Veterinary Medicines Directorate

UK Veterinary Antibiotic Resistance and Sales Surveillance Report

UK-VARSS 2020

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Published on 9th November 2021

Contents

Foreword

Following on from last year, this year's report shows that the reductions in antibiotic use achieved in previous years have been held, with many sectors holding level or seeing modest reductions. This in itself is an achievement given the gains already made, and while a continuing national downward trend for antibiotic consumption is still necessary, it is likely to be more gradual than in recent years.

The Responsible Use of Medicines in Agriculture (RUMA) Alliance Targets Task Force (TTF) report released a year ago shows that the UK agriculture sectors remain focused on the road ahead. As they outline in their report, different sectors' new ambitions fall broadly into three categories: 1) maintaining sizeable reductions already secured; 2) forging ahead with further significant reductions; and 3), for those who have further to go in their antimicrobial usage journey, understanding usage in their sectors.

It is clear over the course of the VARSS reports since the first one published in 2014 (presenting data from 2013), that data on antibiotic sales and use are powerful tools for understanding patterns of antibiotic prescribing and on-farm use at every level – from providing prescribing pattern insight to the farmer and their vet, to describing sectoral and national trends – and galvanising action.

Arguably, the most important of these levels is at the point of veterinary prescribing, and with the increasing coverage of usage data across many sectors this is becoming more and more of a focus. Indeed, the farmer-vet relationship has and will continue to be central to animal health policies across the governments of the four UK nations.

'Farm Vet Champions' is an initiative inspired by a programme pioneered by the Welsh Government, spearheaded by the ruminant sector targets in the TTF 2020 report, given a platform by the RCVS Knowledge and supported by us here at the VMD. It is a training and engagement programme which has the potential to embed antimicrobial stewardship in practices across the country, linked back to resources at its central hub. Although it is still in its first year it is already showing good uptake and has significant potential to complement the work of the RUMA-chaired TTF.

Also building on the principle of empowering vets as prescribers of antibiotics, we are proud to include in the VARSS report for the first time this year, some early results of our enhanced antimicrobial resistance (AMR) surveillance programme for veterinary bacterial pathogens. This programme incorporates an upgrade of our antibiotic sensitivity testing methodology to gold standard broth microdilution and minimum inhibitory concentration (MIC) testing and optimises the panel of antibiotics against which we test for resistance. This not only facilitates better prescribing choices, but also puts the UK at the forefront of veterinary clinical surveillance for AMR internationally. It enhances our ability to detect emerging resistances of concern to animal and/or human health and to compare

resistance trends between countries and over time. This in turn supports our commitment to achieve truly integrated surveillance of AMR across the UK.

And finally, two significant areas have seen a surge in global profile in the past year: sustainability in the way we live our lives, and the importance of taking a ‘One Health’ approach where humans, animals, and the environments we share are interconnected. Both these areas are fundamentally important in how we have tackled, and how we continue to tackle, AMR. As we reach the point in our UK National AMR Action Plan where we take stock of our progress and turn our attention to working up ambitions for the next five years from 2024, these themes are likely to be foundational.

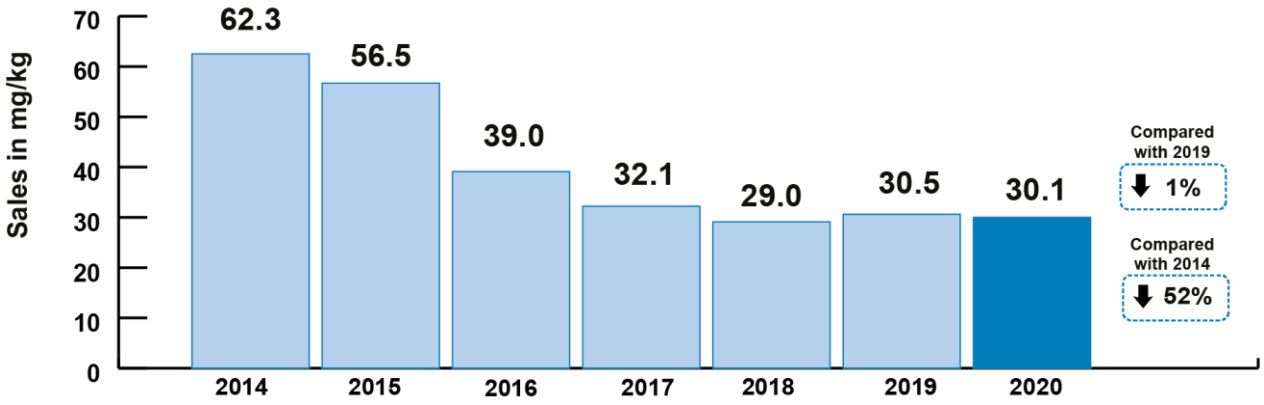
Dr Kitty Healey BVSc PhD MRCVS
Head of Surveillance Division, Head of Antimicrobial Resistance

Highlights

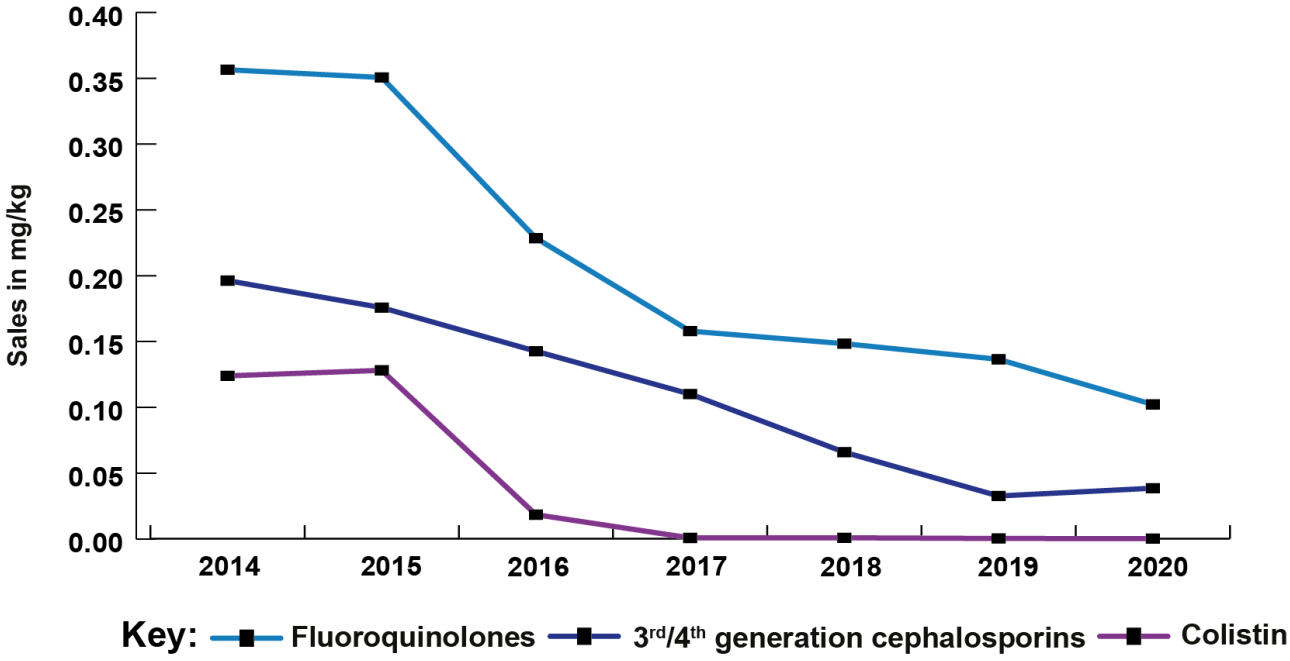
Antibiotic sales

Sales for food-producing animals (mg/kg)

Sales of veterinary antibiotics for use in food-producing animals, adjusted for animal population, were 30.1 mg/kg; a 0.3 mg/kg (1%) decrease since 2019 and a 32.2 mg/kg (52%) decrease since 2014.



Sales of Highest Priority Critically Important Antibiotics (HP-CIAs) in food-producing animals account for 0.5% of total sales and have dropped by 0.03 mg/kg since 2019 and 0.5 mg/kg (79%) since 2014.

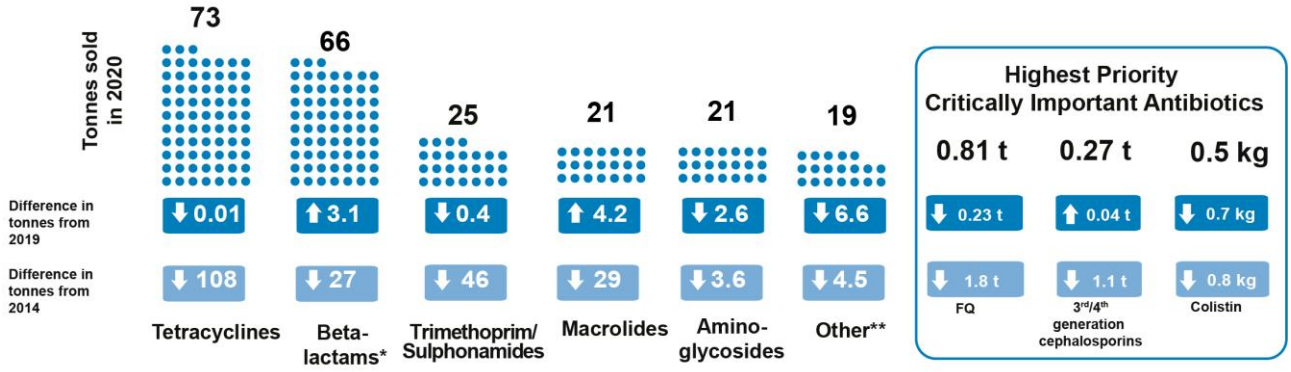


Sales for all animals (tonnes)

In 2020 the total quantity of antibiotic active ingredient sold in the UK was 226.0 tonnes.

	2014	2015	2016	2017	2018	2019	2020	Compared with 2014	Compared with 2019
Total sales (all animals, tonnes)	447	406	293	246	223	229	226	⬇ 49%	⬇ 1%

Sales of HP-CIAs reduced by 0.18 tonnes between 2019 and 2020 (from an already low level) and have now fallen by 3.7 tonnes (77%) since 2014. Tetracyclines remain the most sold antibiotic class (32% of total sales), followed by beta-lactams (29% of total sales). Sales of HP-CIAs in all animal species represent a small proportion (0.48%) of the overall antibiotic sales.



● = 1 tonne
t = tonnes
FQ = fluoroquinolones
* Includes 3rd and 4th generation cephalosporins.
** Includes amphenicols, lincomycins, pleuromutilins, steroidal antibiotics and polymyxins (including colistin).

Antibiotic Usage

Antibiotic usage refers to the amount of antibiotics prescribed and/or administered per sector. The data have been collected and provided to the VMD by the animal industry on a voluntary basis.

Antibiotic usage by food-producing animal species

	Total coverage %*	2020 Total tonnage**	2020 Total per unit***	Longer term change****	1 year change
Pigs	>95	83.1	105 mg/kg	↓ 172.7 mg/kg (62%)	↓ 5.5 mg/kg
Turkeys	90	21.0	25.7 mg/kg	↓ 194 mg/kg (88%)	↓ 16.3 mg/kg
Broilers			16.3 mg/kg	↓ 32.5 mg/kg (67%)	↓ 1.2 mg/kg
Ducks			2.6 mg/kg	↓ 12.5 mg/kg (83%)	↑ 0.9 mg/kg
Laying hens	90	3.1	0.47 % bird days	↓ 0.19 %bird days (29%)	↓ 0.21 %bird days
Gamebirds	91	6.0	—	↓ 14.2 tonnes† (71%)	↓ 4.4 tonnes†
Salmon	100	5.6	29.3 mg/kg	↑ 13.2 mg/kg (82%)	↑ 15.8 mg/kg
Trout	90	0.16	13.9 mg/kg	↓ 5.4 mg/kg (28%)	↑ 4.2 mg/kg

Highest Priority Critically Important Antibiotics by food-producing animal species

	Total coverage %*	2020 Total kg**	2020 Total per unit***	Longer term change****	1 year change
Pigs	>95	41	0.05 mg/kg	↓ 0.93 mg/kg (95%)	↑ 0.01 mg/kg
Meat Poultry	90	12	0.008 mg/kg	↓ 1.2 mg/kg (99%)	↓ 0.001 mg/kg
Gamebirds	91	22	—	↓ 42.5 kg† (66%)	↓ 36.2 kg†
Trout	90	48	4.3 mg/kg	↓ 2.3 mg/kg (35%)	↑ 1.8 mg/kg
Salmon	100	2.5	0.01 mg/kg	↓ 0.11 mg/kg (89%)	↓ 0.01 mg/kg

* Represents the % animals covered by the data, except gamebirds which represents an estimate of the total % antibiotics sales
** Relates to the weight of antibiotic active ingredient, using ESVAC methodology
*** mg/kg relates to the amount of active ingredient standardised by kg biomass and calculated using ESVAC methodology, % doses refers to 'actual daily bird-doses/100 bird-days at risk'
**** This represents the change from when antibiotic usage was first published, which was 2015 for pigs, 2014 for meat poultry, 2016 for laying hens, 2016 for gamebirds and 2017 for salmon and trout
† Note that industry estimates suggest that, due to Covid restrictions, gamebird rearing reduced by 30% during 2020

Antibiotic Resistance in Zoonotic and Commensal Bacteria from Healthy Animals at Slaughter

Resistance in *Escherichia coli* from broilers and turkeys

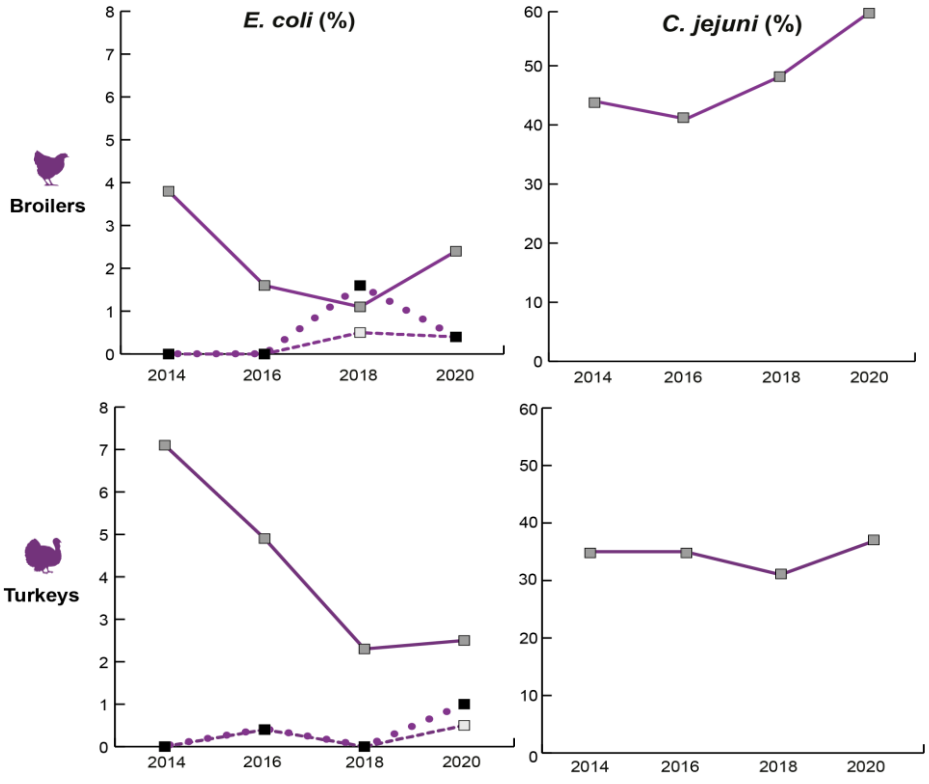
Overall, the UK can report trends of decreasing AMR in *E. coli* from healthy broilers at slaughter since 2014. Resistance to HP-CIAs remains undetected or at low or very low levels in both turkeys and broilers. There has also been a decrease in ESBL/AmpC-producing *E. coli* detected in broilers and turkeys since 2016, with less than 5% of caecal samples testing positive at slaughter in 2020.

Resistance in *Salmonella* spp. from broilers, laying hens and turkeys

In *Salmonella* collected from broilers and layers as part of the National Control Programmes (NCPs), susceptibility to the full panel of antibiotics tested has decreased since 2018; however, in broilers, it is still higher than in 2014. All *Salmonella* isolated from poultry through the NCPs were fully susceptible to the HP-CIAs tested, with the exception of nine isolates from layer flocks, which belong to a serovar that is naturally resistant to colistin.

Resistance in *Campylobacter jejuni* from broilers and turkeys

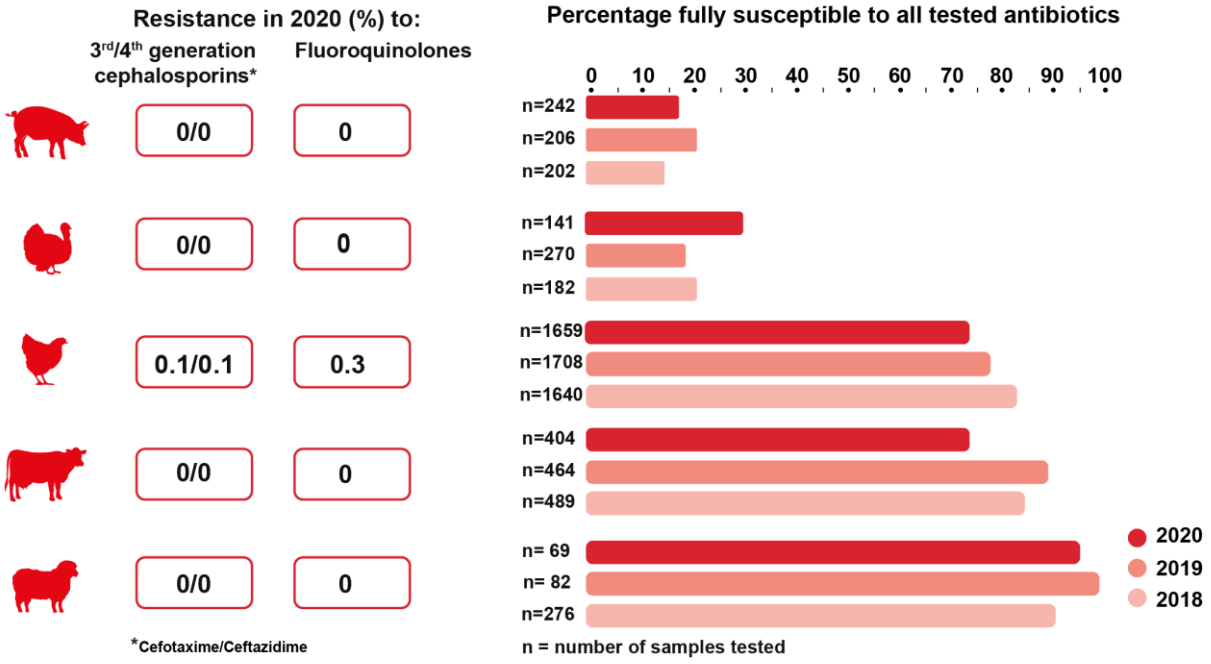
This year, *C. jejuni* isolates from broilers showed increasing and very high resistance to ciprofloxacin. This situation is not unique to the UK and is occurring despite very low fluoroquinolone use in meat poultry. In turkeys, resistance levels are more stable, but remain high. Resistance to erythromycin, a first-line treatment for *Campylobacter* infection in people, remained very low in broilers and turkeys (<1%). A description of resistance levels can be found in Annex B.



Antibiotic Resistance - Clinical Surveillance

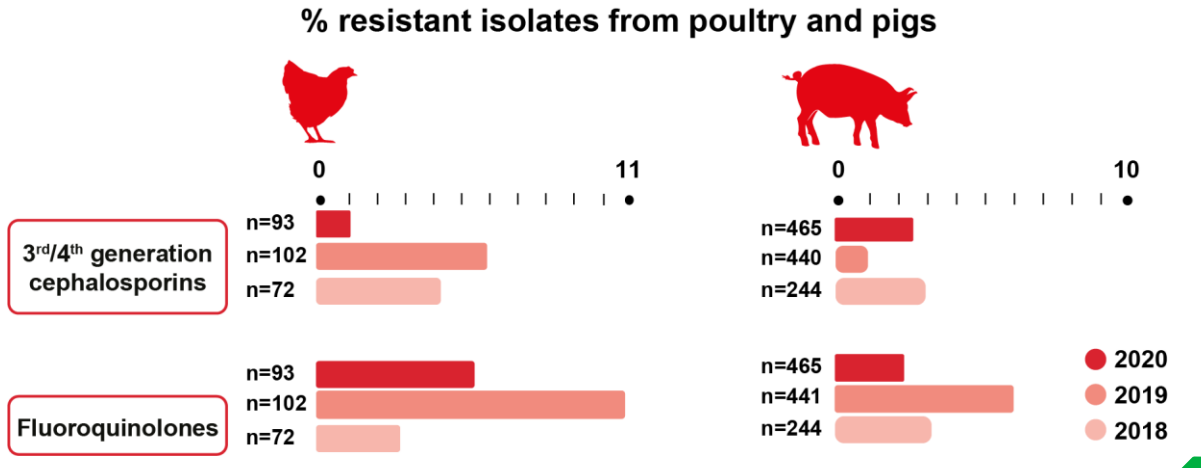
Resistance in *Salmonella* spp.

Of the 4,205 *Salmonella* isolates tested, 68% were susceptible to all of the antibiotics tested. No resistance to third/fourth generation cephalosporins and fluoroquinolones was detected in cattle, pigs, sheep and turkeys. In chickens, resistance to third/fourth generation cephalosporins (0.1%) and fluoroquinolones (0.3%) was very low. Resistance to ciprofloxacin was detected in a small number of isolates which were detected from chickens, feed and related samples, a pheasant and other non-avian species showed resistance to ciprofloxacin. Two isolates detected in an equine environment were multi-drug resistant.



Resistance in *Escherichia coli*

Resistance to fluoroquinolones and third generation cephalosporins remains low (≤10%) compared to 2018 for all animal species, the exception being for chickens where in 2019, fluoroquinolone resistance was 11%.



MIC testing of veterinary pathogens

This year's clinical surveillance programme has been enhanced to include MIC testing for a core range of key veterinary bacterial pathogens against commonly used clinical antibiotics. This improves the usefulness of our AMR surveillance and will also help vets make better prescribing choices.

Many isolates were susceptible to the panel of antimicrobials tested and when resistance was detected, alternative therapeutic options were likely to be available amongst antimicrobials authorised for veterinary use. Resistance was uncommon or not detected amongst antimicrobials which are often used as second- or third-line treatment options.

Introduction

The Veterinary Antibiotic Resistance and Sales Surveillance report of the United Kingdom (UK-VARSS) presents combined data on veterinary antibiotic sales and antibiotic resistance in bacteria from food-producing animals in the UK.

The antibiotic sales data from 2014 to 2020 are presented in **Chapter 1** and are based on sales of antibiotic veterinary medicinal products authorised for use in animals in the UK. Sales data are generally used as an estimate for antibiotic usage. The first report on sales figures for antibiotic veterinary medicinal products, collated and published by the Veterinary Medicines Directorate (VMD), covered 1993 to 1998. The figures were provided voluntarily by the veterinary pharmaceutical companies marketing these products. From 2005, sales data were collected as a statutory requirement (Veterinary Medicines Regulations) and in 2014 the first Veterinary Antibiotic Resistance and Sales Surveillance (VARSS) report of the United Kingdom was published (presenting data from 2013).

However, as many antibiotics are authorised for use in multiple species, it is not possible to determine how much is used by each animal species. The UK-VARSS report has increasingly included data on usage by animal production sector, working in partnership with livestock sectors to develop, facilitate and coordinate antibiotic usage data collection systems; these data reported voluntarily by the livestock sectors and are presented in **Chapter 2**.

While the term antimicrobial resistance (AMR) encompasses resistance of different types of organisms (bacteria, viruses, fungi, and parasites) to the drugs used to treat them, it is used throughout this report to refer to bacterial resistance to antibiotics specifically. The VMD collates data from government laboratories on antibiotic resistance (referred to as AMR in this report) in bacteria obtained from food-producing animals, which are collected under the framework of two surveillance schemes. The surveillance activities focus on the occurrence of antibiotic resistance in pathogens that cause infections in animals, zoonotic bacteria, and commensals. Zoonotic bacteria are covered in the surveillance because they can develop resistance in the animal reservoir, which may subsequently compromise treatment outcomes in people. Results from the harmonised antibiotic resistance monitoring scheme are presented in **Chapter 3.** Results from the scanning surveillance are presented in **Chapter 4**.

Details on methodology and results not presented in the report are included in the supplementary material. The supplementary material and previous UK-VARSS reports are available to download at https://www.gov.uk/government/collections/veterinary-antimicrobial-resistance-and-sales-surveillance.

CHAPTER 1
Sales of veterinary antibiotics

1.1 Summary

UK sales of veterinary antibiotics for food-producing animals, adjusted for animal population, were 30.1 mg/kg in 2020, a 0.3 mg/kg (1%) decrease from 2019 and a 32.2 mg/kg (52%) decrease from 2014. Sales of highest priority critically important antibiotics (HP-CIAs) for food-producing animals reduced for the sixth consecutive year and was 0.14 mg/kg in 2020 (a reduction of 0.5 mg/kg, or 79%, since 2014), representing only 0.5% of the total antibiotic sales.

Sales of veterinary antibiotics for dogs and cats, adjusted for animal population, were 58.8 mg/kg in 2020, a 4.4 mg/kg (7%) reduction since 2019 and a 17.2 mg/kg (23%) reduction since 2014. Sales of HP-CIAs accounted for 0.65 mg/kg (1% of total sales) in 2020, a decrease of 0.34 mg/kg (35%) since 2014, although an increase of 0.02 mg/kg since 2019.

When considering sales for all animals, the total quantity of antibiotics sold during 2020 was 226.0 tonnes, a 2.6 tonne (1%) decrease since 2019, and a 220.5 tonne (49%) decrease since 2014. Sales of HP-CIAs were 1.1 tonnes, representing 0.5% total sales, and have reduced by 0.18 tonnes since 2019 and 3.7 tonnes (77%) since 2014.

1.2 Introduction

Pharmaceutical companies have reported the quantity of authorised veterinary antibiotics sold throughout the UK to the VMD since 1993; this has been a statutory requirement since 2005 (see section S1.1 in the supplementary material for further details). The data reported in this chapter do not take into account wastage, imports or exports of veterinary antibiotics, but they serve as the best currently available approximation of the quantity of antibiotics administered to all animal species within the UK (further details on data limitations can be found in Annex E).

Data has been analysed using European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) methodology. As described in Section 1.4, this methodology had some upgrades in 2020 and these have been applied retrospectively, which is why figures for previous years differ slightly from previous UK-VARSS publications.

Note that for ease of reading, the data has been rounded to one decimal place. However, the percentage changes have been calculated using the exact number. Antibiotics are considered HP-CIAs if they are within “Category B” in the Antimicrobial Expert Group (AMEG) report, that is to say, third and fourth generation cephalosporins, polymyxins (that is to say, colistin) and quinolones/fluoroquinolones[1].

[1] https://www.ema.europa.eu/en/documents/report/infographic-categorisation-antibiotics-use-animals-prudent-responsible-use_en.pdf.

Data has been presented graphically throughout the report for ease of reading. Data tables can be found in the Supplementary material.

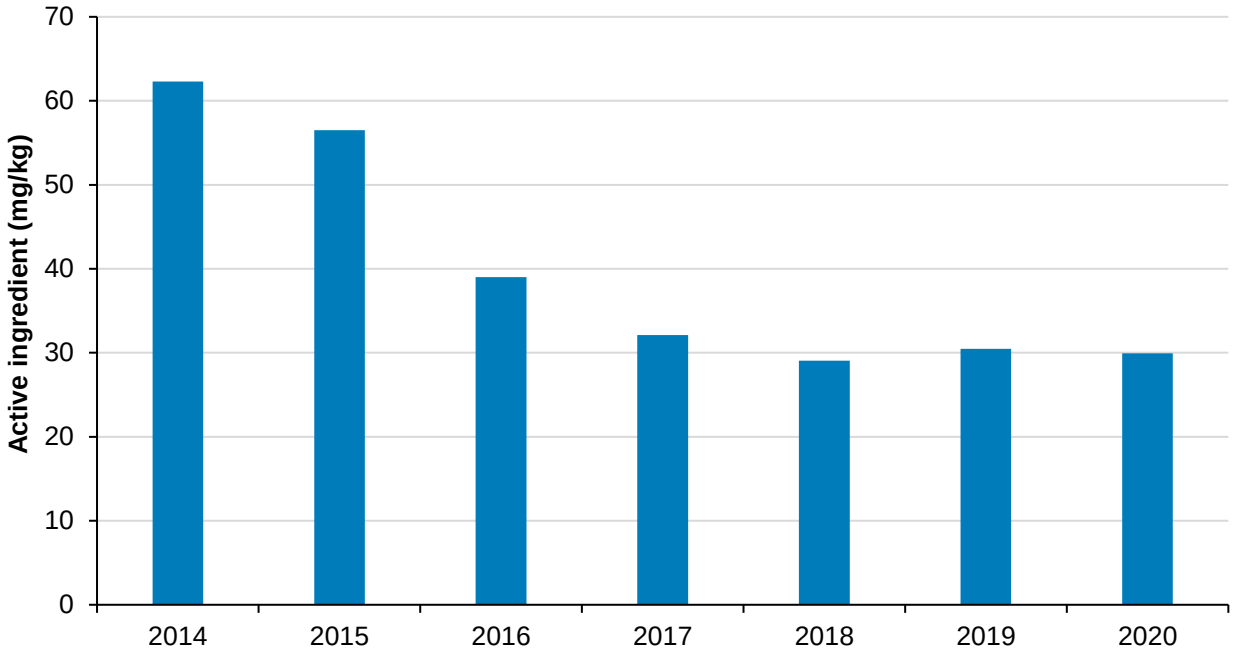
1.3 Results and discussion

1.3.1 Sales of antibiotics for food-producing animal species (mg/kg)

1.3.1.1 Total sales for food-producing animals (mg/kg)

The sales of antibiotics licensed for food-producing animal species decreased by 0.3 mg/kg (1%) between 2019 and 2020 to 30.1 mg/kg and by 32.2 mg/kg (52%) between 2014 and 2020 (**Figure 1.1**). In the UK Five Year National Action Plan[2], there was a target to reduce antibiotic use in food-producing animals by 25% to 29.3 mg/kg between 2016 and 2020 (which was based on the targets that the livestock sectors set in 2017). This target was met ahead of schedule in 2018 (when usage was 29 mg/kg). In 2020, however, sales were marginally above the target, with a 8.9 mg/kg (23%) reduction since 2016.

Figure 1.1: Active ingredient (mg/kg) of antibiotics sold for use in food-producing animals, 2014 to 2020

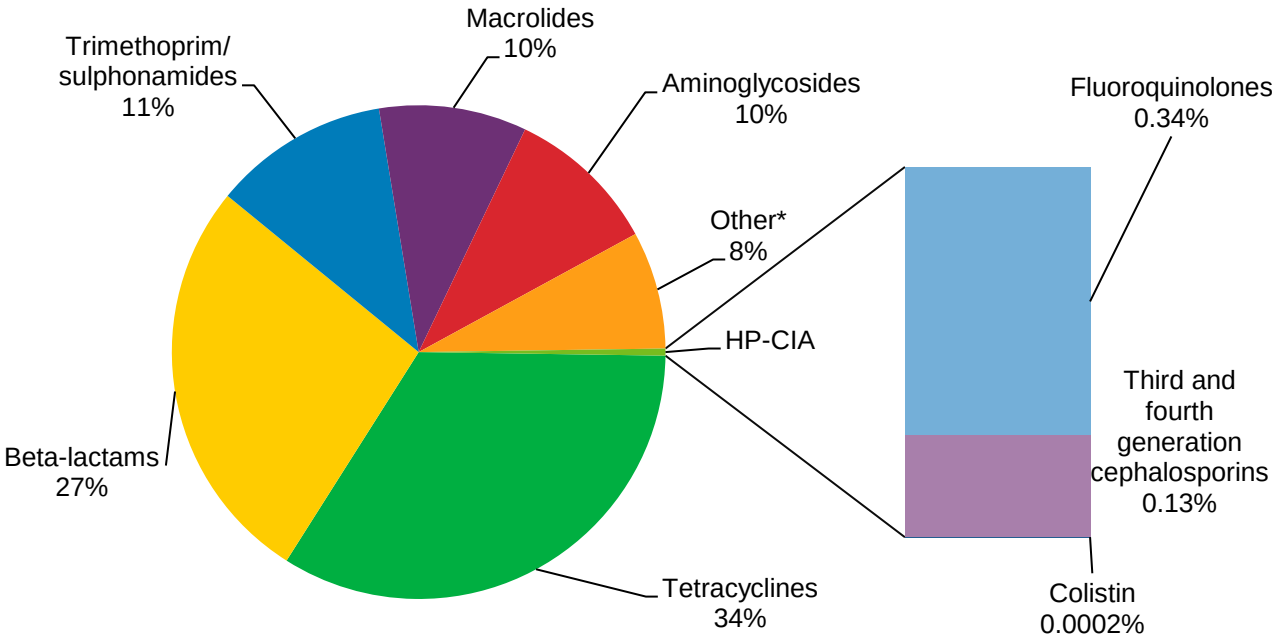


1.3.1.2 Sales by antibiotic class for food-producing animals (mg/kg)

Sales by antibiotic class for food-producing animals are shown in **Figure 1.2** and **Figure 1.3**.

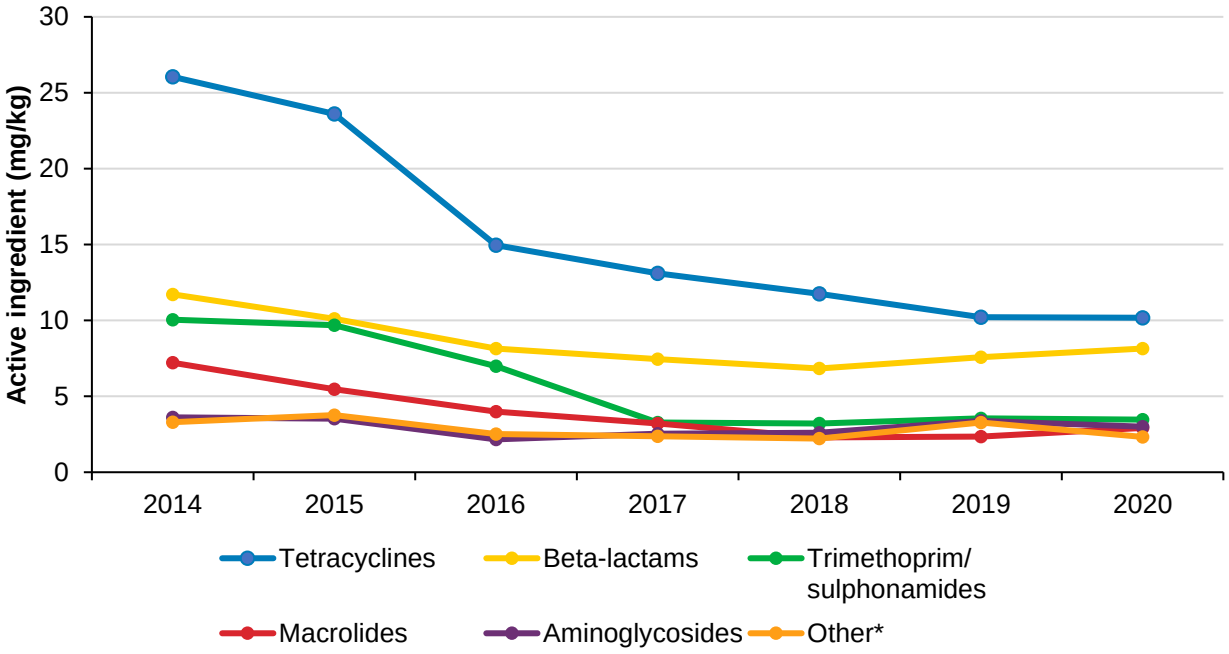
[2]https://assets.publishing.service.gov.uk/government/uploads/system/uploads/attachment_data/file/784894/UK_AMR_5_year_national_action_plan.pdf

Figure 1.2: Active ingredient (% weight) of antibiotics by antibiotic class sold for use in food-producing animals, 2020



* Amphenicols, lincomycins, pleuromutilins, steroidal antibiotics and imidazole derivatives

Figure 1.3: Active ingredient (mg/kg) of antibiotics by antibiotic class sold for use in food-producing animals, 2014 to 2020



* Amphenicols, lincomycins, pleuromutilins, polymyxins (including colistin), steroidal antibiotics and imidazole derivatives.

Tetracyclines and beta lactams are the most sold antibiotic class for food-producing animals, representing 34% and 27% of total antibiotics sold respectively. However,

tetracycline use remained stable between 2019 and 2020 whereas the use of beta-lactams increased by 0.6 mg/kg – in particular amoxicillin, which increased by 0.7 mg/kg. This is largely due to a 0.8 mg/kg increase in amoxicillin oral powders/oral solutions, which are licensed for pigs and/or poultry. Since 2014, tetracycline sales for food-producing animals have reduced by 15.9 mg/kg (61%) whereas beta lactams have fallen to a lesser degree, by 3.6 mg/kg (31%). This is partly linked to the trend away from in-feed use and towards medicating in-water (see Section 1.3.1.3), as in 2020 59% tetracycline use was for in-feed in 2020 (compared with just 18% for beta-lactams).

When looking at the other antibiotic classes, aminoglycoside sales reduced by 0.4 mg/kg between 2019 and 2020. In particular, neomycin (the majority of which is available as an oral powder licensed for pigs, poultry, and cattle) sales increased from 0.5 mg/kg to 1 mg/kg between 2018 and 2019, but then dropped back to 0.5 mg/kg in 2020. Since 2014, trimethoprim-sulphonamides have also reduced by 6.6 mg/kg (65%) and aminoglycosides have fallen by 0.6 mg/kg (17%).

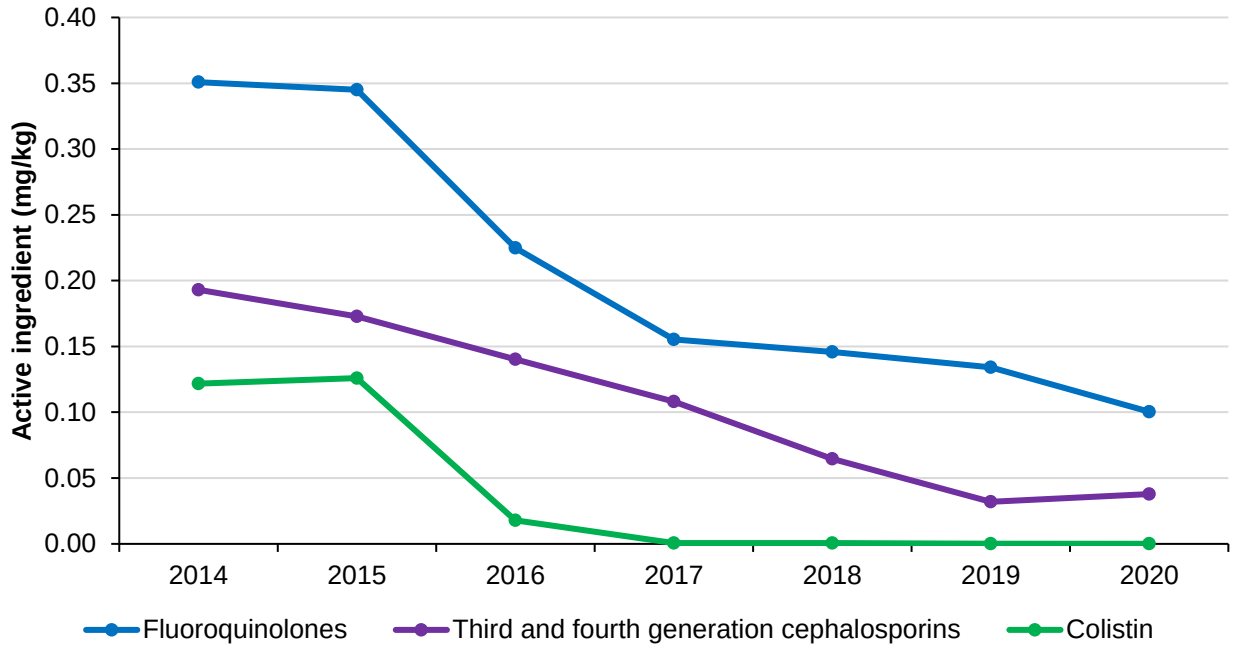
Macrolide sales increased by 0.6 mg/kg between 2019 and 2020, driven by a 0.5 mg/kg increase in tylosin, in particular for the tylosin premixes (which are licensed for pigs +/- chickens). However, macrolide sales are still 4.3 mg/kg (60%) less than in 2014. Sales of pleuromutilin tiamulin also fell by 1.0 mg/kg between 2019 and 2020, mainly due to reductions of in-feed tiamulin (which is licensed for pigs, chickens and turkeys).

Sales of HP-CIAs for food-producing animals are shown in **Figure 1.4**. Sales of HP-CIAs for food-producing animals were 0.14 mg/kg, which represents 0.5% of the overall antibiotic sales, and is a reduction of 0.03 mg/kg between 2019 and 2020. HP-CIA sales for food-producing animals have now decreased for the sixth year running, with total reductions of 0.5 mg/kg (79%) since 2014.

Fluoroquinolone sales reduced by 0.03 mg/kg between 2019 and 2020. This was driven by a 0.04 mg/kg reduction in fluoroquinolones for oral solution, due to reductions in products licensed for chickens and turkeys. By contrast, injectable fluoroquinolones increased by 0.01 mg/kg due to increases in the sale of products licensed for cattle and pigs. Colistin sales continued to decrease in 2020, reducing by 0.0001 mg/kg (59%) since 2019. Colistin sales were attributed to one product with only 2 packs sold.

Despite the overall reduction in HP-CIAs, there was a 0.006 mg/kg increase in the sales of third and fourth generation cephalosporins. This is due to an 0.005 mg/kg increase in intramammary use and a 0.001 mg/kg increase in injectable use (the latter of which was due to an increase in products licensed for cattle and pigs).

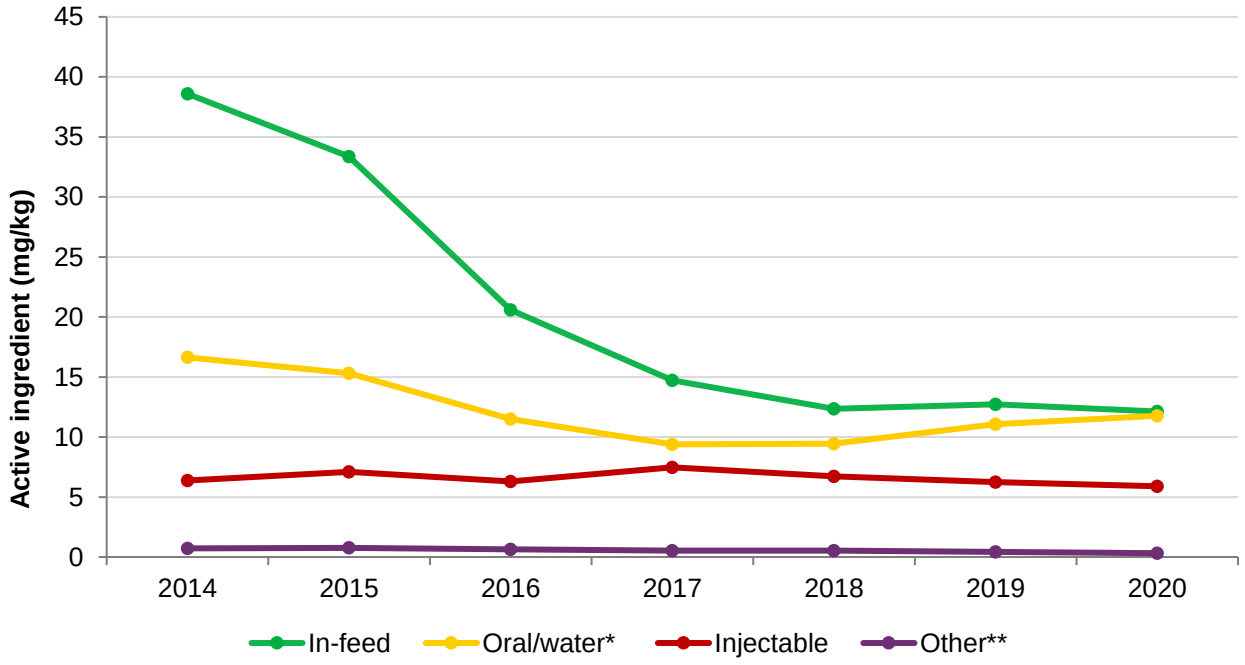
Figure 1.4: Active ingredient (mg/kg) of HP-CIAs sold for use in food-producing animals, 2014 to 2020



1.3.1.3 Sales by route of administration for food-producing animals (mg/kg)

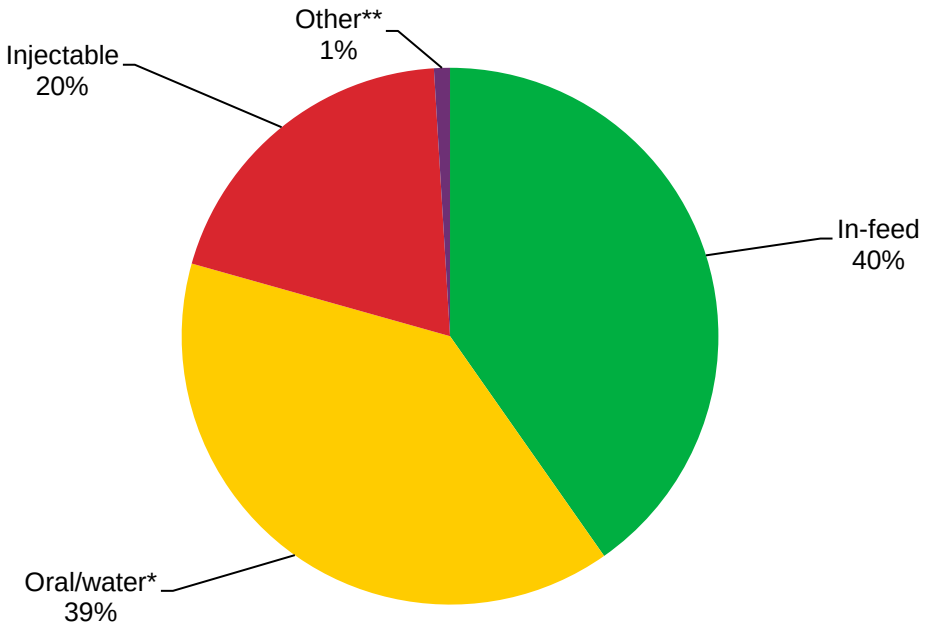
Sales by route of administration for food-producing animals are shown in **Figure 1.5** and **Figure 1.6**.

