ARHAI Scotland

Antimicrobial Resistance and Healthcare Associated Infection

NHS
National Services Scotland

Scottish One Health Antimicrobial Use and Antimicrobial Resistance in 2021

Annual Report

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Introduction

Antimicrobial Resistance (AMR) arises when micro-organisms, such as bacteria, develop the ability to withstand antimicrobial treatments making infections harder to treat which could result in severe disease and potentially death.

Antimicrobial Use (AMU) and spread of infection in humans, animals and the environment contribute to the development of resistant infections. A co-ordinated cross sectoral response is needed to address the threat from AMR. The UK five-year national action plan (NAP) 'Tackling antimicrobial resistance 2019–2024' acknowledges that a 'One Health' approach is required to mitigate the threat from AMR.[1] ARHAI Scotland coordinates the implementation of the UK AMR National Action Plan in Scotland by delivery partners through the Scottish One Health National AMR Action Plan (SOHNAAP) group.

The UK AMR NAP acknowledges that intelligence and evidence for action are essential for supporting the vision to optimise antibiotic use and contain and control AMR across all sectors. The Scottish One Health Antimicrobial Use and Antimicrobial Resistance (SONAAR) Health Protection programme contributes to ARHAI Scotland's mission to improve the health and wellbeing of the population by reducing the burden of infection and AMR. This is delivered through development of epidemiological evidence on trends in antibiotic use and resistance to inform local and national interventions and initiatives in human and animal health. In line with the One Health approach, this report includes information from 2021 on antimicrobial use and resistance in humans, animals and the environment.

In 2021, the impact of the Coronavirus 2019 (COVID-19) pandemic was still evident across society. While some healthcare services resumed during 2021, patterns of service delivery, patient population, risk factors and hospital activity levels had not yet returned to pre-pandemic levels. This makes comparison of results for 2021 with previous years challenging and results presented in this report must be interpreted in the context of the ongoing impact of the pandemic.

AMR was an important clinical and public health issue before the emergence of the pandemic and remained as important in 2021, the second pandemic year. As society starts to recover and the NHS remobilises from the COVID-19 pandemic, national and local strategies for reduction of AMR will once again become more prominent and concerted efforts across all sectors will be required to reduce resistant infections and preserve the effectiveness of antibiotics for prevention and treatment of bacterial infections.

Main Points

The ongoing COVID-19 pandemic has had an impact on prescribing practice during 2021, including antibiotic use, which will affect the data reported. Further information on changes in hospital activity can be found in the ARHAI Scotland 2021 Annual Report.

Antibiotic use in humans

- Total antibiotic use in humans has decreased by 16.9% since 2017.
- In 2021, Access antibiotics (recommended first line narrow spectrum agents) accounted for 62.4% of total antibiotic use in humans and this percentage has increased year-on-year over the last five years.
- The majority of antibiotic use in humans occurs in primary care.
- Antibiotic use in primary care has decreased by 18.8% since 2017.
- 23.0% of the Scottish population received at least one course of antibiotics prescribed in primary care.
- Antibiotic use in acute hospitals has decreased by 8.6% since in 2017.
- Use of Watch and Reserve (restricted) antibiotics in acute hospitals has decreased by 20.6% since 2017.

Antibiotic use in animals

- Antibiotics are essential medicines in animal health to ensure high standards of animal welfare and support production of safe food.
- Among the small number of participating veterinary practices, the percentage of consultations for companion animals resulting in the prescription of at least one antibiotic has decreased over the last five years.

- The percentage of antibiotics prescribed for companion animals which were Highest Priority Critically Important (HP-CIAs) has decreased over the last five years.
- Trends in AMU suggest that there has been increasing awareness of prescribing guidelines among veterinary clinicians contributing to surveillance in Scotland.
- Scotland's Healthy Animals website has been extensively revised and upgraded and continues to offer guidance for vets and animal keepers on disease avoidance and antibiotic stewardship.

Antimicrobial resistance in humans

- Gram-negative bacteria are a common cause of serious infections in both healthcare and community settings.
- Antimicrobial non-susceptibility in Gram-negative bacteria significantly contributes to the overall burden of AMR.
- In 2021, *Escherichia coli* (*E. coli*) was the most common cause of Gram-negative bacteraemia in Scotland with 4,292 cases reported and an incidence of 78.5 per 100,000 population. This incidence has decreased year-on-year over the last five years.
- Non-susceptibility in *E. coli* blood isolates has remained stable between 2020 and 2021 except for a decrease in non-susceptibility to co-amoxiclav.
- In 2021, 743 cases of *Klebsiella pneumoniae* (*K. pneumoniae*) bacteraemia were reported in Scotland with an incidence of 13.6 per 100,000 population. The incidence has remained stable over the last five years.
- Non-susceptibility in *K. pneumoniae* blood isolates remained stable between 2020 and 2021.
- In 2021, 516 cases of *Enterococcus faecalis* (*E. faecalis*) and 276 cases of *Enterococcus faecium* (*E. faecium*) bacteraemia were reported in Scotland. The incidence of *E. faecalis* bacteraemia (9.4 per 100,000 population) and *E. faecium* bacteraemia (5.0 per 100,000 population) has remained stable over the last five years.

- Non-susceptibility in *E. faecalis and E. faecium* blood isolates has remained stable between 2020 and 2021.
- In 2021, 40.4% of *E. faecium* blood isolates were non-susceptible to vancomycin.
- Urinary tract infections (UTI) are commonly diagnosed in community, healthcare and hospital settings and antimicrobial non-susceptibility in urinary isolates significantly adds to the burden of AMR.
- *E. coli* is the most frequently isolated bacteria from urine specimens.
- Between 2020 and 2021, antimicrobial non-susceptibility of *E. coli* urinary isolates has decreased except for an increase in non-susceptibility to fosfomycin.
- In 2021, 55 carbapenemase-producing organisms (CPO) were reported with an incidence of 1.0 per 100,000 population.

Antimicrobial resistance in animals

- Monitoring AMR in animals is a vital component of understanding and mitigating risk of AMR across the entire ecosystem.
- Intelligence relating to AMR in animals continues to be developed to inform the evidence base supporting a One Health approach to AMR.
- Animal stakeholder organisations in all sectors are working hard to improve coverage of surveillance systems.

Results and Commentary

Since the beginning of the COVID-19 pandemic in 2020, there have been changes in healthcare delivery and treatment options. While more services resumed in 2021, routine hospital activity levels had not yet returned to pre-pandemic levels. This continued disruption to healthcare delivery and the changes in patient population risk factors makes comparisons with the years prior to the pandemic challenging and, for this reason, results presented in this report must be interpreted in the context of the pandemic.

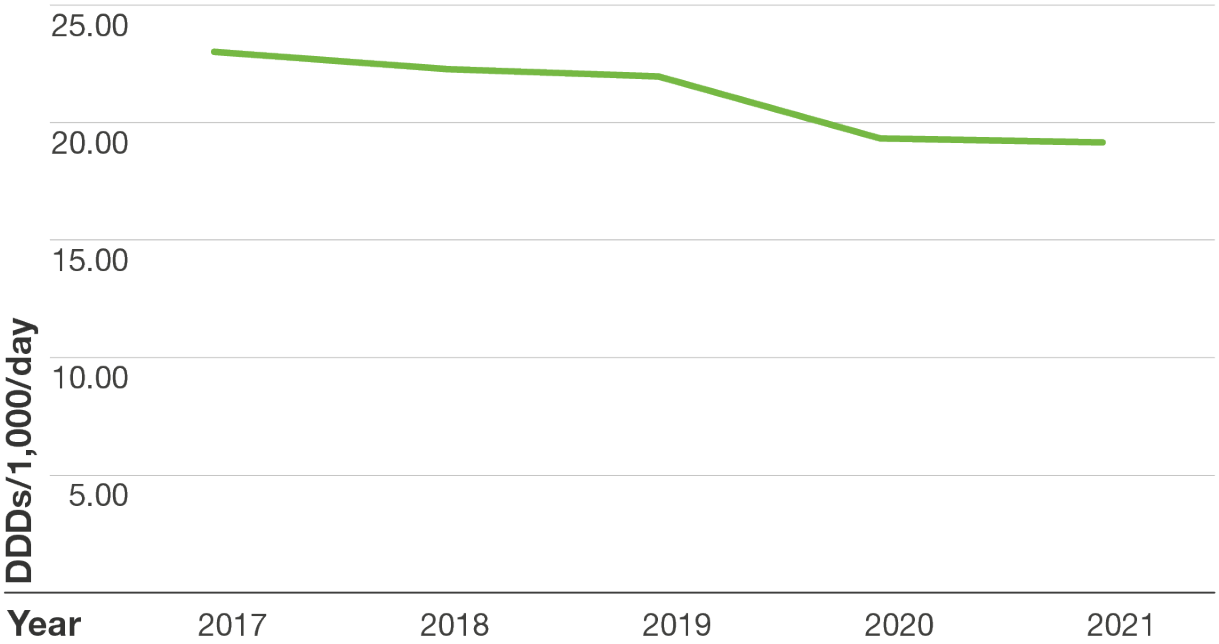
For further information on how COVID-19 has impacted healthcare delivery please see the ARHAI Scotland 2021 annual report.

Antibiotic use in humans

Optimising antibiotic use in humans is one of the three key ways of tackling AMR set out in the UK's five-year National Action Plan (NAP) 2019 to 2024.[1] The NAP includes targets on antibiotic use to act as a focus for improvement activity to preserve the effectiveness of the currently available antibiotics. The generation and sharing of intelligence, developed from monitoring trends in antibiotic use, undertaken by ARHAI Scotland is crucial to the planning, prioritisation and evaluation of the impact of antimicrobial stewardship (AMS) interventions. The interventions are led by the Scottish Antimicrobial Prescribing Group (SAPG) which coordinates the national antimicrobial stewardship programme in humans. This chapter will describe antibiotic use in 2021, during the second year of the COVID-19 pandemic.

In 2021, the total use of antibiotics in humans across all settings was 19.0 defined daily doses (DDDs) per 1,000 population per day (DDDs/1,000/day), this compares to 19.2 DDDs/1,000/day in 2020. Between 2017 and 2021, there has been a year-on-year decrease of 5.0% ($p<0.001$) since 2017, with an overall reduction of 16.9% between 2017 and 2021 (**Figure 1**).

Figure 1: Total number of defined daily doses per 1,000 population per day (DDDs/1,000/day) for all antibiotics prescribed in Scotland, 2017 to 2021, by year.



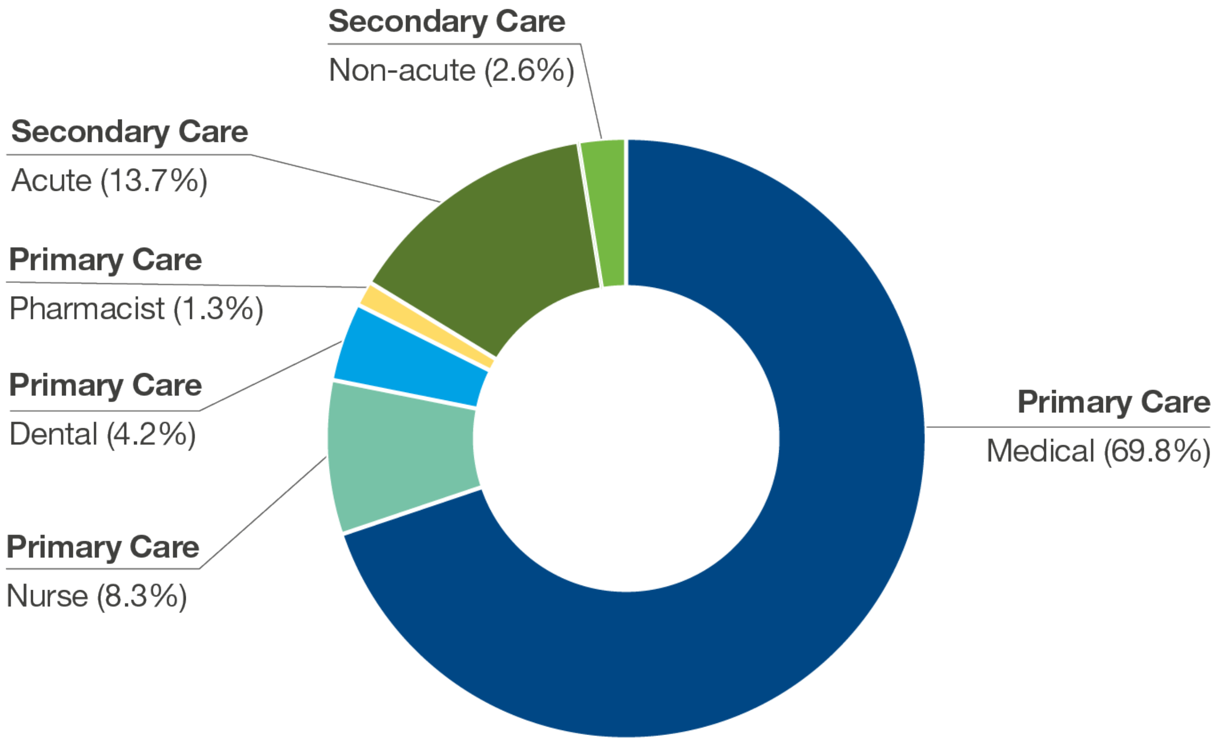
[Data Source: Prescribing Information System (PIS), Hospital Medicines Utilisation Database (HMUD) and National Records of Scotland (NRS)]

Before and throughout the COVID-19 pandemic there have been changes in the types of clinicians prescribing antibiotics as a result of the evolution in health professional roles in delivery of NHS services. As the NHS continues to evolve to meet the changing demand and expectations from the public, so too will how the public access antibiotics for treatment of infection. Optimisation of antibiotic use by all clinicians in all settings is required.

In 2021, 83.7% 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 13.7% of antibiotic use in humans (DDDs) with non-acute hospitals accounting for 2.6% (**Figure 2**).

Using the nationally available data, the prescriber type can only be identified in primary care. In 2021, of the total use of antibiotics in humans (total DDDs), primary care medical prescribers accounted for 69.8% of antibiotic use, followed by nurses (8.3%), dentists (4.2%) and pharmacists (1.3%) (**Figure 2**).

Figure 2: Percentage of all antibiotics prescribed (DDDs) in Scotland by prescriber type, for 2021.



[Data Source: Prescribing Information System (PIS) and Hospital Medicines Utilisation Database (HMUD)]

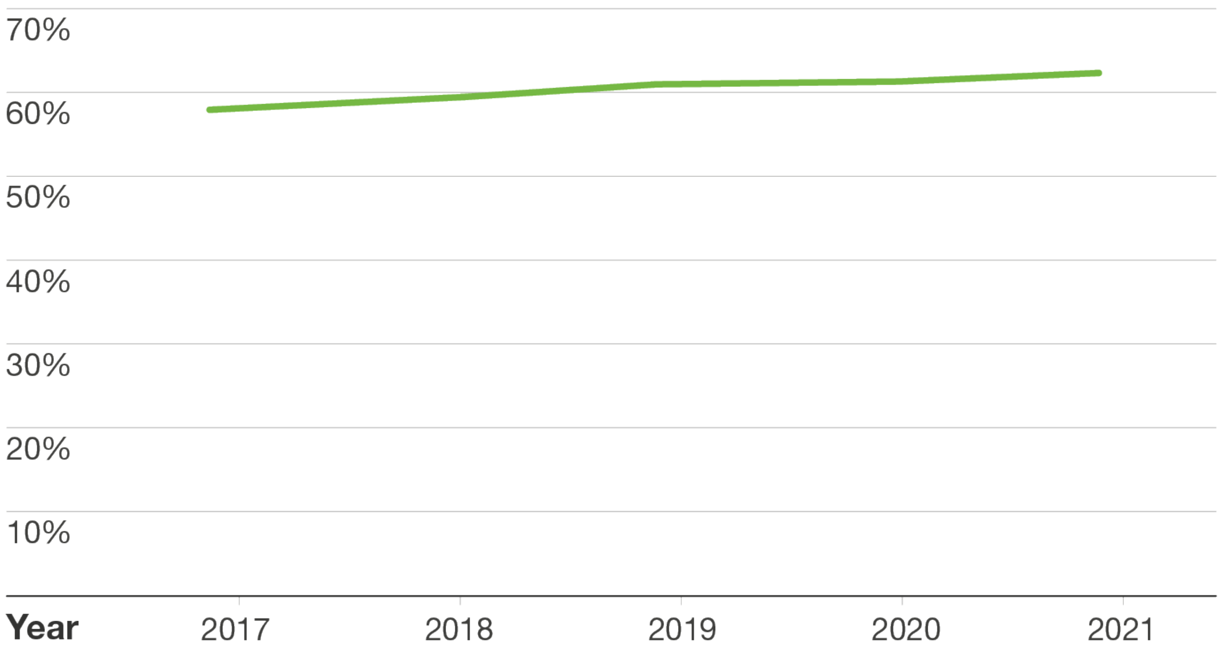
An important element of AMS is the choice of which antibiotic is used. Where there is a clinical need to use antibiotics, it is important to avoid unnecessary use of broad spectrum antibiotics when a narrower spectrum agent would be sufficient. In Scotland, as in elsewhere in the UK, an adapted version of the World Health Organization (WHO) Access, watch, reserve, classification of antibiotics for evaluation and monitoring use classification system (AWaRe) has been adopted to support surveillance of trends in antibiotic use. In this system antibiotics are split into three groups:

- Access group antibiotics 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;
- 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.

In 2021, Access antibiotics accounted for 62.4% of total antibiotic use in humans (DDDs in all primary care and secondary care settings) and compares to 61.3% in 2020. Access antibiotic use as a proportion all antibiotic DDDs in humans has been increasing year-on-year since 2017 (1.8%, $p<0.001$) (**Figure 3**). The increasing proportion of Access antibiotics indicates that during the second year of the pandemic, clinicians across all sectors continued to implement antimicrobial stewardship and follow treatment choice recommendations within local antibiotic prescribing guidelines to minimise unnecessary use of Watch and Reserve antibiotics. When considering monitoring of antibiotic use in animals Watch and Reserve antibiotics are known as highest priority critically important antimicrobials (HP-CIA). (See **Table 1** and **Figure 12** for the use of these antibiotics in animals.)

Figure 3: Percentage of all antibiotics prescribed (DDDs) in Scotland that belonged to the 'Access' group, 2017 to 2021, by year.



[Data Source: Prescribing Information System (PIS) and Hospital Medicines Utilisation Database (HMUD)]

ARHAI Scotland will continue to make available clinically meaningful intelligence on antibiotic use in humans through Discovery dashboards to influence practice and optimise antibiotic use to help contain and control AMR. This enables NHS boards to track local progress against Scottish Government standards on antibiotic use and to identify areas for targeted local improvement activity. ARHAI Scotland will also develop intelligence to inform a review of the current national antibiotic prescribing standards and their associated targets and, in collaboration with the SAPG, provide recommendations for potential refreshed antibiotic use measures for the next UK AMR NAP.

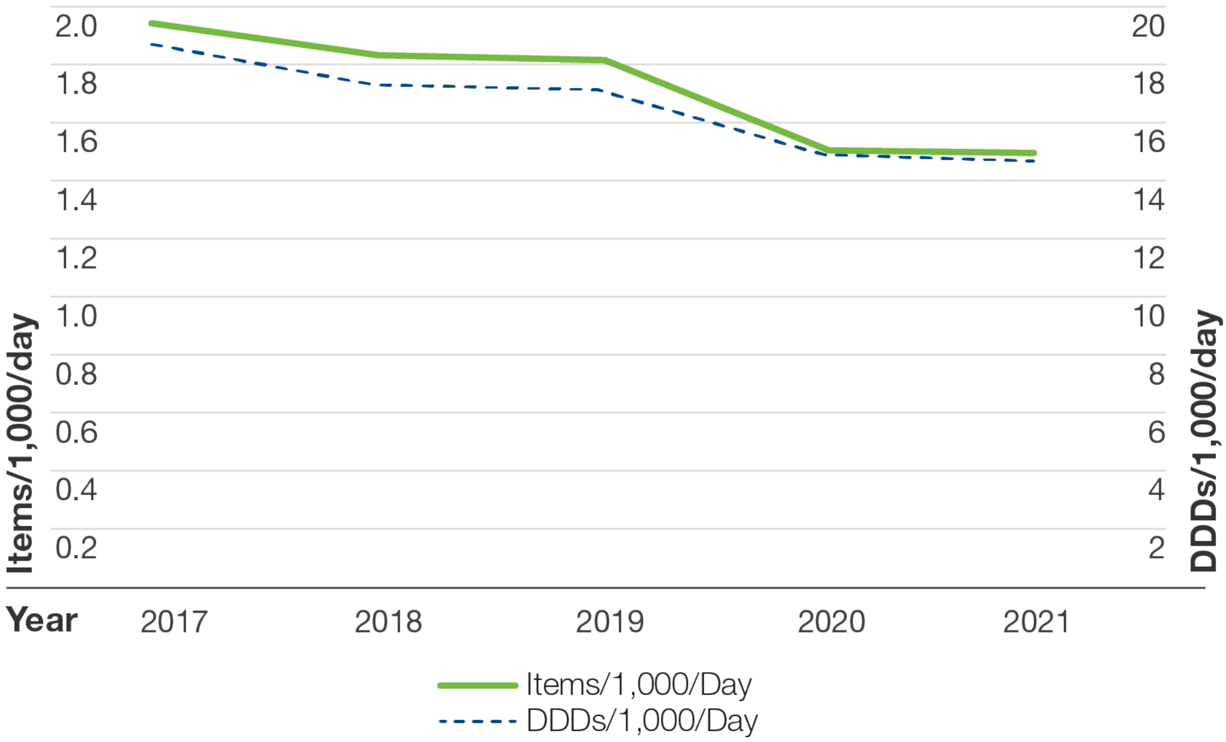
Total antibiotic use in humans key points

- **Antibiotic use in humans decreased by 16.9% since 2017.**
- **The majority of antibiotic use occurs in primary care.**
- **The proportion of total antibiotic use which are WHO Access (first-line) antibiotics has continued to increase during the COVID-19 pandemic.**

Antibiotic use in primary care

Resistance is a natural consequence of using antibiotics, but overuse and inappropriate use can unnecessarily increase the rate of development of resistance. A key approach to optimising antibiotic use in primary care is minimising their use for symptoms such as coughs, colds, sore throats, and earache in otherwise fit and healthy people. The use of antibiotics in primary care (excluding dental prescribing) in 2021 was 1.56 items per 1,000 population per day, this compares with 1.55 items per 1,000 population per day in 2020. Since 2017 there has been a year-on-year decrease of 5.6% ($p < 0.001$), with an overall reduction of 18.8% between 2017 and 2021 (Figure 4). When expressed using DDDs, antibiotic use in 2021 was 15.2 DDDs per 1,000 population per day compared to 15.4 in 2020; a year-on-year decrease of 5.2% ($p<0.001$) since 2017, with an overall reduction of 18.0% between 2017 and 2021. The proportion of the Scottish population that received at least one course of antibiotics (in primary care, excluding dental) was 23.0% in 2021 compared to 22.3% in 2020, the first year of the pandemic, and 26.8 % in 2019, the year preceding the pandemic.

Figure 4: Antibiotic prescribing in primary care (excluding dental prescribing) in Scotland, 2017 to 2021, 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: Prescribing Information System (PIS) and National Records of Scotland (NRS)]

During 2021, ARHAI Scotland monitored and reported trends in antibiotic use in primary care to assess the impact of the COVID-19 pandemic on prescribing behaviour and antibiotic use in humans. This assessment used near real time monitoring of weekly trends in antibiotics used for respiratory infection with reporting for action within NHS boards. ARHAI Scotland will continue this regular monitoring and reporting in 2022 to enable assessment of the impact of NHS remobilisation from COVID-19 and generate evidence for optimisation of antibiotic prescribing.

A second key pillar of AMS in primary care is to avoid the use of broad spectrum antibiotics for empirical treatment of infection. In 2021, 77.6% of antibiotic items dispensed in primary care (excluding dental prescribing) were from the WHO Access group, (recommended first line narrow spectrum agents). This compares to 76.8% in 2020 and indicates that clinicians in primary care continued to follow antibiotic prescribing guidelines throughout the second year of the COVID-19 pandemic. For more detail on use of particular antibiotics and antibiotic classes, see **Supplementary Data**.

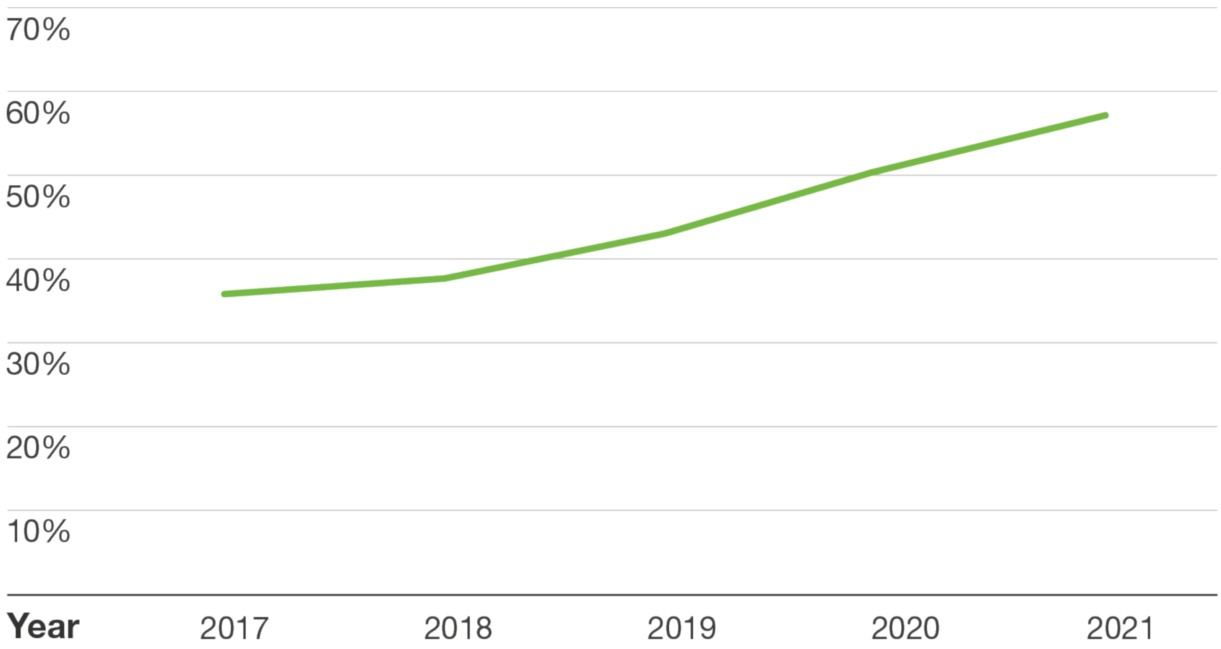
The third key pillar of AMS in primary care is to avoid unnecessary exposure by using antibiotics for the recommended evidenced based duration specified with prescribing guidelines. Respiratory infections are commonly encountered in primary care and prescribing guidelines reflect the evidence that for treatment of respiratory infection, when antibiotics are clinically indicated, a five-day course is recommended.[2] Previous ARHAI Scotland SONAAR reports have highlighted optimising duration of antibiotics commonly used for respiratory infections as an area for improvement.

