ARHAI Scotland

Antimicrobial Resistance and Healthcare Associated Infection

NHS National Services Scotland

Scottish One Health Antimicrobial Use and Antimicrobial Resistance report 2019

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Contents

Introduction

Antimicrobial resistance (AMR) arises when micro-organisms such as bacteria develop the ability to withstand antimicrobial treatments making infections harder to treat with resultant severe disease and potentially death. The concept of AMR is not a new one. As early as 1945, Sir Alexander Fleming highlighted the risk of AMR in his speech accepting the Nobel prize for his discovery of penicillin. One can only wonder if Fleming could have predicted how antibiotics would revolutionise health and healthcare in the decades that followed his speech. Antibiotics have become central to the delivery of healthcare in the 21st century and unfortunately, we have taken them for granted. A post-antibiotic age where bacteria are resistant to antibiotics, leading to many routine healthcare procedures becoming impossible or more dangerous is now a real possibility, and in some parts of the world, already a reality.

Should we fail to tackle AMR it is predicted to cause 10 million global deaths in thirty years' time, with more people dying from drug resistant infections than from cancer. However, actions to tackle AMR in Scotland, within the United Kingdom and internationally are underway. The UK government with input from the Scottish Government and the other devolved nations have published a long term vision which recognises AMR will not be eradicated but could be contained and controlled. This 20-year vision is complemented by a five-year action plan focussing on three key areas: reducing need for and unintentional exposure to antimicrobials; optimising use of antimicrobials; and investing in innovation, supply and access to tackle AMR.

The Scottish One Health Antimicrobial Use and Antimicrobial Resistance (SONAAR) programme, part of ARHAI Scotland, continues to provide intelligence and evidence for action to inform the development of local and national interventions and initiatives to tackle AMR. A One Health approach to tackling AMR was adopted in Scotland in 2016 and acknowledges that the health of humans, animals and the environment are interconnected. Antimicrobial use and spread of infection in humans, animals and the environment contribute to the development of resistant infections. In line with this approach, this report includes information from 2019 on antimicrobial use and resistance in humans, animals and the environment. The data included in this report pre-date the COVID-19 pandemic and accordingly do not provide intelligence on the impact of the pandemic on antimicrobial use and resistance.

This report has been produced during the COVID-19 pandemic which has had a profound impact on healthcare services and for citizens of all ages in Scotland and beyond. There have been and will continue to be the emergence of new models of care and changes in the way antimicrobials are used. The impact of these changes on AMR are as yet unknown. However, tackling AMR, which has been described as a slow burning pandemic, remains vitally important and sustained action to preserve antibiotics and reduce drug resistant infections is crucial to secure the future delivery of healthcare.

Main Points

Antimicrobial use in humans

- Critical to containing and controlling antimicrobial resistance is reducing the Scottish population's unnecessary exposure to antibiotics
- Total antibiotic use in humans has decreased by 7.6% since 2015
- Over 60% of all antibiotic use in Scotland was Access antibiotics (recommended first line narrow spectrum agents)
- The majority of antibiotic use in humans occurs in primary care
- Antibiotic use in primary care has decreased by 9.1% since 2015; the lowest figure since data became available in 1993
- 26.8% of the Scottish population received at least one course of antibiotics prescribed in primary care; the lowest proportion since data became available in 2010
- Over three quarters of antibiotic prescriptions in primary care were Access antibiotics
- Antibiotic use in acute hospitals increased by 12.6% since 2015; however, the rate of increase has slowed compared to previous years
- Over 60% of antibiotic use in acute hospitals was Access antibiotics, exceeding the national standard
- Use of Watch and Reserve (restricted) antibiotics in acute hospitals has decreased by 9.8% since 2015
- Optimisation of antibiotic use through antimicrobial stewardship by all clinicians in all settings is essential to minimise antimicrobial resistance and improve patient outcomes

Antimicrobial use in animals

- Antibiotic use data from a sample of small animal veterinary practices were available
- For the first time in Scotland, these antibiotic use data were available by presenting problem
- Nearly one in five consultations resulted in an antibiotic being prescribed; nine in ten of these were not from the group of antibiotics considered to be high priority critically important in humans
- Scotland's Healthy Animals website continues to provide guidance for vets and animal keepers on disease avoidance and antimicrobial stewardship

Antimicrobial resistance in humans

- Gram-negative bacteria are a common cause of serious infection in both healthcare and community settings
- AMR in Gram-negative bacteria significantly contributes to the overall burden of AMR

- *Escherichia coli* is the most common cause of Gram-negative bacteraemia and contributes significantly to the burden of AMR
- Since 2018 non-susceptibility in *E. coli* bacteraemia (ECB) has remained stable with the exception of an increase in co-amoxiclav and a decrease in piperacillin with tazobactam
- CPO incidence has increased significantly since 2015 ($p<0.001$)
- Urinary Tract Infections are commonly diagnosed in community, healthcare and hospital settings and AMR in urinary isolates significantly adds to the burden of AMR
- *E. coli* is the most frequently isolated bacteria from urine specimens; non-susceptibility of *E. coli* to co-amoxiclav and ceftazidime has increased since 2018
- Incidence of *E. faecalis* and *E. faecium* bacteraemia has remained stable since 2015
- 41.9% of *E. faecium* are non-susceptible to vancomycin
- 78.7% of *E. faecium* isolates are non-susceptible to high-level gentamicin

Antimicrobial resistance in animals

- Monitoring AMR in animals is a vital component of understanding and mitigating risk of AMR across the entire ecosystem
- Non-susceptibility for veterinary clinical isolates has been relatively stable since 2015
- Intelligence relating to AMR in animals will continue to be developed to inform the evidence base

Results and Commentary

Antimicrobial Use

Antibiotic use in humans

Antibiotics are used for the prevention and treatment of bacterial infections and are vital to provision of healthcare in 2020. Antimicrobial resistance (AMR) and drug resistant infections are a growing threat to modern clinical practice. A post-antibiotic age where bacteria are resistant to antibiotics, leading to many routine healthcare procedures becoming impossible or more dangerous is now a real possibility, and in some parts of the world, a reality.

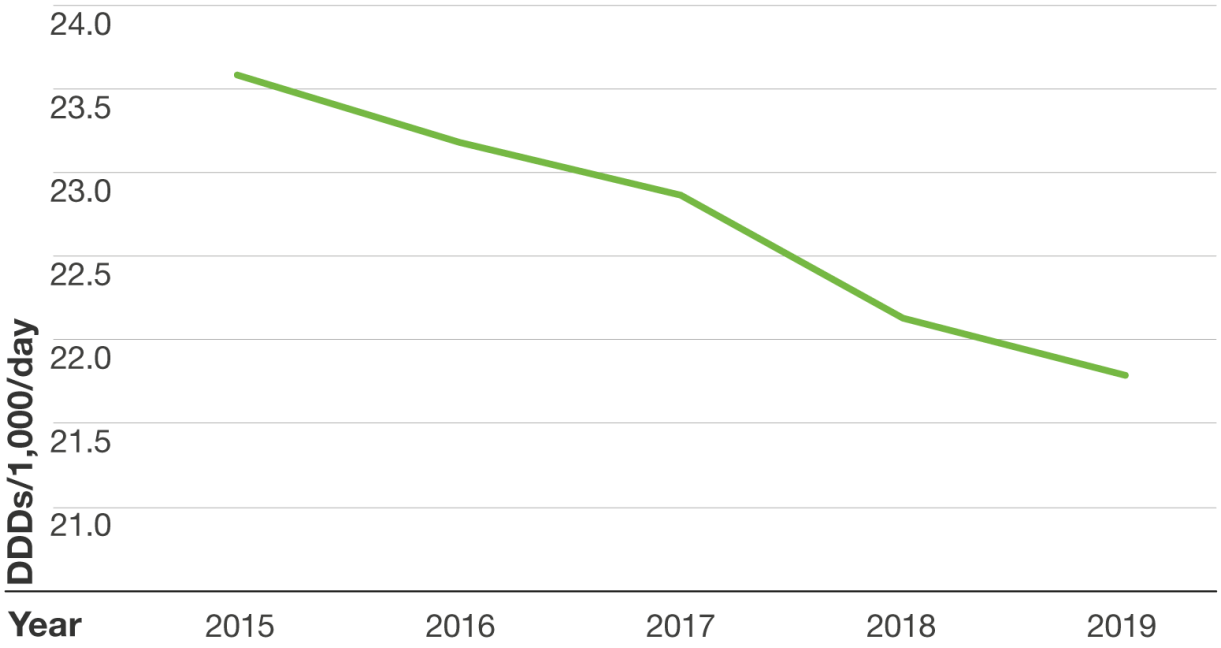
The UK's 2019–2024 National Action Plan (NAP)[1] to tackle AMR acknowledges optimising antibiotic use will slow the development of resistance and help preserve the effectiveness of the antibiotics currently available. The action plan contains measures of success to drive progress, including ambitious targets on antibiotic use.

Antimicrobial stewardship (AMS) is a coordinated set of approaches to optimise the use of antibiotics, making the best use of antibiotics to prevent and treat infection to improve outcomes for patients and reduce harm to both patients and wider society. In Scotland, the Scottish Antimicrobial Prescribing Group (SAPG) coordinates the national antimicrobial stewardship programme.

A key component of AMS is the measurement and reporting of trends in antibiotic use. This surveillance of antibiotic use undertaken by the SONAAR programme is crucial to the planning, prioritisation and evaluation of the impact of interventions intended to optimise the use of antibiotics.

In 2019, the total use of antibiotics in humans across all settings was 21.8 defined daily doses (DDDs) per 1,000 population per day (DDDs/1,000/day); 7.6% lower ($p<0.001$) than in 2015 (Figure 1, and see Appendix). It is now important to consolidate and build upon this progress in the years ahead in order to achieve the UK national action plan ambition to reduce antibiotic use in humans by 15% by 2024.

Figure 1: Total number of defined daily doses per 1,000 population per day (DDDs/1,000/day) for all antibiotics prescribed in Scotland, 2015 to 2019, by year

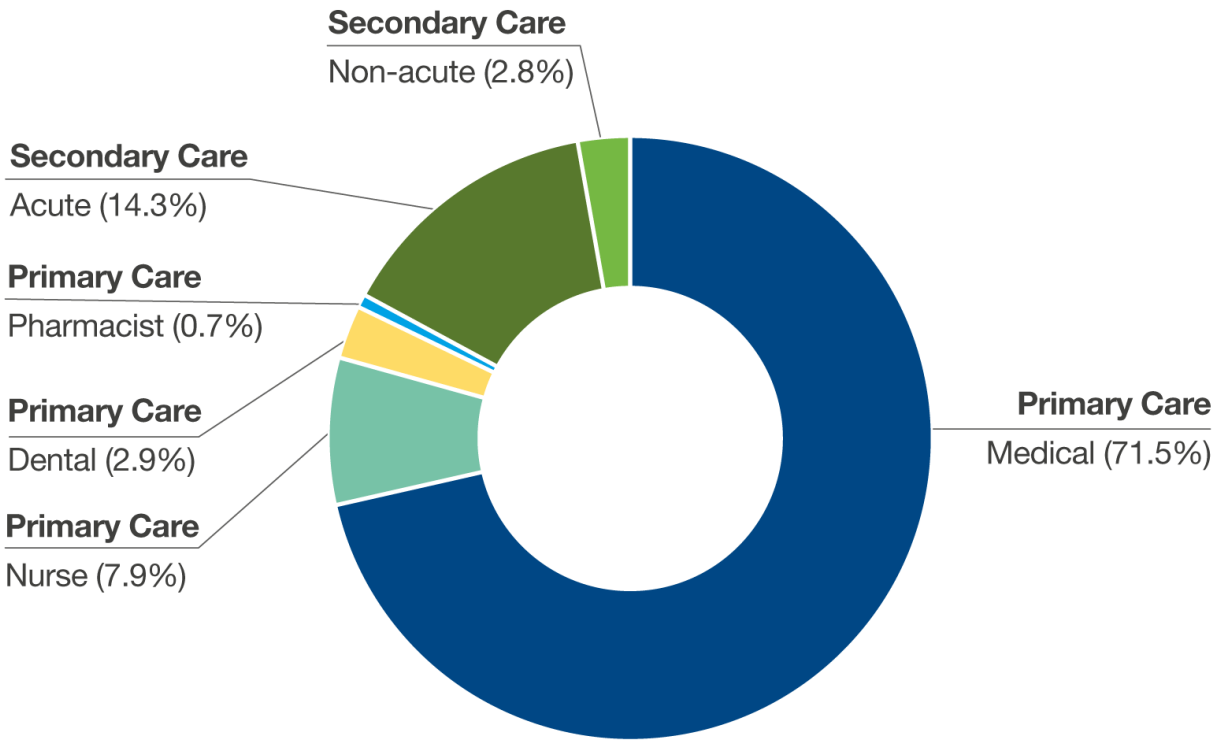


[Data Source: NHS National Services Scotland (NSS) and Public Health Scotland (PHS)]

Antibiotics are used to prevent and treat infections in all care settings. In 2019, 82.9% of antibiotic use (DDDs) occurred in primary care (community setting) with the remainder in secondary care (hospital setting). Antibiotic use in acute hospitals accounted for 14.3% of antibiotic use in humans (DDDs) with non-acute hospitals accounting for 2.8% (Figure 2, and see Appendix). AMS is important in all settings to optimise antibiotic use.

With moves towards a multi-professional approach to delivery of healthcare in Scotland the clinicians prescribing antibiotics are changing. Currently within the national datasets the prescriber type can only be identified in primary care. In 2019, of the total use of antibiotics in humans (total DDDs), medical prescribers accounted for 71.5% of antibiotic use followed by nurses (7.9%), dentists (2.9%) and pharmacists (0.7%) (Figure 2 and see Appendix).

Figure 2: Percentage of all antibiotics prescribed (defined daily doses, DDDs) in Scotland by prescriber type, for 2019



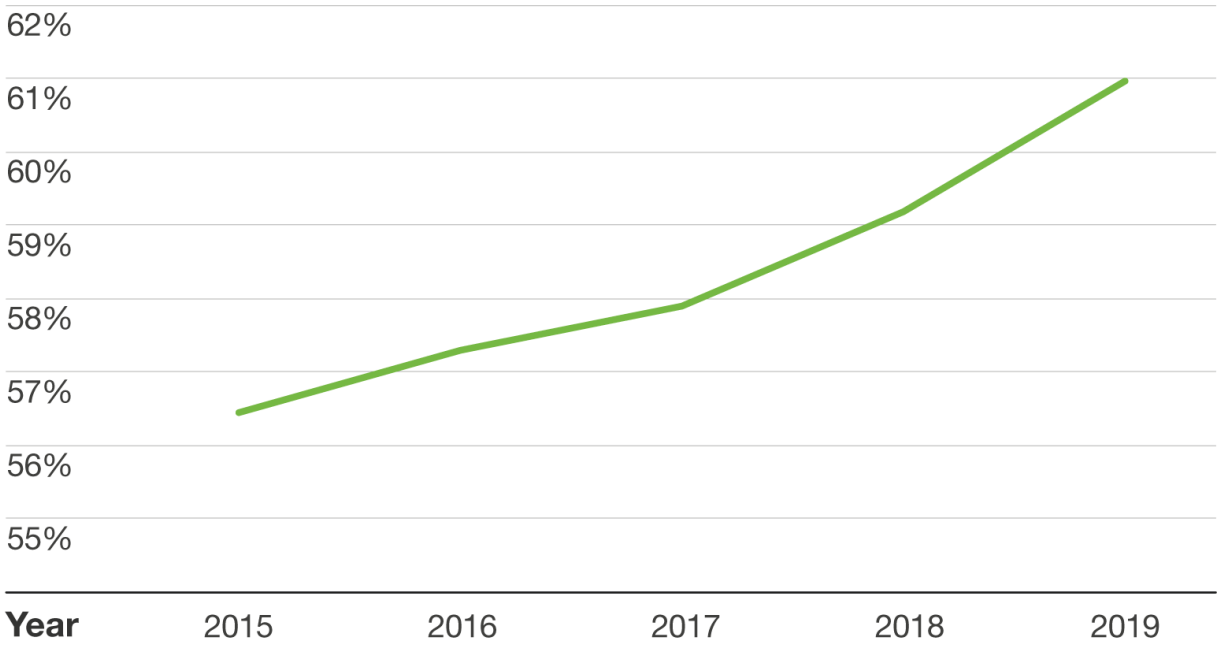
[Data Source: NHS National Services Scotland (NSS) and Public Health Scotland (PHS)]

Antibiotic prescribing guidelines support clinicians in all settings to decide on the most appropriate empirical treatment (where the bacteria causing the infection and its susceptibility to antibiotics are not known) by providing recommendations on treatment choice for commonly encountered infections. Guidelines promote the use of narrow spectrum antibiotics over broad spectrum antibiotics where this is possible and provide recommended duration of treatment. Continuing antibiotics for longer than necessary and inappropriate use of broad spectrum therapy are modifiable prescribing factors which increase the risk of development of AMR.

The World Health Organization has developed a classification system (adapted for use in the UK) which is used to monitor which antibiotics are being used. This system is known as AWaRe and splits antibiotics into three groups: Access are those that should be used as first line treatment for most common infections; Watch group antibiotics are not generally used first line but may be used in specific circumstances; and the Reserve group are those antibiotics that should be preserved for use when other treatment options are not appropriate as a result of known or suspected multi-drug resistance.

Access antibiotic use in DDDs as a proportion all antibiotic DDDs in humans has been increasing since 2015. In 2019, Access antibiotics accounted for 61.0% of total antibiotic use in humans (DDDs in all primary care and secondary care) (Figure 3, and see Appendix). This is the first year where greater than 60% of Access antibiotics use has been achieved. This suggests clinicians across all sectors of care are following treatment choice recommendations included in antibiotic prescribing guidelines.

Figure 3: Percentage of all antibiotics prescribed (defined daily doses, DDDs) in Scotland that belonged to the 'access' group, 2015 to 2019, by year



[Data Source: NHS National Services Scotland (NSS) and Public Health Scotland (PHS)]

Total Antibiotic in Humans Key Points

- **Antibiotic use in humans decreased by 7.6% since 2015**
- **The majority of antibiotic use occurs in primary care**
- **Antibiotics are prescribed by a range of health professionals**
- **The proportion of total antibiotic use which are WHO Access (first-line) antibiotics has increased**
- **Maintaining antimicrobial stewardship during the COVID-19 pandemic is important to optimise antibiotic use**

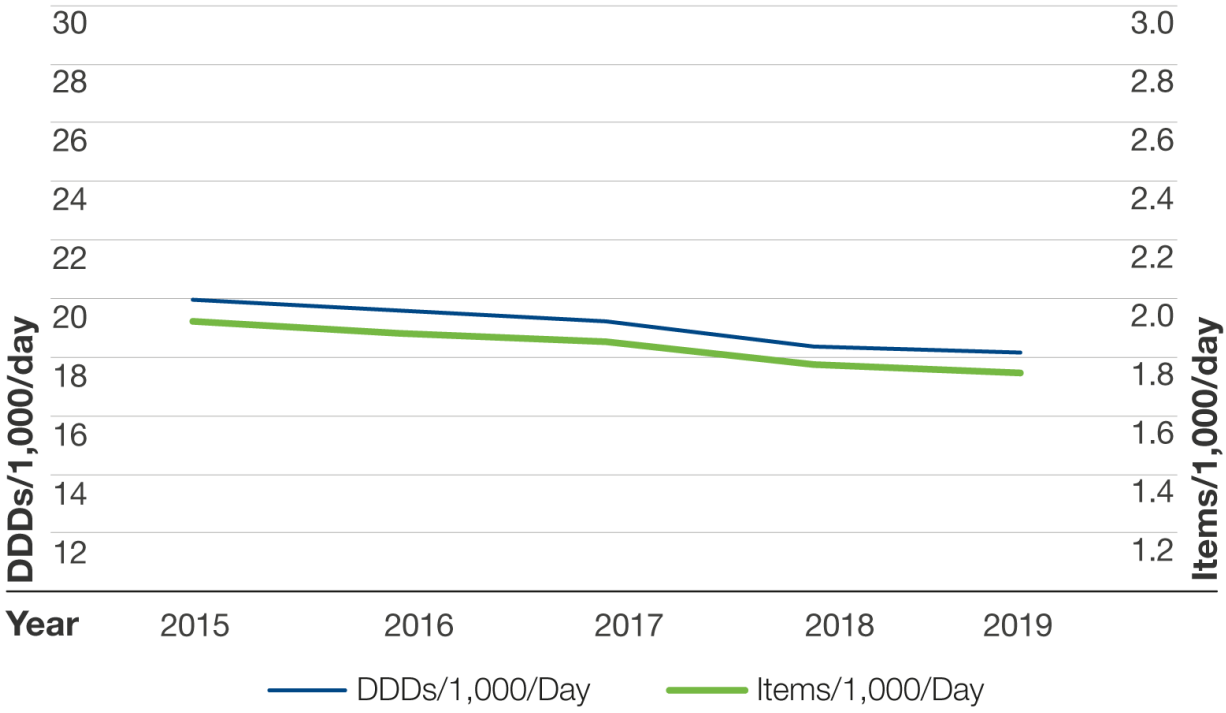
Antimicrobial use in primary care

There is evidence that the majority of drug resistant infections in Scotland originate in the community[2]. In 2019, 82.9% of all antibiotic use occurred in the primary care setting therefore optimising antibiotic use in primary care is a major target for AMS in Scotland. There is a tripartite approach to optimising antibiotic use in primary care. Firstly, it is important to minimise antibiotic use in healthy people presenting with self-limiting infections such as coughs, sore throats, colds and earache. Secondly, when antibiotics are clinically required, it is important to avoid inappropriate use of broad spectrum antibiotics, and thirdly, avoiding unnecessary exposure to antibiotics by using antibiotics for no longer than evidenced based duration of treatment is vital.

In 2019, the use of antibiotics in primary care (excluding dental prescribing) was 1.81 items per 1,000 population per day; 9.1% lower ($p<0.001$) than in 2015 (Figure 4 and see Appendix). This is the seventh consecutive annual decrease and means that antibiotic prescribing in primary care is at its lowest point since data became available in 1993. When expressed using DDDs, antibiotic use was 17.4 DDDs per 1000 population per day; 9.3% lower ($p<0.001$) than in 2015. The proportion of the Scottish population that received at least one course of antibiotics (in primary care, excluding dental) was 26.8% in 2019 compared to 29.6% in 2015, the lowest proportion since this data became available in 2010.

The steady reduction in the rate of antibiotic use expressed as the number of antibiotic items per 1,000 population per day and in the proportion of the population receiving antibiotics together suggests that public understanding and clinicians' attitudes and behaviours around the need to use antibiotics prudently are becoming embedded in practice. However, there is no time for complacency and there is a need to build on and accelerate this change in practice through continued development of AMS and public engagement through and beyond the COVID-19 pandemic.

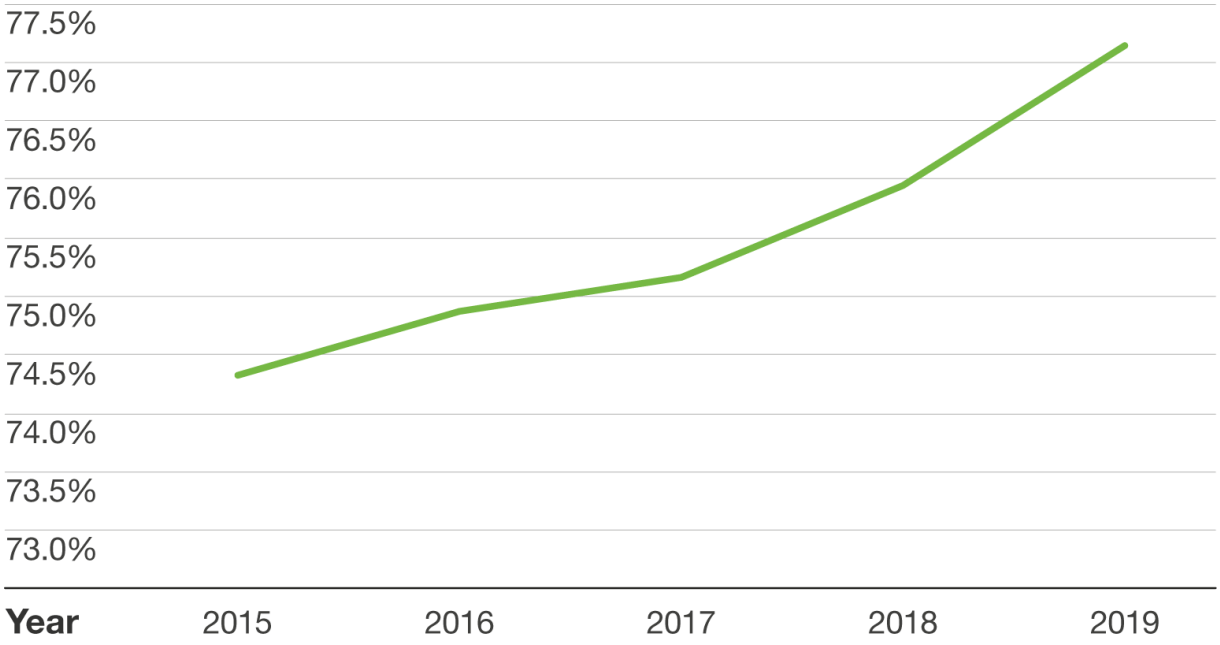
Figure 4: Antibiotic prescribing in primary care (excluding dental prescribing) in Scotland, 2015 to 2019, by defined daily doses per 1,000 population per day (DDDs/1,000/Day) and items per 1,000 population per day (Items/1,000/Day), by year



[Data Source: NHS National Services Scotland (NSS) and Public Health Scotland (PHS)]

Guideline driven empirical antibiotic treatment for common infections in primary care has been an important element of optimising antibiotic use in primary care since SAPG was established. This is intended to reduce the inappropriate use of broad spectrum antibiotics due to their association with AMR and *Clostridioides difficile* infection. In 2019, 77.1% of antibiotic items dispensed in primary care (excluding dental prescribing) were from the WHO Access group, i.e. recommended first line narrow spectrum agents, suggesting that clinicians are following local prescribing guidelines (Figure 5). For more detail on use of particular antibiotics and antibiotic classes, see Appendix.

