DF01
Nitroimidazoles	metronidazole	J01XD01
Nitroimidazoles	tinidazole	J01XD02
Nitroimidazoles	tinidazole	P01AB02
Other antibiotics	chloramphenicol	J01BA01
Other antibiotics	colistin	J01XB01
Other antibiotics	colistin	A07AA10
Other antibiotics	fosfomycin	J01XX01
Other antibiotics	fucidic_acid	J01XC01
Other antibiotics	quinupristin	J01FG02

Antibiotic surveillance group	Individual antibiotic name	ATC codes
Oxazolidinones	linezolid	J01XX08
Oxazolidinones	linezolid	J01XX10
Oxazolidinones	tedizolid	J01XX11
Penicillins	amoxicillin	J01CA04
Penicillins	ampicillin	J01CA01
Penicillins	benzathine-benzylpenicillin	J01CE08
Penicillins	benzylpenicillin	J01CE01
Penicillins	co-fluampicil	J01CA51
Penicillins	co-fluampicil	J01CR50
Penicillins	flucloxacillin	J01CF05
Penicillins	phenoxymethylpenicillin	J01CE02
Penicillins	pivmecillinam	J01CA08
Penicillins	procaine	J01CE09
Penicillins	temocillin	J01CA17
Penicillins with beta lactamase inhibitors	co-amoxiclav	J01CR02
Penicillins with beta lactamase inhibitors	piperacillin/tazobactam	J01CR05
Penicillins with beta lactamase inhibitors	ticarcillin with clavulanic_acid	J01CR03
Quinolones	ciprofloxacin	J01MA02
Quinolones	levofloxacin	J01MA12
Quinolones	moxifloxacin	J01MA14
Quinolones	norfloxacin	J01MA06
Quinolones	ofloxacin	J01MA01
Tetracyclines and related drugs	demeclocycline	J01AA01
Tetracyclines and related drugs	doxycycline	J01AA02
Tetracyclines and related drugs	lymecycline	J01AA04
Tetracyclines and related drugs	minocycline	J01AA08
Tetracyclines and related drugs	oxytetracycline	J01AA06
Tetracyclines and related drugs	tetracycline	J01AA07
Tetracyclines and related drugs	tigecycline	J01AA12

Appendix 3: Testing data

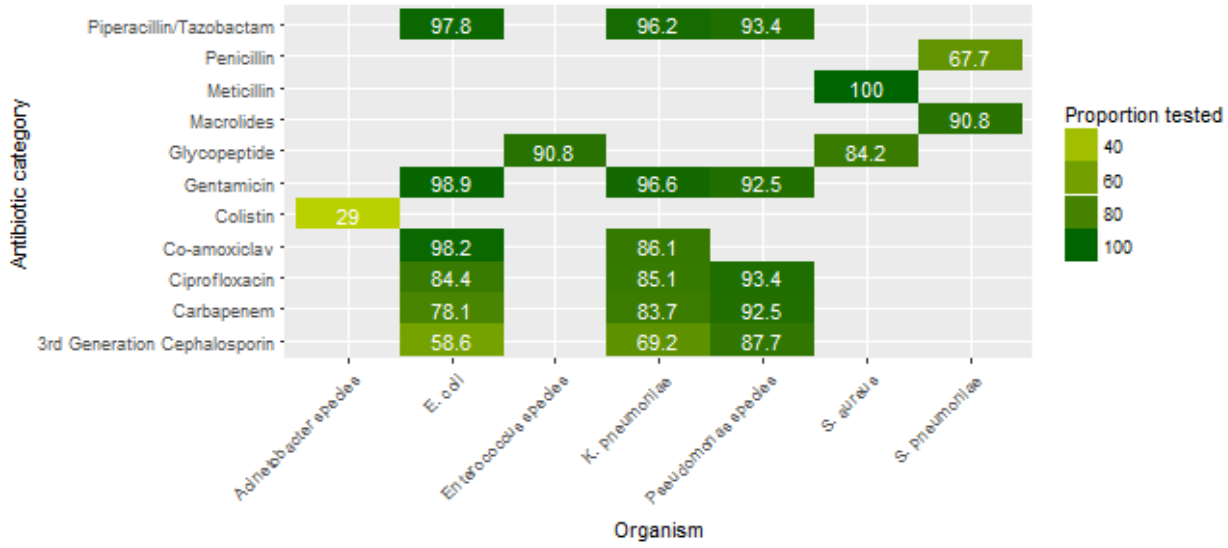

Figure 39: The proportion of key bacteraemias where selected antibiotic susceptibility results were reported to the PHA

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