Amoxicillin is recommended as first line treatment of respiratory infections. In 2021, 58.1% 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 51.7% in 2020 (**Figure 5**).

Between 2017 and 2021, there has been a year-on-year increase in the percentage of amoxicillin prescribed for five-day duration of 13.2% ($p<0.001$). For more detail on duration of other antibiotics commonly used for treatment of respiratory infection and for which use of courses of five-day duration has increased since 2017, see **Supplementary Data.**

Use of shorter courses, in line with published evidenced based guidance, is an important way to reduce individual and population exposure thereby reducing the development of AMR. These data suggest that in 2021, in the second year of the pandemic, clinicians are increasingly following recommendations on treatment duration.

Figure 5: Proportion of amoxicillin 500mg capsule prescriptions with five-day course durations in general practice, 2017 - 2021, by year.



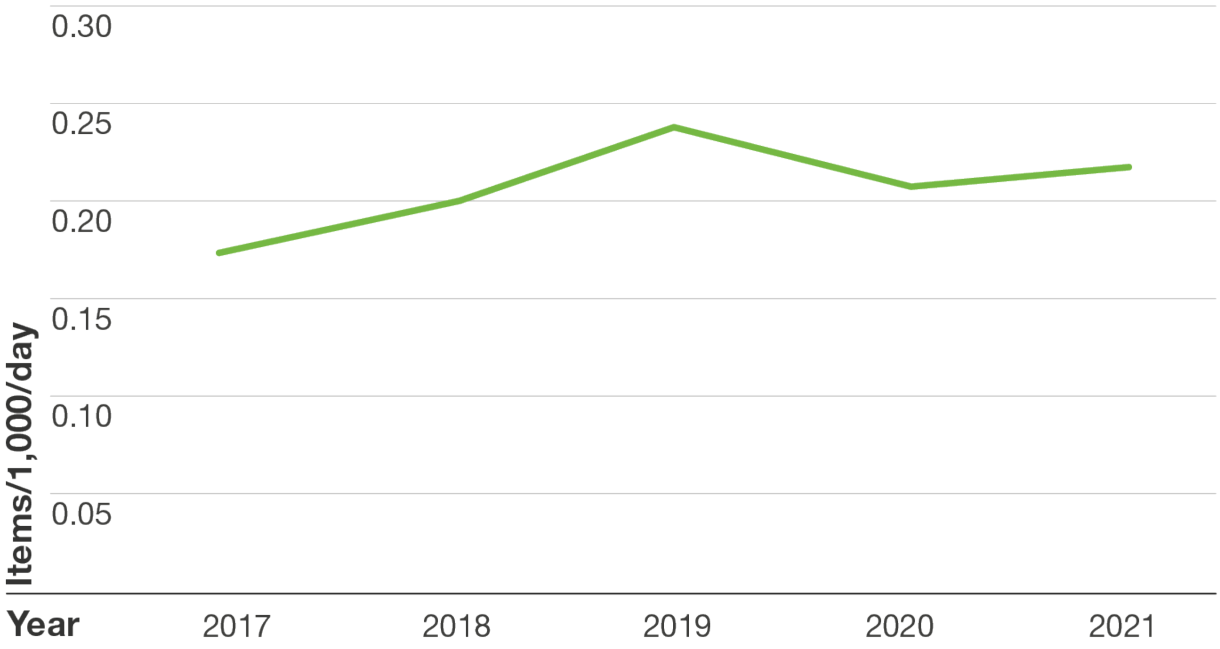
[Data Source: Prescribing Information System (PIS)]

In primary care, new models of healthcare delivery have continued to evolve during the COVID-19 pandemic. The 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.

General practitioners (GPs) remain responsible for the majority of antibiotic prescriptions in primary care. In 2021, GPs accounted for 73.8% of all antibiotic items compared to 74.8% in 2020.

In 2021, nurses accounted for 12.5% of all antibiotic items dispensed in the community. Between 2017 and 2021, there has been a year-on-year increase in the items per 1,000 patients per day prescribed by nurses (4.8%, $p<0.001$) (**Figure 6**). WHO Access antibiotics (items) accounted for 86.3% of nurse prescribing in 2021, no different to 2020, indicating that nurses have continued to follow local guideline recommendations on treatment choice through the COVID-19 pandemic.

Figure 6: Antibiotic prescribing by nurses in primary care in Scotland (items per 1,000 population per day; Items/1,000/Day), 2017 to 2021.

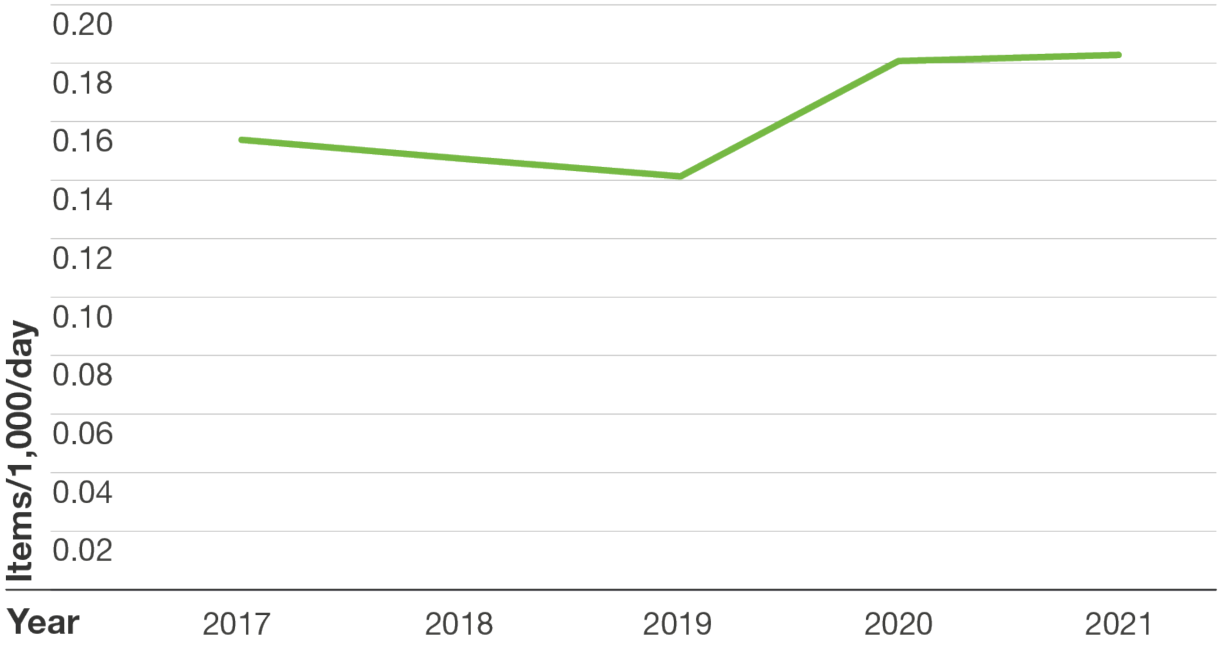


[Data Source: Prescribing Information System (PIS) and National Records of Scotland (NRS)]

In 2021, antibiotic use by dentists was 0.18 items per 1,000 patients per day, similar to 2020, compared to 0.14 items per 1,000 patients per day in 2019 (**Figure 7**). In 2021, the changes to dental service provision and patient activity seen since the emergence of the COVID-19 pandemic have continued. The SAPG Dental Stewardship subgroup continues to coordinate work by stakeholders to support optimisation of dental antibiotic use as dental practices continue to remobilise and move toward normalisation of dental services.

Dentists can prescribe a limited range of antibiotics on NHS prescriptions in Scotland and in 2021, three antibiotics accounted for the majority of dental antibiotic use (items): amoxicillin (50.2%); metronidazole (28.6%); and phenoxymethylpenicillin (penicillin V) (18.9%). In 2020 the use of phenoxymethylpenicillin (penicillin V) accounted for 1.6% of dental antibiotic use. The increase followed advice from SAPG Dental Stewardship subgroup which recommended that phenoxymethylpenicillin was used first line when antibiotics are required for acute dento-alveolar infections. These data indicate that although the overall volume of antibiotic use in dentistry in 2021 remained higher than prior to the COVID-19 pandemic, dental prescribers were optimising antibiotic use through moving toward national advice on choice of treatment.

Figure 7: Antibiotic prescribing by dentists in primary care in Scotland (items per 1,000 population per day; Items/1,000/Day), 2017 to 2021.



[Data Source: Prescribing Information System (PIS) and National Records of Scotland (NRS)]

Through the continued development of NHS Pharmacy First and Pharmacy First Plus (Common Clinical Conditions) the role of community pharmacists continues to evolve to meet the needs to the population. This enables people with common conditions to be reviewed by a community pharmacist to support self-care, provide timely antibiotic treatment where clinically appropriate, or for referral to other NHS services. In 2021, there were 113,199 antibiotic prescriptions written and dispensed by pharmacists in Scotland, representing 3.3% of total antibiotic use in primary care (items) compared to 2.8% in 2020. Of pharmacist antibiotic prescriptions, 62.3% were for trimethoprim, the recommended first line antibiotic for lower urinary tract infection in women in Pharmacy First.

In 2022, ARHAI Scotland will maximise the utility of the national information on antibiotic use in primary care through providing reports on GP practice level antibiotic use. These reports will support practice teams to identify areas for improvement through provision of the practice's own data for measures of total antibiotic use, antibiotic use in children and duration of antibiotic treatment.

Antibiotic use in primary care key points

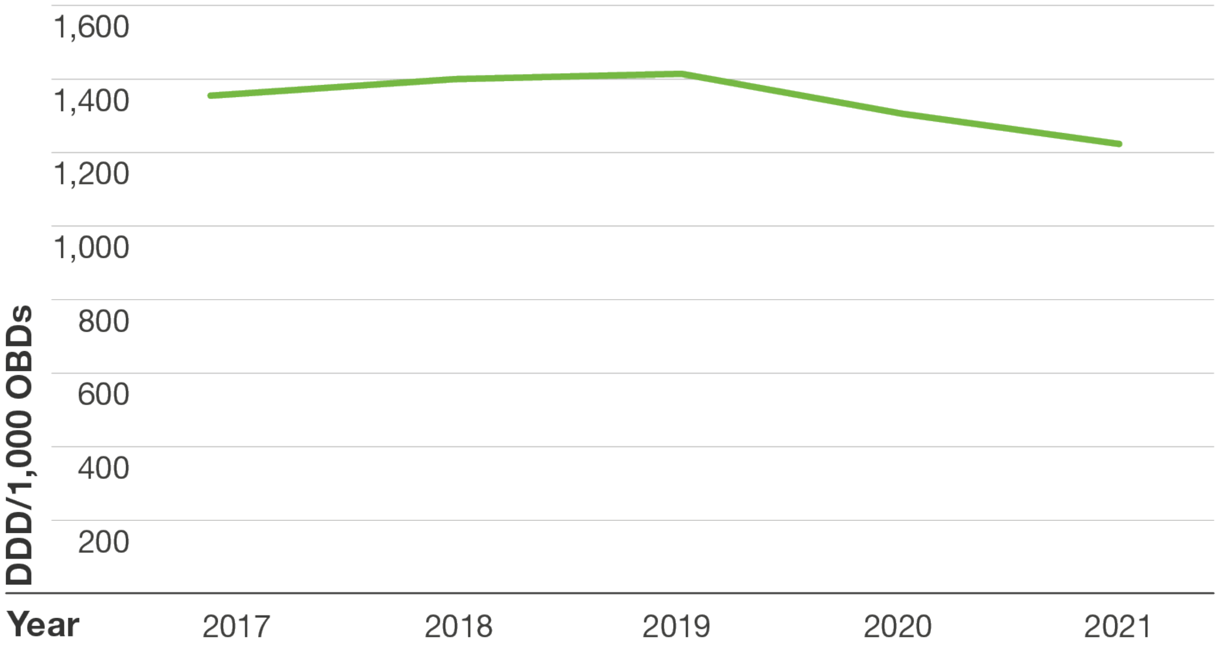
- **Over 80% of total antibiotic use occurs in primary care.**
- **Antibiotic use was 18.8% lower than in 2017.**
- **WHO Access (first line) antibiotics accounted for more than three quarters of all antibiotic use.**
- **Proportion of amoxicillin five-day courses continued to increase in 2021.**
- **Use of antibiotics by dentists remained higher in 2021 compared to pre pandemic.**
- **COVID-19 pandemic has had an ongoing impact on antibiotic use in 2021.**

Antibiotic use in acute hospitals

The second year of the COVID-19 pandemic in 2021 was characterised by ongoing changes in healthcare delivery. There was an increase in routine and non-COVID-19 emergency hospital activity in 2021 but activity had not yet returned to pre-pandemic levels. Although there was an increase of 9.2% in total occupied bed days in 2021 compared to 2020, total occupied bed days in 2021 remained 6.4% lower than in 2019. Emergency admissions in 2021 were 9.2% lower than in 2019 with elective admissions in 2021 being 34.2% lower than in 2019.[3] These changes have influenced the trends in antibiotic use and limit comparison of 2021 with 2019 and other years before the emergence of the COVID-19 pandemic.

In 2021, 13.7% of total antibiotic use (DDDs) in humans occurred in acute hospitals. There were 5,235,181 antibiotic DDDs used in 2021 compared to 5,040,997 in 2020, an increase of 194,184. When expressed as rate using DDDs per 1,000 occupied bed days (OBD), antibiotic use was 1,268.1 DDDs/1,000 OBD in 2021 compared to 1,364.1 DDDs/1,000 OBD in 2020 (**Figure 8**). There has been an overall decrease in the rate of antibiotic use (DDDs/1,000 OBD) of 8.6% ($p<0.001$) between 2017 and 2021. As NHS services remobilise after the COVID-19 pandemic it will be important to optimise antibiotic use through AMS. ARHAI Scotland will continue to support the SAPG through regular monitoring and reporting of trends in antibiotic use to identify areas for improvement. In 2022, work will be undertaken to enable more meaningful comparisons of antibiotic use at hospital level. This will be delivered through developing intelligence on the key factors associated with antibiotic use at hospital level and using these factors to develop adjusted rates based on hospital speciality and case mix.

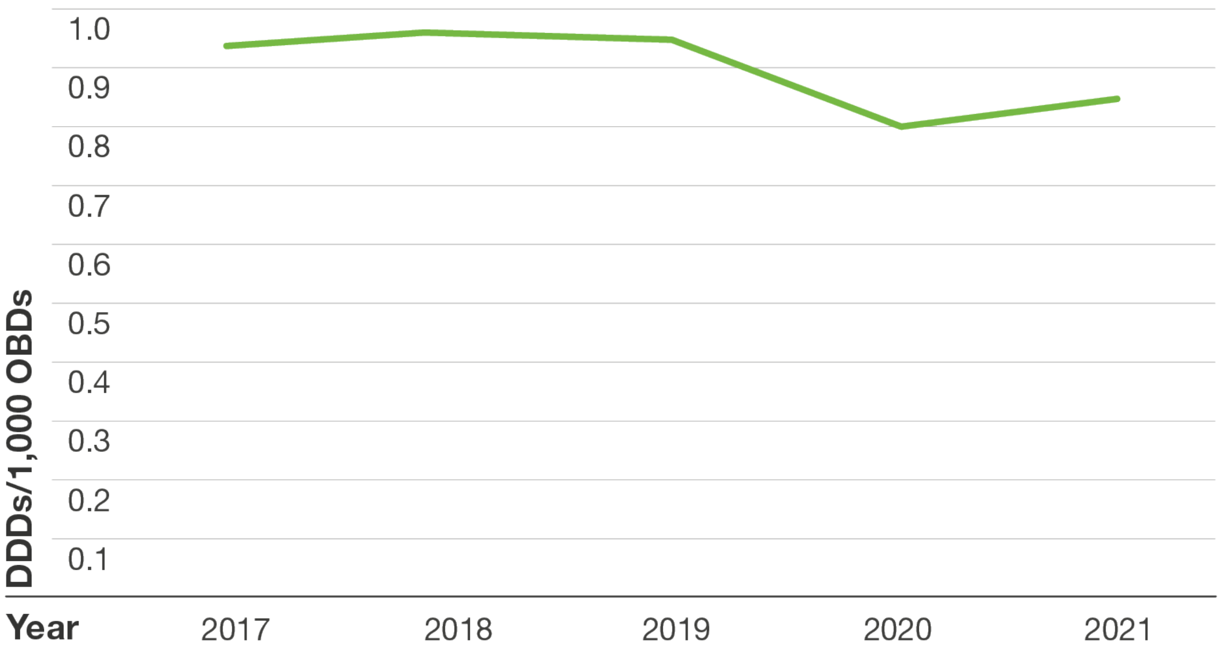
Figure 8: Antibiotic prescribing in acute hospitals in Scotland (defined daily doses per 1,000 occupied bed days; DDDs/1,000 OBDs), 2017 to 2021, by year.



[Data Source: Hospital Medicines Utilisation Database (HMUD) and Information Services Division (ISD(S)1)]

During 2021, a key element of AMS in acute hospitals was a continued focus on regular clinical review of patients receiving antibiotics by intravenous (IV) injection to switch to oral therapy or discontinue antibiotics as soon as was clinically appropriate. In 2021, antibiotics given intravenously accounted for 31.8% of total antibiotic use (DDDs) in acute hospitals. The rate of IV antibiotic use in all secondary care was 0.85 DDDs per 1,000 population per day compared to 0.80 in 2020 and 0.95 in 2019 (**Figure 9**). In 2019, a national indicator was developed, by Scottish Government with support from ARHAI Scotland and SAPG, to measure progress with achieving reliable and timely review of IV antibiotic therapy. This indicator and its associated target was that use of IV antibiotics in hospitals will be no higher in 2022 than it was in 2018 and the data for 2021 show this is on track. ARHAI Scotland publishes these data in NSS Discovery dashboards on a quarterly basis to enable NHS boards to monitor local progress.

Figure 9: Acute and Non-Acute Hospital Use of Parenteral Antibiotics in Scotland, (defined daily doses per 1,000 occupied bed days; DDDs/1,000 OBDs), 2017 to 2021, by year.

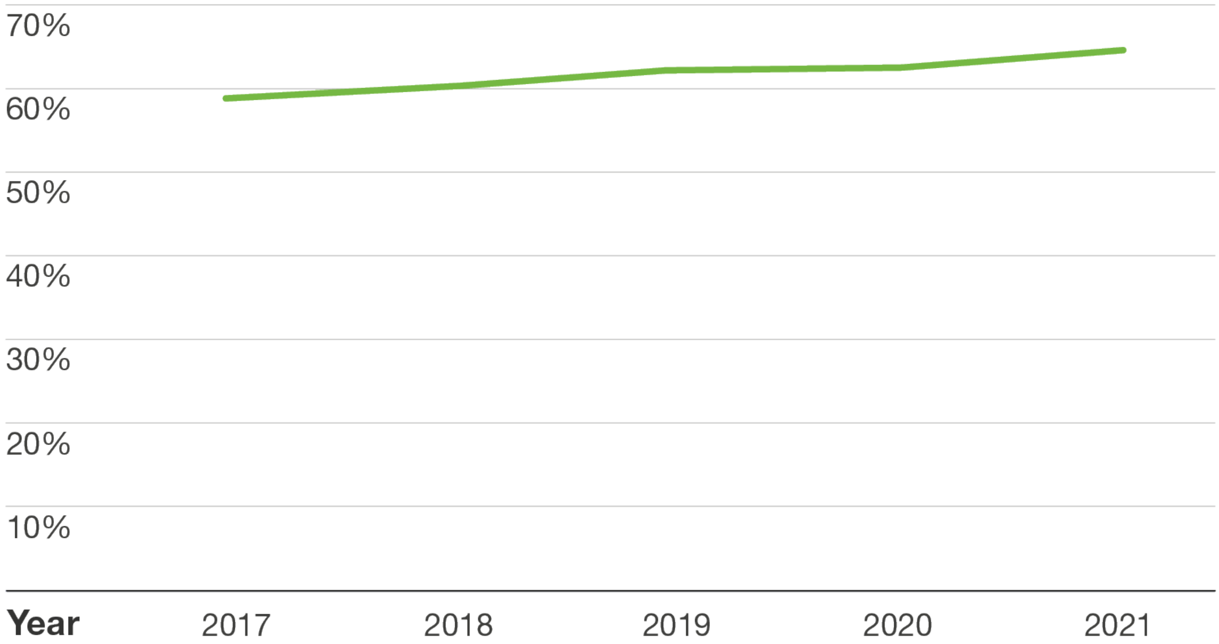


[Data Source: Hospital Medicines Utilisation Database (HMUD) and Information Services Division (ISD(S)1)]

Most suspected bacterial infections in patients in acute hospitals will be managed empirically, where the clinician has no information on the infecting organism nor on antibiotic susceptibility at the initiation of treatment. In such cases the choice of initial antibiotic treatment will be based on evidenced based antibiotic guidelines. These guidelines are intended to support clinicians through promoting use of narrow spectrum antibiotics where appropriate and minimising inappropriate use of broader spectrum treatments.

In 2021, 64.4% of antibiotic use (DDDs) in acute hospitals was Access group antibiotics compared to 63.1% in 2020 and 62.5% in 2019 (**Figure 10**). For more detail on use of particular antibiotics and antibiotic classes, see **Supplementary Data**.

Figure 10: Percentage of all antibiotics prescribed (DDDs) in acute hospitals in Scotland that belonged to the 'Access' group, 2017 to 2021.



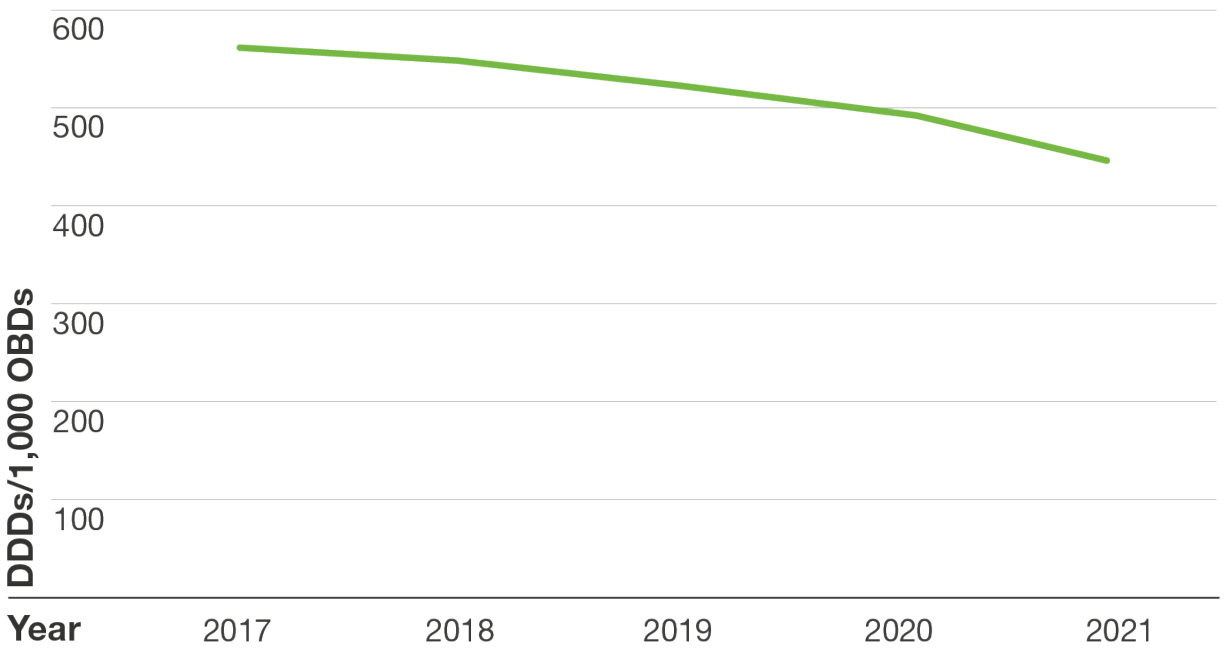
[Data Source: Hospital Medicines Utilisation Database (HMUD)]

One of the ambitions in the UK AMR NAP is a target to reduce by 10% the use of WHO Reserve and Watch categories of antibiotics in acute hospitals by 2024 (using 2018 as baseline).

In 2021, the rate of use of WHO Watch and Reserve antibiotics was 446.9 DDD/1,000 OBD, compared to 499.6 in 2020 and 524.4 DDD/1,000 OBD in 2019 (**Figure 11**). This is a year-on-year decrease of 5.3% ($p<0.001$) since 2017, with an overall reduction of 20.6% between 2017 and 2021.

These most recent data on use of Access, Watch and Reserve antibiotics suggest that hospital clinicians have continued to follow antibiotic guidelines and in this the second year of the COVID-19 pandemic there has been no move away from use of Access antibiotics for treatment or prophylaxis of infection in acute hospitals and at national level the ambition in the UK NAP for a 10% reduction in use of Watch and Reserve antibiotics remains on track.