Figure 5: Percentage of all antibiotics prescribed (items) in primary care (excluding dental prescribing) in Scotland that belonged to the 'Access' group, 2015 to 2019, by year

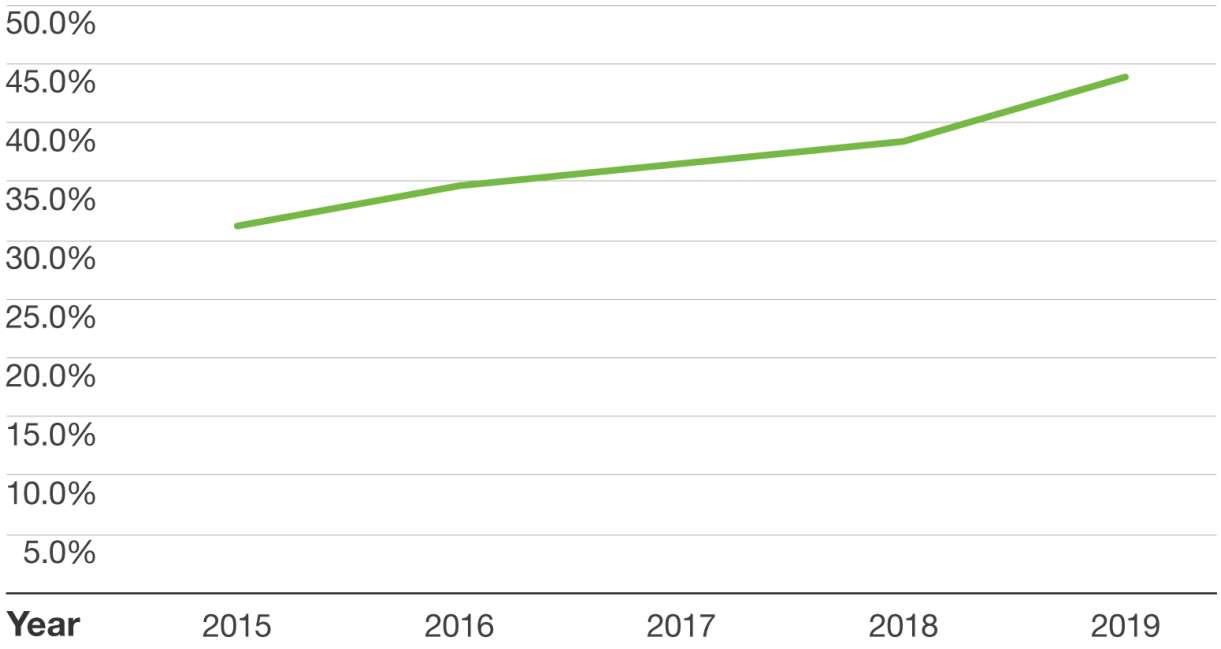


[Data source: NHS National Services Scotland (NSS) and Public Health Scotland (PHS)]

Treatment of respiratory infection is the most common reason for antibiotic use in primary care[3] and the evidence supports that where antibiotics are required (recognising antibiotics are not always needed), five-days treatment with amoxicillin is the recommended first line treatment[4].

In 2019, 43.9% of all prescriptions for amoxicillin dispensed in primary care (excluding dental) were, on the basis of the quantity supplied, for five-day duration compared to 31.2 in 2015 (Figure 6). For more detail on duration of other antibiotics, see Appendix. Optimising antibiotic use through encouraging shorter courses of antibiotics in line with evidenced based recommendations in antibiotic prescribing guidelines has been recognised by the SAPG[5] as an important opportunity to avoid AMR caused by unnecessary over exposure of individuals and the population to antibiotics. These data suggest a change in patterns of prescribing with a move toward shorter courses. This improvement work commenced in 2019 and there is a need to reinforce the importance of following guideline recommendations on treatment duration. It will additionally contribute to the UK national action plan target to reduce antibiotic use by 15% by 2024.

Figure 6: Proportion of amoxicillin 500mg capsule prescriptions with five-day course durations in general practice, 2015 - 2019, by year



[Data source: NHS National Services Scotland (NSS) and Public Health Scotland (PHS)]

As models of service delivery have been transformed in primary care, so too have the professionals responsible for prescribing antibiotics in that setting. GPs remain responsible for the majority of antibiotic prescriptions; in 2019, GPs accounted for 78.6% of all antibiotic items compared to 86.6% in 2015.

In 2019, nurses accounted for 12.2% of all antibiotic items dispensed in the community compared to 5.4% in 2015. Since 2015 the rate of antibiotic use by nurses has more than doubled (Figure 7, and see Appendix). WHO Access antibiotics (items) accounted for 86.7% of nurse prescribing suggesting good compliance with local guideline recommendations. It is important to recognise not only the direct impact of nurse prescribers, but also the role of all nurses to influence and promote the principles and practice of AMS through their roles in medicines management and direct patient care.

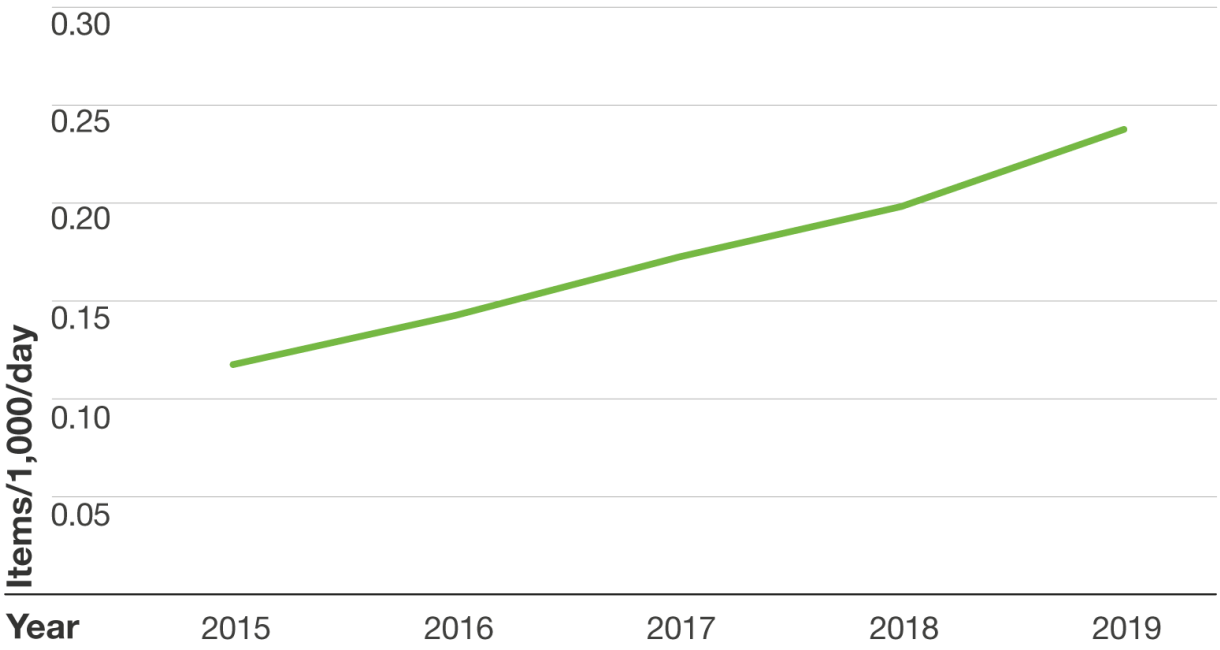
The use of antibiotics by dentists continues to decrease, accounting for 7.2% of total antibiotic use (items) in primary care in 2019, similar to the proportion reported in 2018. Since 2015, the rate of antibiotic use by dentists has reduced by 17.7% ($p<0.001$) (Figure 8, and see Appendix). Dentists can prescribe a limited range of antibiotics on NHS prescription in Scotland with two antibiotics, amoxicillin (68.0%) and metronidazole (28.8%) accounting for the majority of dental antibiotic use (items). The SAPG Dental Stewardship subgroup continues to coordinate work by stakeholders and support optimisation of dental antibiotic use.

A key focus in the coming year will be promoting the re-introduction of phenoxymethylpenicillin as the first line antibiotic in dental infections as an alternative to amoxicillin.

The role of pharmacists, especially community pharmacists, as prescribers of antibiotics continues to evolve. In 2019, there were 77,373 of antibiotic prescriptions written and dispensed by pharmacists in Scotland, representing 2% of total antibiotic use in primary care (items) compared to 0.1% in 2015. Of pharmacist antibiotic prescriptions, 79.2% were for trimethoprim, the recommended first line antibiotic for lower urinary tract infection in women. This is a result of the continued development of Pharmacy First service which enables people with common conditions to be reviewed by a community pharmacist to support self-care, provide timely antibiotic treatment or referral to other NHS services.

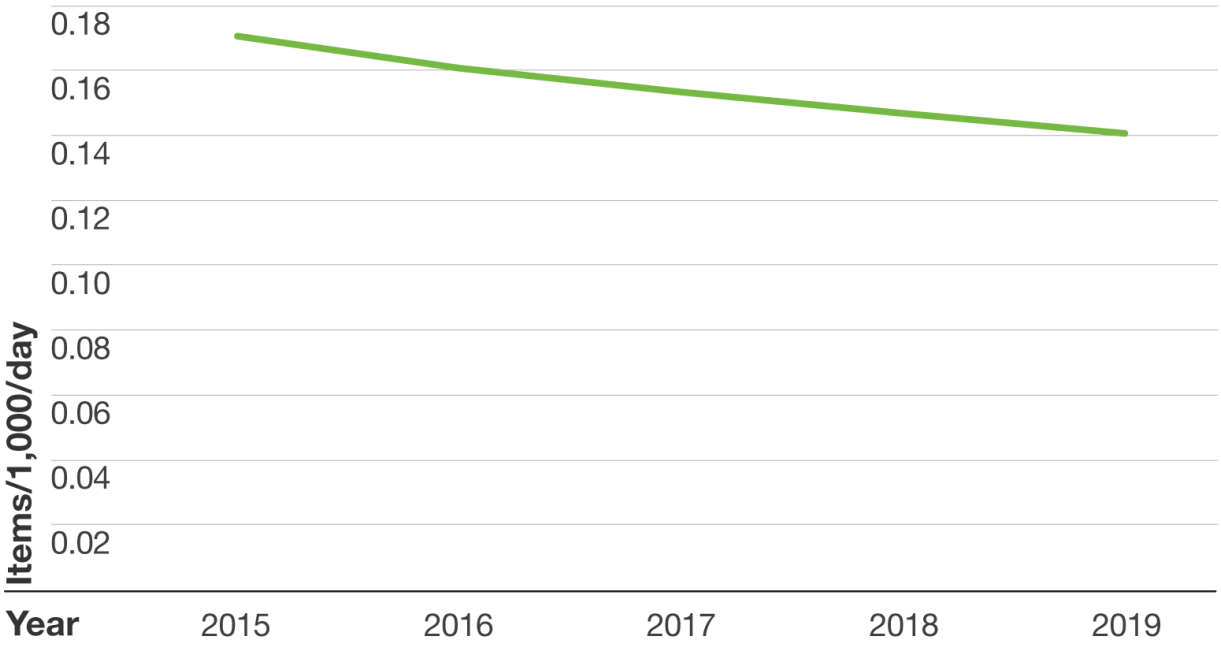
The increasingly multi-professional approach to antibiotic prescribing in primary care in Scotland reinforces the need to ensure all prescribers and clinicians irrespective of profession must be included in communications and education to optimise antibiotic use through local and national AMS initiatives.

Figure 7: Antibiotic prescribing by nurses in primary care in Scotland (items per 1,000 population per day; Items/1,000/Day), 2015 to 2019, by year



[Data source: NHS National Services Scotland (NSS) and Public Health Scotland (PHS)]

Figure 8: Antibiotic prescribing by dentists in primary care in Scotland (items per 1,000 population per day; Items/1,000/Day), 2015 to 2019, by year



[Data source: NHS National Services Scotland (NSS) and Public Health Scotland (PHS)]

Antibiotic Use in Primary Care Key Points

- **Over 80% of antibiotic use occurs in primary care**
- **Antibiotic use in 2019 was at the lowest rate on record and 9.1% lower than in 2015**
- **WHO Access (first line) antibiotics accounted for more than three quarters of all antibiotic use**
- **Increased use of shorter courses of amoxicillin**
- **Following local prescribing guidance and adopting antimicrobial stewardship is important to optimise antibiotic use during the COVID-19 pandemic**

> “It is a testament to the hard work of our colleagues in primary care that we have achieved the lowest antibiotic prescribing rate on record and over three quarters of this from the WHO Access (first line) list. More than 80% of antibiotic use occurs in primary care, with a large proportion for respiratory conditions. So with the COVID-19 pandemic, it remains even more important to avoid antibiotics in suspected viral infections (including COVID-19 where bacterial co-infection is very uncommon). When antibiotics are required we need to optimise their use by following local prescribing guidance, and using the shortest course possible.”
>
> **Dr Gail Haddock**
> GP and Vice Chair of SAPG

Antibiotic use in acute hospitals

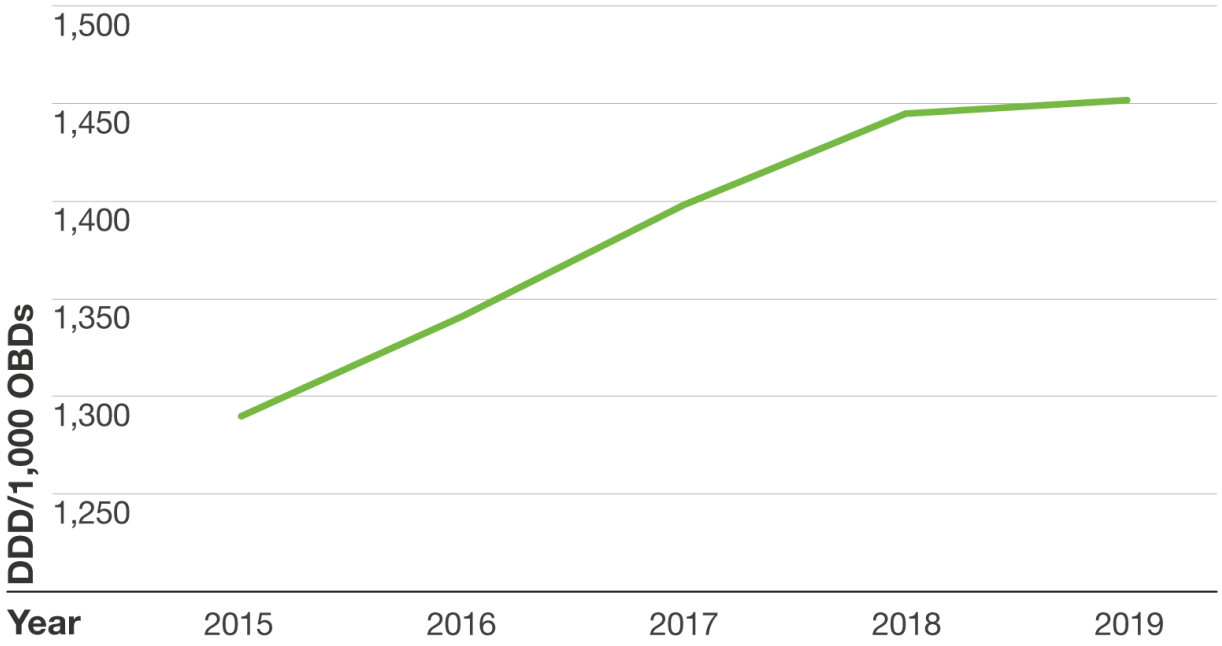
Antibiotic use in hospitals is common. On any day one third of people in Scottish hospitals will be receiving antibiotics[6]. Antibiotics are vital to prevent and treat infections in hospitalised patients, many of whom will have other comorbidities and where infections can be more severe and complex. Severe and drug resistant infections may require treatment with a wide range of antibiotics, including broad and very broad spectrum agents therefore AMS in hospitals is vital to preserve the effectiveness of antibiotics and optimise outcomes for patients.

In 2019, 14.3% of total antibiotic use (DDDs) in humans occurred in acute hospitals, 1,452.1 DDDs per 1,000 occupied bed days (OBD) which is 12.6% higher ($p<0.001$) than in 2015 (Figure 9 and see Appendix).

In 2018, as a result of increased use of antibiotics in acute hospitals being reported, SAPG commenced work to support clinicians to reliably implement timely clinical review of patients receiving antibiotics.[5] This ensures that treatment is personalised based on clinical signs and symptoms and microbiology results and that the intended duration of treatment is documented in the notes and on the medicine chart. Work is also underway to encourage the use of shorter antibiotic courses where published evidence of effectiveness supports this. Optimising duration of treatment in line with evidenced based practice will minimise unnecessary exposure of patients to antibiotics and will support the ambition to reduce antibiotic use to prevent the development of resistance.

In 2019, antibiotic use in acute hospitals was 1,452.1 DDDs per 1,000 OBD compared to 1,444.9 DDDs per 1,000 OBD in 2018. It is not yet possible to determine if this is the start of a new trend. This may suggest the start of a slowing down of previous increasing trends in antibiotic use in acute hospitals, and it may be an early sign that the focus on optimising antibiotics through clinical review and use of shorter courses may be having an impact. Continued development and embedding of behaviour change should be accelerated to drive further optimisation of antibiotic use in acute hospitals.

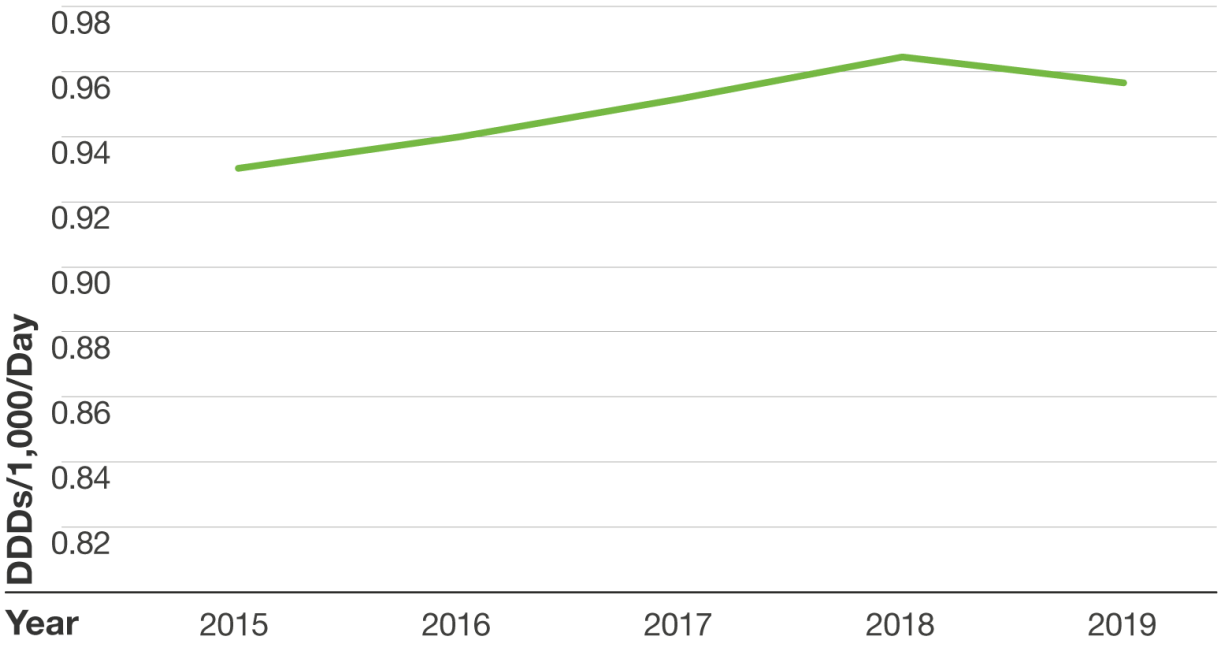
Figure 9: Antibiotic prescribing in acute hospitals in Scotland (defined daily doses per 1,000 occupied bed days; DDDs/1,000 OBDs), 2015 to 2019, by year



[Data Source: NHS National Services Scotland (NSS) and Public Health Scotland (PHS)]

In 2019, antibiotics given intravenously accounted for 30.0% of total antibiotic use (DDDs) in acute hospitals. The work on clinical review led by SAPG has focussed on patients started on IV antibiotics and aims for a documented management plan within 72 hours of treatment starting. This will reduce unnecessary continuation of antibiotics, ensure personalised treatment and appropriate IV to oral switch with associated benefits for patients of reduced risk of device-related infections and potential for earlier discharge from hospital. To measure progress with achieving reliable and timely review of IV antibiotic therapy, a national indicator has been developed with a target that use of IV antibiotics in hospitals will be no higher in 2022 than it was in 2018. The rate of intravenous (IV) antibiotic use in all secondary care in 2019 was 0.96 DDDs per 1,000 population per day showing a marginal reduction compared to 2018; the first reduction since 2015 (Figure 10 and see Appendix).

Figure 10: Parenteral antibiotic use in secondary care in Scotland (defined daily doses (DDDs) per 1,000 population per day (DDDs/1,000/Day), 2015 to 2019, by year

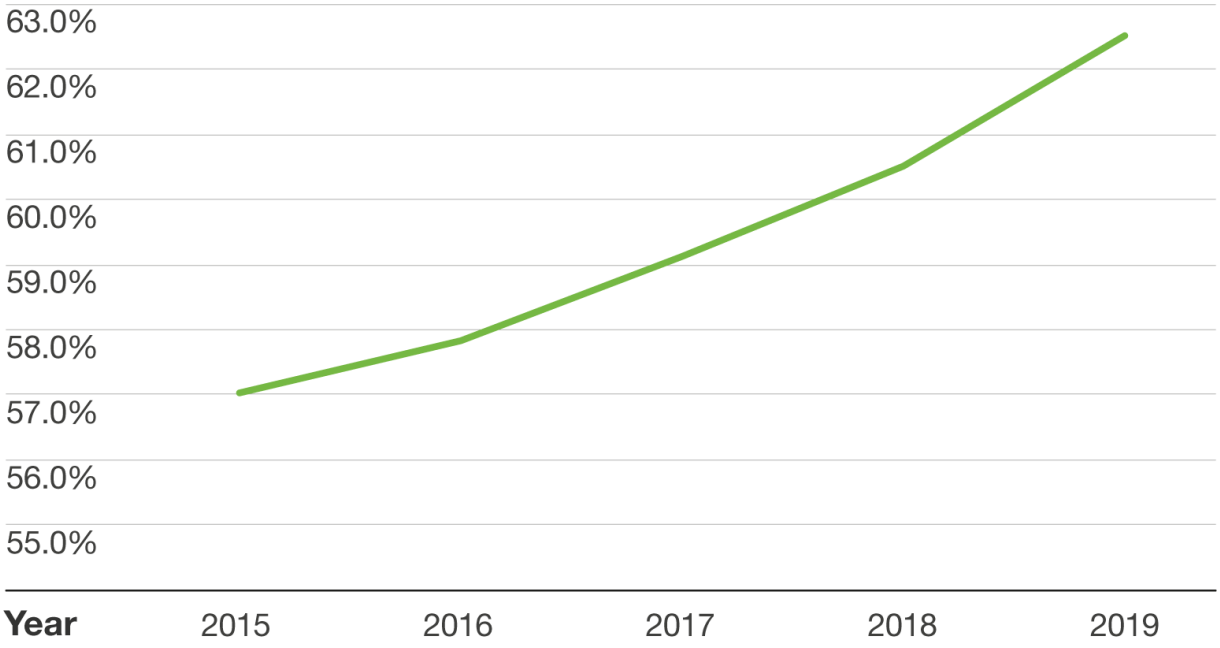


[Data Source: NHS National Services Scotland (NSS) and Public Health Scotland (PHS)]

The choice of initial empiric antibiotic treatment of infection in hospitalised patients remains an important component of hospital AMS and use of local antibiotic guidelines are embedded in clinical practice across NHS Scotland. These guidelines are evidenced based and will where clinically appropriate promote the use of narrower spectrum antibiotics and preserve the use of broader spectrum treatments where possible.

In 2019, 62.5% of antibiotic use (DDDs) in acute hospitals was Access group antibiotics compared to 57.0% in 2015 (Figure 11Figure 11). For more detail on use of particular antibiotics and antibiotic classes, see Appendix. A national indicator was launched in 2019 with a target that at least 60% of all antibiotic use in acute hospitals should be Access antibiotics. These most recent data suggest that hospital clinicians are following antibiotic guidelines, resulting in the Access target being achieved.

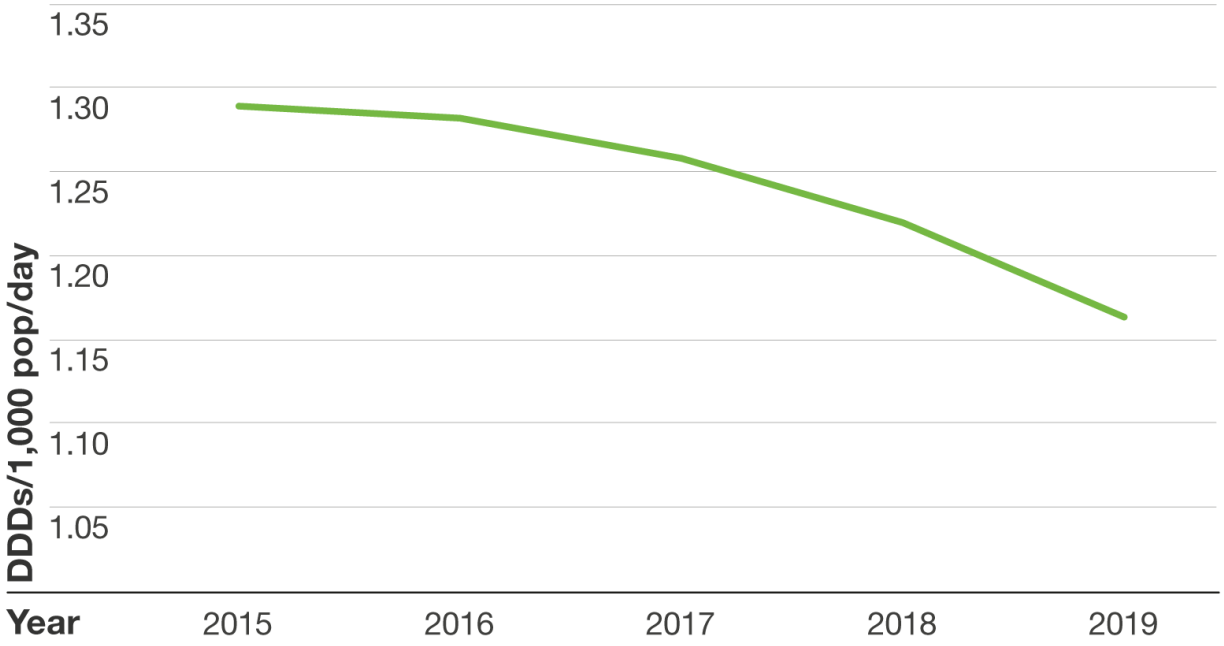
Figure 11: Percentage of all antibiotics prescribed (daily defines doses, DDDs) in acute hospitals in Scotland that belonged to the 'access' group, 2015 to 2019, by year



[Data Source: NHS National Services Scotland (NSS) and Public Health Scotland (PHS)]

In 2019, the rate of use of WHO Watch and Reserve antibiotics was 1.16 DDDs per 1,000 population per day 9.8% ($p<0.001$) lower than in 2015 (Figure 12). One of the ambitions in the UK AMR national action plan is a target to reduce by 10% the use of WHO Reserve and Watch categories of antibiotics in acute hospitals by 2024 (using 2017 as baseline). In 2019, the use of Reserve and Watch antibiotics was 7.5% lower than 2017 ($p<0.001$). This suggests that clinicians in acute hospitals are following treatment choices recommended in local prescribing guidelines.