Figure 1.5: Active ingredient (mg/kg) of antibiotics by route of administration sold for use in food-producing animals, 2014 to 2020



* Oral powders, oral pastes, oral solutions and bolus preparations.
** Includes intramammary dry and lactating cow, bolus and intrauterine preparations.

Figure 1.6: Active ingredient (% weight) of antibiotics by route of administration sold for use in food-producing animals, 2020



* Oral powders, oral pastes, oral solutions and bolus preparations.
** Includes intramammary dry and lactating cow, bolus and intrauterine preparations.

When considering route of administration for food-producing animals, 40% is in-feed and 39% is for oral/water use. However, between 2019 and 2020, in-feed use reduced by 0.6 mg/kg whereas oral/water use increased by 0.7 mg/kg. In-feed use has now reduced by 26 mg/kg (69%) since 2014 and, as a percentage of total use, has decreased every year since 2014. By contrast, oral/water use has reduced to a lesser degree, by 4.9 mg/kg (29%) since 2014 and has increased by 2.3 mg/kg (25%) in the last two years. This reflects a shift away from in-feed and towards oral/water treatments, a trend which has also been demonstrated in the antibiotic usage data from the pig and gamebird sectors.

1.3.1.4 Sales of intramammary antibiotic products (course doses)

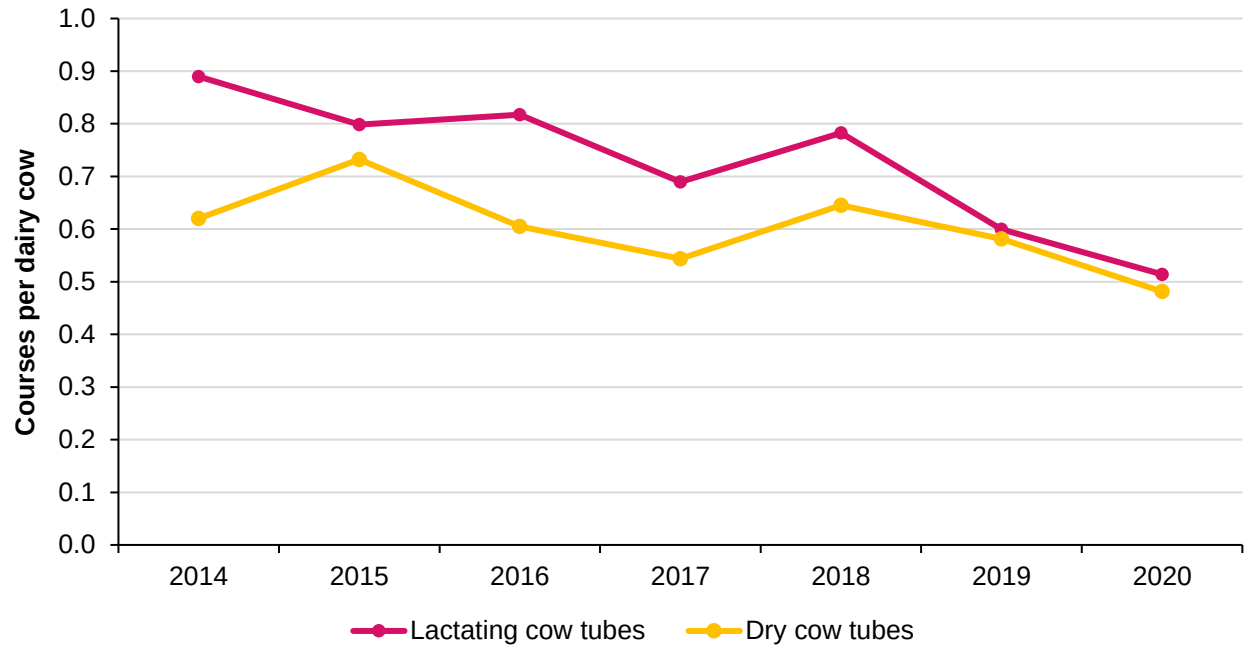
Sales of dry and lactating cow products analysed using the ESVAC defined course dose methodology (DCDvet) are shown in **Figure 1.7**. The DCDvet represents the average number of courses per dairy cow using a standard course dose of four tubes per dry cow and three tubes for most lactating cow treatments. Since 2018 sales of dry and lactating cow products reduced by 0.16 course doses (25%) and 0.27 course doses (34%) respectively. As reported in last year's VARSS report, sales of HP-CIA intramammary products decreased by 0.34 course doses (92%) between 2014 and 2019; however, between 2019 and 2020 there was an increase of 0.04 course doses.

It should be noted that there were availability issues with lactating cow intramammary products in 2020, which may have affected product choice. Additionally, if the available products were considered clinically unsuitable by the veterinary surgeon, alternative

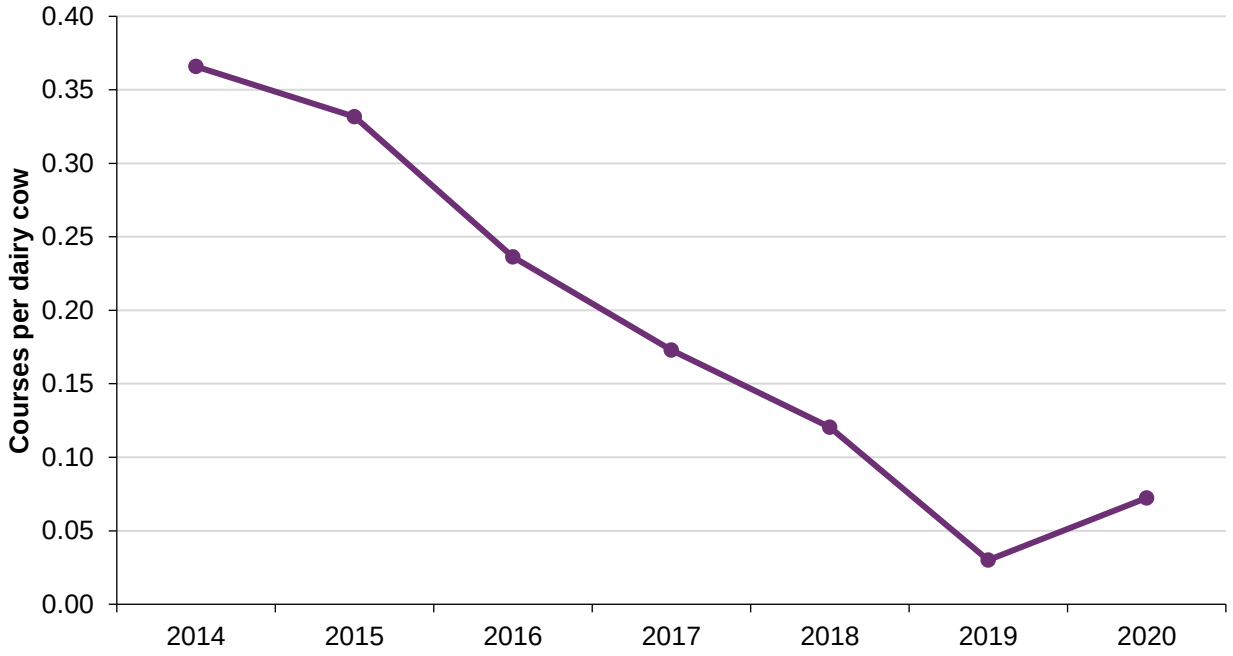
products authorised outside the UK can be imported on a case-by-case basis under the Special Import Scheme. These products are not captured in the antibiotic sales data.

Figure 1.7: Sales of (A) dry and lactating cow intramammary products (courses per dairy cow), 2014–2020, (B) Sales of HP-CIA intramammary products (courses per dairy cow, 2014 to 2020

(A)



(B)

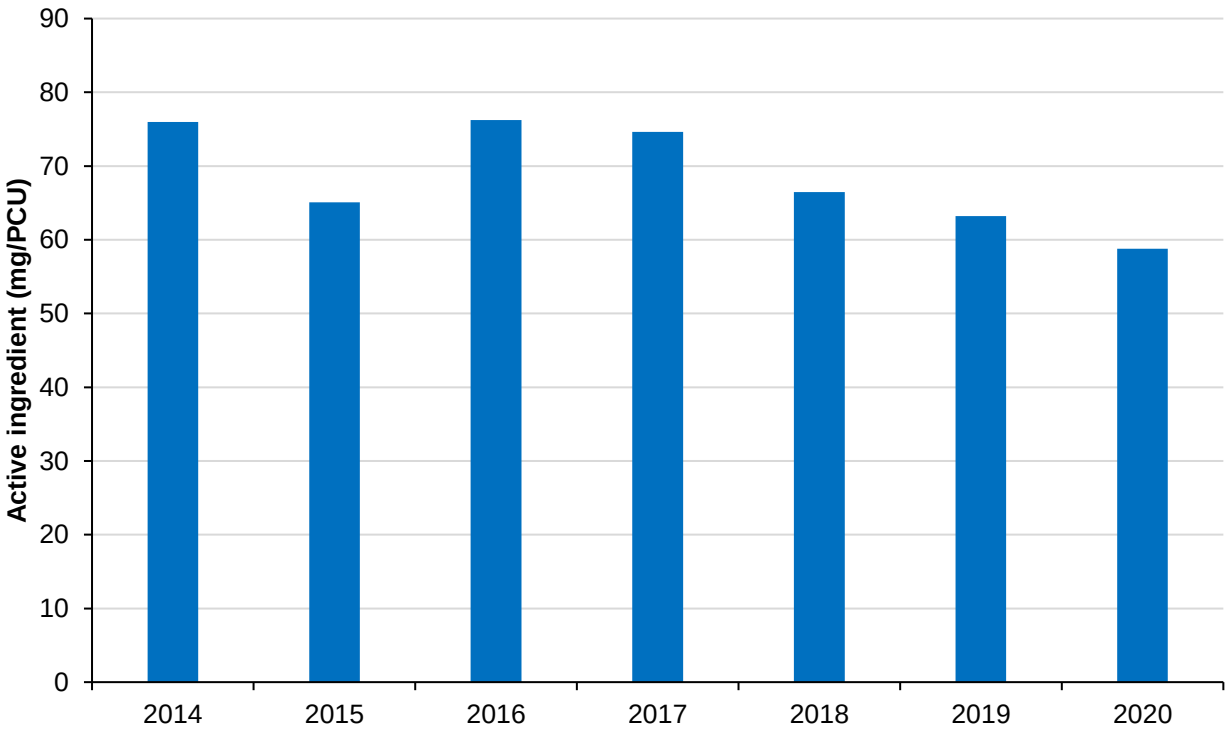


1.3.2 Sales of antibiotics for dogs and cats (mg/kg)

Sales of antibiotics for dogs and cats are shown in **Figure 1.8**, **Figure 1.9** and **Figure 1.10**. For the data presented in this section, the ESVAC methodology was used for calculating the amount of active ingredient, analysing sales data of all products (including tablets) licensed for dogs only, cats only, or licensed for a combination of dogs and cats. Products licensed for multiple companion animal species (rabbits, exotics and horses in combination with dogs and cats) were not included in the analysis, but these products only represent 110 kg of active ingredient, compared to 11.7 tonnes of active ingredient sold for cats and dogs.

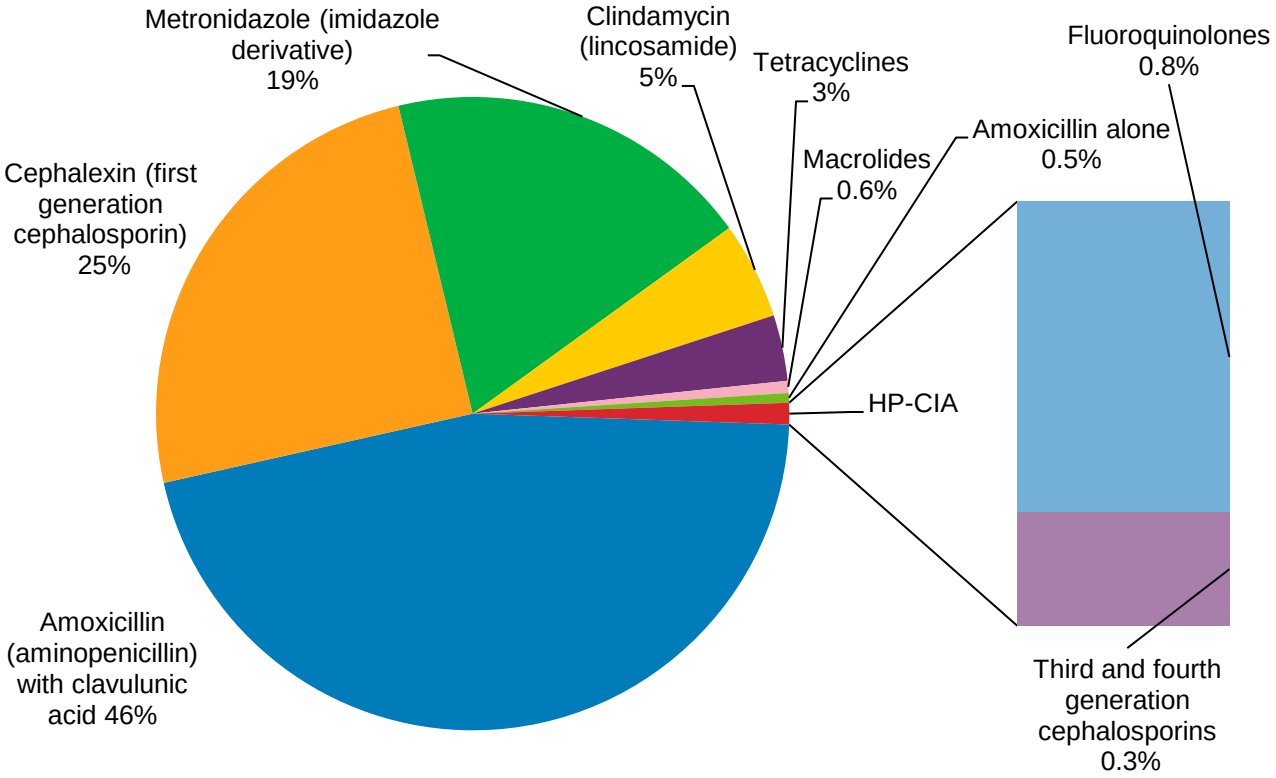
Sales of antibiotic products licensed for dogs and cats combined was 58.8 mg/kg in 2020. This is a 4.4 mg/kg reduction since 2019, and 17.2 mg/kg (23%) reduction since 2014. Nearly all sales were for tablet preparations (99% in 2020).

Figure 1.8: Active ingredient (mg/kg) of antibiotics sold for use in dogs and cats, 2014 to 2020



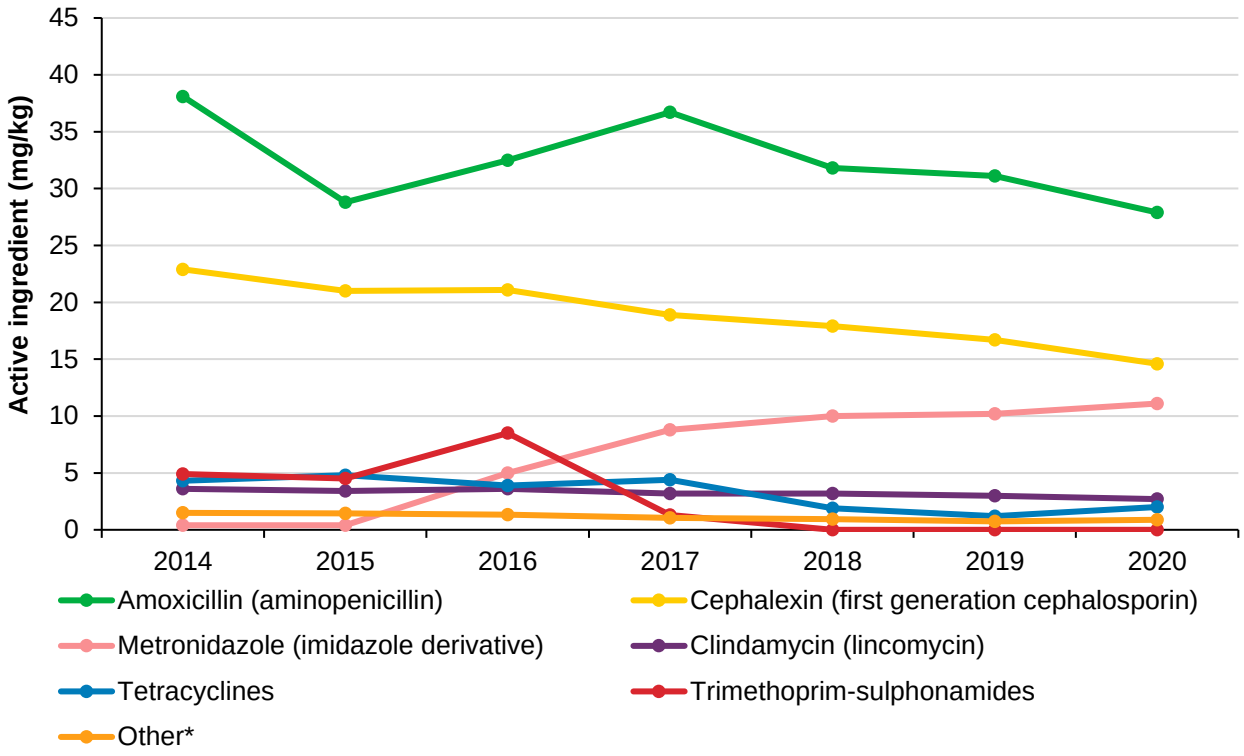
Beta-lactams were the most sold antibiotic class, representing 42.2 mg/kg (72% of total sales) in 2020, of which 65% comprises the aminopenicillin amoxicillin and 34% comprises first generation cephalosporin cephalexin. In 2020 99% of amoxicillin was prescribed alongside the beta lactamase inhibitor clavulanic acid. Antibiotics in the ‘other’ category represented 13.7 mg/kg (23% of total sales) in 2020, with 11.0 mg/kg of this (80%) relating to the imidazole derivative metronidazole.

Figure 1.9: Active ingredient (% weight) of antibiotics by antibiotic class sold for use in dogs and cats, 2020



The biggest reductions have been seen with cephalexin products (which have reduced by 2.2 mg/kg since 2019 and 8.4 mg/kg (37%) since 2014) and amoxicillin products (which have reduced by 3.5 mg/kg since 2019 and 10.5 mg/kg (28%) since 2014). By contrast, sales of metronidazole increased by 0.8 mg/kg compared with 2019 and 10.7 mg/kg since 2014, increasing every year since 2015, which coincides with the launch of new metronidazole products.

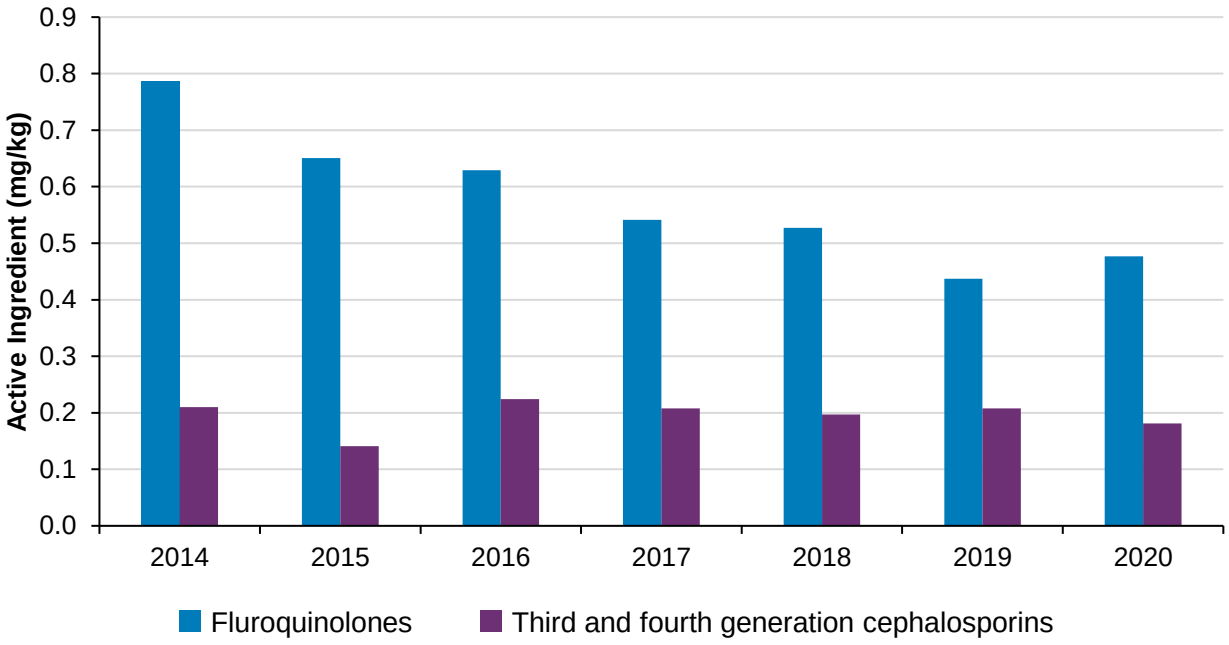
Figure 1.10: Active ingredient (mg/kg) of antibiotics by antibiotic class sold for use in dogs and cats, 2014 to 2020



* Third generation cephalosporins, fluoroquinolones and macrolides

Sales of HP-CIAs accounted for 0.66 mg/kg (1% of total sales) and these increased by 0.01 mg/kg since 2019. This is due to a 0.04 mg/kg increase in the sales of fluoroquinolones, although cefovecin (the only third and fourth generation cephalosporin licensed for dogs and cats) reduced by 0.03 mg/kg. When considering longer term trends, HP-CIAs have reduced by 0.34 mg/kg (34%) since 2014, with fluoroquinolones reducing by 0.3 mg/kg (39%) and third generation cephalosporins reducing by 0.03 mg/kg (14%) (**Figure 1.11**).

Figure 1.11: Active ingredient (mg/kg) of HP-CIAs, sold for use in dogs and cats, 2014 to 2020

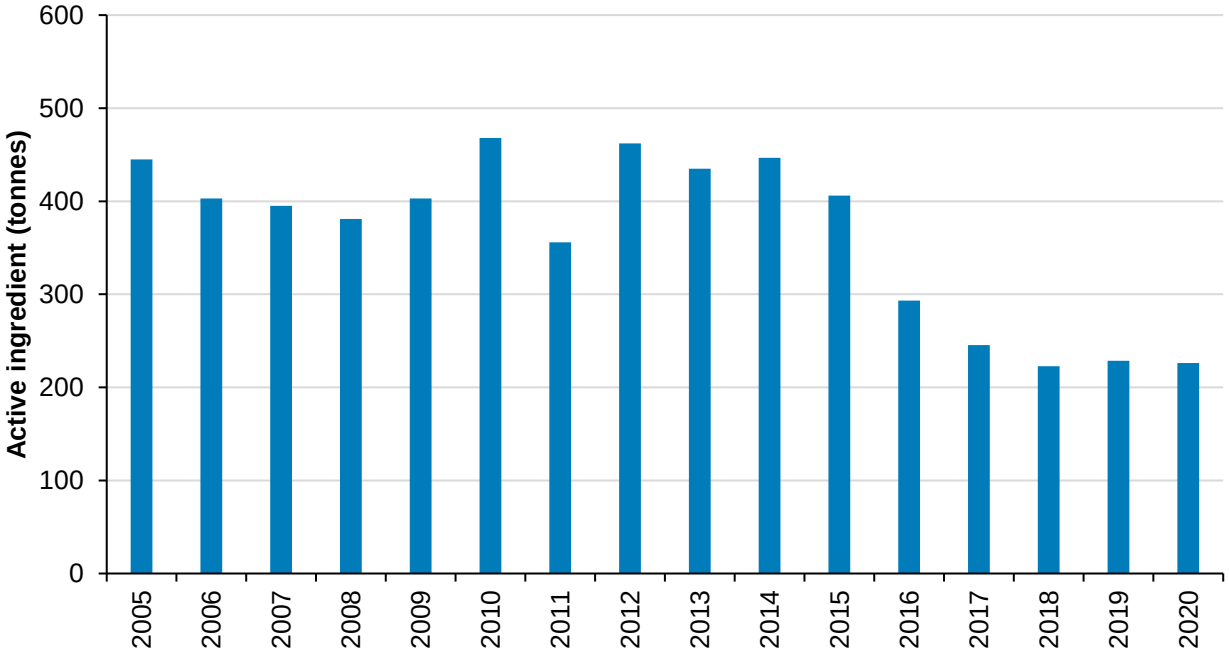


1.3.3 Total sales of antibiotics for all animals (tonnes)

Total sales of antibiotics and sales of HP-CIAs for all animals are shown in **Figure 1.12** and **Figure 1.13** (with data tables contained in Supplementary Material). Sales data analysed using the ESVAC methodology are available from 2005; the ESVAC project was launched in September 2009 and the first report published aggregated sales data for the years 2005–2009. Prior to these years, data (covering 1993–2005) were analysed using the UK-VARSS methodology, further details of which can be found in S1.5 of the supplementary material.

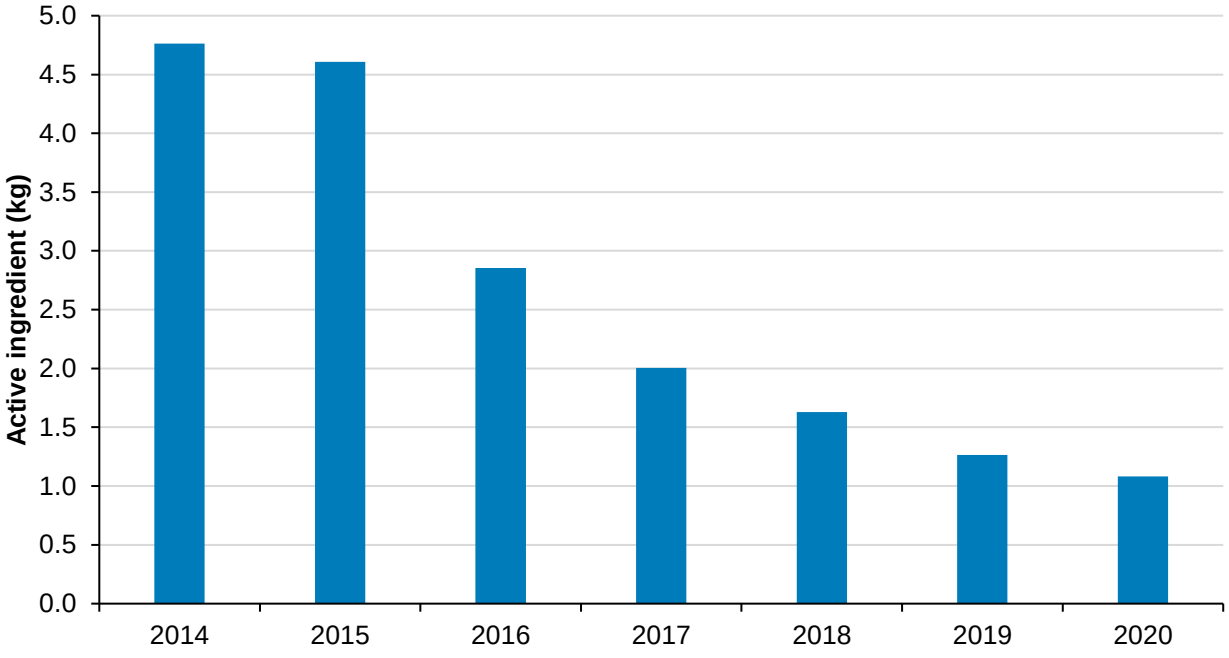
The total quantity of antibiotic active ingredient sold in 2020 was 226.0 tonnes, a 2.6 tonne (1%) decrease since 2019, and a 220.5 tonne (49%) decrease since 2014.

Figure 1.12: Active ingredient (tonnes) of antibiotics sold for use in all animals, 2005 to 2020



When considering HP-CIAs, these have reduced every year since 2014 by a total of 3.7 tonnes (77%) to 1.1 tonnes in 2020. HP-CIA sales now account for 0.5% total antibiotic sales.

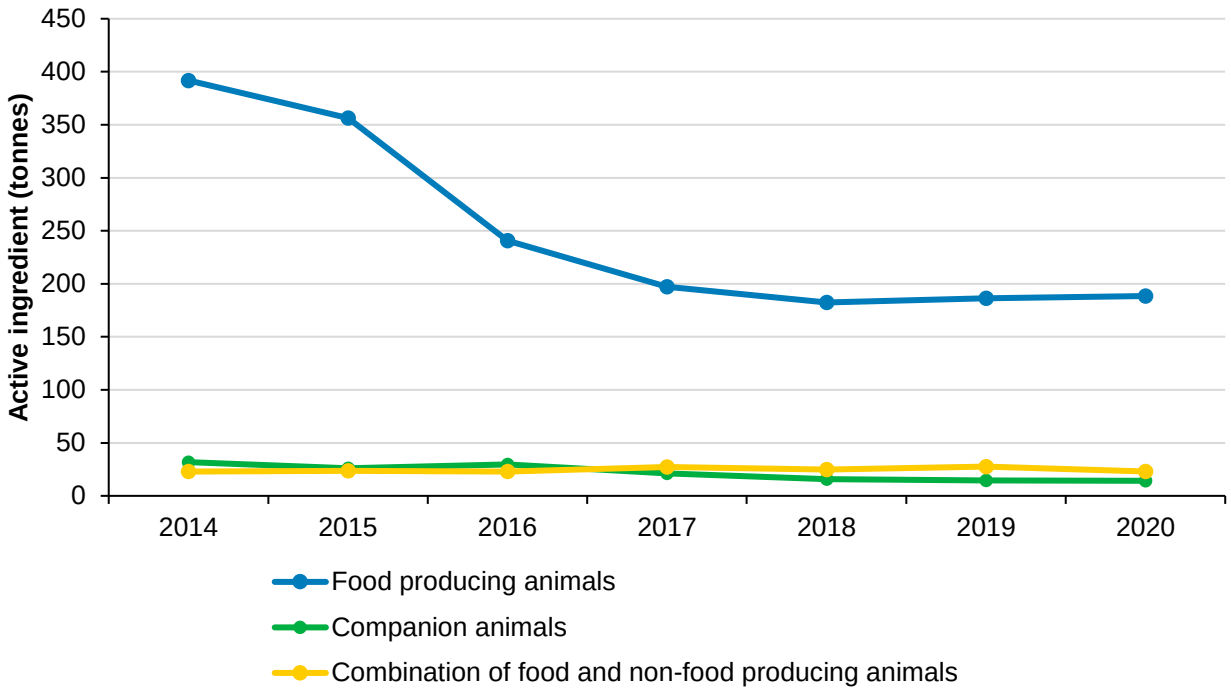
Figure 1.13: Active ingredient (kg) of HP-CIAs sold for use in all animals, 2014 to 2020



1.3.4 Total sales of antibiotics by species indication (tonnes)

Sales of antibiotics by species indication are shown in **Figure 1.14** (with full data tables included in the supplementary material):

Figure 1.14: Active ingredient (tonnes) of antibiotics sold by species indication, 2014 to 2020



In 2020, 188.8 tonnes (84%) of antibiotic sales were attributed to products licensed for food-producing animal species only. This is a 2.4 tonne increase since 2019, largely due to a 2.0 tonne increase in products authorised for fish. Sales of products licensed for pigs and/or poultry and multiple food-producing animals also increased slightly (by 0.5 tonnes and 0.6 tonnes respectively) whereas products licensed for cattle only decreased by 0.8 tonnes.

Products licensed for non-food-producing animal species accounted for 14.2 tonnes in 2020 (6% of total sales) and these reduced by 0.4 tonnes since 2019. This is due to a 0.8 tonne decrease in sales for companion animals (primarily dogs and cats) whereas products licensed for horses only increased by 0.3 tonnes.

In 2020, sales of antibiotics indicated for a combination of food and non-food producing animal species were 23.0 tonnes (10% of the total) and this has decreased by 4.6 tonnes since 2019. This category comprises of 99.8% injectable products.

To provide some context, the weight of food producing animals using the PCU methodology (but excluding horses) increased by 0.24% between 2019 and 2020,

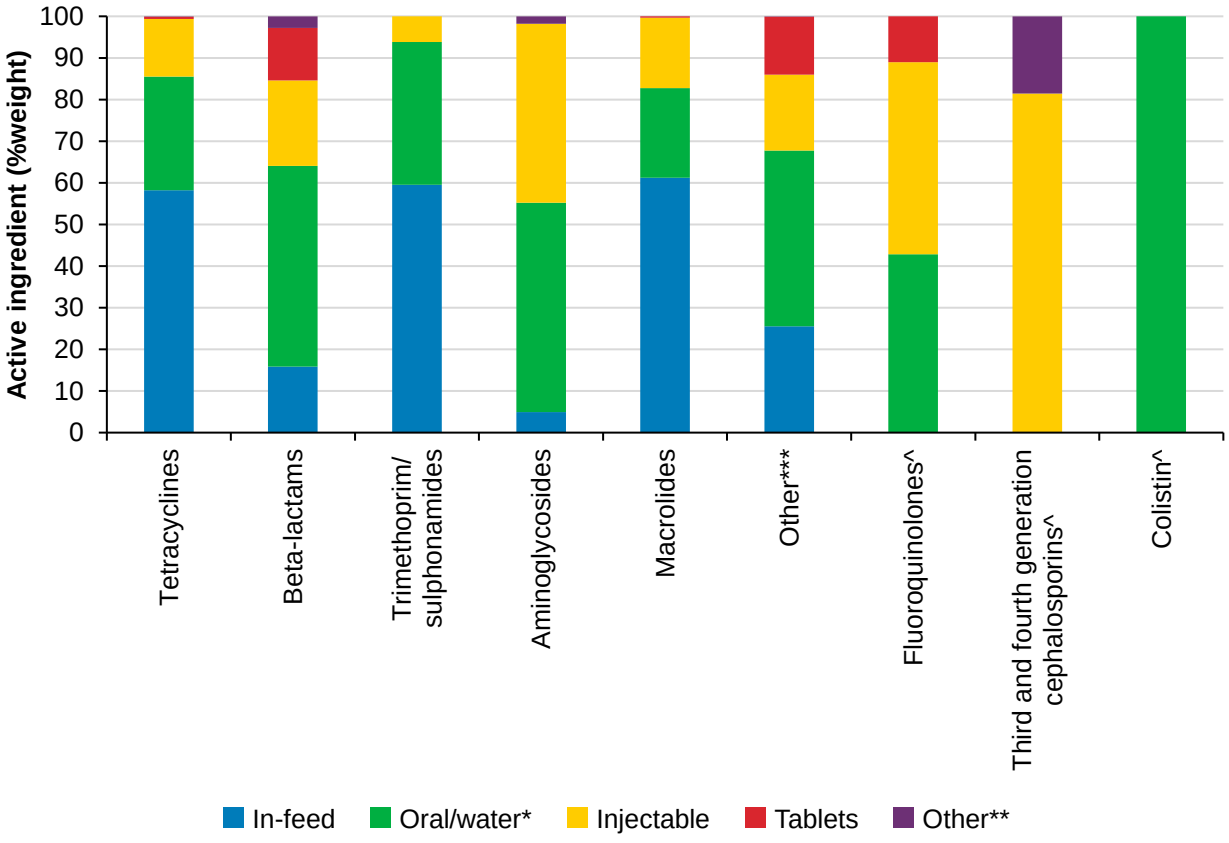
whereas the weight of the dog and cat population increased by 1% and the horse population is estimated to have remained the same.

Where antibiotic usage data are available per species or sector and represent a high proportion of the industry (for example pigs, meat poultry, laying hens, gamebirds, trout and salmon, see **Chapter 2**), these can be extrapolated and compared with the antibiotic sales of products authorised for those species. This analysis shows that these figures are comparable and follow the same trend.

1.3.4.1 By active ingredient and route of administration for all animal species (tonnes)

Sales different routes of administration for each active ingredient are shown in **Figure 1.15** (with data tables contained within the supplementary material).

Figure 1.15: Active ingredient (% weight) of antibiotics by antibiotic class and route of administration sold for all animals, 2020



^ HP-CIAs
***** Oral powders, oral pastes, oral solutions and bolus preparations
** Intramammary and intrauterine preparations
*** Amphenicols, lincomycins, pleuromutilins, polymyxins (including colistin), steroidal antibiotics and imidazole derivatives

When looking at antibiotic sales for all animal species, tetracyclines accounted for 72.8 tonnes (32%) of total sales, 58% of which is in-feed whereas 27% is for oral/water use. However, beta lactam sales comprise 66.2 tonnes (29%) of total sales, but these are most commonly administered for oral/water use (48%) or as an injectable (21%).

The sales of trimethoprim-sulphonamides, aminoglycosides and macrolides are fairly similar (accounting for 11%, 9% and 9% of total sales respectively). However, while trimethoprim-sulphonamides and macrolides are mostly administered in-feed (accounting for 59% and 61% of their use respectively), aminoglycosides are most commonly administered by oral/water (51% total use) and injection (43% total use).

When considering route of administration for HP-CIAs, 81% of third and fourth generation cephalosporins were used via the injectable route, with the remainder as intra-mammary preparations for cattle; 48% of fluoroquinolones were used as injectables, with the remainder used as oral/water (21%) and tablets (13%); all colistin sales were for oral/water use.

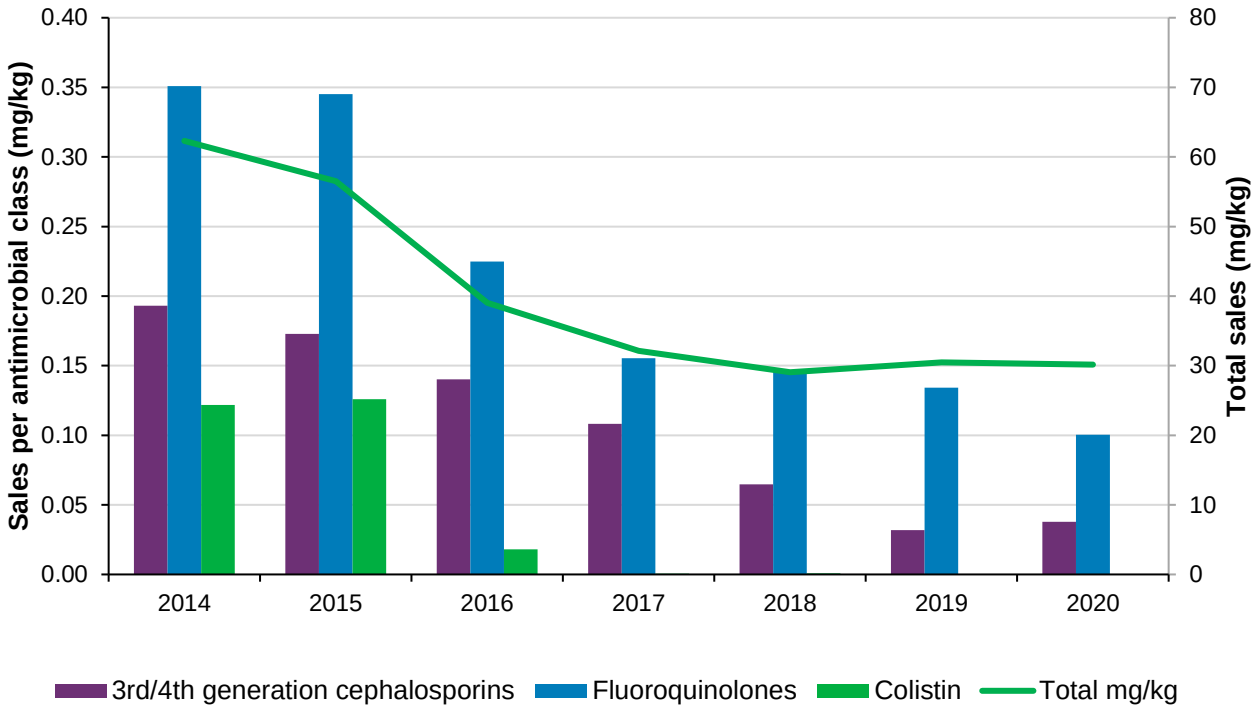
1.3.5 Harmonised outcome indicators for antibiotic use

In 2017, the European Centre for Disease Prevention and Control (ECDC), European Food Safety Authority (EFSA) and EMA published a set of harmonised outcome indicators for comparable monitoring of key indicators for antibiotic consumption in food-producing animals in the EU[3].

The primary indicator is "*the overall sales of veterinary antibiotics in milligram of active substance per kilogram of estimated weight at treatment of livestock and of slaughtered animals in a country (mg/PCU)*" (**Figure 1.1**). Secondary indicators are the sales in mg/PCU for third and fourth generation cephalosporins, quinolones (and percentage of fluoroquinolones) and polymyxins (**Figure 1.4**). In the UK all quinolones sold for use in food-producing animals are fluoroquinolones (although the quinolone oxolinic acid is imported for the fish sector; Section 2.3.6), and colistin is the only polymyxin sold for use in food-producing animals. The data show that all indicators have decreased since 2016 (**Figure 1.16**).

[3] https://www.ecdc.europa.eu/en/publications-data/ecdc-efsa-and-ema-joint-scientific-opinion-list-outcome-indicators-regards

Figure 1.16: EU harmonised primary (total sales of veterinary antibiotics in mg/kg and secondary (sales in mg/kg for third and fourth generation cephalosporins, quinolones and polymyxins) outcome indicators for antibiotic consumption in food-producing animal species in the UK; 2014 to 2020



Harmonised indicators for antibiotic use have also been developed by the tripartitie (World Health Organization (WHO), Food and Agriculture Organization of the United Nations (FAO) & World Organisation for Animal Health (OIE) monitoring and evaluation framework[4]. These include a core indicator measuring total volumes of sales or used based on a mg/kg biomass metric and the percentage of total sales classified by the WHO as Highest Priority Critically Important Antimicrobials. The data using these metrics (presented regionally) can be found in the OIE antimicrobial use report[5].

[4] https://apps.who.int/iris/handle/10665/325006
[5] https://www.oie.int/fileadmin/Home/eng/Our_scientific_expertise/docs/pdf/AMR/A_Fifth_Annual_Report_AMR.pdf

1.4 Methods

Data collection and validation

Pharmaceutical companies supplied annual sales of all authorised veterinary antibiotics to the VMD in accordance with the Veterinary Medicines Regulations[6]. Upon receipt, data were collated and validated. Product data entries were compared to those submitted in previous years. If there are large discrepancies between data provided in successive years, data validity is investigated and queried with the pharmaceutical company. Sales data contained in returned Periodic Safety Update Reports (PSURs) for antibiotic veterinary medicinal products were also compared to the sales data returned by the pharmaceutical companies, and any discrepancies investigated (further details can be found in Annex E).

Tonnes of active ingredient

The weight of antibiotic active ingredient sold is a measurement obtained by multiplying the quantitative composition of active ingredient for each product, taken from the Summary of Product Characteristics (SPC), by the number of units sold as reported by the pharmaceutical companies. For some active ingredients that are either prodrugs or expressed in International Units (IU), a conversion factor is applied. These conversion factors are recommended by the European Medicines Agency (EMA) in the framework of the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project[7].

Since UK-VARSS 2015 (published in 2016), sales data have been reported using ESVAC methodology. Further details on historical methodology for the calculation of quantity of active ingredient (as well as mg/PCU, see below) can be found in S1.5 of the supplementary material. Note that data presented in mg/kg for food-producing animals (which equals mg/PCU) do not include tablets, as, in line with the ESVAC methodology, these are assumed to be exclusively administered to companion animals.

The data reported here are presented according to the ATCvet Classification System for veterinary medicinal products shown in Table S1.5.2 of the supplementary material[8]. Sales of dermatological preparations and preparations for sensory organs (described as ‘other’ route of administration in this and previous UK-VARSS reports) are not included in calculations. Sales of these products have remained stable and account for no more than 3 tonnes of active ingredient (Table S1.5.3 of the supplementary material).

Population Correction Unit

Trends in sales of antibiotics over time are determined by taking into consideration variations in the size and number of the animal population. To achieve this, sales data were analysed using the Population Correction Unit (PCU), a theoretical unit of measure formulated by the EMA and adopted by the countries participating in the ESVAC project to

[6] http://www.legislation.gov.uk/uksi/2013/2033/contents/made
[7] https://www.ema.europa.eu/en/documents/report/sales-veterinary-antimicrobial-agents-31-european-countries-2018-trends-2010-2018-tenth-esvac-report_en.pdf
[8] https://www.whocc.no/atcvet/atcvet_index/

standardise sales against an animal population denominator. Using the PCU, overall sales of products authorised for use in food-producing animal species can be presented as mg/PCU.

The mg/PCU can be considered as the average quantity of active ingredient sold per kg bodyweight of food-producing animal in the UK based on an estimated weight at the point of treatment and enables year-on-year comparisons to be made. Further details on these calculations are presented in S1.6 of the supplementary material and full technical details on PCU methodology can be found in the 2011 ESVAC report[9].