Figure 11: 'Watch' and 'Reserve' group antibiotic prescribing in acute hospitals in Scotland (defined daily doses per 1,000 Occupied Bed Days; DDDs/1,000 OBDs), 2017 to 2021, by year.



[Data Source: Hospital Medicines Utilisation Database (HMUD) and Information Services Division (ISD(S)1)]

In 2022, ARHAI Scotland will collaborate with Public Health Scotland (PHS) to undertake preliminary analysis of patient level antibiotic use in acute hospitals using data from a new emerging national datamart. This will contain information generated from Hospital Electronic Medicines Prescribing and Medicines Administration (HEMPA) systems in NHS Scotland.

The data submission process is being automated and should provide near real-time data from inpatient electronic prescribing systems (excluding discharge prescriptions) on individual prescriptions and individual administrations. As these data are at patient level, basic patient characterisation and linkage to other data will be possible.

After discussion with stakeholders the initial priority for analysis of these data will be generation of intelligence on duration of antibiotic treatment in hospitalised patients. Use of shorter courses of antibiotics is a key stewardship area for the SAPG as evidence suggests that shorter courses of antibiotics for common infections are as effective as longer courses.

Currently, the only way to assess duration of treatment in hospitalised patients is by undertaking audit and point prevalence studies. These approaches are labour intensive. ARHAI Scotland, working with PHS, aims to develop intelligence from HEMPA using individual inpatient treatment data - total exposure to antibiotics for an infective episode including via different routes and different antibiotics. These data will provide intelligence on trends on duration of treatment over time, between geographical locations and before and after interventions all of which will be used to drive improvement.

Antibiotic use in acute hospitals key points

- **Antibiotic use was 8.6% lower than in 2017.**
- **The COVID-19 pandemic continues to have an impact on quantity of antibiotics used in acute hospitals.**
- **Use of WHO Access (first-line) antibiotics as proportion of total antibiotic use has increased in 2021.**
- **There has been a continued decreased use of WHO Watch and Reserve (restricted) antibiotics since 2017.**

Antibiotic use in animals

In the same way that optimisation of antibiotic use in humans is required to tackle the risk of AMR, the optimisation of antibiotic use in animals is also important. Historically, data on antibiotic use in animals have comprised sales data compiled at the UK level and published in the annual UK-Veterinary Antibiotic Resistance and Sales Surveillance (VARSS) Report.[4] The publication of animal AMU data in the Responsible Use of Medicines in Agriculture Alliance (RUMA) Targets Task Force 2 – One Year On 2021 Report[5] and VARSS Report of 2021[4] continue to demonstrate serious commitment to antibiotic stewardship in the face of ongoing bacterial disease challenge in animal species as part of a One Health response to AMR in the UK.

Scottish companion animal AMU data were made available from veterinary practices in Scotland contributing voluntarily to the Small Animal Veterinary Surveillance Network (SAVSNET). This provided an opportunity to further describe antibiotic prescribing in the animal component of the One Health ecosystem.

The recently updated Scotland's Healthy Animals website was created and is maintained by ARHAI Scotland working with stakeholders in the animal health sector and brings together expert advice on keeping animals healthy and antibiotic stewardship. Trusted guidance is signposted for all animal keepers and their vets, for countryside users, and for wildlife and rescue centres, and the website also hosts Scotland's Poultry Hub for poultry keepers, in particular smallholders.

Antibiotic use in companion animals

For the following section it should be noted that these data are obtained from a relatively small number of practices in Scotland contributing voluntarily to SAVSNET, and therefore cannot be assumed to be representative of all companion animal practices in Scotland. Additionally, COVID-19 is likely to have affected the level of contact of companion animals with their vets, with resultant impact on the number of consultations, reported in 2020 and 2021.

ARHAI will continue to work with animal health stakeholders, including the veterinary corporate practices, to attempt to increase the availability of antibiotic use surveillance data in animals.

A summary of the available data is provided in **Table 1**. In 2021, 13 veterinary practices in Scotland contributed data from 42,181 individual consultations and 25,228 individual animals. For this analysis, highest priority critically important antibiotic (HP-CIAs) 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.[6, 7]

Table 1: Summary characteristics for all companion animals in veterinary practices in Scotland contributing to SAVSNET, 2017 to 2021.

	2017	2018	2019	2020	2021
Number of contributing practices	11	15	15	13	13
Number of animals	26,138	30,145	36,933	24,181	25,228
Number of antibiotics prescribed	12,885	11,832	13,132	6,888	8,238
Number of consultations	57,886	54,824	69,992	37,794	42,181
Number of consultations resulting in prescription of at least one antibiotic	10,445	9,750	11,433	6,129	7,339
Percentage of consultations resulting in prescription of at least one antibiotic	18.0%	17.8%	16.3%	16.2%	17.4%
Percentage of antibiotics prescribed that were high priority critically important antibiotics (HP-CIAs)*	10.0%	9.6%	9.7%	9.4%	8.1%

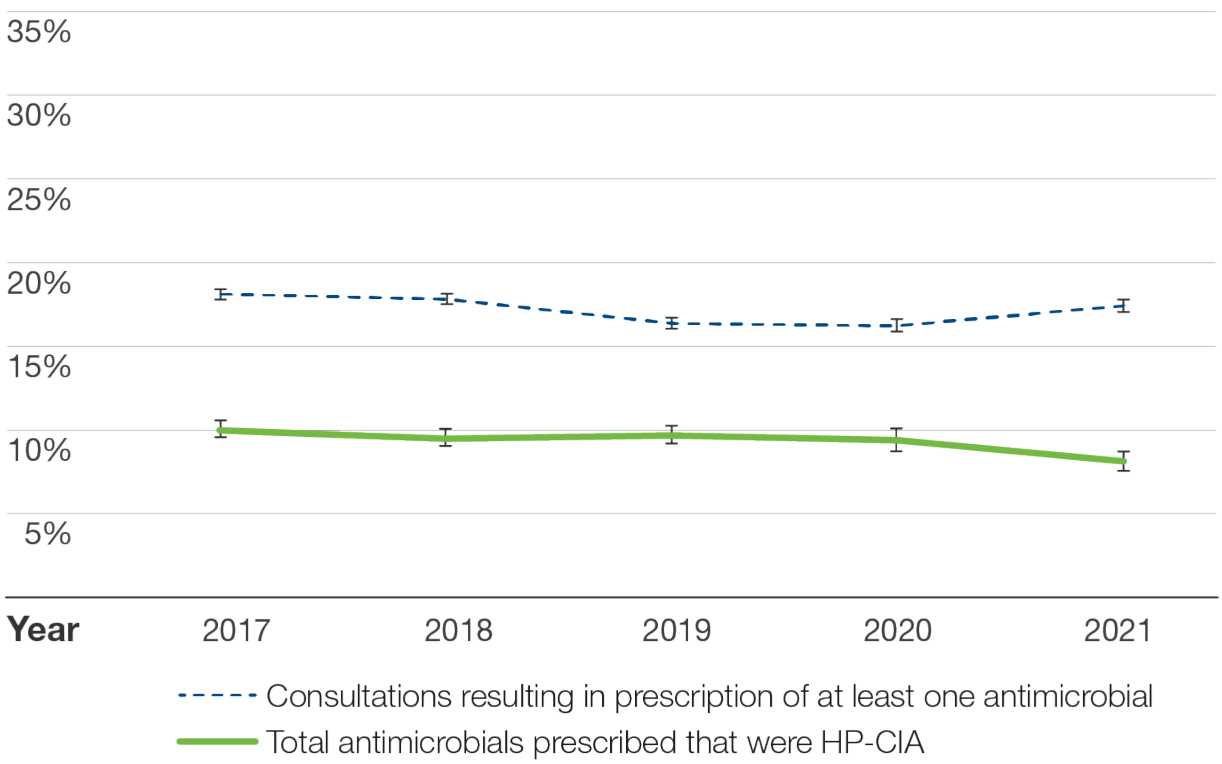
*Highest priority critically important antibiotics (HP-CIAs) are: cefovecin, ciprofloxacin, enrofloxacin, marbofloxacin, ofloxacin, orbifloxacin and pradofloxacin.

Footnote: These data are obtained from a relatively small number of practices in Scotland contributing voluntarily to SAVSNET, and therefore cannot be assumed to be representative of all companion animal practices in Scotland.

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

In 2021, among the participating veterinary practices, 17.4% of consultations for all companion animals resulted in the prescription of at least one antibiotic (**Figure 12**). This is a year-on-year decrease of 1.8% ($p<0.001$) since 2017. There has also been a year-on-year decrease in the percentage of antibiotics prescribed which were HP-CIAs since 2017 (3.9%, $p<0.001$) with a 13.4% ($p<0.05$) reduction between 2020 and 2021 for all companion animals (**Figure 12**). This is the lowest recorded usage of HP-CIAs since our monitoring of AMU began in the small number of practices contributing to SAVSNET in Scotland. This suggests that there is increasing awareness of prescribing guidelines among these veterinary practices. HP-CIAs would be considered as WHO Watch and Reserve antibiotics when used in human health. For information on trends in use of these antibiotics groups in humans see **Figure 3** and **Figure 11**.

Figure 12: Trends in prescribing of antibiotics (including HP-CIAs) for all companion animals, in veterinary practices in Scotland contributing to SAVSNET, 2017 to 2021.



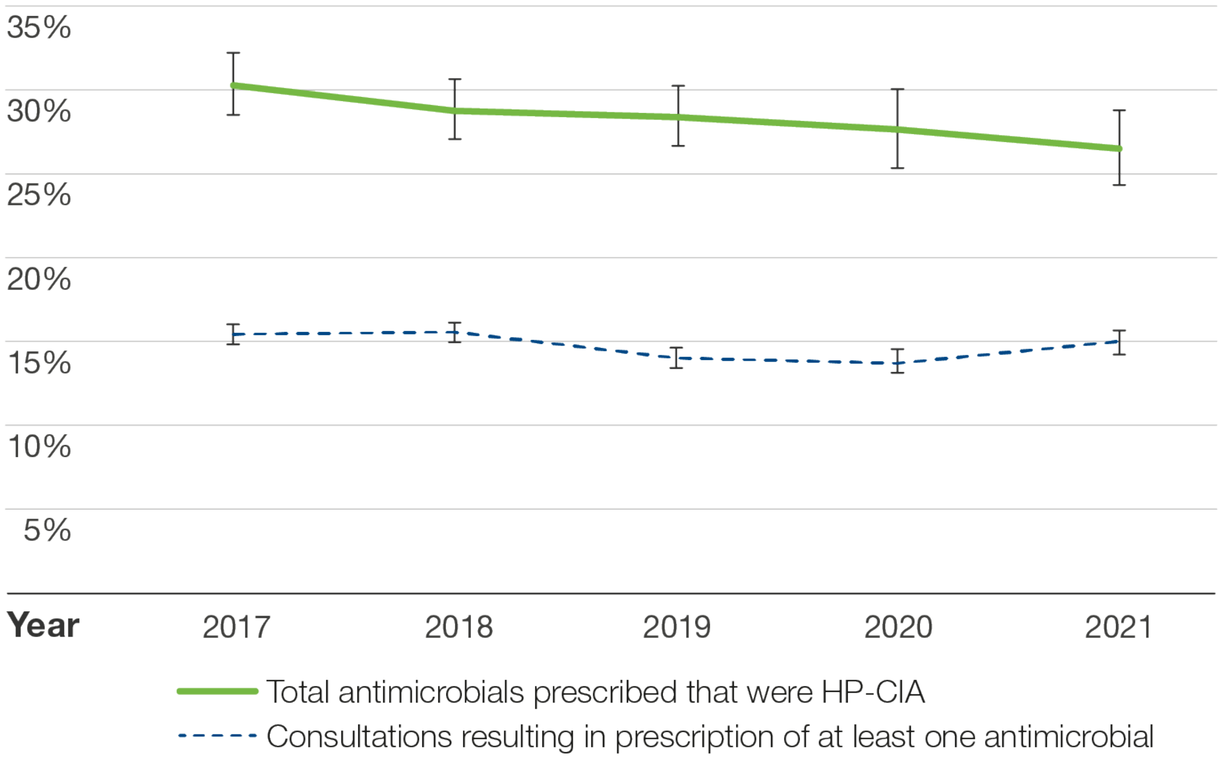
Footnote: These data are obtained from a relatively small number of practices in Scotland contributing voluntarily to SAVSNET, and therefore cannot be assumed to be representative of all companion animal practices in Scotland.

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

The following figures summarise overall trends in aspects of AMU for cats and dogs in in the small number of veterinary practices submitting to SAVSNET for 2017 to 2021. These include antibiotics prescribed, routes of administration and main reasons for consultation. It is important to be aware of the contextual realities of veterinary practice when interpreting this information. For example, some species are difficult to medicate by some routes of administration; for some species there is a very limited range of therapeutic options due to either or both toxicity and authorisation of products for use in a particular species.

Between 2017 and 2021, there has been a year-on-year decrease in the percentage of consultations for cats which resulted in the prescription of at least one antibiotic (2.0%, $p<0.05$). There has also been a year-on-year decrease in the percentage of antibiotics prescribed for cats which were HP-CIAs (3.1%, $p<0.05$) (**Figure 13**). There is a higher recorded usage of HP-CIAs in cats than dogs (**Figure 13** and **Figure 14**), largely because of a single long-acting injectable product containing 3rd generation cephalosporin (**Figure 15** and **Figure 16**). Some cats are difficult to medicate by the oral route and this product offers an effective alternative means of ensuring adequate treatment that might otherwise be impossible to achieve. However, 3rd generation cephalosporins are classified by EMA AMEG as Category B (Restrict) antibiotics which means that they should only be used when supported by antibiotic susceptibility testing, where drugs in categories C (Caution) or D (Prudence) are not effective AND where topical therapy is not feasible or effective.

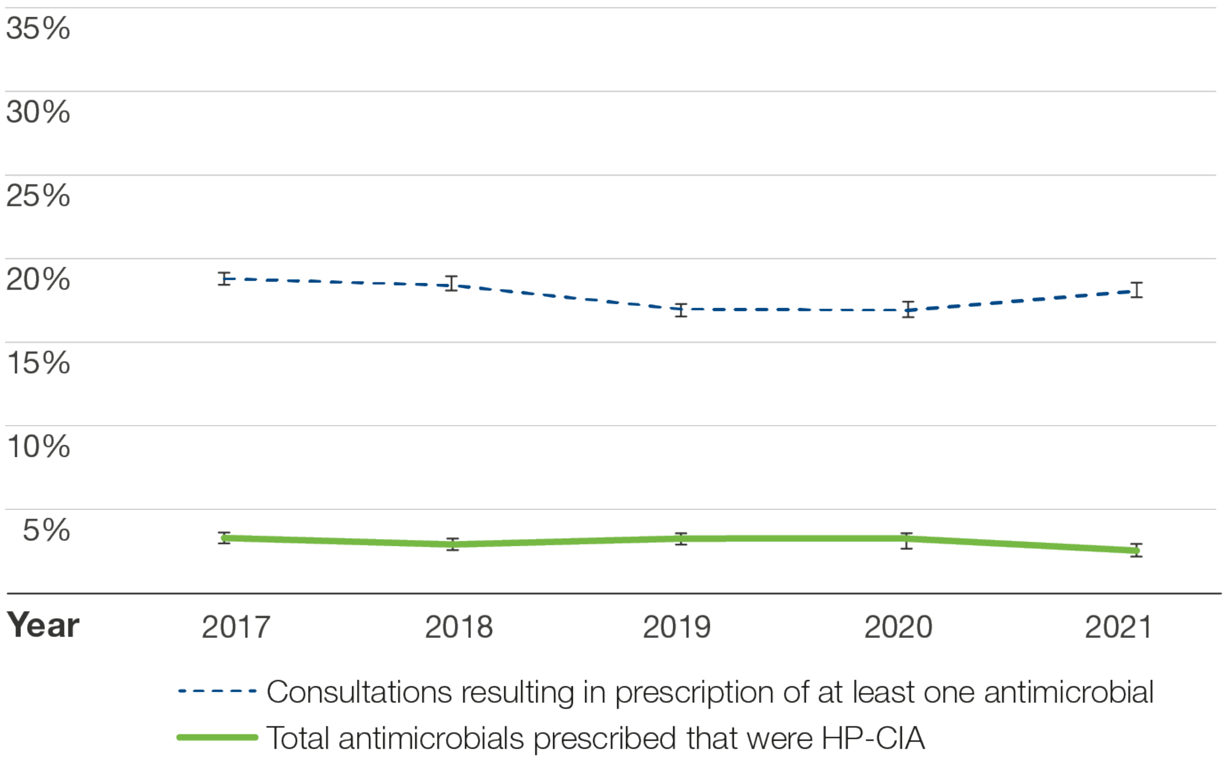
Figure 13: Trends in prescribing of antibiotics (including HP-CIAs) for cats, in veterinary practices in Scotland contributing to SAVSNET, 2017 to 2021.



Footnote: These data are obtained from a relatively small number of practices in Scotland contributing voluntarily to SAVSNET, and therefore cannot be assumed to be representative of all companion animal practices in Scotland.

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

Figure 14: Trends in prescribing of antibiotics (including HP-CIAs) for dogs, in veterinary practices in Scotland contributing to SAVSNET, 2017 to 2021.



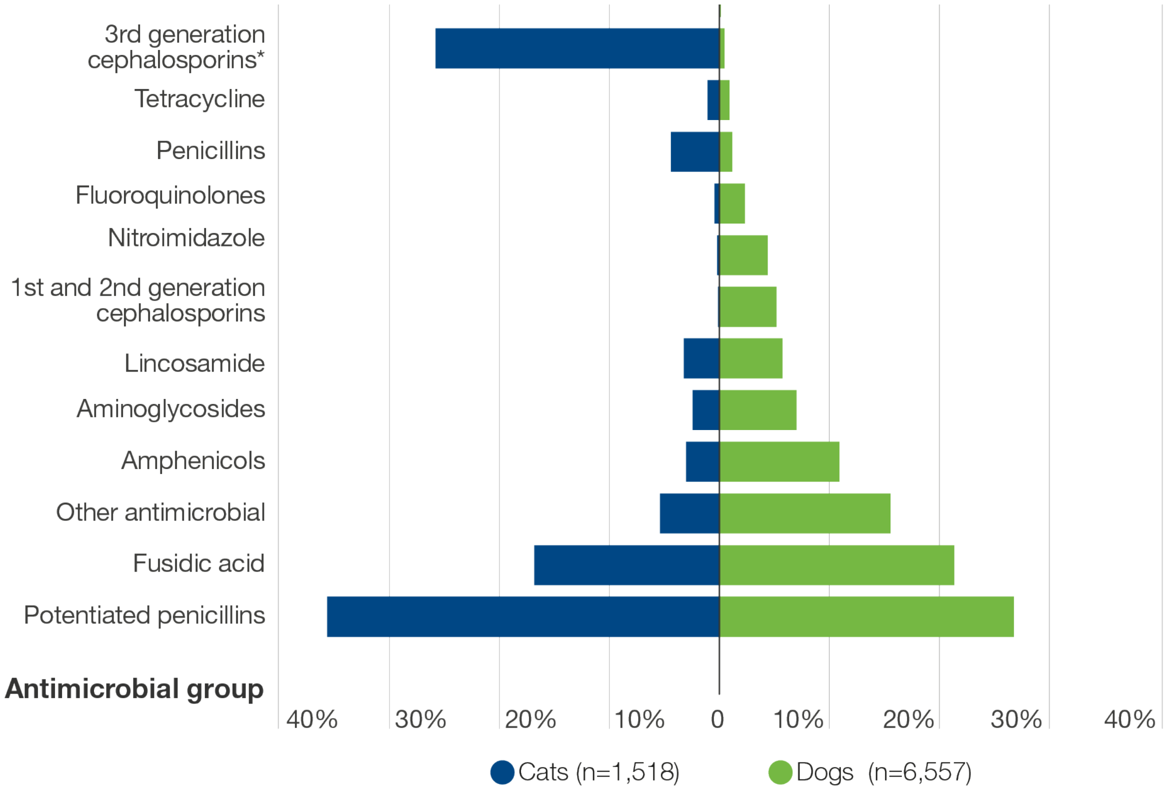
Footnote: These data are obtained from a relatively small number of practices in Scotland contributing voluntarily to SAVSNET, and therefore cannot be assumed to be representative of all companion animal practices in Scotland.
[Data source: Small Animal Veterinary Surveillance Network (SAVSNET)]

Between 2017 and 2021, there has been year-on-year decreases in the percentage of consultations for dogs which resulted in the prescription of at least one antibiotic (1.8%, $p<0.001$) and in the percentage of antibiotics prescribed for dogs which were HP-CIAs (4.2%, $p<0.05$) (**Figure 14**).

Antibiotic groups

In the small number of participating practices in 2021, there were 6,557 antibiotics prescribed for dogs and 1,518 antibiotics prescribed for cats. The most frequently prescribed antibiotic group was potentiated penicillins for cats (35.7%) and dogs (26.6%), followed by third generation cephalosporins for cats (25.9%) and topical antibiotic fusidic acid for cats (16.9%) and dogs (21.2%) (Figure 15).

Figure 15: Percentage of total antibiotics prescribed, by antibiotic family, for cats and dogs in veterinary practices in Scotland contributing to SAVSNET for 2021.



Footnote: These data are obtained from a relatively small number of practices in Scotland contributing voluntarily to SAVSNET, and therefore cannot be assumed to be representative of all companion animal practices in Scotland.

Proportions of macrolides, sulphonamides and other beta-lactams not displayed due to small numbers.

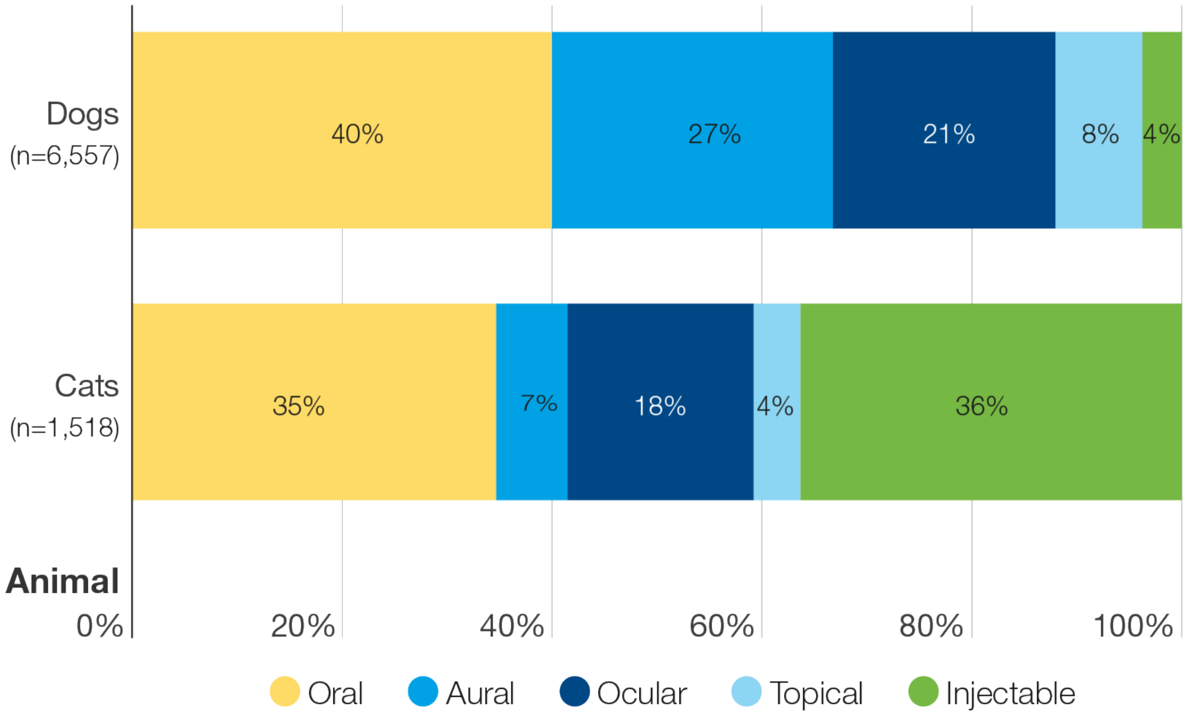
*3rd generation cephalosporins are usually categorised as part of a '3rd/4th/5th generation cephalosporin' grouping, but no 4th or 5th generation cephalosporins are used in animals.

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

Route of administration

The route of administration of antibiotics for dogs and for cats are shown in **Figure 16**. This is likely to reflect differences in the ease of medication by some routes of administration. For cats, the injectable route of administration was most common (36.3%). In contrast, for dogs, oral route of administration was most common (40.1%).

Figure 16: Route of administration of antibiotics for cats and dogs in veterinary practices in Scotland contributing to SAVSNET, 2021.



Footnote: These data are obtained from a relatively small number of practices in Scotland contributing voluntarily to SAVSNET, and therefore cannot be assumed to be representative of all companion animal practices in Scotland.