Figure 12: 'Watch' and 'Reserve' group antibiotic prescribing in acute hospitals in Scotland (defined daily doses per 1,000 population per day; DDDs/1,000/Day), 2015 to 2019, by year



[Data Source: NHS National Services Scotland (NSS) and Public Health Scotland (PHS)]

Antibiotic Use in Acute Hospitals Key Points

- Antibiotic use in acute hospitals increased by 12.6% since 2015
- In 2019 the rate of increase in use of antibiotics in hospitals has slowed compared to previous years
- Over 60% of total antibiotic use in acute hospitals was WHO Access (first-line) antibiotics
- Decreased use of WHO Watch and Reserve (restricted) antibiotics compared to previous years
- A continued focus on clinical review and recording the duration of treatment is required to drive further optimisation of antibiotic use in acute hospitals
- Maintaining antimicrobial stewardship during the COVID-19 pandemic is important to optimise antibiotic use and prevent resistance

> “This year’s report shows some really important trends: The year on year increase in antibiotic prescribing in hospitals has markedly slowed, there has been a reduction in intravenous antibiotic use and a greater proportion of patients are receiving first line (Access) antibiotics. These data suggest good adherence to treatment guidelines, improved review and rationalisation of treatment. This reflects the growing body of evidence that shorter duration is better and oral therapy is preferred to IV therapy for the majority of bacterial infections in hospital. With the ongoing pressures of COVID-19 in Scottish hospitals antimicrobial stewardship is brought into sharp focus. In line with the latest recommendations from SAPG it is imperative that unjustified empirical and escalating antibiotic therapy is avoided and treatment decisions continue to be reviewed and rationalised in order to minimise unnecessary antibiotic use.”
>
> **Dr Andrew Seaton**
> Consultant Physician and Chair of SAPG

Antibiotic use in animals

In the same way that optimisation of antimicrobial use in humans is required to tackle the risk of AMR, the optimisation of antimicrobial use in animals is also important. Historically, data on antimicrobial use in animals has comprised of sales data compiled at the UK level and published in the annual Veterinary Antimicrobial Resistance and Sales Surveillance (VARSS)[7]. The publication of animal antimicrobial use (AMU) data in the Responsible Use of Medicines in Agriculture Alliance (RUMA)[8] Targets Task Force 2 Report of 2019 and VARSS Report of 2019 demonstrate serious commitment to antimicrobial stewardship in the face of ongoing bacterial disease challenge in livestock species as part of a One Health response to AMR in the UK.

For the second year, this report includes Scottish small animal antimicrobial use data. These data were made available from Scottish veterinary practices contributing to the Small Animal Veterinary Surveillance Network (SAVSNET) and provide an opportunity to further describe antimicrobial prescribing in the animal component of the One Health ecosystem.

In order to optimise disease avoidance and prescribing in veterinary practice, improve education, training and public engagement, and provide better access to and use of surveillance data in animal sectors, the **Scotland’s Healthy Animals website** was developed. The website was developed with stakeholders in the animal health sector and brings together expert advice on keeping animals healthy. Trusted guidance is signposted for all animal keepers and their vets, for countryside users, and for wildlife and rescue centres, and it hosts Scotland’s Poultry Hub for poultry keepers, in particular smallholders.

The Small Animal Veterinary Surveillance Network

The SAVSNET data were collected via electronic health records within the practice management systems of first opinion veterinary practices (these record species, breed, date or year of birth, sex, nature of condition being treated and antimicrobial treatments supplied, and postcode). These data are submitted voluntarily by participating veterinary practices and therefore cannot be interpreted as being representative of all of Scotland. Nevertheless, they provide additional important intelligence relating to another aspect of antimicrobial use in the One Health ecosystem.

This important data stream allows a continuing impression of antimicrobial use in companion animals in Scotland and will enable practitioners to evaluate their own data compared to these preliminary national data.

Antimicrobial Use (AMU) Summary

A summary of the available data is provided in Table 1. In 2019, 15 small veterinary practices in Scotland contributed data from 69,992 individual consultations and 36,933 individual animals. For this analysis, high priority critically important antimicrobials (HP-CIA) are identified according to the categorisation by the Antimicrobial Advice *Ad hoc* Expert Group (AMEG) of the European Medicines Agency (EMA) and include fluoroquinolones, 3rd and 4th generation cephalosporins, and colistin[9;10].

Fewer than one in five consultations resulted in the prescription of at least one antimicrobial (16.2%, 95% CI 15.9 to 16.4) Table 2, (Figure 13). The percentage of consultations that resulted in the prescription of an antimicrobial has shown a downward trend between 2015 and 2019 ($p<0.001$).

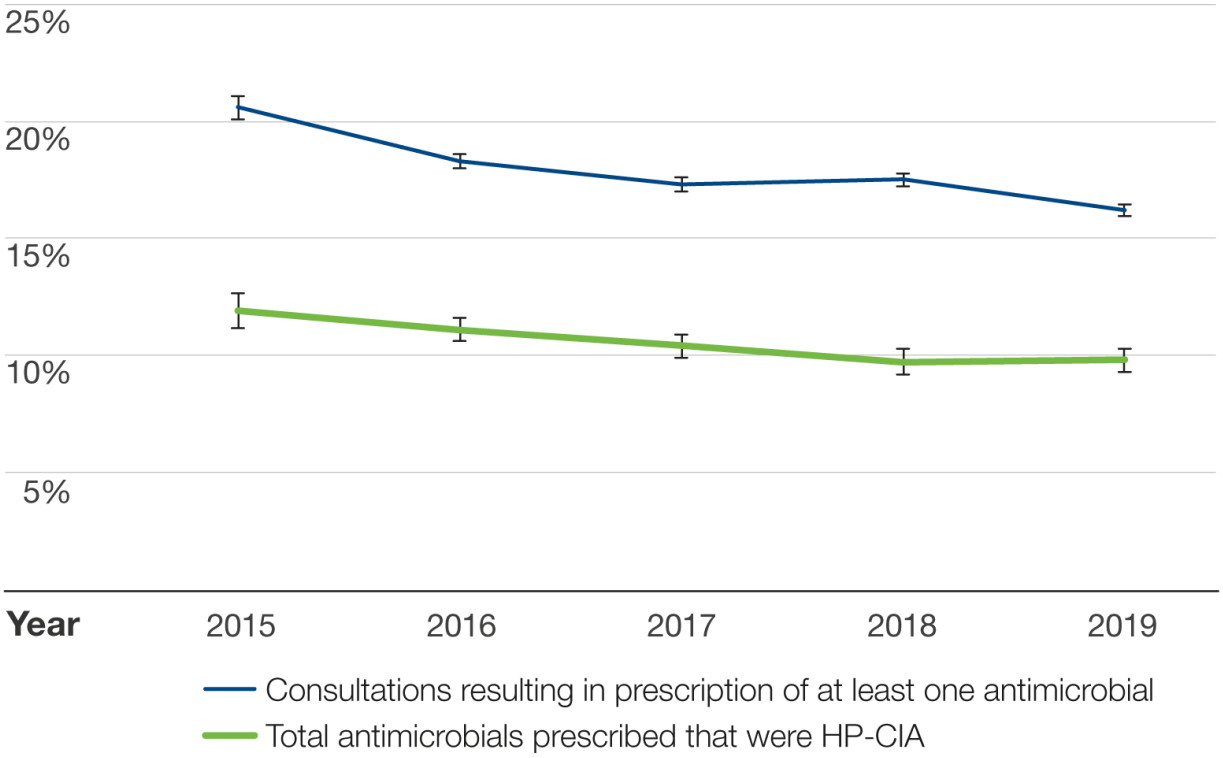
Table 1: Summary characteristics for companion animals in Scottish veterinary practices, extract from SAVSNET database, 2015 to 2019 inclusive

	2015	2016	2017	2018	2019
Number of contributing practices	9	11	11	15	15
Number of individual animals	15,140	26,646	26,138	30,145	36,933
Number of antimicrobials prescribed	7,336	13,963	12,360	11,633	12,968
Number of total consultations of individual animals	28,539	61,542	57,886	54,824	69,992
Number of consultations resulting in prescription of at least one antimicrobial	5,882	11,241	10,006	9,585	11,307
Percentage of consultations resulting in prescription of at least one antimicrobial	20.6% (95% CI=20.1 to 21.1)	18.3% (95% CI=18.0 to 18.6)	17.3% (95% CI=17.0 to 17.6)	17.5% (95% CI=17.2 to 17.8)	16.2% (95% CI=15.9 to 16.4)
Percentage of total antimicrobials prescribed that were high priority critically important antimicrobials (HP-CIA)	11.9% (95% CI=11.2 to 12.7)	11.1% (95% CI=10.6 to 11.6)	10.4% (95% CI=9.9 to 10.9)	9.7% (95% CI=9.2 to 10.3)	9.8% (95% CI=9.3 to 10.3)

*High priority critically important antimicrobials (HP-CIAs) are: cefovecin, ciprofloxacin, enrofloxacin, marbofloxacin, ofloxacin, orbifloxacin and pradofloxacin

[Data Source: The Small Animal Veterinary Surveillance Network (SAVSNET)]

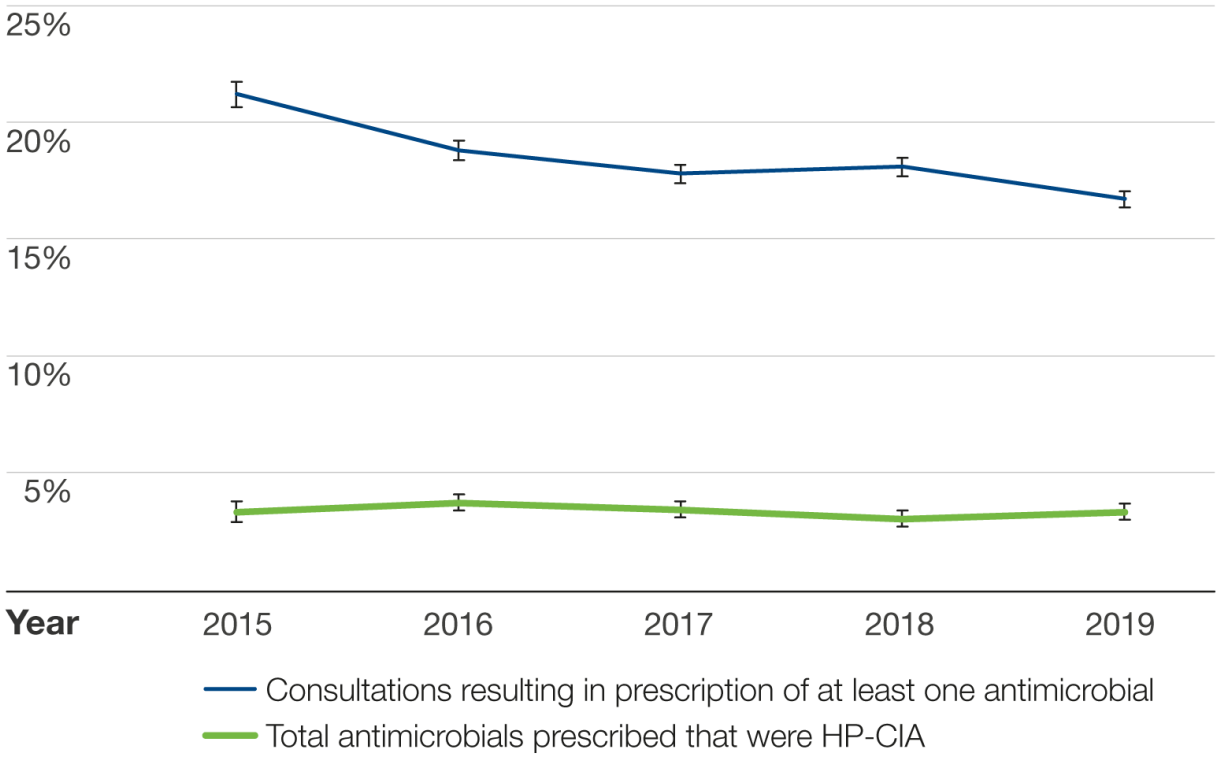
Figure 13: Trends in prescribing of antimicrobials (including HP-CIA) for all companion animals in Scottish practices, extract from SAVSNET database, 2015 to 2019 inclusive



[Data Source: Small Animal Veterinary Surveillance Network (SAVSNET)]

Over the five years from 2015 to 2019, there has been a significant decrease in the percentage of consultations resulting in the prescription of at least one antimicrobial to all companion animals. ($p<0.001$) but no significant difference in the percentage of total antimicrobials being prescribed that were HP-CIA ($p>0.05$) (Figure 13).

Figure 14: Trends in prescribing of antimicrobials (including HP-CIA) for dogs in Scottish practices, extract from SAVSNET database, 2015 to 2019 inclusive

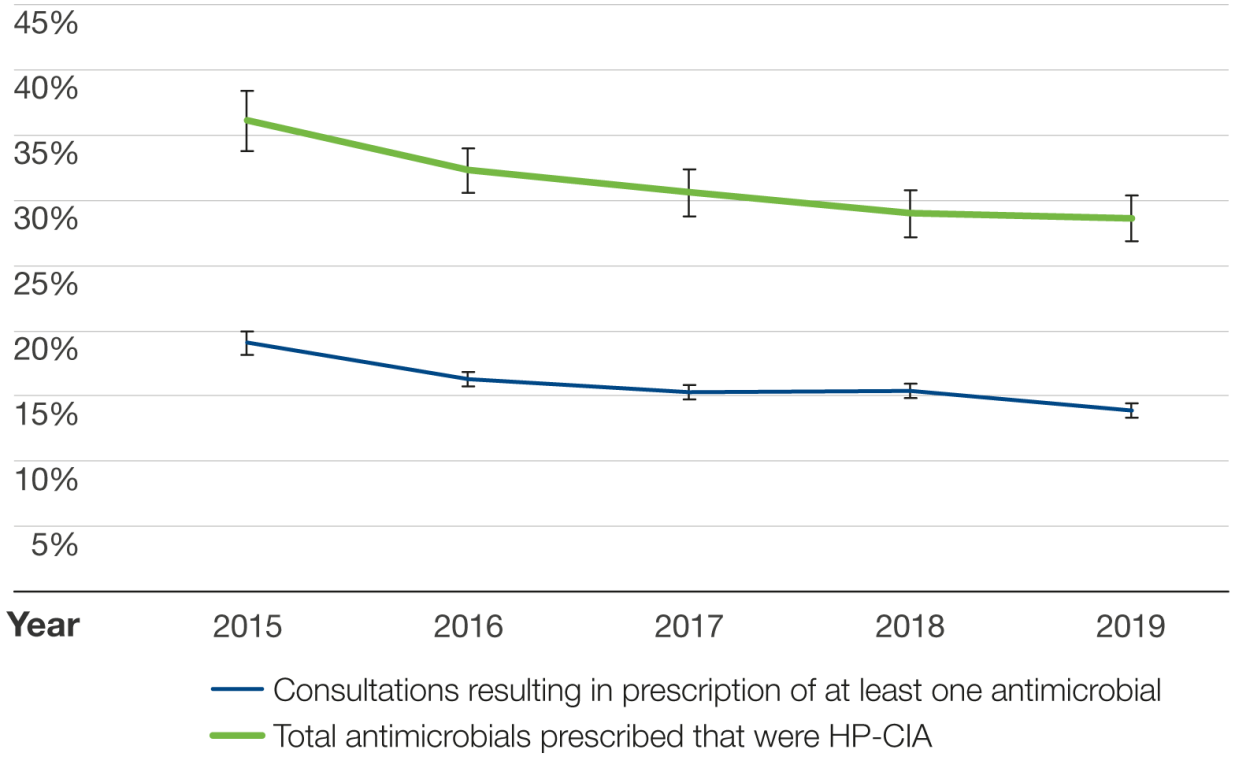


[Data Source: Small Animal Veterinary Surveillance Network (SAVSNET)]

Over the last five years, from 2015 to 2019, there has been a significant decrease in the percentage of consultations resulting in the prescribing of at least one antimicrobial to dogs ($p<0.001$).

Over the last five years, from 2015 to 2019, there was no significant difference in the percentage of total antimicrobials being prescribed that were HP-CIA ($p>0.05$) (Figure 14).

Figure 15: Trends in prescribing of antimicrobials (including HP-CIA) for cats in Scottish practices, extract from SAVSNET database, 2015 to 2019 inclusive



[Data Source: Small Animal Veterinary Surveillance Network (SAVSNET)]

Over the last five years, from 2015 to 2019, there has been a significant decrease in the percentage of consultations resulting in the prescribing of at least one antimicrobial to cats ($p<0.001$) (Figure 15).

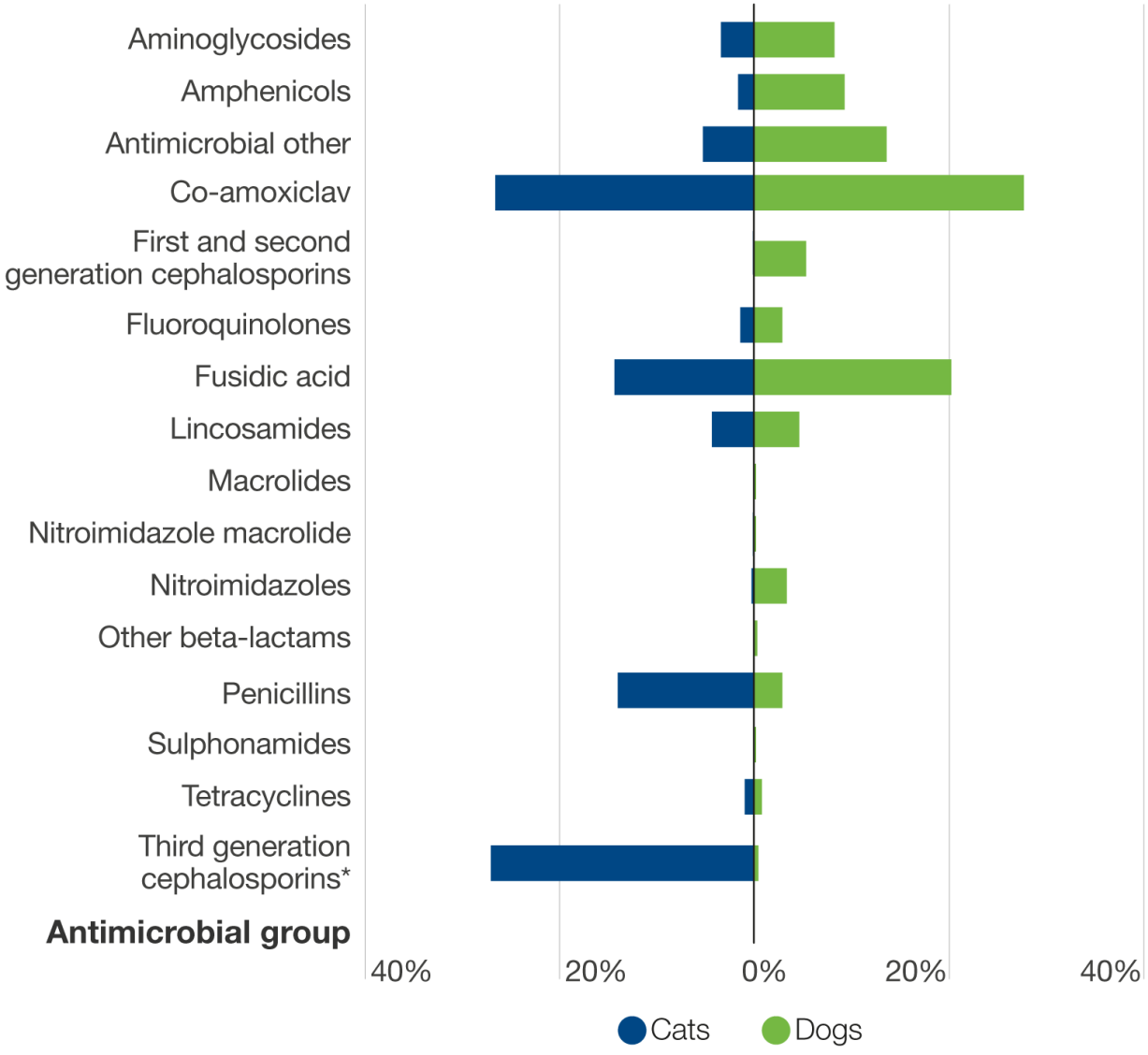
Over the last five years, from 2015 to 2019, there was no significant difference in the percentage of total antimicrobials being prescribed that were HP-CIA ($p>0.05$)

The differences between dogs and cats reflect to a great extent differences in formulation, with injectable antimicrobials used more frequently in cats (Figure 18).

Antimicrobial groups

The most frequently prescribed antimicrobial group for dogs was co-amoxiclav (27.8%) (Figure 16), followed by the topical antibiotic fusidic acid (20.2%), and the most frequently prescribed antimicrobial group for cats was 3rd generation cephalosporins (27.2%) followed by co-amoxiclav (26.6%).

Figure 16: Percentage of total antimicrobials prescribed, by antimicrobial group, for dogs and cats for 2019



*3rd generation cephalosporins are usually categorised as part of a '3rd/4th/5th generation cephalosporin 'grouping, but no 4th or 5th generation cephalosporins are used in animals.

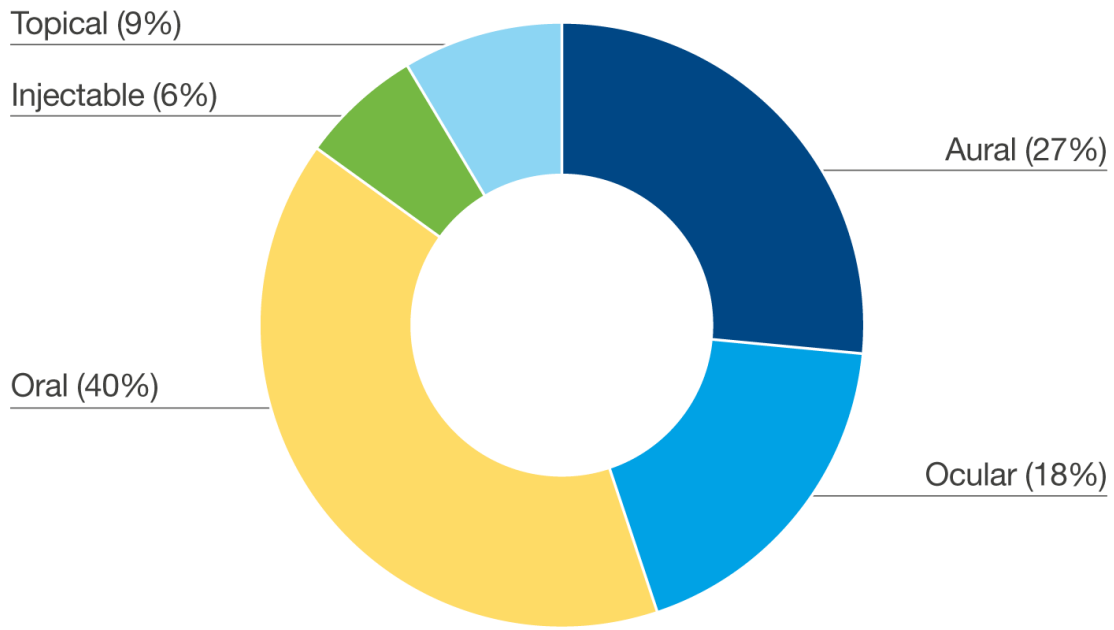
[Data Source: Small Animal Veterinary Surveillance Network (SAVSNET)]

Route of Administration

The route of administration of antimicrobials for dogs and for cats are shown in

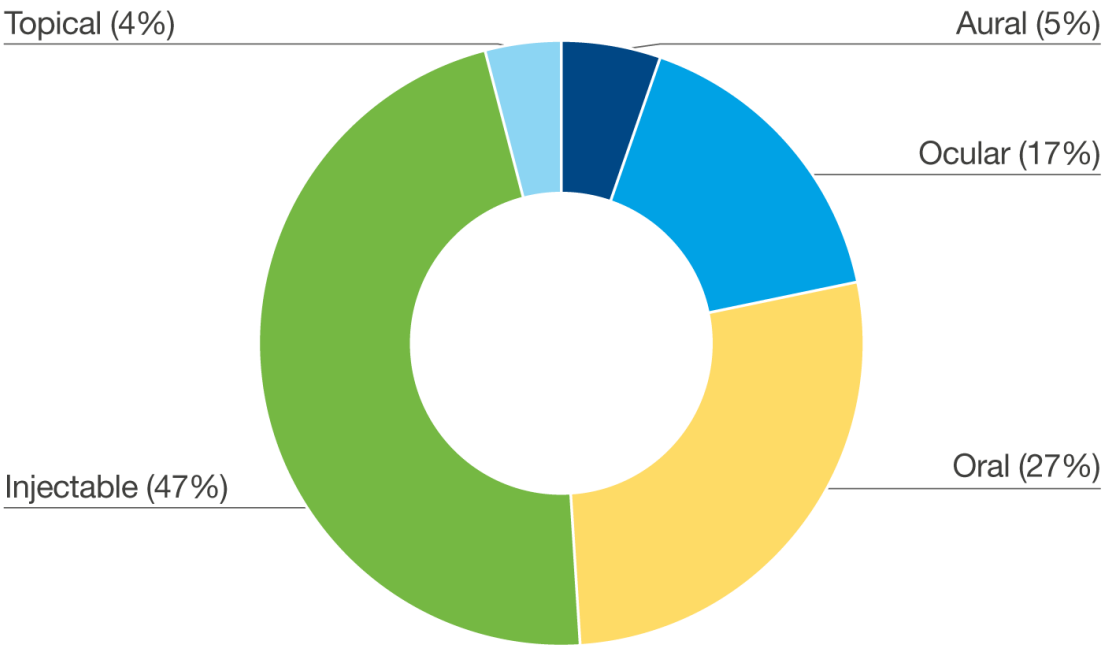
Figure 17 and Figure 18, respectively.

Figure 17: Route of administration of antimicrobials for dogs, 2019



[Data Source: Small Animal Veterinary Surveillance Network (SAVSNET)]

Figure 18: Route of administration of antimicrobials for cats, 2019

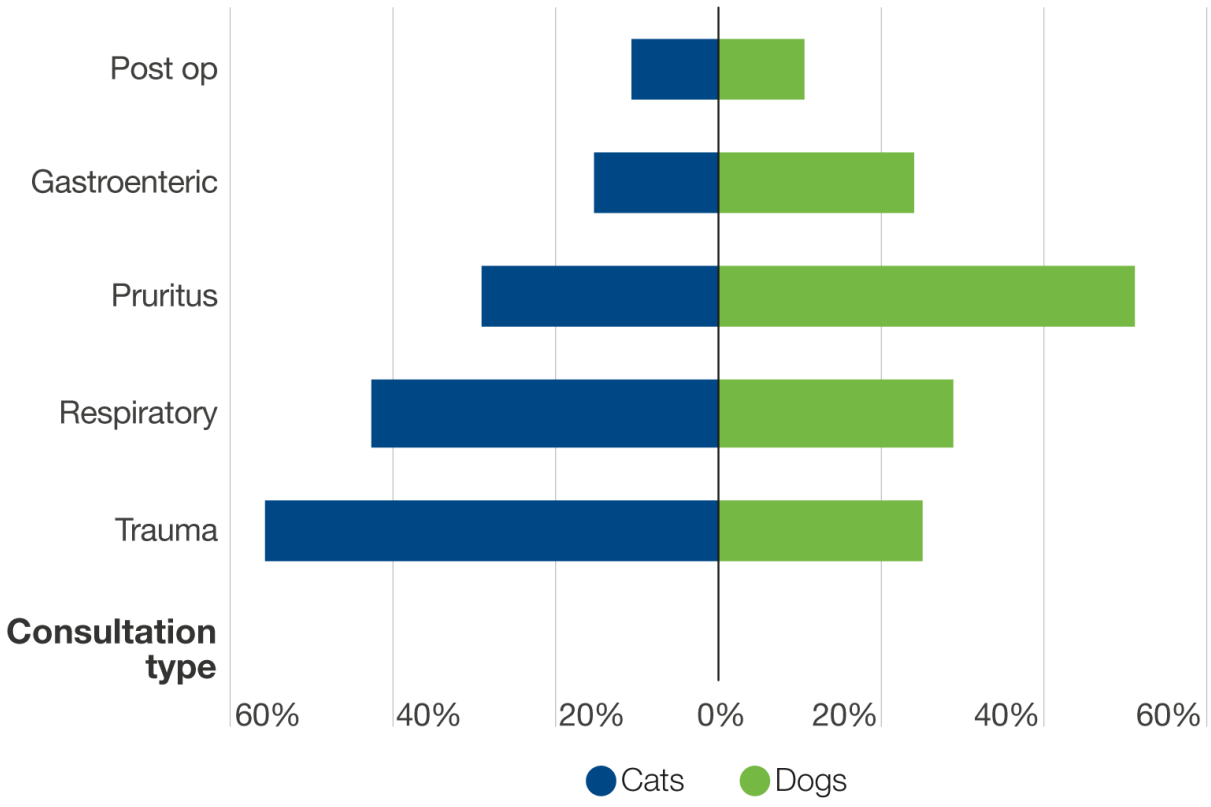


[Data Source: Small Animal Veterinary Surveillance Network (SAVSNET)]

The data on route of administration provides context to the antimicrobial use findings. For example, almost all (>99%) aminoglycoside, amphenicol, fusidic acid and other antimicrobial use are ocular, aural or topical. Similarly, differences in 3rd generation cephalosporin use between cats and dogs match those in injectable antimicrobials.