In order to calculate the mg/kg for dogs and cats, a combined dog and cat weight of animal at risk (in kg) was calculated using population data from the Pet Food Manufacturers' Association[10] and average cat and dog weights provided by SAVSNET[11] (see S1.3 of the supplementary material). Within the sales section of this UK-VARSS report, all references to mg/kg for food-producing animals equate to mg/PCU.

Corrections for historical data

The VARSS methodology changed in 2020, with amendments to International Unit factors and now the weight of the salt is excluded if the weight of the active itself is included in the "Qualitative and Quantitative Composition" section of the product's SPC, even if the product name includes the weight of the salt, for example for the product "Citramox 1000 mg/g Powder for Use in Drinking Water for Chickens, Turkeys, Ducks and Pigs", 1000 mg/g represents the weight of Amoxicillin trihydrate. However, the SPC says this is equivalent to 871.2 mg/g amoxicillin, so this is the figure now chosen. These changes have been applied to the historical data.

[9] https://www.ema.europa.eu/en/documents/report/trends-sales-veterinary-antimicrobial-agents-nine-european-countries_en.pdf
[10] https://www.pfma.org.uk/statistics and average cat and dog weights provided by SAVSNET
[11] University of Liverpool, Small Animal Veterinary Surveillance Network (SAVSNET) project, personal communication, 2020

CHAPTER 2

Usage of veterinary antibiotics by animal species

2.1 Summary

The key trends are as follows:

- **Pigs –** Total usage reduced by 5.5 mg/kg between 2019 and 2020 to 105 mg/kg, and usage has now reduced 62% since 2015. There was a slight (0.01 mg/kg) increase in HP-CIA use since 2019, although this has still reduced 95% since 2015. The sector also demonstrates an ongoing shift away from in-feed medication towards in-water.
- **Broilers –** Total usage reduced by 1.2 mg/kg between 2019 and 2020 to 16.3 mg/kg, and usage has now reduced 67% since 2014. HP-CIA use was 0.001 mg/kg.
- **Turkeys –** Total usage reduced by 16.3 mg/kg to 25.7 mg/kg, which represents an 88% reduction since 2014. HP-CIA use also dropped from 0.11 mg/kg to 0.08 mg/kg
- **Ducks –** Total usage increased by 0.9 mg/kg to 2.6 mg/kg since 2019. No HP-CIAs were used by the sector.
- **Gamebirds –** Usage dropped by 4.4 tonnes (43%) to 6.0 tonnes of active ingredient since 2019. However, it should be noted that, due to Covid restrictions, the industry estimate that gamebird rearing reduced by 30% in 2020, which will explain some of the reduction in usage. Nonetheless, relative use of HP-CIAs reduced from 0.6% active ingredient in 2019 to 0.4% in 2020. The sector also demonstrates an ongoing shift away from in-feed medication towards in-water.
- **Trout –** Usage increased by 4.2 mg/kg to 13.9 mg/kg since 2019, although this is still 28% lower than usage in 2017. Usage of oxolinic acid (which, since 2020, is now classified as an HP-CIA) increased by 1.8 mg/kg to 4.3 mg/kg between 2019 and 2020, although is still 35% lower than the levels seen in 2017.
- **Salmon –** Usage increased by 15.8 mg/kg since 2019, 13.2 mg/kg (82%) higher than in 2017. Usage of oxolinic acid decreased by 0.012 mg/kg since 2019, representing a 0.11 mg/kg (89%) reduction since 2017.

2.2 Introduction

Many antibiotics are authorised for use in multiple animal species, so it is not possible to determine from sales data how much is used per species. The VMD is working in partnership with food-producing animal sectors to develop, facilitate and coordinate antibiotic usage data collection systems.

Antibiotic usage refers to the amount of antibiotics purchased, prescribed and/or administered. Capturing antibiotic usage data by animal species provides a baseline against which trends and the impact of interventions, such as those designed to reduce antibiotic use, can be measured. The data can also be used to investigate better any correlation between changing antibiotic use and antibiotic resistance. Data collection

systems also allow for benchmarking, enabling farmers to compare themselves with their peers and encouraging veterinarians and farmers to identify and share good practice and make interventions.

This chapter describes the progress achieved so far, with updates from the food-producing animal sectors. Methodology is outlined in Section 2.4.

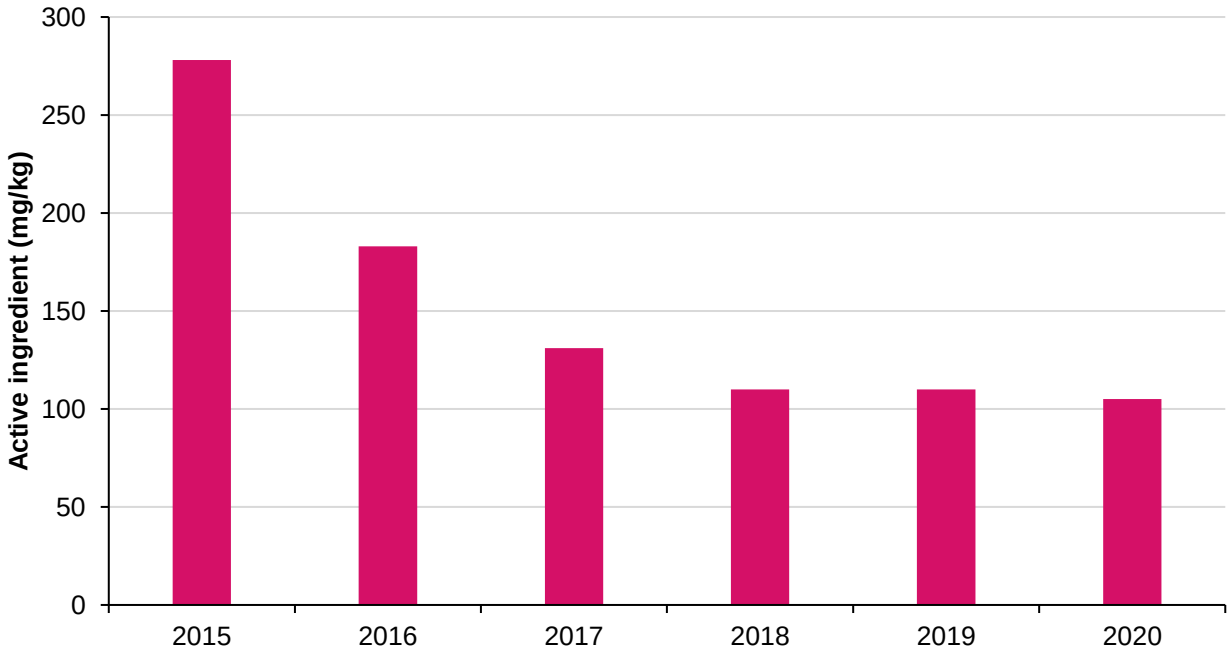
2.3 Results

2.3.1 Pigs

2.3.1.1 Antibiotic usage data

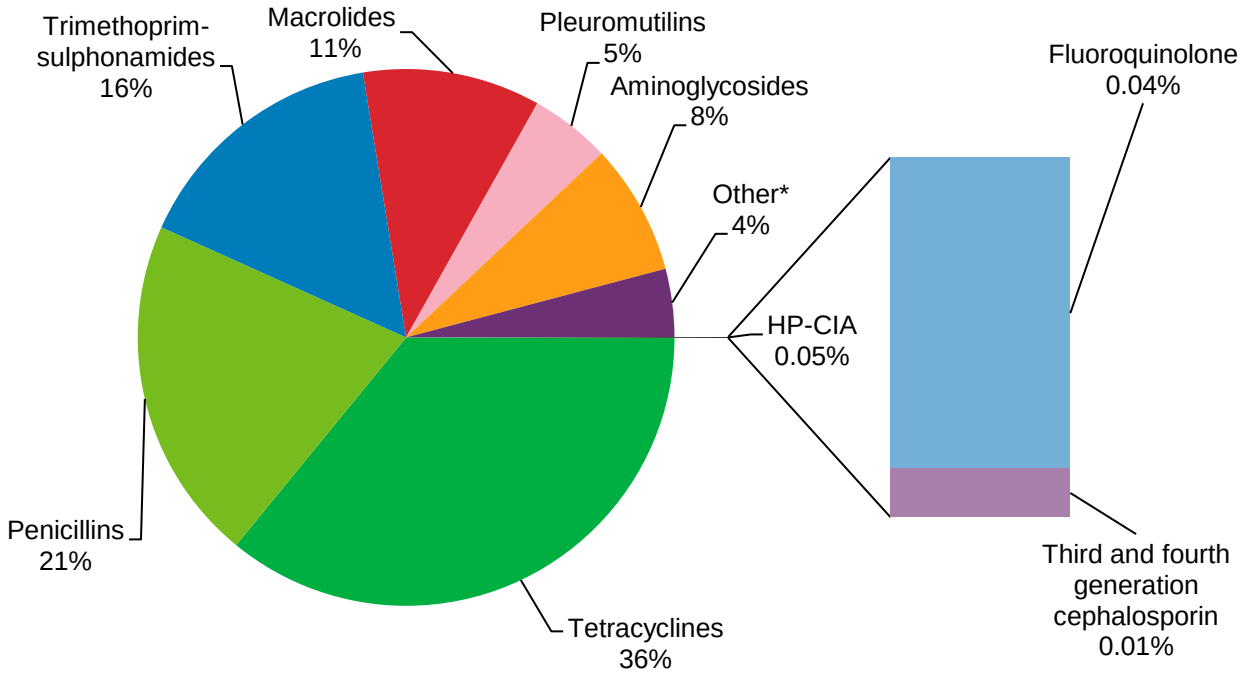
Total electronic Medicines Book for Pigs (eMB Pigs) data shows that total antibiotic usage in pigs was 83.0 tonnes for 2020, which represents 105 mg/kg. This is a decrease of 5.5 mg/kg (5%) since 2019, and a reduction of 172.7 mg/kg (62%) since 2015 (**Figure 2.1**).

Figure 2.1: Active ingredient (mg/kg) of antibiotics reported in eMB pigs, 2015 to 2020



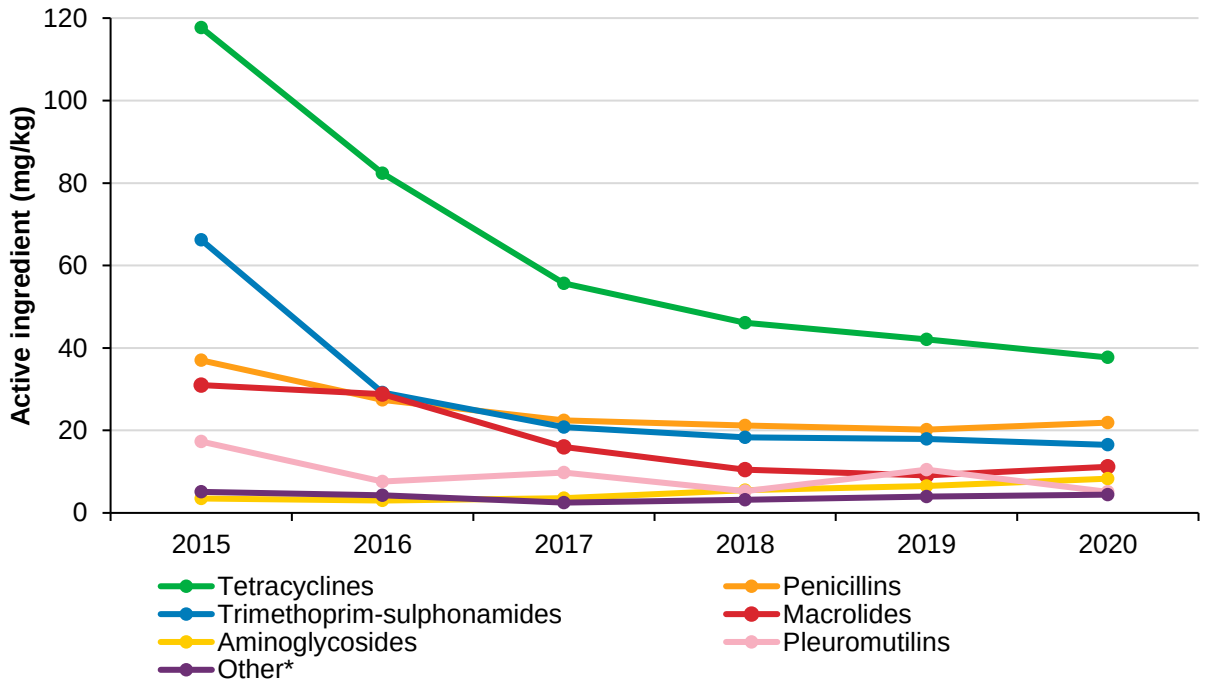
The different antibiotic classes used are shown in **Figure 2.2** and **Figure 2.3.**

Figure 2.2: Active ingredient (% weight) of antibiotics by antibiotic class reported in eMB pigs, 2020



*lincosamides and amphenicols

Figure 2.3: Active ingredient (mg/kg) of antibiotics by antibiotic class reported in eMB Pigs, 2015 to 2020



* Lincosamides, amphenicols, polymyxins, fluoroquinolones and third and fourth generation cephalosporins.

Tetracyclines remain the most used antibiotic class, representing 36% of antibiotic used in 2020. However, it is notable that tetracyclines (74% of which are administered in-feed) and trimethoprim-sulphonamides (75% of which are administered in-feed) have both reduced

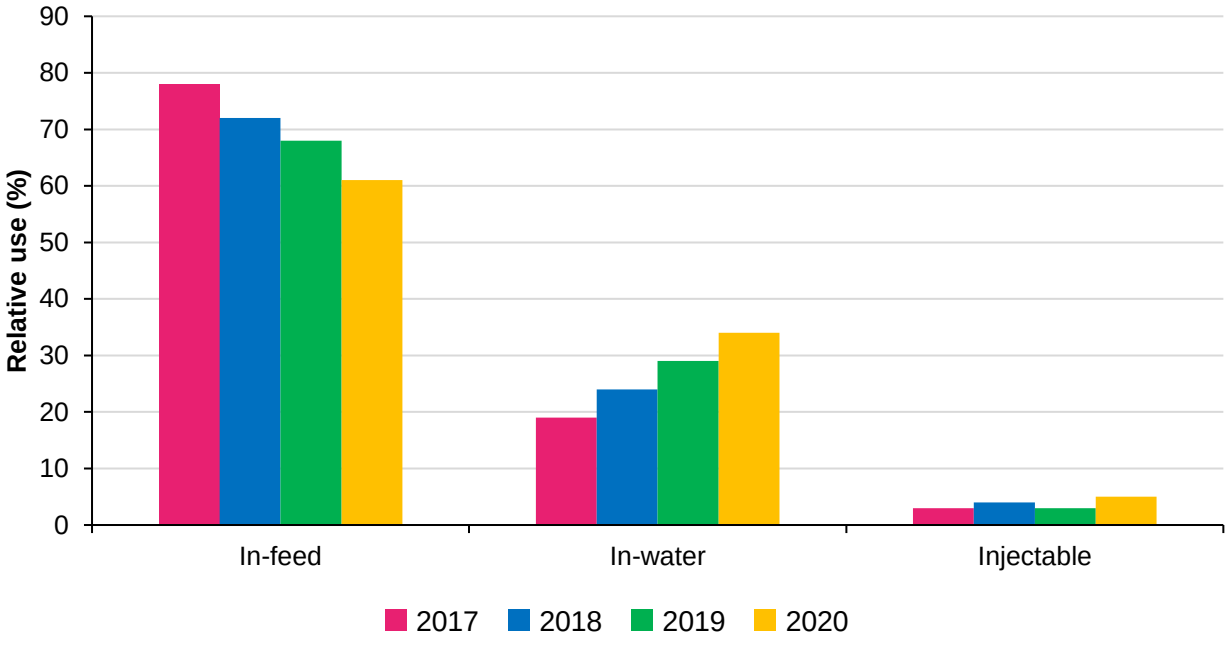
every year since 2015, by 80.0 mg/kg (68%) and 49.8 mg/kg (75%) respectively. Penicillins were the second most used antibiotic class (representing 21% use) and use has reduced by 15.1 mg/kg (41%) since 2015. However, penicillin usage increased by 1.7 mg/kg between 2019 and 2020. In 2020, 45% of penicillin use was in-feed and 43% in-water.

Pleuromutilin use (65% of which is given in-feed) decreased from 10.5 mg/kg in 2019 to 5.1 mg/kg (5%) in 2020 (to similar usage levels that were seen in 2018). The increase in pleuromutilins in 2019 is likely to be due to antibiotic treatments for swine dysentery outbreaks in 2019.

Macrolides (91% of which are administered in-feed) increased by 2.1 mg/kg since 2019 but have decreased by 19.7 mg/kg (64%) since 2015. Aminoglycoside use also increased between 2019 and 2020, by 1.8 mg/kg, now representing 8% overall use. Usage of this class has increased every year since 2016. In 2020, the majority of aminoglycosides were administered in-water (64%) or by injection (27%).

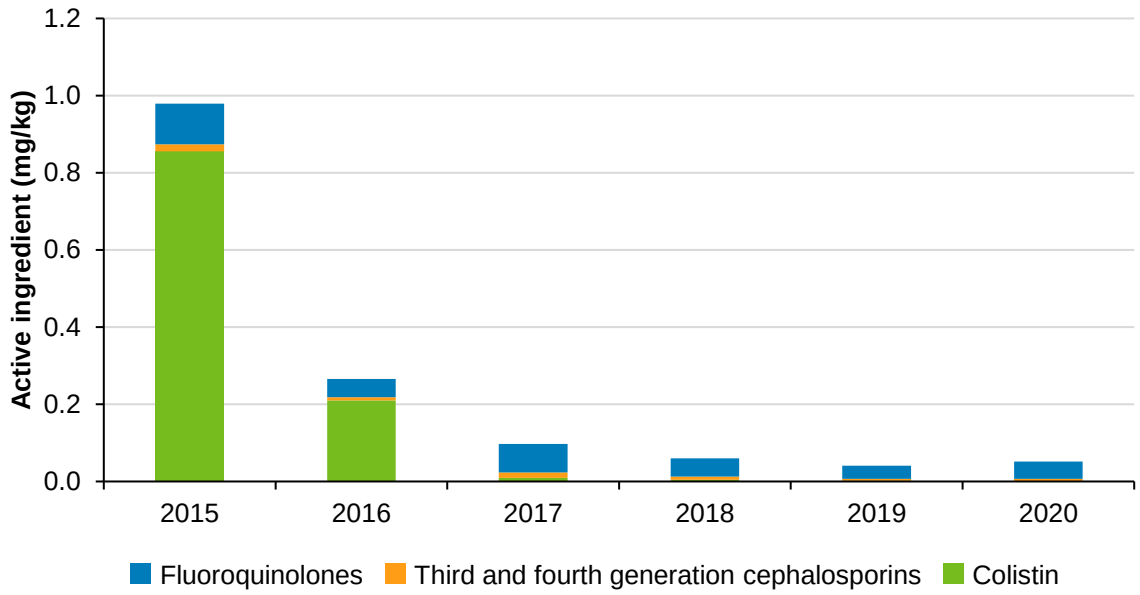
In-feed is still the most common route of administration in pigs; however, in-feed has continued to fall, representing 78% in 2017 and 61% in 2020 (see **Figure 2.4**). The most common antibiotic classes for in-feed use in 2020 were tetracyclines (42%), trimethoprim-sulphonamides (19%), macrolides (16%) and penicillins (15%). Correspondingly, in-water administration now accounts for 34% active ingredient used (compared with 19% in 2017). The most common antibiotic classes for in-water use were tetracyclines (26%), beta lactams (26%) and aminoglycosides (19%).

Figure 2.4: Active ingredient (% weight) of antibiotics by route of administration reported in eMB Pigs, 2017 to 2020



The use of HP-CIAs in pigs is shown in **Figure 2.5**. Usage of HP-CIAs in pigs increased by 0.01 mg/kg between 2019 and 2020, with both fluoroquinolones and third and fourth generation cephalosporins increasing by 0.01 mg/kg and 0.002 mg/kg (28%). Despite these slight increases, HP-CIA usage has reduced by 0.93 mg/kg (95%) since 2015. All the third generation cephalosporins and 99.7% of the fluoroquinolones were administered by injection. No products containing colistin were used in 2020, representing a decrease of 0.002 mg/kg since 2019.

Figure 2.5: Active ingredient (mg/kg) of HP-CIAs reported in eMB Pigs, 2015 to 2020



2.3.1.2 Statement from Pig Health and Welfare Council (PHWC) Antimicrobial Usage Subgroup

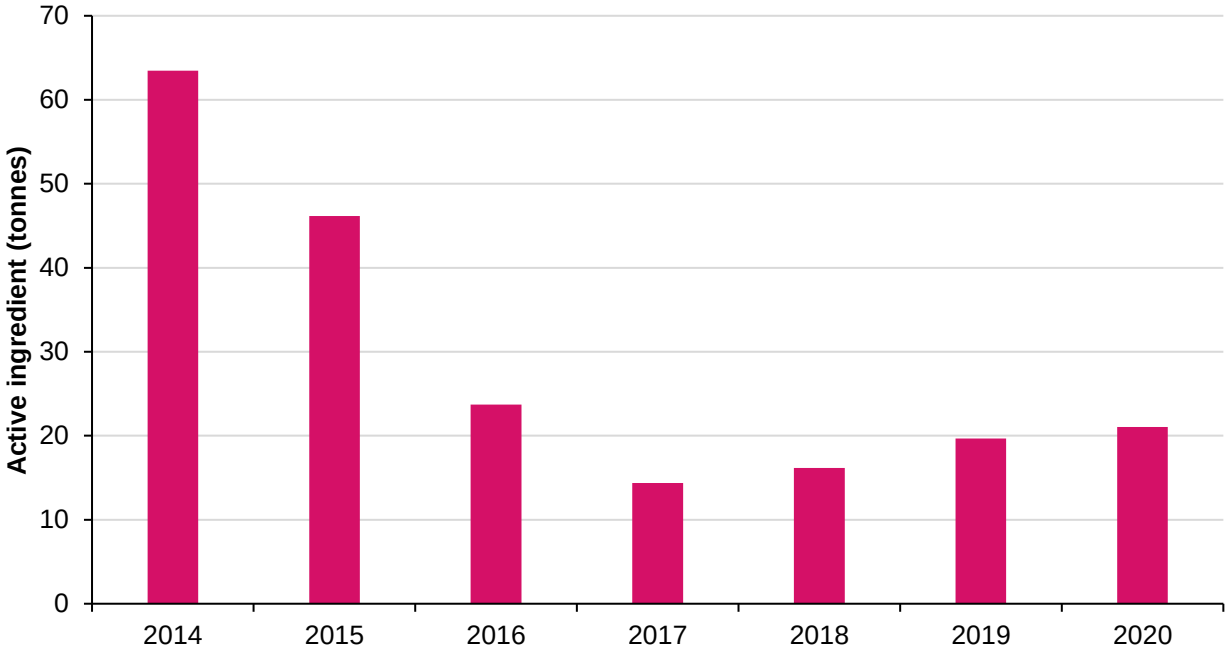
“The antibiotic reductions seen in 2020, alongside the maintenance of low levels of HP-CIA use, are encouraging and demonstrate the on-going progress in reducing and stewarding antibiotic use that has been achieved by the pig sector. In 2020, the pig sector also set further targets, aiming to reach 73 mg/kg (a 30% reduction from the use in 2020) by 2024. This will be achieved through a number of strategies, including: implementing a programme to support and encourage Persistently High Users to undertake efforts to reduce antibiotic usage (as detailed in a unit specific Antibiotic Reduction plan), developing a best practice plan for weaner management, encouraging the move from in-feed to more targeted in-water administration where appropriate, as well as evaluating and increasing the uptake of medicine training. Pig health metrics will also continue to be monitored carefully to assess the effects of reduced antibiotic usage. Many challenges remain, but the sector is committed to continually improving how antibiotics are being used and encouraging responsible use.”

2.3.2 Meat poultry

2.3.2.1 Antibiotic usage data

In 2020, the British Poultry Council (BPC) reported the use of 21 tonnes of active ingredient, nearly all of which is licensed for in-water use. This is a 1.3 tonne (7%) increase since 2019. However, it should be noted that both the number of breeders, turkeys and chickens placed, and the weight of birds reared increased by 8.5% and 24% respectively between 2019 and 2020, which is consistent with the increase in antibiotic usage. Since 2014, antibiotic usage has decreased by 42.4 tonnes (67%) (**Figure 2.6**).

Figure 2.6: Active ingredient (tonnes) of antibiotics used by members of BPC Antibiotic Stewardship, 2014 to 2020



When considering the size of the animal population, between 2019 and 2020 antibiotic usage in the chicken sector decreased by 1.2 mg/kg to 16.3 mg/kg. While this is 6.4mg/kg higher than in 2018 (the year with the lowest recorded use), it is still 32.5 mg/kg (67%) lower than 2014, the first year when accurate usage figures were available. Antibiotic usage in the turkey sector decreased by 16.3 mg/kg to 25.7 mg/kg since 2019 (this is the lowest use recorded for the sector) and has reduced by 193.8 mg/kg (88%) since 2014. The duck sector demonstrated a slight increase of 0.9 mg/kg to 2.6 mg/kg; however, usage remains very low and has reduced by 12.5 mg/kg (83%) since 2014. For both the chicken and turkey sectors, usage remains below the sector targets of 25 mg/kg and 50 mg/kg respectively (**Figure 2.7** and **Figure 2.8**).

Figure 2.7: Active ingredient (mg/kg) of antibiotics by species used by members of BPC Antibiotic Stewardship, 2014 to 2020

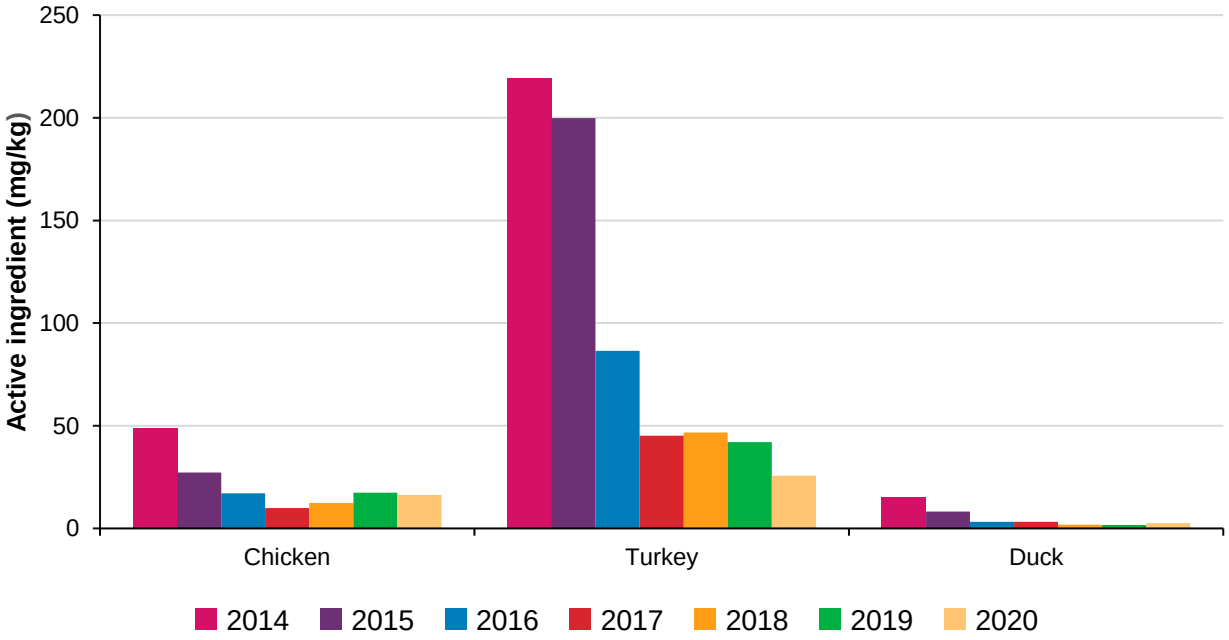
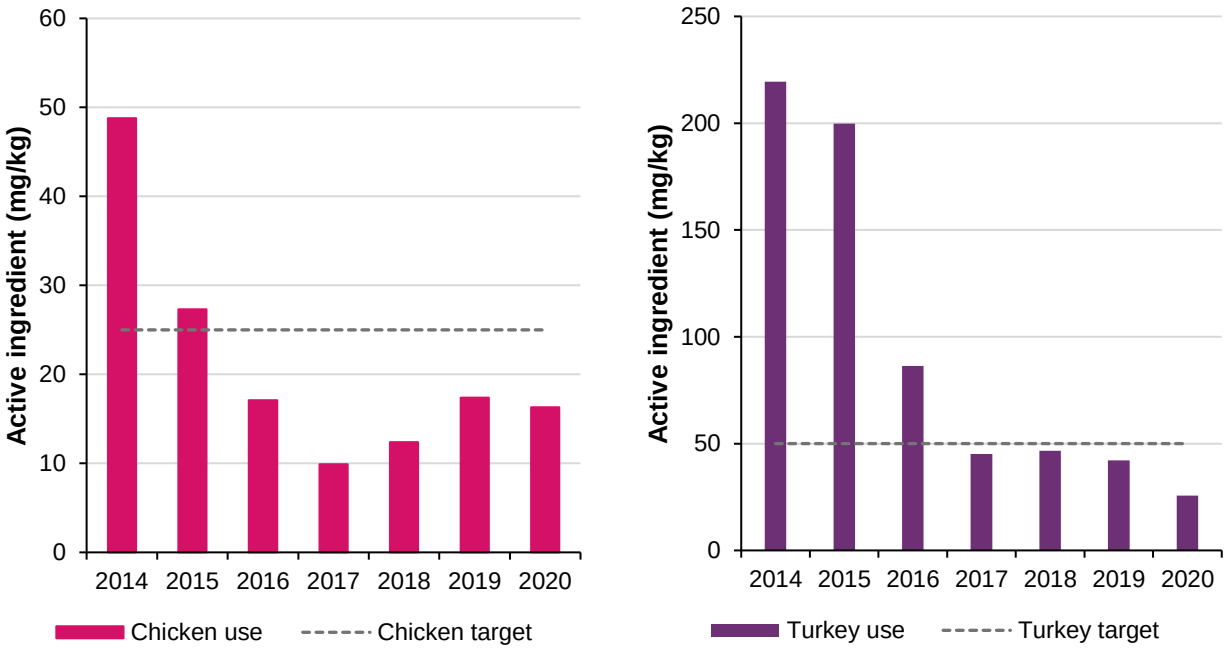
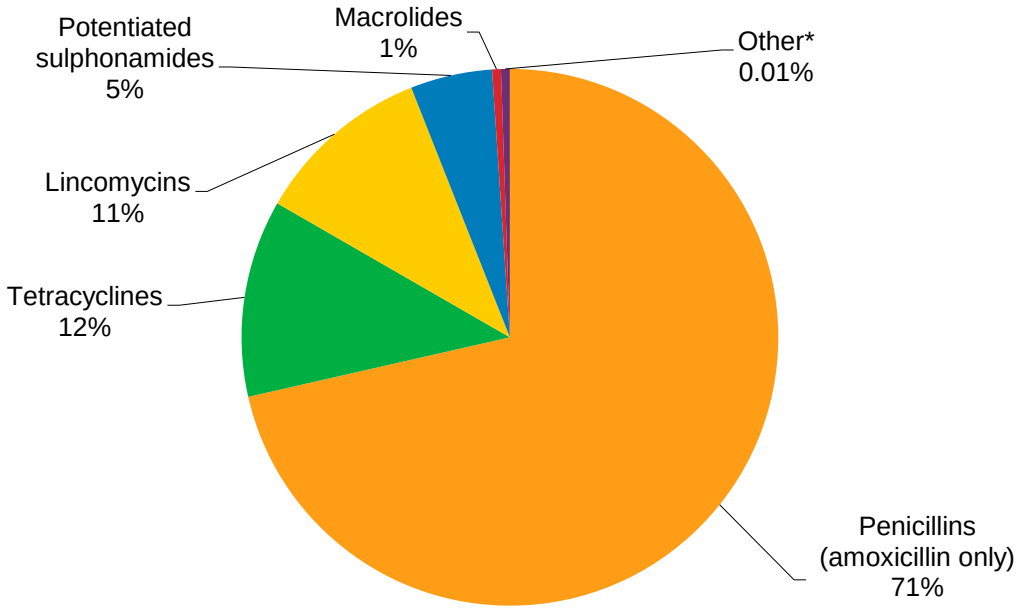


Figure 2.8: Active ingredient (mg/kg) of antibiotics by species used by members of BPC Antibiotic Stewardship and compared with the sector target, 2014 to 2020



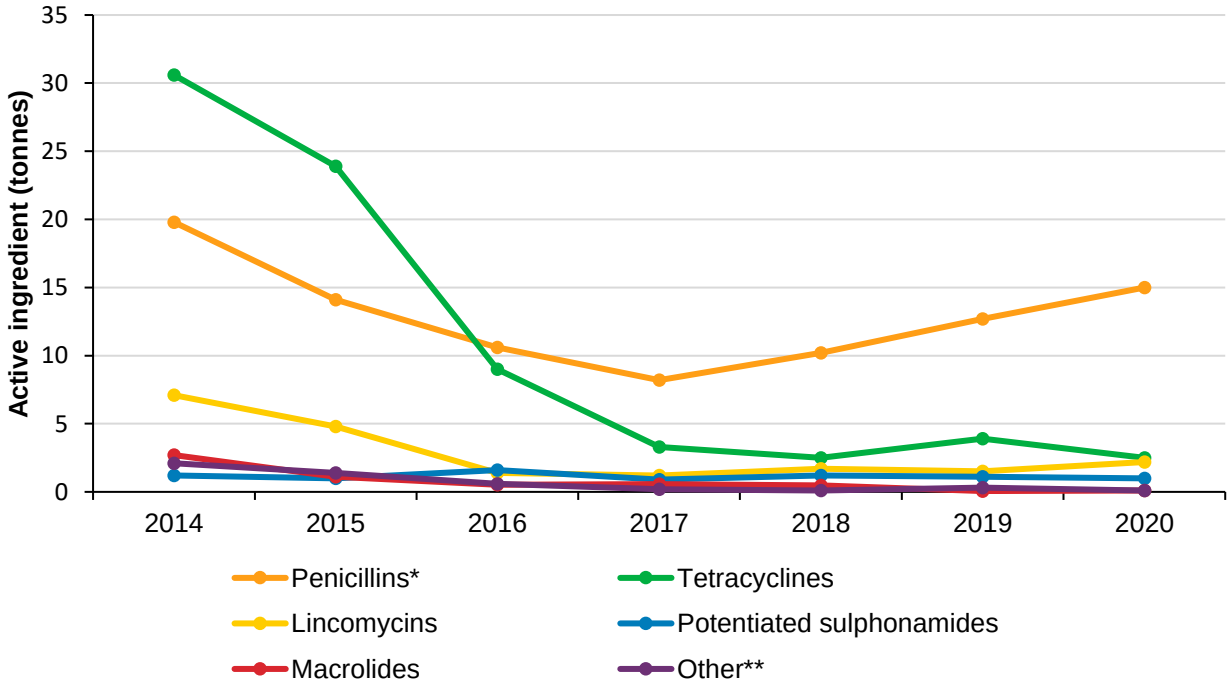
The sales of antibiotics in meat poultry broken down by active ingredient are shown in **Figure 2.9** and **Figure 2.10**.

Figure 2.9: Active ingredient (% weight) of antibiotics by antibiotic class used by members of BPC Antibiotic Stewardship, 2020



* Aminoglycosides, pleuromutilins, fluoroquinolones and products under the cascade.

Figure 2.10: Active ingredient (tonnes) of antibiotics by antibiotic class used by members of BPC Antibiotic Stewardship, 2014 to 2020



* Amoxicillin and phenoxymethylpenicillin.
** Aminoglycosides, pleuromutilins, fluoroquinolones, colistin and products under the cascade.

In 2020, 71% of active ingredient classes comprised penicillins (which was all amoxicillin), compared with 65% in 2019 and 31% in 2014. By contrast, tetracyclines (which are the second most used antibiotic class) accounted for 12% of antibiotic use in 2020, compared with 20% in 2019 and 48% in 2014.

When considering HP-CIAs, Colistin and third and fourth generation cephalosporins were once again not used by the meat poultry sectors in 2020, and overall use of fluoroquinolones has reduced by 2.3 kg since 2019 to 12.1 kg. In 2020, overall use of fluoroquinolones was 0.001 mg/kg in broilers (compared to zero use in 2019) and 0.08 mg/kg in turkeys (compared to 0.11 mg/kg in 2019).

2.3.2.2 Statement from British Poultry Council

"In 2020, the poultry meat sector was again able to deliver within its responsible use targets[12] of 25mg/kg for broilers and 50mg/kg for turkeys, with continued reductions in the use of HP-CIAs. The vast majority of birds go without needing any treatment and it's only those challenged directly by disease in any cycle that receive veterinary prescription of antibiotic in the interests of safeguarding bird health and welfare. A new set of targets for the meat poultry sectors was published in 2020. The sector will continue to be open and transparent in its antibiotic usage, and the key focus is now to drill down into the antibiotic data and look at the challenges facing producers and the reason for usage and treatment outcome, as well as identifying and encouraging any persistent high users within each business to develop farm action plans, with targeted veterinary and management input, to drive change."

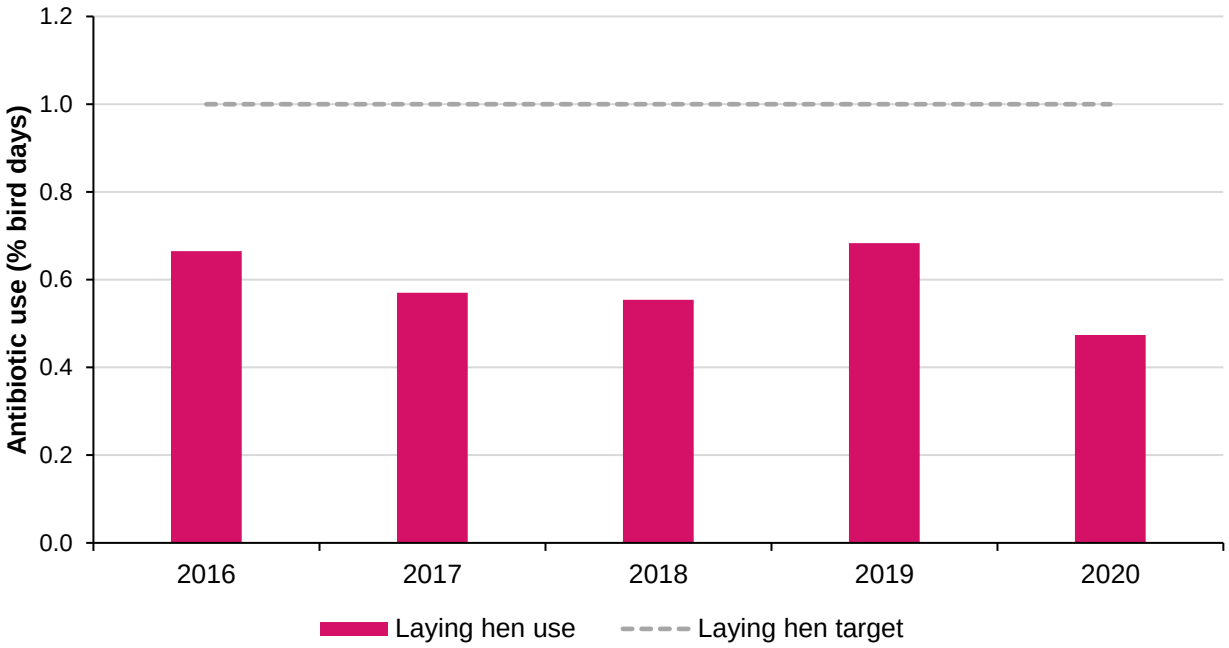
2.3.3 Laying hens

2.3.3.1 Antibiotic usage data

A total of 3.1 tonnes of antibiotic active ingredient was used by the laying hen industry in 2020. This represents 0.47 actual bird days treated/100 bird days at risk (% bird days), a decrease of 0.21 (31%) and 0.19 (29%) since 2019 and 2016 respectively and below the sector target of 1% (**Figure 2.11**). The methodology for this metric is explained in Section 2.4.

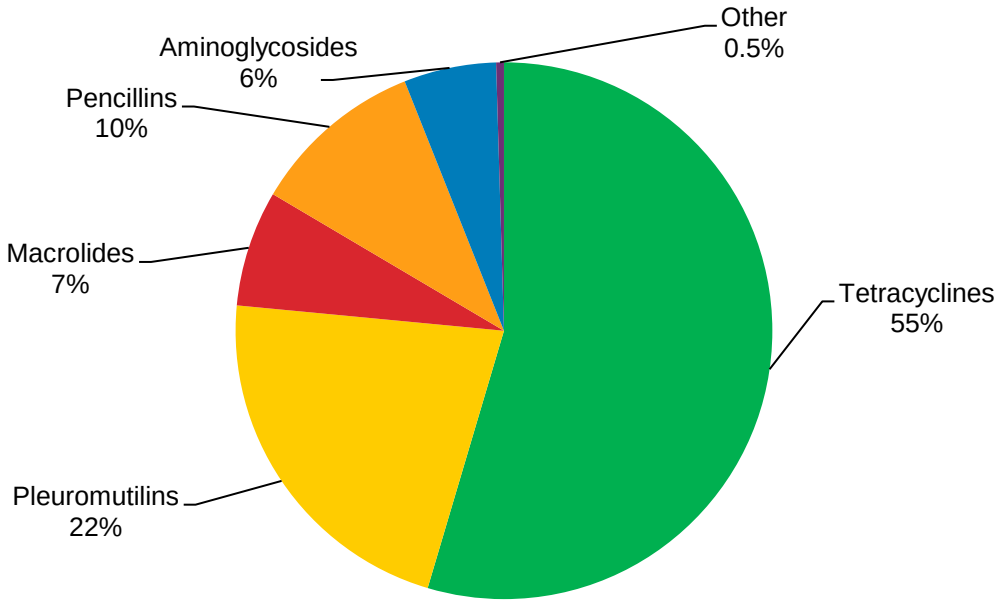
[12] https://www.ruma.org.uk/targets-task-force-2021-2024/

Figure 2.11: Antibiotic use (% bird days) by members of the British Egg Industry Council Lion Code alongside the sector target, 2016 to 2020



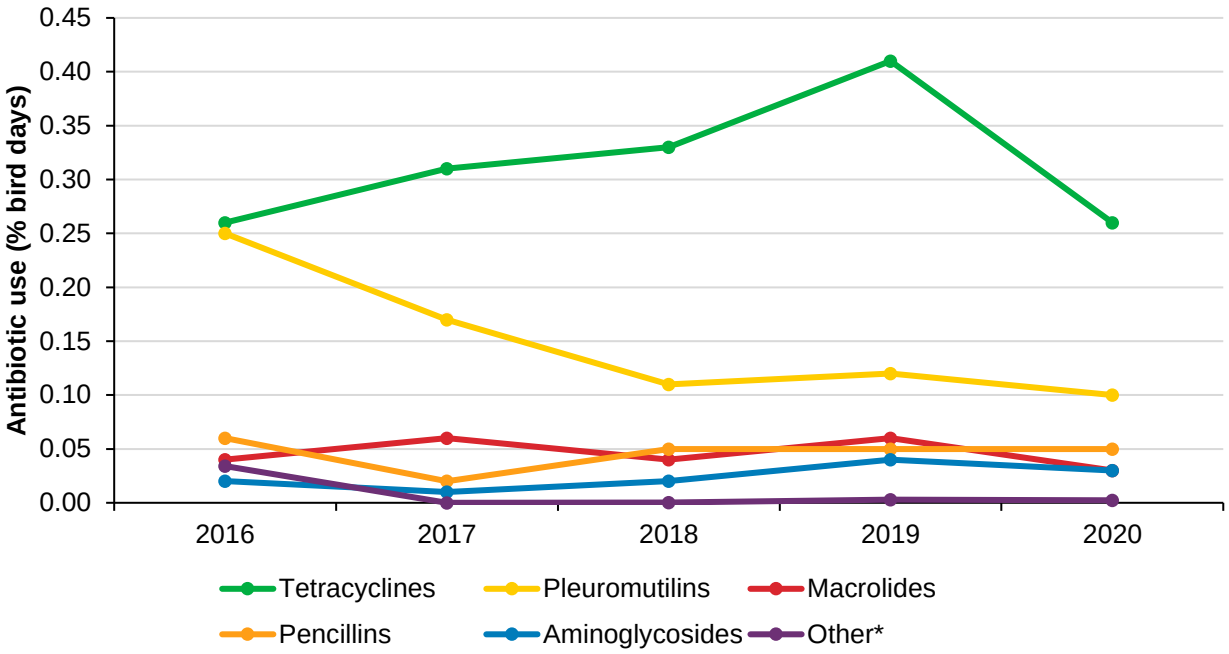
Antibiotic use broken down by antibiotic class is shown in **Figure 2.12** and **Figure 2.13**.

Figure 2.12: Antibiotic use (% of total bird days) by antibiotic class by members of the British Egg Industry Council Lion Code, 2020



* Lincosamide/aminoglycoside combination product

Figure 2.13: Antibiotic use (% bird days) by antibiotic class by members of the British Egg Industry Council Lion Code, 2016 to 2020



*Includes fluoroquinolones, polymyxins, sulphonamides, lincosamides and combination products

Tetracyclines and pleuromutilins accounted for 77% of total use. Tetracyclines have decreased by 0.002% bird days (1%) since 2016 whereas pleuromutilins have reduced by 0.15% bird days) during the same period. Aminoglycosides were the only class to increase between 2016 and 2020, increasing by 0.01% bird days (32%). For the fourth year running there were no HP-CIAs used by the laying hen sector in 2020.