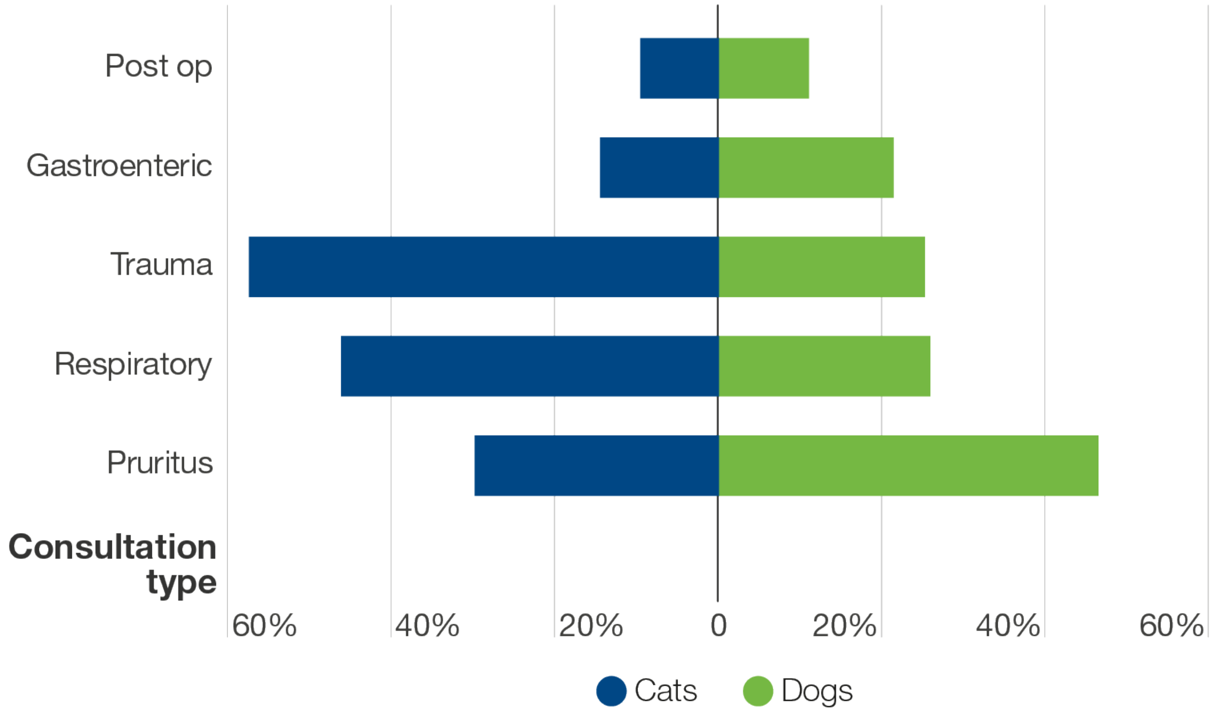
The following routes of administration were excluded from the visualisation but not the dataset: Dogs: Unknown (n=5, 0%), Cats: Unknown (n=2, 0%).

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

Prescription of antibiotic by syndrome

The caveats at the beginning of this section should be noted. **Figure 17** shows the percentage of consultations by the main presenting syndrome that resulted in prescription of an antibiotic in cats and dogs. **Figure 18** and **Figure 19** focus on the importance of topical treatment of pruritus without recourse to systemic therapy.

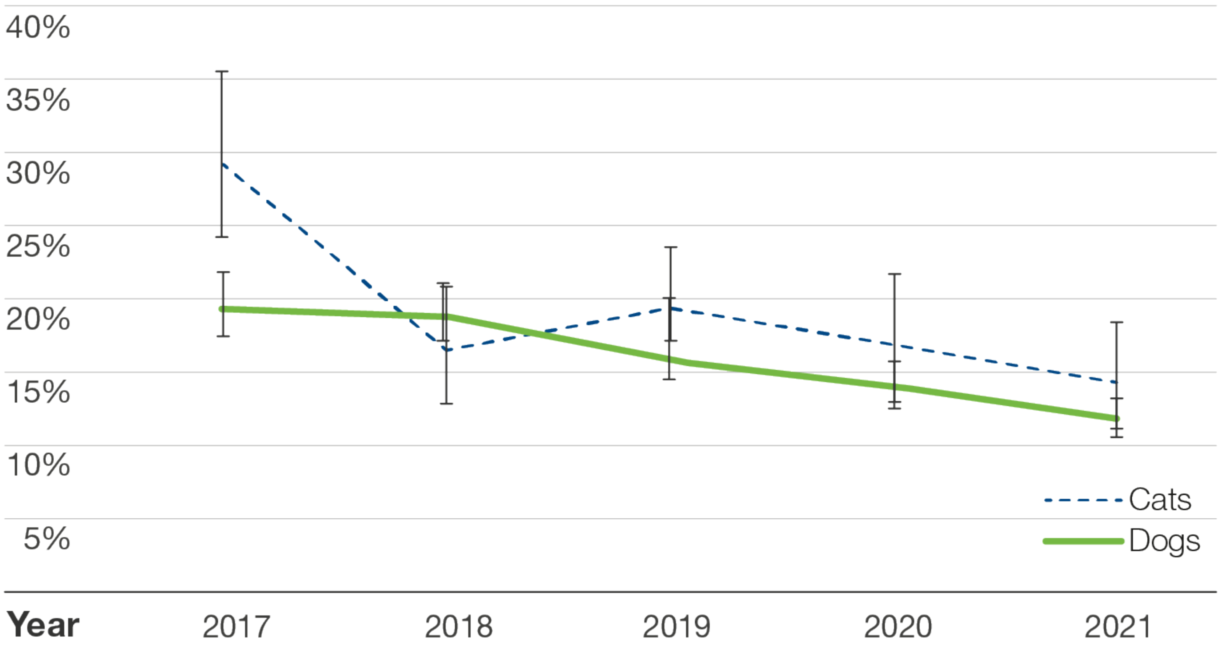
Figure 17: Percentage of consultations which resulted in prescription of an antibiotic by main presenting syndrome for cats and dogs in veterinary practices in Scotland contributing to SAVSNET for 2021.



Footnote: These data are obtained from a relatively small number of practices in Scotland contributing voluntarily to SAVSNET, and therefore cannot be assumed to be representative of all companion animal practices in Scotland.
[Data source: Small Animal Veterinary Surveillance Network (SAVSNET)]

Between 2017 and 2021, there has been a year-on-year decrease in the percentage of pruritus consultations for cats which resulted in the prescription of a systemic antibiotic (14.2%, p<0.001); there has also been a year-on-year decrease in the percentage for dogs (12.4%, p<0.001) (**Figure 18**).

Figure 18: Proportion of pruritus consultations during which antibiotics authorised for systemic administration were prescribed for cats and dogs in veterinary practices in Scotland contributing to SAVSNET, 2017 to 2021.

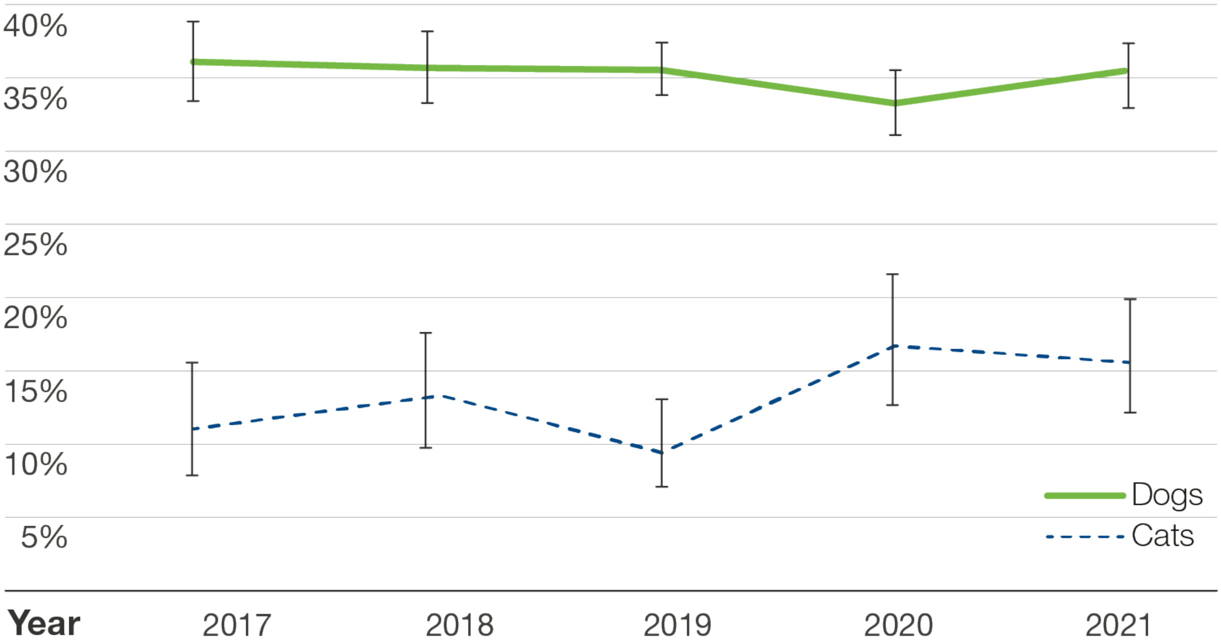


Footnote: These data are obtained from a relatively small number of practices in Scotland contributing voluntarily to SAVSNET, and therefore cannot be assumed to be representative of all companion animal practices in Scotland.

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

Between 2017 and 2021, the percentage of pruritus consultations for cats and dogs which resulted in the prescription of topical antibiotic remained stable (**Figure 19**).

Figure 19: Proportion of pruritus consultations during which antibiotics authorised for topical administration were prescribed for cats and dogs in veterinary practices in Scotland contributing to SAVSNET, 2017 to 2021.



Footnote: These data are obtained from a relatively small number of practices in Scotland contributing voluntarily to SAVSNET, and therefore cannot be assumed to be representative of all companion animal practices in Scotland. For further information on prescribing patterns by other types of consultations for cats and dogs, see **Supplementary Data**.

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

Animal antimicrobial use key points

- **Antibiotics are very important medicines in animal species and ongoing data collection contributes to developing the evidence base pertaining to AMU in animals and their impact on AMR.**
- **Overall antibiotic use in companion animals is reducing over time in the small number of veterinary practices which contribute to SAVSNET in Scotland.**
- **Trends in AMU suggest that there is increasing awareness of prescribing guidelines among veterinary clinicians contributing to surveillance in Scotland.**
- **Engagement and support from animal stakeholder groups continues to be essential in the development of this intelligence. Over the course of the last year, RUMA has launched its Companion Animal & Equine Group to support antibiotic stewardship in these species.**
- **Further close working with SAVSNET to encourage practices to participate in the network is important.**
- **The recently updated Scotland's Healthy Animals website continues to provide guidance for vets and animal keepers on disease avoidance and antibiotic stewardship.**

Antimicrobial resistance in humans

AMR is a major global threat across human, animal, plant, and environmental sectors threatening the effective prevention and treatment of common pathogens. AMR is a natural phenomenon but is accelerated by the overuse and misuse of antimicrobials.[8]

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.[1]

Surveillance data, as presented in this ARHAI Scotland 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.

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 2021, there were an estimated 1,288 bloodstream infections (BSI) caused by antibiotic resistant bacteria of public health concern compared to 1,312 in 2020 (**Table 2**). There were an estimated 1,133 and 174 Gram-negative and Gram-positive antibiotic resistant bacteraemia, respectively. Drug resistant bacteraemia caused by Gram-negative bacteria accounted for 86.5% of all drug resistant bacteraemia. Importantly, nearly a quarter of *E. coli* bacteraemia (ECB) in Scotland were resistant to one or more key antibiotics, accounting for an estimated 962 cases, with *K. pneumoniae* and *E. faecium* being the next most common drug resistant organisms reported in blood isolates.

ARHAI Scotland share these data with the UK 4 Nations Surveillance Group and the Advisory Committee on Antimicrobial Prescribing, Resistance and Healthcare Associated Infection thus allowing the UK Government to monitor progress against the ambitions laid out in the five-year AMR NAP. Wider Gram-negative bacteraemia surveillance to support NHS Boards and the AMR NAP is being developed by ARHAI Scotland.

Table 2: Estimated number of drug resistant bacteraemia in Scotland, 2021, by organism.

Organisms (n=total number of bacteraemia)	Percentage resistant to at least one key antibiotic	Estimated number of resistant bacteraemia
Gram-negative bacteraemia (n = 5,600)	**19.9%**	**1,113.4**
Escherichia coli (n=4,292)	22.4%	962.5
Klebsiella pneumoniae (n=743)	15.0%	111.8
Klebsiella oxytoca (n=247)	5.3%	13.1
Acinetobacter species (n=57)	0.0%	0.0
Pseudomonas aeruginosa (n=261)	10.0%	26.1
Gram-positive bacteraemia (n = 2,646)	**6.6%**	**174.2**
Enterococcus faecium (n=276)	40.4%	111.4
Enterococcus faecalis (n=516)	0.6%	3.2
Staphylococcus aureus (n=1,590)	3.6%	57.0
Streptococcus pneumoniae (n=264)	1.0%	2.6
Total number of bacteraemia (n = 8,246)	**15.6%**	**1,287.6**

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

Burden of AMR key points

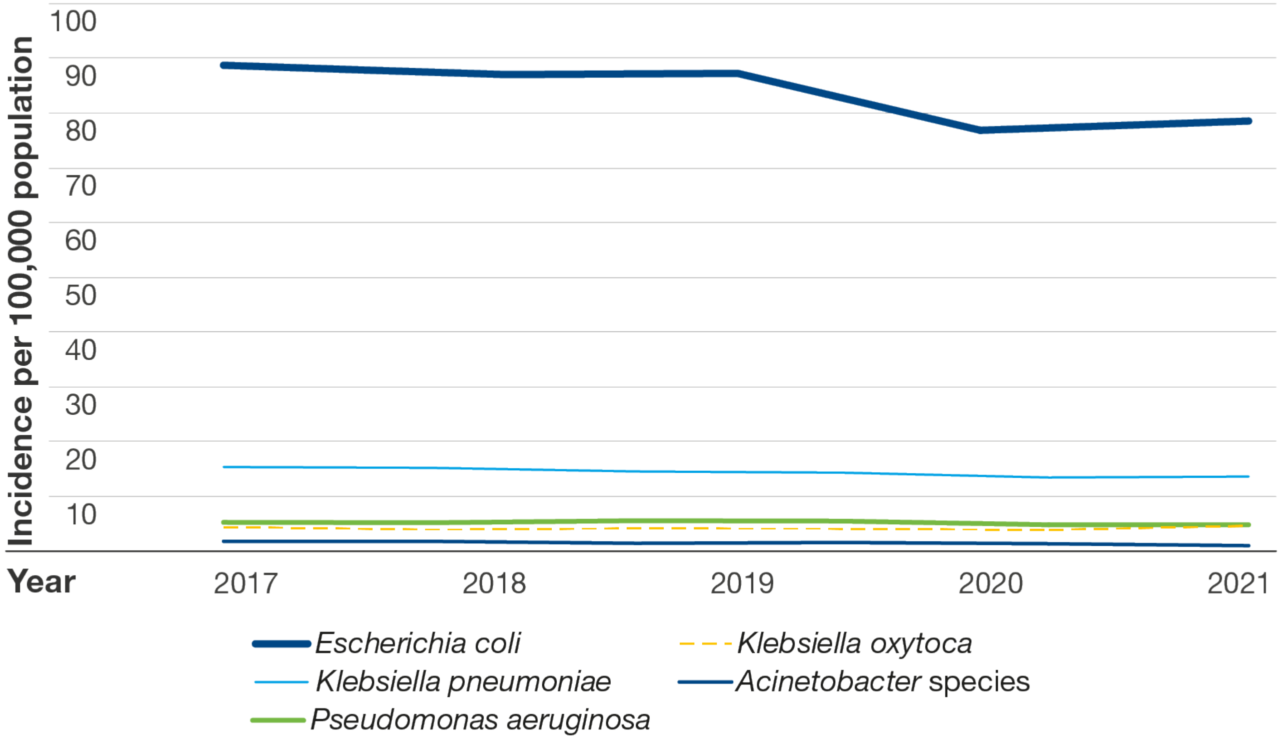
- **Reducing the burden of drug resistant infections is critical to controlling and containing AMR.**
- **There were an estimated 1,288 drug resistant bacteraemia in 2021.**
- **86.5% of drug resistant bacteraemia were caused by Gram-negative bacteria with the remaining 13.5% caused by Gram-positive bacteria.**
- **Nearly a quarter of *E. coli* bacteraemia (ECB) in Scotland were resistant to one or more key antibiotics.**
- **Continued focus on reducing Gram-negative infections is essential.**
- **Robust intelligence and metrics are required to plan, prioritise and evaluate interventions to reduce the burden.**

Gram-negative bacteraemia

Gram-negative bacteria are an important cause of serious infections in both healthcare and community settings. In the UK one of the biggest drivers of AMR is a rise in the incidence of infections, particularly Gram-negatives infections.[9] In 2021, *E. coli* was the most common cause of Gram-negative bacteraemia in Scotland with 4,292 cases reported and an incidence of 78.5 per 100,000 population (**Figure 20**). There has been an overall 3.4% (p<0.001) year-on-year decrease in ECB incidence over the last five years but the incidence remained stable between 2021 and 2022 (p=0.4).

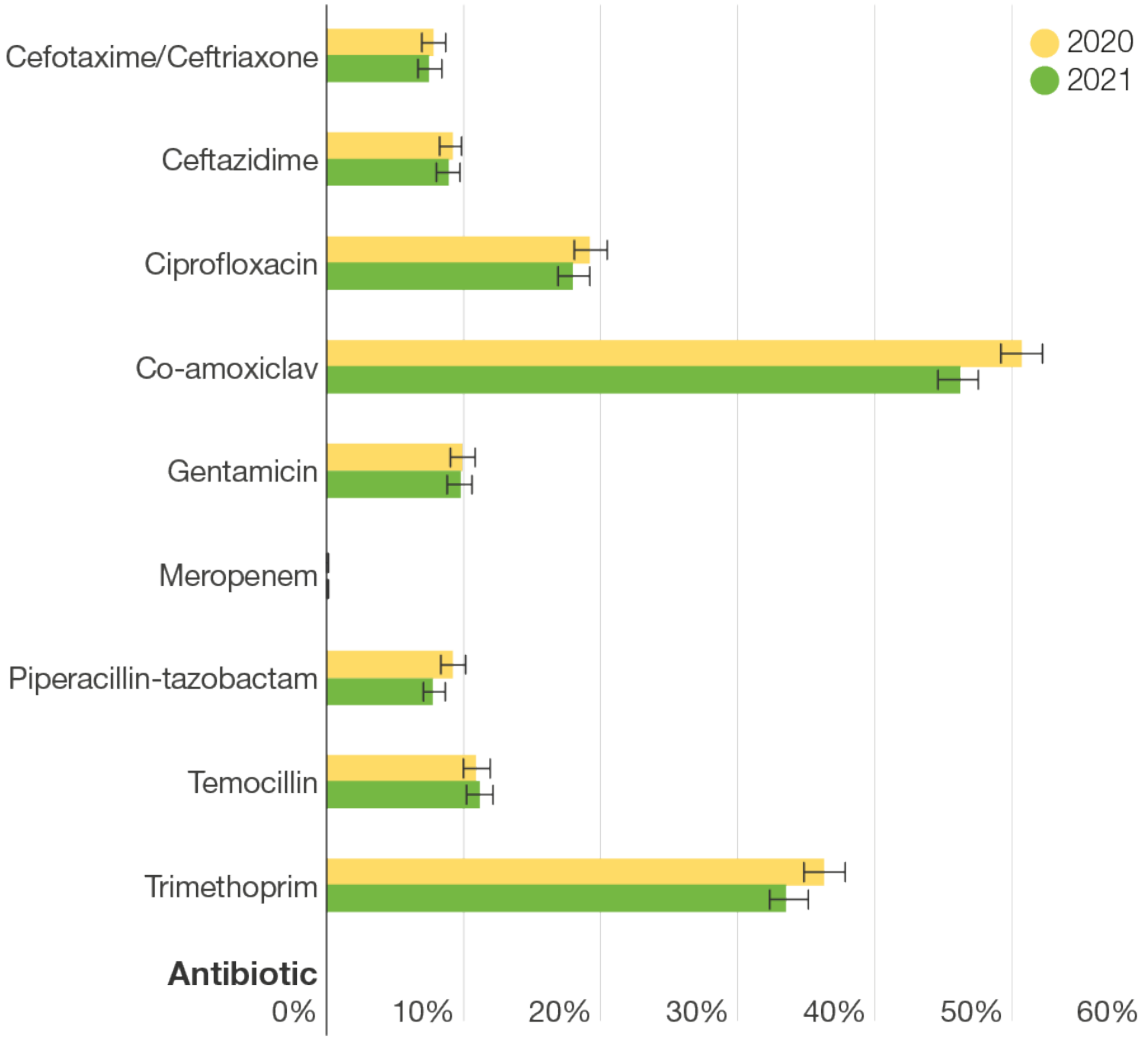
Non-susceptibility in ECB isolates has remained stable between 2020 and 2021 except for a decrease in co-amoxiclav non-susceptibility from 50.7% to 46.2% (p<0.001) (**Figure 21**). Co-amoxiclav is a WHO Watch antibiotic on the UK amended list, commonly used in acute hospitals, it is therefore encouraging to observe a reduction in non-susceptibility. (See **Supplementary Data** for data on hospital use of co-amoxiclav.)

Figure 20: Annual incidence of Gram-negative bacteraemia per 100,000 population in Scotland, 2017 to 2021, by five most frequently reported organisms.



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

Figure 21: Non-susceptibility of *E. coli* bacteraemia isolates in Scotland, 2020 to 2021.

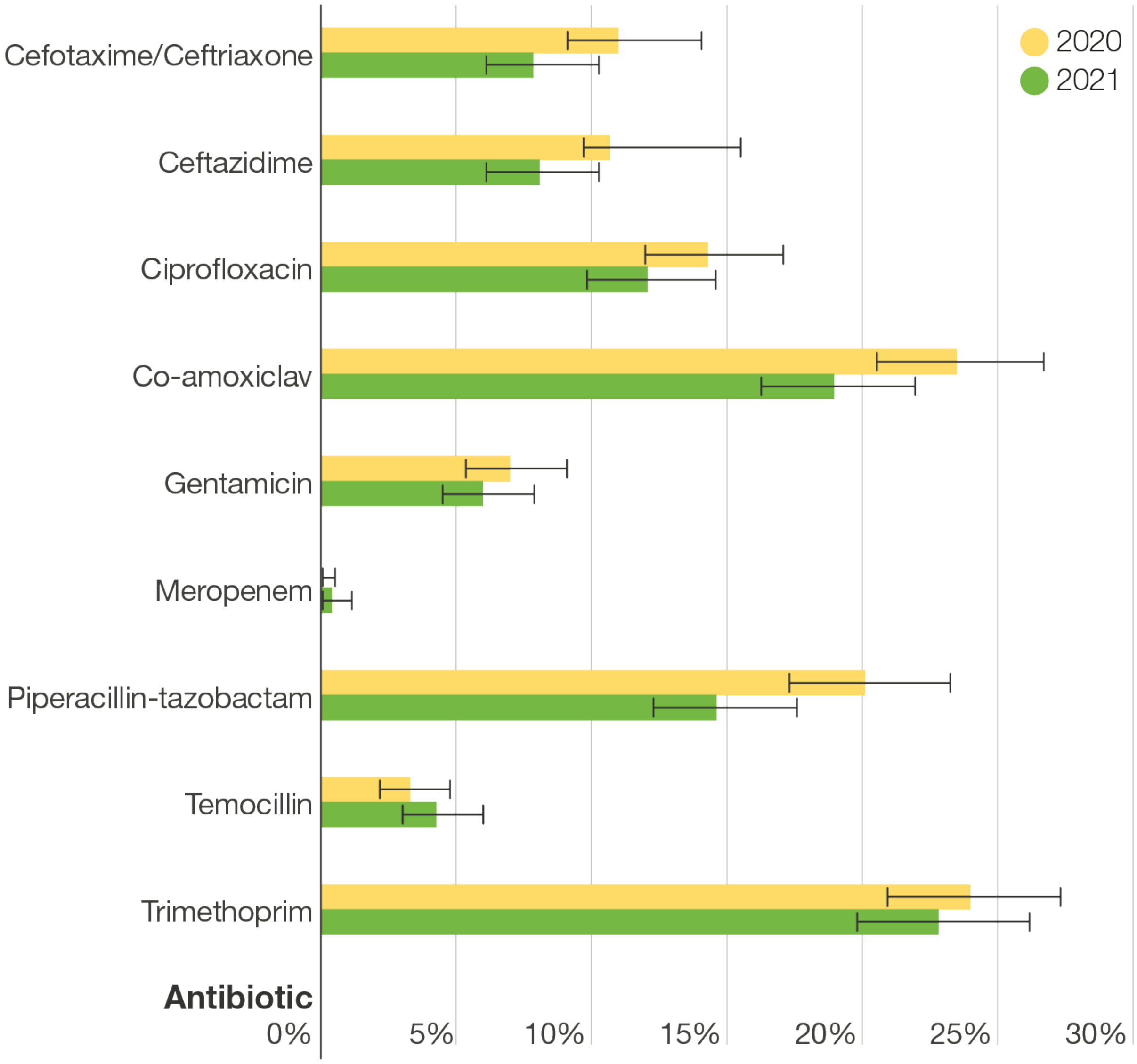


[Data source: Electronic Communication of Surveillance in Scotland (ECOSS)]

Since 2017, the incidence of bacteraemia caused by *K. pneumoniae*, *Pseudomonas aeruginosa* (*P. aeruginosa*), *Klebsiella oxytoca* (*K. oxytoca*) and *Acinetobacter* species has remained stable (**Figure 20**). Despite their combined incidence being lower than that of *E. coli* bacteraemia alone, *K. pneumoniae, P. aeruginosa, K. oxytoca* and *Acinetobacter* species still represent a significant burden of infection.

In 2021, 743 cases of *K. pneumoniae* bacteraemia were reported, with an incidence of 13.6 per 100,000 population. *K. pneumoniae,* are an important cause of healthcare associated infection (HCAI), especially UTIs, respiratory tract infections and bacteraemias.[10] Clinical management of *Klebsiella* infections is becoming increasingly difficult due to AMR, particularly with regards to acquired carbapenemases.[11] Non-susceptibility of *K. pneumoniae* blood isolates remained stable between 2020 and 2021 (**Figure 22**).

Figure 22: Non-susceptibility of *K. pneumoniae* bacteraemia isolates in Scotland, 2020 to 2021.