For the first time in Scotland, we have been able to report data on the percentage of consultations where at least one antimicrobial was prescribed by presenting problem (Figure 19).

Figure 19: Percentage of consultations which resulted in prescription of an antimicrobial by presenting problem for dogs and cats in 2019 [R]



[Data Source: Small Animal Veterinary Surveillance Network (SAVSNET)]

Further detail on prescribing in syndromic categories can be found in the SAVSNET surveillance series published in the Veterinary Record[11-13].

Animal Antimicrobial Use Key Points

- **Antimicrobials are very important medicines in animal species**
- **Overall antimicrobial use in companion animals is reducing over time in Scotland**
- **Ongoing data collection contributes to developing evidence base pertaining to AMU in animals and the impact on AMR**
- **Engagement and support from animal stakeholder groups is essential in the development of this intelligence**
- **Further close working with SAVSNET to encourage practices to participate in the network is important**
- **Scotland's Healthy Animals website provides guidance for vets and animal keepers on disease avoidance and antimicrobial stewardship**

"Collaborating with ARHAI Scotland has given us an unparalleled opportunity to witness data collected by ourselves from voluntary veterinary practices being used to produce outputs of real value not just for the veterinary profession, but for public health as well. This report drives the conversation relating to responsible antimicrobial prescribing practices forward, enabling findings to be incorporated into stewardship action."

Dr David Singleton
Veterinary Epidemiologist, SAVSNET, The University of Liverpool

"The SAVSNET results give us a much better overview of antimicrobial use compared to sales information. Analysing antimicrobial prescriptions by drug, route, species and presentation significantly improves monitoring. It's great to see the sustained reduction in antimicrobial use and the emphasis on 1st line and topical drugs. However, continued use of High Priority-Critically important Antibiotics, particularly in cats, is an area for further work. Encouraging practices to join SAVSNET will give us more and better data, which will help improve antimicrobial stewardship."

Dr Tim Nuttall
Senior Lecturer in Small Animal Veterinary Dermatology, The University of Edinburgh

What is the current burden of drug resistant infections in Scotland?

Reducing the burden of drug resistant infections is critical to controlling AMR by reducing the need for antimicrobials and reducing the risk of further spread of drug resistant micro-organisms. In Europe in 2015, there was an estimated 671,689 infections with antibiotic resistant bacteria, accounting for 33,110 attributable deaths and 874,541 disability adjusted life years[14].

In 2019, there were an estimated 1,476 BSI caused by antibiotic resistant bacteria of public health concern compared to 1,424 in 2018 (Table 2, and see Appendix). There were 1,294 and 182 Gram-negative and Gram-positive antibiotic resistant bacteraemia, respectively. Drug resistant bacteraemia caused by Gram-negative bacteria accounted for 87.7% of all drug resistant bacteraemia. Importantly, nearly a quarter of *Escherichia coli* bacteraemia (ECB) in Scotland were resistant to one or more key antibiotics, accounting for over 1,100 cases. Whilst *E. coli* accounted for the majority of drug resistant infections, vancomycin resistant *Enterococcus faecium* were the second most common organism. The overall burden of infection was low; however, the proportion of resistance to vancomycin was 43.1%.

Preliminary analyses will be further developed by the SONAAR programme in collaboration with UK colleagues to measure and monitor the wider burden and impact of drug resistant infections (including other infection types) using methods developed by Cassini *et al* 2019 [14].

Table 2: Estimated number of drug resistant bacteraemia in Scotland, 2019, by organism [R]

Organisms (n=total number of bacteraemia)	Estimated number of resistant bacteraemia	% resistant to at least one key antibiotic*
Gram negative bacteraemia (n=6,127)	**1,293.8**	21.12%
E. coli (n=4767)	1,145.4	24.03%
K. pneumoniae (n=777)	109.2	14.05%
K. oxytoca (n=215)	15.1	7.04%
Acinetobacter species (n=79)	1.2	1.49%
P. aeruginosa (n=289)	23.0	7.94%
Gram positive bacteraemia (n=2,827)	**181.8**	6.43%
E. faecium (n=295)	126.7	43.10%
E. faecalis (n=451)	1.0	0.23%
S. aureus (n=1499)	46.0	3.07%
S. pneumonia (n=583)	8.0	1.38%
Total number of bacteraemia (n=8,954)	**1,475.6**	16.48%

[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

> “Now more than ever Infection Protection and Control precautions are at the forefront of everyone’s minds. Preventing infections in the community and across healthcare settings is vital and will reduce the need to use antibiotics which in turn will help contain antimicrobial resistance. At ARHAI Scotland we will continue to work with our partners across all settings to monitor infections and provide evidence for action.”
>
> **Laura Imrie**
> Consultant Lead, ARHAI Scotland, Procurement, Commissioning and Facilities

Burden of AMR Key Points

- Reducing the burden of drug resistant infections is critical to controlling and containing AMR
- There were 1,476 drug resistant bacteraemia during 2019, the majority caused by drug resistant Gram-negative bacteraemia
- Almost a quarter of *E. coli* bacteraemia were resistant to one or more key antibiotics, accounting for over 1,100 cases in 2019
- Continued focus on reducing Gram-negative infections is essential
- Gram-positive infections also contribute to the burden of AMR
- Robust intelligence and metrics are required to plan, prioritise and evaluate interventions to reduce the burden

Antimicrobial Resistance

Antimicrobial resistance in humans

AMR is a serious worldwide public health challenge, threatening the effective prevention and treatment of an ever increasing number of pathogens. Although resistance occurs naturally, the inappropriate use of antimicrobials amplifies the rate at which it develops and spreads[15]. With a limited pipeline of new antimicrobials under development, AMR renders once standard treatments ineffective and is associated with increased morbidity and mortality, longer treatment durations and higher healthcare costs[16].

Surveillance data, as presented in this report, provides essential evidence to prevent, control and contain AMR, drive appropriate prescribing, inform national policy and preserve the effectiveness of antibiotics for future generations.

This section of the report focuses on AMR of key public health importance in Scotland. Additional data published in the appendix can be used to make comparisons to other European countries.

Infections caused by Gram-negative bacteria

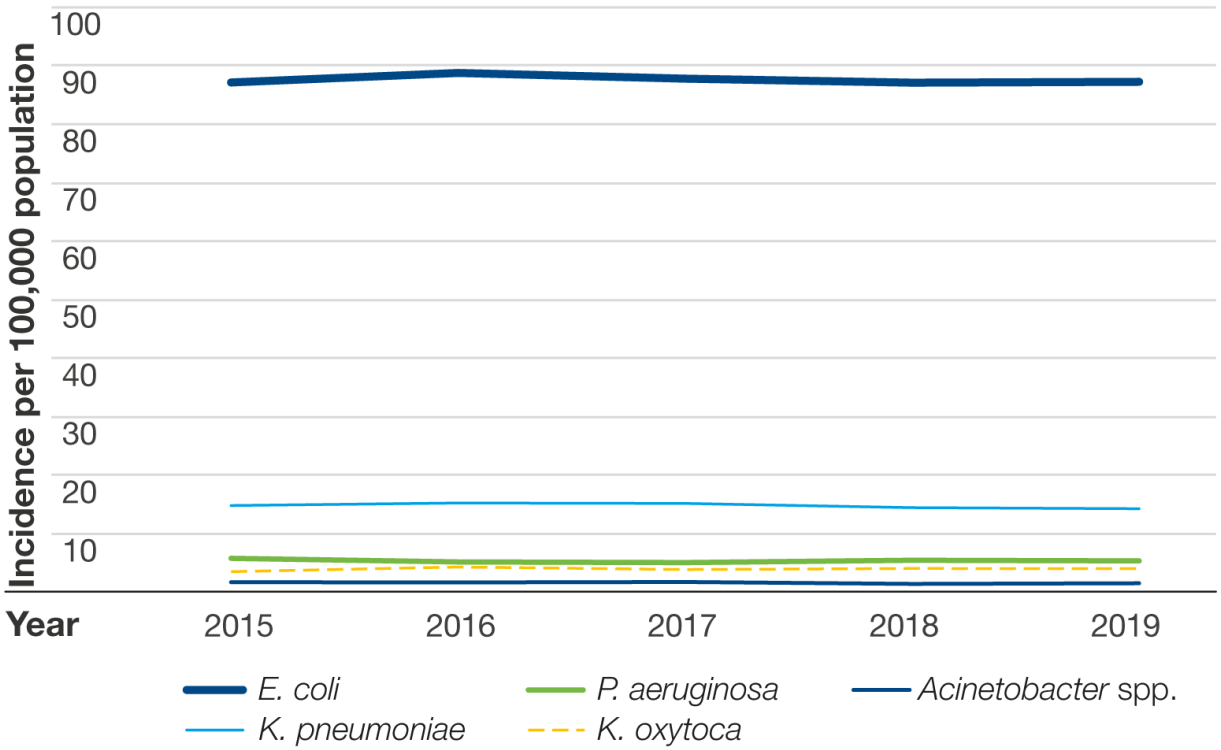
Gram-negative bacteria are an important cause of serious infections in both healthcare and community settings. Globally, the prevalence of these infections is increasing and Gram-negative bloodstream infections (BSIs) are associated with excess morbidity, mortality and length of hospital stay[17;18].

The reduction of healthcare associated Gram-negative infections is one of the priority areas identified in the UK NAP to tackle AMR.[1] The UK NAP includes a target to reduce Gram-negative bacteraemia by 25% by 2021/22 and 50% by 2023/24.

Effective infection prevention and control in addition to antibiotic stewardship, including limiting the use of unnecessary antibiotics, is key to reducing the burden of invasive Gram-negative infections[19;20].

The incidence of key Gram-negative bacteraemia is described in Figure 20. *E. coli* was the most common cause of Gram-negative bacteraemia in 2019 in Scotland, followed by *Klebsiella pneumoniae (K. pneumoniae), Pseudomonas aeruginosa (P. aeruginosa), Klebsiella oxytoca (K. oxytoca) and Acinetobacter* spp. The incidence of bacteraemia caused by these bacteria has remained stable over the last five years.

Figure 20: Incidence of Gram-negative bacteraemia per 100,000 population in Scotland, 2015 to 2019, by five most frequently reported organism and year [R]



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

Escherichia coli bacteraemia

Incidence of of *E. coli* bacteraemia

E. coli bacteraemia (ECB) typically develops as a complication of a primary infection, most commonly within the genital/urinary tract[21;22].

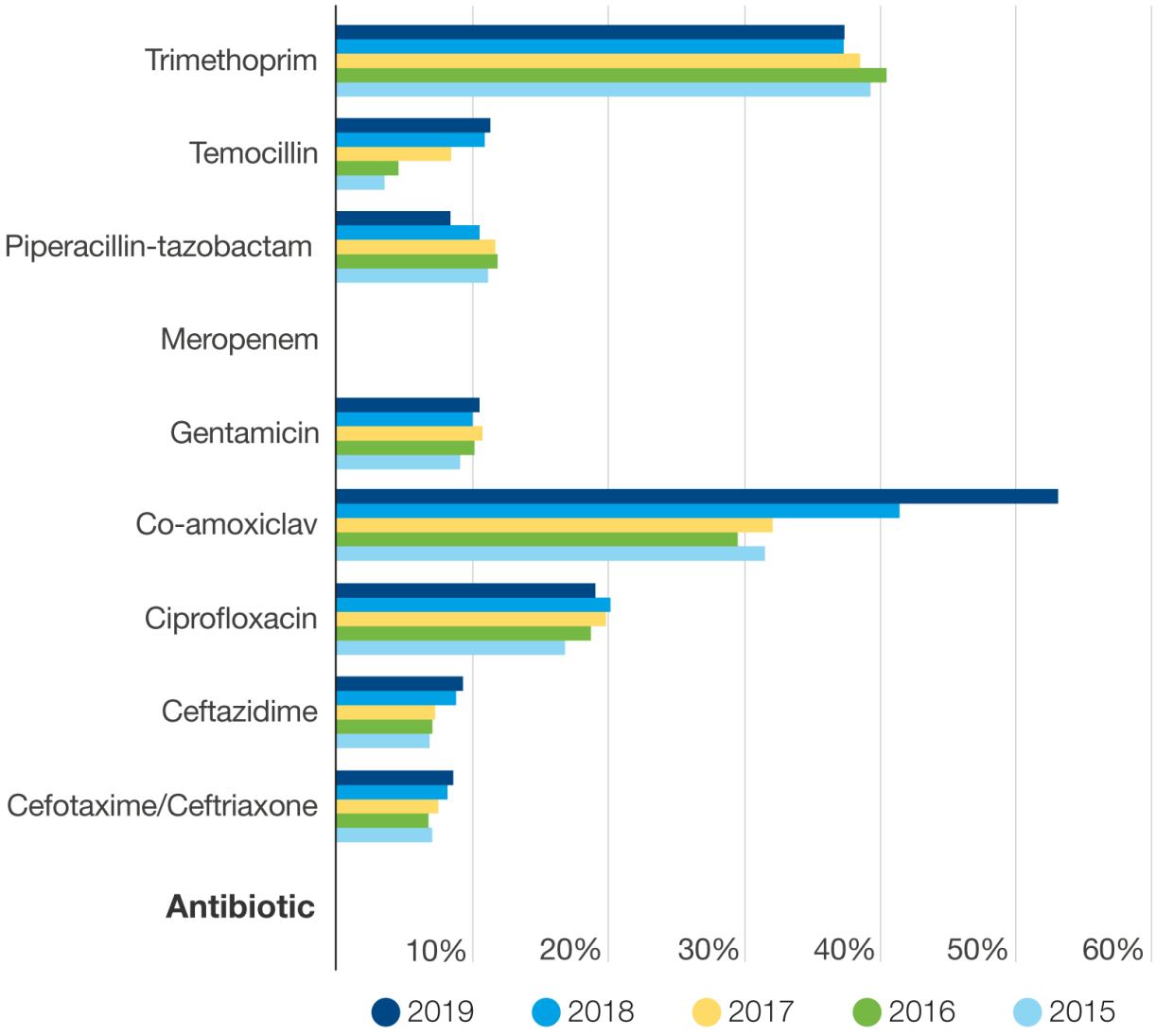
The incidence of ECB has remained stable in Scotland over the last five years. In 2019, there were 4,767 cases of ECB which equates to an incidence of 87.3 per 100,000 population (Figure 20), compared to an incidence of 70.7 per 100,000 population for the most recent (2018) Public Health England (PHE) surveillance data, from England, Wales and Northern Ireland[23].

Non-susceptibility in *E. coli* blood isolates

As the primary causative organism of bacteraemia, *E. coli* infections pose a significant antibiotic resistance burden.

Within the last year there has been an increase in co-amoxiclav non-susceptibility from 41.5% in 2018 to 53.1% in 2019 ($p<0.001$) (Figure 21). However, this may not be representative of a true increase and is likely to have resulted from the implementation of new Biomerieux® Vitek AST cards in late 2018 that test amoxicillin in combination with a fixed clavulanic acid concentration of 2 mg/L. During this period piperacillin with tazobactam non-susceptibility decreased significantly ($p=0.001$) from 10.6% in 2018 to 8.5% in 2019. No increase in the 3rd generation cephaloporins have been observed unlike elsewhere in the UK and also in Europe[24].

Figure 21: Non-susceptibility of *Escherichia coli* bacteraemia (ECB) isolates in Scotland, 2015 to 2019 [R]



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

Bacteraemia caused by other Gram-negative micro-organisms

Despite their collective incidence being lower than that of *E. coli* bacteraemia alone, *K. pneumoniae*, *P. aeruginosa*, *K. oxytoca* and *Acinetobacter* spp. still represent a significant burden of infection.

Incidence of *Klebsiella pneumoniae* and *Klebsiella oxytoca* bacteraemia

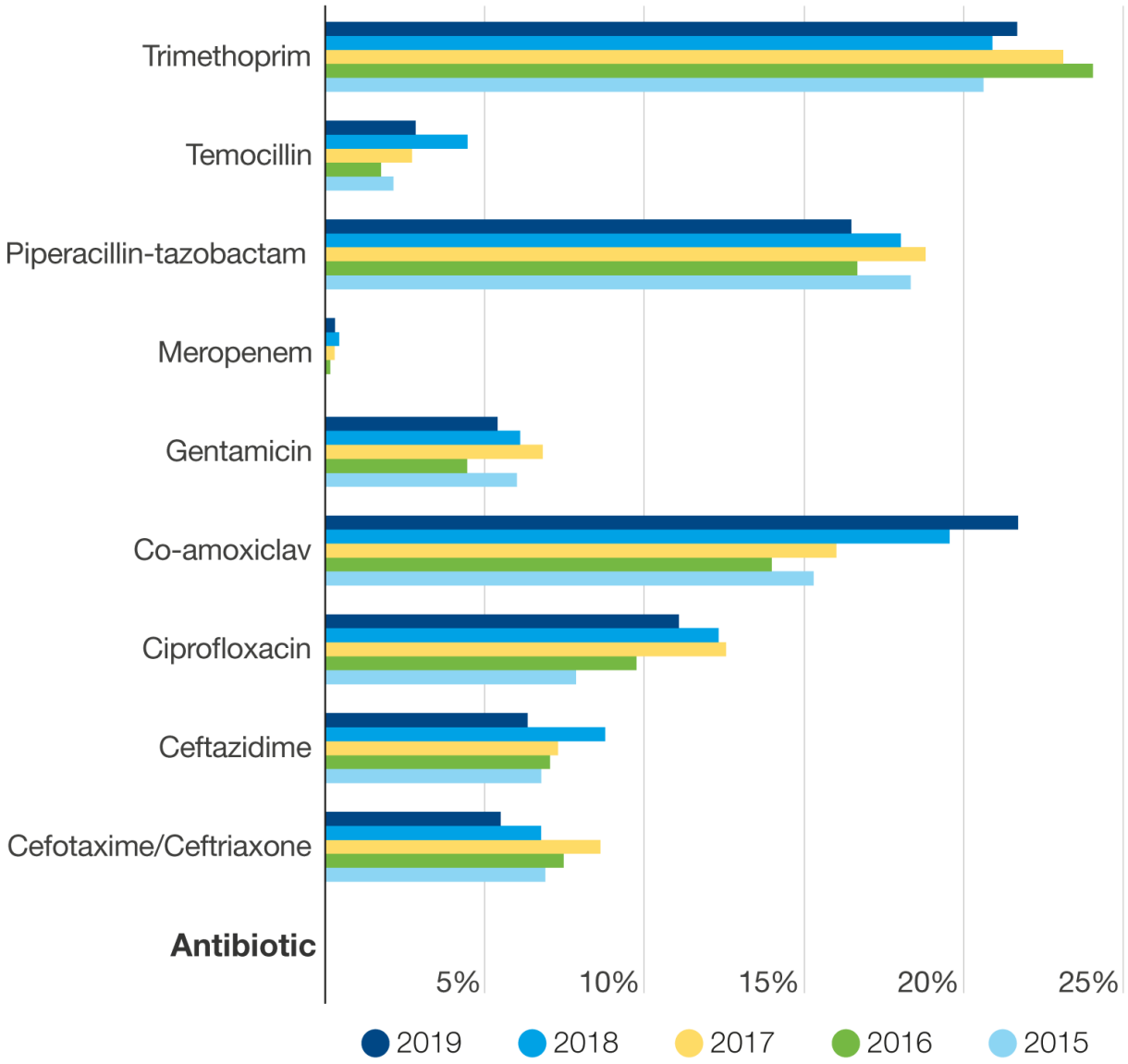
Klebsiella spp. and in particular *K. pneumoniae,* are an important cause of healthcare associated infection (HCAI), especially urinary tract infections (UTIs), respiratory tract infections and BSIs[25]. Clinical management of *Klebsiella* infections is becoming increasingly difficult due to antimicrobial resistance, particularly with regards to acquired carbapenemases[26].

The incidence of both *K. pneumoniae* and *K. oxytoca* bacteraemia over the last five years in Scotland has remained stable (**Figure 20**). In 2019, 777 cases of *K. pneumoniae* and 215 cases of *K. oxytoca* bacteraemia were reported, equating to an incidence of 14.2 and 3.9 per 100,000 population, respectively, compared to an incidence of 12.5 and 2.8 per 100,000 population, respectively, for the most recent available data (2018), from England, Wales and Northern Ireland[27].

Non-susceptibility in *Klebsiella pneumoniae* and *Klebsiella oxytoca* blood isolates

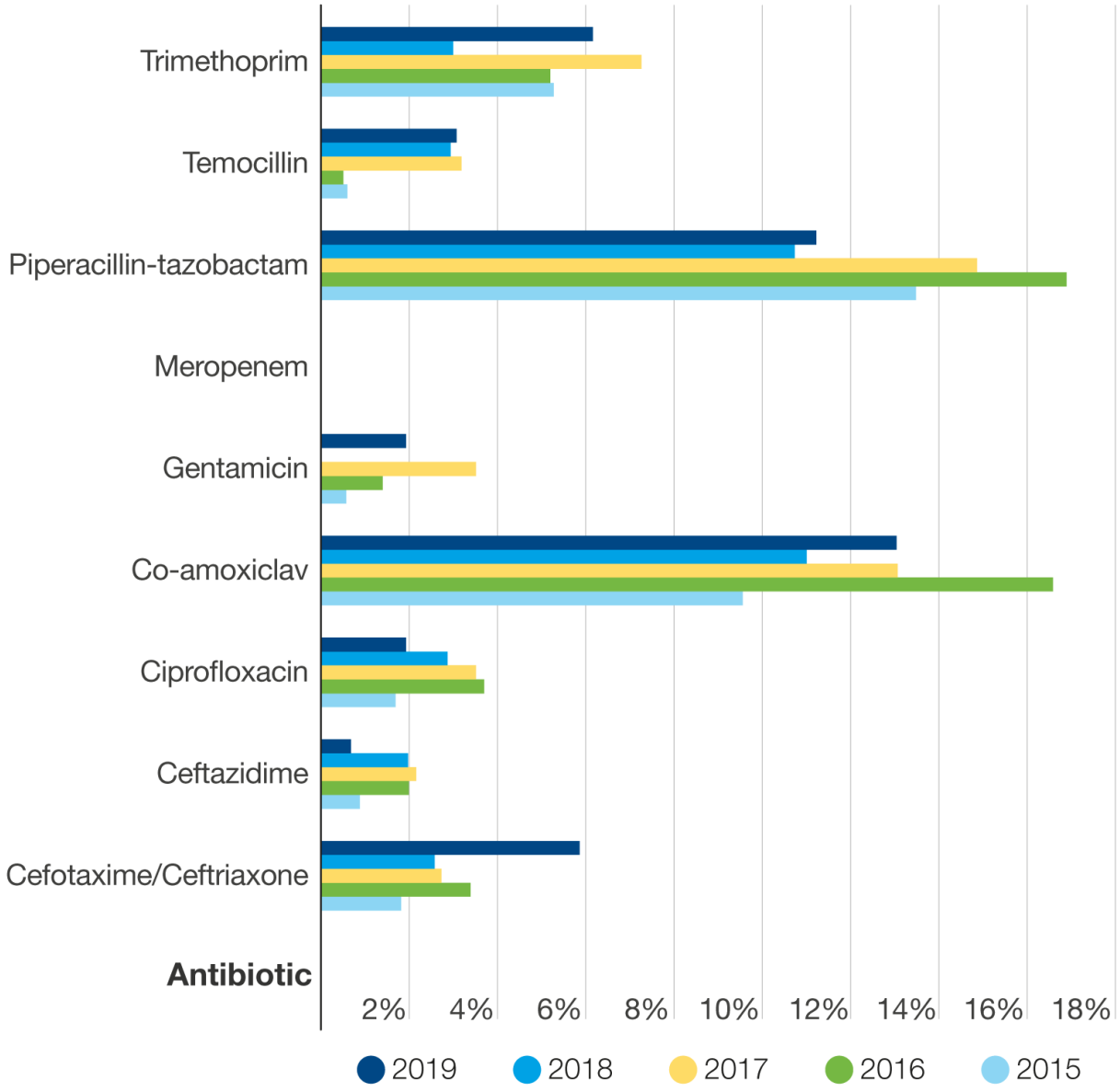
In 2019, 21.7% of *K. pneumoniae* and 13.0% *K. oxytoca* blood isolates were non-susceptible to co-amoxiclav, 21.7% and 6.2% to trimethoprim, 16.5% and 11.2% to piperacillin with tazobactam and 11.1% and 1.9% to ciprofloxacin respectively. Non-susceptibility to the remaining antibiotics, including the third-generation cephalosporins remained low (**Figure 22** and **Figure 23**). Non-susceptibility proportions have remained stable in comparison to last year. Susceptibility trends among *K. pneumoniae* and *K. oxytoca* blood isolates were broadly comparable to recent (2018) PHE surveillance data[27].

Figure 22: Non-susceptibility of *Klebsiella pneumoniae* bacteraemia isolates in Scotland, 2015 to 2019 [R]



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)

Figure 23: Non-susceptibility of *Klebsiella oxytoca* bacteraemia isolates in Scotland, 2015 to 2019 [R]



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

Incidence of of *Pseudomonas aeruginosa* bacteraemia

P. aeruginosa is a non-fermenting Gram-negative bacteria found commonly throughout the environment[28]. As an opportunistic pathogen, *P. aeruginosa* is associated with a variety of acute and chronic infections and is a leading cause of hospital-acquired infections, particularly in immunocompromised patients[29].