2.3.3.2 Statement from the British Egg Industry Council (BEIC)

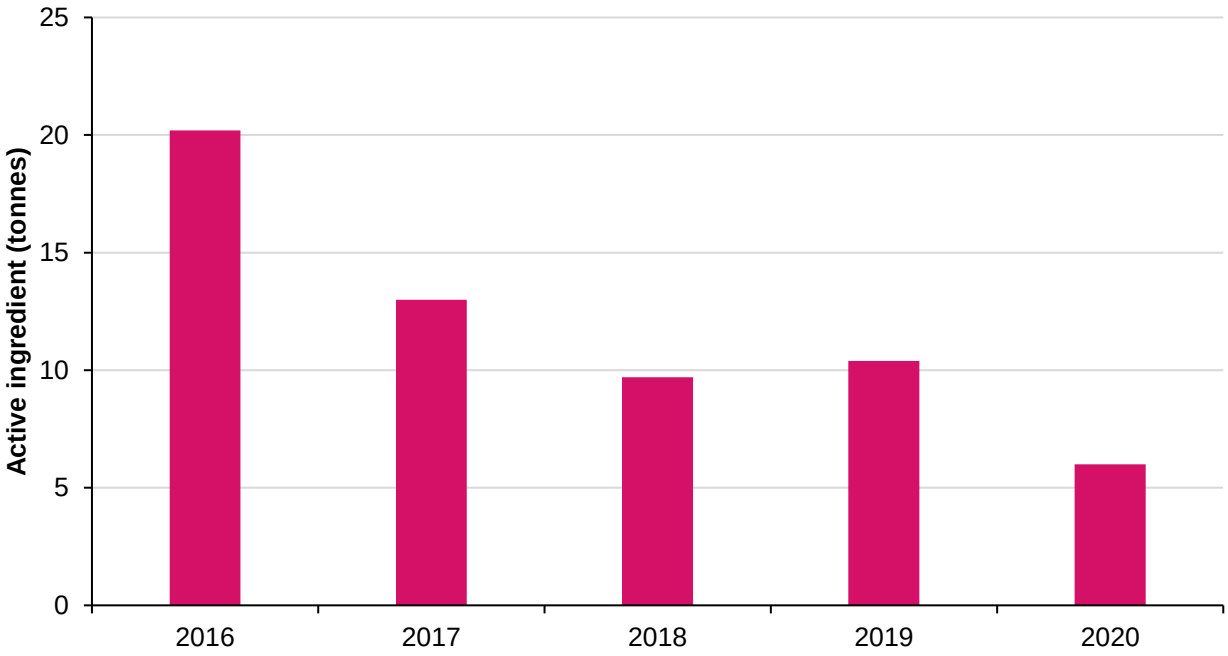
"The antibiotic usage data from members of the British Egg Industry Council (BEIC) Lion Scheme for 2020 continues to be below the 1% bird days, and no HP-CIAs were used for the fourth consecutive year. In 2020, this was collected through an online portal for the first time, which has facilitated the analysis of the data and improved feedback to subscribers, producers, and vets. It has also made it possible to share data on reasons for medication with prescribing veterinarians. In the laying hen sector, there continues to be a focus on disease prevention, including widespread vaccination programmes. It is also a requirement for all farms to have a written biosecurity and veterinary health plan and, in addition, the Lion Training Passport provides a common training standard on key topics, including welfare, biosecurity and medicine usage. From January 2021 the Lion Training Passport, which includes medicine training has been a required standard for all farms. There are currently some significant structural changes of the industry with a move away from enriched colony cage production for retail supply towards 'barn' production. While this will create challenges, we are confident that, through a continued focus on disease prevention and antibiotic stewardship, we will remain below our on-going target of keeping below 1% bird days, and 0.05% bird days for HP-CIAs."

2.3.4 Gamebirds

2.3.4.1 Antibiotic usage data

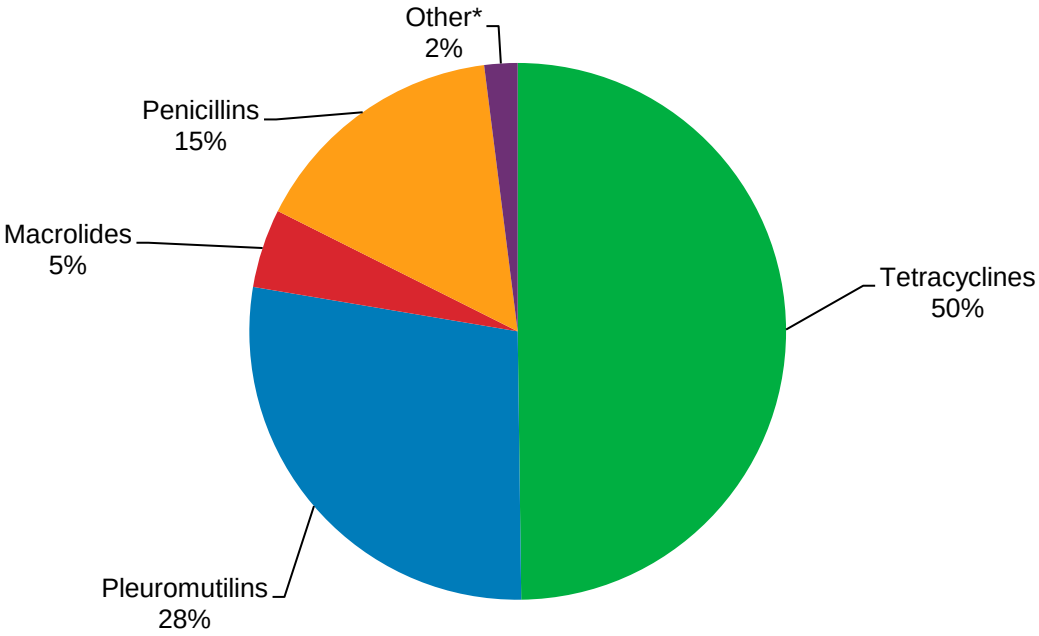
In 2020, 6.0 tonnes of active ingredient were reported through the Game Farmers' Association (GFA) and British Veterinary Poultry Association (BVPA) gamebird subcommittee data collection programme. This represents a decrease in 4.4 tonnes (43%) between 2019 and 2020, and a reduction of 14.2 tonnes (70%) since 2016 (**Figure 2.14**). However, it should be noted that, due to Covid restrictions, the industry estimates that gamebird rearing reduced by 30% in 2020.

Figure 2.14: Active ingredient (tonnes) of antibiotics used in gamebirds, collected by the GFA and BVPA data collection programme, 2016 to 2020



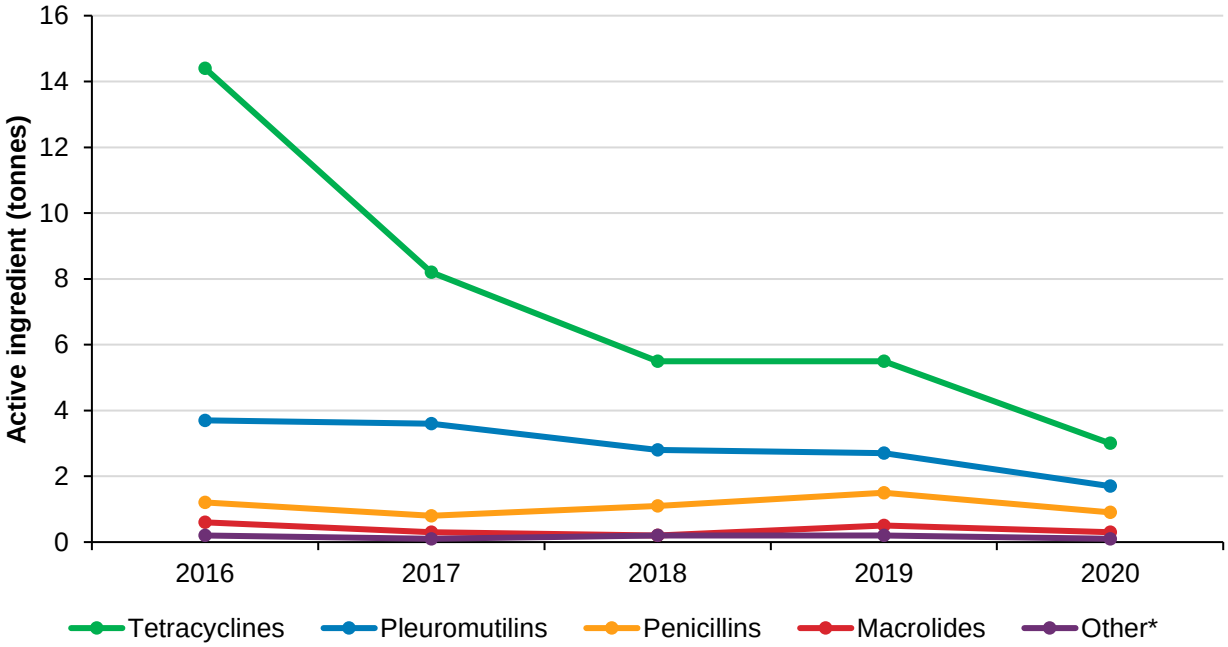
The use of antibiotics broken down by active ingredient is shown in **Figure 2.15** and **Figure 2.16**.

Figure 2.15: Active ingredient (% weight) of antibiotics by antibiotic class used in gamebirds, collected by the GFA and BVPA data collection programme, 2020



* Aminoglycosides, amphenicols, fluoroquinolones, lincomycin, trimethoprim/sulphonamides

Figure 2.16: Active ingredient (tonnes) of antibiotics by antibiotic class used in gamebirds, collected by the GFA and BVPA data collection programme, 2016 to 2020



* Aminoglycosides, amphenicols, fluoroquinolones, lincomycin, trimethoprim/sulphonamides

Tetracyclines and pleuromutilins represented 78% of antibiotics used in 2020. Analysis of usage data by route of administration shows that in-feed medication accounted for 40% antibiotic use (with the remainder in-water), compared with 41% in 2019 and 74% in 2016.

Within the HP-CIAs, there was a 36 kg (63%) decrease in fluoroquinolone use between 2019 and 2020, and HP-CIAs accounted for 0.4% of overall use (compared with 0.6% in 2019).

2.3.4.2 Statement from the Game Farmers' Association and the British Poultry Veterinary Association gamebird subcommittee

"The antibiotic usage results for the gamebird industry for the 2020 season are very positive, with overall antibiotic use reducing by 43% and HP-CIA use reducing by 63% (bearing in mind the number of animals reared, which is thought to have been reduced by 30%).This is testament to the work of the gamebird sector and the key role vets play in working with rearers to optimise flock health and welfare with the key focuses in 2020 on: improving husbandry and reducing the need to treat with antibiotics, tightening up on the prescription of in-feed antibiotics, increasing the number of audits (via the British Game Alliance) and ensuring that HP-CIA are only used as a last resort, backed up where possible and appropriate by diagnostic and sensitivity testing. However, there are still improvements to be made and, in 2020, the gamebird sector published a new set of targets aiming for a 40% reduction in antibiotic use from the 2019 baseline (2020 is not a representative baseline year due to reduced rearing as a result of Covid restrictions). This will be achieved through a continued focus on improving animal husbandry and prescribing as well as the development of antibiotic benchmarking, allowing vets to identify and support persistently high users. The welfare effects of antibiotic reduction will also continue to be monitored, to help ensure that reductions are safe and sustainable."

2.3.5 Cattle

2.3.5.1 Cattle sales targets

There is no antibiotic usage data reported for cattle this year, but it is possible to monitor sales of intramammary product and injectable HP-CIAs that are licensed for cattle (although some of these products include other species in their licence indication, industry feedback suggests that the majority (75%) are used in cattle).

In the sector-specific targets document produced by Responsible Use of Medicines in Agriculture Alliance (RUMA)[13], the dairy and beef sectors made a commitment to reduce the use of injectable HP-CIAs from 2016 levels by 50% by 2020. **Table 2.1** shows that this target has been more than met, with a 0.63 mg/kg (68%) reduction in cattle injectable HP-CIAs since the baseline year of 2016. There was, however, an increase in injectable HP-CIA use of 0.03 mg/kg between 2019 and 2020.

[13] https://www.ruma.org.uk/targets-task-force-2021-2024/

For the dairy sector, there are also targets to reduce intramammary HP-CIAs by 50% by 2020 and reduce lactating cow intramammary use and dry cow intramammary use by 10% and 20% respectively, from a 2015 baseline. As shown in **Table 2.1**, the sector has more than met these targets, with a 0.26 course dose (78%) reduction in intramammary HP-CIA use, as well as reductions of 0.3 course dose (38%) and 0.25 course dose (34%) in lactating cow and dry cow therapy sales, respectively. Despite this reduction, intramammary HP-CIA use has increased by 0.04 course doses between 2019 and 2020. As noted earlier, there were availability issues with lactating cow intramammary products in 2020, which may have affected product choice. Additionally, if the available products were considered clinically unsuitable by the veterinary surgeon, alternative products authorised outside the UK can be imported on a case-by-case basis under the Special Import Scheme. These products are not captured in the antibiotic sales data.

Table 2.1: Sales (mg/kg) of injectable HP-CIAs with a licensed indication for cattle and of intramammary tubes (course doses, DCDvet), using methodology defined by ESVAC; 2014 to 2020

Antibiotic	2014	2015	2016	2017	2018	2019	2020	2020 Target
Injectable HP-CIA products licenced for cattle (mg/kg)	1.10	1.10	0.92*	0.70	0.50	0.26	0.29	**0.46**
Intramammary HP-CIA products (DCDvet)	0.37	0.33*	0.24	0.17	0.12	0.03	0.07	**0.17**
Intramammary tubes – lactating cow (DCDvet)	0.89	0.80*	0.82	0.69	0.78	0.60	0.51	**0.73**
Intramammary tubes – dry cow (DCDvet)	0.62	0.73*	0.61	0.54	0.64	0.58	0.48	**0.59**

*Baseline year

2.3.5.2 Statement from the Cattle Antibiotic Guardian Group

“In 2020, there is no antibiotic usage data reported for cattle. This is because the sector has focused on the development of Medicine Hub (which was launched in January 2021). The Medicine Hub will provide an independent, central repository to collate, report and compare antibiotic use at farm level for both cattle and sheep. Medicine Hub will be used to report 2021 national data in next year’s VARSS report and, in 2020, the sector set ambitious targets for the medicine hub to capture data from 95% UK dairy herds, 50% UK calf rearing units and 10% UK beef herds by 2024. These targets have also focused on other key areas, including increased training of vets (through the Farm Vet Champions initiative), farmers and vet/agriculture students, and a focus on improved herd health planning. When looking at the 2020 sales data, the ongoing reductions in intramammary lactating and dry cow sales are encouraging, the latter of which highlights the push towards only treating high risk cows at drying off (selective dry cow therapy). There was a slight increase in injectable and intramammary HP-CIA use between 2019 and 2020 and we will investigate the reasons for this. However, it should be noted that injectable and

intramammary HP-CIA use is still significantly below the levels seen in 2018 and there was a lack of availability of some lactating cow intramammary tubes in 2020, which may have limited the number of treatment options available in some cases."

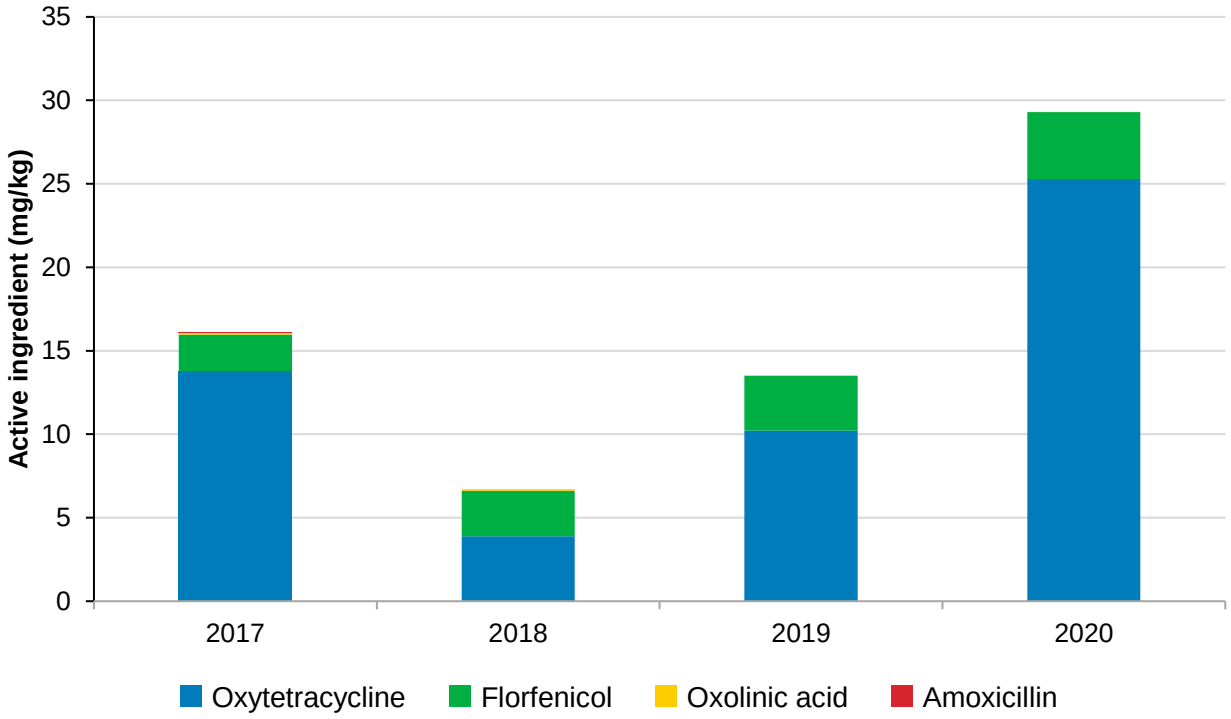
2.3.6 Aquaculture

2.3.6.1 Salmon

2.3.6.1.1 Results

In 2020, 5.6 tonnes of antibiotic active ingredient were used, representing 29.3 mg/kg (**Figure 2.17**), which is 15.8 mg/kg higher than the use reported in 2019, and 13.2 mg/kg (82%) higher than 2017.

Figure 2.17: Active ingredient (mg/kg) of antibiotics by antibiotic class used in salmon, 2017 to 2020



Oxytetracycline remains the most used antibiotic class (accounting for 86% of total use in 2020) and usage has increased by 15.1 mg/kg since 2019, and 11.5 mg/kg (83%) since 2017. Florfenicol was the second most commonly used antibiotic class, and this has increased by 0.7 mg/kg since 2019 and 1.8 mg/kg (84%) since 2017. Under the new Antimicrobial Expert Group (AMEG) advice published in January 2020, the quinolone oxolinic acid is now considered an HP-CIA, although this was not the case in 2019. In 2020, oxolinic acid usage decreased by 0.012 mg/kg from 2019 and has reduced by 0.11 mg/kg (89%) since 2017.

2.3.6.1.2 Statement from the Scottish Salmon Producers' Organisation

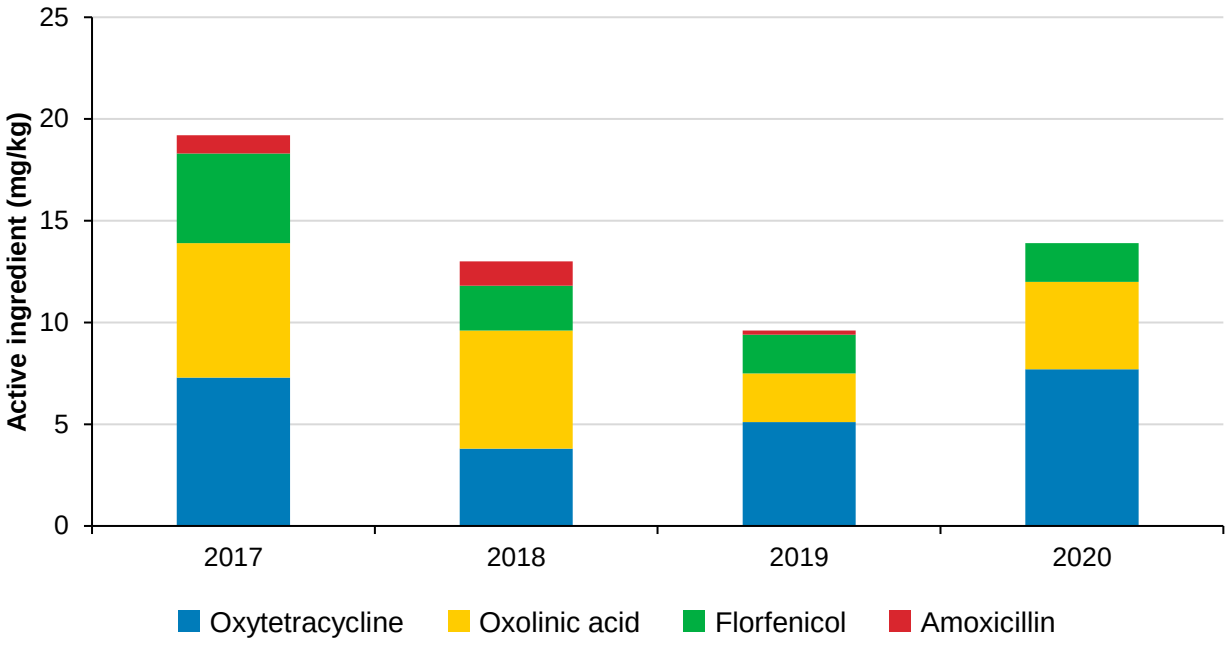
"The 2020 data records an increase in antibiotic use between 2019 and 2020. This relates to an increase in use during the marine phase of production, with a decrease recorded in freshwater. Antibiotic use and stewardship are routinely discussed within a dedicated Prescribing Vets forum. It is important to state that antibiotic treatments are still relatively infrequent in the salmon farming sector, with only 6.9% of freshwater farms and 4.4% of marine farms reporting any antibiotic use in 2020. Antibiotics are only ever used in response to the clinical presentation of bacterial infection: there is no prophylactic use of antibiotics and any use is supported by appropriate sensitivity testing. Despite the overall increase, use of the HP-CIA oxolinic acid has continued to decrease and now represents only 0.04% of total use. In 2020, the Salmon sector published further targets surrounding antibiotic stewardship, which continue to focus on a holistic and preventative approach to health management, including vaccination, antibiotic stewardship, biosecurity and health and welfare planning. It should also be noted that the overall production cycle for Salmon is 3 years, so single year mg/kg figures can be difficult to interpret. The sector remains committed to responsible use of antibiotics, balancing a drive to reduce use against the need to safeguard fish health and welfare."

2.3.6.2 Trout

2.3.6.2.1 Results

The sample obtained from approximately 90% of the UK trout production demonstrates that a total of 0.16 tonnes of antibiotic active ingredient was used, representing 13.9 mg/kg, an increase of 4.2 mg/kg (44%) since 2019. However, the level of antibiotic use is similar to that seen in 2018 and 5.3 mg/kg (28%) lower than usage in 2017, remaining below the industry target of 20 mg/kg (see **Figure 2.18**).

Figure 2.18: Active ingredient (mg/kg) of antibiotics by antibiotic class used in trout, 2017 to 2020



When considering usage by class, oxytetracycline remains the most used antibiotic (accounting for 55% of overall use) and this has increased by 2.6 mg/kg since 2019 and 0.3 mg/kg (4%) since 2017. Under the new AMEG advice published in January 2020, the quinolone oxolinic acid is now considered an HP-CIA. Oxolinic acid use increased by 1.8 mg/kg since 2019 but it is still 2.3 mg/kg (35%) and 1.6 mg/kg (27%) lower than the levels of use seen in 2017 and 2018 respectively.

2.3.6.2.2 Statement from the British Trout Association

“The data from 2020 shows that the trout sector remains below the target of using less than 20 mg/kg. The increases seen in oxolinic acid and oxytetracycline reflect an increase in disease challenge for *Yersinia ruckeri* (enteric redmouth) and *Aeromonas salmonicida* (furunculosis) respectively in 2020. However, there is no preventative use in the trout sector, and antibiotics are only used when they are required for clinically diagnosed disease, balancing the desire to reduce overall use against the need to protect fish health and welfare. In 2020, the sector published a new set of antibiotic targets and key commitments include: a focus on vaccination, ensuring that all trout farms are compliant with Quality Trout UK standards, the setting up of a new “bug bank” for monitoring resistance levels (and supporting the development of autogenous vaccines, that the HP-CIA oxolinic acid will only be used when clinically necessary (and no effective alternatives are available) and that overall use will continue to remain below 20 mg/kg.”

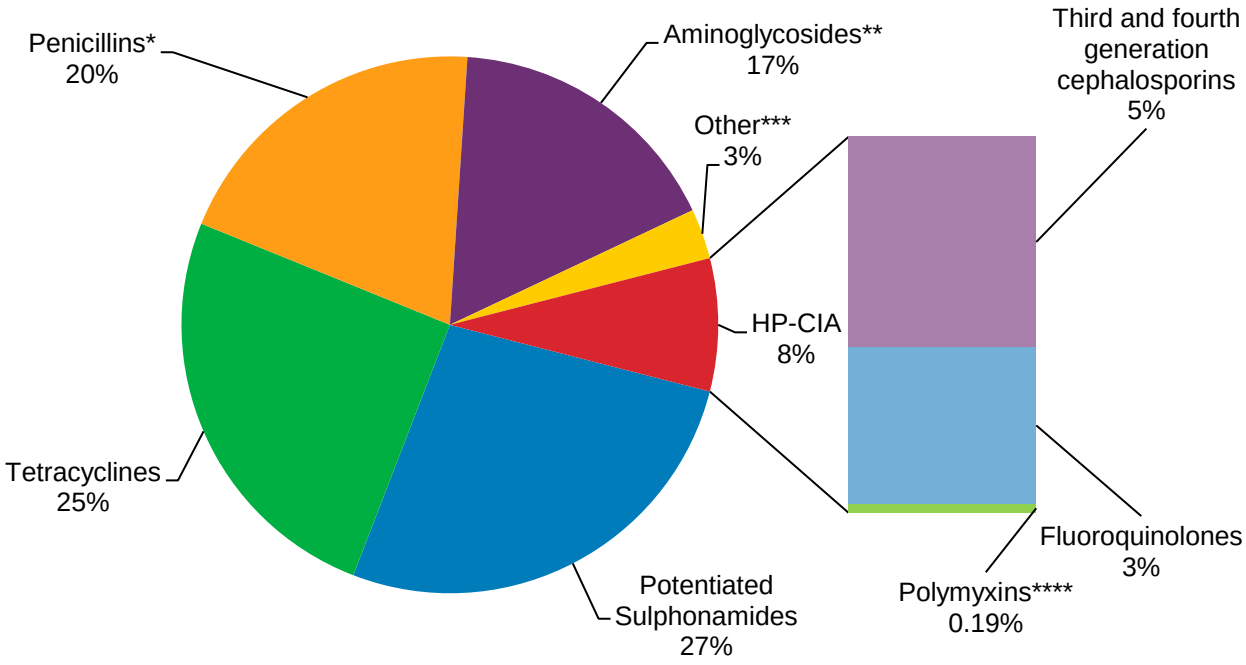
2.3.7 Companion Animals

2.3.7.1 Horses

In the equine sector, a new study which was funded by the VMD and carried out by the Royal Veterinary College, explored systemic (oral or parenteral) antibiotic use in UK equine practice[14]. The study analysed anonymised electronic patient records (EPRs), collected via the VetCompass™ programme, for all equines attended by 39 UK veterinary practices between 1st January and 31st December 2018.

The study population included 64,322 equines (7% of the UK population). Overall, 19.5% of equines received a systemic antimicrobial during the study period. The total number of prescription events (where each event relates to the sale of a unique antimicrobial product prescribed on a given day) was 40,066. Potentiated sulphonamides were the most prescribed class of antibiotics, followed by tetracyclines and then penicillins (**Figure 2.19**), of which 98.4% were natural penicillins.

Figure 2.19: Antibiotic prescription events split by antibiotic class from 64,322 equines:



* Includes natural penicillins and aminopenicillins but excludes natural penicillin/ aminoglycoside combination products.
** Excludes aminoglycosides in combination with lincosamides, natural penicillins and sulphonamides.
*** Includes amphenicols, first generation cephalosporins, lincosamides, lincosamide/aminoglycoside combination products, macrolides, rifamycins, natural penicillin/ aminoglycoside combination products, nitroimidazoles, sulphonamides and sulphonamide/ aminoglycoside combination products.
**** Polymyxin B

[14] Allen, S.E., Verheyen, K.L.P, O'Neill, D.G and Brodbelt, D.C. (2021) Use of Systemic Antimicrobials in UK Equine Practice. Veterinary Medicines Directorate, UK.

Systemic HP-CIAs were prescribed to 1.9% of equines in the study population and in total, accounted for 8% of antibiotic prescriptions given. Third generation cephalosporins and fluoroquinolones were the most commonly used HP-CIAs and were prescribed in 4.5% and 3.3% of antibiotic prescriptions respectively.

Culture and sensitivity testing was used in 4.9% of all systemic antibiotic courses and 19% of HP-CIA courses.

Within the study, five equine practices had available data from both 2016/17 (representing 25,693 equines) and 2018 (representing 30,858 equines). This allowed trends to be explored. The results showed that the % equines receiving systemic antibiotics declined from 25.2% of in 2016/17 to 23.1% in 2018 ($p<0.001$). Additionally, prescription of HP-CIAs declined from 11.2% in 2016/17 to 10.0% in 2018 ($p<0.001$), largely due to a reduction in fourth generation cephalosporins caused by a removal of a product from the market.

While the study is a convenience sample and tends to be skewed towards larger veterinary hospitals (with a range of 150 – 9,489 equines per practice and a median of 508) the study provides a valuable insight into the use of antibiotics, and the usage trends, in equines.

2.3.7.2 Dogs and Cats

In dogs and cats, a new study, which was funded by the VMD (VM0520) and carried out by the University of Liverpool, explored antibiotic prescription patterns in the UK for both cats and dogs by looking at the proportion of consultations (as a percentage) where antibiotics are prescribed[15]. This is calculated as follows:

(Number of consultations where an antibiotic is prescribed / Total number of consultations) x 100

The study used data from Electronic Health Records (EHR) collected by The Small Animal Veterinary Surveillance Network (SAVSNET) covering 1,482,001 dogs and 765,312 cats from 300 veterinary practices between 2014 and 2020.

In 2020, systemic antibiotics were prescribed to dogs in 9.6% of consultations and to cats in 12.0% consultations (**Figure 2.20**). For both dogs and cats, this represents a 3% increase since 2019 but a decrease of around 1/3 since 2014. The increase in 2020 for both dogs and cats is primarily due to fewer consultations taking place (the number of consultations per practice dropped by 30% for both dogs and cats in 2020 compared with 2019). However, for those consultations which did take place during Q2 2020, antibiotics were prescribed 24% and 33% more frequently for dogs and cats than the other quarters

[15] Singleton, D. A, Broadfoot, F., Noble, P. J. M., Pinchbeck, G. L., Williams, N. J., Radford, A. D. Temporal analysis of antimicrobial agent prescription in a sentinel population of canine and feline veterinary practices in the United Kingdom: 2014-2020.

in 2020 (see **Figure 2.21**). The reason for this is that, due to covid restrictions, many practices reduced preventive health interventions during Q2 2020[16], and focused on emergency treatment only. Therefore, although fewer animals were seen, a higher percentage of the animals required antibiotic treatment.

Figure 2.20: Antibiotic use (% consultations) by species, collected by SAVSNET, 2014 to 2020

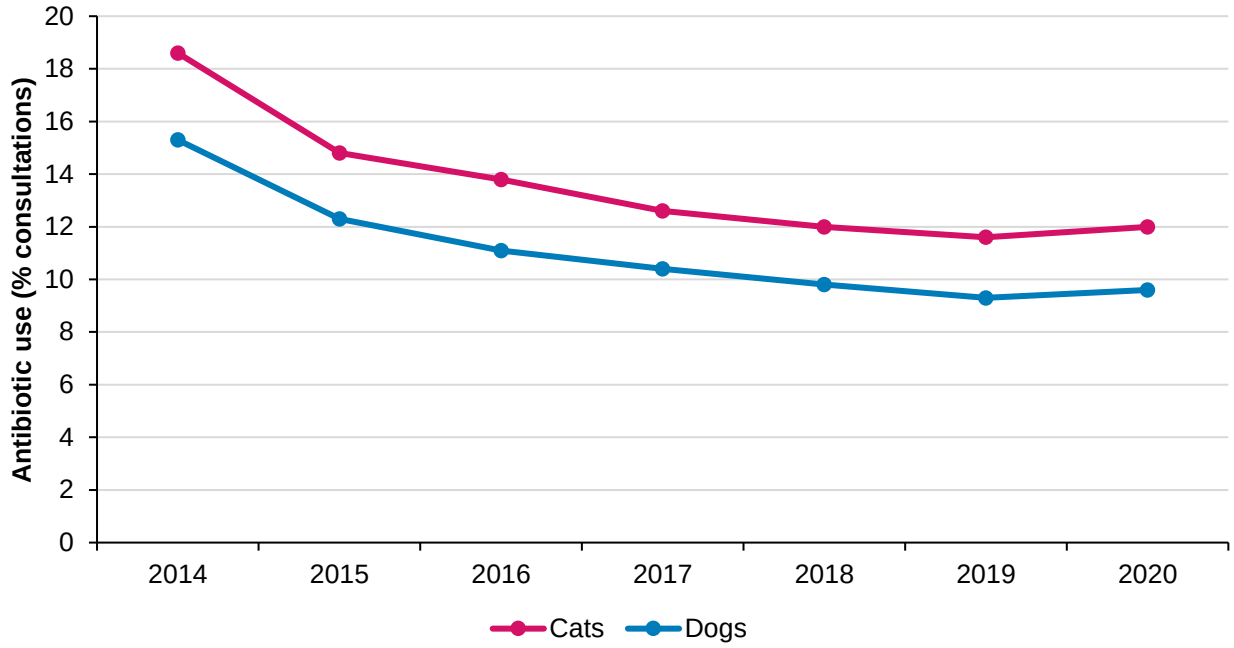
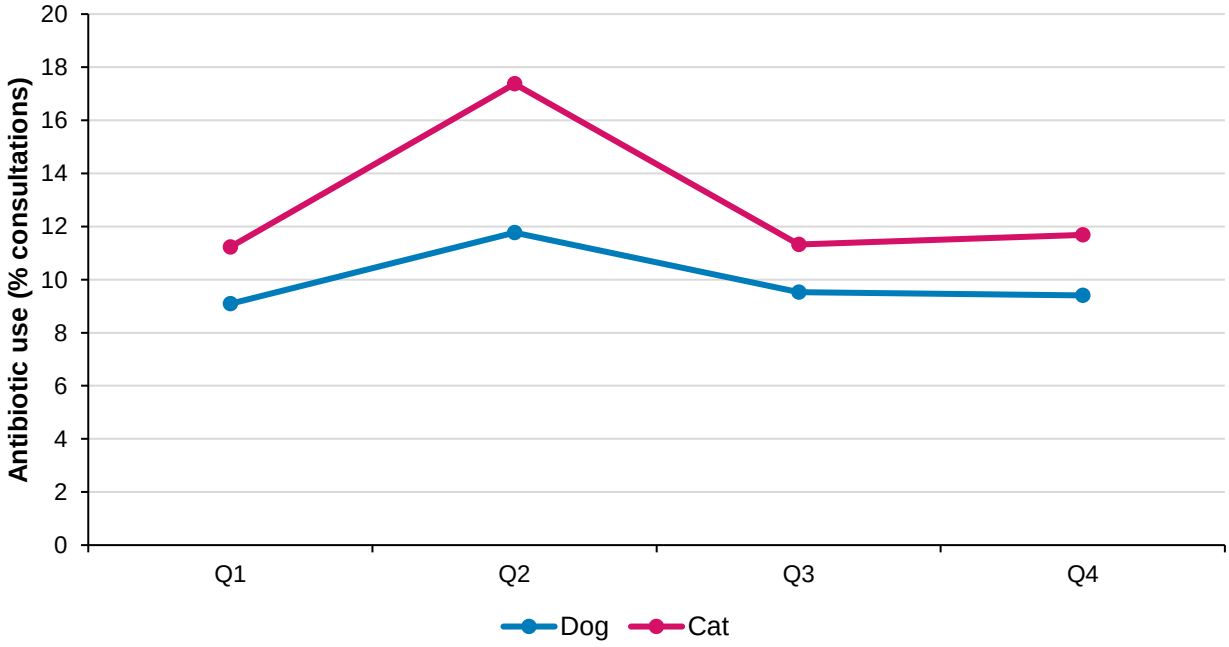


Figure 2.21: Antibiotic use (% consultations) of antibiotics by species, collected by SAVSNET, 2020

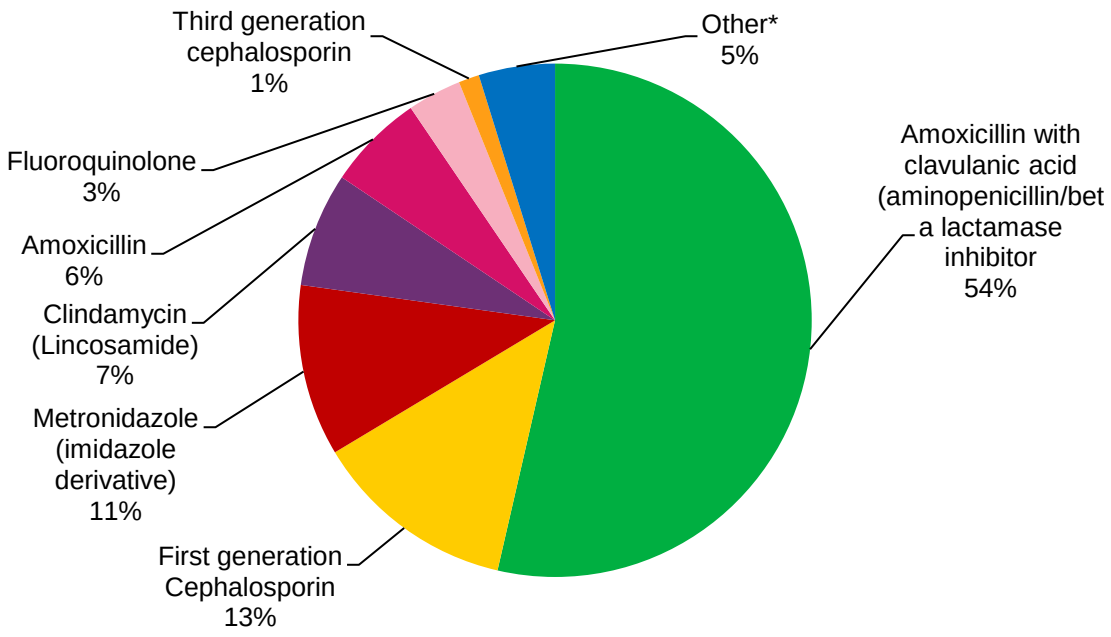


[16] Littlehales, R., Noble, P. J. M., Singleton, D. A., Pinchbeck, G. L. & Radford, A. D. Impact of Covid-19 on veterinary care. Vet. Rec. 186, 650 LP – 651 (2020).

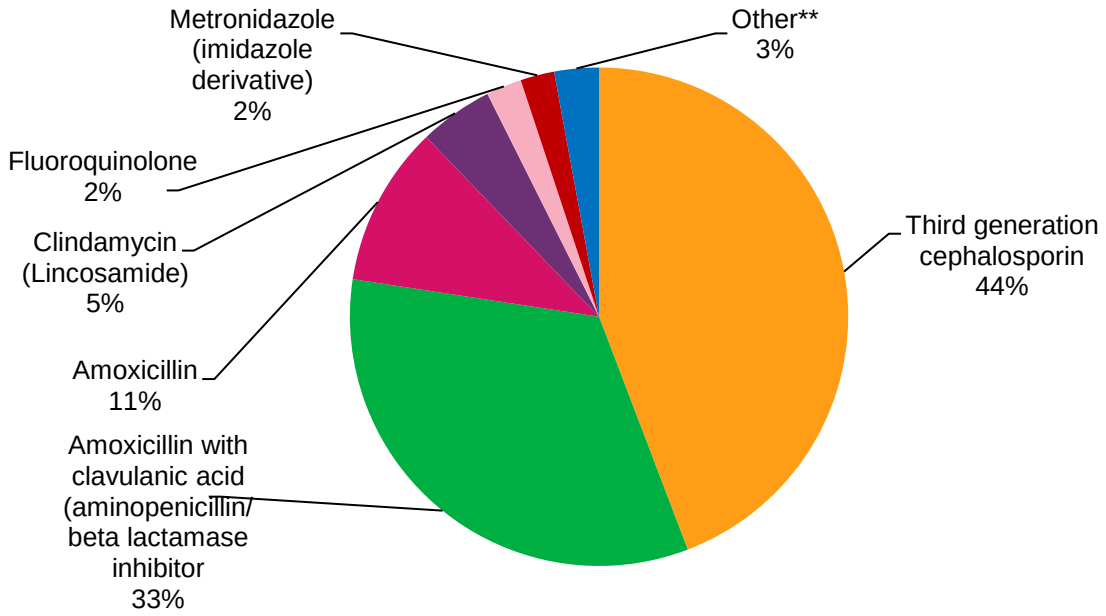
In dogs, between 2014 and 2020, beta-lactams accounted for 74% prescriptions in dogs and 89% in cats, with amoxicillin alongside clavulanic acid the most prescribed antibiotic for dogs and third generation cephalosporins the most prescribed for cats (**Figure 2.22**).

Figure 2.22: Antibiotic use (% of antibiotics prescribed per consultation) by class in (A) dogs, (B) cats, collected by SAVSNET, 2020

(A)



(B)

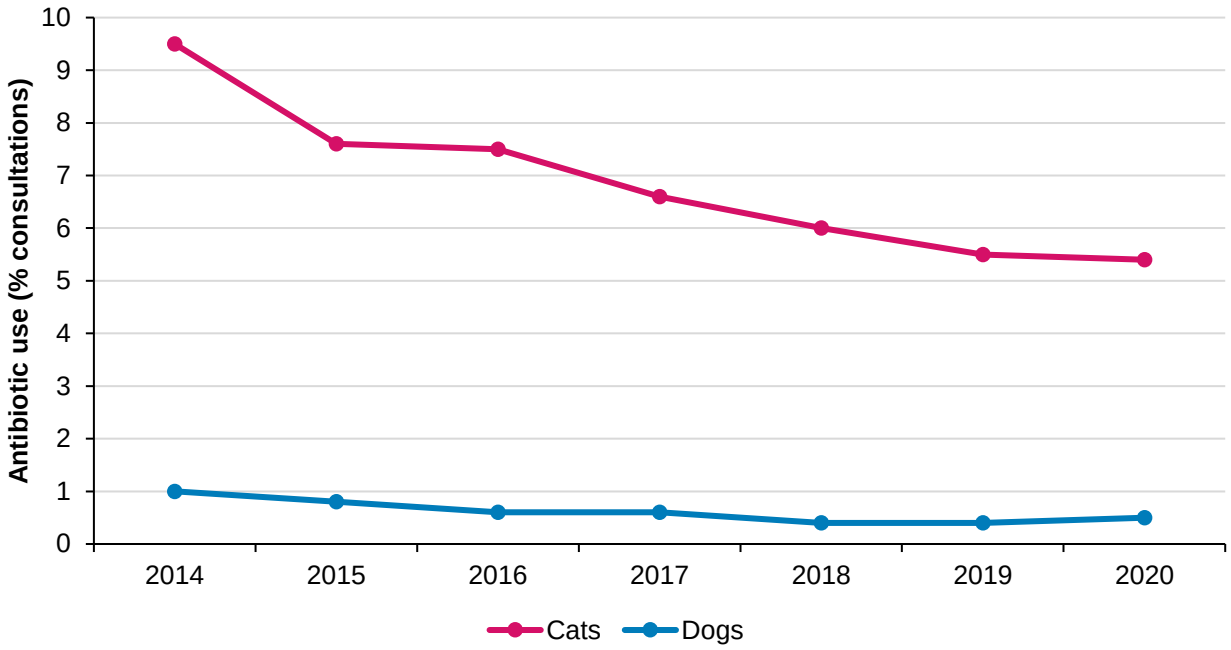


* Includes combination products, sulphonamides, tetracyclines macrolides, aminoglycosides and simple penicillins

** Includes tetracyclines, sulphonamides, macrolides, aminoglycosides, first/second generation cephalosporins, simple penicillins and combination products

In 2020, HP-CIAs (AMEG category B) accounted for 5% of systemic antibiotic prescriptions in dogs, and their use has fallen 54% since 2014, although there was an increase of 0.08% consults between 2019 and 2020. Fluoroquinolones account for 72% HP-CIA prescriptions in dogs, with the remainder being third generation cephalosporins. In cats, HP-CIAs represented 45% of systemic antibiotic prescriptions and this has fallen by 43% since 2014. In cats, the majority of HP-CIA use (95% in 2020) relates to the third generation cephalosporin cefovecin (**Figure 2.23**).

Figure 2.23: Antibiotic use (% consultations) of HP-CIAs by species, collected by SAVSNET, 2014 to 2020



Overall, the study demonstrates some encouraging trends, with both overall use and use of HP-CIAs decreasing since 2014 – which is consistent with the sales data (reported in Section 1.3.2). The use of HP-CIAs, however, is still high, particularly in cats. This is despite industry advice that these should only be used when "first-line antibacterials are inappropriate or ineffective"[17] and, where possible, based on culture and sensitivity.