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

P. aeruginosa is an opportunistic pathogen found in a wide variety of environments including soil and water. It is a major cause of illness and death in humans with immunosuppressive and chronic conditions, and infections in these patients are difficult to treat due to a number of antibiotic resistance mechanisms.[12] In 2021, there were 261 cases of *P. aeruginosa* bacteraemia in Scotland with a rate of 4.8 per 100,000 population. Non-susceptibility in *P. aeruginosa* blood isolates has remained stable ($p>0.05$) between 2020 and 2021 (see **Supplementary Data**).

Acinetobacter spp. is a widespread environmental opportunistic pathogen frequently responsible for outbreaks in health-care facilities, particularly in Intensive Care Units (ICU).[13] It can easily survive in the hospital setting for long periods.[13] In 2021, there were 57 cases of *Acinetobacter* spp. bacteraemia with a rate of 1.0 per 100,000 population. Non-susceptibility in *Acinetobacter* spp. blood isolates was 40.4%, 2.1% and 0.0% in 2021 for ciprofloxacin, gentamicin and meropenem respectively, compared to 33.9%, 6.2% and 1.6% in 2020. It should be noted that numbers are small for *Acinetobacter* spp. and so changes in non-susceptibility should be interpreted with caution (see **Supplementary Data**).

Throughout 2021, ARHAI Scotland have continued to monitor Gram-negative bacteraemia and routinely report the findings in NSS Discovery. This enables NHS Boards to benchmark against other Boards and identify strengths and areas for improvement and implementation of quality improvement initiatives. Furthermore, the intelligence generated for AMR in Gram-negative bacteria is used to guide empirical antibiotic use and improve patient outcomes.

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 2020, non-susceptibility in ECB has remained stable except for a decrease in co-amoxiclav.**
- **Since 2020, non-susceptibility of *K. pneumoniae* blood isolates has remained stable.**

Urinary tract infections caused by *Escherichia coli*

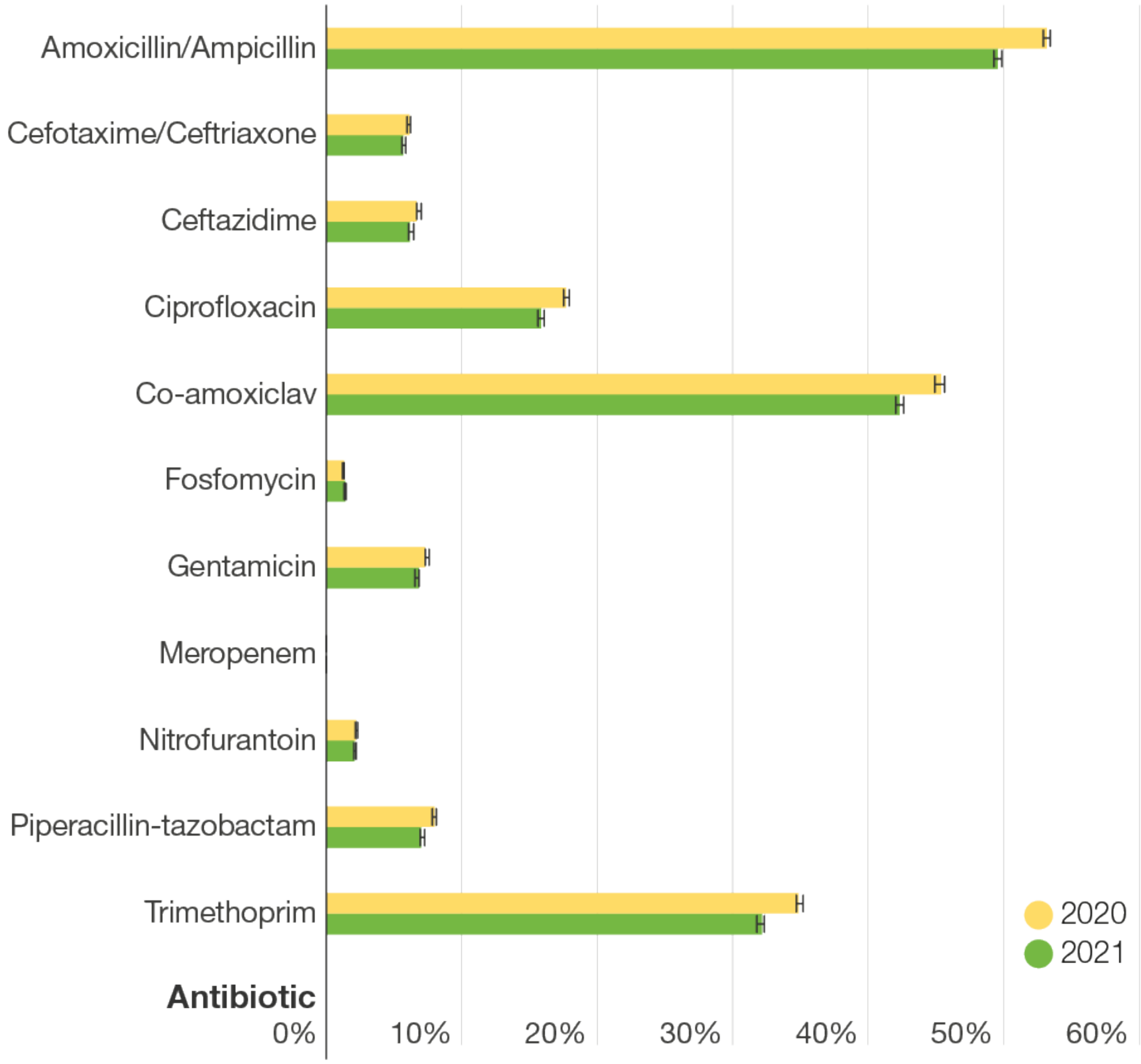
Urinary tract infections (UTIs) are among the most common bacterial infections acquired in the community and in hospitals. In individuals without anatomical or functional abnormalities, UTIs are generally self-limiting, but have a propensity to recur. Although generally self-limiting, treatment of UTIs with antibiotics leads to a more rapid resolution of symptoms and is more likely to clear bacteriuria, but also selects for resistant uropathogens and commensal bacteria, adding to the burden of AMR.[14] The development of resistance in urinary isolates can act as an early warning of resistance in bacteria causing more serious infections.[15] Increasing resistance necessitates prudent use of antibiotics. Knowledge of the common causative uropathogens, including local susceptibility patterns, is essential in determining appropriate empiric therapy.[16]

ARHAI Scotland use these data to support SAPG and NHS Boards Antimicrobial Management Teams (AMTs) to optimise antibiotic prescribing and stewardship ensuring empiric guidelines are based on current AMR.

ARHAI Scotland lead on the National Hydration Adult and Children's Think2DrinkH2O campaigns, and the National Catheter Passport, adopting a collaborative approach to reducing UTI and catheter associated urinary tract Infection (CAUTI). These resources support reduction of ECB and prudent antibiotic prescribing.

E. coli is the most common bacteria isolated from urine specimens. In 2021, there were 127,377 cases of *E. coli* from urine samples reported through Electronic Communication of Surveillance in Scotland (ECOSS), compared to 115,845 in 2020. *E. coli* bacteriuria results in ECOSS are used as a proxy indicator of UTI and continue to be monitored, generating evidence for optimisation of antibiotic prescribing. Between 2020 and 2021, antimicrobial non-susceptibility in *E. coli* urinary isolates has seen a reduction in all commonly used antibiotics tested, except for fosfomycin which increased from 1.4% to 1.6% ($p<0.001$) (**Figure 23**). Oral fosfomycin is commonly used to treat UTIs and is on the WHO Watch and Reserve list. (See **Supplementary Data** for data on WHO Watch and Reserve antibiotics used in primary and secondary care.)

Figure 23: Non-susceptibility of *E. coli* urinary isolates in Scotland, 2020 to 2021.



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

AMR in urinary tract infections key points

- **UTIs are commonly 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.**
- **Between 2020 and 2021, non-susceptibility of *E. coli* urinary isolates has reduced apart from an increase in fosfomycin.**

Carbapenemase-producing organisms

Carbapenems are potent beta-lactam antibiotics with a broad spectrum of activity, often reserved as last-line agents for the treatment of bacterial infections.[17] Carbapenem-resistant organisms (CROs) have been gradually increasing worldwide since they were first identified more than 30 years ago.[18] 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 rendering many beta-lactams ineffective.[19] Carbapenemase enzymes are often carried on mobile genetic elements allowing for horizontal transfer between strains, species and genera.[19, 20]

In 2021, 55 carbapenemase-producing organisms (CPO) were reported with a rate of 1.0 per 100,000 population. This compares to 59 CPOs in 2020 with a rate of 1.1 per 100,000 population. The rate of CPO has remained stable between 2020 and 2021, however there has been an overall year-on-year decrease of 14.3% (p<0.001) between 2017 and 2021 (**Figure 24**). This decrease can likely be attributed to the impact of the COVID-19 pandemic, with a reduction in foreign travel and changes in hospital activity.

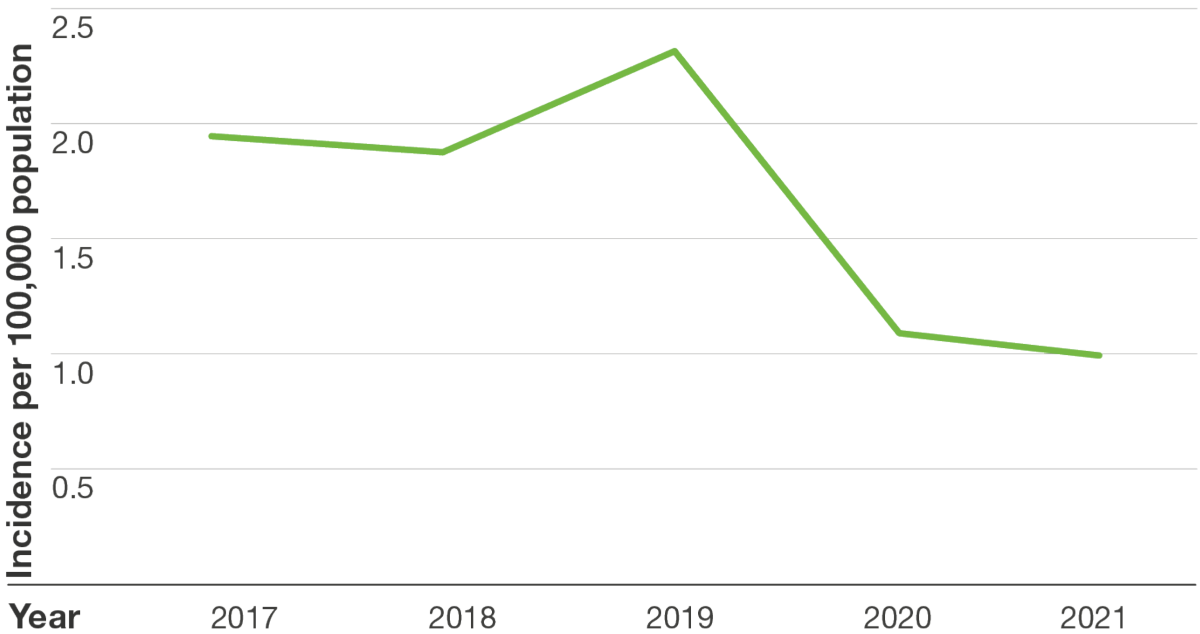
The majority of CPOs identified in 2021 were carbapenemase-producing *Enterobacterales* (CPE), (n= 56, 94.9%), and the remaining were non-fermenters such as *Acinetobacter* spp. and *P. aeruginosa*. In 2021 the most frequently identified enzyme genes were oxacillinase

(OXA)-48 followed by New Delhi Metallo-beta-lactamase (NDM) and Verona integrin-encoded metallo-beta-lactamase (VIM) (**Figure 25**).

For the first time, this report contains antimicrobial minimum inhibitory concentrations (MICs) corresponding to enzyme type. Each enzyme confers various spectrums of resistance impacting on the choice of therapeutic options (see **Supplementary Data**).

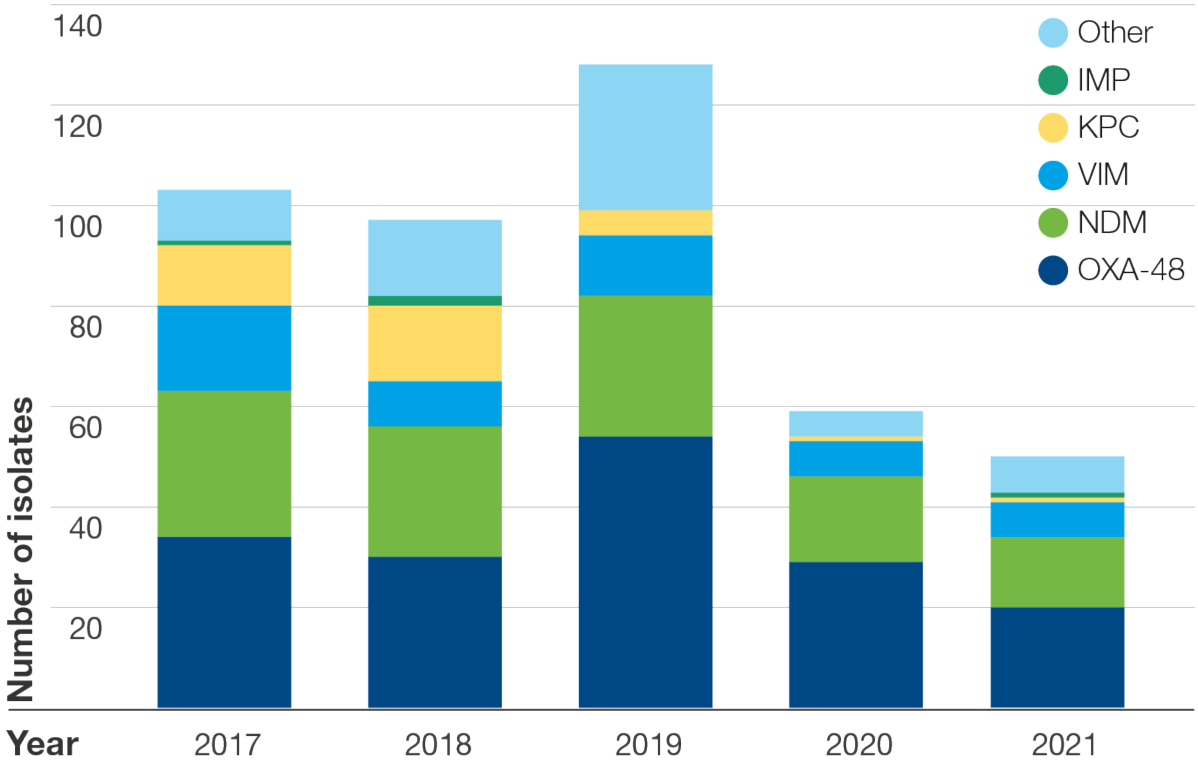
ARHAI Scotland will continue to develop further intelligence relating to CPO epidemiology in Scotland. This will include a review of the literature and linkage of CPO enzymes and MIC data to risk factors and patient outcome. As ARHAI Scotland gather more information, the findings will be used to support SAPG and the Scottish Microbiology and Virology Network, driving forward the antibiotic stewardship agenda.

Figure 24: Incidence of CPOs per 100,000 population in Scotland, 2017 to 2021.



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

Figure 25: Number of CPO isolates (first isolation from all body sites) reported in Scotland, 2017 to 2021, by enzyme type and year.



[Data source: Electronic Communication of Surveillance in Scotland (ECOSS) and Scottish Microbiology Reference Laboratory (SMiRL)]

Gram-positive bacteraemia

Gram-positive bacteria are significant pathogens and can cause a range of infections in both the healthcare and community setting. (See **Supplementary Data** for AMR in *Staphylococcus aureus.)*

Enterococcal bacteraemia

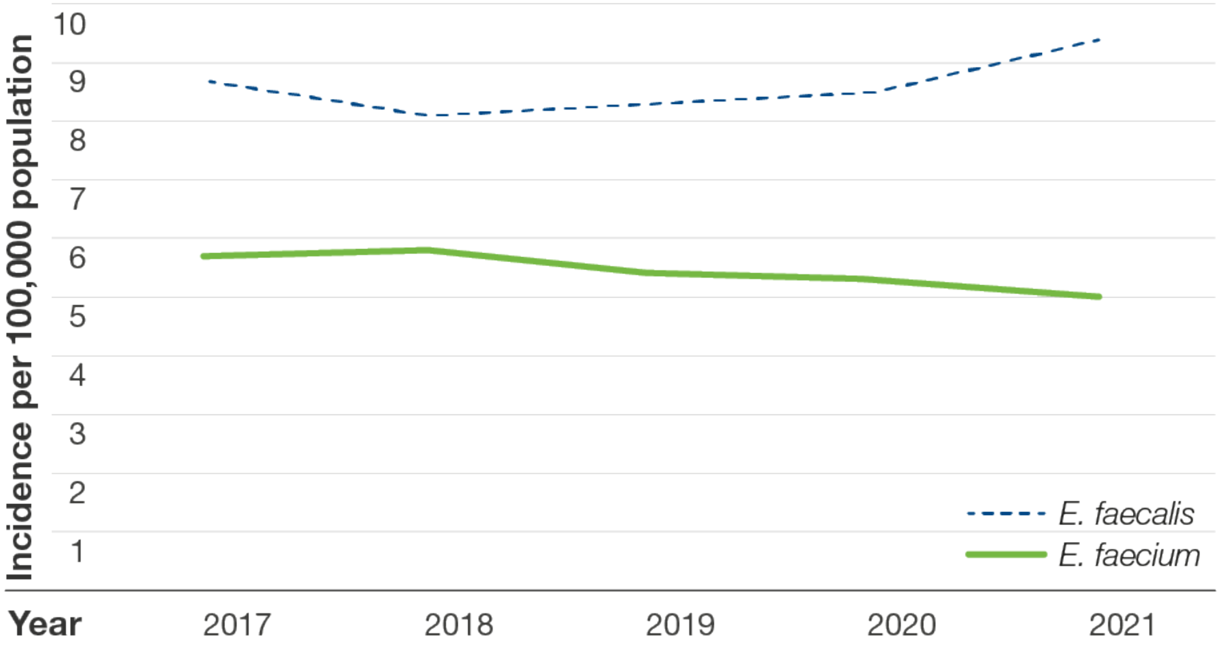
Enterococci are distributed widely in nature and are found in humans, animals, soil, food and plants and are a commensal of the gastrointestinal tract of most species, including humans. Enterococci are important healthcare associated pathogens and are a common cause of UTIs but can also lead to more serious infections such as intra-abdominal infections, endocarditis, bacteraemias, neonatal infections and meningitis.[21] Enterococci have intrinsic resistance to several antimicrobial classes, and the ability to acquire additional resistance, limiting treatment options. They also have a propensity to survive in harsh environments.[22, 23] Enterococci can disseminate within healthcare facilities if standard infection control precautions (SICPs) and transmission-based precautions (TBPs) are not followed. The causative agents of the majority of human infections are *E. faecalis* and *E. faecium.*

In 2021, 516 cases of *E. faecalis and* 276 *cases of E. faecium* bacteraemia were reported in Scotland. The incidence of *E. faecalis* bacteraemia (9.4 per 100,000 population) *and E. faecium* bacteraemia (5.0 per 100,000 population) has remained stable (p>0.05) since 2017 (**Figure 26**).

Vancomycin non-susceptibility of *E. faecium* blood isolates remained high at 40.4% but stable (p>0.05) between 2020 and 2021. Scotland has one of the highest reported proportions of vancomycin resistance in *E. faecium* bacteraemia isolates in Europe with the most recent European Antimicrobial Resistance Surveillance Network (EARS-Net) report stating that this is a growing issue across Europe.[24] Infections caused by vancomycin resistant enterococci (VRE) are associated with higher mortality rates compared with those caused by vancomycin sensitive enterococci (VSE).[21] Vancomycin non-susceptibility in *E. faecalis* is less common and was 0.6% in 2021. There are a number of factors known to increase the risk of infection with VRE including previous antibiotic therapy, previous or prolonged hospitalisation, medical devices and severe underlying illnesses or immunosuppression.[21]

There is currently a lack of intelligence on the epidemiology of VRE in Scotland. This information is needed to better understand the population at risk and to inform future programmes of work, policies or interventions with respect to VRE. In 2022, ARHAI Scotland will work with both the Scottish Environment Protection Agency (SEPA) and Scotland's Rural College (SRUC), adopting a One Health approach, to gather more intelligence on strains of VRE circulating in Scotland.

Figure 26: Incidence of *E. faecalis* and *E. faecium* bacteraemia per 100,000 population in Scotland, 2017 to 2021, by organism and year.



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

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 between 2017 and 2021.**
- **Non-susceptibility in *E. faecium* blood isolates has remained stable between 2020 and 2021.**
- **Vancomycin non-susceptibility was found in 40.4% of *E. faecium* blood isolates and 0.6% of *E. faecalis* blood isolates.**
- **Further work is underway to identify the appropriate public health actions.**

Streptococcus pneumoniae bacteraemia

Streptococcus pneumoniae is a common cause of bacterial infections of the respiratory system, middle ear infection, bacteraemia, meningitis, and pneumonia.[25]

Between 2020 and 2021 there was a 67.7% (p=0.015) decrease in resistance to tetracyclines, although numbers remain small (see **Supplementary Data**).

Streptococcus pyogenes bacteraemia

Streptococcus pyogenes (Lancefield group A streptococcus; GAS) is a major pathogen causing infectious diseases in children. It causes diseases such as erysipelas, tonsillitis, scarlet fever, rheumatic fever, and glomerulonephritis.

Between 2020 and 2021 there was an increase in non-susceptibility to tetracyclines (81.3%, p=0.001). Numbers are small, and increases in AMR should be interpreted with caution, however, against the background of increased reports of scarlet fever, clinicians should remain vigilant.

Unusual resistance identified through the AMR Alerts Early Warning System (AMR-EWS) in 2021

ARHAI Scotland monitoring of unusual phenotypes enables a timely scientific and public health response to potential emerging AMR issues informing infection control practices and appropriate therapy. 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.

The unusual 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.[26] 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.

Monitoring of unusual resistance continued throughout the pandemic. In 2021, the total number of laboratory confirmed unusual phenotypes identified from the AMR-EWS was 317 (see **Supplementary Data**).

Throughout 2022, the European Committee on Antimicrobial Susceptibility Testing (EUCAST) unusual phenotype list has been reviewed. This list now takes into account the epidemiology of Scottish isolates. Conjointly, work has commenced on reviewing the Reference Laboratory Referral Document for unusual phenotypes.

Unusual phenotype monitoring key points

- **Monitoring of unusual resistance is critical for identifying emerging AMR threats and enables the development of appropriate public health actions.**
- **Monitoring of unusual resistance in a timely manner supports quality improvement initiatives in NHS Boards.**

Salmonella antimicrobial resistance in humans and animals

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.[27] *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 extraintestinal 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, and snack foods such as chocolate[28] have been recognised as vehicles of transmission,[29-31] where contamination can occur at any point along the food chain from raw through to finished/cooked products. Contact with companion animals including dogs (often infected through consumption of raw pet food) and reptiles (often infected through feeding of raw, often imported feeder mice) have also been recognised as a significant source of *Salmonella* infection in humans with related outbreaks.[32]

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 and dogs are required to send suspect isolates for confirmation and typing to the SMiRL.

Whole Genome Sequencing (WGS) was introduced into routine use in the Scottish Microbiology Reference Laboratories in late 2017 for the identification and characterisation of *Salmonella* isolates. Following a review of published reports[33, 34] and an extensive validation confirming the high degree of correlation observed between the two approaches, the *in silico* prediction of AMR phenotype from WGS was introduced in January 2020. The predictive tools in use allow the identification of many thousands of individual AMR genes. New AMR mechanisms identified by other laboratories can quickly be identified by searching within the SMiRL existing sequence dataset without the need to repeat the wet laboratory processes.

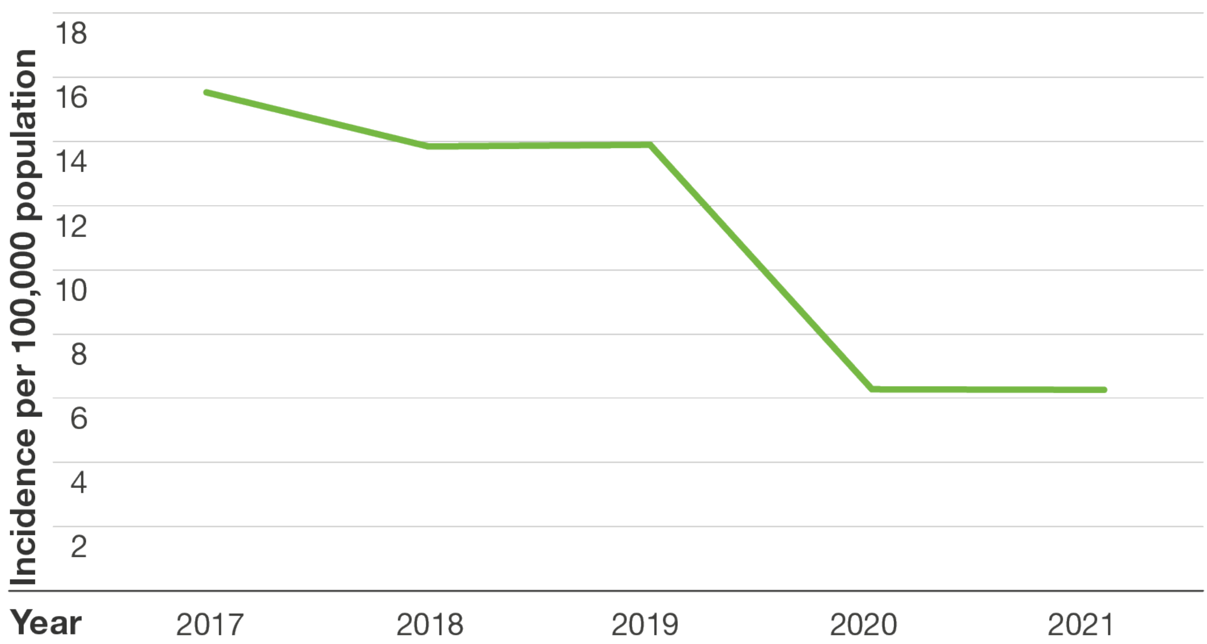
The availability of data from isolates from different source populations (humans and animals) which have undergone the same processing by the same laboratory offers an opportunity to monitor the trends in resistance and identify epidemiological links in these populations.