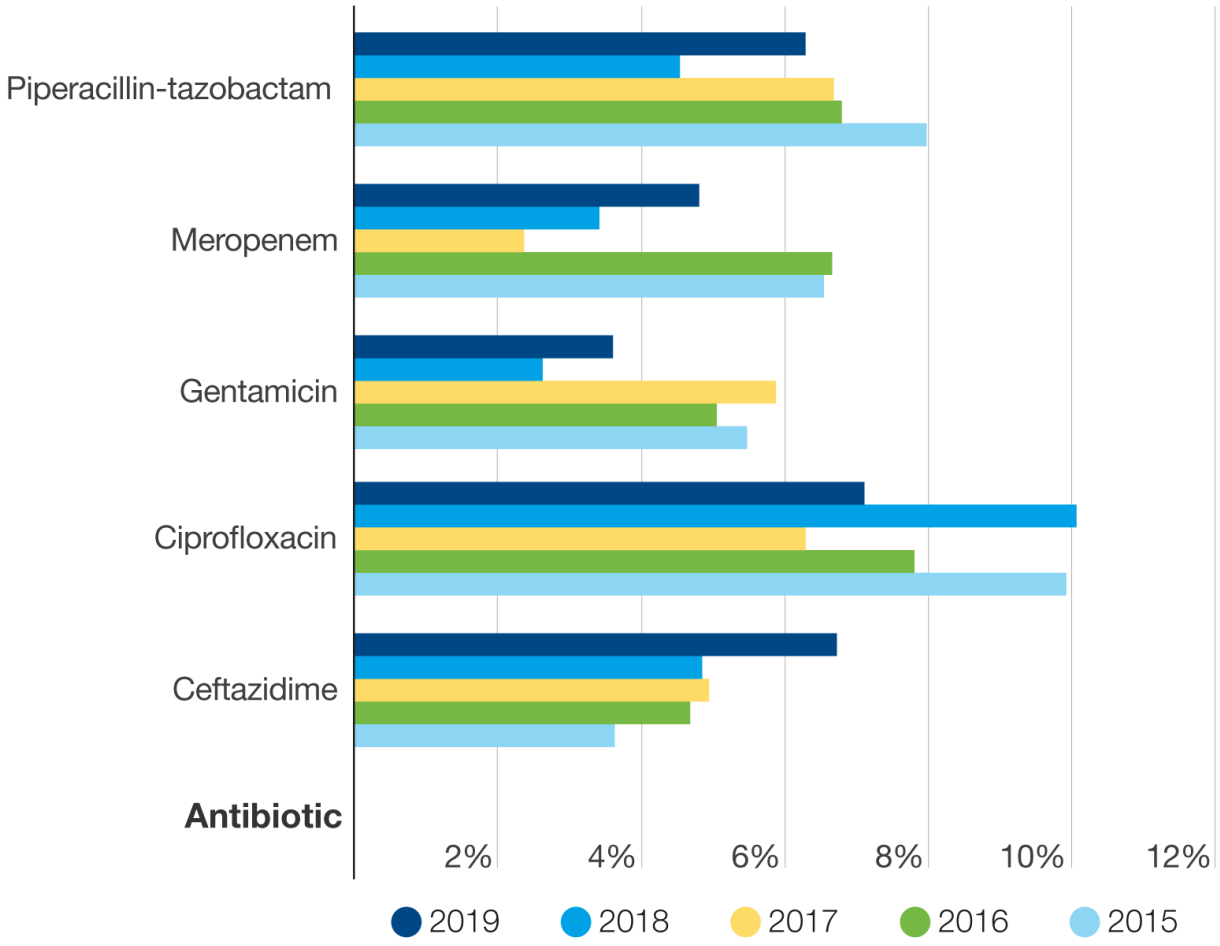
The incidence of *P. aeruginosa* bacteraemia over the last five years in Scotland has remained stable (Figure 20). In 2019, there were 289 cases of *P. aeruginosa* bacteraemia in Scotland which equates to an incidence of 5.3 per 100,000 population, compared to an incidence of 7.8 per 100,000 population for the most recent available data (2018) across England, Wales and Northern Ireland[30].

Non-susceptibility in *P. aeruginosa* blood isolates

P. aeruginosa is not only intrinsically resistant to a broad range of antibiotics but can easily develop additional resistance via chromosomal mutations or horizontal acquisition of resistance determinants[28]. The development of multi-drug resistant (MDR) and extensively drug resistant (XDR) *P. aeruginosa* is cause for concern due to limited treatment options and associated high mortality[31].

Non-susceptibility in *P. aeruginosa* blood isolates has remained stable over the last five years for all reported agents. In 2019, 7.1% of isolates were non-susceptible to ciprofloxacin, 6.7% to ceftazidime, 6.3% to piperacillin/tazobactam, 4.8% to meropenem and 3.6% to gentamicin (Figure 24). Susceptibility trends among *P. aeruginosa* blood isolates were broadly comparable to recent (2018) PHE surveillance data[30].

Figure 24: Non-susceptibility of *Pseudomonas aeruginosa* bacteraemia isolates in Scotland, 2015 to 2019 [R]



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

Incidence of *Acinetobacter* spp. bacteraemia

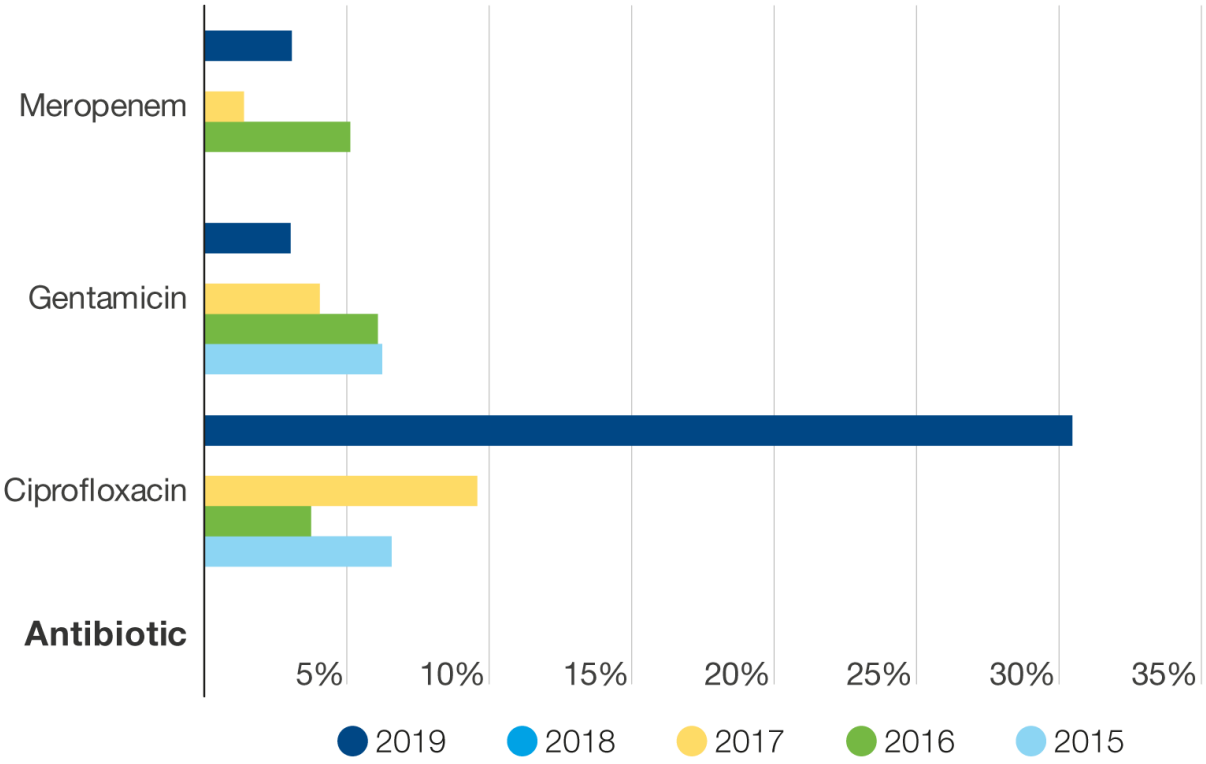
Acinetobacter spp. are opportunistic pathogens commonly associated with a variety of HCAI, particularly in intensive care units (ICUs) and immunocomprised patients with central-venous catheters. In addition to being intrinsically resistant to most antibiotics, *Acinetobacter* spp. are recognised for their ability to acquire resistance via chromosomal mutations and acquisition of plasmid-mediated resistance genes[32]. Similar to *P. aeruginosa*, infections associated with carbapenem and/or colistin resistant isolates, as well as MDR isolates are of particular concern due to very limited treatment options.

The incidence of *Acinetobacter* spp. bacteraemia over the last five years in Scotland has remained stable (**Figure 20**). In 2019, there were 79 cases of *Acinetobacter* spp. bacteraemia in Scotland which equates to an incidence of 1.4 per 100,000 population, compared to an incidence of 1.6 per 100,000 population for the same year, across England, Wales and Northern Ireland[33].

Non-susceptibility in *Acinetobacter* spp. blood isolates

In 2019, 30.5% of isolates were non-susceptible to ciprofloxacin, 3.1% to meropenem and 3.0% to gentamicin (**Figure 25**). In comparison to last year, non-susceptibility to ciprofloxacin appears elevated. Unfortunately, due to the small annual number of isolates reported, the statistical significance of this could not be determined. This increase is likely to have occurred as a result of the revised EUCAST breakpoints that were implemented for ciprofloxacin in 2019 (v9.0)[34] which saw the susceptible MIC breakpoint lowered from ≤1 mg/L to ≤ 0.06 mg/L and creation of an intermediate (I) category. At the time of writing, no comparable data was available for 2019 to assess the wider impact of the revised ciprofloxacin breakpoints. (Note: no non-susceptible isolates were reported in 2018.)

Figure 25: Non-susceptibility of *Acinetobacter* species bacteraemia isolates in Scotland, 2015 to 2019 [R]



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

AMR in Gram-negative Bacteria Key Points

- **Gram-negative bacteria are a common cause of serious infection in both healthcare and community settings**
- **AMR in Gram-negative bacteria significantly contributes to the overall burden of AMR**
- ***E. coli* is the most common cause of Gram-negative bacteraemia and contributes significantly to the burden of AMR**
- **Since 2018, non-susceptibility in ECB has remained stable with the exception of an increase in co-amoxiclav and a decrease in piperacillin with tazobactam**
- **CPO incidence has increased since 2015 ($p<0.001$)**

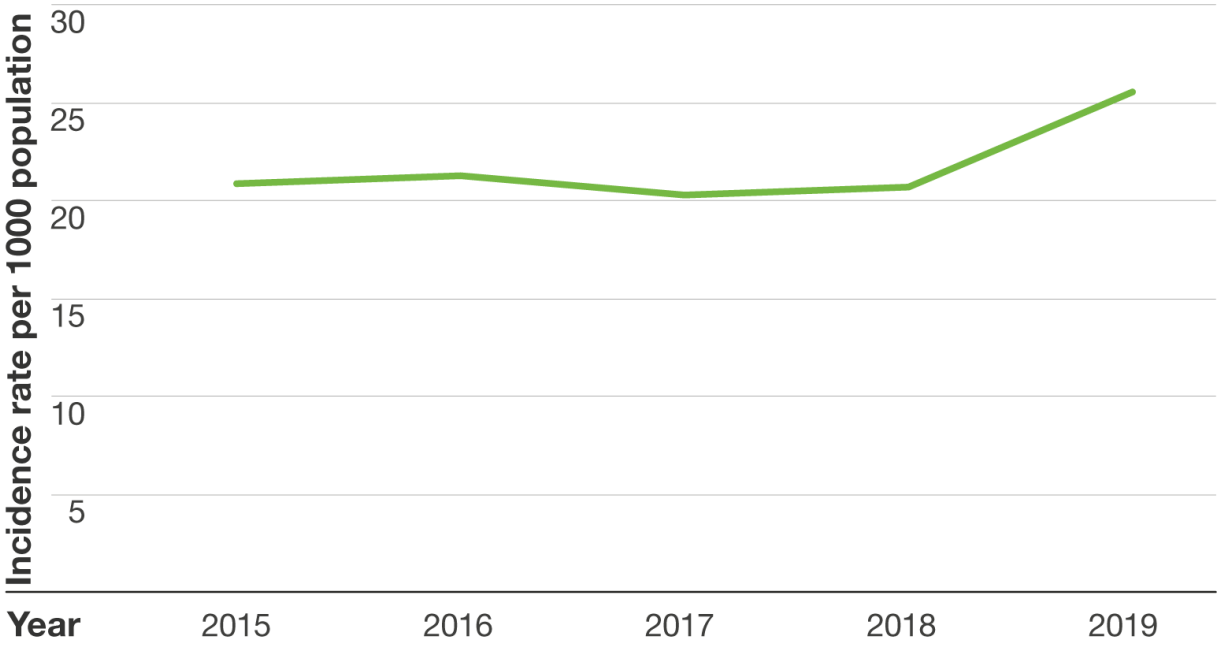
Urinary Tract Infections caused by *Escherichia coli*

Due to the high prevalence of urinary tract infections (UTI) in both community and healthcare settings, these constitute a significant public health priority. Frequent recurrence rates and increasing antibiotic resistance among urinary bacteria threaten to increase the burden of these infections. In turn, the development of resistance in urinary isolates can act as an early warning of resistance in bacteria causing more serious infections[35]. Increasing resistance necessitates judicious use of antibiotics. Knowledge of the common causative pathogens, including local susceptibility patterns, is essential in determining appropriate empiric therapy[36].

The majority of Gram-negative BSIs are considered to arise due to primary UTIs[37], therefore, to achieve significant reductions in morbidity and mortality caused by ECB in particular, interventions aimed at preventing UTI are necessary.

In 2019, there were 139,276 cases of *E. coli* from urine samples reported to the Electronic Communication of Surveillance in Scotland (ECOSS) system, equating to an incidence of 25.5 per 1,000 population (Figure 26). This is a significant increase ($p<0.001$) in incidence compared with 2018 and is largely attributed to the alignment of testing methods via the implementation of the Vitek-2 within a large NHS board in Scotland.

Figure 26: Incidence of *Escherichia coli* urinary isolates per 1,000 population in Scotland, 2015 to 2019 [R]



Note: per 1,000 population denominator due to large numbers

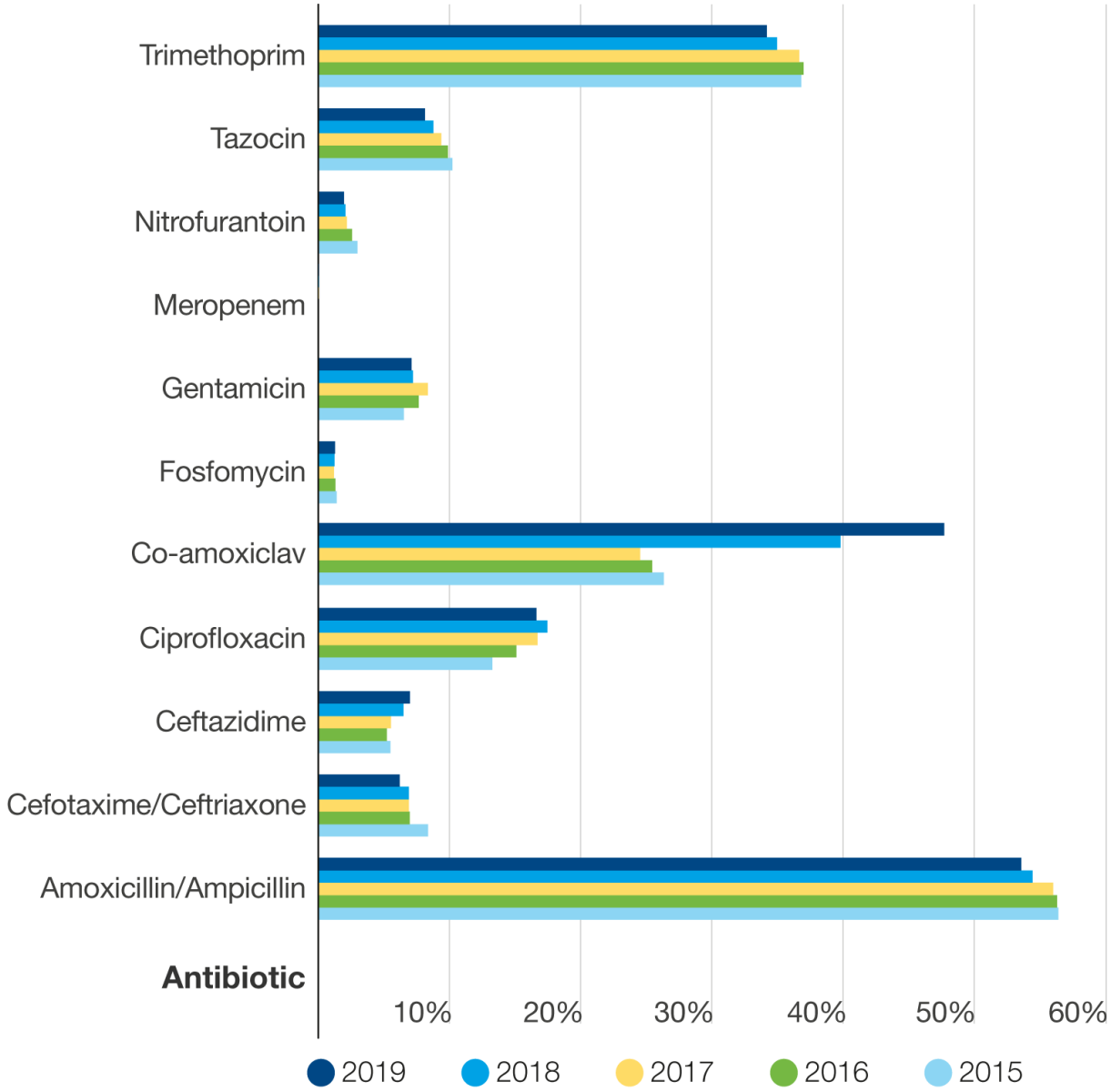
[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

Non-susceptibility in *Escherichia coli* urinary isolates

UTI caused by antibiotic resistant Gram-negative bacteria are a concern due to limited therapeutic options, particularly oral antibiotics available in the community setting. Gram-negative bacteria, specifically *Enterobacterales*, are common causes of both community and hospital acquired UTI. In particular, these micro-organisms can acquire genes that encode for multiple antibiotic resistance mechanisms, including extended spectrum beta-lactamases (ESBLs) and carbapenemases[36].

Since 2018 non-susceptibility in *E.coli* urinary isolates has remained stable or decreased across the majority of antibiotics with the exception of co-amoxiclav and ceftazidime which have increased. As per the E.coli BSIs, the increase in co-amoxiclav may, in part, be due to the change in Biomerieux® Vitek AST cards.

Figure 27: Non-susceptibility of *Escherichia coli* urinary isolates in Scotland, 2015 to 2019 [R]



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

AMR in Urinary Tract Infections Key Points

- **UTI are the most common infections diagnosed in community and healthcare settings**
- **AMR in urinary isolates significantly adds to the burden of AMR**
- ***E. coli* is the most common bacteria isolated from urine specimens**
- **Non-susceptibility to co-amoxiclav and ceftazidime has increased significantly within the last year**

Carbapenemase-producing organisms

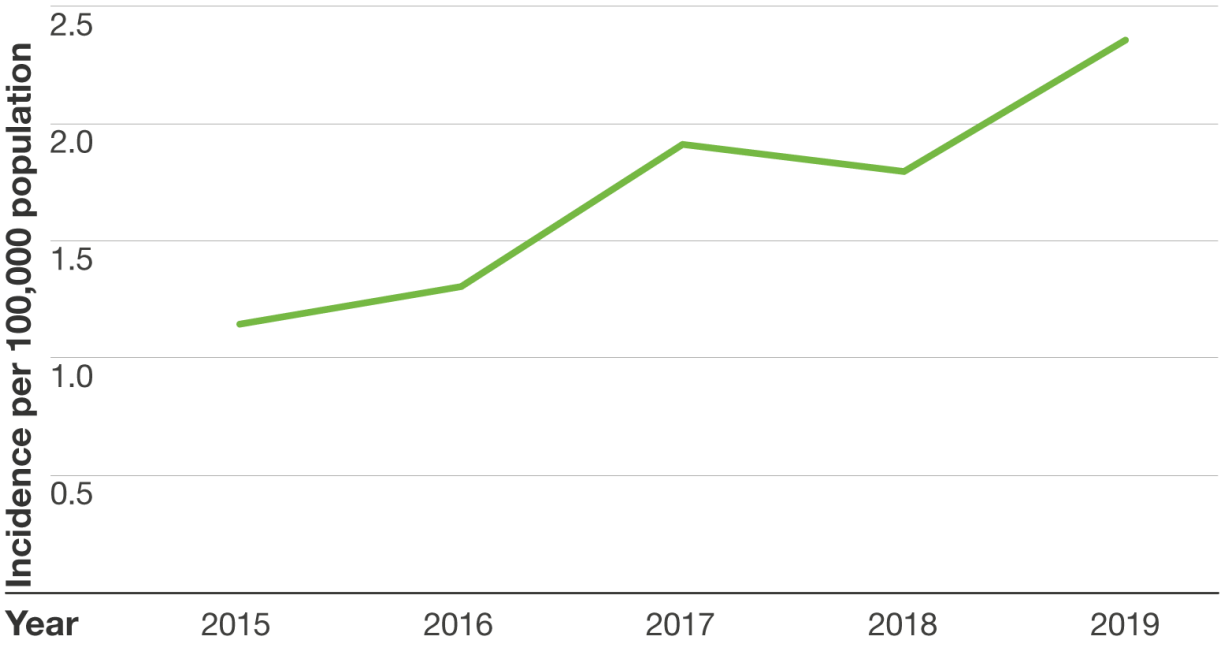
Carbapenems are potent β-lactam antibiotics with a broad spectrum of activity, often reserved as last-line agents for the treatment of bacterial infections[38]. Consequently, carbapenem resistance is of major and on-going public health concern, particularly in Gram-negative bacteria where the primary mechanism of resistance is the production of acquired carbapenemases, enzymes which inactivate carbapenem antibiotics[39]. Carbapenemase enzymes hydrolyse a broad variety of β-lactams, with few exceptions[19] and are often carried on mobile genetic elements allowing for horizontal transfer between strains, species and genera[39;40].

The Scottish Microbiology Reference Laboratory (SMiRL) currently performs confirmation of status by means of carbapenemase gene detection. The CPOs described in this report were isolated from both screening and clinical specimens including urine, respiratory and blood samples.

CPO incidence has increased significantly since 2015 ($p<0.001$) (Figure 28), although there was no significant difference between 2018 and 2019 ($p=0.043$). In 2019, 128 isolates were reported compared to 97 isolates in 2018. The majority of CPO identified were carbapenemase-producing *Enterobacterales* (CPE), (n=104, 81.3%), and the remaining were non-fermenters such as *Acinetobacter* spp. and *P. aeruginosa* (n=24, 18.8%). The most frequently identified enzyme gene was oxacillinase (OXA)-48 (n=54, 42.2%) followed by New Delhi Metallo-beta-lactamase (NDM) (n=28, 21.9%). Figure 29 shows the number of CPO isolates by enzyme type and supporting data by micro-organism can be found in Appendix.

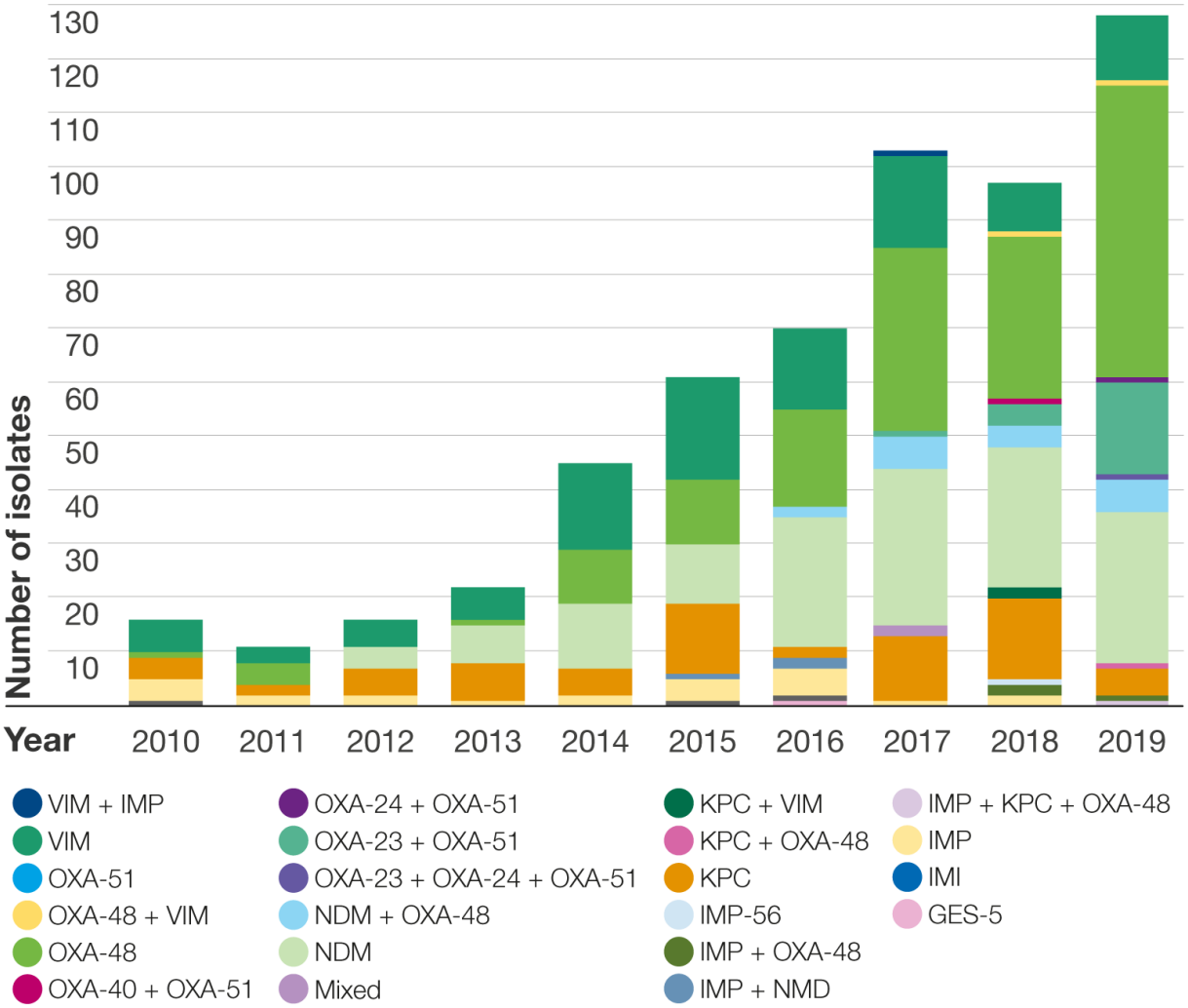
As per the UK's five-year national action plan[1], developments are currently underway to have CPOs added to the list of notifiable organisms.