2.3.7.3 Statement from RUMA Companion Animal and Equine Alliance

"A new cross-sectoral collaboration has been formed to promote the responsible use of medicines in companion animals and horses**.** Inspired by the success of the UK farm animal sector in reducing antibiotic use during the past five years, the newly formed RUMA Companion Animal and Equine Alliance (RUMA CA&E) will draw on those learnings to help protect important medicines for future human and animal use. This new collaboration will cover the responsible use of medicines in dogs, cats, rabbits, small mammals, exotic

[17] https://www.bsavalibrary.com/content/chapter/10.22233/9781910443644.chap6_1#supplementary_data

animals kept as pets, and equines. The aim is for the UK to lead the way in these sectors through evidence-based and measurable activities that will promote and enhance stewardship. The Alliance has appointed Chairman Gwyn Jones, who will bring previous experience from The Responsible use of Medicines in Agriculture Alliance (RUMA), and includes representation from regulators, veterinary professional associations and many of the leading stakeholders from the sectors. RUMA CA&E will focus initially on the responsible use of antibiotics and welcomes the inclusion of more detailed data and insight for companion animals into this years' VARSS report. Further details can be found here - www.rumacae.org.uk."

2.4 Methods

Pigs

The antibiotic usage data in pigs were extracted from the electronic Medicines Book for Pigs (eMB), developed by the pig sector with support from the VMD, and launched by the Agriculture and Horticulture Development Board Pork (AHDB-Pork) in 2016.

The scope and limitations of the data (as provided by AHDB-Pork) are presented below:

- These data are national, aggregated figures for antibiotic usage calculated from individual unit data held in the eMB for pig farms across the UK.
- eMB uptake to date has been voluntary and this sample may not be representative for the whole of the UK.
- In terms of pig production, this eMB data covers English slaughter pigs only for 2015 and 2016, and UK slaughter pigs for 2017 to 2019. The eMB data as a percentage of the total clean pig slaughter figures for the relevant region are: 61% in 2015, 70% in 2016, 87% in 2017, 89% in 2018, 95% in 2019 and above 95% in 2020.
- The data are inputted by producers and, although clear outliers have been identified and queried, AHDB is not able to validate every individual producer's data. However, at a national, aggregated level, the data provide an estimation of national usage and allow year on-year comparisons to be made.
- The data for 2020 were extracted from eMB on 7th June 2021 and these figures will now be fixed as the reference levels for 2020. Data in Method of Administration and Breakdown by Product and Class tabs were extracted from eMB on 24th August 2021 based on the same criteria used during June, but changes to the concentrations of certain products made in July 2021 have reduced the amount of active ingredient.
- The eMB database and the calculations within it are subject to a series of quality assurance checks to ensure national aggregated figures are as accurate as possible. As a result of this process, the eMB system is continuing to develop and work to further improve data accuracy is ongoing.

- The calculations used for the eMB data are in-line with the methods used by the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project, to allow comparisons to be made with European counterparts.

Meat poultry

The British Poultry Council (BPC) provided antibiotic usage data for the poultry meat (chicken, turkey and duck) sectors. BPC runs BPC Antibiotic Stewardship, which covers 90% of UK poultry meat production. This process of data collection started in 2012 and producers are responsible for submitting quarterly (chicken, duck) or annual (turkey and all breeders) antibiotic usage data in the form of an aggregate spreadsheet. BPC then collate the data and report usage by sector in their annual report. This includes the overall annual amount of active ingredient used (in tonnes), which covers both breeders and producers.

For the producers, this is then compared with the population at risk of treatment to create a mg/kg usage figure. BPC calculates the population at risk of treatment by using annual slaughter numbers and standardised estimated weights at time of treatment (chickens: 1.0 kg as derived by ESVAC; turkeys: 6.5 kg as derived by ESVAC; ducks: 1.75 kg as derived by BPC based on ESVAC principles).

BPC carries out the calculations using ESVAC methodology. The process of calculating the quantity of antibiotic active ingredient has been validated by the VMD.

Laying hens

The collection of antibiotic usage data for the laying hen industry is organised by the British Egg Industry Council (BEIC). Sharing these data with BEIC is mandatory through the Lion Scheme, which represents over 90% of the UK laying hen industry.

All egg producers, pullet rearers and breeding companies are required to report any use of an antibiotic to their subscriber. This is then reported to the BEIC on a quarterly basis. The BEIC collated aggregate annual antibiotic pack level data and provided it to the VMD, who carried out the calculations and validation of the usage by active ingredient using ESVAC methodology. Denominator data are available from monthly records of the total number of birds in the scheme, averaged over the year.

The data published here as ‘actual daily bird days/100 bird days at risk’ represent the average number of days treatment administered per chicken over a 100-day period.

Note that a ‘mg/kg’ figure has not been included, as ESVAC methodology does not include a standardised method for laying hens.

Gamebirds

The Game Farmers’ Association (GFA) and the British Veterinary Poultry Association (BVPA) gamebird subcommittee coordinated a comprehensive, voluntary data collection exercise to measure the use of antibiotics throughout the sector for 2020. This involved the collection of in-feed medication records from game feed producers (which supply 95% of game farmers and rearers) and prescribing records from specialist gamebird vets (of which 75% of game farmers and rearers are clients).

Each company was asked to provide a spreadsheet showing the amount of antibiotics used in 2018. GFA aggregated the results and provided them to the VMD, who then used ESVAC methodology to calculate the amount of antibiotic active ingredient administered by the game sector.

Note that a ‘mg/kg’ figure has not been included, as ESVAC methodology does not include a standardised method for gamebirds.

Aquaculture

The trout data were collected from the main veterinary practices dealing with trout in England and Scotland and represent approximately 90% of UK trout production. The salmon usage data were collected by the Scottish Salmon Producers’ Organisation (SSPO) from all veterinary practices treating salmon in Scotland and therefore represent 100% of Scottish salmon production. The aggregated data were analysed as mg/kg using ESVAC methodology, where kg represents the weight of slaughtered fish as live weight.

It is important to note that around 30% of trout are reared for restocking waters for angling rather than directly for food production. Antibiotic use on these restocking fish will be captured in the weight of active ingredient, but not in the weight denominator, leading to a potential overestimate of the mg/kg. It should also be noted that salmon have a three-year production cycle, so the tonnes of fish produced in any one year do not fully represent the overall salmon population that may require treatment.

CHAPTER 3

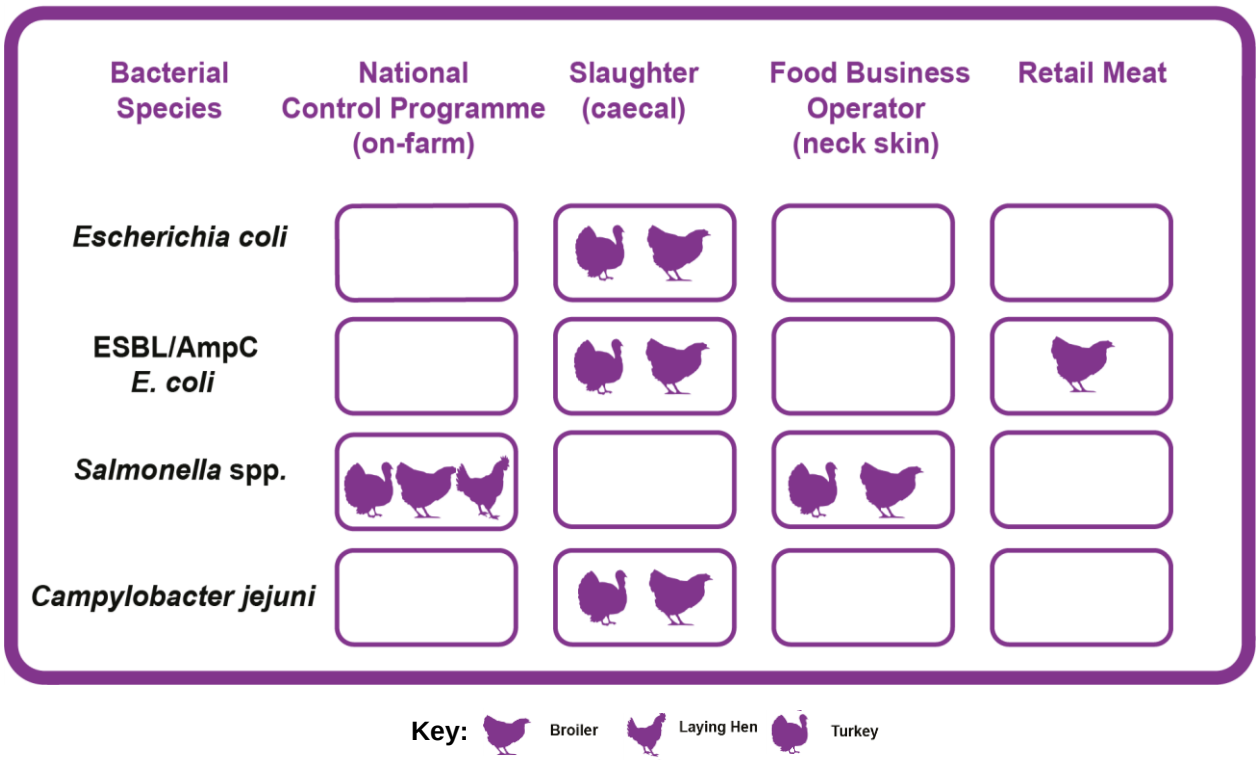
Harmonised monitoring of antibiotic resistance

This programme was originally developed to harmonise monitoring and reporting of antimicrobial resistance (AMR) in the food chain across Europe[18]. It involves testing for resistance in zoonotic and commensal bacteria from healthy food-producing animals at slaughter, *Salmonella* isolates from the National Control Program[19] and food products at retail. In the UK, key livestock species are monitored in alternating years (poultry in even years, pigs in odd years).

The points in the food chain at which different poultry species are sampled are summarised in **Figure 3.1**. The results of the testing of isolates from caecal samples, neck skin samples and on farms are presented in this chapter. The caecal samples collected for this programme are designed to be representative of the UK poultry population and are collected from slaughterhouses processing at least 60% of domestic production. An overview of the sampling plan is summarised in Table S3.1.1 of the supplementary material. The Food Standards Agency (FSA) lead on the testing and reporting of AMR in retail meat.

[18] Commission Implementing Decision of 12 November 2013 on the monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria (notified under document C(2013) 7145)Text with EEA relevance (europa.eu)
[19] Salmonella in Livestock Production 2020 (publishing.service.gov.uk)

Figure 3.1: Harmonised AMR monitoring requirements in 2020



3.1 Summary

Escherichia coli

- All harmonised outcome indicators show continued improvement (decreasing resistance/increasing susceptibility).
- There was no resistance detected to colistin, meropenem or tigecycline in broilers or turkeys in 2020.
- Resistance to the third generation cephalosporins cefotaxime and ceftazidime was detected in 0.4% of isolates from broilers, for both antibiotics, and in 1.0% and 0.5% of isolates from turkeys, respectively.
- Prevalence of ESBL and AmpC-producing *E. coli* phenotypes continued to reduce in both broilers and turkeys. In 2020, 3.4% of broiler caecal samples yielded *E. coli* with an ESBL phenotype and 1.1% with an AmpC phenotype. For turkeys, 1.2% of caecal samples yielded *E. coli* with an ESBL phenotype and 0.3% within an AmpC phenotype.
- Carbapenemase-producing *E. coli* were not detected in either broilers or turkeys.
- Resistance to the fluoroquinolone ciprofloxacin has remained at low levels in both broilers (2.4%) and turkeys (2.5%), although it has increased slightly since 2018.
- Resistance to all non-HP-CIAs has decreased since 2018 in broilers; resistance to some non-HP-CIAs has increased very slightly in turkeys. In both broilers and turkeys, resistance to all non-HP-CIA antibiotics is lower than in 2014.

Salmonella spp.

- A total of 72% of *Salmonella* isolates from broiler flocks were susceptible to all the antibiotics tested. This was 78% for layer flock isolates and 22% for turkey flock isolates. Full susceptibility has decreased since 2018 in broilers and layers and increased slightly in turkeys.
- Resistance to HP-CIAs in *Salmonella* spp. isolated from poultry flocks under the National Control Programmes (NCPs) was maintained at 0%, with the exception of colistin resistance in layers (see following bullet point). No resistance to the third generation cephalosporins cefotaxime and ceftazidime or the fluoroquinolone ciprofloxacin, was detected in *Salmonella* isolated from broiler, layer or turkey flocks in 2020.
- Resistance to colistin was detected in nine *S*. Enteritidis isolates (12%) from layer flocks. *S*. Enteritidis is a group D *Salmonella*, which can show a degree of intrinsic resistance to colistin.
- No resistance to meropenem or tigecycline was detected in *Salmonella* isolated from broiler, layer or turkey flocks in 2020.
- No resistance to gentamicin in broiler and turkey flocks was detected in 2020, however gentamicin resistance was detected at low levels (2.7%) in layers.

- In *Salmonella* isolated from broilers through the FBO programme, no resistance was detected to cefotaxime, ceftazidime, ciprofloxacin, gentamicin, meropenem or tigecycline. One isolate was resistant to colistin.

Campylobacter jejuni

- Resistance to the ciprofloxacin was detected in 59% of isolates from broilers, and 37% of isolates from turkeys: an increase in resistance in both species since 2014.
- Resistance to erythromycin was detected in 0.6% of isolates from broilers and 0.6% of isolates from turkeys.
- Resistance to tetracyclines has been maintained at very high levels in broilers (67%) and high levels in turkeys (40%).
- The remaining antibiotics tested in the panel (streptomycin and gentamicin) have remained at low levels (<3%) over the monitoring period, with no decreased susceptibility detected to gentamicin for both broilers and turkeys in 2020.

3.2 Methods

3.2.1 Sample collection

Caecal samples were taken from healthy broilers and turkeys at slaughter, in accordance with Decision 2013/652/EU[20], by Food Standards Agency (FSA) personnel. The sampling plan was randomised, stratified and weighted by slaughter throughput. Samples were collected from the biggest slaughterhouses, jointly covering 80% of the UK turkey throughput and 65% of the UK broiler throughput in 2020. Sample collection was randomised and evenly distributed throughout the year. One caecal sample was collected per epidemiological unit (flock) sampled.

Boot/dust swabs were collected in accordance with EU Regulation (EC) No. 2160/2003[21] and the National Control Programme (NCP) for layers, broilers and turkeys. Swabs were taken from all flocks included in the NCPs and all isolated *Salmonella* were tested, unless there were 170 isolates or more, in which case a randomised sample of the isolates obtained from those swabs was further analysed.

Under the requirements of Commission Regulation (EC) No. 2073/2005[22] on microbiological criteria for foodstuffs (process hygiene criteria only) Food Business Operators (FBOs) collect neck skin samples which are submitted to private laboratories for bacteriological culture. Any isolated *Salmonella* should then be submitted to the Animal and Plant Health Agency (APHA) for serotyping and susceptibility testing.

[20] https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:303:0026:0039:EN:PDF
[21] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:32003R2160
[22] https://eur-lex.europa.eu/legal-content/EN/TXT/PDF/?uri=CELEX:02005R2073-20140601

3.2.2 Antibiotic susceptibility testing (AST)

AST was carried out by the national reference laboratories (NRLs). Caecal samples were cultured for *E. coli* and *C. jejuni* using appropriate media and a single typical colony was selected for speciation and susceptibility testing. *Salmonella* isolates are not cultured from these caecal samples and are instead received by the NRLs for serotyping and susceptibility testing via the sample collection procedures outlined in Section 3.2.1. Standardised broth microdilution was used to determine the minimum inhibitory concentration (MIC) against a panel of antibiotics in accordance with Decision 2013/652/EU and the EFSA manual[20].

In addition, caecal samples were cultured for ESBL-/AmpC-/carbapenemase-producing *E. coli* following the selective procedures outlined in Decision 2013/652/EU. Whole genome sequencing (WGS) and *in silico* bioinformatic tools were used to detect the antibiotic resistance determinants present in the isolates with ESBL- or AmpC-phenotypes.

Detailed methodology for the susceptibility testing is presented in S.3.2 of the supplementary material.

3.2.3 Interpretation of results

Both the European Committee on Antimicrobial Susceptibility Testing (EUCAST) human clinical breakpoints (CBPs) and EUCAST epidemiological cut-off values (ECOFFs) were used to assess susceptibility of the bacterial isolates. CBPs relate the laboratory results to the likelihood of clinical treatment success or failure. Therefore, 'resistant' results using CBPs correspond to a likelihood of human treatment failure when using the antibiotic in question to treat a human clinical infection caused by that bacterial isolate. ECOFFs represent the point at which bacteria have developed a higher level of resistance to an antibiotic than the background level of resistance that exists naturally for that bacterial species. A 'decreased susceptibility' (or 'resistant') result based on ECOFFs does not necessarily imply a level of resistance that would correspond to clinical treatment failure.

In this report, the ECOFF and CBP values applied are in accordance with Decision 2013/652/EU[23]. Where CBPs were available, these were used for interpreting resistance; when no CBP was available, ECOFF values were used instead. Results interpreted using both human CBPs and ECOFFs are provided in full in Sections S3.3, S3.4 and S3.5 of the supplementary material.

Please note that some historical AMR results referred to in this chapter are different to those previously published in UK-VARSS 2018. AMR data in UK-VARSS 2018 was reported using resistance breakpoints proposed by EFSA[24], which were not formally adopted. This meant that resistance levels to some antibiotics were over-stated in 2018.

[23] https://eur-lex.europa.eu/LexUriServ/LexUriServ.do?uri=OJ:L:2013:303:0026:0039:EN:PDF
[24] Technical specifications on harmonised monitoring of antimicrobial resistance in zoonotic and indicator bacteria from food-producing animals and food - - 2019 - EFSA Journal - Wiley Online Library

Historical data in this report have been amended to interpret resistance using the breakpoints in the Commission Implementing Decision 2013/652/EU, ensuring comparability with previous UK-VARSS reports and EFSA publications. Details of these corrections can be found in Tables S3.3.1 to S3.5.2 of the supplementary material.

3.3 Results

Certain active ingredients included in the panel are not authorised for use in food-producing animals. These are included to monitor resistances of concern to public health (for example, carbapenem resistance), or because they are representative of an antibiotic class. Please refer to Table S.1.7.2 of the supplementary material to see a table of these compounds. All isolates collected were tested against the full antibiotic panel. The number of isolates tested are shown in S3.3 to S3.5 of the supplementary material. Where a figure shows no data for certain antibiotics or years, this is because no resistance was detected.

Additionally, please note that EFSA definitions for levels of resistance have been used to denote whether resistance levels are low, moderate, high etc. throughout the report. A table highlighting these definitions can be found in Annex B.

3.3.1 *Escherichia coli*

3.3.1.1 Broilers

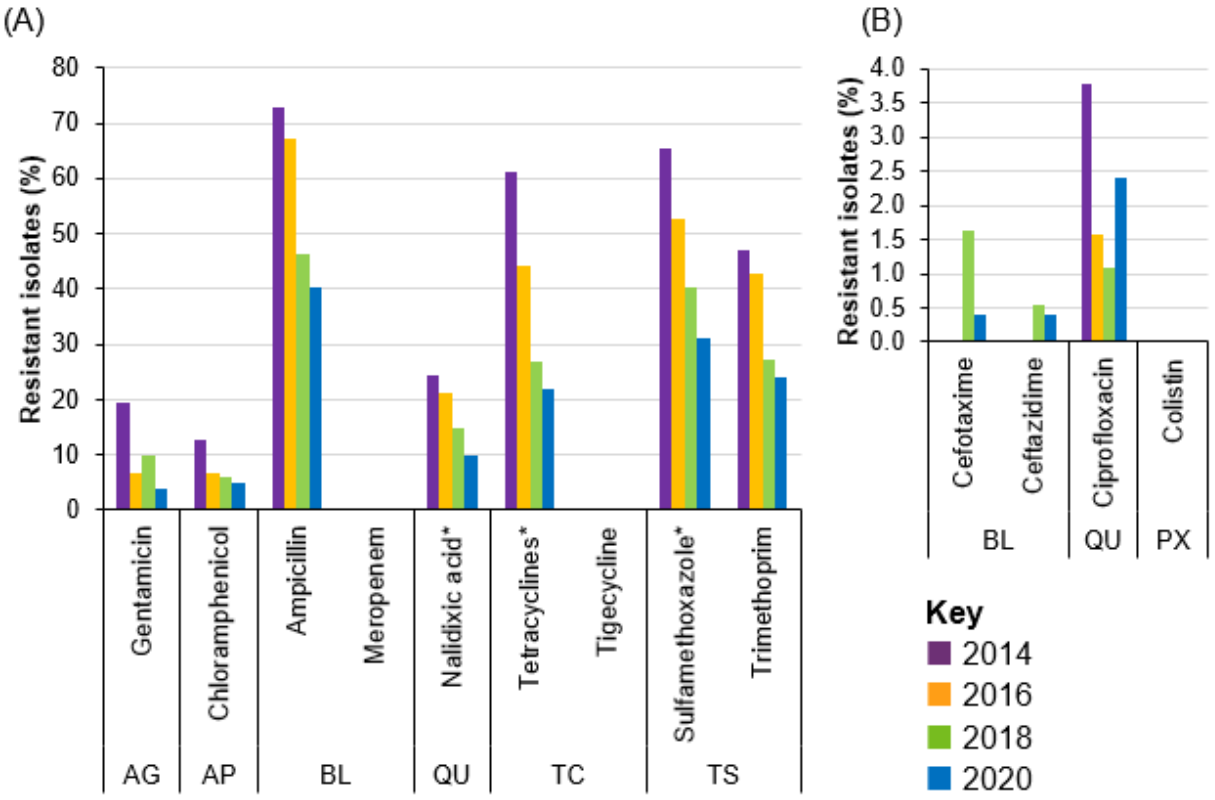
Resistance of indicator *E. coli* isolates from broiler caecal samples is shown in **Figure 3.2**.

Of the HP-CIAs, resistance to the third generation cephalosporins cefotaxime and ceftazidime was detected in 0.4% of *E. coli* isolates for each antibiotic, a decline since the highest reported levels in 2018 (1.6% and 0.5% respectively). Resistance to the fluoroquinolone ciprofloxacin remained at low levels over the monitoring period 2014 to 2020. Although resistance has increased since 2016 and 2018, to 2.4% of isolates in 2020, resistance was still at overall lower levels than those detected in 2014. *E. coli* from broiler caecal samples remained susceptible to colistin, meropenem and tigecycline throughout 2014 to 2020.

In 2020, resistance levels to antibiotics where CBPs were available were detected to ampicillin (40%) and trimethoprim (24%) at high levels, in both cases a consistent decrease since 2014. Resistance to chloramphenicol (4.8%) and gentamicin (4.0%) remained low; the former also consistently declining since 2014 and the latter detected at its lowest levels in 2020.

For antibiotics where only ECOFF values were available, in 2020, levels of decreased susceptibility were similar to those seen in previous years. Decreased susceptibility to sulfamethoxazole and tetracyclines was high (31% and 22% respectively) and to nalidixic acid was low (10.0%). Resistance to all three antibiotics has consistently decreased since 2014.

Figure 3.2: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Escherichia coli* isolates from broilers at slaughter. Interpreted using EUCAST CBPs unless otherwise indicated. Note scale differs between graphs.



* Interpreted using EUCAST ECOFF values
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, PX: polymyxins, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

3.3.1.2 Turkeys

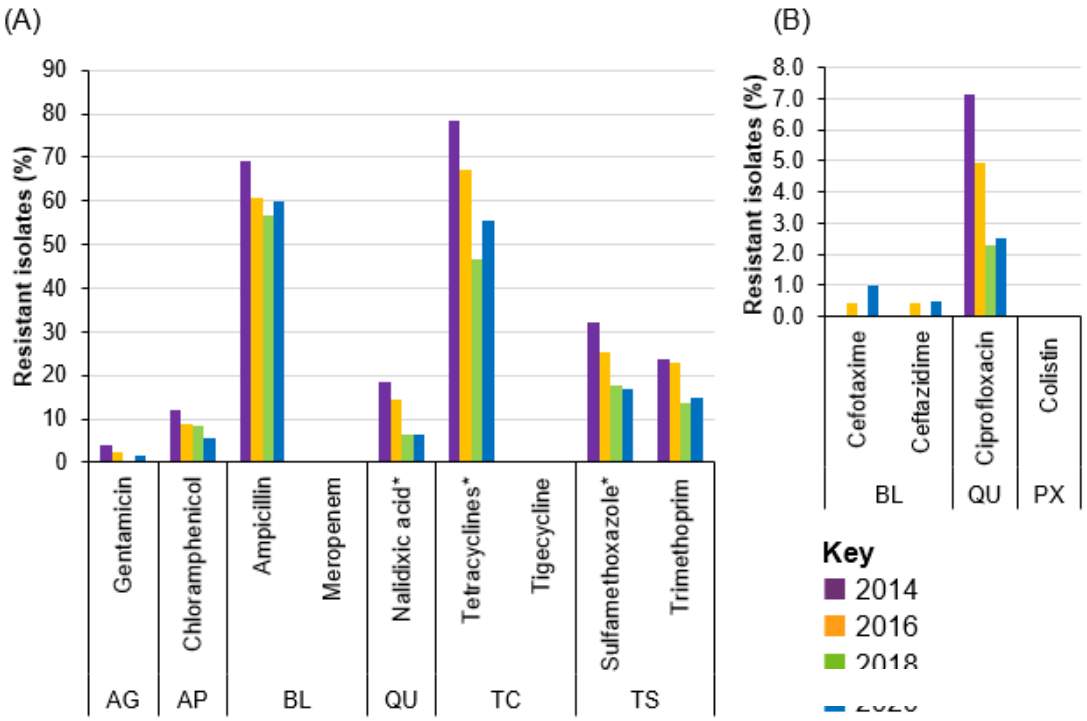
Resistance of *E. coli* isolates from turkey caecal samples is shown in **Figure 3.3**.

Resistance to the third generation cephalosporins cefotaxime and ceftazidime was detected at very low levels from 2014 and 2020. Although resistance levels were at their highest in 2020 (1.0% and 0.5% respectively), this reflects a very low number of resistant isolates (two and one respectively). Resistance to the fluoroquinolone ciprofloxacin fluctuated over the monitoring period and was at lower levels in 2020 compared to 2014 (2.5% compared to 7.1% respectively), but slightly higher than 2018 (2.3%). Susceptibility to colistin, meropenem and tigecycline was maintained throughout the monitoring period.

In 2020, resistance levels to antibiotics where CBPs were available were lower than those seen in 2014 and 2016, however, apart from chloramphenicol (5.6%) – which has continually declined since 2014 – resistance levels all increased slightly compared to 2018. Resistance to ampicillin (60%) remained very high, to trimethoprim (15%) remained moderate and to gentamicin (1.5%) remained low.

For antibiotics where only ECOFF values were available, a continued decline in decreased susceptibility to sulfamethoxazole was noted between 2014 and 2020, with resistance remaining at moderate levels (17%). Decreased susceptibility to tetracyclines (55%) remained very high and to nalidixic acid (6.6%) remained low.

Figure 3.3: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Escherichia coli* isolates from turkeys at slaughter. Interpreted using EUCAST CBPs unless otherwise indicated. Note scale differs between graphs.



* Interpreted using EUCAST ECOFF values.
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, PX: polymyxins, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

3.3.2 ESBL-, AmpC- and/or carbapenemase-producing *E. coli*

All resistances referred to under Section 3.3.2 are denoted in ECOFF values indicating decreased susceptibility.

3.3.2.1 Broilers

There has been a continued decline in the percentage of broiler caecal samples yielding ESBL or AmpC-producing *E. coli* over the period 2016 to 2020 (no ESBL/AmpC data are available for 2014).

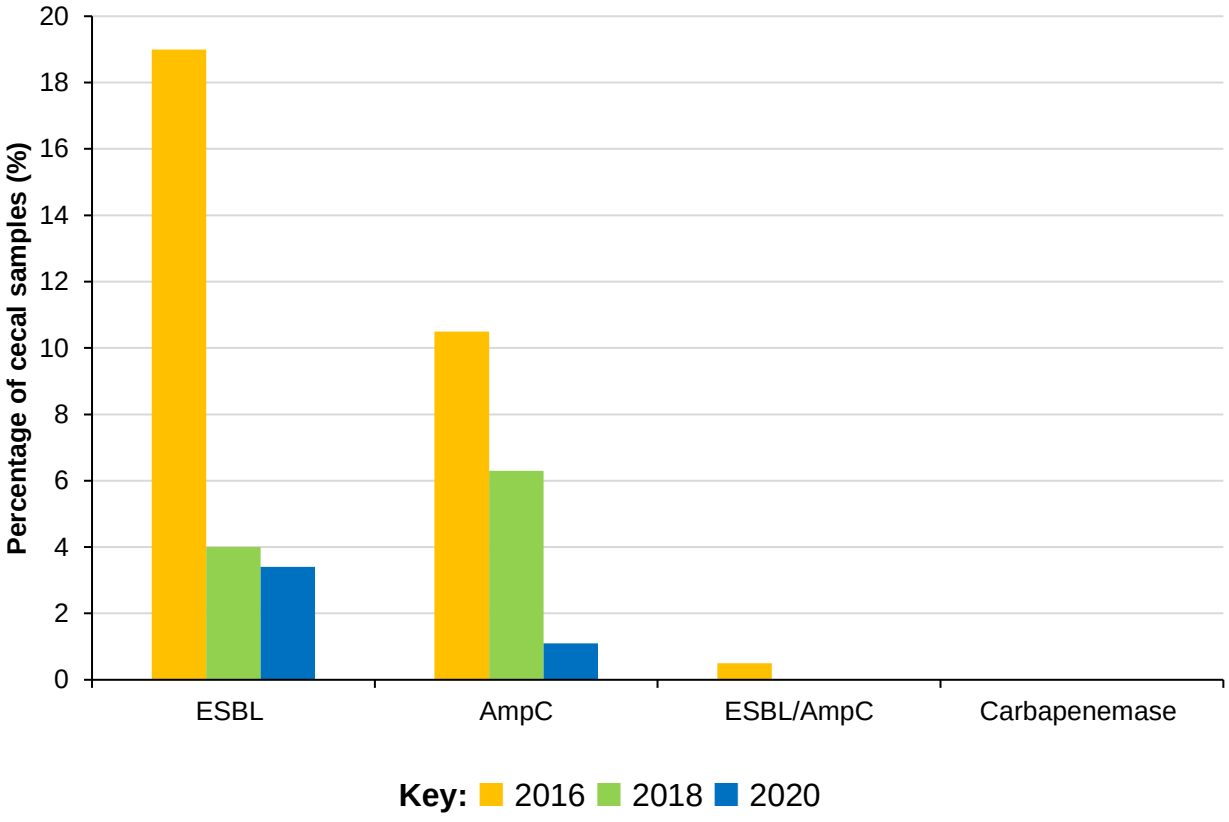
The total number of caecal samples examined from different broiler flocks in 2020 was 350, of which 17 (4.9%) yielded growth of *E. coli* on selective MacConkey plates containing the third generation cephalosporin cefotaxime. Resistance was not detected to colistin, ertapenem, meropenem, imipenem, gentamicin, temocillin or tigecycline in these 17 *E. coli* isolates.

E. coli with an ESBL phenotype were present in 3.4% of caecal samples (twelve isolates) and an AmpC phenotype in 1.1% of caecal samples (four isolates). None of the isolates were positive for both phenotypes (**Figure 3.4**).

Of the 16 *E. coli* isolates which had an ESBL or AmpC phenotype, all were resistant to ampicillin, as expected. Resistance to other antibiotic classes was higher in isolates with an ESBL phenotype compared to an AmpC phenotype. Six of the isolates with an ESBL phenotype were resistant to ciprofloxacin, five of which were also resistant to nalidixic acid, whereas only one of the isolates with an AmpC phenotype was resistant to ciprofloxacin and none were resistant to nalidixic acid. Eight of the ESBL-positive isolates were resistant to tetracyclines, ten to sulfamethoxazole, and nine to trimethoprim, whereas none of the AmpC-positive isolates were resistant to any of these antibiotics. The percentage of ESBL-positive isolates that showed resistance to chloramphenicol was higher than those with an AmpC phenotype.

No carbapenemase-producing *E. coli* were detected.

Figure 3.4: ESBL-/AmpC- and carbapenemase producing *Escherichia coli* cultured on selective agars, from caecal samples from healthy broilers at slaughter in the UK.



Whole genome sequencing (WGS) results showed that 17 *E. coli* isolates from broilers were positive for ESBL/AmpC-encoding genes. Around 1% of all caecal samples were positive for *E. coli* harbouring either the *bla*$_{CTX-M-1}$ or *bla*$_{CTX-M-55}$ gene. Of these, *bla*$_{CTX-M-55}$ was the most common ESBL-encoding gene, detected in five isolates (29%), followed by *bla*$_{CTX-M-1}$ which was detected in four isolates (24%) and *bla*$_{SHV-12}$ which was detected in three isolates (18%).

The *bla*$_{CMY-2}$ gene was the only transferable *ampC* gene detected and was present in two isolates (12%) with an ESBL/AmpC phenotype. An additional *E. coli* isolate was positive for *bla*$_{CMY-2}$ but was phenotypically sensitive to cefoxitin. In three isolates (18%) mutations in the promoter region associated with upregulation of chromosomal *ampC* expression were detected, but no ESBL/AmpC enzyme-encoding genes were detected.

The four isolates positive for the *bla*$_{CTX-M-1}$ gene were associated with three different multi locus sequence types (MLSTs), indicating possible transmission of a plasmid harbouring this gene. However, four of the five isolates harbouring the *bla*$_{CTX-M-55}$ gene belonged to ST752, indicating a possible clonal dissemination. All isolates harbouring *bla*$_{SHV-12}$ and *bla*$_{CMY-2}$ genes were assigned to different STs.

3.3.2.2 Turkeys

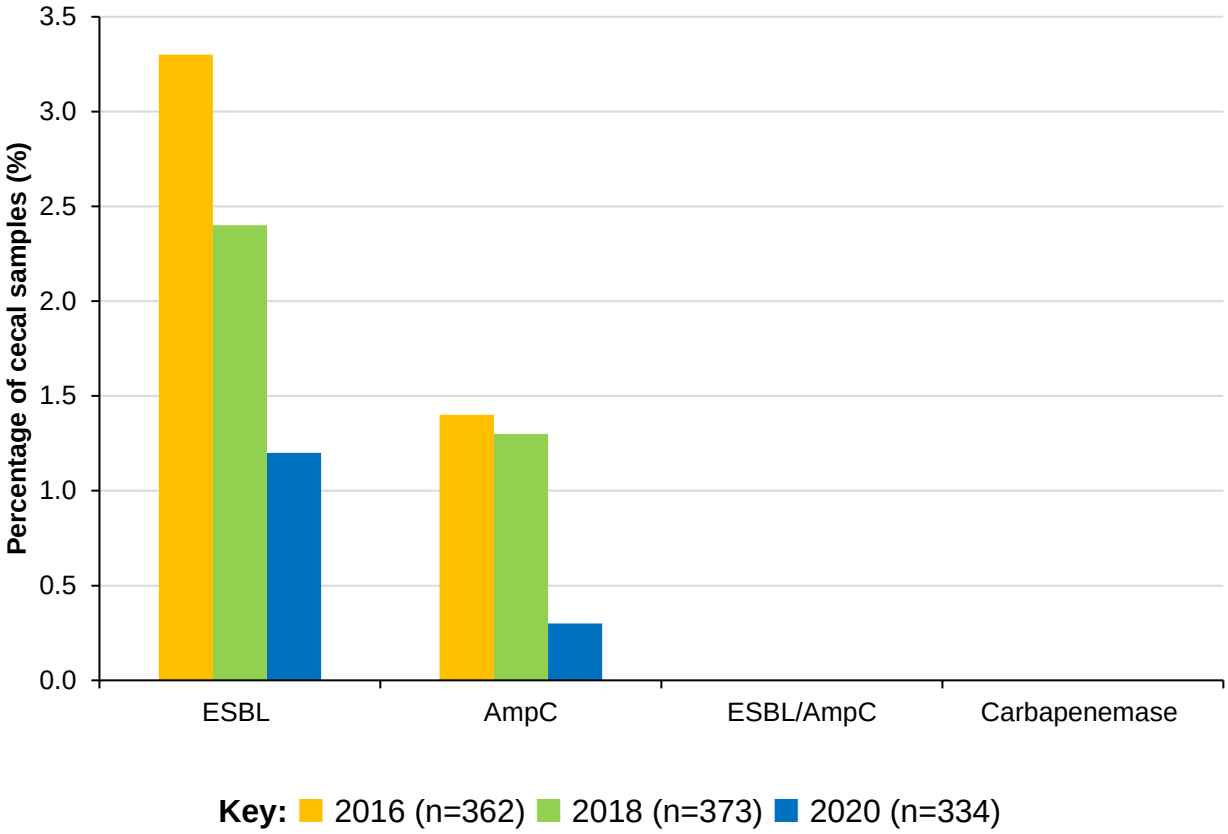
There has been a continued decline in the percentage of turkey caecal samples yielding AmpC or ESBL-producing *E. coli* over the period 2016 to 2020 (no ESBL/AmpC data are available for 2014).

The total number of caecal samples examined from different turkey flocks in 2020 was 334, of which five (1.5%) yielded growth of *E. coli* on selective MacConkey plates containing the third generation cephalosporin cefotaxime. Resistance was not detected to colistin, ertapenem, meropenem, imipenem, gentamicin, temocillin or tigecycline in these five *E. coli* isolates.

E. coli with an ESBL were present in 1.2% of caecal samples (four isolates) and an AmpC phenotype in 0.3% of caecal samples (one isolate) (**Figure 3.5**). The five *E. coli* isolates which had an ESBL or AmpC phenotype were all resistant to ampicillin, as expected. Those with an AmpC phenotype also showed resistance to the fluoroquinolone ciprofloxacin and trimethoprim. Three of the isolates with an ESBL phenotype were resistant to ciprofloxacin, only one of which was also resistant to nalidixic acid. The phenotype of ciprofloxacin resistance without nalidixic resistance suggests transferable mechanisms of fluoroquinolone resistance. The proportion of isolates with an ESBL phenotype that showed resistance to chloramphenicol, tetracycline, sulfamethoxazole, and nalidixic acid, was between 25% and 50%. Only one AmpC-producing isolate harbouring co-resistance to ciprofloxacin and trimethoprim was detected.

No carbapenemase-producing *E. coli* were detected.

Figure 3.5: ESBL-/AmpC- and carbapenemase producing *Escherichia coli* cultured on selective agars, from caecal samples from healthy turkeys at slaughter in the UK.



As a proportion of the total turkey caecal samples, 0.6% contained *bla*$_{\text{CTX-M-15}}$-positive *E. coli*. WGS results showed that five *E. coli* isolated from turkeys were positive for ESBL/AmpC-encoding genes. Of these, 80% harboured genes encoding CTX-M enzymes. *bla*$_{\text{CTX-M-15}}$ was the most common gene detected and was found in two isolates (40%), followed by *bla*$_{\text{CTX-M-1}}$ and *bla*$_{\text{CTX-M-55}}$. One isolate harboured the *bla*$_{\text{DHA-1}}$ gene, encoding AmpC, but none harboured *bla*$_{\text{CMY-2}}$ or a mutation in the *ampC* promoter region.

The five ESBL/AmpC isolates were generally of different STs, although both isolates harbouring the *bla*$_{\text{CTX-M-15}}$ gene belonged to ST1011.

3.3.3 *Salmonella* spp.

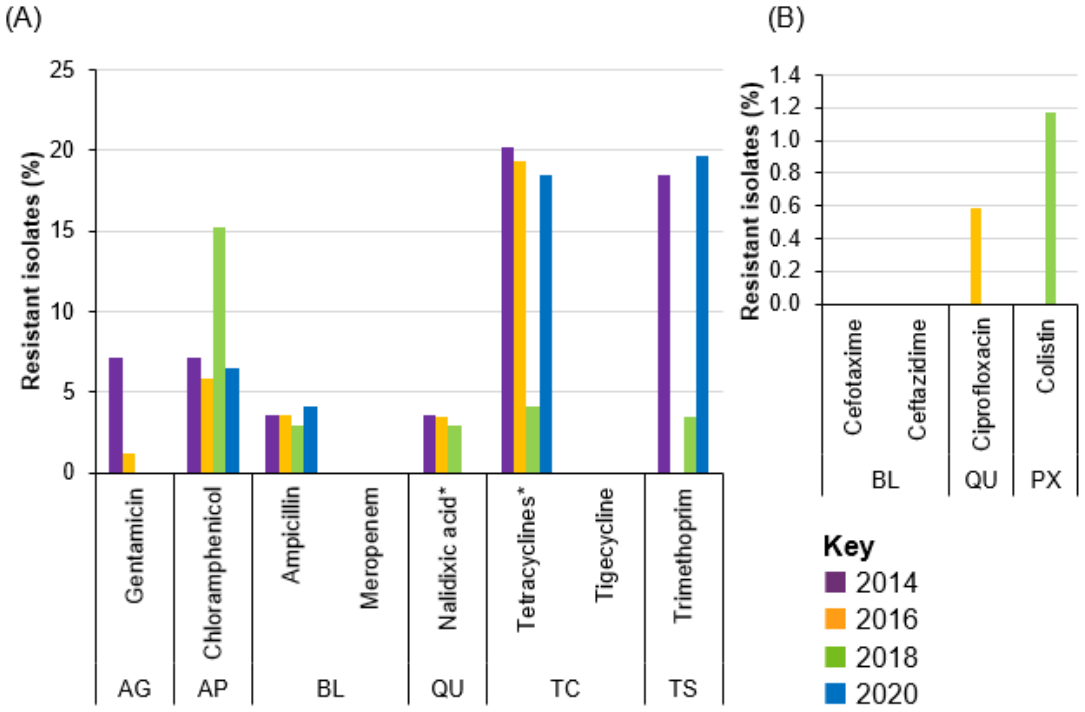
3.3.3.1 Broilers

3.3.3.1.1 National Control Programme for *Salmonella*

Susceptibility to the full panel of antibiotics tested was determined using ECOFFs rather than CBPs, as the latter are not available for all antibiotics. Of the *Salmonella* isolates from broiler flocks, 72% were susceptible to the full panel of antibiotics tested, representing a decline since 2018 (84%), however this is still an increase compared to 2014 levels (64%).

Full susceptibility to the third generation cephalosporins cefotaxime and ceftazidime was maintained between 2014 and 2020 and to the fluoroquinolone ciprofloxacin since 2018. Resistance to colistin was only detected in two isolates in 2018 and was not detected throughout the rest of the monitoring period. *Salmonella* isolates remained susceptible to meropenem and tigecycline between 2014 and 2020 and to gentamicin since 2018 (**Figure 3.6**).

Figure 3.6: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Salmonella* isolates from broiler flock NCP samples. Interpreted using EUCAST CBPs unless otherwise indicated. Note scale differs between graphs.



* Interpreted using EUCAST ECOFF values
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, PX: polymyxins, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

The total number of *Salmonella* isolates investigated was 168. These included the incomplete serovar 13,23:i:- (55 isolates), *S.* Kedougou (37 isolates), *S.* Montevideo (32 isolates) and *S.* Mbandaka (19 isolates). This is similar to the serovars noted in 2018, which included the incomplete serovar 13,23:i:- (61 isolates), *S*. Mbandaka (54 isolates), *S*. Kedougou (18 isolates), *S.* Montevideo (8 isolates) and *S.* Ohio (7 isolates). There were no isolates of *S.* Enteritidis, or monophasic *S*. Typhimurium included in the randomised sample of *Salmonella* isolates from broiler samples. Two *S.* Typhimurium isolates were present and showed resistance to ampicillin; one isolate was additionally resistant to chloramphenicol and had decreased susceptibility to tetracyclines.

In 2020, for antibiotics where CBPs were available, resistance to ampicillin (4.2%) and chloramphenicol (6.5%) fluctuated between 2014 and 2020; for chloramphenicol,

resistance is still lower than 2014 levels however this is not the case for ampicillin. Resistance to trimethoprim increased from 3.5% in 2018 to 20% in 2020, although this is similar to resistance levels noted in 2014 (19%). This increase can largely be attributed to the spread of *S*. Kedougou, which is resistant to sulphonamides/tetracyclines.

Regarding antibiotics where only ECOFF values were available, for the first time during the monitoring period no isolates showed decreased susceptibility to nalidixic acid. Decreased susceptibility to tetracyclines (19%) fluctuated between 2014 and 2020, although 2020 levels are still lower than 2014 and 2016 levels.

3.3.3.1.2 FBO neck skin samples

For isolates detected through the FBO monitoring programme, there is limited scope to draw trends from the data. This is because historically, the number of isolates detected through this programme has been very low, except for data obtained between 2018 and 2020. Consequently, in this report, trends only refer to data obtained from this period.

The number of *Salmonella* isolates investigated was 69, including *S.* Agona (27 isolates), *S.* Montevideo (13 isolates) and *S.* Kedougou (7 isolates). The other serovars recovered were *S.* Coeln, *S.* Indiana, *S.* Mbandaka and *S.* Ohio and two incomplete serovars. *S.* Enteritidis, *S.* Typhimurium and monophasic Typhimurium were not detected. The majority of isolates (48, 70%) were susceptible to the full panel of antibiotics tested.

Full susceptibility to the third generation cephalosporins cefotaxime, ceftazidime and the fluoroquinolone ciprofloxacin has been maintained, as well as to the antibiotic's gentamicin, meropenem and tigecycline (see Table S3.4.4 of the supplementary material). A single isolate with colistin resistance was detected for the first time in this sampling programme in 2020.

Other than for chloramphenicol (1.4%), resistance to the remaining antibiotics where CBPs were available increased between 2018 and 2020: resistance to ampicillin increased from 0% to 23%, and resistance to trimethoprim increased from 1.0% to 29%. These increases can be attributed to the spread of *S*. Agona with resistance to ampicillin, tetracycline and trimethoprim, which was first detected in feed in early 2020 and subsequently appeared in FBO broilers and layers.

For antibiotics where only ECOFF values were available, decreased susceptibility to tetracyclines increased from 0% to 26%, which can also be attributed to the *S*. Agona clone.