Human and animal non-typhoidal *Salmonella*

Human

Figure 27In 2021, there were 338 confirmed laboratory reports of *Salmonella* in humans*,* an incidence of 6.2 per 100,000 population*.* This incidence was stable compared with 2020 but there was a year-on-year decrease of 21.4% (p<0.001) over the last five years (**Figure 27**). COVID-19 pandemic restrictions, in particular restrictions on foreign travel, were the most likely reason for this reduction. The three most commonly reported serotypes in 2021 were *Salmonella* Enteritidis (67, 19.8%), *Salmonella* Typhimurium (50, 14.8%), and monophasic Typhimurium (4,5,12:i:-) (42, 12.4%), collectively accounting for 47.0% of all human *Salmonella* isolates.

Figure 27: Incidence of *Salmonella* species per 100,000 population in Scotland, 2017 to 2021.

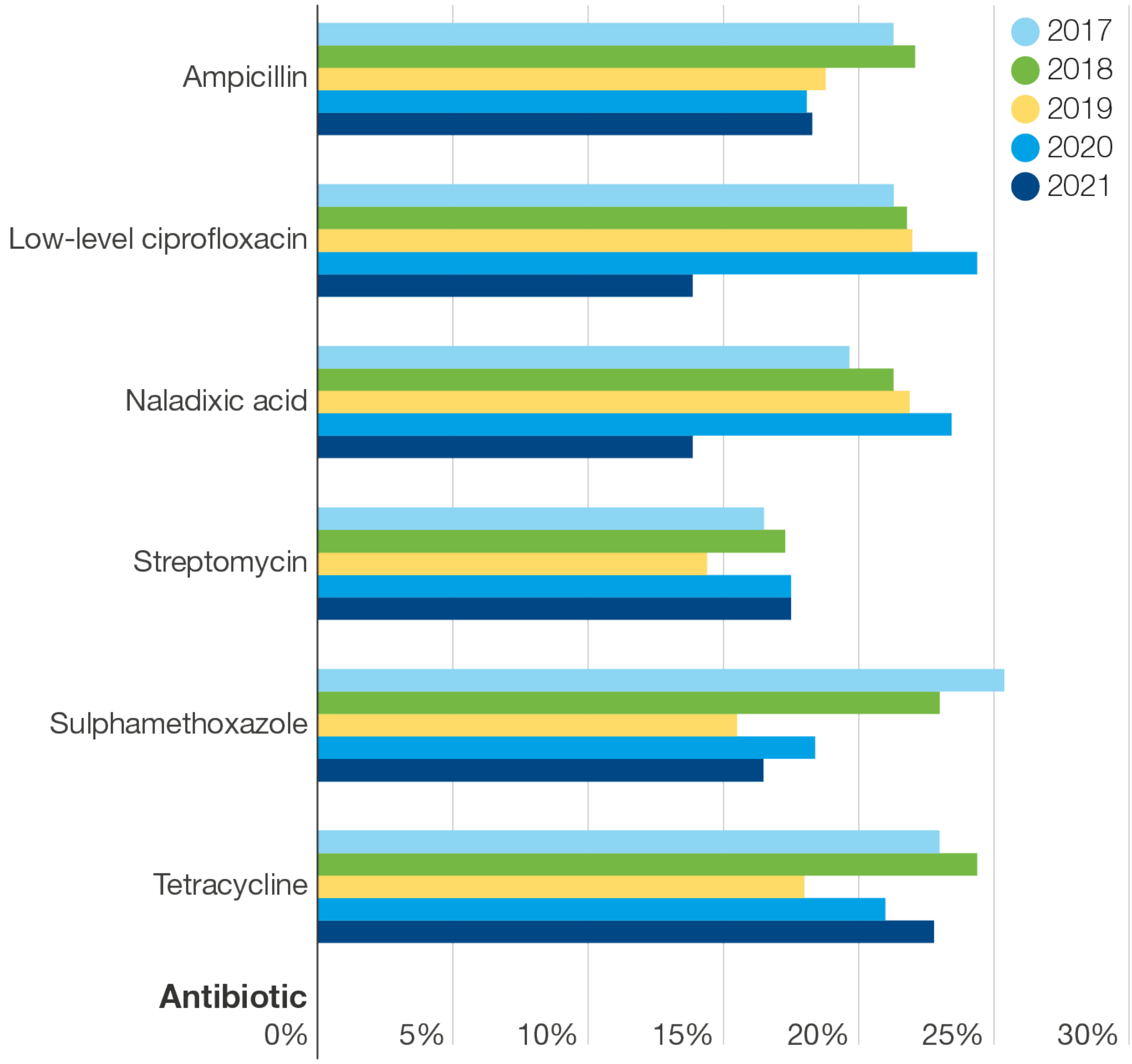


[Data source: Electronic Communication of Surveillance in Scotland (ECOSS) and National Records of Scotland (NRS)]

Susceptibility of human non-typhoidal *Salmonella*

During 2021, 67.0% of the 333 human *Salmonella* isolates tested were fully susceptible by genotype due to the absence of any detectable AMR genes or genetic markers; this compares to 60.2% in 2020 (see **Supplementary Data**). **Figure 28** shows non-susceptibility of human *Salmonella* isolates in Scotland by year from 2017-2021.

Figure 28: Non-susceptibility of human *Salmonella* isolates in Scotland, 2017 to 2021, by year.



[Data source: Scottish Microbiology Reference Laboratory (SMiRL)]

Interpretation of *Salmonella* resistance to individual antimicrobials 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 antimicrobials 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.

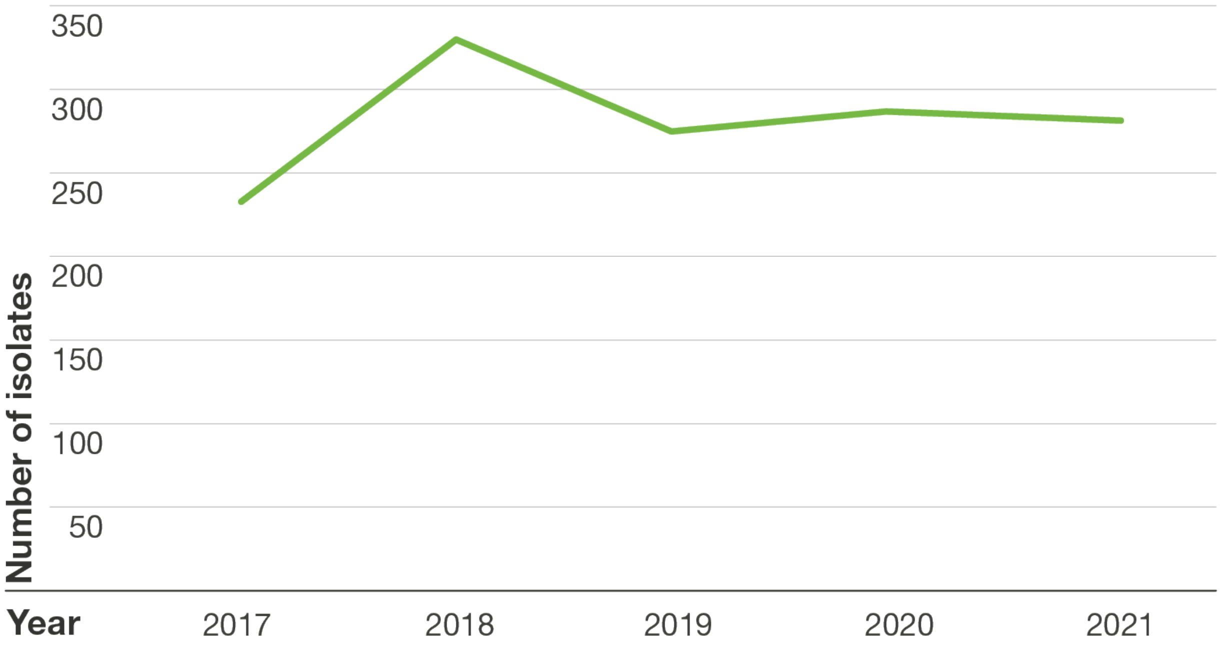
Animal

In Scotland, *Salmonella* is a reportable animal pathogen: all veterinary diagnostic laboratories isolating *Salmonella* spp. from livestock or dogs 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 by inference of AMR phenotype from Whole Genome Sequencing (WGS) data in the same way as for human isolates.

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.

In 2021 there were 282 reports of *Salmonella* in animals (**Figure 29**).

Figure 29: Number of laboratory confirmed *Salmonella* isolates from animals in Scotland, 2017 to 2021.



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

Most reports were from cattle (52.8%), sheep (17.7%) and pigs (13.1%). The remaining reports were from a variety of animals including dogs, cats, reptiles, tropical fish, birds and wild animals. Isolates from companion animals (dogs/cats/reptiles) accounted for 7.8% of the animal isolates.

Susceptibility of animal non-typhoidal *Salmonella*

In 2021, a total of 230 (83.3%) of the 276 isolates tested were fully susceptible by genotype. In 2020, 79.1% (n=227) of *Salmonella* reported from animals were fully susceptible as determined by phenotypic inference from WGS. This compares to phenotypically susceptible proportions of 77.7% in 2019, 64.8% in 2018 and 72.1% in 2017.

Non-susceptibility was 13.0% for tetracycline, 14.9% for sulphamethoxazole, 14.1% for ampicillin, 5.8% for ciprofloxacin and 13.8% for streptomycin (see **Supplementary Data**).

Salmonella antimicrobial resistance determination in the genomic era

The advantages 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".

Extended spectrum beta-lactamase (ESBL) genes were detected in three human isolates (0.9%), with one example of CMY-2 detected in an isolate of *S.* Minnesota, and two of SHV-12 in single isolates of *S.* Haifa and *S.* Typhimurium. There was no recorded travel history for any of these cases. No ESBL genes were detected in isolates of veterinary origin.

The predominant beta-lactamase genes detected in both human and animal isolates were the TEM beta-lactamases and the CARB-2 beta-lactamase. The TEM genes were identified in a diverse group of serotypes including Bovismorbificans, Braenderup, Brancaster, Enteritidis, Infantis, Java, Kentucky, Mbandaka, Rissen, Typhimurium ST19, and the monophasic variant of Typhimurium ST34, and were commonly associated with the carriage of *strA/strB* (streptomycin), *tetA* (tetracycline) and *sul-2* (sulphonamides). The CARB-2 gene was exclusively associated with a clonal group of *S.* Typhimurium ST19 strains which have been identified as most likely belonging to the historically important "DT104 complex", and also carried the integron-associated classical combination *aadA* (streptomycin), *floR* (chloramphenicol), *tetG* (tetracycline) and *sul-1* (sulphonamides).

Apart from the streptomycin resistance genes discussed above, genes encoding resistance to other aminoglycosides (gentamicin and kanamycin) were rare in both human and animal isolates (<1%).

Fluoroquinolone (FQ) resistance determinants were, as in 2020, more commonly found in human isolates (13.9%) than in animal isolates (5.8%) (p=0.001). However, these proportions have changed in comparison with 2020. The presence of FQ resistance genotypes has fallen in human isolates compared with 2020 (80 isolates; 23.4%) (p<0.05) while it has increased in animal isolates compared with 2020 (5 isolates; 1.7%) (p<0.05). This increase in animals is due to the identification of 11 isolates possessing the *gyrA*[87:D-N] mutation in a cluster of Typhimurium ST19 from cattle, and two isolates of Enteritidis ST3347 with the *gyrA*[83:S-Y] mutation isolated from pet dogs. Genetic signatures for higher level ciprofloxacin resistance

(MIC >. 0.5mg/L) were identified in four human isolates (1.2%) but not in animal isolates. Plasmid mediated *qnr* (quinolone resistance) resistance genes were identified in 16 (4.8%) of human isolates. Three (18.8%) of these human *qnr* containing isolates were from cases that reported foreign travel. This compares with a previous Scottish study[35] from 2008 in which 18/34 isolates (52.9%) identified as containing *qnr* genes were from cases where foreign travel had been reported.

The mobile colistin resistance gene *mcr*1.1 was detected in human isolate of *S*. Typhimurium ST19, no travel history reported. No colistin resistance genes were detected in animal isolates in 2021.

Antimicrobial resistance in animals

AMR in veterinary clinical isolates from livestock

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

For 2021, data are only presented from livestock species. These data derive from clinical specimens submitted to the farm animal diagnostic services offered by Scotland's Rural College (SRUC) Veterinary Services. 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 isolates from animals 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 existing 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 microorganisms that cause morbidity in humans.

Staphylococcus spp.

Staphylococcus spp. are common commensal organisms that can act as important opportunist pathogens of humans and other animals.

The sensitivity patterns for *Staphylococcus aureus (S. aureus)* for 2020 and 2021 are shown in the **Supplementary Data**. Meticillin resistance was not detected in *S. aureus* from livestock in either year.

Streptococcus spp.

Streptococcus spp. can be important pathogens or opportunist colonisers of livestock species, with the potential to cause severe disease of the skin, respiratory tract, body cavities, wounds and urinary tract. Some species, including *Streptococcus agalactiae*, *Streptococcus dysgalactiae*, and *Streptococcus suis*, are also recognised in human infections. The non-susceptibility patterns for selected *Streptococcus* spp. for 2020 and 2021 are shown in the **Supplementary Data**.

Pasteurellaceae

Pasteurellaceae are important causes of potentially severe respiratory and soft tissue infections in 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* (cattle, sheep, pigs), *Mannheimia haemolytica* (cattle and sheep), *Bibersteinia trehalosi* (cattle and sheep) and *Actinobacillus pleuropneumoniae* (pigs). The non-susceptibility patterns for the selected *Pasteurellaceae* for 2020 and 2021 from livestock animals are shown in the **Supplementary Data**.

Escherichia coli

E. 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 2020 and 2021 from livestock animals are shown in the **Supplementary Data**.

Klebsiella pneumoniae

K. pneumoniae is a cause of significant economic loss to the livestock industry and is potentially zoonotic. The non-susceptibility patterns for *K. pneumoniae* for 2020 and 2021 are shown in the **Supplementary Data**.

Extended-spectrum beta-lactamase producing *Enterobacterales*

ESBL were identified in *Enterobacterales* from one diagnostic isolate in 2020 - *K. pneumoniae* from a cow's milk. This was further identified as blaCTX-M-15 harbouring *K. pneumoniae* ST187. ESBL were identified in *Enterobacterales* from four diagnostic isolates in 2021, all from cattle: *K. pneumoniae* ST127, all CTX-M15, from cows' milk from mastitis cases (three from the same and one from a different dairy farm).

Carbapenemases

Carbapenemases were not detected in any animal isolates.

AMR in companion animals (SAVSNET)

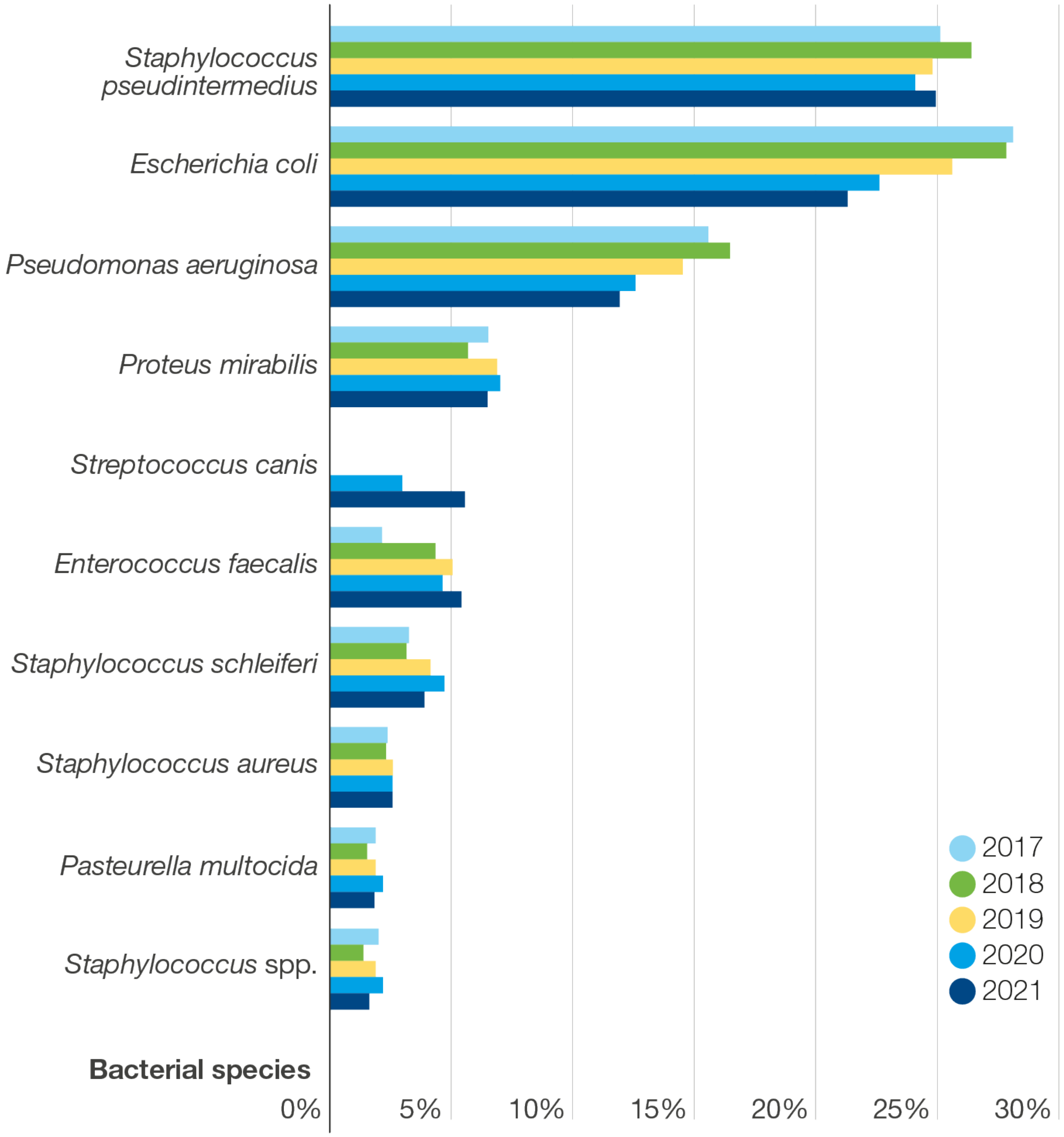
For the following section it should be noted that these data are obtained from private veterinary diagnostic laboratories contributing voluntarily to SAVSNET, that receive samples submitted from veterinary practices in Scotland. As these data come directly from participating laboratories, the number of veterinary practices contributing these samples is unknown. Therefore, data presented here cannot be assumed to be representative of samples submitted to laboratories from all companion animal practices in Scotland. Additionally, COVID-19 is likely to have affected the level of contact of companion animals with their vets, with resultant impact on the number of consultations, reported in 2020 and 2021.

ARHAI Scotland will continue to work with animal health stakeholders, including the veterinary corporate practices, to attempt to increase the availability of AMR surveillance data in animals.

Data on AMR in small companion animals were available from Scottish veterinary practices that contribute to SAVSNET for 2020 and 2021. A total of 4,763 and 6,313 bacterial isolates were reported in 2020 and 2021, respectively. In 2020, 86.1% (n=4,101) of the total 4,763 isolates were from dogs and 13.9% (n=662) from cats. In 2021, 87% (n=5,493) of the total 6,313 isolates were from dogs and 13% (n=820) from cats.

The distribution of bacterial species isolated is presented in **Figure 30**. *Staphylococcus pseudintermedius* (*S. pseudintermedius*) (n=1,580; 25%) and *E. coli* (n=1,346; 21.3%) were the most frequently isolated bacteria in 2021.

Figure 30: The 10 most common bacterial isolates in companion animals from samples submitted to private laboratories contributing to SAVSNET that come from veterinary practices in Scotland in 2021 as a percentage of the total isolates per year, 2017 to 2021.



Footnote: These data are obtained from private veterinary diagnostic laboratories contributing voluntarily to Small Animal Veterinary Surveillance Network (SAVSNET), that receive samples submitted from veterinary practices in Scotland. Therefore, they cannot be assumed to be representative of all companion animal practices in Scotland. In 2021, there were a further 108 bacterial species accounting for 887 isolates (14.1%), each with a prevalence of <1.5%.

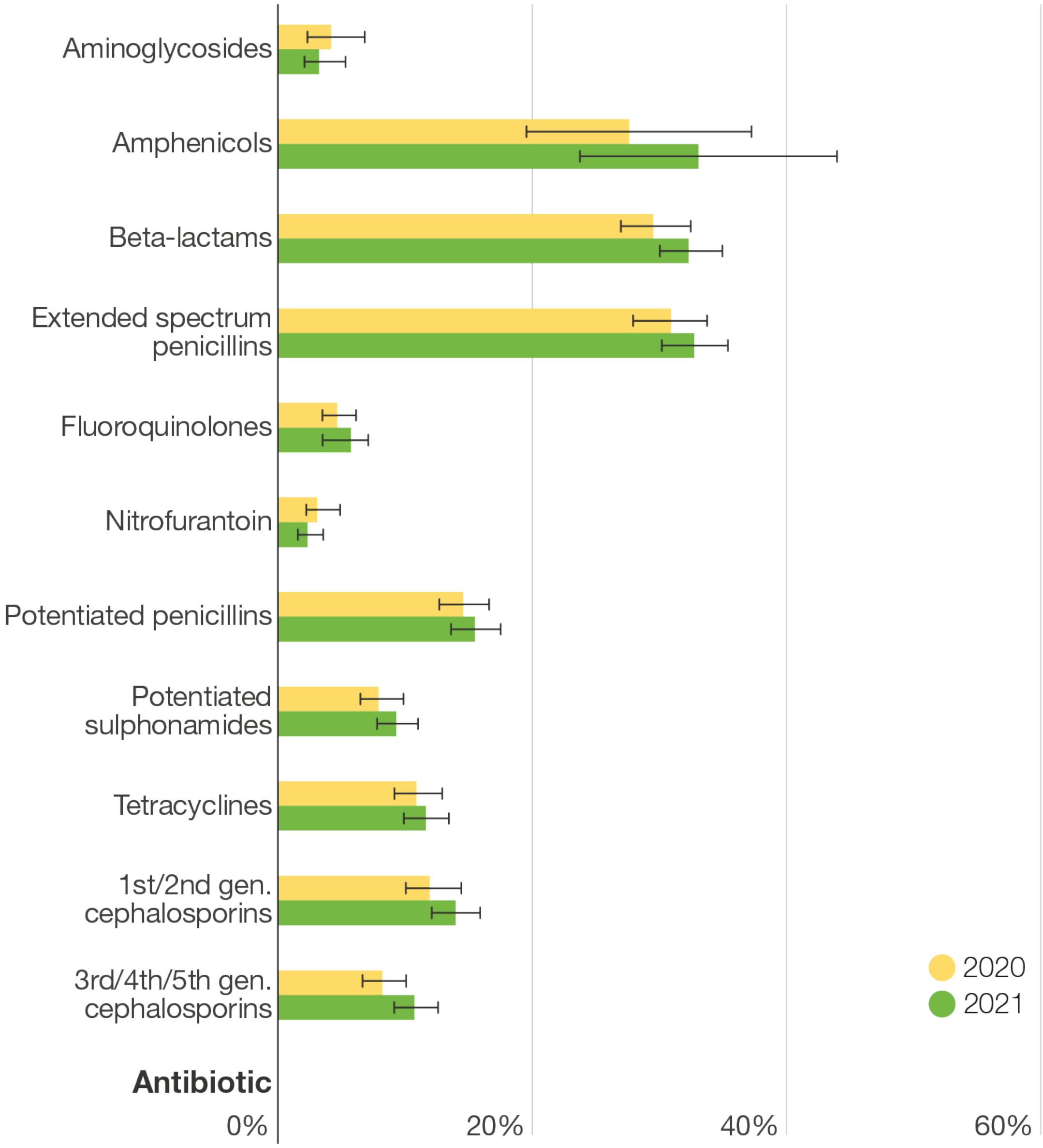
The following graphs present the percentage of isolates of *E. coli*, *S. pseudintermedius* and *S. aureus* from all companion animals non-susceptible to pathogen-appropriate antimicrobial classes for 2020 and 2021.

There was a total of 1,080 (80.4% from dogs) and 1,346 (81.4% from dogs) isolates of *E. coli* reported for 2020 and 2021, respectively. The percentage of isolates that were non-susceptible to selected antimicrobial classes in each year is shown in **Figure 31**.

There was a total of 1,153 (98.4% from dogs) and 1,580 (98.7% from dogs) isolates of *S. pseudintermedius* reported for 2020 and 2021, respectively. The percentage of isolates that were non-susceptible to selected antimicrobial classes in each year is shown in **Figure 32**.

There was a total of 123 (65.9% from dogs) and 163 (62.6% from dogs) isolates of *S. aureus* reported for 2020 and 2021, respectively. The percentage of isolates that were non-susceptible to selected antimicrobial classes in each year is shown in **Figure 33**.