Figure 28: Incidence of carbapenemase producing organisms (CPOs) per 100,000 population in Scotland, 2015 to 2019 [R]



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

Figure 29: Number of carbapenemase producing organism (CPO) isolates (first isolation from all body sites) reported in Scotland by AMRHAI (PHE) and the SMiRL, 2015 to 2019, by enzyme type and year [R]



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

> “Antimicrobial resistance continues to make the treatment of patients challenging. As this report shows there has been an increase in the number of very resistant CPO type organisms in Scotland. These difficult to treat pathogens have been steadily increasing over the years. Making these organisms notifiable, as part of a Public Health response to antimicrobial resistance, is fundamental in understanding how they spread, what treatments are best used for infected patients and how we can minimise the spread of these organisms.”
>
> **Professor Alistair Leanord**
> Director of Scottish Microbiology Reference Laboratories

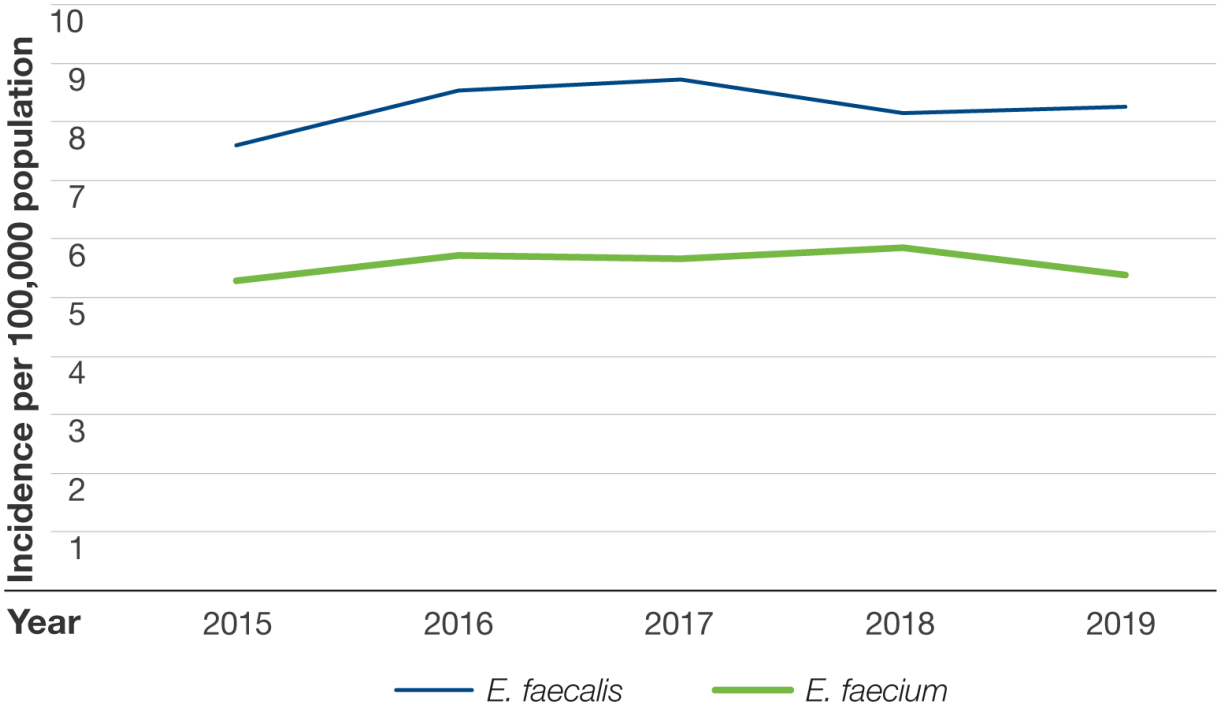
Antimicrobial resistance in *Enterococcus* species

As commensals of the gastrointestinal tract in both humans and animals, enterococci are opportunistic pathogens capable of causing a range of infections including urinary tract infections (UTIs), wound infections, bacteraemia and endocarditis[41]. In humans, the majority of infections are caused by *E. faecalis* and *E. faecium.* Enterococci are well established as a leading cause of HCAIs and their success is due, in part, to their intrinsic resistance and capacity to rapidly acquire and disseminate resistance genes coupled with their ability to survive in harsh environments[42;43].

Incidence of *Enterococcus faecalis* and *Enterococcus faecium* bacteraemia

In 2019, 451 cases of *E. faecalis and* 294 *cases of E. faecium* bacteraemia were reported. The incidence of *E. faecalis* bacteraemia (8.3 per 100,000 population) *and E. faecium* bacteraemia (5.4 per 100,000 population) has remained stable since 2015 (Figure 30). The incidence for *Enterococcus* spp bacteraemia in Scotland is 13.7 per 100,000 and is comparable to the most recent (2018) combined rate of 13.3 per 100,000 published by PHE for England, Wales and Northern Ireland[44].

Figure 30: Incidence of *Enterococcus faecalis* and *Enterococcus faecium* bacteraemia per 100,000 population in Scotland, 2015 to 2019, by organism and year [R]



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS) and National Records of Scotland (NRS)]

Non-susceptibility in *Enterococcus* spp. blood isolates

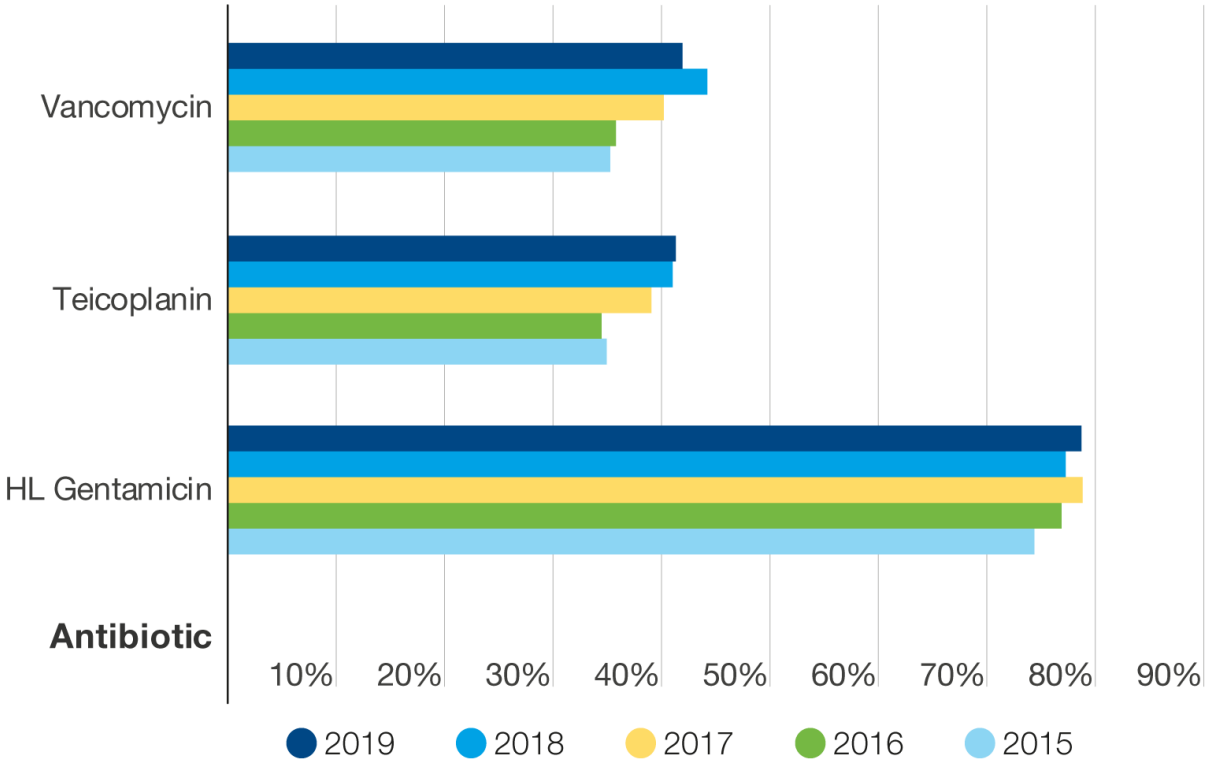
In 2019, vancomycin non-susceptibility in *E. faecium* blood isolates remained stable at 41.9%, whilst non-susceptibility in *E. faecalis* blood isolates remained low at 0.2% (Figure 31). Infections caused by vancomycin resistant enterococci (VRE) are associated with higher mortality rates compared with those cause by vancomycin sensitive enterococci (VSE)[41]. There are a number of factors known to increase the risk of infection with VRE including previous antibiotic therapy, previous/prolonged hospitalisation, medical devices and severe underlying illnesses or immunosuppression[41].

High-level gentamicin non-susceptibility data was collated for the first time for *E. faecalis* and *E. faecium* blood isolates. According to the latest surveillance data from 2019[45]; the United Kingdom has the highest (89.3%) reported high-level gentamicin non-susceptibility in *E. faecium* blood isolates in Europe with other countries reporting between 0.0% and 77.8%. Non-susceptibility to high-level gentamicin in Scotland has remained stable over the last five years and in 2019 was lower (78.7%) than the UK proportion. High-level gentamicin resistance has treatment implications as it eliminates the bacterial synergism that occurs when gentamicin is used in combination with penicillins or aminoglycosides. *E. faecalis* blood isolates conversely have shown a significant ($p<0.001$) decrease in high-level gentamicin non-

susceptibility from 42.4% in 2015 to 27.4% in 2019. The SONAAR programme will undertake further analysis and will work with stakeholders to identify appropriate public health actions.

Linezolid, is an oxazolidinone antibiotic used for the treatment of multi-drug resistant (MDR) Gram-positive infections, including VRE. Although resistance to linezolid has been reported[46] non-susceptibility in Scotland remains low with no *E. faecalis* and *E. faecium* blood isolates reported in 2019.

Figure 31: Non-susceptibility of *Enterococcus faecium* bacteraemia isolates in Scotland, 2015 to 2019 R



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

AMR in *Enterococcus* species Key Points

- ***Enterococcus* species have the ability to survive in harsh environments**
- **Incidence of *E. faecalis* and *E. faecium* bacteraemia has remained stable since 2015**
- **41.9% of *E. faecium* were non-susceptible to vancomycin**
- **78.7% of *E. faecium* isolates were non-susceptible to high-level gentamicin**
- **Further work is required to identify the appropriate public health actions**

"This year's report shows relative stability in resistance of many common Gram-negative infections. Whilst there is significant concern worldwide regarding MDR GNBs it is important to also consider resistant Gram-positive infections as glycopeptide and high level gentamicin resistance rates in *E. faecium* bacteraemias are of significant concern. These are exceptionally difficult to treat infections and further investigation is required to understand the high rates seen in Scotland compared to the rest of Europe."

Dr Mairi MacLeod
Consultant Microbiologist, Head of Service, Microbiology & Virology, NHS GGC

Exceptional resistance identified through the AMR Alerts Early Warning System (AMR-EWS) in 2019

National monitoring of exceptional phenotypes enables a timely scientific and public health response to potential emerging AMR issues. Detection of emerging AMR is critical to contain the development and spread of resistance at a national, regional and local level and allows ARHAI Scotland to gather intelligence relating to national trends and to communicate any identified issues with other public health bodies, as necessary.

In 2018, the SONAAR team at ARHAI Scotland introduced an electronic process to run a twice weekly interrogation of ECOSS to identify exceptional resistance phenotypes and contact the submitting laboratory requesting confirmation of reported resistance. All alerts are assessed by ARHAI Scotland and if of potential public health concern are drawn to the attention of the wider public health community for appropriate action.

The exceptional phenotypes monitored in the ARHAI Scotland AMR-EWS are also detailed in **Appendix 13** of the National Infection Prevention & Control Manual (NIPCM) as a mandatory alert micro-organism/condition list[47]. Local monitoring ensures that microbiology clinicians, infection prevention and control teams (IPCTs), health protection teams (HPTs) and

antimicrobial management teams (AMT), as appropriate, are aware of each identified case as per local protocols.

A short life working group comprising of representatives from the ARHAI Scotland SONAAR team and the SMVN-AMR diagnostic subgroup review the exceptional phenotype list on an annual basis.

2019 AMR-EWS alert results

The summary contained within the appendix is based on de-duplicated (one isolate per patient per micro-organism/resistance per year) AMR-EWS alert results for a time period spanning 1st January 2019- 31st December 2019.

The following caveats should be noted when interpreting the results:

The identification of an alert is dependent on laboratories actively performing antimicrobial susceptibility testing (AST) and submitting results to ECOSS. This may result in underreporting, or no reporting, of a particular micro-organism/antibiotic resistance combination if there is limited or no testing performed.

In addition, it is possible that in a small number of instances, not all data related to exceptional resistance is currently captured by ECOSS. A programme of work to enhance the data captured was implemented in 2019 by the Scottish Health Protection Network (SHPN) Public Health Microbiology Team and it is anticipated that this will improve the quality of the data captured by the system.

Approximately 20% of isolates identified via the AMR-EWS were communicated as having had occurred due to testing/reporting errors. The same error frequency was reported in 2018. Informing laboratories of these increases vigilance for errors and improves the information available at a local level. The remainder of isolates were confirmed as having the exceptional resistance phenotype (Appendix).

The annual number of isolates with reported exceptional resistance varies by micro-organism/antibiotic. Some micro-organisms, although still considered to be rare (prevalence typically ≤ 1%), are identified on a weekly basis i.e. ciprofloxacin resistant *Haemophilus influenzae*, azithromycin resistant *Neisseria gonorrhoeae* and carbapenem resistant Gram-negatives. Public health actions, by microbiology laboratories and others including local IPCT and HPT, are well established for these micro-organisms in particular.

The total number of isolates identified from the EWS has increased from 403 in 2018 to 604 in 2019. The majority of this increase is attributable to azithromycin resistant *N. gonorrhoeae.* This increase has been observed across the whole of the UK[48] and accordingly new treatment guidelines for gonorrhoea in the UK were published in January 2019 recommending

ceftriaxone monotherapy instead of ceftriaxone in combination with azithromycin. No isolates were resistant to ceftriaxone and there were no documented treatment failures in 2019[49].

Exceptional Phenotype Monitoring Key Points

- **Monitoring of exceptional resistance is critical for identifying emerging AMR threats**
- **National monitoring is essential for collating and developing epidemic intelligence**
- **Most common exceptional phenotypes identified were *Neisseria gonorrhoea* – azithromycin, *Haemophilus influenza* – ciprofloxacin, and *Klebsiella pneumoniae* – meropenem**
- **Monitoring emerging exceptional phenotypes enables the development of appropriate public health action**

Antimicrobial resistance in humans and animal: Salmonella in Scotland

Salmonella is a Gram-negative bacterium, ubiquitous in nature and a common cause of gastrointestinal illness in humans. It is the second most commonly reported cause of bacterial infectious intestinal disease in Scotland after *Campylobacter* spp[50]. *Salmonella* is usually a self-limiting infection and treatment with antibiotics is not routinely recommended. However, in some individuals, antimicrobial therapy may be required, particularly for severe or extra-intestinal infections.

Salmonella is a zoonosis - a wide range of domestic and wild animals can act as a reservoir, including cattle, sheep, pigs, poultry, reptiles and household pets. Infected animals are often asymptomatic. In recent years, fresh produce such as fruits and vegetables have been recognised as vehicles of transmission[51-53], where contamination can occur at multiple steps along the food chain. Feeder mice and reptiles have also been recognised as a source of *Salmonella* with related outbreaks[54].

Salmonella is notifiable in humans and a reportable animal pathogen in the UK. All medical diagnostic laboratories are required to forward suspect isolates from humans to the Scottish Microbiology Reference Laboratory (SMiRL) which is responsible for testing antimicrobial susceptibility in a range of organisms, including *Salmonella* and *Shigella* species. All veterinary diagnostic laboratories isolating *Salmonella* spp. from livestock species are required to send suspect isolates for confirmation and typing to the SMiRL. Human and animal *Salmonella* isolates were tested for susceptibility to 14 antibiotic agents of veterinary and human health significance. The availability of data from isolates from different source populations (humans and animals) processed in exactly the same way by the same laboratory offers an opportunity to monitor the trends in resistance whilst developing the inference to evaluate the epidemiological linkages at play.

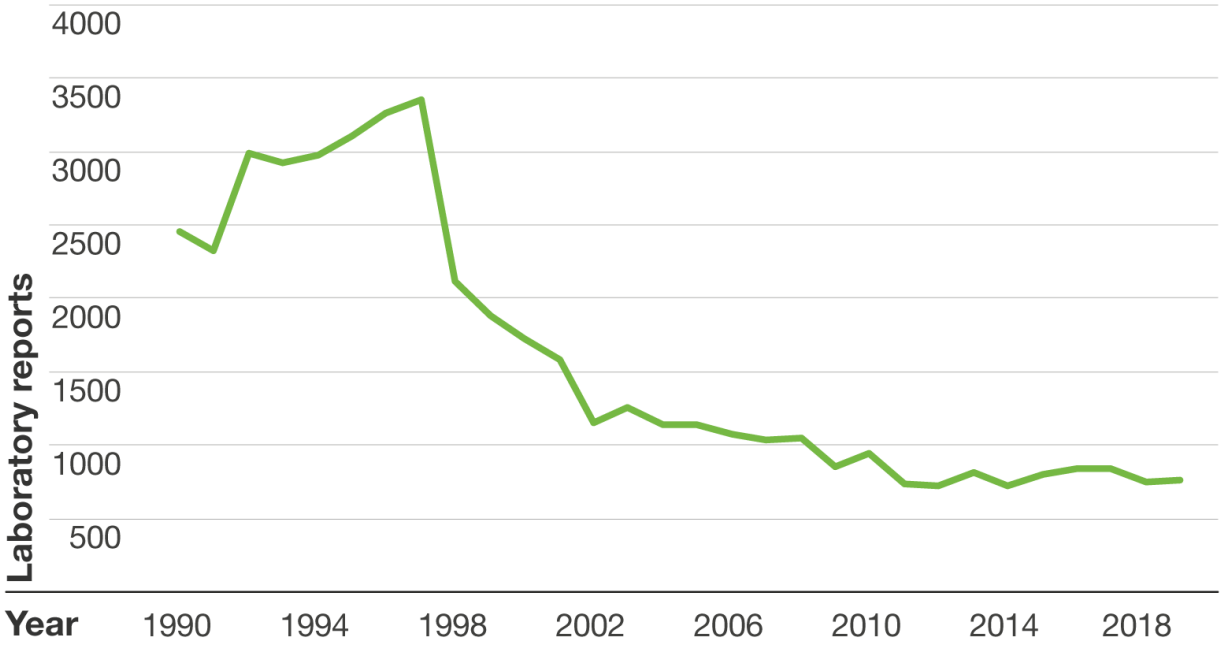
Human and animal non-typhoidal *Salmonella*

Human

In 2019, there were 757 laboratory reports of *Salmonella*, similar as that seen in 2018 (751 reports). The two most commonly reported serotypes were *Salmonella* Enteritidis and *Salmonella* Typhimurium which accounted for 58% of all *Salmonella* isolates reported in 2019. This figure is comparable with previous years; between 2014 and 2018, around 55% of reports were represented by these two serotypes.

In 2019, 35% of cases were thought to have acquired their infection abroad. This figure (Figure 32), however, is an underestimate as PHS does not receive travel histories for all cases.

Figure 32: Number of laboratory-confirmed human *Salmonella* reports in Scotland, 1990 to 2019

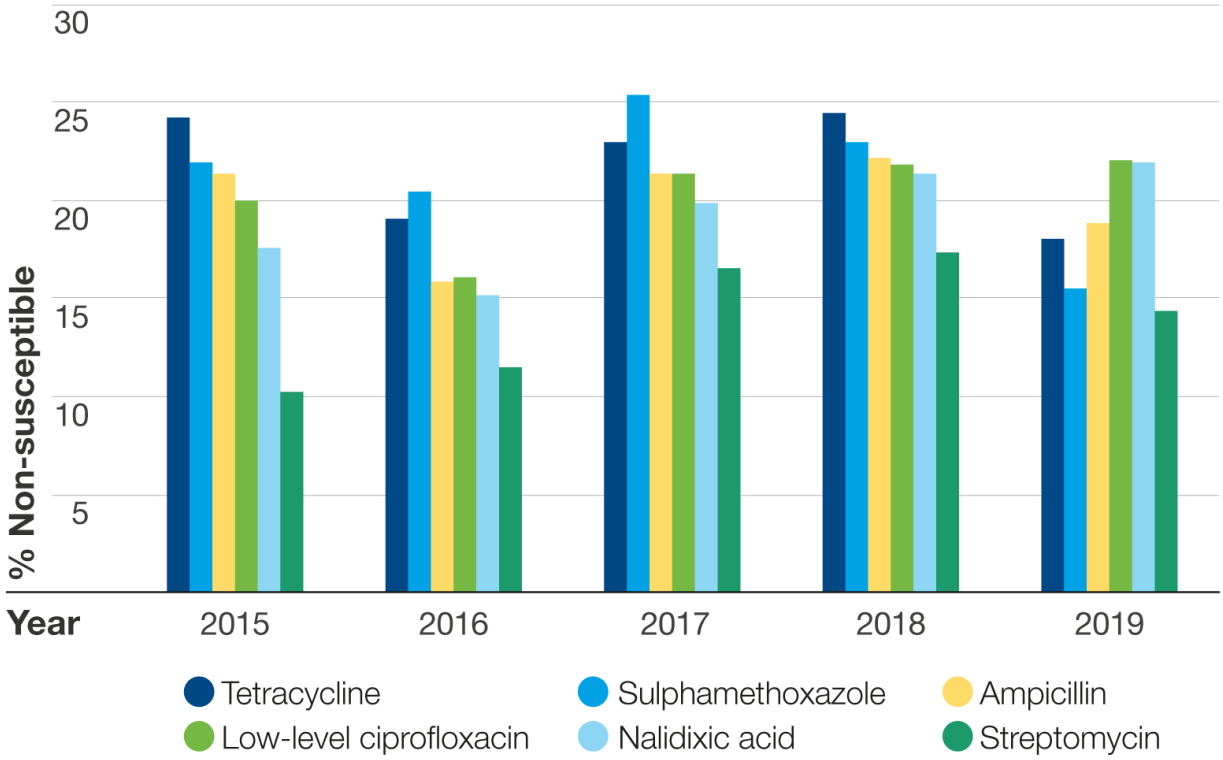


[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

Susceptibility of human non-typhoidal *Salmonella*

In 2019, 61.6% of human *Salmonella* isolates were fully susceptible to all antibiotics tested (see Appendix).

Figure 33: Non-susceptibility of human *Salmonella* isolates in Scotland, 2014 to 2019, by year



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

Interpretation of *Salmonella* resistance to individual antibiotics is complicated by the fact that in some subtypes there are well-recognised genetic elements encoding resistance to multiple agents. Thus, the occurrence of resistance to individual antibiotics is not always independent and the apparent prevalence of resistances to different agents can be strongly influenced by the abundance of *Salmonella* sub-types in the sample set for each reporting period.

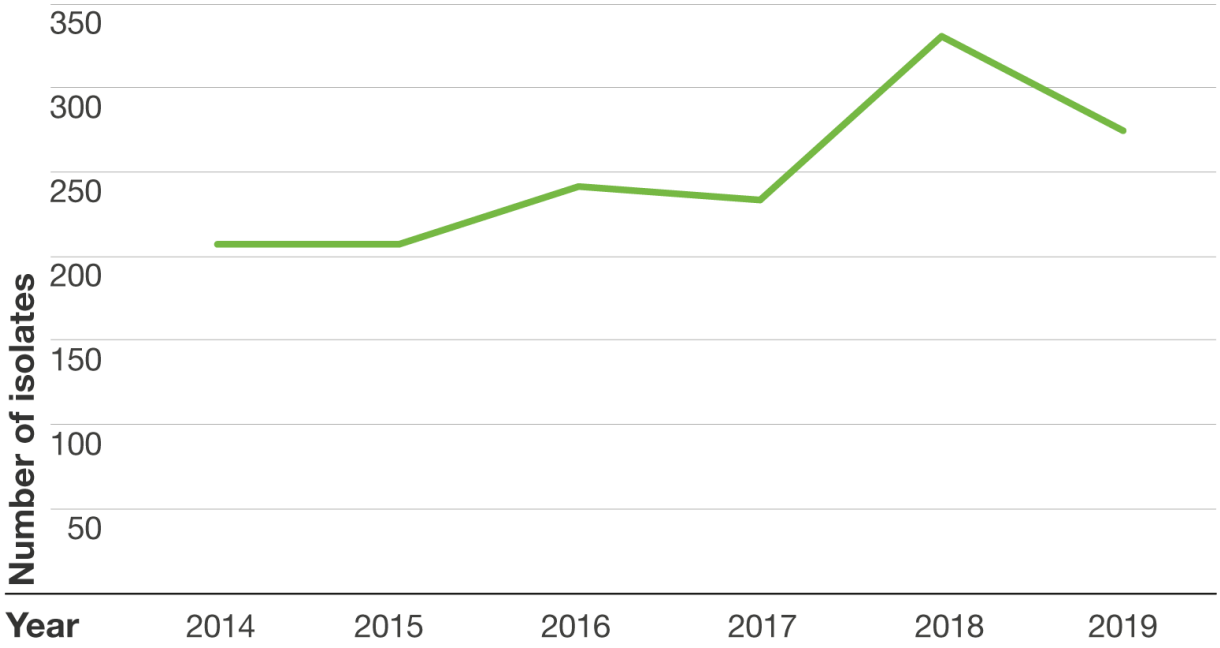
Animal

In Scotland, *Salmonella* is a reportable animal pathogen; all veterinary diagnostic laboratories isolating *Salmonella* spp. from livestock in Scotland are also required to forward suspect isolates for confirmation and typing to the SMiRL. No information on prior antibiotic treatment is available for *Salmonella* isolates identified from animal samples. *Salmonella* isolates were tested for susceptibility to the same 14 antibiotic agents of veterinary and human significance (see Appendix). The submission of samples is affected by the willingness of an animal keeper to pay the costs of laboratory testing to inform treatment, in addition to the clinical presentation in the affected animal(s). A number of *Salmonella* spp. are adapted to particular animal host species and are only found rarely in others. Generally, *Salmonella* infection in animals can

result in clinical syndromes suggestive of bacteraemia and systemic illness and, in these cases, antibiotic therapy would sometimes be part of the treatment regimen instituted by an attending veterinarian. Vaccines against some serotypes of *Salmonella* spp. are available for some animal species, and are used to a greater of lesser extent depending on a number of factors including assessed risk of infection in the particular group of animals.

Whilst the number of reports of *Salmonella* in animals has remained relatively stable, in recent years there have been somewhat greater fluctuations for which the reasons are not clear.

Figure 34: Number of laboratory confirmed *Salmonella* isolates from animals in Scotland, 2014 to 2019 by year



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

The majority of reports were from cattle (61%), pigs (15%) and sheep (14.5%). The remaining reports were from a variety of animals including dogs, birds and wild animals.

Susceptibility of animal non-typhoidal *Salmonella*

In 2019, 77.7% (n=213) of *Salmonella* reported from animals were fully susceptible to all antibiotics against which they were tested. This compares to 64.8% of isolates in 2018 and 72.1% of isolates in 2017.

Non-susceptibility was 13.9% for tetracycline, 16.1% for sulphamethoxazole, 19.3% for streptomycin and 16.1% for ampicillin (see Appendix).

Antimicrobial Resistance Determination in the Genomic Era

Until the end of January 2020, antimicrobial susceptibility in Salmonella was carried out at SMiRL using an in-house agar plate breakpoint method providing AMR phenotype data for the defined set of 14 antimicrobials for surveillance purposes.

Following a review of published reports[55;56] and an extensive in-house evaluation by SMiRL involving over 1000 previously phenotyped isolates which confirmed the high degree of correlation observed between the two approaches, SMiRL began using *in silico* prediction of AMR phenotype from whole genome sequencing. The predictive tools in use allow the identification of many thousands of individual AMR genes. This allows the differentiation, for example, of ampicillin resistance encoded by the TEM-1 (a broad spectrum β-lactamase) gene from that encoded by CARB-2. It has also allowed discrimination of the many different ESBL genes encountered, as well as the accurate identification of carabapenemase genes. SMiRL abilities have been further enhanced in that it is now possible to identify genes which were not accessible to the phenotypic methods previously in use (colistin resistance genes, transferrable quinolone resistance genes and macrolide resistance genes). New mechanisms identified by other laboratories can quickly be identified by searching within our existing sequence dataset without the need to repeat the wet laboratory processes.

The power of using WGS for detailed molecular epidemiology is now being further enhanced by using a genotypic approach for AMR surveillance. Increased knowledge on the prevalence of individual AMR genes in human, veterinary and environmental sources will be important in the evaluation of the impact of resistance on “One Health”.

Antimicrobial resistance in animals

Antimicrobial resistance in veterinary clinical isolates

This is the fourth year that data on resistance in veterinary clinical isolates from Scotland have been reported in the SONAAR report. Knowledge on AMR in bacterial isolates from animals with disease is necessary to understand more fully the epidemiology of AMR in a 'One Health' context.