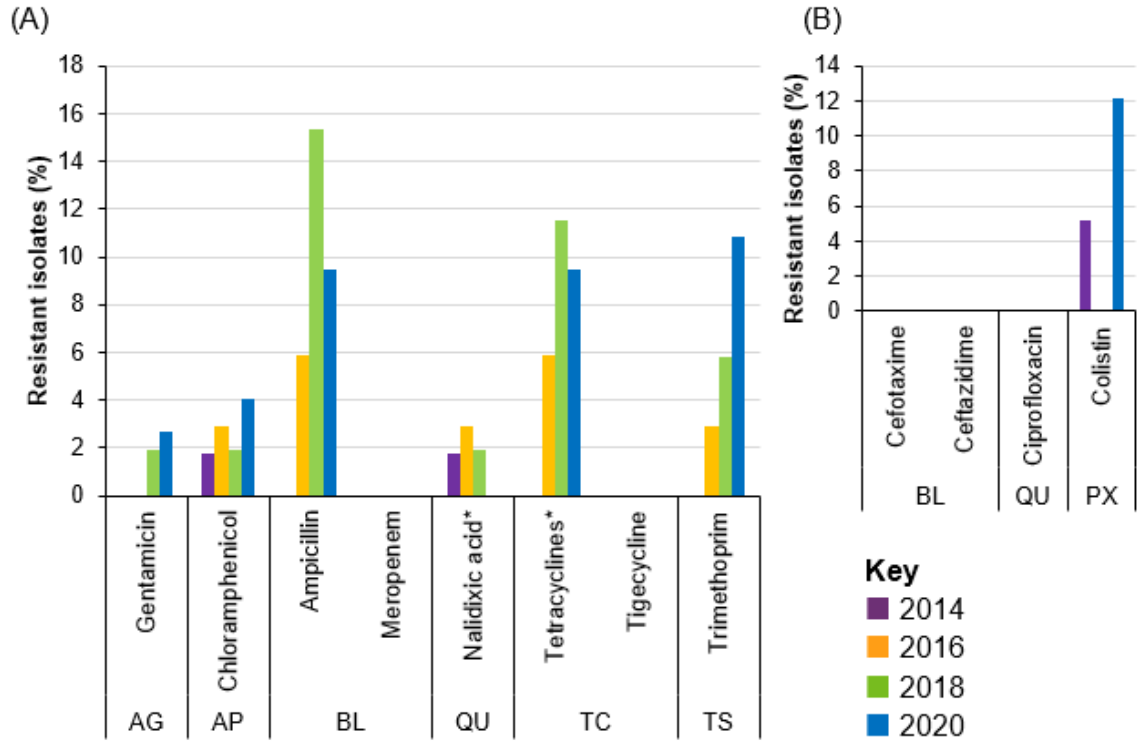
3.3.3.2 Laying hens

3.3.3.2.1 National Control Programme (NCP) for *Salmonella*

The number of *Salmonella* isolates investigated from laying hens was 74, including *S.* Enteritidis (18 isolates), *S.* Typhimurium (12 isolates) and *S.* Agona (7 isolates). There were two isolates of monophasic *S.* Typhimurium.

Susceptibility to the full panel of antibiotics tested was determined using ECOFFs rather than CBPs, as the latter are not available for all antibiotics. Susceptibility to all the antibiotics tested was shown in 78% of isolates representing a decrease since 2018 (81%) and since 2014 (93%). Resistance in 2020 is influenced by the colistin resistance observed in nine *S*. Enteritidis isolates. *S.* Enteritidis is a Group D *Salmonella*, which are intrinsically more resistant to colistin than other *Salmonellas*, due to their cell wall structure. Susceptibility to the third generation cephalosporins cefotaxime, ceftazidime and the fluoroquinolone ciprofloxacin was maintained over the monitoring period. Susceptibility was also maintained to meropenem and tigecycline (**Figure 3.7**).

Figure 3.7: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Salmonella* isolates from layer flock NCP samples. Interpreted using EUCAST CBPs unless otherwise indicated. Note scale differs between graphs.



* Interpreted using EUCAST ECOFF values
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, PX: polymyxins, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

In 2020, for antibiotics where CBPs were available, resistance to ampicillin (9.5%) and chloramphenicol (4.1%) fluctuated over the monitoring period; ampicillin resistance declined since 2018, whereas chloramphenicol resistance increased. Resistance to gentamicin and trimethoprim increased over the monitoring period; although gentamicin resistance remains low (2.7%), resistance to trimethoprim increased from 0% in 2014 to 10.8% in 2020.

For antibiotics where only ECOFF values were available, no isolates had decreased susceptibility to nalidixic acid, a decline from 1.9% in 2018. Decreased susceptibility to tetracyclines (9.5%) fluctuated over the monitoring period, with resistance detected at lower levels in 2020 than in 2018.

The twelve *S.* Typhimurium isolates from laying hens were susceptible to the panel of antibiotics tested. The 18 *S.* Enteritidis isolates were susceptible to the panel of antibiotics tested, with the exception of the nine isolates which were resistant to colistin, mentioned above.

3.3.3.3 Turkeys

3.3.3.3.1 National Control Programme (NCP) for *Salmonella*

The number of *Salmonella* isolates investigated was 166, including *S.* Kedougou (57 isolates), *S.* Anatum (44 isolates), *S.* Derby (20 isolates), the incomplete serovars 3,10:e,h:- (12 isolates) and 13,23:i:- (11 isolates) and *S.* Senftenberg (eight isolates) with the other serovars reported occurring in lower numbers. There were no isolates of *S.* Typhimurium, monophasic *S.* Typhimurium or *S.* Enteritidis included in the sample of isolates from turkeys.

Susceptibility to the full panel of antibiotics tested was determined using ECOFFs rather than CBPs, as the latter are not available for all antibiotics. Susceptibility to the full panel of antibiotics tested was shown by 22% of the NCP *Salmonella* isolates, a slight increase from 2018 (20%). This is a decline since susceptibility levels noted in 2014 (31%), but 2020 levels are the same as those seen in 2016. Susceptibility to the HP-CIAs cefotaxime, ceftazidime, ciprofloxacin and colistin was maintained over the monitoring period, as well as to meropenem and since 2016, to tigecycline as well (see **Figure 3.8**).

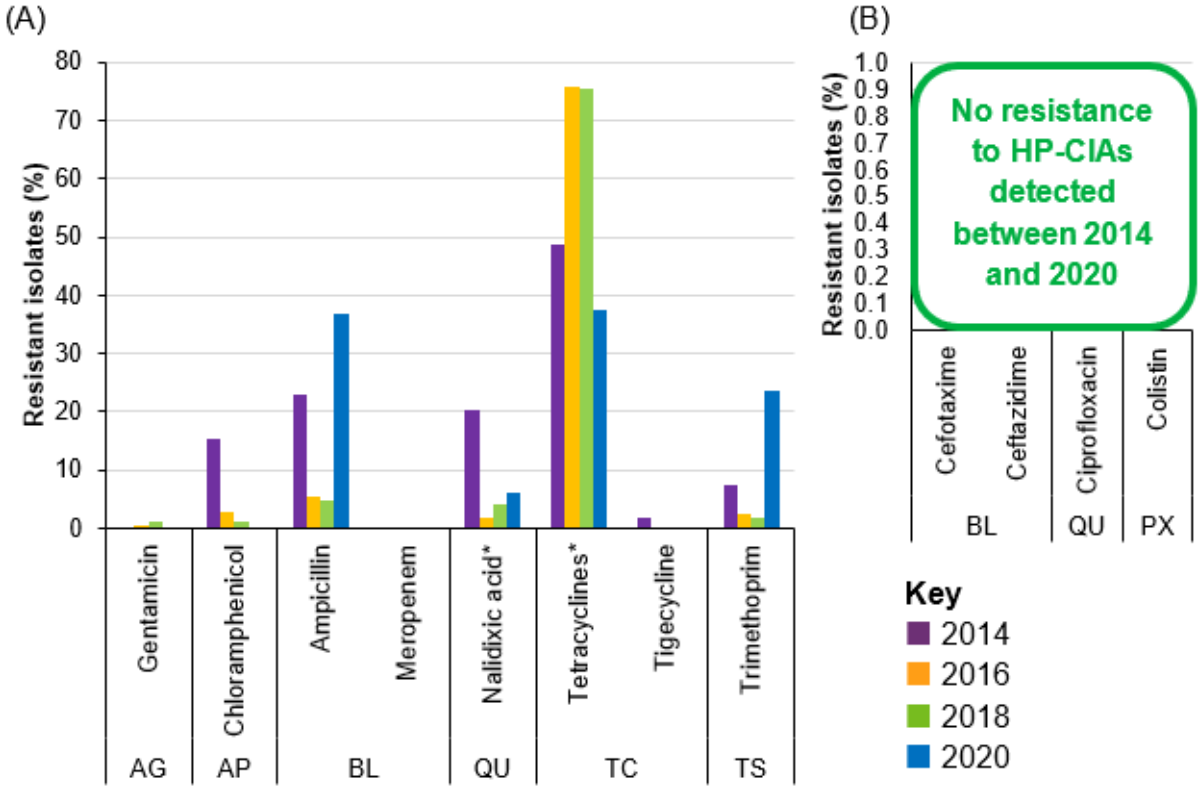
In 2020, for antibiotics where CBPs were available, resistance to gentamicin fluctuated at low levels over the monitoring period and was not detected in 2020. Resistance to chloramphenicol decreased over the monitoring period, dropping to 0% for the first time in 2020. Increases in resistance were noted to ampicillin and trimethoprim: the former is largely attributed to the *Salmonella* serovar *S*. Anatum, which has increased ten-fold, likely associated with contaminated feed[25]; the latter to *S.* Kedougou, which is associated with combined sulphonamides/tetracyclines/trimethoprim resistance, as seen in broilers.

[25] Salmonella in livestock production in Great Britain - GOV.UK (www.gov.uk)

Resistance to ampicillin and trimethoprim exceeded 2014 levels, increasing from 4.7% to 37% and from 1.8% to 24% respectively.

For antibiotics where only ECOFF values were available, decreased susceptibility to tetracyclines decreased between 2014 and 2020, declining from 75% in 2018 to 37% in 2020. Decreased susceptibility to nalidixic acid remained low (6.0%) and at lower levels than those seen in 2014.

Figure 3.8: Resistance to non-HP-CIAs (A) and HP-CIAs (B) in *Salmonella* isolates from turkey flock NCP samples. Interpreted using EUCAST CBPs unless otherwise indicated. Note scale differs between graphs.



* Interpreted using EUCAST ECOFF values
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, PX: polymyxins, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

3.3.3.3.2 Isolates from FBO neck skin samples

No *Salmonella* isolates were recovered from turkey carcass samples from Food Business Operators in 2020.

3.3.4 *Campylobacter jejuni*

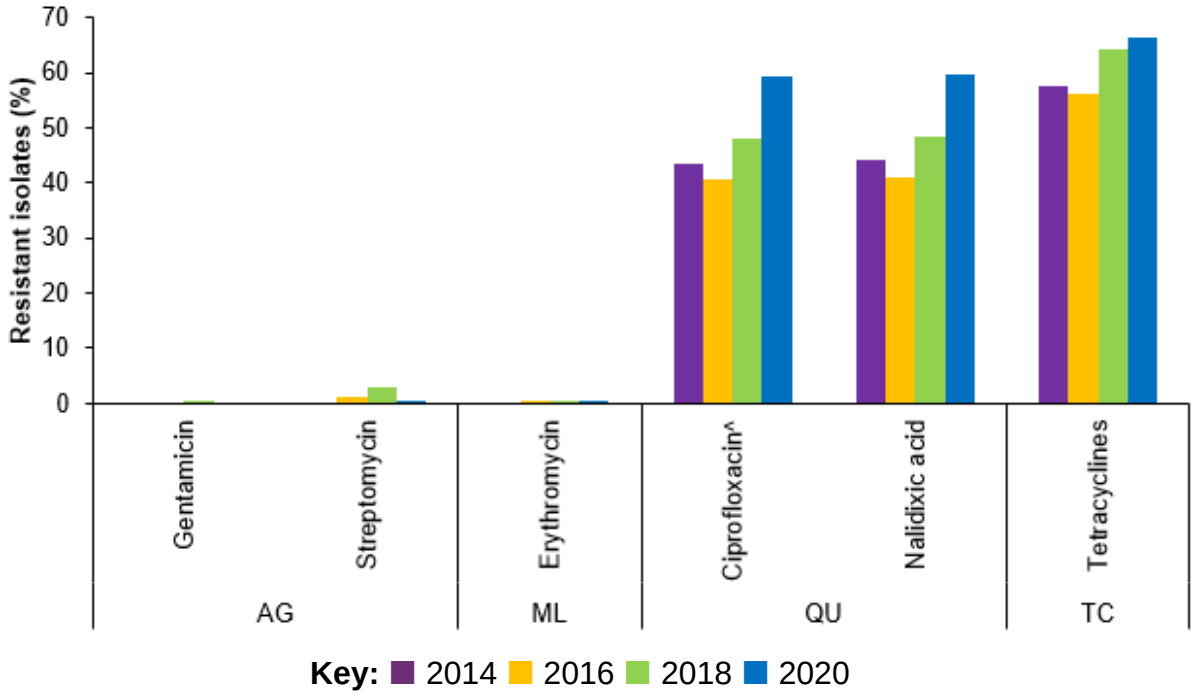
3.3.4.1 Broilers

Resistance in *C. jejuni* to ciprofloxacin, tetracyclines and nalidixic acid in broilers remains a concern, as similarly high levels have been detected in isolates from both retail meat[26] and human patients[27]. In 2020, for antibiotics where CBPs were available, resistance to the fluoroquinolone ciprofloxacin was detected at very high levels, increasing from 44% in 2014 to 59% in 2020. Most isolates (98%) resistant to ciprofloxacin were also resistant to nalidixic acid. Similarly, most isolates resistant to ciprofloxacin were also resistant to tetracyclines (89%). Resistance to tetracyclines increased from 58% in 2014 to 67% in 2020. However, macrolides remain the treatment of choice for human campylobacteriosis, and resistance to erythromycin in *C. jejuni* in broilers remains was very low, with only one isolate (0.6%) resistant in 2020. This isolate had a high MIC value of >128mg/l but was susceptible to ciprofloxacin. WGS was performed and confirmed the isolate did not contain any of the known transferable macrolide resistance genes (including *erm* genes).

For antibiotics where only ECOFF values were available, decreased susceptibility to nalidixic acid increased from 44% in 2014 to 60% in 2020 (**Figure 3.9**). Decreased susceptibility to gentamicin was only noted in 2018 (0.6%) throughout the reporting period and to streptomycin was detected at low levels in 2020 (0.6%).

[26] Antimicrobial resistance in Campylobacter jejuni and Campylobacter coli from retail chilled chicken in the UK | Food Standards Agency
[27] UK One Health Report: antibiotic use and antibiotic resistance in animals and humans - GOV.UK (www.gov.uk)

Figure 3.9: Resistance (to both non-HP-CIAs and HP-CIAs) in *Campylobacter jejuni* isolates from broilers at slaughter.



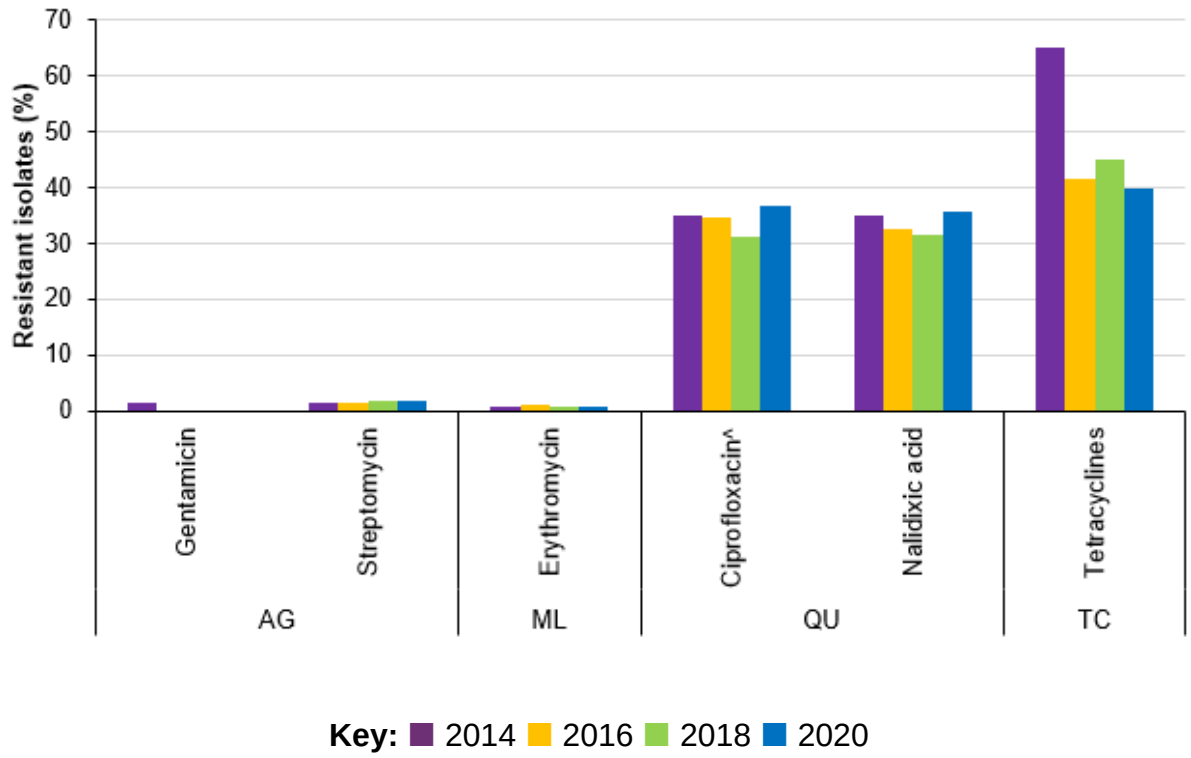
^ HP-CIA
AG: aminoglycosides, ML: macrolides, QU: quinolones, TC: tetracyclines

3.3.4.2 Turkeys

Resistance to the fluoroquinolone ciprofloxacin remained at high levels over the monitoring period and in 2020 was recorded at 37% (**Figure 3.10**). As in broilers, most (84%) *C. jejuni* isolates from turkeys which were resistant to ciprofloxacin were also resistant to tetracyclines and nalidixic acid. Resistance to tetracyclines has been maintained at high levels over the monitoring period but was recorded at its lowest levels in 2020 at 40%. Resistance to erythromycin was very low in 2020, with only one out of 169 (0.6%) *C. jejuni* isolates showing resistance. This isolate had an MIC of >128 mg/l but was susceptible to ciprofloxacin. WGS was performed and confirmed the isolate did not contain any transferable macrolide genes (including *erm* genes). This prevalence of resistance is the same as in 2014 and 2018 and a decline from 2016 levels (1.1%).

Decreased susceptibility to nalidixic acid (36%) has been maintained at high levels and was highest in 2020. Decreased susceptibility to streptomycin increased between 2014 and 2020 (from 1.3% to 1.8%) but levels remain low. Susceptibility to gentamicin has been maintained since 2016.

Figure 3.10: Resistance (to both non-HP-CIAs and HP-CIAs) in *Campylobacter jejuni* isolates from turkeys at slaughter.



^ HP-CIA
AG: aminoglycosides, ML: macrolides, QU: quinolones, TC: tetracyclines

3.3.5 EU harmonised AMR outcome indicators

In 2017, the ECDC, EFSA and EMA recommended harmonised outcome indicators for presenting data on antibiotic resistance in food-producing animal species[28]. These comprise one primary and three secondary indicators. *E coli* is the indicator organism due to its ubiquitous nature in animals, food and humans and its ability to readily develop or transfer antibiotic resistance between these reservoirs. The indicators **are averaged over two years** due to the alternating schedule for AMR pig and poultry sampling and are weighted by population size (expressed in PCU), to ensure the data includes both groups for each indicator.

Primary indicator:

- Proportion of indicator *E. coli* isolates from broilers, fattening turkeys and fattening pigs (as collected in the framework of Decision 2013/652/EU) fully susceptible to the entire panel of antibiotics defined in the Decision, weighted by PCU.

[28] https://www.ecdc.europa.eu/en/publications-data/ecdc-efsa-and-ema-joint-scientific-opinion-list-outcome-indicators-regards

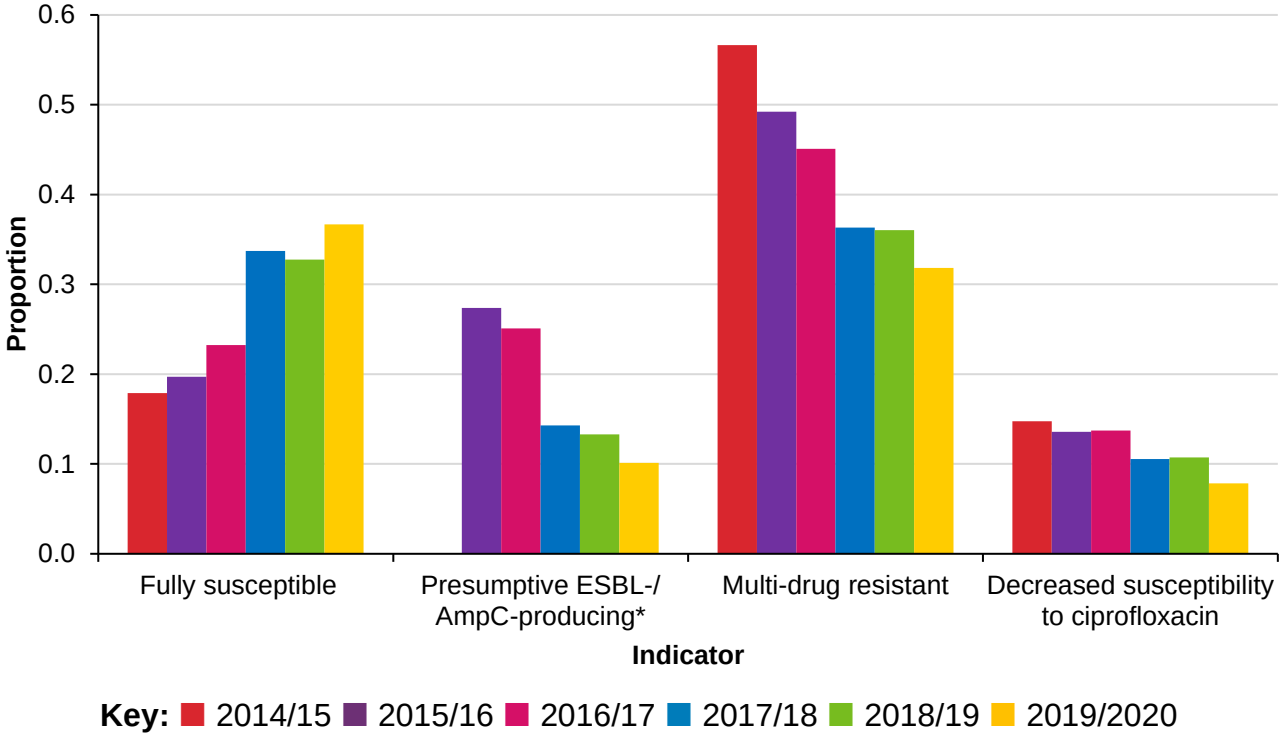
Secondary indicators:

- Proportion of indicator *E. coli* isolates from the three animal species, weighted by PCU, showing decreased susceptibility to at least three antibiotics from different classes from the predefined panel of antibiotics (multi-drug resistant);
- Proportion of indicator *E. coli* isolates from the three animal species, weighted by PCU, showing decreased susceptibility to the fluoroquinolone ciprofloxacin;
- Proportion of samples identified as positive for presumptive ESBL-/AmpC-producing indicator *E. coli* under the specific monitoring for ESBL-/AmpC-/carbapenemase-producing indicator *E. coli* from the three animal species, weighted by PCU.

All indicators show decreasing resistance and increasing susceptibility in the 2019 to 2020 period (**Figure 3.11**). The proportion of fully susceptible *E. coli* (the primary indicator) has more than doubled and multi-drug resistant *E. coli* (a secondary indicator) decreased by 44% since the 2014 to 2015 monitoring period.

The other secondary indicators also showed an increase in susceptibility. The proportion of samples identified as positive for presumptive ESBL-/AmpC-producing *E. coli* has more than halved (63% decrease) since the 2015 to 2016 monitoring period (no data available for the 2014 to 2015 period) and the proportion of *E. coli* isolates that showed decreased susceptibility to ciprofloxacin decreased by almost half (47%) since the 2014 to 2015 monitoring period.

Figure 3.11: Proportion of harmonised monitoring indicator *Escherichia coli* isolates from broilers, fattening turkeys and fattening pigs weighted by PCU, averaged over two years



* Data not available for 2014/15.

CHAPTER 4

Clinical surveillance of antibiotic resistance

Clinical surveillance is a programme of passive surveillance which evaluates AMR in bacteria of relevance to animal health. These bacteria are isolated from post-mortem carcases or other diagnostic samples submitted by private veterinary surgeons to APHA and partner veterinary laboratories in England and Wales. When a bacterial pathogen is identified, susceptibility testing is performed to provide the practitioner with relevant information for treatment. Similar programmes are conducted by Scottish (SRUC Veterinary Services) and Northern Irish (Agri-Food Biosciences Institute, AFBI-NI) laboratories. This chapter for the majority reports the APHA methods and results; results from SRUC and AFBI-NI are included in the supplementary material.

As this is a passive programme, the results in this chapter should not be considered representative of the UK as a whole, and should be interpreted with caution (see Section 4.2 below and S4.1 of the supplementary material). The primary aim of the programme is to provide scanning surveillance of animal disease. However, it also helps to identify new and emerging patterns of resistance, particularly since treatment failure is a frequent reason for submission of samples. The programme also incorporates results from the susceptibility testing of *Salmonella* isolates recovered from animals and their environment, as part of the UK Zoonoses Order 1989[29]. Any findings considered to pose a particular risk to human or animal health are reported to the Defra Antibiotic Resistance Coordination (DARC) group and to the VMD for consideration and management in accordance with protocols outlined in the VMD AMR Contingency Plan.

For the first time, this report presents the results of minimum inhibitory concentration (MIC) testing to assess susceptibility to antibiotics of important veterinary respiratory pathogens. This enhancement of the clinical surveillance programme applies recent recommendations for monitoring AMR from food-producing animals[30] in a way that will generate robust and comparable susceptibility testing outputs for relevant combinations of antibiotics and

[29] The Zoonoses Order 1989 (legislation.gov.uk)

[30] A proposed scheme for the monitoring of antibiotic resistance in veterinary pathogens of food animals in the UK - Teale - 2021 - Veterinary Record - Wiley Online Library

veterinary pathogens. Results will help veterinarians make better prescribing choices and support responsible use of antibiotics, as well as increase the ability of clinical surveillance to detect emerging resistance issues in the UK.

4.1 Summary

The resistance levels observed in many veterinary bacteria showed limited change over the monitoring period covered by this report (2018 to 2020). Because scanning surveillance is subject to biases and differences in the intensity of sampling, results in this chapter cannot be extrapolated to the general livestock population.

Respiratory pathogens:

- Major respiratory pathogens (*Pasteurella multocida, Mannheimia haemolytica*, *Bibersteinia trehalosi, Actinobacillus pleuropneumoniae*) were tested for the first time against the most clinically relevant antibiotics using a microbroth dilution method to generate MIC results.
- Many isolates remain susceptible to the panel of antibiotics tested, including those that have been authorised for many years.
- When resistance was detected, alternative therapeutic options could be identified. Resistance was uncommon or not detected to those antibiotics which are often used as second- or third-line treatment options.

Mastitis pathogens:

- *E. coli* was the most-frequently isolated bacteria in bovine mastitis submissions in 2020 and resistance both to HP-CIAs and non-HP-CIAs has remained low or stable over the reporting period, with the exception of ampicillin, which has increased to 45% in 2020.
- Penicillin resistance was not detected in bovine mastitis streptococci (*Streptococcus agalactiae*, *Streptococcus dysgalactiae* and *Streptococcus uberis*) in 2020.

LA-MRSA:

- Livestock-associated methicillin-resistant *S. aureus* (LA-MRSA) clonal complex (CC) 398, was detected in four pig herds in scanning surveillance performed at APHA in 2020.
- This is the first time LA-MRSA has been detected in England and Wales since 2018, where it was detected in a turkey, and the first detection in a pig since 2017.

Clinical *E. coli*:

- HP-CIA resistance in diagnostic *E. coli* from neonatal calves declined in 2020, with resistance to cefotaxime (an indicator third generation cephalosporin used to detect

ESBL and other beta-lactamases) and enrofloxacin detected in 7.0% and 3.5% of isolates, respectively, compared to 7.6% and 5.3% in 2019.

- In 2020, HP-CIA resistance in diagnostic *E. coli* from neonatal piglets was low, with cefpodoxime (also a third generation cephalosporin important in human medicine) resistance detected in 3.2% of isolates and enrofloxacin resistance in 2.2% of isolates (compared to 1.1% and 9.6% respectively in 2019).
- Resistance to cefotaxime in diagnostic *E. coli* isolates from lambs in 2020 was 2.0%, a slight increase from 0.0% reported in 2019. Enrofloxacin resistance declined to 3.4% from 4.8% in 2019.
- Cefpodoxime resistance in *E. coli* from chickens was 1.1% in 2020, a decline from 5.9% in 2019. Use of third generation cephalosporins has not been permitted in poultry since 2012. Enrofloxacin resistance in diagnostic *E. coli* isolates from chickens in 2020 was 5.4%, a decrease from 11% reported in 2019.

Clinical *Salmonella*:

- For all *Salmonella* isolates tested in 2020, 2871 (68%) were sensitive to all the antibiotics tested.
- The proportion of *Salmonella* isolates resistant to third generation cephalosporins and fluoroquinolones (HP-CIAs) was very low in 2020.
- A single *S.* Indiana isolate with multi-drug resistance (including to third generation cephalosporins) was recovered from a lorry swab taken at a poultry farm, which is likely a result of environmental contamination.
- Third generation cephalosporin resistance was also detected in two multi-drug resistant *S.* Typhimurium isolates from equine environment.
- No third generation cephalosporin or fluoroquinolone resistance was detected in *S.* Enteritidis from animals in 2020.
- Susceptibility in *S.* Dublin isolates decreased in 2020 (from 99.6% to 89%).

4.2 Methods

4.2.1 Sample sources

Bacteria were isolated from clinical or post-mortem samples submitted to APHA by practising veterinary surgeons.

For *Salmonella* spp., any laboratory isolating these from animals under the UK Zoonoses Order 1989[31] and their environment in Great Britain is required to notify and submit an isolate to a Defra-approved laboratory for characterisation including antibiotic sensitivity testing.

[31] The Zoonoses Order 1989 (legislation.gov.uk)

4.2.2 Susceptibility testing methodology

Detailed methodology for the susceptibility testing is presented in S4.1.1 of the supplementary material.

For the results in the main sections of this chapter, the method used was that formerly recommended by the British Society for Antimicrobial Chemotherapy (BSAC). The susceptibility tests were performed (unless otherwise stated) by disc diffusion and interpreted using BSAC human breakpoints, where available. Isolates have been classed as either sensitive or resistant; intermediate isolates under the BSAC guidelines are considered resistant.

Data presented in Section 4.3.1.1 (MIC testing of veterinary pathogens) and Section 4.3.2.6 (Private Laboratory Initiative) utilised different methods, which are described separately in S4.1.2 and S4.1.3 of the supplementary material respectively.

4.3 Results

For some bacterial pathogens, very few isolates are recovered in any one year and therefore the prevalence of resistance and any trends need to be interpreted with caution. When more than 20 isolates of any pathogen are recovered in any given year the results are presented graphically in the main body of the report, with additional numerical data available in the supplementary material. When fewer than 20 isolates are recovered consistently, results are presented in the supplementary material only.

Certain active compounds included in the antibiotic testing panels are not authorised for use in food-producing animals. These are included to monitor the emergence or risk of resistance to these antibiotics in bacteria in humans, or because they are representative of an antibiotic class. Please refer to Table S1.7.2 of the supplementary material to see a table of these compounds. Panels of antibiotics can vary between years and individual isolates. Where a figure shows no data against specific antibiotics or years as a result of this panel variation, this has been identified in a footnote.

Additionally, please note that EFSA definitions for levels of resistance have been used to denote whether resistance levels are low, moderate, high etc. throughout the report. A table highlighting these definitions can be found in Annex B.

4.3.1 Respiratory pathogens

4.3.1.1 MIC testing of veterinary pathogens

Minimum inhibitory concentration (MIC) testing under the clinical surveillance programme has historically been limited to specific organisms, such as *Brachyspira hyodysenteriae*, which causes swine dysentery. For the first time, bacterial susceptibility determined by MIC testing of a broader range of veterinary pathogens is presented in this report, focusing on

key respiratory pathogens. The results in this section are based on recommendations published in a recently proposed scheme developed by APHA and VMD for monitoring AMR in key veterinary bacterial pathogens from food-producing animals[32].

The disc diffusion methodology used to date for assessing susceptibility of veterinary pathogens from scanning surveillance (detailed in S4.1.1 of the supplementary material) are limited by the availability of suitable breakpoints for all relevant antibiotic and organism combinations. Assessing the susceptibility of veterinary pathogens by determination of the MIC using a standardised broth microdilution method provides a higher quality, internationally recognised output, which is comparable with other monitoring programmes (such as the harmonised monitoring programme in **Chapter 3**).

Results have been interpreted using available veterinary clinical breakpoints (CBPs) from the Clinical and Laboratory Standards Institute (CLSI), and where these are unavailable, veterinary CBPs from the Antibiogram Committee of the French Society of Microbiology (CASFM) and human CBPs from European Committee on Antimicrobial Susceptibility Testing (EUCAST). Further details on the methods and interpretation criteria can be found in S4.1.2 of the supplementary material. Multi-drug resistance (MDR) was assessed using veterinary CBPs (or human CBPs where a veterinary CBP was not available) and was considered to indicate resistance to any three or more classes of antibiotics.

Application of established clinical veterinary pathogen breakpoints for relevant antibiotic-pathogen combinations provides useful data for vets to support their prescribing choices. Antibiotics were chosen for the panel according to their clinical importance and licensing in the UK and across Europe, as well as their suitability as representatives or class representatives of resistance. More than one antibiotic could be chosen within a class, for example, on the respiratory panel, tetracyclines were represented by doxycycline and tetracycline. Additionally, antibiotics which are not used in animals but are important indicators of resistance to relevant veterinary antibiotics were also included[33].

In future years, our aim is to expand this surveillance methodology to a wider range of relevant veterinary pathogens. Results for 2020 concentrate on respiratory pathogens and include the following bacterial species: *Mannheimia haemolytica* from cattle and sheep, *Pasteurella multocida* from cattle, sheep and pigs, *Bibersteinia trehalosi* from sheep and *Actinobacillus pleuropneumoniae* from pigs.

4.3.1.1.1 *Mannheimia haemolytica*

M. haemolytica is a common cause of respiratory disease in both cattle and sheep in the UK although different serotypes predominantly affect each species. Healthy animals can

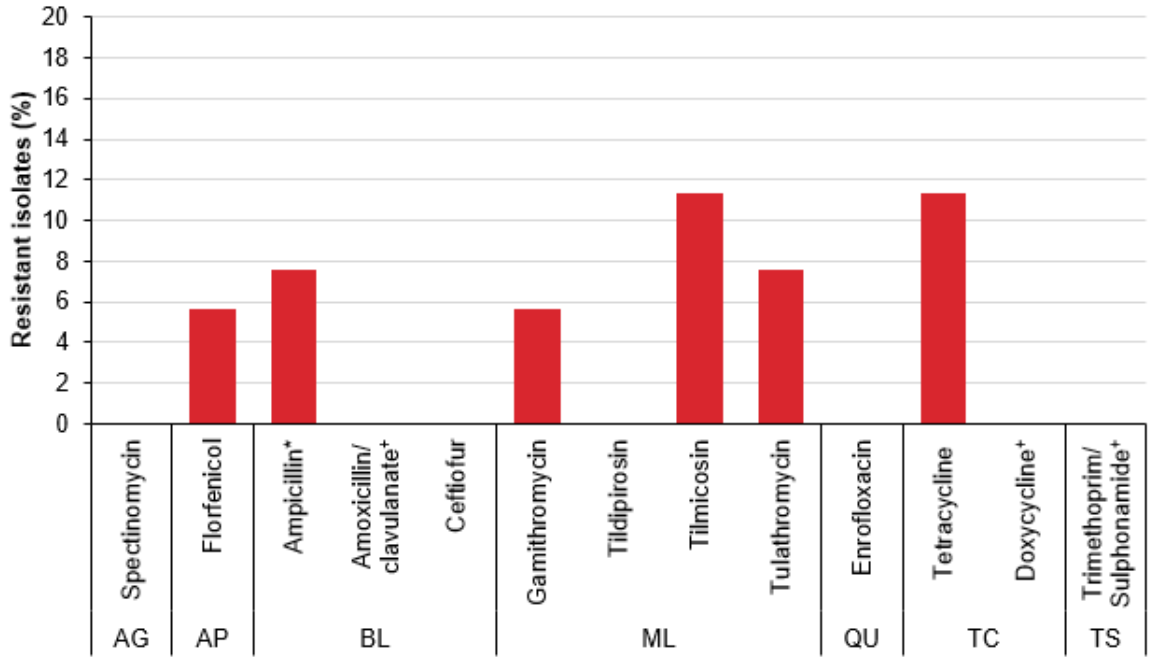
[32] A proposed scheme for the monitoring of antibiotic resistance in veterinary pathogens of food animals in the UK - Teale - 2021 - Veterinary Record - Wiley Online Library
[33] A proposed scheme for the monitoring of antibiotic resistance in veterinary pathogens of food animals in the UK - Teale - 2021 - Veterinary Record - Wiley Online Library

carry the bacteria in the upper respiratory tract. Ovine *Mannheimia* strains can also cause mastitis; *M. haemolytica* has been more rarely recorded as causing mastitis in cattle.

In *M. haemolytica* from cattle (n=53) (**Figure 4.1**), 21% of isolates were resistant to at least one of the antibiotics tested, and 3.8% of isolates were considered MDR. Aminoglycoside (spectinomycin) resistance was not detected. Amphenicol (florfenicol) resistance was observed in 5.7% of bovine *M. haemolytica.* Of the beta-lactams, resistance to ampicillin was observed in 7.6% of isolates; resistance to amoxicillin/clavulanate and the HP-CIA ceftiofur was not detected. Fluoroquinolone resistance was also not observed. Of the macrolides, resistance was detected to gamithromycin (5.6%), tilmicosin (11%) and tulathromycin (7.6%), whilst trimethoprim/sulphonamide resistance was not observed.

Resistance to tetracycline (which in this case also represents oxytetracycline and chlortetracycline) was detected in 11% of bovine *M. haemolytica*, although all isolates were susceptible to doxycycline, indicating that the latter antibiotic may remain effective in cases of *in vitro* resistance to tetracycline treatments. This is because some mechanisms of resistance confer resistance only to tetracycline and not to doxycycline[34].

Figure 4.1: Antibiotic resistant isolates of *Mannheimia haemolytica* isolates from respiratory infections of cattle in 2020 (interpreted using cattle CLSI veterinary breakpoints unless indicated otherwise).

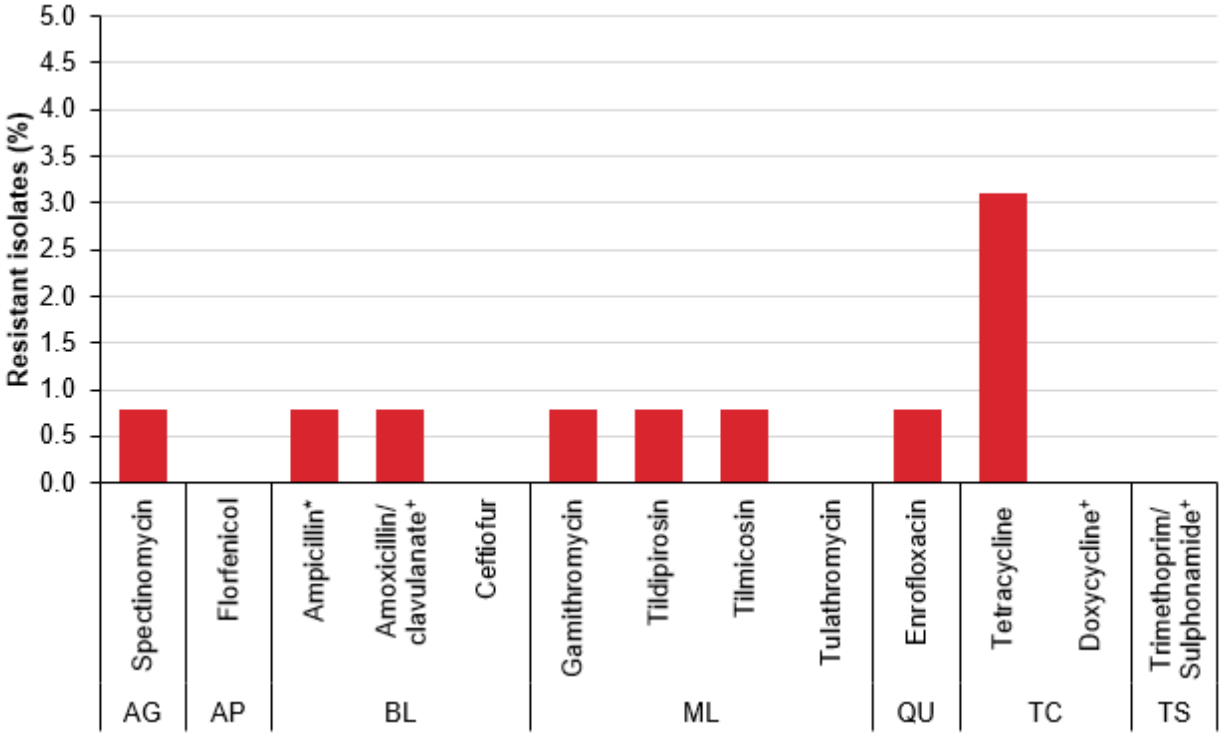


* Interpreted using EUCAST human CBP for *P. multocida*
+ Interpreted using CA-SFM veterinary CBP
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

[34] Interpretative reading: recognizing the unusual and inferring resistance mechanisms from resistance phenotypes | Journal of Antimicrobial Chemotherapy | Oxford Academic (oup.com)

The percentage of *M. haemolytica* isolates from sheep susceptible to the panel of antibiotics tested was higher than those recovered from cattle, which could reflect lower antibiotic usage in this species. Of *M. haemolytica* from sheep (n=129) (**Figure 4.2**), 3% of isolates were resistant to at least one of the antibiotics tested, though a single isolate (0.8%) was multi-drug resistant to ampicillin, amoxicillin/clavulanate, tetracycline, spectinomycin, enrofloxacin, gamithromycin, tildipirosin and tilmicosin. Tetracycline resistance was detected in 3.1% of *M. haemolytica* from sheep, though doxycycline resistance was not detected.

Figure 4.2: Antibiotic resistant isolates of *Mannheimia haemolytica* isolates from respiratory infections of sheep in 2020 (interpreted using cattle CLSI veterinary breakpoints unless indicated otherwise)



* Interpreted using EUCAST human CBP for *P. multocida*
+ Interpreted using CA-SFM veterinary CBP
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

The occurrence of amoxicillin/clavulanate resistance in a single isolate of *M. haemolytica* from sheep is an interesting finding, not only because the other pathogens studied were not resistant to this compound but also because the common mechanism of resistance in *M. haemolytica* is the beta-lactamase ROB-1, which is inhibited by clavulanate[35]. Further investigation is warranted.

4.3.1.1.2 *Pasteurella multocida*

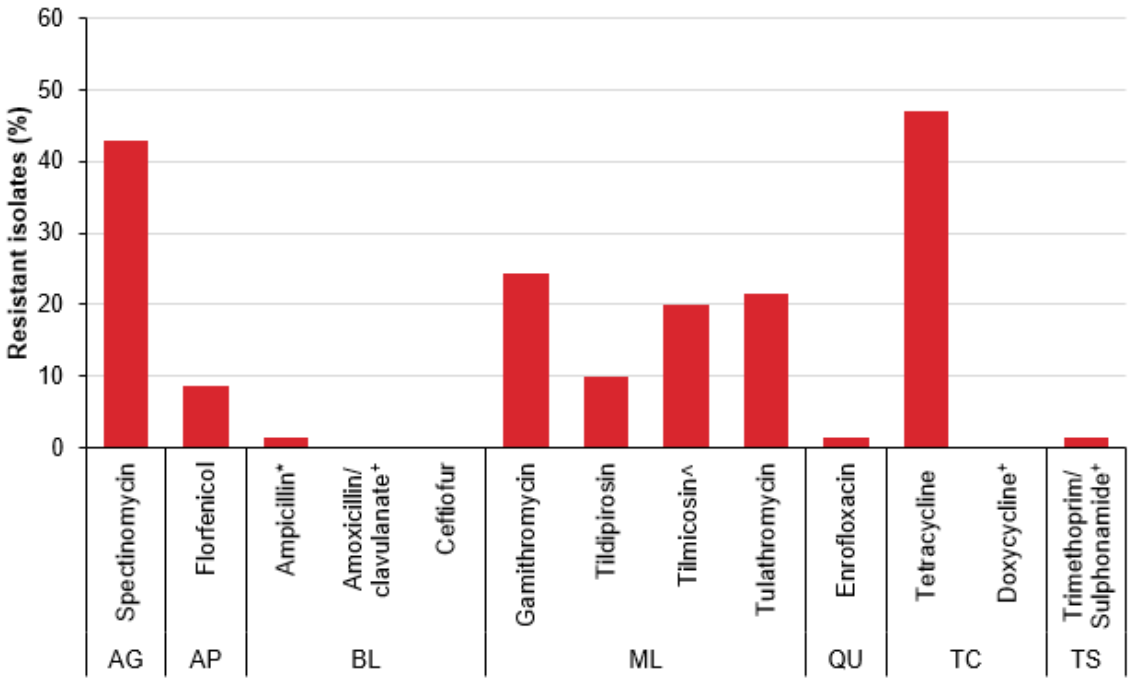
[35] Antimicrobial Resistance in Haemophilus influenzae | Clinical Microbiology Reviews (asm.org)

P. multocida causes primarily respiratory disease in cattle and (more rarely) sheep in the UK. It can also affect poultry (fowl cholera) and toxigenic strains are responsible for the development of atrophic rhinitis in pigs.