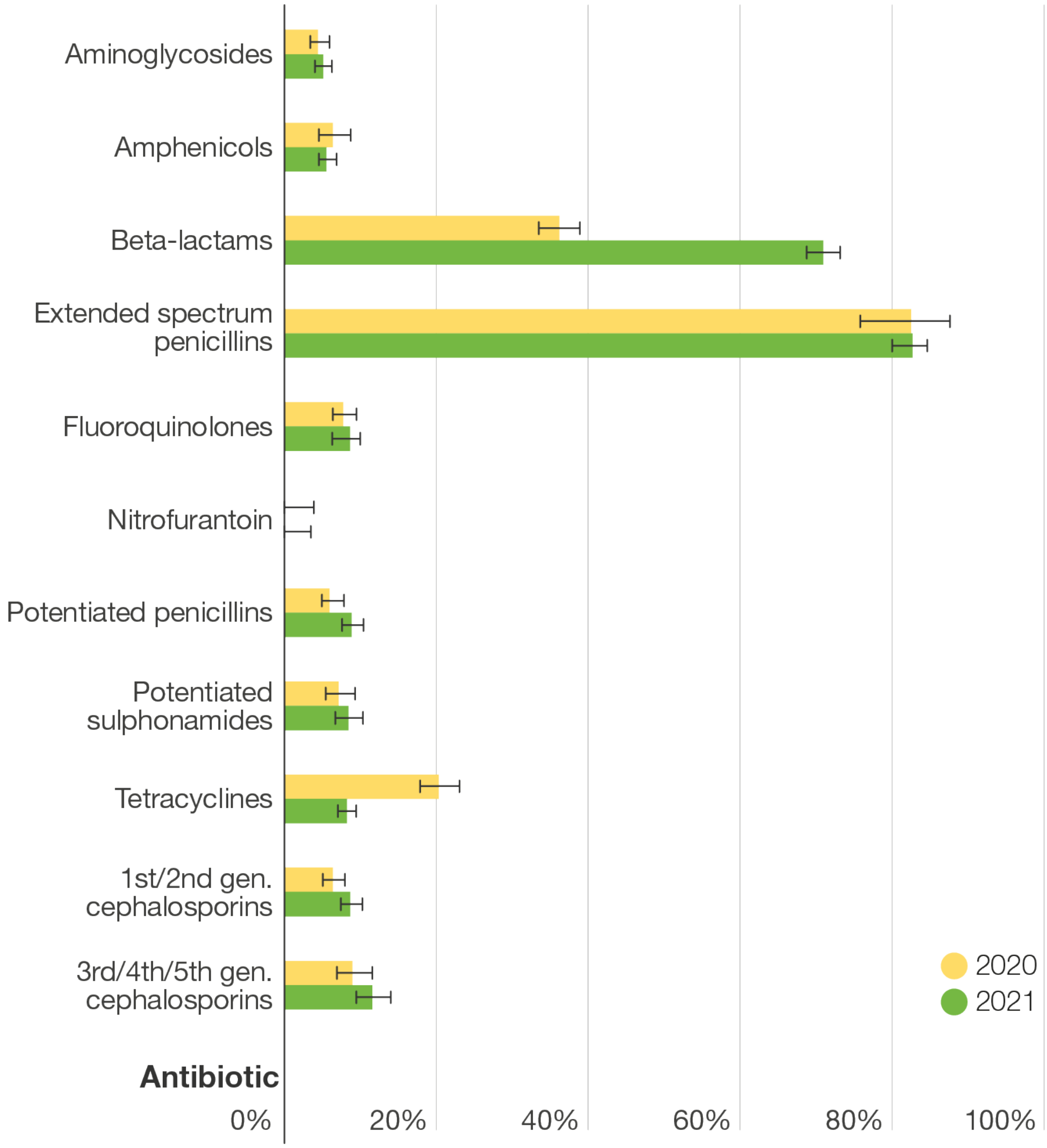
Figure 31: Percentage of *E. coli* cat and dog isolates non-susceptible to antimicrobial classes, from samples submitted to private laboratories contributing to SAVSNET that come from veterinary practices in Scotland, 2020 to 2021.



Footnote: These data are obtained from private veterinary diagnostic laboratories contributing voluntarily to Small Animal Veterinary Surveillance Network (SAVSNET), that receive samples submitted from veterinary practices in Scotland. Therefore, they cannot be assumed to be representative of all companion animal practices in Scotland.

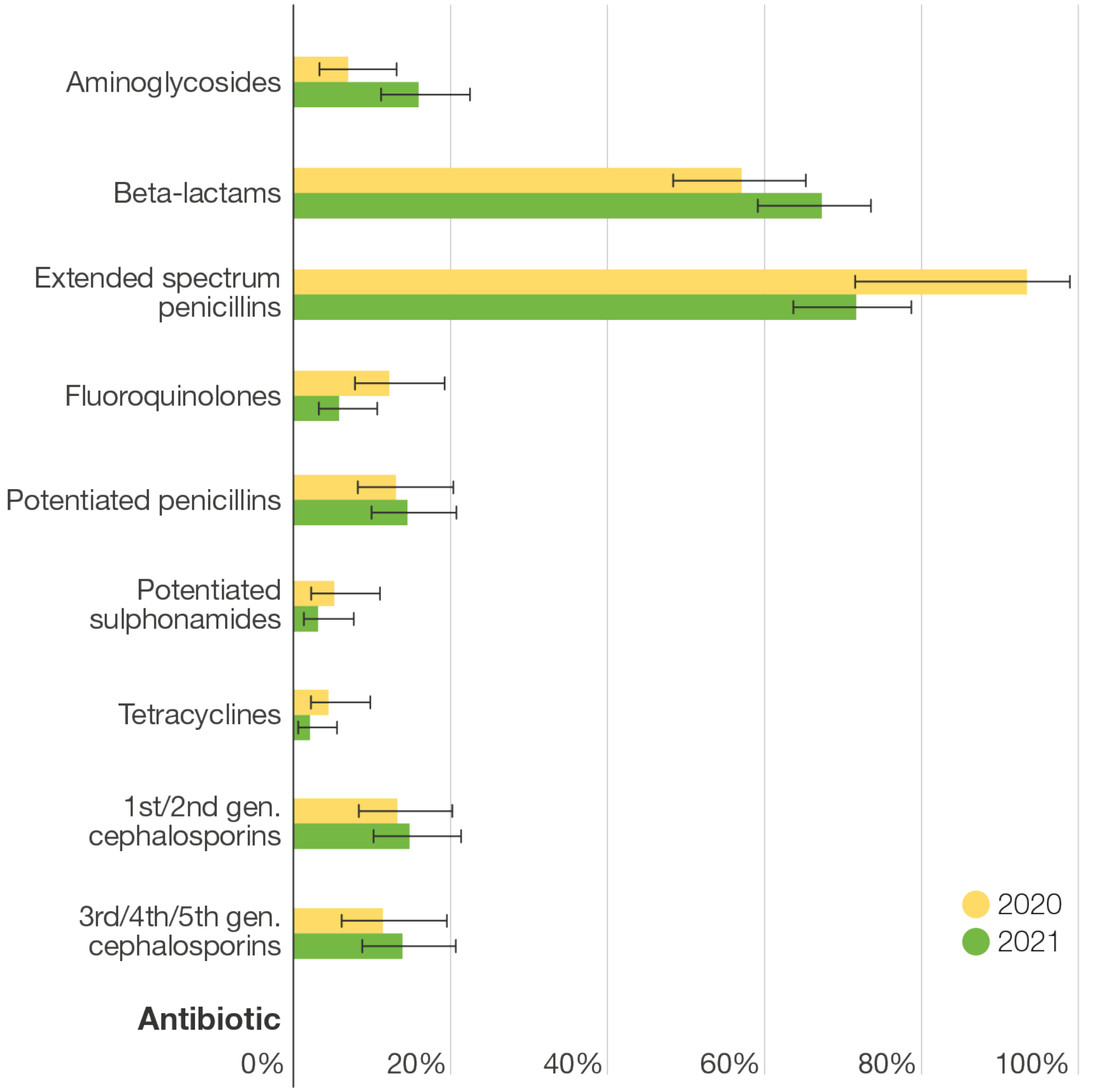
Numbers of isolates tested against polymixins were too small to lend meaningful outputs within this figure, details are available in the **Supplementary Data.**

Figure 32: Percentage of *S. pseudintermedius* cat and dog isolates non-susceptible to antimicrobial classes, from samples submitted to private laboratories contributing to SAVSNET that come from veterinary practices in Scotland, 2020 to 2021.



Footnote: These data are obtained from private veterinary diagnostic laboratories contributing voluntarily to Small Animal Veterinary Surveillance Network (SAVSNET), that receive samples submitted from veterinary practices in Scotland. Therefore, they cannot be assumed to be representative of all companion animal practices in Scotland. Numbers of isolates tested against polymixins were too small to lend meaningful outputs within this figure, details are available in the **Supplementary Data.**

Figure 33: Percentage of *S. aureus* cat and dog isolates non-susceptible to antimicrobial classes, from samples submitted to private laboratories contributing to SAVSNET that come from veterinary practices in Scotland, 2020 to 2021.

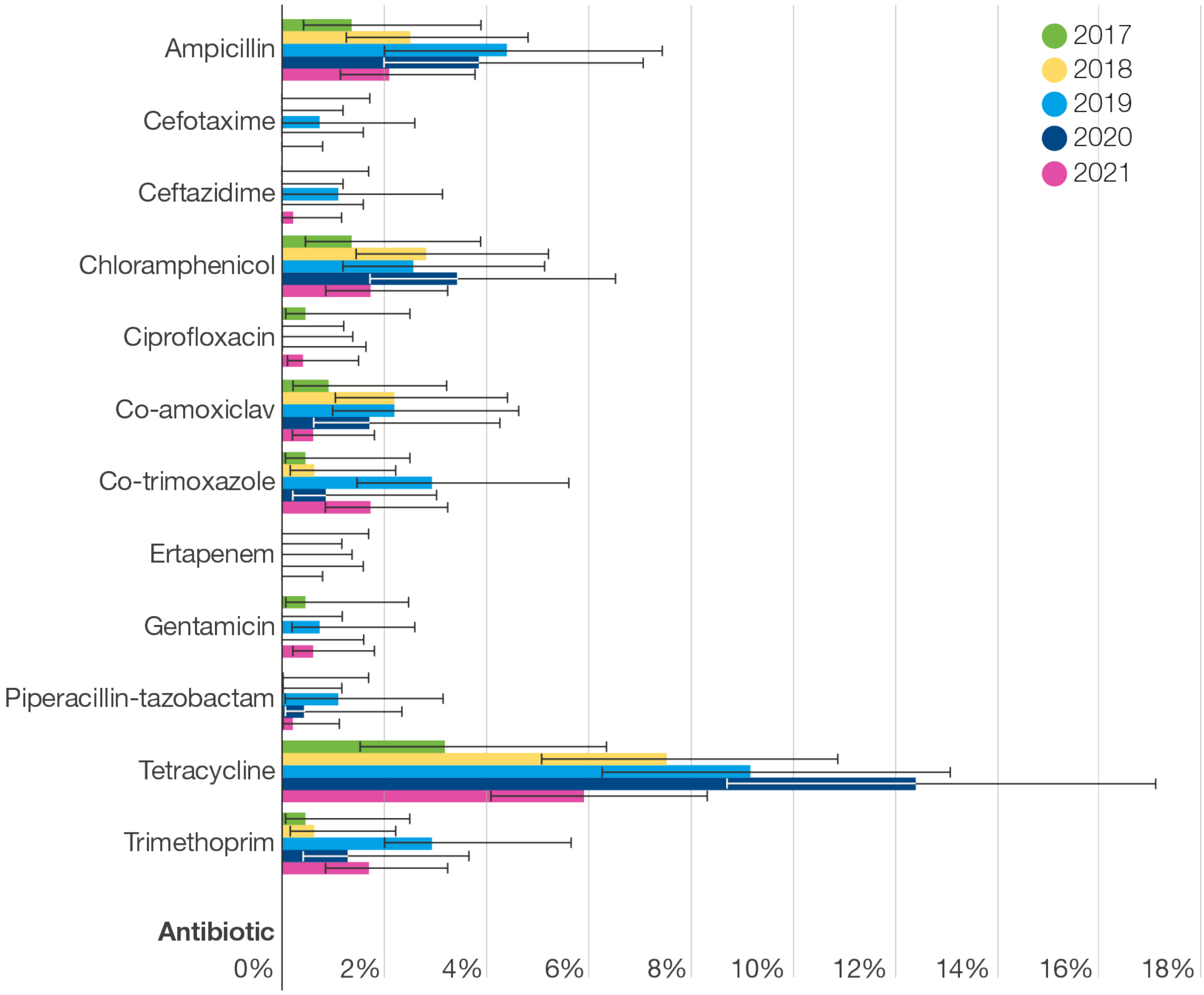


Footnote: These data are obtained from private veterinary diagnostic laboratories contributing voluntarily to Small Animal Veterinary Surveillance Network (SAVSNET), that receive samples submitted from veterinary practices in Scotland. Therefore, they cannot be assumed to be representative of all companion animal practices in Scotland. Numbers of isolates tested against amphenicols, nitrofurantoin and polymyxins were too small to lend meaningful outputs within this figure, details are available in the **Supplementary Data.**

AMR in *E. coli* isolates from healthy livestock

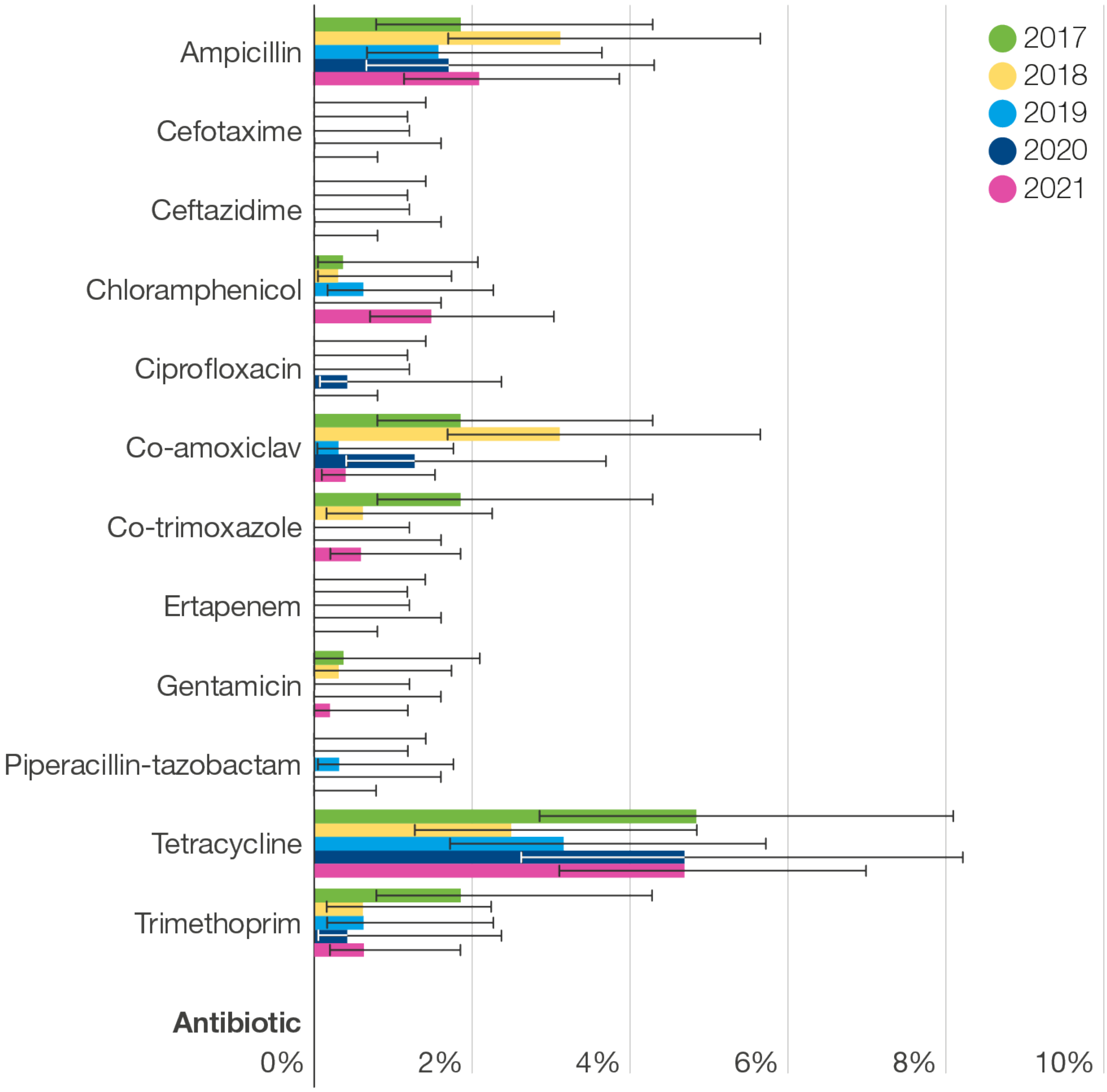
In addition to diagnostic isolates, *E. coli* collected from enteric samples of healthy animals are tested as a measure of the background resistance in livestock entering the food chain. Since 2017, an ongoing project in collaboration with Food Standards Scotland monitors the prevalence of resistance 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 for susceptibility against were selected specifically for their relevance for human treatment, rather than veterinary practice. Results for each of the four years for each livestock host are presented in **Figure 34**, **Figure 35**, **Figure 36** and **Figure 37**. Continued monitoring is important for comparison over several years. In 2021, as was reported in previous years, 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 very low (see **Supplementary Data**). Amongst high priority critically important antimicrobials (HP-CIAs), non-susceptibility was not detected to ertapenem. Non-susceptibility to third generation cephalosporins remained low and was only detected from cattle (ceftazidime, 0.2%) and poultry (cefotaxime 0.9%; ceftazidime 0.9%). In 2021, ciprofloxacin (fluoroquinolone) non-susceptibility was detected from cattle (0.4%), pigs (1.9%), but in 7.4% of poultry isolates, which is a decrease (p=0.001) from 15.5% in 2020. As in previous years, there was again a notable proportion of isolates from poultry non-susceptible to gentamicin and isolates from pigs non-susceptible to chloramphenicol. These proportions are lower (p=0.003) in 2021 compared to those seen in 2020.

Figure 34: Percentage of *E. coli* isolates that were non-susceptible to selected antimicrobials in healthy cattle in Scotland, 2017 to 2021, by antimicrobial.



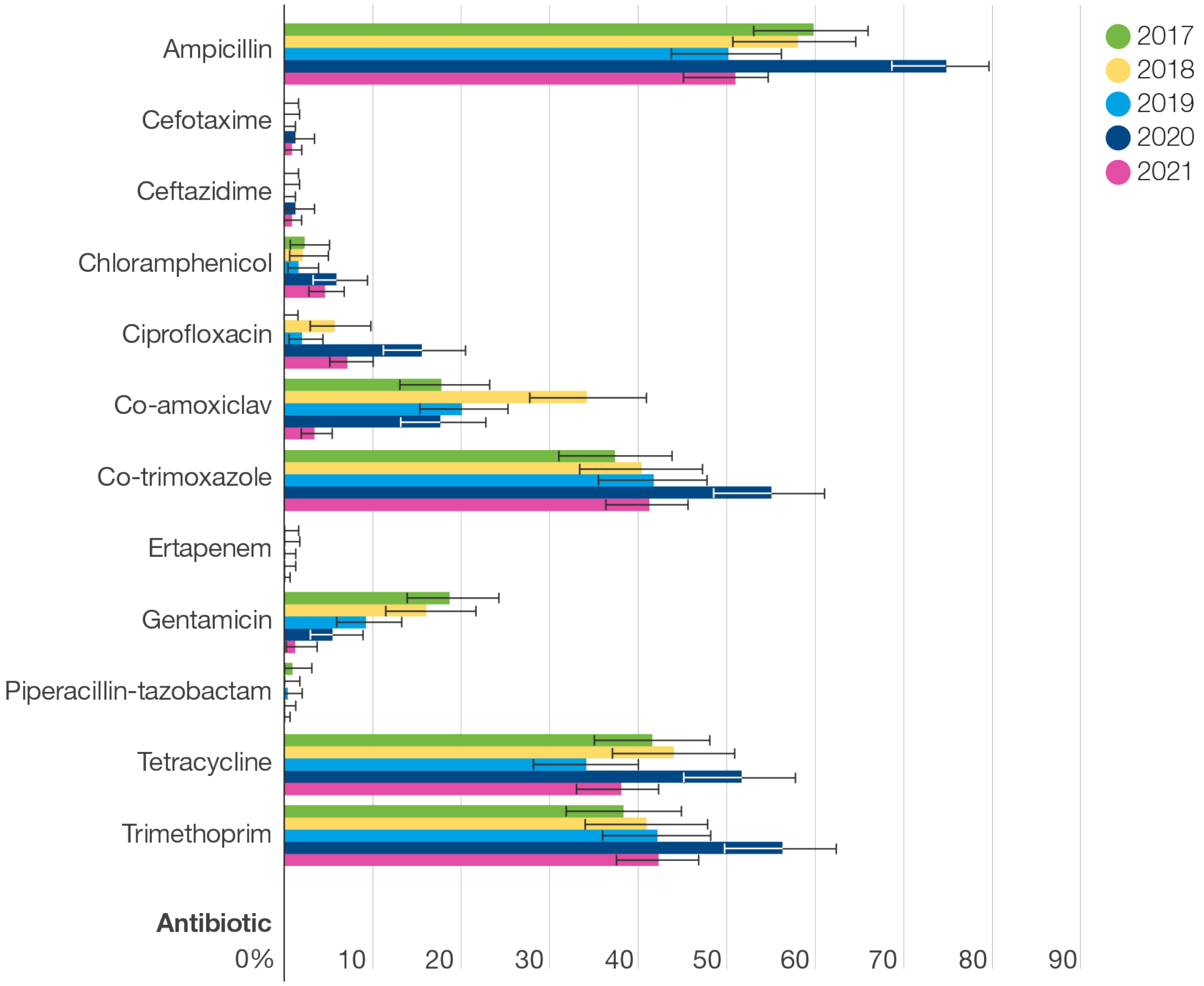
[Data source: Scotland's Rural College (SRUC)]

Figure 35: Percentage of *E. coli* isolates that were non-susceptible to selected antimicrobials in healthy sheep in Scotland, 2017 to 2021, by antimicrobial.



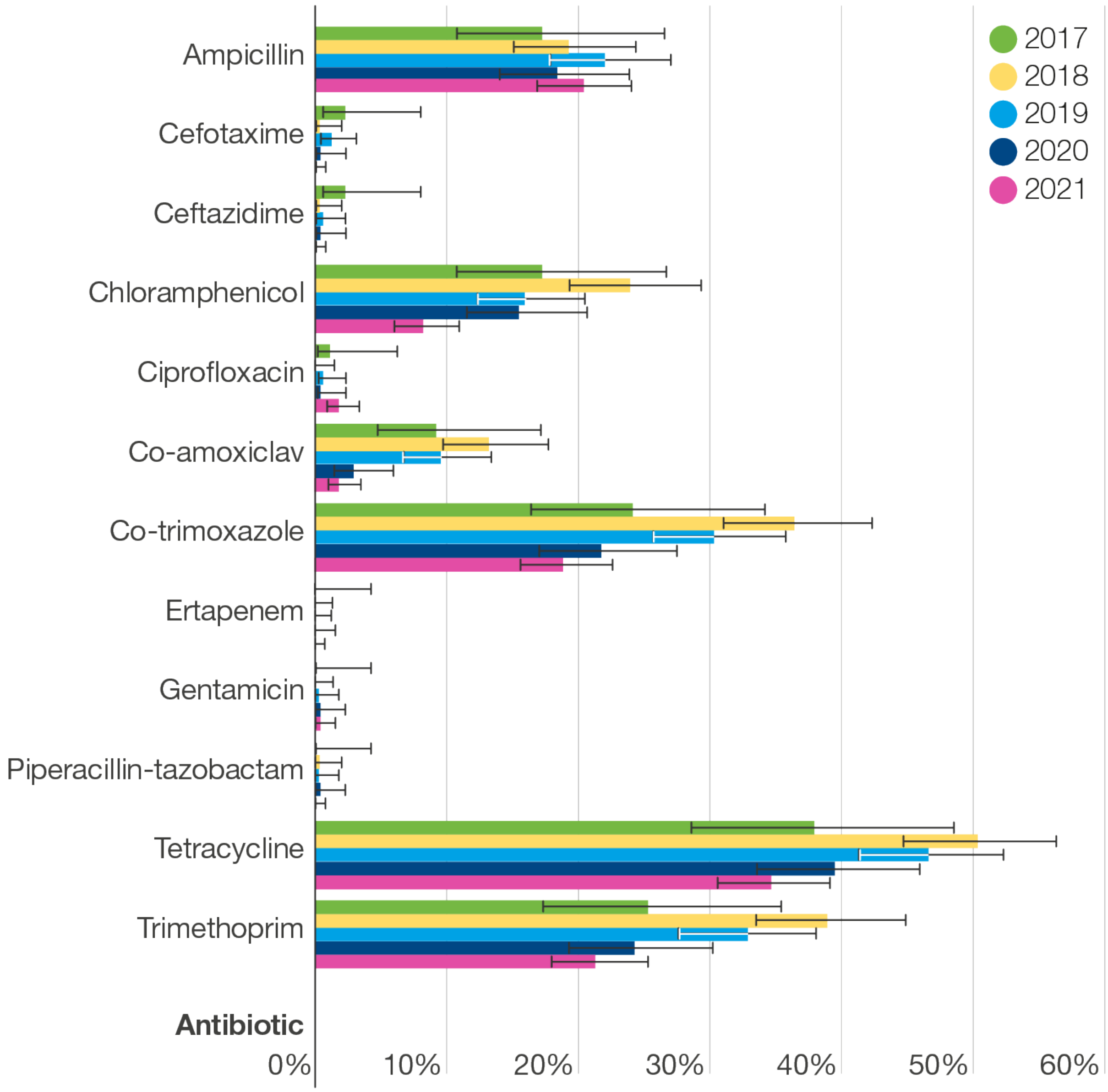
[Data source: Scotland's Rural College (SRUC)]

Figure 36: Percentage of *E. coli* isolates that were non-susceptible to selected antimicrobials in healthy poultry in Scotland, 2017 to 2021, by antimicrobial.



[Data source: Scotland's Rural College (SRUC)]

Figure 37: Percentage of *E. coli* isolates that were non-susceptible to selected antimicrobials in healthy pigs in Scotland, 2017 to 2021, by antimicrobial.