These data derive from clinical specimens submitted to the farm and companion animal diagnostic services offered by Scotland's Rural College (SRUC) Veterinary Services and Capital Diagnostics.

The data from veterinary clinical isolates are subject to a number of important biases. Unlike the clinical samples in humans in Scotland, the samples are tested on a 'charged for' basis to inform private veterinary treatment of diseased animals. There is a cost to the animal keeper that affects the submission of samples to these services. In addition, the primary purpose of screening for AMR is to inform veterinary treatment and they are tested against a panel of antimicrobials relevant for that purpose at, where they exist, species-relevant clinical breakpoints.

Interpretation of these data in terms of their relevance to public health is challenging beyond the notion of evidence of impact of a selection pressure being applied in another compartment of the ecosystem that humans share closely with animals. The micro-organisms included are selected based both on their prevalence among all submissions, i.e. their importance as causes of animal morbidity, as well as, in some cases, their similarity to micro-organisms that cause morbidity in humans.

AMR in farm and companion animals (Scotland's Rural College)

In 2019, antimicrobial sensitivity testing was undertaken on bacterial isolates from veterinary clinical samples:

Staphylococcus spp.

Staphylococcus spp. are common commensal organisms that can act as important opportunist pathogens of humans and other animals. *Staphylococcus pseudintermedius* infections of humans have been recognised more frequently in the recent few years, in large part due to methodology changes in NHS microbiology laboratories. In most cases, these human infections will have been transmitted from a pet, most likely a dog[57], whereas the reverse is likely to apply for *S. aureus*, with canine and also some feline infections being acquired from their owners or other human contacts.[58]

The sensitivity patterns for selected *Staphylococcus* spp. for 2013 to 2019 are shown in the Appendix. Non-susceptibility for *S. aureus* and *S. pseudintermedius* isolates from companion animals, for several antibiotics, has fallen; however, relatively high levels of non-susceptibility

to penicillins and the topical agent fusidic acid are a concern for animal treatment. Fusidic acid is a recommended and commonly used antibiotic for the management of *S. pseudintermedius*-associated otitis externa. For *Staphylococcus* spp. from livestock, non-susceptibility was generally unchanged in 2019 and remained low for the majority of antimicrobials.

Meticillin-resistant *Staphylococcus* sp.

For coagulase positive staphylococci isolates from companion animals, meticillin resistance was identified in 9/132 *S. pseudintermedius* tested from dogs and 1/3 *S. aureus* tested from cats; meticillin resistance was not detected in *S. aureus* from four dogs or three horses; nor from 17 *S. schleiferi* subsp. *coagulans* recovered from dogs or a single *S. pseudintermedius* from a cat. Levels of meticillin-resistance are broadly similar to those for 2018.

In 2019, meticillin resistance was not detected in *S. aureus* from livestock (39 cattle, 10 sheep, two pigs and two goats). In the four years that SRUC data have been reported, an MRSA recovered from a pheasant in 2017 remains the only meticillin resistant strain of *S. aureus* recovered from farmed animals.

Streptococcus spp.

Streptococcus spp. can be important pathogens or opportunist colonisers of livestock and companion animal species, with the potential to cause severe disease of the skin, ear, respiratory tract, body cavities, wounds and urinary tract. Some species, including *S. agalactiae*, *S. dysgalactiae*, *S. suis*, *S. equi* subsp. *zooepidemicus* and *S. canis* are also recognised in human infections. The non-susceptibility patterns for selected *Streptococcus* spp. for 2014 to 2019 are shown in the Appendix.

Pasteurellaceae

Pasteurellaceae are important causes of potentially severe respiratory and soft tissue infections in companion and livestock animals. In livestock animals, high levels of morbidity and mortality can result with consequential significant economic losses. Important bacterial species included in this report are *Pasteurella multocida* (companion animals, cattle, pigs and sheep), *Mannheimia haemolytica* (cattle and sheep), *Bibersteinia trehalosi* (cattle and sheep) and *Actinobacillus pleuropneumoniae* (pigs). Of these, *P. multocida* can cause severe disease in humans.

The non-susceptibility patterns for the selected *Pasteurellaceae* for 2019 from companion and livestock animals are shown in the Appendix.

Escherichia coli

Escherichia coli are a major constituent of the normal faecal flora of humans and warm-blooded animals. However, some strains can cause intestinal and extraintestinal disease. The

non-susceptibility patterns for the selected *E. coli* for 2014 to 2019 from companion and livestock animals are shown in the Appendix.

Klebsiella pneumoniae

Klebsiella pneumoniae is a cause of significant economic loss to the livestock industry and is potentially zoonotic. The non-susceptibility patterns for *K. pneumoniae* for 2014 to 2019 are shown in the Appendix. Spectinomycin remains the recommended treatment for *K. pneumoniae* in animals.

Extended-spectrum beta-lactamase producing *Enterobacterales*

Extended spectrum beta-lactamases were identified in *Enterobacterales* from four diagnostic isolates in 2019: *E. coli* from a bovine lung sample, *Proteus mirabilis* from a canine urine specimen and *K. pneumoniae* from a cow's milk and from a tortoise. The latter was further identified as *bla*$_{\text{CTX-M-15}}$ harbouring *K. pneumoniae* ST307, an emerging MDR clone in humans globally, and represented the first report of this organism from an animal in Europe (Foster et al., 2020).

Carbapenemases were not detected from any animal isolates.

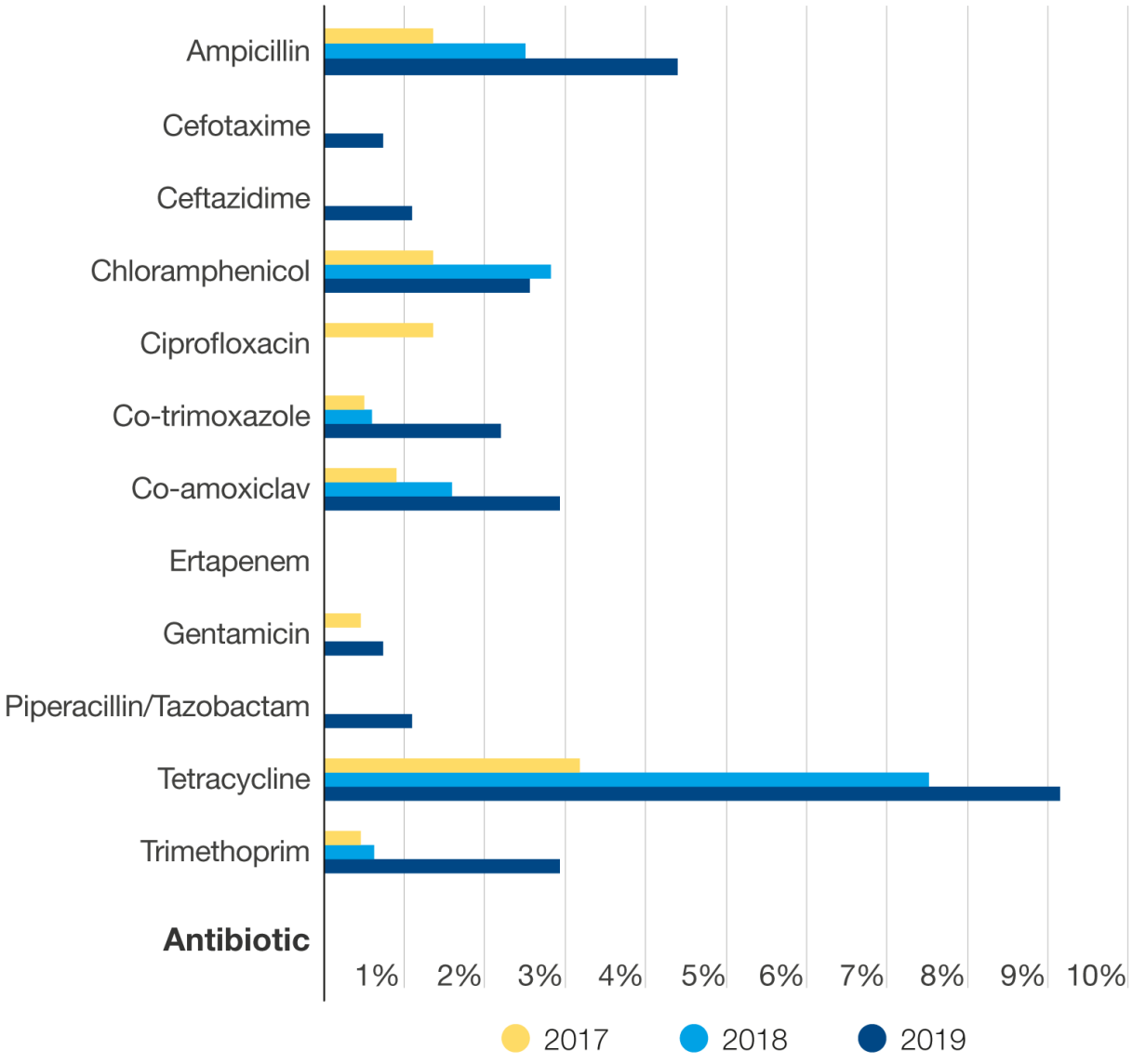
Corynebacterium spp.

Corynebacterium spp. are associated with serious soft tissue infections and otitis externa in the dog (*Corynebacterium auriscanis*), but invasive corynebacteriosis in companion animals remains rare. *Corynebacterium* spp. are also associated with soft tissue infections in livestock. The non-susceptibility patterns for *Corynebacterium* spp. for 2014 to 2019 are shown in the Appendix.

Antimicrobial resistance in *E. coli* from healthy animals

In addition to diagnostic isolates, *E. coli* collected from enteric samples of healthy animals are tested as a measure of the background resistance in livestock entering the food chain. Since 2017, an ongoing project monitors the prevalence of resistance in *E. coli* cultured from cattle, sheep, pigs and poultry presenting at abattoirs in Scotland for slaughter for human consumption. The antimicrobials that the *E. coli* isolates from healthy animals were tested against were selected specifically for their relevance for human treatment, rather than veterinary practice. Results for each of the three years for each livestock host are presented in Figure 35-Figure 38.

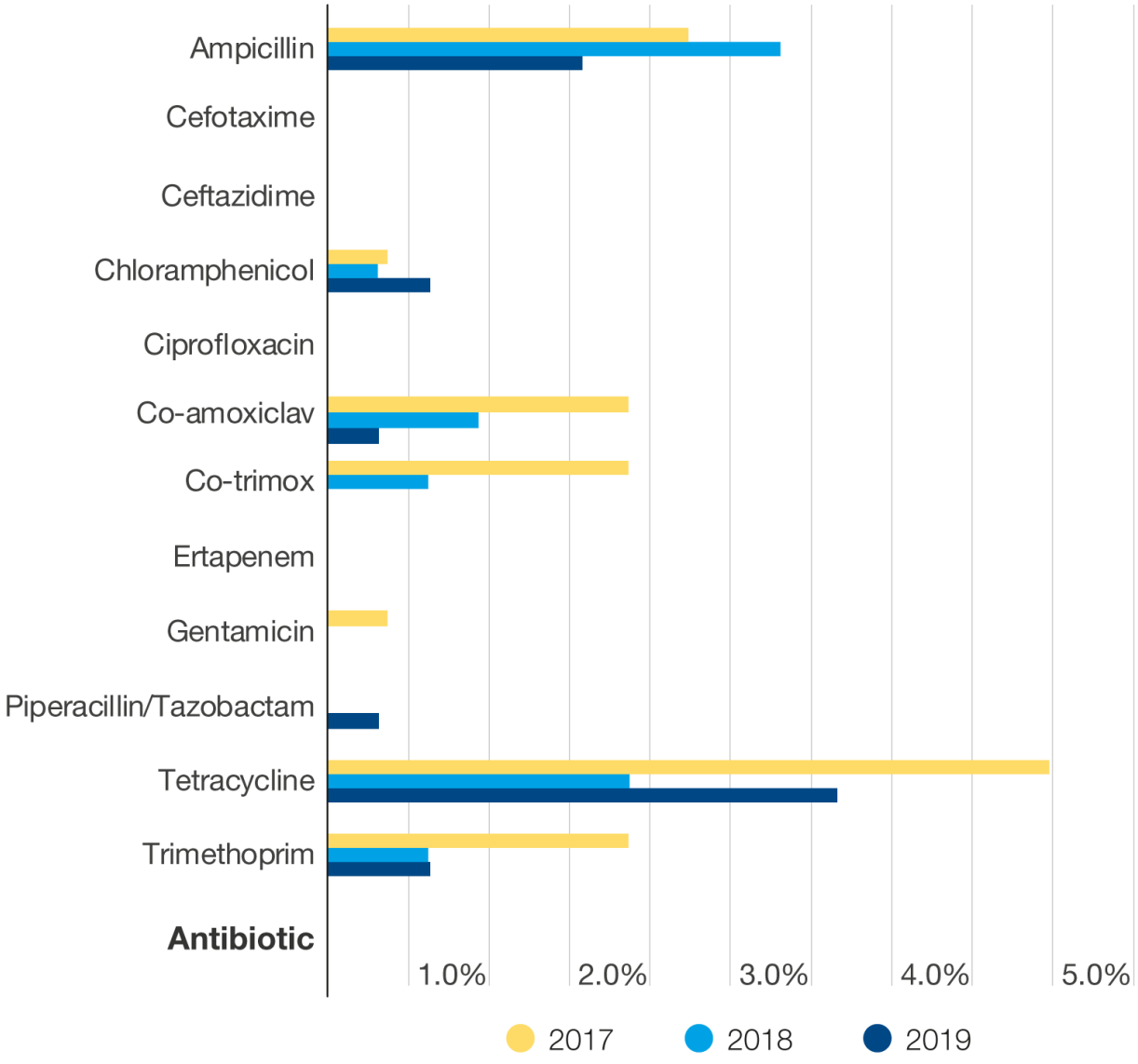
Figure 35: Percentage of *Escherichia coli* isolates that were non-susceptible to selected antimicrobials in healthy cattle in Scotland, SRUC, from 2017 to 2019, by antimicrobial



Footnote: The microbiological thresholds at which resistance is considered to be present changed for antimicrobials ampicillin, co-trimoxazole, tetracycline and trimethoprim for the data from 2019, so care is needed in interpreting changes in percentage of isolates not susceptible to these from 2018 to 2019.

[Source: Scottish Rural Collage (SRUC)]

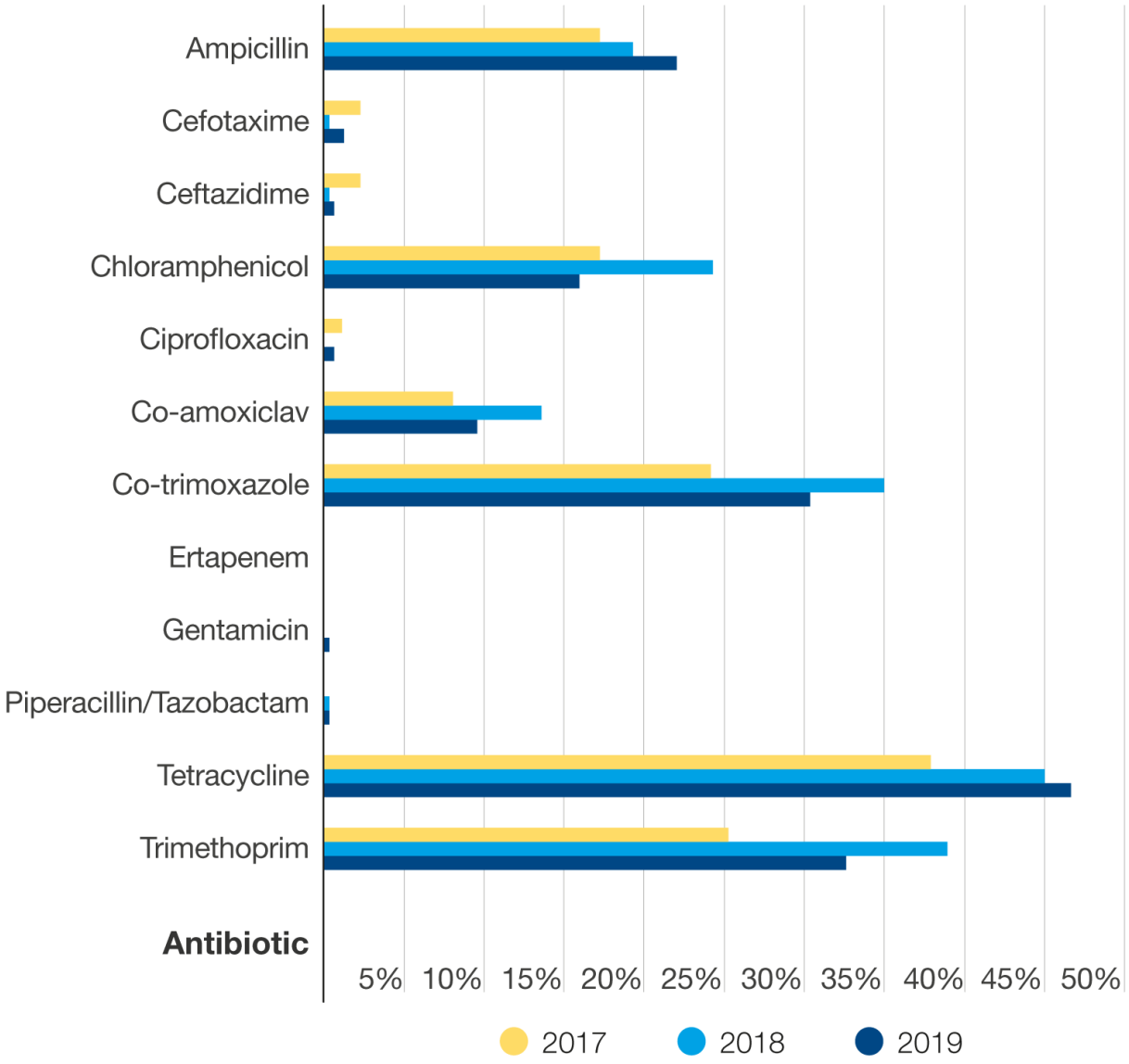
Figure 36: Percentage of *Escherichia coli* isolates that were non-susceptible to selected antimicrobials in healthy sheep in Scotland, SRUC, from 2017 to 2019, by antimicrobial



Footnote: The microbiological thresholds at which resistance is considered to be present changed for antimicrobials ampicillin, co-trimoxazole, tetracycline and trimethoprim for the data from 2019, so care is needed in interpreting changes in percentage of isolates not susceptible to these from 2018 to 2019.

[Source: Scottish Rural Collage (SRUC)]

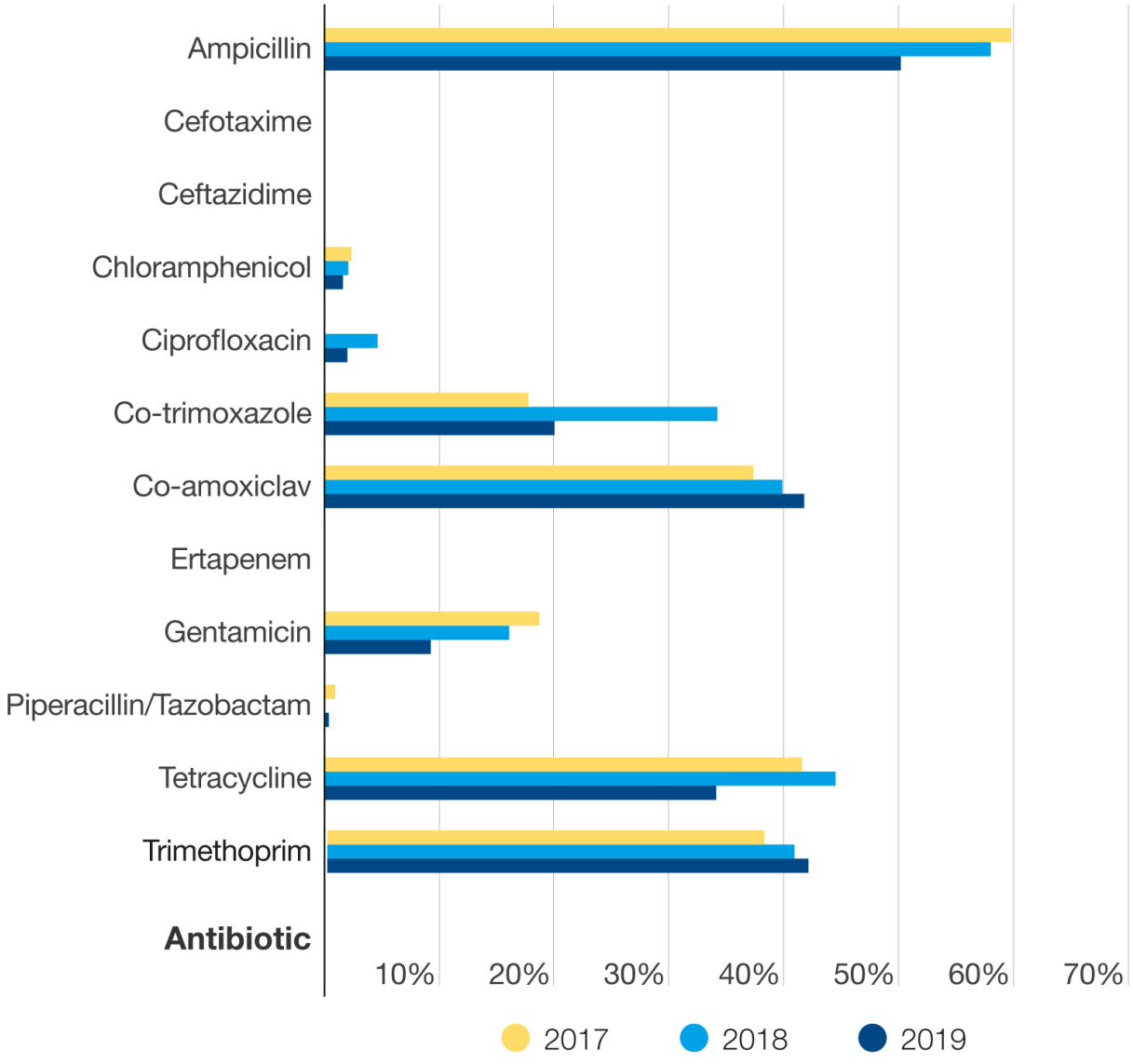
Figure 37: Percentage of *Escherichia coli* isolates that were non-susceptible to selected antimicrobials in healthy pigs in Scotland, SRUC, from 2017 to 2019, by antimicrobial



Footnote: The microbiological thresholds at which resistance is considered to be present changed for antimicrobials ampicillin, co-trimoxazole, tetracycline and trimethoprim for the data from 2019, so care is needed in interpreting changes in percentage of isolates not susceptible to these from 2018 to 2019.

[Source: Scottish Rural Collage (SRUC)]

Figure 38: Percentage of *Escherichia coli* isolates that were non-susceptible to selected antimicrobials in healthy poultry in Scotland, SRUC, from 2017 to 2019, by antimicrobial



Footnote: The microbiological thresholds at which resistance is considered to be present changed for antimicrobials ampicillin, co-trimoxazole, tetracycline and trimethoprim for the data from 2019, so care is needed in interpreting changes in percentage of isolates not susceptible to these from 2018 to 2019.

[Source: Scottish Rural Collage (SRUC)]

Continued monitoring is important for comparison over several years. In 2019 as was reported in 2018, proportions of non-susceptibility in isolates from pigs and poultry sampled were greater than in those from cattle and sheep, for which numbers of non-susceptible isolates were either absent or very low (see Appendix). Amongst high priority critically important antimicrobials, non-susceptibility was not detected to ertapenem, and to third generation

cephalosporins remained low and was only detected from cattle and poultry. Ciprofloxacin non-susceptibility was detected from five porcine and two poultry samples. As in the two previous years, there was again a notable proportion of isolates from poultry non-susceptible to gentamicin and isolates from pigs non-susceptible to chloramphenicol[57;58].

Animal AMR Key Points

- **AMR is a feature of bacterial pathogens affecting all domestic animal species**
- **Non-susceptibility for veterinary clinical isolates is relatively stable over 5 years**
- **AST to support veterinary treatment comes primarily from private laboratories but is not currently part of a formal surveillance system**
- **Monitoring of AMR in animals is a vital component of understanding and mitigation of AMR across the entire ecosystem**
- **Responsible Use of Medicines in Agriculture Alliance (RUMA) Targets Task Force Report of 2019 and Veterinary Antimicrobial Resistance and Sales Surveillance Report of 2019 demonstrate serious commitment to antimicrobial stewardship in UK livestock**

"The inclusion of veterinary data in the SONAAR report for the third successive year is a valuable contribution to the ongoing challenge of AMR. This One Health approach is an essential component in enhancing the growing interactions between medical and veterinary professionals for the benefit of public and animal health.

Antimicrobial resistance rates in diagnostic samples from livestock and companion animals have remained relatively stable over the four years that animal data have been included in the SONAAR report. Sampling of healthy livestock shows minor fluctuations over its three-year lifespan."

Dr Geoff Foster
Microbiologist, SRUC Veterinary Services

Minimising the spread of AMR through the environment

Minimising the spread of AMR through the environment remains a UK priority and the UK's five-year NAP[1] sets out the ambitions in this area.

The role of the environment as a transmission route for many bacterial pathogens has long been recognised, often associated with insufficient sewage infrastructure, faecal contamination of water or organic fertilisers). More recently, the understanding has developed that many of the resistance genes that we find in pathogens today originate from bacteria normally thriving in the environment. Hence, the environment acts as a dispersal route and reservoir of resistant pathogens, and also as an arena for the evolution of resistance[59-61].

The NAP states that there should be increased activity to identify and assess sources, pathways and exposure risks including their interdependencies that create the opportunity to impact on the presence and persistence of AMR in the environment. The action plan also advocates the evaluation of existing regulations to evaluate whether they can be applied, and if not amended, to encompass monitoring of AMR in the environment. Engagement at a global level also remains a key priority.

ARHAI Scotland has engaged with environmental and veterinary agencies and academia to scope out collaborative areas of work. Initial work with the Scottish Environmental Protection Agency (SEPA), SRUC and Napier University has centred around *E. coli* cefotaxime resistance in human bacteraemia isolates, healthy animal isolates and bathing water isolates. Cefotaxime was chosen as it is widely used to treat human infection and is currently routinely tested against human, healthy animal and bathing water isolates. Whilst caution should be exercised when drawing conclusions from these baseline data, it is worth noting that in 2018, the proportion of *E. coli* resistant to cefotaxime in human bacteraemia was 8.0% while it was markedly lower in bathing water and healthy animal isolates (1.5% and 0.4%, respectively). In 2019 an increase in the proportion of *E. coli* resistant to cefotaxime was observed in samples from all three areas (human 8.8%, bathing water 1.8% and healthy animal 0.6%).

ARHAI Scotland will continue to work closely with SEPA to monitor the increasing trend in AMR in *E. coli* bathing water isolates.