In *P. multocida* from cattle (n=70) (**Figure 4.3**), 50% were resistant to at least of the antibiotics tested and 21% were MDR. Resistance to the aminoglycoside spectinomycin was high at 43%. Amphenicol resistance was observed in 8.6% of *P. multocida*. Of the beta-lactams, ampicillin resistance was seen in 1.4% of isolates from cattle and resistance to ceftiofur was not detected. Fluoroquinolone resistance was detected in 1.4% of bovine *P. multocida.* Of the macrolides (which have not previously been tested for this pathogen), resistance was detected to gamithromycin (24%), tildipirosin (10%), tilmicosin (20%) and tulathromycin (21%). Tetracycline resistance was common, occurring in 47% of isolates, however, doxycycline resistance was not detected. Trimethoprim/sulphonamide resistance was observed in 1.4% of bovine *P. multocida.*

P. multocida from sheep (n=11) were fully susceptible to the panel of antibiotics tested.

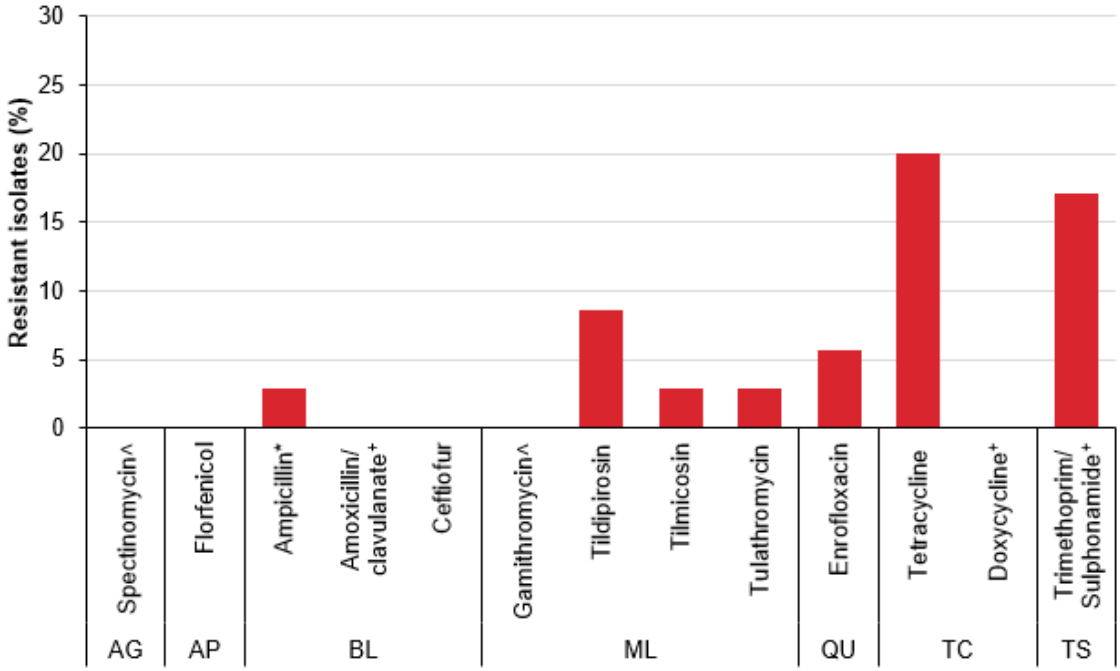
Figure 4.3: Antibiotic resistant isolates of *Pasteurella multocida* isolates from respiratory infections of cattle in 2020 (interpreted using cattle CLSI veterinary breakpoints unless indicated otherwise).



* Interpreted using EUCAST human CBP for *P. multocida*
+ Interpreted using CA-SFM veterinary CBP
^ Tilmicosin breakpoint for porcine isolates applied
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

In pigs, 34% of *P. multocida* (n=35) were resistant to at least one of the antibiotics tested and 2.9% were MDR. Resistance to aminoglycosides and amphenicols was not detected (**Figure 4.4**). Of the beta-lactams, 2.9% of isolates were resistant to ampicillin and ceftiofur resistance was not detected. Enrofloxacin resistance was detected in 5.7% of porcine *P. multocida*. Of the macrolides tested, tildipirosin resistance was observed in 8.6% of *P. multocida* from pigs and tilmicosin resistance was observed in 2.9%. The same figure was observed for tulathromycin, whilst resistance to gamithromycin was not detected. Tetracycline resistance (20%) exceeded doxycycline resistance (0%). Resistance to trimethoprim/sulphonamides (17%) exceeded the values observed in *P. multocida* from ruminants.

Figure 4.4: Antibiotic resistant isolates of *Pasteurella multocida* isolates from respiratory infections of pigs in 2020 (interpreted using CLSI veterinary breakpoints unless indicated otherwise).



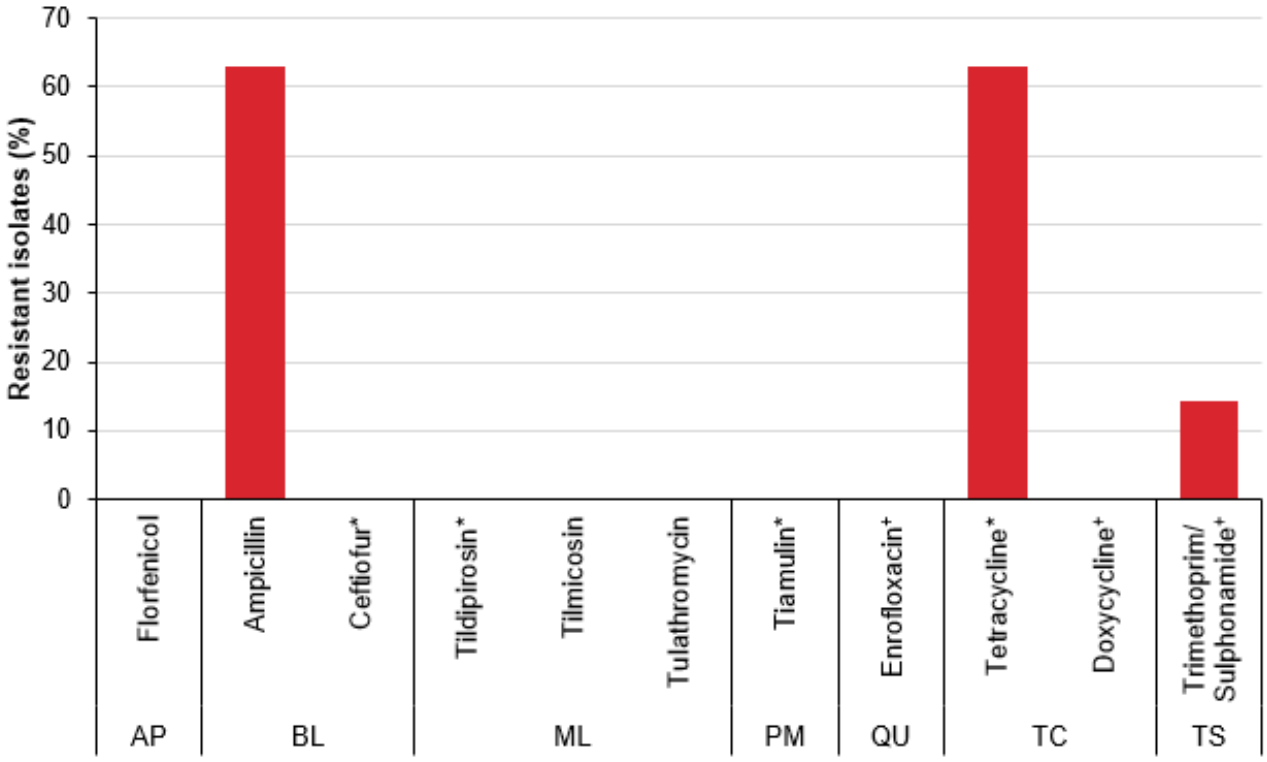
* Interpreted using EUCAST human CBP for *P. multocida*
+ Interpreted using CA-SFM veterinary CBP
^ Spectinomycin and gamithromycin breakpoint for bovine isolates applied.
AG: aminoglycosides, AP: amphenicols, BL: beta-lactams, ML: macrolides, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

4.3.1.1.3 *Actinobacillus pleuropneumoniae*

A. pleuropneumoniae is a cause of pneumonia in pigs. In 35 isolates from pigs, resistance to at least one of the antibiotics tested was seen in 74% of isolates and MDR in 11%. Of the beta-lactams, ampicillin resistance was observed in 63% of isolates (**Figure 4.5**). Resistance was not detected to ceftiofur, macrolides, or the pleuromutilin compound tiamulin. Tetracycline resistance was observed in 63% of isolates, although these isolates

were susceptible to doxycycline. Trimethoprim/sulphonamide resistance was seen in 14% of isolates.

Figure 4.5: Antibiotic resistant isolates of *Actinobacillus pleuropneumoniae* isolates (n=35) from respiratory infections of pigs in 2020 (interpreted using CLSI veterinary breakpoints unless indicated otherwise)



* Interpreted using EUCAST human CBP for *P. multocida*
+ Interpreted using CA-SFM veterinary CBP
AP: amphenicols, BL: beta-lactams, ML: macrolides, PM: pleuromutilin, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

4.3.1.1.4 *Bibersteinia trehalosi*

B. trehalosi causes septicaemia in growing lambs. Isolates from sheep (n=55) were fully susceptible to the panel of antibiotics tested.

4.3.1.1.5 Discussion

These results show the value of this new improved testing protocol for veterinary pathogens. Where appropriate, the panels of antibiotics were designed to include multiple, clinically relevant antibiotics within the same class. This protocol therefore has an important role in improving selection and refinement of possible treatment options. Many isolates remain susceptible to the panel of antibiotics tested and resistance was uncommon or not detected to those antibiotics which are often used as second- or third-

line treatment options. Differences between the occurrence of tetracycline and doxycycline resistance warrant further investigation; there are some mechanisms of resistance that affect tetracycline but not doxycycline and thus doxycycline may remain a therapeutic option when tetracycline (or oxytetracycline or chlortetracycline) resistance is present.

These results demonstrate the benefits of gold-standard MIC testing, which enables resistance to classes of antibiotics of veterinary clinical importance to be measured more accurately. These results show that resistance to tetracyclines in *M. haemolytica,* and in *P. multocida*, has previously been over-estimated (see Section 4.3, 4.4 and 4.5 in the supplementary material), meaning that oxytetracycline and chlortetracycline are likely to remain viable treatment options in many cases. This discrepancy is due to use of legacy breakpoints for disc diffusion (see S4.1.2 in the supplementary material). Conversely, another legacy breakpoint (for enrofloxacin resistance in *P. multocida* in pigs) used in disc diffusion could have resulted in a slight under-estimation of resistance. MIC also enables us to distinguish between high-level and low-level resistance.

Resistance of selected respiratory pathogens to macrolides, which was not tested using the previous disc diffusion method, was reported. Isolates with the resistance gene *erm*(42) have been reported to show greatly elevated MICs (that is to say, are much more resistant) for the macrolides tildipirosin and tilmicosin, while smaller MIC increases are reported for the smaller molecules tulathromycin and gamithromycin. However, the resistance genes *msr(E)* and *mph(E)* (which are frequently linked genetically) are associated with large increases in MICs for tilmicosin, tulathromycin, and gamithromycin but not for tildipirosin. All three of these genes have been shown to occur on the same mobile genetic element[36][37]. All *P. multocida* isolates from cattle resistant to tildipirosin (n=7) were also resistant to tulathromycin, tilmicosin and gamithromycin; tulathromycin resistance (n=15) usually occurred in conjunction with tilmicosin resistance (n=13) and always with gamithromycin resistance (n=15). The macrolide resistance phenotype therefore in many cases appears to correlate well with the described mechanisms of resistance; determination of genotype by whole genome sequencing would be useful to confirm predicted genotype and to investigate the phenotypic patterns of resistance.

4.3.1.2 Other respiratory pathogens

The remaining respiratory pathogens were tested under the previous disc diffusion protocol (see S4.1 in the supplementary material).

Glaesserella (Haemophilus) parasuis – is included in this section because it is a member of the *Pasteurellaceae*. Harmonised susceptibility testing methods and breakpoints for this organism are still being established. Considering the *G. parasuis*

[36] Multiplex PCR To Identify Macrolide Resistance Determinants in Mannheimia haemolytica and Pasteurella multocida (asm.org)
[37] Increased MICs of gamithromycin and tildipirosin in the presence of the genes erm(42) and msr(E)-mph(E) for bovine Pasteurella multocida and Mannheimia haemolytica | Journal of Antimicrobial Chemotherapy | Oxford Academic (oup.com)

isolates recovered in 2020, resistance was detected to tetracyclines (5.9%) and trimethoprim/sulphonamides (65%).

Histophilus somni - *H. somni* (formerly known as *Haemophilus somnus*) is a cause of pneumonia and thromboembolic meningoencephalitis in calves. All isolates tested between 2018 and 2020 were susceptible to the panel of antibiotics, with the exception of a single isolate in 2019 which was resistant to ampicillin.

Trueperella (Arcanobacterium) pyogenes – Data on this less frequently isolated ovine respiratory pathogen can be found in Table S4.5.1 of the supplementary material. Resistance to tetracyclines and trimethoprim/sulphonamides was detected in isolates over the period 2018 to 2020 from respiratory and other infections of cattle (excluding mastitis cases) and pigs; low numbers of isolates recovered from pigs were resistant to lincosamides whilst sheep isolates were mostly susceptible to the antibiotics tested.

Further details on percentage of resistance for respiratory infections of cattle and pigs are included in Tables S4.3.1 and S4.4.1 of the supplementary material.

4.3.2 Bovine mastitis pathogens

Bovine mastitis is complex and the patterns of resistance observed vary with time and between farms. The data presented are aggregated at a national level and therefore have limited ability to inform treatment protocols. However, they do highlight that acquired resistance does occur in England and Wales and should be considered when veterinarians and farmers develop mastitis control programs for individual farms.

Note that Gram negative (*E. coli*) and Gram positive (*S. aureus* and streptococci) isolates are tested against different panels of antibiotics. Note that the number of isolates tested is highly variable, which is likely to impact the interpretation of percentage resistance. Details on the number of tests performed on bovine mastitis pathogens are in S4.2 of the supplementary material.

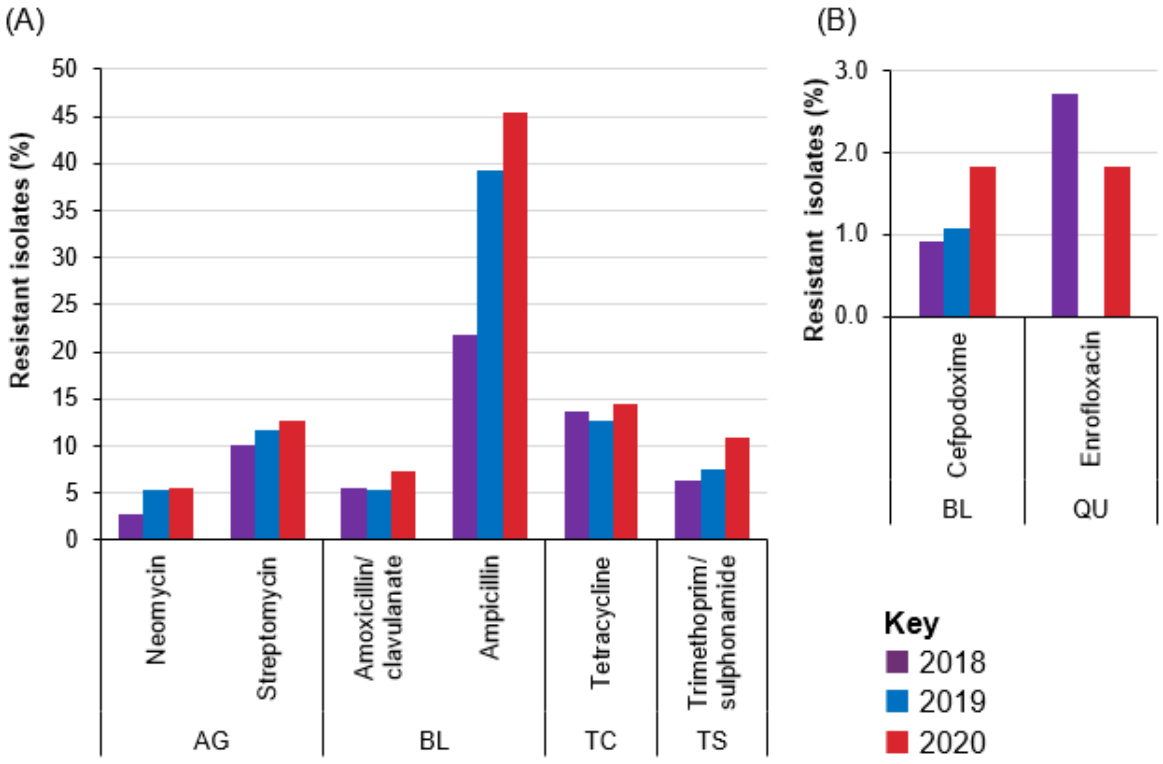
4.3.2.1 *Escherichia coli*

E. coli is a major cause of bovine mastitis and this species was the most-frequently isolated bacteria in mastitis submissions in 2020. Most *E. coli* strains originate from the cow's immediate environment and it is thought that no special virulence factors are required to infect the mammary gland. These *E. coli* isolates therefore represent those strains that are present in the environment of adult dairy cattle, particularly cattle sheds and cubicle houses, and are probably mainly of faecal origin.

The percentage of *E. coli* isolates from mastitis infections resistant to different antibiotics are presented in **Figure 4.6**. The number of isolates tested has decreased in 2020 and are presented in Table S4.2.1 of the supplementary material.

Resistance to HP-CIAs remains low. Resistance to aminoglycosides has remained at low to moderate levels over the reporting period. Ampicillin resistance has increased from 22% in 2018 to 39% in 2019 and 45% in 2020. Ampicillin is rarely used in intramammary preparations for cattle; however, resistance to this antibiotic could be driven by systemic beta-lactam use. Resistance to amoxicillin/clavulanate has remained between 5.5% to 7.3% over this period. Resistance levels to tetracyclines have remained stable over the monitoring period, reported at 15% in 2020, and resistance to trimethoprim/sulphonamide compounds have remained at low to moderate levels over the reporting period.

Figure 4.6: Resistance to non-HP-CIAs (A) and HP-CIAs (B) of *Escherichia coli* isolated from mastitis samples from cattle in England and Wales. Note scale differs between graphs.



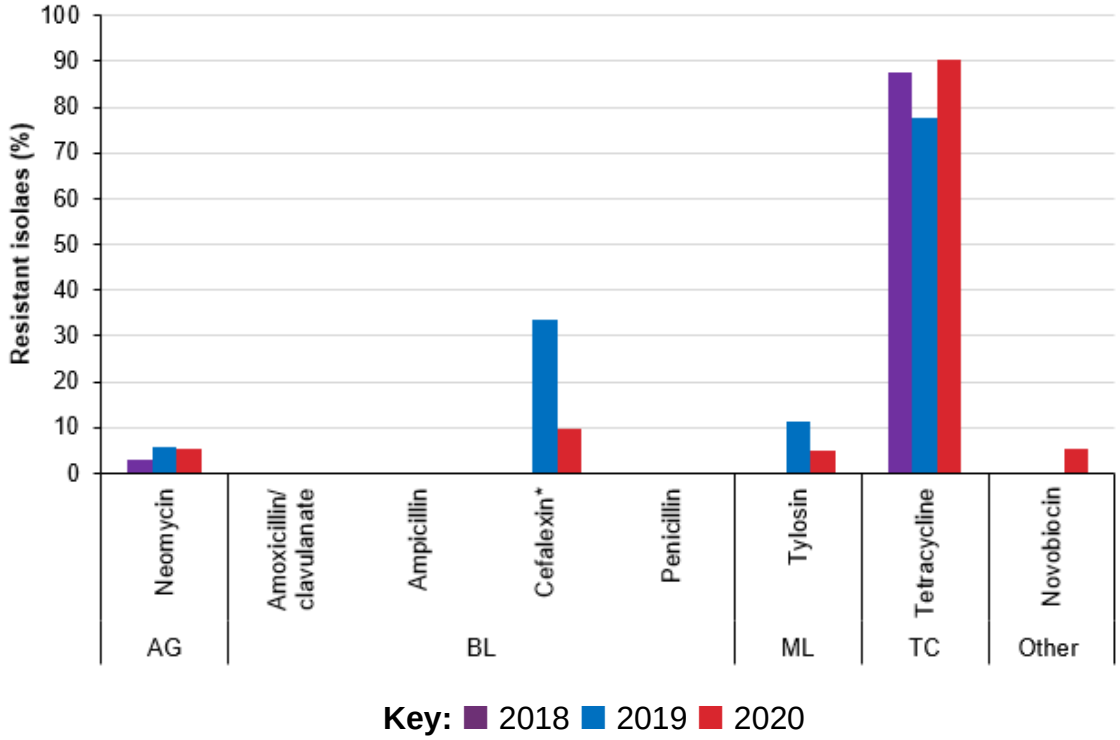
AG: aminoglycosides, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

4.3.2.2 *Streptococcus dysgalactiae*

S. dysgalactiae is a commensal of the mucous membranes of cattle that causes mastitis and occasionally other diseases. It is not considered a zoonosis. **Figure 4.7** presents the percentage of *S. dysgalactiae* isolates from mastitis infections resistant to different antibiotics. The number of isolates tested have varied over the reporting period; these are presented in Table S4.2.3a of the supplementary material.

Streptococci show a degree of intrinsic resistance to aminoglycosides, and therefore, some resistance is to be expected in *S. dysgalactiae.* No resistance to the beta-lactams ampicillin or penicillin was detected over the period 2018 to 2020, and resistance to cefalexin declined between 2019 and 2020 from 33% to 9.5%. In 2019, 11% of isolates were resistant to the macrolide tylosin, whilst 4.8% were resistant in 2020. Resistance to this compound was not detected in 2018. Tetracycline resistance was reported between 78% and 90% of isolates between 2018 and 2020 – this resistance is recognised as being common in *S. dysgalactiae*.

Figure 4.7: Antibiotic resistance of *Streptococcus dysgalactiae* isolated from mastitis samples from cattle in England and Wales.



* No data available for 2018
AG: aminoglycosides, BL: beta-lactams, ML: macrolides TC: tetracyclines

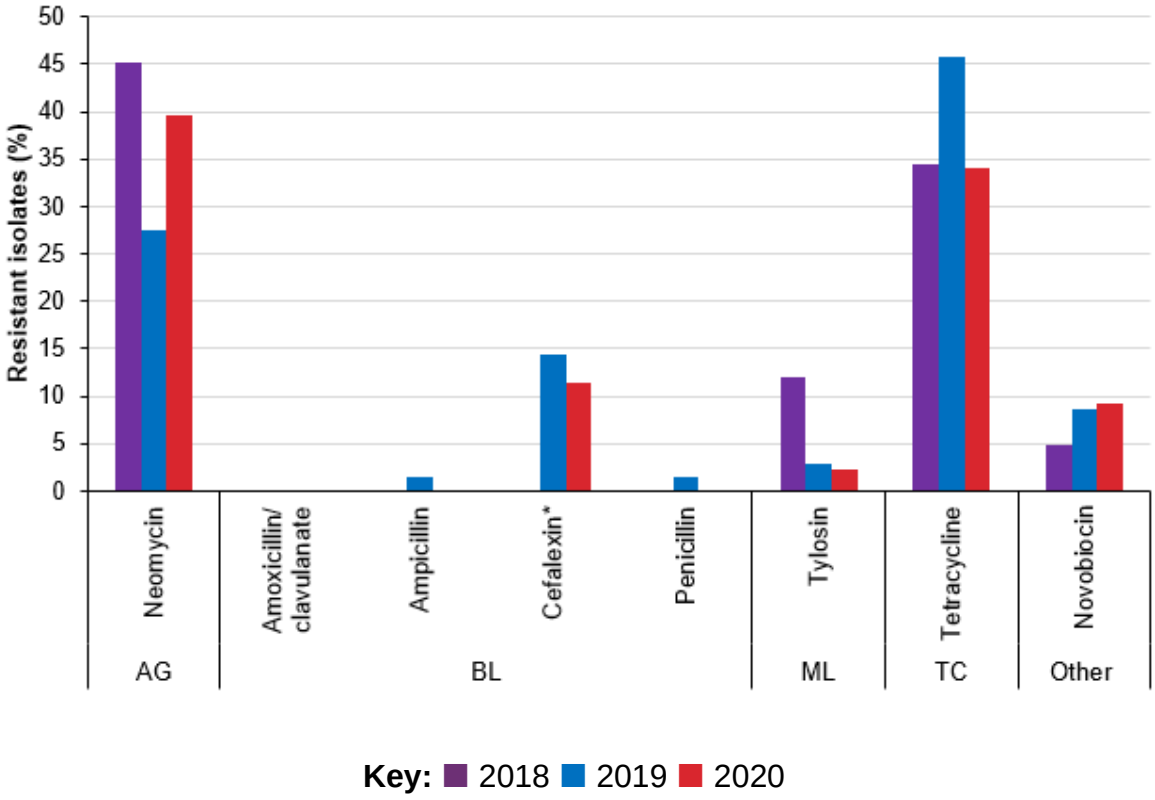
4.3.2.3 *Streptococcus uberis*

S. uberis is widely distributed in the environment and also a normal commensal resident of the bovine vagina, tonsil and skin. It is a common cause of mastitis and not regarded as zoonotic. The percentage of *S. uberis* isolates from mastitis infections resistant to different antibiotics are presented in **Figure 4.8**. The number of isolates tested have declined over the reporting period and are presented in Table S4.2.3b of the supplementary material.

Resistance to the aminoglycoside neomycin is to be expected in *S. uberis* because streptococci show a degree of intrinsic resistance to aminoglycosides. Of the beta-lactams, no resistance to ampicillin or penicillin was detected in *S. uberis* in 2020, although *S. uberis* isolates from bovine mastitis with reduced susceptibility to penicillin have been

reported in France[38]. Between 2018 and 2020, between 2.3% and 12% of *S. uberis* isolates were resistant to the macrolide tylosin. Resistance can be mediated by the induction of a plasmid-encoded enzyme which methylates the 20S ribosomal RNA sub-unit and prevents binding of the macrolide to the ribosome and so disrupts protein synthesis. Resistance to tetracyclines was detected in 34% to 46% of isolates between 2018 and 2020.

Figure 4.8: Antibiotic resistance of *Streptococcus uberis* isolated from mastitis samples from cattle in England and Wales.



* No data available for 2018
AG: aminoglycosides, BL: beta-lactams, ML: macrolides TC: tetracyclines

4.3.2.4 *Staphylococcus aureus*

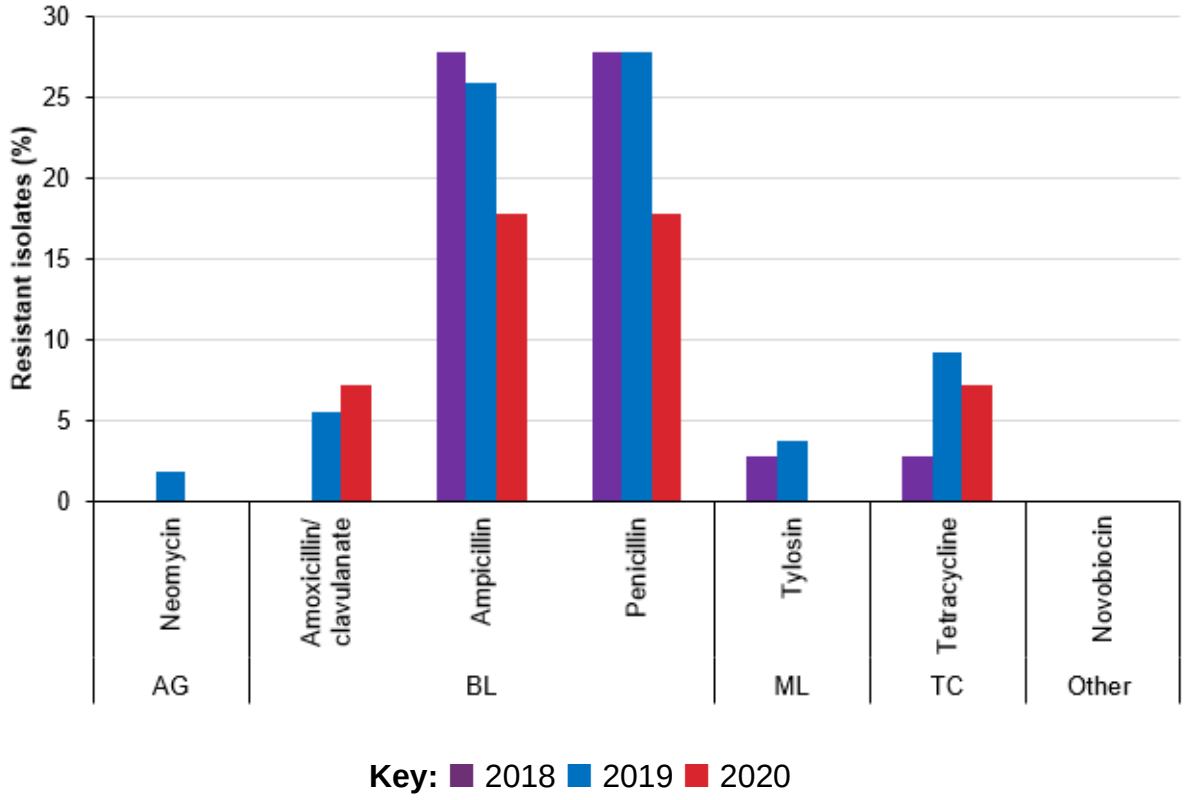
S. aureus is normally resident on the skin and mucous membranes of cattle and is a common cause of mastitis. Bovine *S. aureus* is not generally regarded as zoonotic and although both *mecA* MRSA and *mecC* MRSA have been detected in cattle[39,40], the possible role of cattle as a source of human infection has not been well-defined. The

[38] Penicillin-Binding Protein Gene Alterations in Streptococcus uberis Isolates Presenting Decreased Susceptibility to Penicillin | Antimicrobial Agents and Chemotherapy (asm.org)
[39] Methicillin-resistant Staphylococcus aureus (MRSA) ST398 associated with clinical and subclinical mastitis in Belgian cows - ScienceDirect
[40] Meticillin-resistant Staphylococcus aureus with a novel mecA homologue in human and bovine populations in the UK and Denmark: a descriptive study - PubMed (nih.gov)

percentage of *S. aureus* isolates from mastitis infections resistant to different antibiotics are presented in **Figure 4.9** The number of isolates tested has varied over the reporting period; these are presented in Table S4.2.3c of the supplementary material.

Aminoglycoside resistance was rarely detected with only a single *S. aureus* isolate displaying neomycin resistance between 2018 and 2020. Of the beta-lactams, resistance to ampicillin and penicillin has reduced to moderate levels in 2020 (18% for both antibiotics). Penicillin resistance in bovine *S. aureus* from England and Wales occurs most frequently via the production of beta-lactamases. The genes encoding beta-lactamases can be located on plasmids and often on transposons and may be readily transferable by conjugation. Amoxicillin/clavulanate resistance was reported between 0% and 7.1% between 2018 and 2020. No MRSA isolates were detected from bovine mastitis over the period 2018 to 2020 at APHA. Tylosin (macrolide) resistance was recorded in a low percentage (between 0% and 3.7%) of isolates. No resistance was detected to novobiocin and resistance levels to tetracycline have remained under 10% over the monitoring period.

Figure 4.9: Antibiotic resistance of *Staphylococcus aureus* isolated from mastitis samples from cattle in England and Wales.



AG: aminoglycosides, BL: beta-lactams, ML: macrolides TC: tetracyclines

4.3.2.5 Other mastitis pathogens

Klebsiella pneumoniae - isolates were generally resistant to ampicillin. This reflects the intrinsic resistance to ampicillin shown by this organism; most isolates were susceptible to the other antibiotics reported.

Pseudomonas aeruginosa - commonly resistant to a range of antibiotics and isolates from bovine mastitis proved no exception in this regard. A low number of isolates was available for testing. Efflux pumps and impermeability are frequently responsible for resistance to beta-lactams in *P. aeruginosa* and probably accounted for the observed beta-lactam resistance.

Streptococcus agalactiae - two isolates were recovered in 2020 which were susceptible to the panel of antibiotics tested.

Trueperella (Arcanobacterium) pyogenes - no isolates of *T. pyogenes* were recovered from bovine mastitis in 2020.

See Table S4.2.4 of the supplementary material for further details.

4.3.2.6 Private Laboratory Initiative

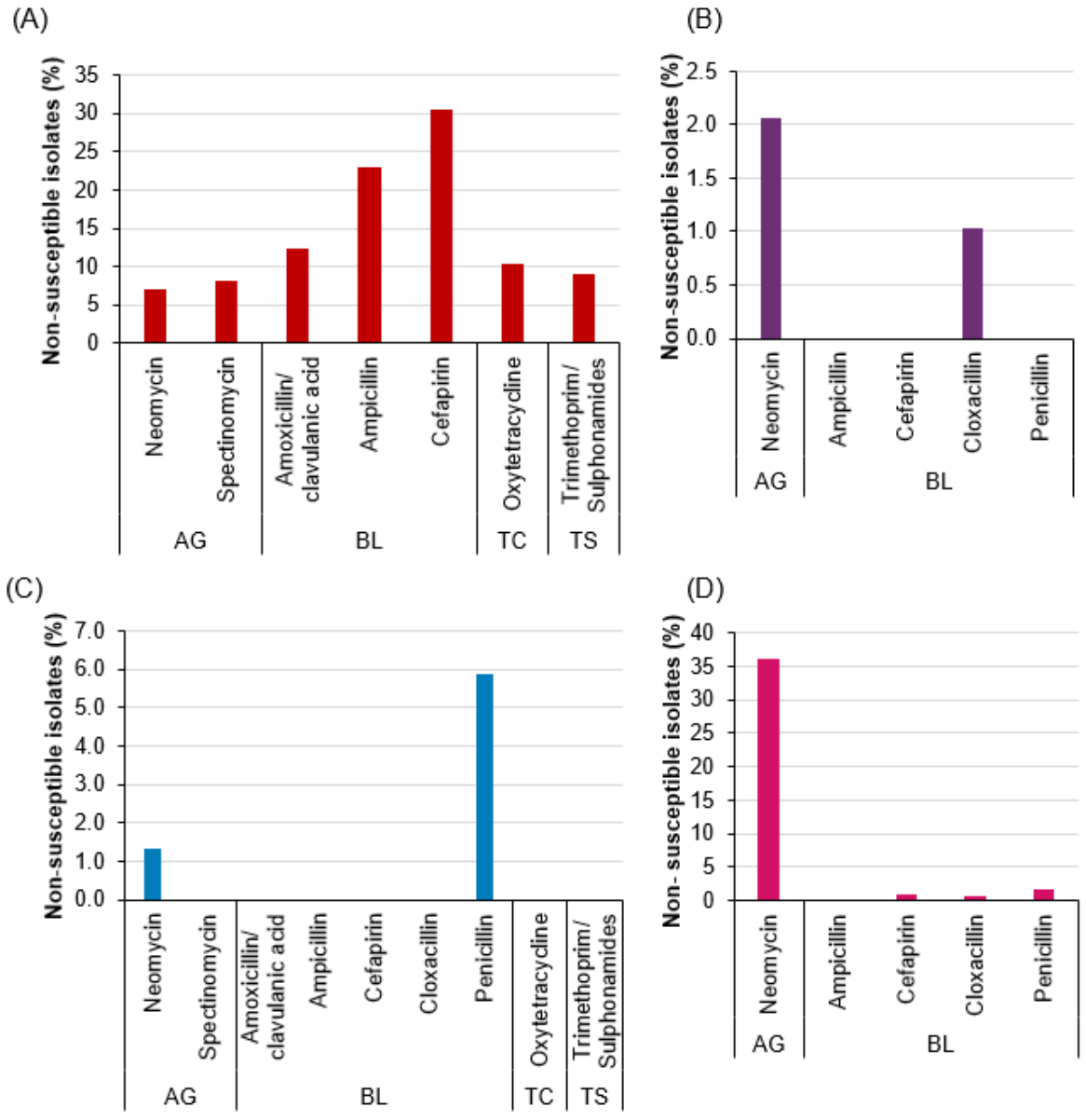
The Private Laboratory Initiative (PLI) is a collaborative project between the Veterinary Medicines Directorate (VMD) and the Animal and Plant Health Agency (APHA). Many veterinarians send mastitis samples to private veterinary laboratories (PVLs) for diagnosis, the results of which do not ordinarily feed into AMR surveillance efforts. The purpose of the project is to collect and analyse data from PVLs to complement the scanning surveillance undertaken by APHA and AMR surveillance undertaken by VMD. This initiative directly supports the UK's ambition to contain and control AMR, by increasing the sensitivity of surveillance and timeliness of detection of potential threats, as well as providing a stronger evidence base for AMR in UK livestock. This project is still in its proof-of-concept stage.

We are grateful to the Vale Veterinary Laboratory for providing data for this project. Presented in **Figure 4.10** are the results from antibiotic susceptibility testing of key mastitis pathogens isolated from cattle by the Vale Laboratory in 2020. This data should be interpreted with caution, as there are differences in the laboratory methods, antibiotic panels and interpretation criteria used by government and private laboratories. A summary of the methodology and breakpoints applied can be found in S4.1.3 of the supplementary material.

Moderate to high levels of resistance were seen in *E. coli* isolates from bovine mastitis cases in 2020 to beta-lactams, with resistance detected to amoxicillin/clavulanic acid (12%), ampicillin (23%) and cefapirin (31%). Lower levels of resistance were seen in *E. coli* to other antibiotic classes, such as trimethoprim/sulphonamides, aminoglycosides and tetracyclines.

In *S. uberis*, 36% of isolates were resistant to neomycin, however, as noted in Section 4.3.2.3, this finding is to be expected as *streptococci* show a degree of intrinsic resistance to aminoglycosides. Low resistance was also detected to cefapirin (0.9%). AMR in *S. aureus* was either not detected or low, with resistance detected only to penicillin (5.9%) and neomycin (1.3%). *S. dysgalactiae* showed low levels of resistance to neomycin (2.0%) and cloxacillin (1.0%).

Figure 4.10: Non-susceptibility of (A) *E. coli* (n=559); (B) *S. dysgalactiae* (n=97), (C) *S. aureus* (n=153) and (D) *S. uberis* (n=555) isolated from bovine mastitis samples submitted to Vale Veterinary Laboratories in 2020.



AG: aminoglycosides, BL: beta-lactams, TC: tetracyclines, TS: trimethoprim/sulphonamides

These results very broadly align with data presented in Section 4.3.1.1, with the exception of the lower levels of resistance to ampicillin in *E. coli* and lower levels of resistance to both ampicillin and penicillin in *S. aureus* isolated by Vale compared to APHA. These discrepancies could be attributed to population and sampling differences, or variation in laboratory techniques and breakpoints used.

Whilst still in early stages of this project, these early results demonstrate the potential for broadening AMR surveillance by collaborating with the private sector. Bringing together and reporting data from additional sources will both improve representativeness of surveillance through an increased number of samples for testing and provide greater information on AMR at a regional level. This will provide direct benefits to both farmers and vets by creating a more detailed picture of AMR in key veterinary pathogens, and better help inform disease management and treatment.

4.3.3 Other animal pathogens

Brachyspira hyodysenteriae – *B. hyodysenteriae* is the causative organism of swine dysentery, an enteric disease of pigs, resulting in serious ill-thrift in its chronic form. A limited range of antibiotics is available for the treatment of swine dysentery. Reliance on ongoing medication without addressing other aspects of disease control, such as hygiene and herd husbandry (for example all-in, all-out management, medical elimination and/or periodic depopulation) risks resistance arising through mutations.

Tiamulin is an important antibiotic used in the treatment of swine dysentery and because of the importance of this disease all available isolates of *B. hyodysenteriae* are tested for tiamulin susceptibility each year. Two *B. hyodysenteriae* isolates of 15 tested in 2020 had a tiamulin MIC $\underline{\geq}$ 0.5 mg/l, which is above the ECOFF cut-off, indicating divergence from the wild type. One of these was within the threshold of clinical susceptibility; the other was resistant.

Staphylococcus aureus **in birds** - *S. aureus* causes a number of infections in poultry and game birds, including septicaemia, yolk sac infection, arthritis and osteomyelitis. Low numbers of isolates were available and resistance to ampicillin/penicillin, tetracyclines, lincosamides, macrolides or trimethoprim/sulphonamides was detected in isolates of *S. aureus* from chickens, turkeys or other avian species in one or more years.

Staphylococcus aureus **in sheep -** *S. aureus* causes mastitis and tick pyaemia as well as other infections in sheep. *S. aureus* isolates from sheep were susceptible to penicillin and the other antibiotics tested between 2019 and 2020, but between 15% and 20% of isolates were resistant to tetracyclines, assumed to reflect usage of this compound in this species.

Streptococcus dysgalactiae **in sheep**- *S. dysgalactiae* is the major cause of infectious arthritis in young lambs and is thought to be carried on the mucous membranes of a small proportion of sheep. Levels of resistance to tetracyclines in ovine isolates of *S.*

dysgalactiae were high (between 74% and 90%) and similar to those recorded for bovine mastitis isolates. No resistance to ampicillin or penicillin was detected in ovine *S. dysgalactiae* isolates, though low numbers of isolates were reportedly resistant to cephalexin or tylosin between 2018 and 2020.

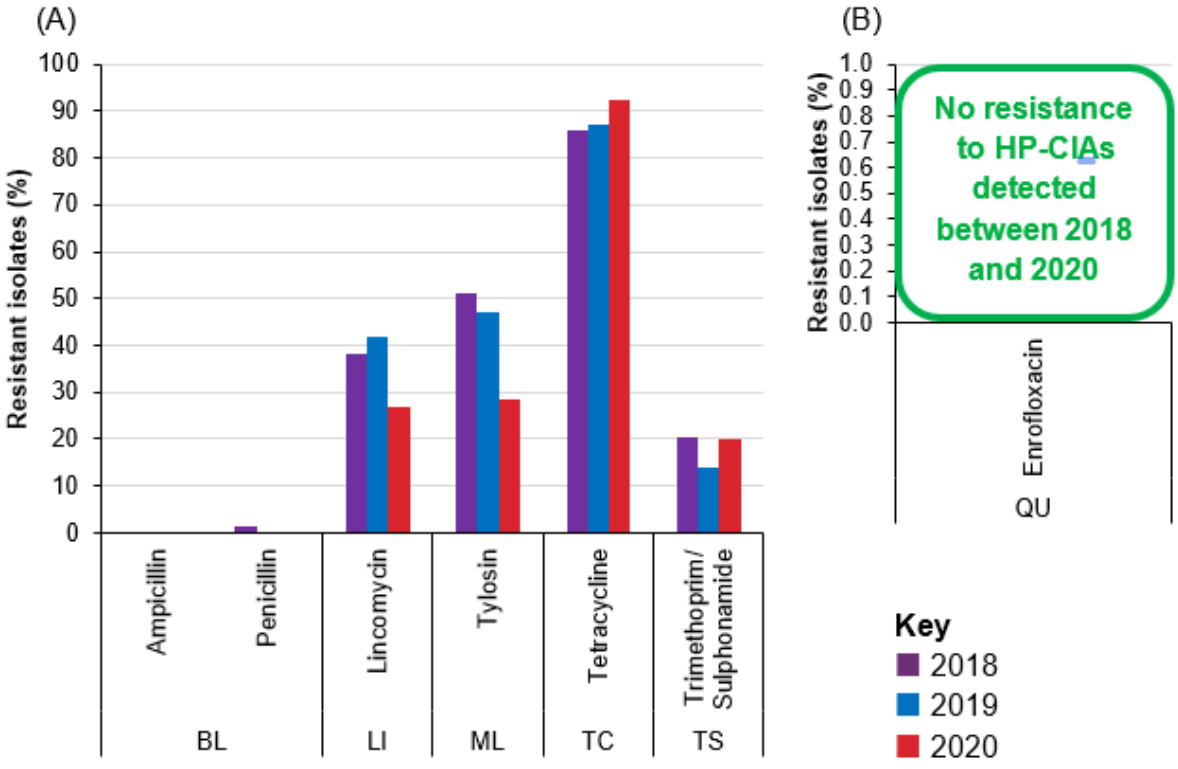
Staphylococcus xylosus – *S. xylosus* is a coagulase-negative *Staphylococcus* which has been reported to cause dermatitis in sheep and mastitis in cattle. In 2020, resistance to ampicillin/penicillin and tetracyclines was detected in bovine *S. xylosus* isolates; there were no isolates recovered from sheep or chickens, but tetracycline resistance was also detected in isolates from pigs.

4.3.4 Zoonotic pathogens

4.3.4.1 *Streptococcus suis*

S. suis is a pathogen of pigs that can cause pneumonia, meningitis and arthritis; it can also infect people. Between 84 and 115 isolates were tested each year over the reporting period between 2018 and 2020. *S. suis* isolates had resistance detected to tetracyclines, trimethoprim/sulphonamide, tylosin and lincomycin. Penicillin resistance was not detected in 2020.

Figure 4.11: Resistance to non-HP-CIAs (A) and HP-CIAs (B) of *Streptococcus suis* isolates from pigs. Note scale differs between graphs.



BL: beta-lactams, LI: lincosamides, ML: macrolides, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

4.3.4.2 Livestock Associated-MRSA (LA-MRSA)

LA-MRSA are different from other types of MRSA, such as hospital or community associated strains, which are more frequently found in humans. Anyone who has contact with colonised livestock can become colonised with LA-MRSA but prolonged colonisation is more likely in humans who have regular, prolonged contact. LA-MRSA usually lives in the nose or on skin and is an opportunist pathogen. Usually this is a local skin infection, but occasionally it can cause diseases such as pneumonia or bacteraemia. Further information for people who work with livestock is available.