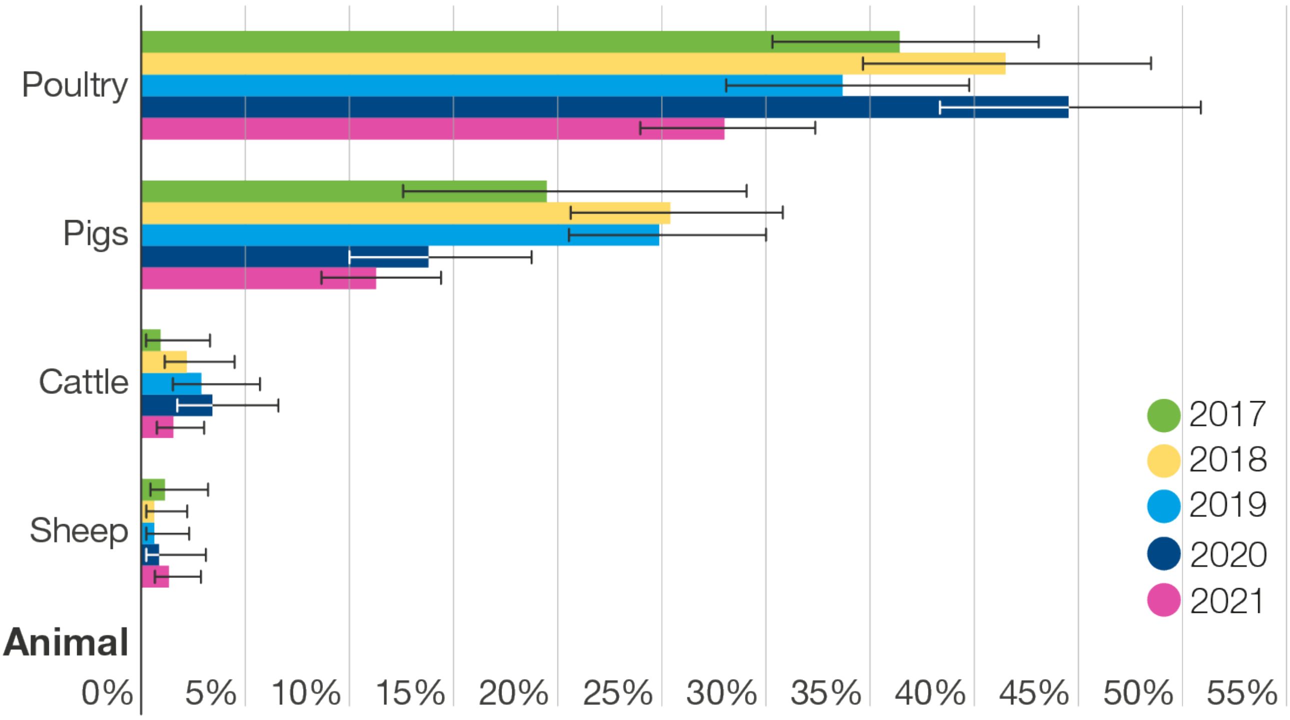


[Data source: Scotland's Rural College (SRUC)]

Multi Drug Resistance (MDR) in *E. coli* isolates from healthy livestock

A year-on-year comparison between 2017 and 2021 of data in terms of the percentage of isolates deemed to be multi drug resistant (MDR), which is defined as non-susceptibility to three or more antimicrobial classes, is presented. These are presented in the following figure, Figure 38, by animal species. These appear to be very low and reasonably stable in cattle and sheep but less so in poultry and pigs. Although derived from samples collected from somewhat different stages of production in the different animal species, and processed using different microbiological methods, data from the periodic European Union Summary Report on Antimicrobial Resistance in zoonotic and indicator bacteria from humans, animals and food may be a relevant basis for cautious comparison.

Figure 38: Percentage of *E. coli* isolates classed as MDR in healthy livestock in Scotland, with 95% confidence intervals, 2017 to 2021.



[Data source: Scotland's Rural College (SRUC)]

Animal AMR key points

- **AMR is a feature of bacterial pathogens affecting all domestic animal species.**
- **Antimicrobial susceptibility testing (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 2: One Year On update and Veterinary Antibiotic Resistance and Sales Surveillance (VARSS) Report of 2021 continue to demonstrate serious commitment to antimicrobial stewardship in UK livestock.**

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 sets out the ambitions in this area.[1] ARHAI Scotland have worked closely with the Scottish Environment Protection Agency (SEPA) to gather more intelligence to progress against the environmental AMR ambition.

The role of the environment as a transmission route for many bacterial pathogens has long been recognised as a dispersal route and reservoir of resistant pathogens, and as an arena for the evolution of resistance. [36-38]

SEPA has tested for and detected cefotaxime resistant *E. coli* in water samples collected from Scotland's designated bathing water sites during the bathing water season (June to mid-September) in 2018, 2019, and 2021. SEPA has also tested cefotaxime resistant *E. coli* isolates for resistance to a range of other antibiotics and detected resistance. Results can be accessed on the SEPA informatics website.

As mentioned previously, during 2022, work in conjunction with SEPA and the SRUC has commenced to gain more intelligence on antibiotic resistant strains of enterococci Enterococcal bacteraemia circulating in Scotland (see **Enterococcal bacteraemia** section).

List of Abbreviations and Acronyms

AMEG	Antimicrobial Advice Ad Hoc Expert Group of the European Medicines Agency
AMR	Antimicrobial Resistance
AMR-EWS	Antimicrobial Resistance Early Warning System
AMRHAI	Antimicrobial Resistance and Healthcare Associated Infections
AMT	Antimicrobial Management Teams
AMU	Antimicrobial Use
AMS	Antimicrobial Stewardship
ARHAI Scotland	Antimicrobial Resistance and Healthcare Associated Infection Scotland
AST	Antimicrobial Susceptibility Testing
AWaRe	WHO access, watch, reserve, classification of antibiotics for evaluation and monitoring of use
BSAC	British Society for Antimicrobial Chemotherapy
BSI	Bloodstream Infection
CAUTI	Catheter Associated Urinary Tract Infection
COVID-19	Coronavirus disease 2019
CPE	Carbapenemase-producing *Enterobacterales*
CPO	Carbapenemase-producing Organism
CRO	Carbapenem-resistant Organism
DDDs	Defined Daily Doses

EARS-Net	European Antimicrobial Resistance Surveillance Network
ECB	*Escherichia coli* bacteraemia
ECDC	European Centre for Disease Prevention and Control
ECOSS	Electronic Communication of Surveillance in Scotland
EMA	European Medicines Agency
EWS	Early Warning System
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FSS	Food Standards Scotland
GP	General Practitioner
HCAI	Healthcare Associated Infection
HEMPA	Hospital Electronic Medicines Prescribing and Medicines Administration
HMUD	Hospital Medicines Utilisation Database
HP-CIA	Highest Priority Critically Important Antibiotics
HPT	Health Protection Team
ICU	Intensive Care Unit
IPCT	Infection Prevention and Control Team
IV	Intravenous
MDR	Multi-Drug Resistant
MIC	Minimum Inhibitory Concentrations

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
PHS	Public Health Scotland
PIS	Prescribing Information System
RUMA	Responsible Use of Medicines in Agriculture Alliance
SAPG	Scottish Antimicrobial Prescribing Group
SAVSNET	Small Animal Veterinary Surveillance Network
SEPA	Scottish Environmental Protection Agency
SICPs	Standard Infection Control Precautions
SMiRL	Scottish Microbiology Reference Laboratory
SMVN	Scottish Microbiology and Virology Network
SOHNAAP	Scottish One Health National AMR Action Plan Group
SONAAR	Scottish One Health Antimicrobial Use and Antimicrobial Resistance

SRUC	Scotland's Rural College
TBPs	Transmission-Based Precautions
UK	United Kingdom
UTI	Urinary Tract Infection
VARSS	Veterinary Antibiotic Resistance and Sales Surveillance
VIM	Verona integrin-encoded metallo-beta-lactamase
VRE	Vancomycin-resistant enterococci
VSE	Vancomycin-sensitive enterococci
WGS	Whole Genome Sequencing
WHO	World Health Organisation

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- Scottish Antimicrobial Prescribing Group (SAPG)
- 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) **and** Scottish Veterinary Antimicrobial Stewardship (SVAS) Groups
- Small Animal Veterinary Surveillance Network (SAVSNET)
- Food Standards Scotland

Appendix 1 – Background information

Table: 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 NHS boards was variable due to laboratories depleting existing stock of older cards. This change was associated with an increase in co-amoxiclav non-susceptibility in 2019.
Implementation of v_11.0 EUCAST breakpoints	2021	Human AMR	Changes can be accessed via this link eucast
Temocillin breakpoints (*Enterobacterales*)	2020	Human AMR	No EUCAST breakpoint available. Initially all Biomerieux® Viteks used BSAC legacy UTI breakpoint of 16. NHS GGC moved to systemic breakpoint of 8 in ~2015. Other NHS boards moved variably up until end 2017. NHS GGC and some others retained an ‘I’ category (MIC 16) up until Oct 2019 when all moved to S<8 and R>8.
Change to episode based reporting for	2020	Human AMR	Data processing antimicrobial susceptibility data:

antimicrobial susceptibility data			For bacteraemias and bacteriurias, only the first isolate (of one specific organism per rolling 14-day period for blood and per rolling 30 day period for urine) is reported as a case. This is equivalent to one episode of infection. The most complete or most resistant AST result during each episode is reported for each case. Where more than one organism was present in a sample deduplication was carried out separately for each organism.
Change to ceftazidime resistance and non-susceptibility figures	2021	Human AMR	Due to an incorrect mapping of antibiotic code in ECOSS, ceftazidime was being incorrectly reported as cefradine. This was limited to one NHS board but accounted for a significant number of results since 2007. This has been corrected and amended retrospectively for data included in this report.

Appendix 2 – Metadata

Publication title

Scottish One Health Antimicrobial Use and Antimicrobial Resistance report, 2021 (SONAAR report, 2021)

Description

This annual report provides data relating to antimicrobial use and antimicrobial resistance in Scotland during 2021.

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), Public Health Scotland (PHS).

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), PHS.

Healthcare associated denominator: Total occupied bed days (OBD), Sum of OBDs for all hospitals in numerator: Information Services Division ISD(S)1, PHS.

Antibiotic use in animals

Antibiotic use in companion animals: Small Animal Veterinary Surveillance Network (SAVSNET).

Human antimicrobial resistance

Bacteraemia: Electronic Communication of Surveillance in Scotland (ECOSS).

Urinary tract infection: ECOSS.

Carbapenemase Producing Organisms (CPOs): ECOSS and the Scottish AMR Satellite Laboratory (SMiRL), Glasgow).

Unusual phenotypes: ECOSS.

***Salmonella* in humans**: ECOSS and Scottish Microbiology Reference Laboratory (SMiRL) via Public Health Scotland.

Animal antimicrobial resistance

Animal *Salmonella*: ECOSS and SMiRL via Public Health Scotland.

AMR in companion animal isolates: SAVSNET.

AMR in livestock animal clinical isolates: Scotland's Rural College (SRUC) Veterinary Services.

***Staphylococcus aureus* animal isolates antimicrobial susceptibility data**: SMiRL via SRUC.

AMR in healthy animals (abattoir): SRUC Veterinary Services.

Date that data are acquired

Antibiotic use in humans

Antibiotic use in primary care:

Patient-based analysis: 20/06/2022

Urinary tract infections (UTI) analysis: 08/08/2022

Primary Care (PC) Trend data: 13/06/2022

PC Duration of course analysis: 13/06/2022

PC Variation analysis: 13/06/2022

PC Antifungal analysis: 13/06/2022

Population denominator data: Mid-year population projections for Scotland: 16/08/2022

Antibiotic use in secondary care:

Secondary Care (SC) Trend analysis: 02/08/2022

SC Antifungal analysis: 18/08/2022

Healthcare denominator data: Total occupied bed days, Sum of OBDs for all hospitals in numerator: 17/06/2022

Antibiotic use in companion animals

Antibiotic use in companion animals: 16/08/2022

Human antimicrobial resistance

Bacteraemia: 07/07/2022

Population denominator data: Mid-year population projections for Scotland: 04/08/2022

Urinary tract Infection: 07/07/2022

Carbapenemase producing organisms (CPOs): 23/09/2022

Unusual Phenotypes: 18/07/2022

Salmonella in humans: 30/08/2022

Animal antimicrobial resistance

Antimicrobial resistance (AMR) in companion animal clinical isolates: 19/08/2022

AMR in livestock animal clinical isolates: 01/08/2022

AMR in healthy animals (abattoir): 02/02/2022

Salmonella in animals: 30/08/2022

Release date

15 November 2022

Frequency

Annual

Timeframe of data and timeliness

Antibiotic use in humans: Data are for 2017 to 2021 and are timely for this report.

Antibiotic use in companion animals: Data are for 2017 to 2021.

Bacteraemia: Data are for 2017 to 2021 and are timely for this report.

Urinary tract infections: Data are for 2017 to 2021 and are timely for this report.

Carbapenemase Producing Organisms (CPOs): Data are for 2017 to 2021 and are timely for this report.

Unusual Phenotypes: Data are for 2021 and are timely for this report.

***Salmonella* in humans**: Data are from 2017 to 2021 and timely for this report.

AMR in companion animal clinical isolates: Data for clinical isolates from cats and dogs from 2017 to 2021 and are timely for this report.

AMR in livestock animal clinical isolates: Data for clinical isolates from livestock animals from 2020 to 2021, with the exception of *Staphylococcus hyicus*, *Actinobacillus suis*, *Histophilus somni* and *Klebsiella oxytoca* complex for which data was only available for 2021.

AMR in healthy animals (abattoir): Data are for 2017 to 2021 and are timely for this report.

***Salmonella* in animals:** Number of laboratory reports from 2017 to 2021. AMR data for 2021 only.

Continuity of data

There are no discontinuities in the reporting period.

Revisions statement

These data are not subject to planned major revisions. However, ARHAI Scotland aims to continually improve the interpretation of the data and therefore analysis methods are regularly reviewed and may be updated in the future.

Revisions relevant to this publication

Gram-negative bacteraemia: Since the 2019 publication, changes were made to the data processing methods used to produce antimicrobial susceptibility figures. The new method identifies the most resistant (non-susceptible) isolates from a patient during each 14-day episode of bacteraemia rather than within each calendar year. The new methods have been applied to historic data to allow year-on-year trend analyses using the same definitions.

Urinary tract infections: Since the 2019 publication, changes were made to the data processing methods used to produce antimicrobial susceptibility figures. The new method identifies the most resistant (non-susceptible) isolates from a patient during each 30-day episode of bacteriuria rather than within each calendar year. The new methods have been applied to historic data to allow year-on-year trend analyses using the same definitions.

Change to previously reported ceftazidime resistance and non-susceptibility figures: Due to an incorrect mapping of antibiotic code in ECOSS, ceftazidime was being incorrectly reported as cefradine. This was limited to one NHS Board but accounted for a significant number of results since 2007. This has been corrected and amended retrospectively for data included in this report.

Concepts and definitions

Statistical significance: Please note where an increase or decrease is stated in this report this refers to a statistical change. Where a trend is referred to as stable, there has been no statistically significant increase or decrease. Statistical significance has been determined by a p-value of less than (<) 0.05. Due to the number of tests being done at the same time a Bonferroni correction has been applied and the p-values adjusted to reflect the number of tests undertaken for each organism. In order to keep the number of multiple testing to a minimum, only organism and drug combinations with enough numbers each year have been tested.

Confidence Intervals: Confidence intervals (95% CI) for proportions were calculated to indicate robustness of the proportions presented. Where a 95% CI has been quoted or displayed in a figure as an error bar around a percentage, the method used is the Wilson Score.[39]

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/

Prescribing time period: All trend data are reported for calendar years 2017 to 2021. 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/statistics-and-data/statistics/statistics-by-theme/population/population-estimates/mid-year-population-estimates

Defined Daily Dose (DDDs, World Health Organisation (WHO)): https://www.whocc.no/atc_ddd_index/

Parenteral antibiotics defined daily doses (DDDs) used to monitor use of intravenous (IV) antibiotics.

Primary care prescribing information sourced from PIS is linked to patient Community Health Index (CHI) numbers. Using patient CHI numbers, it is possible to analyse demographic information on patients prescribed antibiotics such as age and gender. Patients who live in Scotland have a unique CHI number, meaning that it is also possible to count numbers of distinct patients receiving a particular treatment or investigate prescribing patterns for particular individuals over time. From 2009 onwards, the majority of prescriptions can be linked to a valid CHI number, however CHI capture rates can vary by drug, geographical area or prescriber type, with GPs having better capture rates than other prescriber types. When interpreting trends in patient counts over time, the underlying CHI capture rate must also be considered. In this report where patient level data is used, the relevant CHI capture rates are also presented. It is difficult to identify with certainty how much impact increasing CHI completeness has on the number of patients identified, but the evidence available suggests that the impact is small when considering the scale of change in CHI completeness presented in this report and this should not generally be significantly affecting trends in patient counts.

Unless otherwise stated Primary Care figures exclude Dental (GP14) Prescription Forms.

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 antibiotic 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. Practices submitting data are not necessarily the same from year to year. Nevertheless, they provide additional important intelligence relating to another aspect of antibiotic use in the One Health ecosystem.

This important data stream allows a continuing impression of antibiotic 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://bvajournals.onlinelibrary.wiley.com/doi/10.1136/vr.h6174

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 antibiotic 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

Case definitions:

Total numbers, incidence rates and antimicrobial susceptibility testing (AST) results were calculated using the following case definitions:

- 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 bacteriuria 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).

Isolate(s) refers to the organism isolated from each case of bacteraemia or bacteriuria.

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 use validated data collected as part of mandatory surveillance programme as detailed in the ARHAI Scotland Quarterly epidemiological data on *Clostridioides difficile* infection, *Escherichia coli* bacteraemia, *Staphylococcus aureus* bacteraemia and Surgical Site Infection in Scotland.

Please note that bacteriuria (bacteria present in urine) is used as a proxy for UTI and not all cases reported will be validated cases of UTI. As part of the NHS Pharmacy First Scotland service, community pharmacists have the ability to supply via patient group direction trimethoprim or nitrofurantoin for uncomplicated UTIs in females aged 16 to 65. This service has been available in all community pharmacies since August 2020 and is likely to have had an impact on the number of urine samples being referred to laboratories since females with uncomplicated UTIs can be treated by pharmacists without attending their General Practitioner.

Incidence rates were calculated as follows:

Bacteraemia rate per 100,000 population = (Number of cases per year / mid-year Scottish population) x 100,000

Population estimates: https://www.nrscotland.gov.uk/statistics-and-data/statistics/statistics-by-theme/population/population-estimates/mid-year-population-estimates

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.

Burden of drug resistant infection:

The burden of drug resistant infections is estimated for *Escherichia coli*, *Klebsiella pneumoniae* and *Klebsiella oxytoca*, *Acinetobacter* species, Pseudomonas *aeruginosa,* *Enterococcus faecium*, *Enterococcus faecalis, Staphylococcus aureus* and *Streptococcus pneumoniae* bacteraemia cases based on the percentage of organisms resistant (R) to at least one key antibiotic (see Table of Key antibiotics by organisms).

Antimicrobial susceptibility results are not available for all bacteraemia cases, therefore the % resistance from available results is applied to the total number of bacteraemia cases to provide the estimated number of antibiotic resistant bacteraemias.

Table: Key antibiotics by organisms

Organism(s)	Key antibiotic(s)
Escherichia coli, *Klebsiella pneumoniae* and *Klebsiella oxytoca*	Carbapenems (imipenem, meropenem or ertapenem) Third generation cephalosporins (one of ceftazidime, cefotaxime or ceftriaxone and not carbapenems) Gentamicin (and not carbapenems or third generation cephalosporins) Ciprofloxacin (and not carbapenems or third generation cephalosporins or gentamicin)
Acinetobacter species	Carbapenems (imipenem or meropenem) Aminoglycosides (amikacin or gentamicin) AND ciprofloxacin (and not carbapenems)
Pseudomonas aeruginosa	Carbapenems (imipenem or meropenem) Three or more antimicrobial groups (but not carbapenems)
Enterococcus faecium and Enterococcus faecalis	Vancomycin
Staphylococcus aureus	Meticillin

Streptococcus pneumoniae	Penicillin and macrolides Penicillin (and not macrolides)

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/.

Unusual phenotypes:

In 2018, the SONAAR team at ARHAI Scotland introduced an electronic process to run a twice weekly interrogation of ECOSS to identify unusual 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.

Definitions of an unusual phenotype can be accessed here:
http://www.eucast.org/expert_rules_and_intrinsic_resistance/

Appendix 13 of the National Infection Prevention & Control Manual (NIPCM) contains 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, based on British Society for Antimicrobial Chemotherapy (BSAC) breakpoints.

Antimicrobial susceptibility testing (AST) to support veterinary treatment comes primarily from private laboratories but is not currently part of a formal surveillance system.

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.

Changes in European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints for 2020 have been applied to healthy animal data for all antibiotics except tetracycline which uses the Clinical and Laboratory Standards Institute (CLSI) breakpoint value. These breakpoints are the agreed microbiological thresholds at which resistance is considered to be present. Changes to breakpoints have been applied retrospectively to allow year on year comparisons.

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.

WGS was introduced into routine use in the Scottish Microbiology Reference Laboratories in late 2017 for the identification and characterisation of *Salmonella* isolates. Following a review of published reports[31, 32] and an extensive validation confirming the high degree of correlation observed between the two approaches, the *in silico* prediction of AMR phenotype from WGS was introduced in January 2020. The predictive tools in use allow the identification of many thousands of individual AMR genes. New AMR mechanisms identified by other laboratories can quickly be identified by searching within the SMiRL existing sequence dataset without the need to repeat the wet laboratory processes.

The availability of data from isolates from different source populations (humans and animals) which have undergone the same processing by the same laboratory offers an opportunity to monitor the trends in resistance and identify epidemiological links in these populations.

Relevance and key uses of the 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

Antibiotic use in humans

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.

Antibiotic use in animals

Data provided by SAVSNET from a non-random sample of veterinary practices. Analyses carried out by ARHAI Scotland and results quality assured by SAVSNET data provider.

Human antimicrobial resistance

Bacteraemia: Data supplied by United Kingdom Accreditation Service (UKAS) accredited laboratories using standardised testing methodologies.

Urinary tract infections: Data supplied by UKAS accredited laboratories using standardised testing methodologies. PHS are undertaking an ECOSS quality improvement project (ECOSS Roll-out Implementation Programme (EDRIP)) which has highlighted some inconsistent mapping and reporting of urine sample results in ECOSS. Since this project is not yet complete, and missing results may not be retrospectively included, it is not currently possible to report and compare incidence over time.

Carbapenemase Producing Organisms (CPOs): Data supplied by UKAS accredited laboratories using standardised testing methodologies.

Unusual phenotypes: Data supplied by UKAS accredited laboratories using standardised testing methodologies. Unusual 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 available data within ECOSS have been included in the analysis, however, it should be noted that Public Health Scotland are undertaking an ECOSS quality improvement project (ECOSS Roll-out Implementation Programme (EDRIP)) which has highlighted some inconsistent mapping and reporting of urine sample results in ECOSS. Since this project is not yet complete, it is not currently possible to report and compare incidence per 1,000 population over time, however we do not expect this to impact the national antimicrobial susceptibility.

Carbapenmase Producing Organisms (CPOs): All data for the reporting period have been included in the analysis.

Unusual phenotypes: All laboratory confirmed isolates have been included in the analysis.

Animal antimicrobial resistance

AMR in companion animal clinical isolates: Database represents a non-random sample of veterinary practices and veterinary isolates, based on voluntary submission to SAVSNET.

AMR in livestock 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): Samples are collected on a monthly basis from livestock animals presenting at abattoirs and submitted 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 (DDDs) and is comparable to other antibiotic use surveillance programmes using this method. Historic

Secondary Care data may be subject to slight variation due to retrospective location mapping changes the datamart.

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 and *Staphylococcus aureus* bacteraemia: ARHAI Scotland Quarterly epidemiological data on *Clostridioides difficile* infection, *Escherichia coli* bacteraemia, *Staphylococcus aureus* bacteraemia and Surgical Site Infection in Scotland.

ARHAI Scotland Annual report: https://www.nss.nhs.scot/publications/arhai-scotland-2021-annual-report/

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

Unusual 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. European Committee on Antimicrobial Susceptibility Testing (EUCAST) breakpoints for 2020 have been applied for all antibiotics except tetracycline which uses the Clinical and Laboratory Standards Institute (CLSI) breakpoint value. These breakpoints are the agreed microbiological thresholds at which resistance is considered to be present. Changes to breakpoints have been applied retrospectively to allow year-on-year comparisons.

Accessibility

It is the policy of NHS National Services Scotland (NSS) to make its web sites and products accessible according to published guidelines.

Coherence and clarity

Tables and charts are accessible via our website at: https://www.nss.nhs.scot/sonaar2021/

Value type and unit of measurement

Antibiotic use in humans: The number of items per 1,000 population in Scotland per day (items/1000/day) and total DDD per 1,000 population per day (DDD/1000/day).

Antibiotic use in animals: Counts and percentages of antibiotic prescriptions by antibiotic class, animal species, administration routes, and main presenting problems.

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/organism combinations as reported in blood isolates.

Urinary tract infections:

AMR data includes percentage non-susceptible (I & R categories) for antibiotic/organism combinations as reported in urinary isolates.

Carbapenemase Producing Organisms (CPOs):

Number of isolates, number of carbapenemase producers by organisms and enzyme type and incidence per 100,000 population.

Unusual phenotypes:

Number of confirmed unusual phenotype, number of unusual phenotypes per organism/antibiotic combination.

Animal antimicrobial resistance

AMR in companion animal clinical isolates: Counts and percentage of non-susceptible isolates over all tested isolates.

AMR in livestock animal clinical isolates: Counts and percentage of non-susceptible isolates over all tested isolates.

AMR in healthy animals (abattoir): Counts and percentage of non-susceptible isolates over all tested isolates.

Disclosure

The NSS protocol on Statistical Disclosure Protocol is followed.

Official Statistics designation

Not Assessed

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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 – ARHAI Scotland 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'.

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