List of Abbreviations and Acronyms

AMEG	Antimicrobial Advice Ad Hoc Expert Group
AMR	Antimicrobial Resistance
AMR-EWS	Antimicrobial Resistance Early Warning System
AMRHAI	Antimicrobial Resistance and Healthcare Associated Infections
AMT	Antimicrobial Management Teams
AMU	Antimicrobial Use
ARHAI Scotland	Antimicrobial Resistance and Healthcare Associated Infection Scotland
ASP	Antimicrobial Stewardship Programme
AST	Antimicrobial Susceptibility Testing
BASHH	British Association for Sexual Health and HIV
BMD	Broth Microdilution
BSAC	British Society for Antimicrobial Chemotherapy
BSI	Bloodstream Infection
CLSI	Clinical and Laboratory Standards Institute
CPE	Carbapenemase-producing Enterobacterales
CPO	Carbapenemase-producing Organism
DDDs	Defined Daily Doses
ECB	*Escherichia coli* bacteraemia
ECDC	European Centre for Disease Prevention and Control
ECOSS	Electronic Communication of Surveillance in Scotland
EEA	European Economic Area
EMA	European Medicines Agency
ESBL	Extended spectrum beta-lactamases
EWS	Early Warning System
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FSS	Food Standards Scotland
GASS	Gonococcal Antibiotic Surveillance in Scotland
GNB	Gram-negative bacilli
GP	General Practitioner
HCAI	Healthcare Associated Infection
HL-AziR	High level azithromycin resistance
HP-CIA	High Priority Critically Important Antibiotics
HPS	Health Protection Scotland
HPT	Health Protection Team
IPCT	Infection Prevention and Control Team
IQR	Interquartile range
ISD	Information Services Division
IV	Intravenous
MDR	Multi-Drug Resistant
MRSA	Meticillin Resistant *Staphylococcus aureus*
NAP	National Action Plan
NDM	New Delhi Metallo-beta-lactamases
NHS	National Health Service
NICE	National Institute for Health and Care Excellence

NIPCM	National Infection Prevention Control Manual
NRS	National Records of Scotland
OBD	Occupied Bed Days
OXA	Oxacillinase
PCR	Polymerase Chain Reaction
PHE	Public Health England
RUMA	Responsible Use of Medicines in Agriculture Alliance
SAC	Scottish Agricultural College
SAPG	Scottish Antimicrobial Prescribing Group
SARIS	Surveillance of Antimicrobial Resistance in Scotland
SAVSNET	Small Animal Veterinary Surveillance Network
SBSTIRL	Scottish Bacterial Sexually Transmitted Infections Reference Laboratory
SCIEH	Scottish Centre for Infection and Environmental Health
SEAG	Scottish Environmental AMR Group
SEPA	Scottish Environmental Protection Agency
SHPN	Scottish Health Protection Network
SMA	Scottish Microbiology Association
SMVN	Scottish Microbiology and Virology Network
SOHNAAP	Scottish One Health AMR Action Plan
SONAAR	Scottish One Health Antimicrobial Use and Antimicrobial Resistance
SRUC	Scotland's Rural College
SSSCDRL	Scottish *Salmonella*, *Shigella* and *Clostridium difficile* Reference Laboratory
STI	Sexually Transmitted Infection
SUTIN	Scottish UTI Network
ICU	Intensive Care Unit
UK	United Kingdom
UN	United Nations
UTI	Urinary Tract Infections
VARSS	Veterinary Antimicrobial Resistance and Sales Surveillance
VRE	Vancomycin-resistant enterococci
WGS	Whole Genome Sequencing
WHO	World Health Organisation
XDR	Extensively Drug Resistant

List of Tables

List of Figures

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- Scottish Microbiology and Virology Network (SMVN)
- Scottish Environment Protection Agency (SEPA)
- Scotland's Rural College (SRUC) which includes Scottish Agricultural College (SAC) Veterinary Services and Capital Diagnostics in Scotland
- Scottish Animal Health and Antimicrobial Resistance (SAHAMR)
- Scottish Veterinary Antimicrobial Stewardship (SVAS) Groups
- Small Animal Veterinary Surveillance Network (SAVSNET)
- Scottish Environmental AMR Group (SEAG)
- Food Standards Scotland

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Appendices

Appendix 1 – Background information

Revisions to the surveillance

Description of Revision	First report revision applied	Report section(s) revision applies to	Rational for revision
Implementation of new Biomerieux® Vitek AST cards within laboratories	2020	Human AMR	Implementation of new Biomerieux® Vitek AST cards in late 2018 that test amoxicillin in combination with a fixed clavulanic acid concentration of 2 mg/L as per EUCAST recommendations. Roll out across boards was variable due to labs depleting existing stock of older cards. This change was associated with an increase in co-amoxiclav non-susceptibility in 2019
Changes in healthy animal breakpoints	2020	AMR in animals	Changes in health animal breakpoints for ampicillin, co-trimoxazole, tetracycline and trimethoprim. These have not been retrospectively applied to historical data therefore care is needed in interpretating changes between 2018 and 2019.
Implementation of v_9.0 EUCAST breakpoints	2020	Human AMR	Reduction in ciprofloxacin MIC for *Acinetobacter* species from from ≤1 mg/L to ≤ 0.06 mg/L and creation of an intermediate (I) category. Scottish Vitek AST cards only read MIC as low as 0.25 calling range. Introduction of Areas of Technical Uncertainity (ATU) for Enterobacterales against piperacillin-tazobactam and ciprofloxacin. Although in the intermediate (I) catergory, results for these antibiotics may be downgraded to resistant (R) as per EUCAST guidance.
Temocillin breakpoints (Enterobacterales)	2020	Human AMR	No EUCAST breakpoint available. Initially all Viteks used BSAC legacy UTI breakpoint of 16. GGC moved to systemic breakpoint of 8 in ~2015. Other boards moved variably up until end 2017. Glasgow and some others retained an I category(MIC 16) up until Oct 2019 when all moved to S<8 and R>8.

Appendix 2 – Metadata

Metadata Indicator	Description
Publication title:	Scottish One Health Antimicrobial Use and Antimicrobial Resistance report, 2019 (SONAAR report, 2019)
Description:	This annual report provides data relating to antimicrobial use and antimicrobial resistance in Scotland during 2019.
Theme:	Health and Care (ARHAI SCOTLAND, NHS National Services Scotland and Public Health Scotland)
Topic:	Antimicrobial use and resistance in humans and animals.
Format:	Online resource (PDF)
Data source(s):	**Antibiotic Use in Humans** **Antibiotic use in primary care**: Prescribing Information System (PIS), ISD **Population denominator data**: Mid-year population projections for Scotland: National Records of Scotland (NRS) population estimates **Antibiotic use in secondary care**: Hospital Medicines Utilisation Database (HMUD), ISD. **Healthcare associated denominator -Total occupied bed days, Sum of OBDs for all hospitals in numerator**: Data Source: Information Services Division ISD(S)1. **Antibiotic Use in Animals** **Antibiotic use in companion animals**: Small Animal Veterinary Surveillance Network (SAVSNET). **Human Antimicrobial Resistance**

	Bacteraemia: ECOSS (Electronic Communication of Surveillance in Scotland). **Urinary tract infection:** ECOSS (Electronic Communication of Surveillance in Scotland). **Carbapenemase Producing Organisms (CPOs):** ECOSS (Electronic Communication of Surveillance in Scotland) and the Scottish AMR Satellite Laboratory (SMiRL, Glasgow) **Exceptional phenotypes:** ECOSS (Electronic Communication of Surveillance in Scotland) **Animal Antimicrobial Resistance** ***Salmonella***: ECOSS (Electronic Communication of Surveillance in Scotland). ***AMR in animal clinical isolates:*** Scotland's Rural College (SRUC) Veterinary Services and Capital Diagnostics ***Staphylococcus aureus* animal isolates antimicrobial susceptibility data**: MRSA reference laboratory (via SRUC) ***AMR in healthy animals (abattoir):*** Scotland's Rural College (SRUC) Veterinary Services
Date that data are acquired:	**Antibiotic Use in Humans** **Antibiotic use in primary care:** Patient-based analysis 12/08/2020 UTI analysis 21/09/2020 PC Trend data 09/06/2020 PC Duration of course analysis 09/06/2020 PC Variation analysis 09/06/2020 PC Antifungal analysis 09/06/2020 **Population denominator data**: Mid-year population projections for Scotland: 29/05/2019 **Antibiotic use in secondary care numerator**: SC Trend analysis 09/06/2020

	SC Antifungal analysis 09/06/2020 **Healthcare associated denominator -Total occupied bed days, Sum of OBDs for all hospitals in numerator**: 06/05/2020 **Antibiotic Use in Animals** **Antibiotic use in companion animals:** 17/08/2020 **Human Antimicrobial Resistance** **Bacteraemia**: 13/08/2020 03/08/2021 **Population denominator data**: Mid-year population projections for Scotland: 13/08/2019 03/08/2021 **Urinary Tract Infection**: 13/08/2020 03/08/2021 **Carbapenemase producing organisms (CPOs)**: 14/08/2019 03/08/2021 **Exceptional Phenotypes**: 13/08/2020 19/07/2021 ***Salmonella*:** 09/10/2020 05/07/2021 **Animal Antimicrobial Resistance** ***AMR in animal clinical isolates:*** 04/10/2020 ***AMR in healthy animals (abattoir):*** 04/10/2020 ***Salmonella:*** 09/10/2020
Release date:	17 November 2020 Revised content published 07/09/2021
Frequency:	Annual
Timeframe of data and timelines:	**Antibiotic Use in Humans**: Data are for 2015 to 2019 and are timely for this report. **Antibiotic Use in Animals:** Data are for 2015 to 2019 and are timely for this report. **Bacteraemia:** Data are for 2015 to 2019 and are timely for this report. **Urinary Tract Infections:** Data are for 2015 to 2019 and are timely for this report. **Carbapenemase Producing Organisms (CPOs):**

	The data are from 2003 to 2019 and are timely for this report **Exceptional Phenotypes:** Data are for 2019 and are timely for this report. ***Salmonella:*** Number of cases from 1990 to 2019, AMR data 2019 only. Data to end of 2019 presented. ***AMR in animal clinical isolates:*** Data for 2015 to 2019 and timely for this report. ***Staphylococcus aureus* animal isolates antimicrobial susceptibility data:** Data are for 2019 and timely for this report. ***AMR in healthy animals (abattoir):*** Data for 2017 to 2019 and timely for this report. ***Salmonella:*** Number of cases from 2015 to 2019, AMR data 2019 only. Data to end of 2019 presented.
Continuity of data:	There are no discontinuities in the reporting period.
Revisions statement:	**Revision, September 2021:** Revisions to the data and text were made on pages 7, 31, 34-59 & 72. **Animal Antimicrobial Use Figure 19 revision:** An error in the manner in which the total number of consultations denominator for cats and dogs was produced for Figure 19 has been uncovered and corrected. The impact of this is that the percentages of consultations where at least one antimicrobial was prescribed by presenting problem are now larger for all categories shown (approximately doubled for all except post op). **Human AMR revision statement:** Errors uncovered during year-on-year comparisons of figures resulted in a full review of the methodology, including extraction and processing of the data for analysis (further details provided in the metadata of revised report). In compiling the revisions, new source data extracts were used which will account for some of

	the observed changes in the published figures. New extracts of results were taken from Electronic Communication of Surveillance in Scotland (ECOSS) and the National Records of Scotland (NRS) mid-year population estimate for 2019 has now replaced the 2018 mid-year population for calculating 2019 incidence rates. The impact of this is that the key messages regarding the susceptibility of *E. coli* bacteraemia and urinary isolates has changed as follows: • *E. coli* bacteraemia: there is no longer an increase in non-susceptibility to temocillin and ceftazidime between 2018 and 2019, as previously reported. • *E. coli* urinary isolates: there is now an increase in non-susceptibility to both co-amoxiclav and ceftazadime between 2018 and 2019. **Environmental revision statement:** A revision to the text describing *E. coli* resistance to cefotaxime in relation to minimising the spread of AMR through the environment was provided by SEPA.
Revisions relevant to this publication:	EUCAST clinical breakpoint tables v.9.0 (2019 revision)
Concepts and definitions:	**Statistical significance** Please note where an increase or decrease is stated in this report this refers to a statistical change, and where a trend is referred to as stable there has been no significant increase or decrease. **Rounding** Please note that due to rounding to 1 decimal place values may not add to 100%. **Antibiotic Use in Humans** • Prescribing data - **https://www.isdscotland.org/Health-Topics/Prescribing-and-Medicines/** • Occupied bed days - **https://www.isdscotland.org/Health-Topics/Hospital-Care/Beds/**; **https://www.isdscotland.org/Products-and-Services/Excellence-in-Care/_docs/Occupied-Bed-Days-OBD-v1-2.pdf** • Prescribing time period - All trend data are reported for calendar years 2015 to 2019. Data before these time periods may be accessed via older reports which can be found at: **https://www.hps.scot.nhs.uk/a-to-z-of-topics/antimicrobial-use-and-resistance/#publications**

	• Population estimates: **https://www.nrscotland.gov.uk/files//statistics/population-estimates/mid-19/mid-year-pop-est-19-methodology.pdf.** • Time Period – Previous reports which can be found at: **https://www.hps.scot.nhs.uk/a-to-z-of-topics/antimicrobial-use-and-resistance/#publications** • **Defined Daily Dose (DDDs, World Health Organisation (WHO)) - https://www.whocc.no/atc_ddd_index/** **Antibiotic Use in Animals** The SAVSNET data were collected via electronic health records within the practice management systems of first opinion veterinary practices (these record species, breed, date or year of birth, sex, nature of condition being treated and antimicrobial treatments supplied, and postcode). These data are submitted voluntarily by participating veterinary practices and therefore cannot be interpreted as being representative of all of Scotland. Nevertheless, they provide additional important intelligence relating to another aspect of antimicrobial use in the One Health ecosystem. This important data stream allows a continuing impression of antimicrobial use in companion animals in Scotland and will enable practitioners to evaluate their own data compared to these preliminary national data. • SAVSNET website: **https://www.liverpool.ac.uk/savsnet/my-savsnet-amr/** • Description of the methods used by SAVSNET to capture electronic health records: Sánchez-Vizcaíno, F., et al. (2015) Small animal disease surveillance. Veterinary Record 177, 591-594. **https://veterinaryrecord.bmj.com/content/184/21/640** • D.A. Singleton, et al. (2017) Patterns of antimicrobial agent prescription in a sentinel population of canine and feline veterinary practices in the United Kingdom. The Veterinary Journal, Volume 224, Pages 18-24. **https://www.sciencedirect.com/science/article/pii/S1090023317300722#bib0090** • Description of methods used by SAVSNET for syndromic analysis of antimicrobial prescribing:

	• D.A. Singleton, et al. (2019) Small animal disease surveillance: gastrointestinal disease, antibacterial prescription and Tritrichomonas foetus. Veterinary Record 10.1136/vr1722 (14th Feb p211-216) • D.A. Singleton, et al. (2019) Small animal disease surveillance 2019: pruritus, pharmacosurveillance, skin tumours and flea infestations. Veterinary Record 10.1136/vr16074 (19th Oct p470-475) • D.A. Singleton, et al. (2019) Small animal disease surveillance 2019: respiratory disease, antibiotic prescription, and canine infectious respiratory disease complex. Veterinary Record (25th May p640-645) **Human Antimicrobial Resistance** • Population projections: **https://www.nrscotland.gov.uk/files//statistics/population-estimates/mid-18/mid-year-pop-est-18-methodology.pdf.** To align with HAI Annual report, population projection as was available 02/2019 was used. • Time Period – Previous reports which can be found at: **https://www.hps.scot.nhs.uk/a-to-z-of-topics/antimicrobial-use-and-resistance/#publications** **Burden of drug resistant infection** Calculated based on isolates reported as resistant (R) only. AST testing is not performed on all isolates, therefore the % resistance from available results is applied to the total number of bacteraemia cases to provide the estimated number of antibiotic resistant bacteraemias. **Bacteraemia & Urinary tract infections** **Incidence rates** Incidence rates were calculated as follows: Bacteraemia Rate per 100 000 population = (Number of cases/ mid-year Scottish population) x 100 000 Urinary Tract Rate per 1 000 population = (Number of cases/ mid-year Scottish population) x 1 000" **Percentage non-susceptibility:**

	Non-susceptibility is defined as isolates reported as intermediate (I) or resistant (R). % Non-susceptible= non-susceptible (resistant or intermediate) isolates divided by the total number of isolates tested *100. **Case definitions:** To align with data published by HPS in annual and quarterly epidemiological reports, total numbers and incidence rates were calculated using the following case definition: • A new case of bacteraemia is a patient from whom an organism has been isolated from the patient's blood, and who has not previously had the same organism isolated from blood within a 14 day period (i.e. 14 days from date last positive sample obtained). • A new case of UTI is a patient from whom an organism has been isolated from the patient's urine, and who has not previously had the same organism isolated from urine within a 30 day period (i.e. 30 days from date last positive sample obtained). Please note that the UTI case definition used for this report is based on bacteriuria (bacteria present in urine) and not all cases will be clinically significant UTIs. With the exception of *Escherichia coli* bacteraemia and *Staphylococcus aureus* bacteraemia, all human bacteraemia data are based only on positive blood results extracted from ECOSS and are not validated cases. *Escherichia coli* bacteraemia and *Staphylococcus aureus* bacteraemia data used validated data collected as part of mandatory surveillance programme – details below**:** • ARHAI Scotland Quarterly epidemiological data on *Clostridioides difficile* infection, *Escherichia coli* bacteraemia, *Staphylococcus aureus* bacteraemia and Surgical Site Infection in Scotland. The definitions applied to the incidence data can be accessed here: **http://www.hps.scot.nhs.uk/pubs/detail.aspx?id=3340. The surveillance methods and caveats can be accessed here: https://hps.scot.nhs.uk/web-resources-container/quarterly-**

	epidemiological-commentary-for-the-surveillance-of-healthcare-associated-infections-in-scotland-methods-caveats/ • Definitions applied to the antimicrobial susceptibility data are an adaptation of the ECDC EARS-Net protocol, with the most complete/most resistant isolate within the year included in further analysis. The definitions applied to the antimicrobial susceptibility data can be accessed here: **https://www.ecdc.europa.eu/en/publications-data/ears-net-reporting-protocol-2018** **Carbapenemase-producing Organisms (CPOs)*:*** The term CPOs encompasses all acquired carbapenemase-producing Gram-negative bacteria and is not limited to carbapenemase- producing Enterobacterales (CPEs). Case definitions can be accessed here: **https://www.hps.scot.nhs.uk/web-resources-container/toolkit-for-the-early-detection-management-and-control-of-carbapenemase-producing-enterobacteriaceae-in-scottish-acute-settings/** **Exceptional Phenotypes:** • Definitions of an exceptional phenotype can be accessed here: **http://www.eucast.org/expert_rules_and_intrinsic_resistance/** • **Appendix 13** of the National Infection Prevention & Control Manual (NIPCM) as a mandatory alert micro-organism/condition list. Local monitoring ensures that microbiology clinicians, infection prevention and control teams (IPCTs), health protection teams (HPTs) and antimicrobial management teams (AMT), as appropriate, are aware of each identified case as per local protocols. • The identification of an alert is dependent on laboratories actively performing antimicrobial susceptibility testing (AST) and submitting results to ECOSS. This may result in underreporting, or no reporting, of a particular micro-organism/antibiotic resistance combination if there is limited or no testing performed. **Animal Antimicrobial resistance** **AMR in animal clinical isolates:**

	The data from veterinary clinical isolates are subject to a number of important biases. Unlike the clinical samples in humans in Scotland, the samples are tested on a 'charged for' basis to inform private veterinary treatment of diseased animals. There is a cost to the animal keeper that affects the submission of samples to these services. In addition, the primary purpose of screening for AMR is to inform veterinary treatment and they are tested against a panel of antimicrobials relevant for that purpose at, where they exist, species-relevant clinical breakpoints. ***AMR in healthy animals (abattoir):*** Data presented here represent the percentage of non-susceptible isolates over all tested isolates. These isolates are from healthy livestock animals and are tested against a panel of antimicrobials, and at breakpoints, relevant to human clinical isolates. Database represents a non-random sample of veterinary practices and isolates, based on voluntary submission of data and/or samples to SRUC. *An erratum was issued in 2018 relating to a small number of penicillin non-susceptible *Streptococcus* spp. isolates derived from animals from 2012-2016. Careful review of information pertaining to these isolates has identified that they were wrongly classified as non-susceptible; they were in fact all susceptible to penicillin at the relevant break point. ***Salmonella:*** Interpretation of *Salmonella* resistance to individual antibiotics is complicated by the fact that in some subtypes there are well-recognised genetic elements encoding resistance to multiple agents. Thus, the occurrence of resistance to individual antibiotics is not always independent and the apparent prevalence of resistances to different agents can be strongly influenced by the abundance of *Salmonella* sub-types in the sample set for each reporting period. In Scotland, *Salmonella* is a reportable animal pathogen; all veterinary diagnostic laboratories isolating *Salmonella* spp. from livestock in Scotland are also required to forward suspect isolates for confirmation and typing to the SMiRL. No information on prior antibiotic treatment is available for *Salmonella* isolates identified from animal samples. The submission of samples is affected by the willingness of an animal keeper to pay the costs of laboratory testing to inform treatment, in addition to the clinical

	presentation in the affected animal(s). A number of *Salmonella* spp. are adapted to particular animal host species and are only found rarely in others. Generally, *Salmonella* infection in animals can result in clinical syndromes suggestive of bacteraemia and systemic illness and, in these cases, antibiotic therapy would sometimes be part of the treatment regimen instituted by an attending veterinarian. Vaccines against some serotypes of *Salmonella* spp. are available for some animal species, and are used to a greater of lesser extent depending on a number of factors including assessed risk of infection in the particular group of animals.
Relevance and key uses of statistics:	Making information publicly available. The report is intended to support planning, prioritisation and evaluation of initiatives to optimise antimicrobial use and to minimise antimicrobial resistance.
Accuracy:	**<u>Antibiotic Use in Humans</u>** **Antibiotic use in primary care:** A subset of these data are routinely validated by Practitioner Services on a monthly basis **Healthcare associated denominator -Total occupied bed days, Sum of OBDs for all hospitals in numerator**: Standardised methodology used **<u>Human Antimicrobial Resistance</u>** **Bacteraemia:** Data supplied by UKAS accredited laboratories using standardised testing methodologies. **Urinary Tract Infections**: Data supplied by UKAS accredited laboratories using standardised testing methodologies **Carbapenemase Producing Organisms (CPOs):** Data supplied by UKAS accredited laboratories using standardised testing methodologies

	Exceptional Phenotypes: Data supplied by UKAS accredited laboratories using standardised testing methodologies. Exceptional phenotypes are confirmed with the sending laboratory **Animal Antimicrobial resistance** Data supplied by UKAS accredited laboratories using standardised testing methodologies. SRUC (ISO:17025), SMiRL, Glasgow (ISO:15189).
Completeness:	**Antibiotic Use in Humans:** All data for the reporting period have been included in the analysis. **Antibiotic Use in Animals:** Database represents a non-random sample of veterinary practices based on voluntary submission of data to SAVSNET **Human Antimicrobial Resistance** **Bacteraemia:** All data for the reporting period have been included in the analysis **Urinary Tract Infections:** All data for the reporting period have been included in the analysis **Carbapenmase Producing Organisms (CPOs):** All data for the reporting period have been included in the analysis **Exceptional Phenotypes:** All laboratory confirmed isolates have been included in the analysis **Animal Antimicrobial resistance** ***AMR in animal clinical isolates:*** Database represents a non-random sample of veterinary practices and veterinary isolates, based on voluntary submission of data and/or samples to SRUC. ***AMR in healthy animals (abattoir):*** Database represents a non-random sample of veterinary practices and veterinary isolates, based on voluntary submission of data and/or samples to SRUC.

	Salmonella: All laboratory confirmed isolates have been included in the analysis
Comparability:	**Antibiotic Use in Humans** The numerator for antibiotic use includes the number of WHO defined daily doses and is comparable to other antibiotic use surveillance programmes using this method. Occupied bed days (OBDs), is derived using a standardised methodology used allowing comparability across years **Antibiotic Use in Animals** Comparable to prescribing databases from ISD. **Human Antimicrobial Resistance** **Bacteraemia:** Public Health England report on national data on antibiotic resistance **https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report** ECDC report on Antimicrobial resistance surveillance in Europe **https://www.ecdc.europa.eu/en/antimicrobial-resistance/surveillance-and-disease-data/report** ***Escherichia coli*** bacteraemia: Details provided in quarterly publication **https://www.hps.scot.nhs.uk/data/healthcare-associated-infection-quarterly-epidemiological-commentary/** **Urinary Tract Infection:** Public Health England report on national data on antibiotic resistance **https://www.gov.uk/government/publications/english-surveillance-programme-antimicrobial-utilisation-and-resistance-espaur-report.** **Carbapenemase producing Organisms (CPOs):**

	Public Health England report on Carbapenem resistance **https://www.gov.uk/government/collections/carbapenem-resistance-guidance-data-and-analysis** ECDC report on Carbapenem resistance **https://ecdc.europa.eu/en/surveillance-atlas-infectious-diseases** **Exceptional Phenotypes:** N/A **Animal Antimicrobial resistance** SRUC data from healthy livestock animals are tested against a panel of antimicrobials, and at breakpoints, relevant to human clinical isolates so that AMR results are comparable (EUCAST & BSAC)
Accessibility:	It is the policy of NSS to make sure its web sites and products are accessible in accordance with published guidelines
Coherence and clarity:	Tables and charts are accessible via the HPS website at: **https://www.hps.scot.nhs.uk/web-resources-container/scottish-one-health-antimicrobial-use-and-antimicrobial-resistance-in-2019/**
Value type and unit of measurement:	**Antibiotic Use in Humans** Counts & number of prescriptions **Antibiotic Use in Animals** Counts & number of prescriptions **Human Antimicrobial Resistance** **Bacteraemia:** Number of cases and incidence rates (per 100,000 population). AMR data includes percentage non-susceptible (I & R categories) for antibiotic/organisms combinations **Urinary Tract Infections**: Number of cases and incidence rates (per 1000 population).

	AMR data includes percentage non-susceptible (I & R categories) for antibiotic/organisms combinations **Carbapenemase Producing Organisms(CPOs):** Number of isolates, number of carbapenemase producers by organisms and enzyme type and incidence per 100,000. **Exceptional phenotypes:** Number of confirmed exceptional phenotype, number of exceptional phenotypes per organism/antibiotuic combination**.** **Animal Antimicrobial resistance** ***AMR in animal clinical isolates*** Counts, percentage of non-susceptible isolates over all tested isolates ***AMR in healthy animals (abattoir)*** Counts, percentage of non-susceptible isolates over all tested isolates
Disclosure:	The NSS protocol on Statistical Disclosure Protocol is followed
Official Statistics designation:	Not Assessed
UK Statistics Authority Assessment:	Not Assessed
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Help email:	**NSS.hpsSONAAR@nhs.scot**
Date form completed:	20/10/2019 **07/09/2021**

Appendix 3 – Early access details

Pre-Release Access

Under terms of the "Pre-Release Access to Official Statistics (Scotland) Order 2008", ARHAI is obliged to publish information on those receiving Pre-Release Access ("Pre-Release Access" refers to statistics in their final form prior to publication). The standard maximum Pre-Release Access is five working days. Shown below are details of those receiving standard Pre-Release Access.

Standard Pre-Release Access:

- Scottish Government Health Department
- NHS Board Chief Executives
- NHS Board Communication leads

Appendix 4 – HPS and Official Statistics

About ARHAI Scotland

ARHAI Scotland works at the very heart of the health service across Scotland, delivering services critical to frontline patient care and supporting the efficient and effective operation of NHS Scotland.

Official Statistics

Our statistics comply with the **Code of Practice for Statistics** in terms of trustworthiness, high quality and public value. This also means that we keep data secure at all stages, through collection, processing, analysis and output production, and adhere to the '**five safes**'.