Since the first discovery in 2005, LA-MRSA was found to be prevalent in livestock around the world. It was detected in food-producing animals in the UK for the first time in 2013, and sporadic cases are detected annually. Clonal Complex (CC) 398 is a common LA-MRSA CC group isolated from food-producing animal populations in the UK. Isolates are whole genome sequenced and shared with the UK Health Security Agency (UK-HSA) as appropriate to investigate any possible associations with infections in humans.

A summary of all findings identified by UK government veterinary laboratories is provided in S4.6.6 of the supplementary material. These reports should not be interpreted as a prediction of prevalence in the animal population, as samples have been collected through differing methods of passive surveillance in animals which are affected with clinical disease. Results may therefore not be representative of the wider, healthy population.

LA-MRSA CC398 was detected in pigs originating from four different pig farms in England and Wales in 2020. All were recovered from piglets or weaners, either from synovial or pulmonary samples, indicating systemic infection. Two isolates belonged to MRSA CC398 *spa*-type t011; one to each of spa-type t1250 and t1456.

4.3.4.3 Other zoonotic pathogens

Corynebacterium pseudotuberculosis – *C. pseudotuberculosis* the cause of caseous lymphadenitis in sheep, is a zoonosis though it rarely infects humans. Resistance was detected to penicillin and cephalexin (first generation cephalosporin) in 2020, although only low numbers of isolates were available for susceptibility testing. Irrespective of *in vitro* susceptibility, treatment of clinical cases of this infection in sheep is often difficult because of the difficulties in delivering sufficient antibiotic to the typical “onion-ring” abscesses that occur.

Erysipelothrix rhusiopathiae – *E. rhusiopathiae* is widely distributed in nature and occurs as a commensal or pathogen of a very wide range of vertebrate and invertebrate species. The main reservoir amongst the domestic species is probably pigs, though infection of both birds and rodents is said to be common. A low number of isolates of this organism were tested from pigs, sheep, turkeys and chickens and the main resistances detected were to tetracyclines and trimethoprim/sulphonamides. All isolates, irrespective of the

species from which they were isolated, were susceptible to ampicillin/penicillin, which is the usual treatment for infection with this organism.

***Listeria* spp.** – *Listeria* are widely distributed in the environment and can be isolated from soil, decaying vegetation and poorly fermented silage. Asymptomatic faecal carriage occurs in humans and in many species of animal. Only low numbers of *Listeria monocytogenes* isolates were tested. Cephalexin resistance was observed in both bovine and ovine isolates, reflecting the intrinsic resistance of *Listeria* spp. to this compound. Isolates from cattle and sheep were otherwise sensitive to the panel of compounds tested over the period 2018 to 2020.

Klebsiella pneumoniae – A limited number of isolates of *K. pneumoniae* have been recovered from avian species; the isolates were all resistant to ampicillin reflecting intrinsic resistance to ampicillin of this organism. Resistance to tetracyclines and trimethoprim/sulphonamides was also observed in avian *K. pneumoniae*.

***Yersinia* spp.** – A singe isolate of *Y. pseudotuberculosis* was reported in 2020 from sheep and was susceptible to the antibiotics tested. There were no isolates of *Yersinia enterocolitica* reported.

4.3.5 *Escherichia coli*

E. coli is an important zoonotic organism. *E. coli* is a commensal of animals and humans and has the capacity to function as a reservoir of transferable resistance determinants. *E. coli* can also cause a range of clinical problems in animals and people. The strains affecting animals are often different from those affecting humans but there is some overlap and *E. coli* can be important as a reservoir of resistance genes.

This section includes all isolates of *E. coli*, with the exception of bovine isolates recovered from milk which are included in the section on cattle mastitis organisms. The majority of isolates reported in this section were recovered from faeces or intestinal contents. The *E. coli* isolates referred to in this report will include some *E. coli* strains which are pathogenic for animals as well as commensal strains. Collated AMR data from England and Wales are presented in the main body of the report, with the numbers of isolates tested included in S4.7 of the supplementary material. Due to differences in methodology, data for Scotland and Northern Ireland are presented in S4.7 of the supplementary material only.

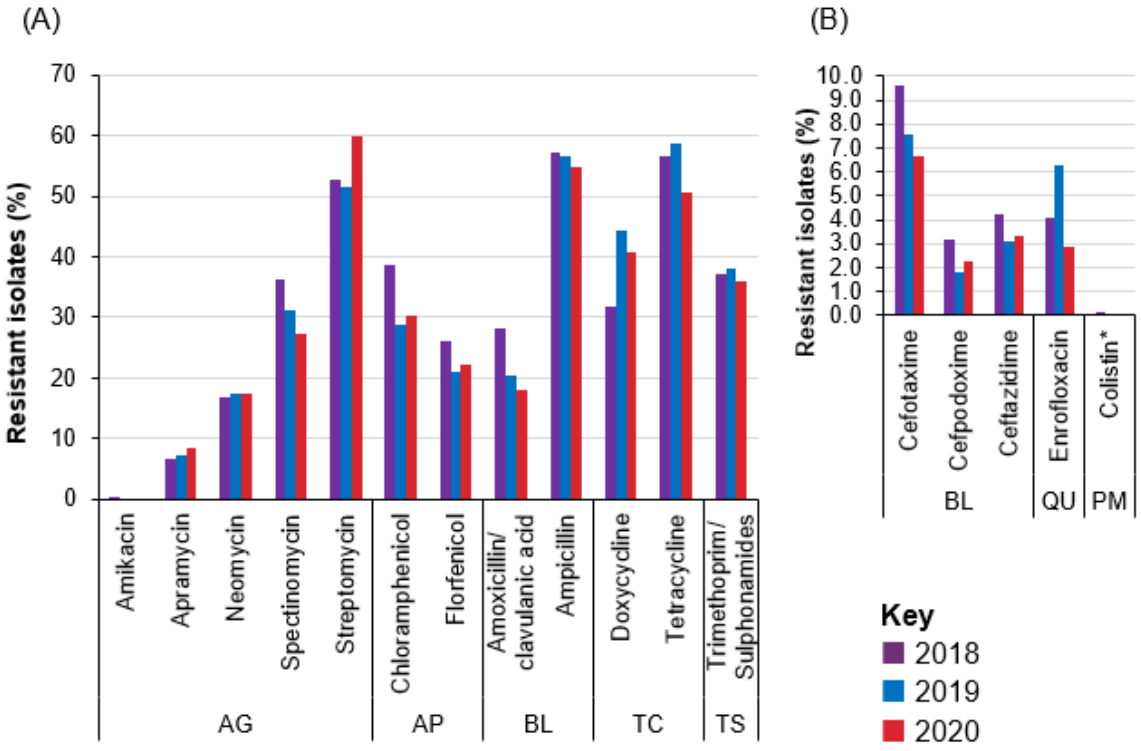
For cattle, sheep and pigs the data are analysed by the age categories of neonatal, pre- or post-weaning and adult for each species. Definitions of these age categories can be found in the supplementary material.

There is a general trend towards higher levels of resistance in isolates from younger animals in all species. This is consistent with previous surveillance data and with studies

recorded in the literature[41], and likely reflects the more frequent treatment of young animals with antibiotics. This trend is particularly evident when resistance in *E. coli* from adults is compared to resistance in *E. coli* from younger animals.

In 2020, however, resistance to ampicillin, apramycin, neomycin, tetracyclines and trimethoprim/sulphonamides was slightly higher in *E. coli* from piglets at post-weaning than in isolates from neonates, likely reflecting the frequent occurrence of disease, and antibiotic treatment, of pigs post-weaning. Similarly, in calves, the occurrence of resistance to florfenicol in neonatal calves was lower than that observed in pre-weaning calves and this may reflect greater use of florfenicol in pre-weaning calves to treat (for example) respiratory disease. In sheep, the occurrence of resistance in *E. coli* for most antibiotics was in general highest in neonates, again reflecting antibiotic usage in this age group, and declined with age, although neomycin resistance was higher in pre-weaning lambs than in neonates.

Figure 4.12: Resistance to non-HP-CIAs (A) and HP-CIAs (B) of *Escherichia coli* isolates from cattle, pigs, sheep, broilers and turkeys (all ages, combined). Note scale differs between graphs.



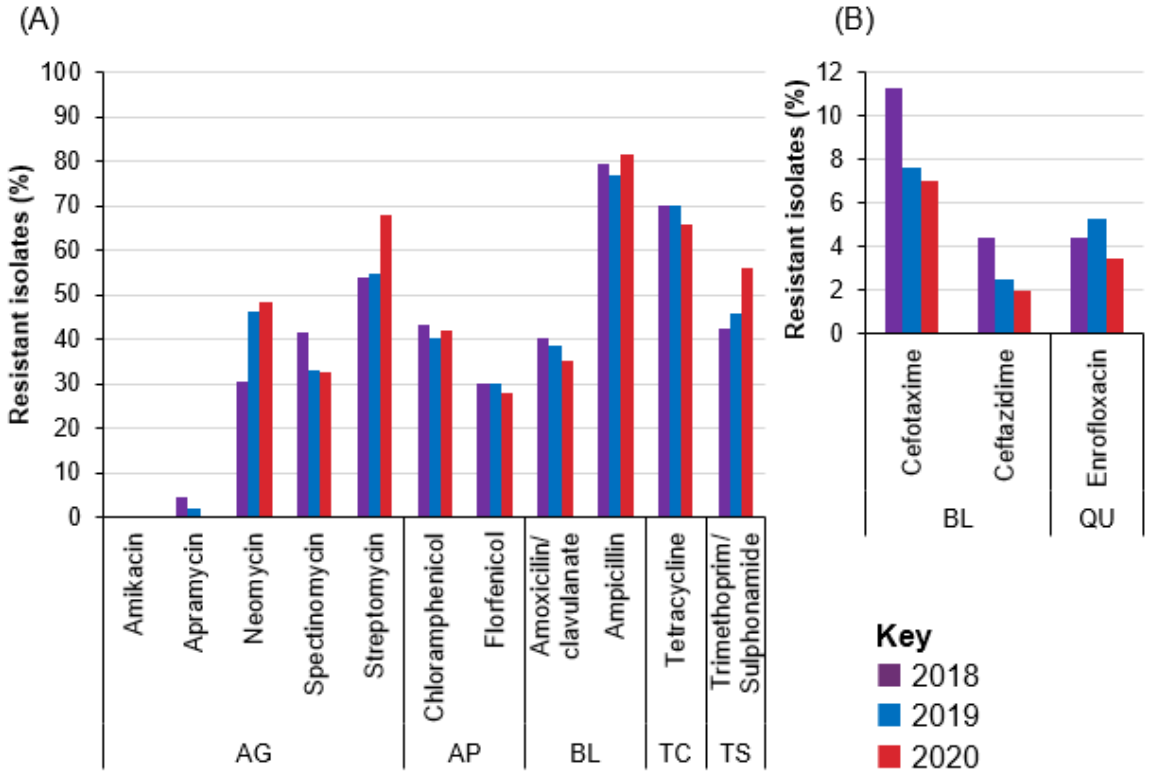
* No isolates tested in 2019 and 2020
AG: aminoglycoside, AP: amphenicols BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

[41] https://pubmed.ncbi.nlm.nih.gov/3538639/

4.3.5.1 Cattle

The AMR in *E. coli* results from cattle during the reporting period are predominantly from the neonatal age category and are presented in **Figure 4.13**; results for pre-weaning calves are presented in **Figure 4.14.** Data for adult cattle and the number of isolates tested are in Tables S4.7.8 to S.4.7.10 of the supplementary material.

Figure 4.13: Resistance to non-HP-CIAs (A) and HP-CIAs (B) of *Escherichia coli* isolates from neonatal calves. Note scale differs between graphs.



AG: aminoglycoside, AP: amphenicols BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

Resistance to certain third generation cephalosporins can indicate the presence of ESBL or Amp C enzymes. In general, a higher prevalence of resistance to cefotaxime than ceftazidime (third generation cephalosporins) was observed in neonatal calves and this is likely to reflect the occurrence of those ESBL enzymes which are cefotaximases, rather than ceftazidimases. An overall decline in resistance in *E. coli* from neonatal calves to third generation cephalosporins was noted, reported at 7.0% in 2020 for cefotaxime, and 2.0% for ceftazidime. Similar to the situation in previous years, the percentage of isolates (1.8%) resistant to cefpodoxime in *E. coli* isolated from mastitis cases in 2020 was much lower than the percent resistant to cefotaxime isolated from neonatal calves. Cefotaxime resistance in pre-weaned calves did not show a decline from 2018, although this could be due to the smaller sample size for this age class.

Resistance to enrofloxacin was between 3.5% and 5.3% in *E. coli* from neonatal calves over the period 2018 to 2020, and between 6.2% and 14% in older calves pre-weaning.

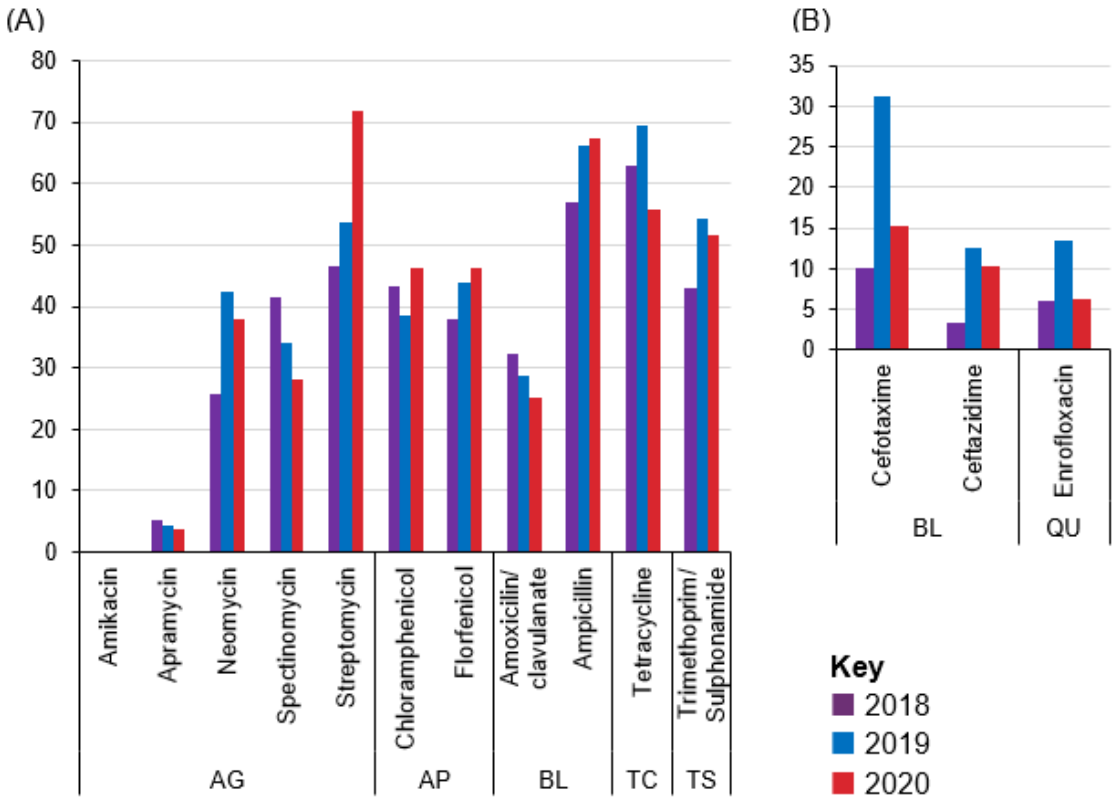
Of the aminoglycosides, streptomycin resistance is highest in both neonatal and pre-weaning calves. This is likely to reflect usage patterns, with streptomycin and dihydrostreptomycin the most frequently used aminoglycosides in cattle. Resistance to apramycin was low in *E. coli* from neonatal calves (between 0% and 4.6% between 2018 and 2020), whilst resistance to neomycin (between 31% and 48%) and spectinomycin (between 32% and 42%) was higher; a similar situation was observed in older calves, pre-weaning. This could be associated with differences in the availability of these antibiotics in intramammary formulations: neomycin is available in dry cow intramammary tubes, whereas apramycin is not. Alternatively, these differences could reflect differences in systemic use of the different aminoglycosides in dairy cattle. Amikacin resistance was not detected in *E. coli* from cattle in 2018 to 2020. Amikacin is not authorised for treatment of animals but was included in some of the panels to detect the possible occurrence of 16S rRNA methyltransferase enzymes which can confer resistance to many aminoglycosides.

Florfenicol resistance was at 28% to 30% in neonatal calves and 38% to 46% in older calves over the reporting period. These differences probably reflect patterns of antibiotic usage, related to the occurrence of pneumonia, in the different age groups of calves.

Considering beta-lactams, the relatively high frequency at which *E. coli* isolates resistant to ampicillin are recovered from young calves (77% to 82% over the period 2018 to 2020) may reflect the use of dry cow intra-mammary infusions containing aminopenicillins in the dam and transfer of residual antibiotics to calves in colostrum, which may then exert a selective pressure on the intestinal bacterial flora of the neonatal calf. Although ampicillin resistance remained consistently high at 77% to 82% in neonatal calves over the period 2018 to 2020, it was lower in older, pre-weaned calves: between 57% and 67%. Similarly, amoxicillin/clavulanate resistance ranged between 35% and 40% in neonatal calves but was lower in older, pre-weaned calves over the same period: between 25% and 32%.

Tetracycline and trimethoprim/sulphonamide resistance were high in *E. coli* from neonatal and older calves, probably reflecting widespread usage in cattle.

Figure 4.14: Resistance to non-HP-CIAs (A) and HP-CIAs (B) of *Escherichia coli* isolates from pre-weaning calves. Note scale differs between graphs.



AG: aminoglycoside, AP: amphenicols BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

4.3.5.2 Pigs

The percentage of resistance in *E. coli* from pigs in neonatal and post-weaning age categories over the reporting period are shown in **Figure 4.15** and **Figure 4.16** – in 2020, the results are predominantly from the post-weaning age category. Details on the number of isolates tested, and AMR data for adult pigs, can be found in Tables S4.7.11 to S4.7.13 on the supplementary material.

Considering HP-CIA resistance, cefpodoxime resistance in *E. coli* isolates from pigs was detected in neonatal and post-weaning piglets at consistently low levels over the monitoring period, detected in 3.2% of neonatal isolates in 2020 and 1.3% of post-weaning isolates. Resistance to enrofloxacin was 2.2% in *E. coli* from neonatal piglets and 1.7% in *E. coli* from post-weaning pigs in 2020.

For aminoglycosides, apramycin resistance in neonatal pigs increased to 13% in 2020. The occurrence of apramycin resistance was higher in post-weaning pigs, at 20%. This is assumed to reflect the use of apramycin in treating post-weaning diarrhoea in pigs. Resistance to neomycin was also higher in *E. coli* from post-weaning pigs (10% to 15% over

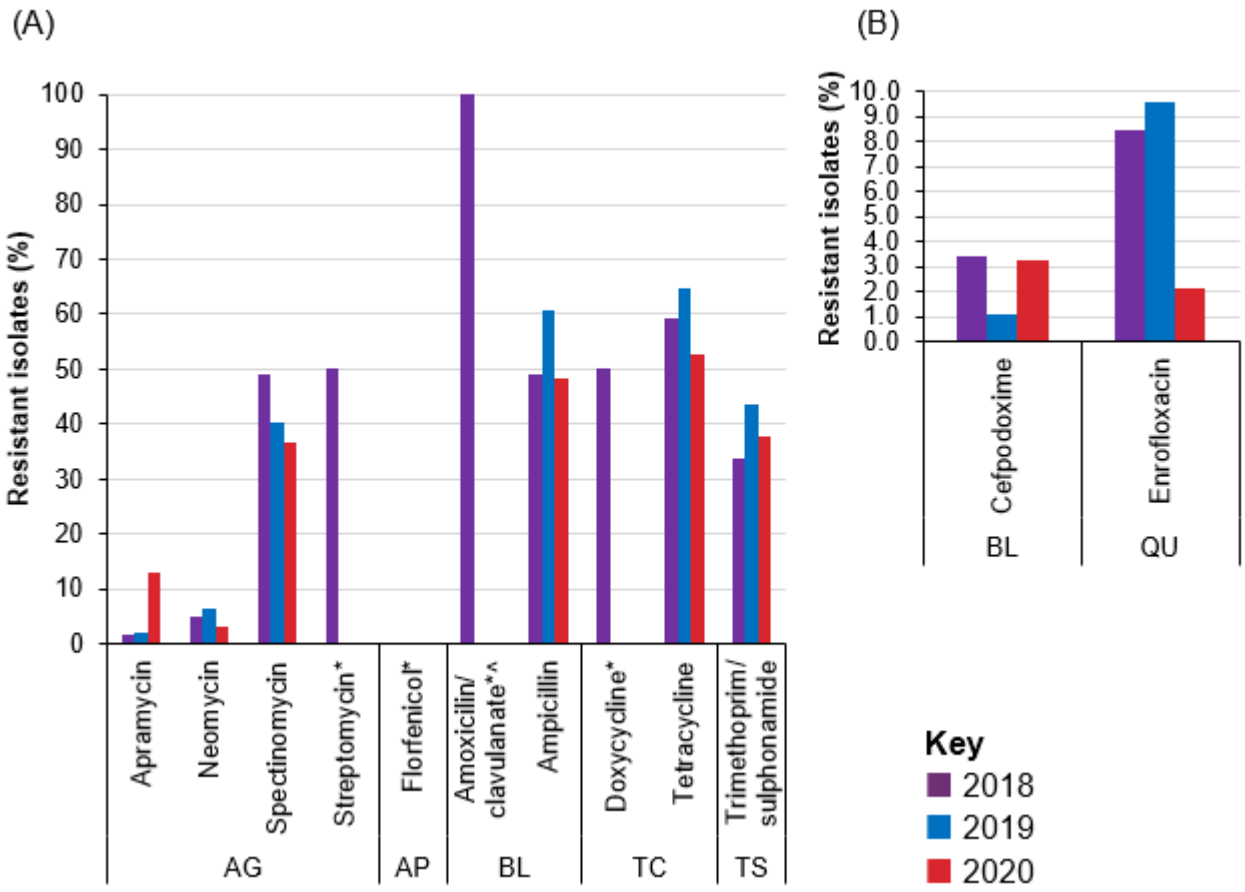
the period 2018 to 2020) compared to neonatal pigs (3.2% to 6.4%), again, probably reflecting patterns of usage. Spectinomycin resistance in *E. coli* from neonatal piglets ranged from 37% to 49% and was 33% to 39% in pigs after weaning.

Of the beta-lactams, ampicillin resistance was high both in neonatal pigs (between 48% and 61%) and in pigs after weaning (between 55% and 67%) during the reporting period.

Resistance to tetracyclines was relatively high in post-weaning pigs (60% to 71%), with slightly lower levels of resistance observed in neonatal pigs (53% to 65%) – levels showed small fluctuations over the reporting period.

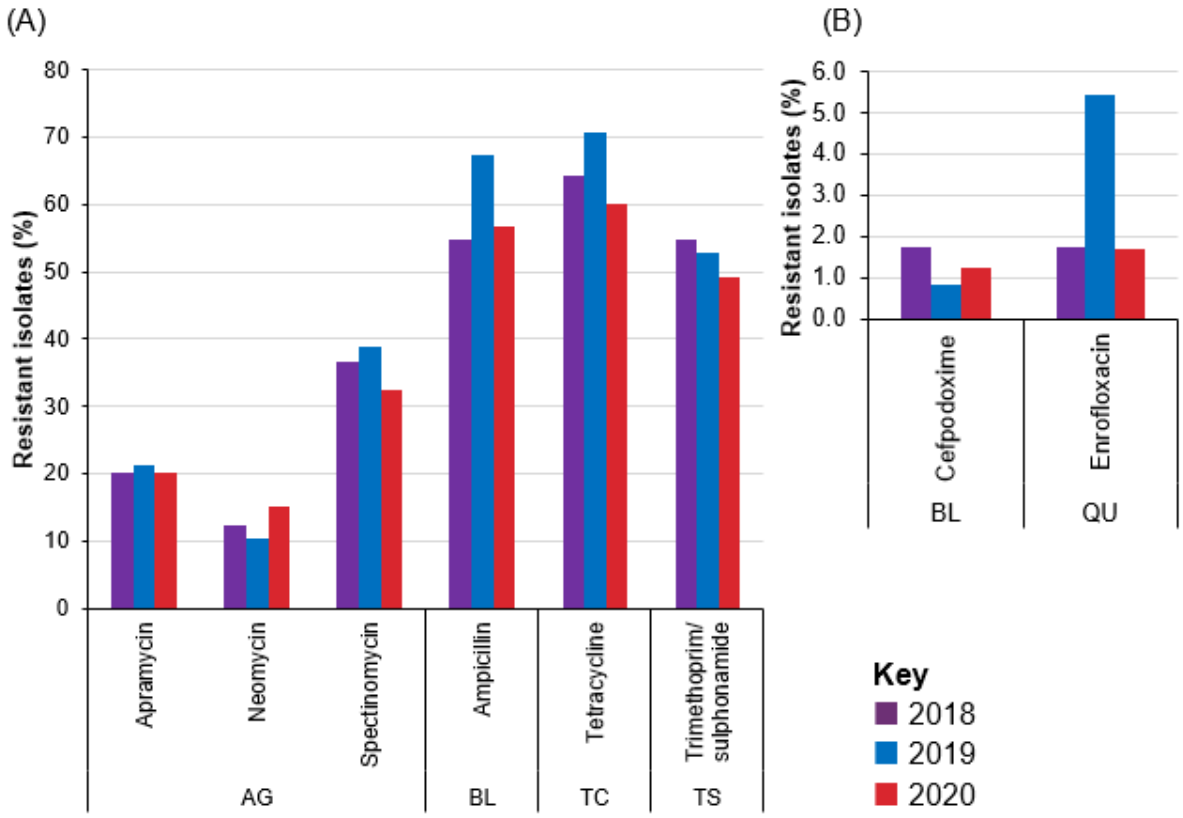
Resistance to trimethoprim/sulphonamides was high in post-weaning pigs (49% to 55%), with lower levels of resistance observed in neonatal pigs (34% to 44%).

Figure 4.15: Resistance to non-HP-CIAs (A) and HP-CIAs (B) of *Escherichia coli* isolates from neonatal piglets. Note scale differs between graphs.



* No isolates tested in 2019 and 2020
^ Only two isolates tested
AG: aminoglycoside, AP: amphenicols BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

Figure 4.16: Resistance to non- HP-CIAs (A) and HP-CIAs (B) of *Escherichia coli* isolates from post-weaning piglets. Note scale differs between graphs.



AG: aminoglycoside, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

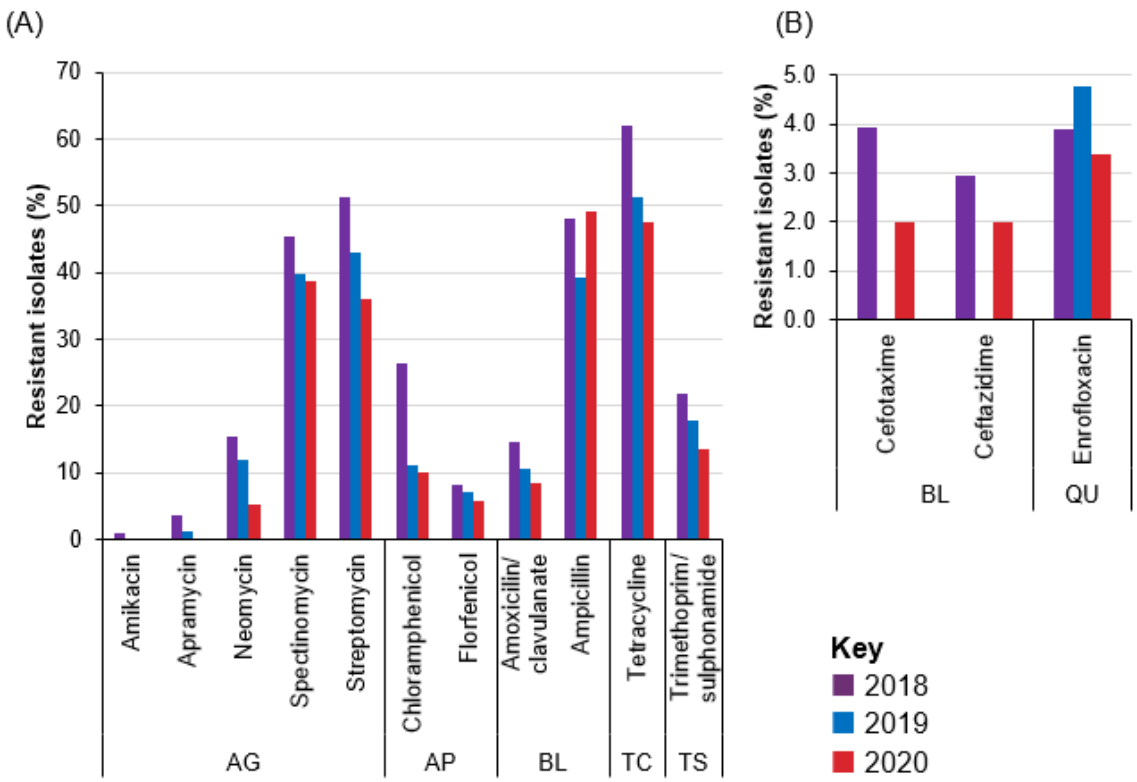
4.3.5.3 Sheep

The AMR results for sheep are predominantly from neonatal lambs and presented in **Figure 4.17**. The sample size for pre-weaning and adult sheep of approximately 30 isolates was low and is likely to have been a factor in the variation in the occurrence of resistance observed in different years. Full details are included in Tables S.4.7.14 to S.4.7.16 of the supplementary material.

For most antibiotics reported in 2020, the levels of resistance in *E. coli* from neonatal lambs were lower than those reported for neonatal calves, with the exception of spectinomycin where resistance in lambs (39%) exceeded that in calves (32%). This may reflect the high levels of oral spectinomycin use in lambs. Cefotaxime/ceftazidime (third generation cephalosporins) resistance was detected in 2.0% of *E. coli* from neonatal lambs, contrasting with the detection of cefotaxime resistance in 7.0% of *E. coli* from neonatal calves. This may be explained by the greater use of third and fourth generation cephalosporins, both as injectables and intramammary preparations, in cattle. Enrofloxacin resistance was 3.4% and 3.3% in *E. coli* from neonatal and pre-weaning lambs, slightly lower than the figures of 3.5% and 6.3% seen in calves.

A decline in resistance to ampicillin and tetracyclines in *E. coli* from neonatal lambs had been observed over the period 2016 to 2019; this continued in 2020 for tetracyclines but not for ampicillin. Declines in resistance were also observed over the period 2018 to 2020 in *E. coli* from neonatal lambs to amoxicillin/clavulanate, apramycin, florfenicol, neomycin, spectinomycin and trimethoprim/sulphonamides and these declines may reflect efforts to reduce antibiotic treatment of new-born lambs, in particular oral neomycin and spectinomycin.

Figure 4.17: Resistance to non-HP-CIAs (A) and HP-CIAs (B) of *Escherichia coli* isolates from neonatal lambs. Note scale differs between graphs.



AG: aminoglycoside, AP: amphenicols BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

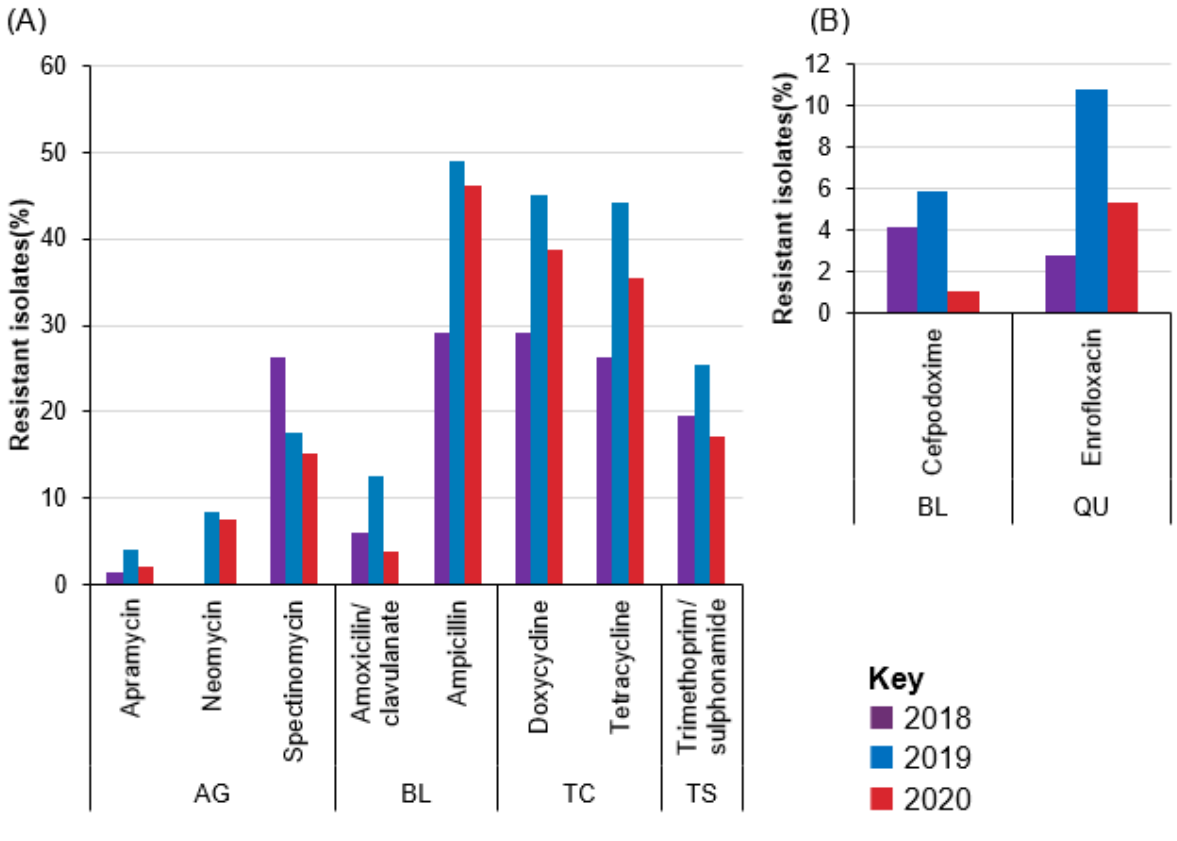
4.3.5.4 Chickens and turkeys

Cefpodoxime resistance was 1.1% in *E. coli* from chickens in 2020 (**Figure 4.18**), which has declined from 11% recorded in 2015. This reflects an industry-wide ban on usage of third generation cephalosporins in poultry since 2012. Persistence of low levels of resistance could be attributable to the timescales required for resistant strains to be outcompeted; it could also reflect the use of other antibiotics. Other beta-lactam compounds can exert a degree of selective pressure for third generation cephalosporin resistance.

Tetracycline and doxycycline resistance has increased in *E. coli* from chickens between 2018 and 2020 (from 26% and 29% to 35% and 39% respectively), although 2020 levels are lower than in those in 2019 (44% and 45% resistant). The position was similar for ampicillin which was reported at 29% in 2018 and 46% 2020. Levels of resistance detected to the fluoroquinolone enrofloxacin in *E. coli* from chickens over the reporting period have remained low, temporally coincident with industry initiatives to reduce use of fluoroquinolones in broilers. While resistance to enrofloxacin increased to 11% in 2019, it declined to 5.4% in 2020.

Resistance in *E. coli* isolates from turkeys is shown in Table S4.7.7 of the supplementary material.

Figure 4.18: Resistance to non-HP-CIAs (A) and HP-CIAs (B) of *Escherichia coli* isolates from chickens (all ages). Note scale differs between graphs.



AG: aminoglycoside, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

4.3.6 *Salmonella* spp.

Salmonella is an important cause of food borne disease in people and can be a cause of disease in animals. The results in this section are derived from data published in the

Salmonella in Livestock Production in Great Britain report[42]. *Salmonella* isolations are reported on a statutory basis and a culture of the organism must be provided to government laboratories. Some farming companies, especially poultry companies, have ongoing monitoring programmes and large numbers of *Salmonella* isolates may be received from a single premise. In this situation, the numbers of isolates of a particular serotype and their antibiotic susceptibility may not reflect the prevalence in the animal population as a whole, but rather the intensity of that monitoring programme. Since 1996, to better indicate the prevalence of AMR in *Salmonella* spp., only the first isolate from a *Salmonella* incident on a given livestock premises is tested.

Antibiotic susceptibility patterns have been useful in conjunction with *Salmonella* serovar and (where appropriate) phage type data to investigate the epidemiology of *Salmonella* infections in humans and animals. When new serovars or phage types or patterns of resistance emerge in humans, comparative analysis used to be done to provide an indication of the possible role or involvement of UK livestock. However, genome sequencing has replaced older methods of *Salmonella* typing for human isolates and is also being increasingly used to characterise and compare isolates from animals and humans. Ongoing liaison takes place between the public and animal health agencies concerned in relation to the strains detected and their resistance.

Most cases of non-typhoidal *Salmonella* infection in humans are non-invasive, limited to the gastro-intestinal tract, and may not require treatment with antibiotics. However, when treatment is required, third generation cephalosporins and fluoroquinolones are important treatment options. Resistance to these antibiotics is therefore considered of most importance in *Salmonella* spp. isolated from animals.

APHA offers an advisory visit when cases of *Salmonella* infection in food-producing animals with resistance to third generation cephalosporins or ciprofloxacin are detected, both to explain the significance of the findings and to provide appropriate advice on control. Collated AMR data from England and Wales are presented in the main body of the report, with the numbers of isolates tested included in S4.8 of the supplementary material. Due to differences in methodology, data for Scotland and Northern Ireland are presented in S4.8 of the supplementary material only.

Of the 4205 *Salmonella* isolates tested in 2020, 2871 (68%) were sensitive to all the antibiotics tested. This is similar to the situation in 2019, when 4533 isolates were tested and 3272 (72%) were sensitive to all of the antibiotics tested.

The percentage of *Salmonella* isolates that were resistant to ciprofloxacin in 2020 was 0.5%. The ciprofloxacin resistant isolates detected in 2020 originated from chicken (*S.*13, 23:i:-[four out of 449 resistant] and *S.* Agona [one out of 67 resistant]), feed and related samples (*S.* Derby [two out of 38 resistant], *S.* Infantis [one out of 50 resistant], *S.* Kentucky [one out of one resistant], *S.* Newport [five out of 19 resistant], *S.* Typhimurium

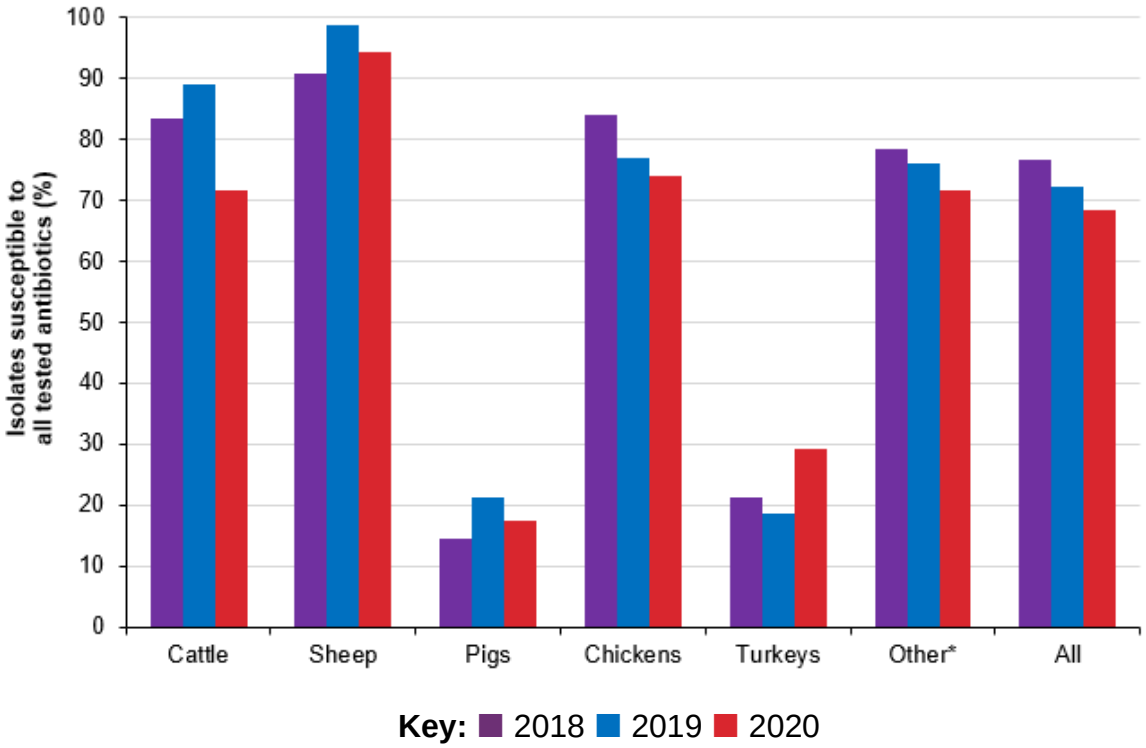
[42] Salmonella in Livestock Production 2020 (publishing.service.gov.uk)

[three out of 53 resistant]), pheasant (a single isolate of *S.* Senftenberg which was resistant), and other non-avian species (a single isolate of *S.* Give which was resistant). Ciprofloxacin resistance was not detected in *Salmonella* isolates from turkeys in 2020.

Resistance to the third generation cephalosporins cefotaxime and ceftazidime was detected in 2020 in three isolates. One *S.* Indiana isolate with resistance to ampicillin, cefotaxime, ceftazidime and amoxicillin/clavulanate recovered from a lorry swab taken at a poultry farm in 2020. This isolate was found to possess the *bla*$_{CMY-2}$ gene, encoding an AmpC beta-lactamase. This strain was not identified in samples directly collected from UK broiler flocks, and it is likely to have been a result of environmental contamination.

S. Typhimurium and *S.* Enteritidis are the two controlled serovars considered of greatest importance to public health[43]. Two equine *Salmonella* Typhimurium isolates (both DT116) detected from environmental swabs from stables were found to be multidrug resistant (resistant to at least four antibiotics in the panel). The isolates were resistant to tetracycline, ampicillin, ceftazidime, trimethoprim, chloramphenicol, gentamicin, streptomycin and sulphonamides. Cefotaxime, ceftazidime or ciprofloxacin resistance was not detected in *S.* Enteritidis from animals in 2020.

Figure 4.19: *Salmonella* spp. isolates susceptible to all tested antibiotics, from different sources and animal species.



* Ducks, horses, dogs, other non-avian species, other avian species, feed and farm environment.

[43] Salmonella in livestock production in Great Britain - GOV.UK (www.gov.uk)

Tetracycline, sulphonamide and streptomycin resistance was commonly found in *Salmonella* isolates originating from pigs and chickens in 2020, similar to in 2019.

Resistance to apramycin in all *Salmonella* serovars was 1.1% in 2020, similar to the level observed in 2019 (1.2%). *Salmonella* isolates from pigs, for which resistance was 14% in 2020, contributed most to the overall apramycin resistance figure; in pigs, apramycin resistance was observed in both monophasic *S.* Typhimurium variants 4,12:i:- and 4,5,12:i:-. In 2020, 36% of *Salmonella* 4,12:i:- isolates (n=33) and 35% of *Salmonella* 4,5,12:i:- isolates (n=48) from pigs were resistant to apramycin. Of all *Salmonella* isolates, 1.3% were resistant to gentamicin. Resistance was detected to the aminoglycoside amikacin in two out of 111 (1.8%) *S.* Typhimurium DT193 isolates from pigs. These isolates were also resistant to tetracycline, neomycin, ampicillin, trimethoprim, gentamicin, streptomycin and sulphonamides.

The highest prevalence of resistance to nalidixic acid in 2020 was observed in *Salmonella* isolates from turkeys, feed, especially raw meat pet food, and dogs. The high proportion of nalidixic acid resistant isolates in feed represents a difference from between 2013 and 2016 when resistance to nalidixic acid was mostly observed in *Salmonella* from turkeys and “other avian species”. In turkeys, 11 out of 11 *S.* Senftenberg isolates and one out of one *S.* 3,19:-:- isolates were resistant to nalidixic acid in 2020. The situation in turkeys was similar in 2013 to 2019, with nalidixic acid resistance frequently detected in this serovar. In chickens, resistance to nalidixic acid was found in *S.* 13,23:i:-, *S.* Indiana, *S.* Infantis, *S.* Enteritidis and *S.* Agona.

4.3.6.1 *Salmonella* by animal species

Data for the resistance levels for *Salmonella* isolates from the different animal species to the antibiotics tested is presented in full in tables S4.8.2 to S4.8.6 of the supplementary material. A summary is given below.

Cattle – No resistance was observed to the HP-CIAs ceftazidime, cefotaxime or ciprofloxacin. The highest levels of resistance were to tetracycline (20%), streptomycin and sulphonamide (both 17%) and ampicillin (13%).

Pigs – No resistance was observed to the HP-CIAs ceftazidime, cefotaxime or ciprofloxacin. The highest levels of resistance were to ampicillin and sulphonamide (both 76%), streptomycin (62%) and tetracycline and chloramphenicol (64.9 and 52% respectively).

Sheep - No resistance to the HP-CIAs ceftazidime, cefotaxime or ciprofloxacin. The highest levels of resistance were to streptomycin, sulphonamide and tetracycline (all 4.3%), followed by ampicillin and chloramphenicol (both 2.9%).

Chickens – One isolate was resistant to the HP-CIAs cefotaxime and ceftazidime (0.1%) and five isolates to ciprofloxacin (0.3%). The highest levels of resistance were to

sulphonamide (22%), tetracyclines (15.4%) trimethoprim/sulphonamides (17%), streptomycin (6.2%) and ampicillin (5.7%).

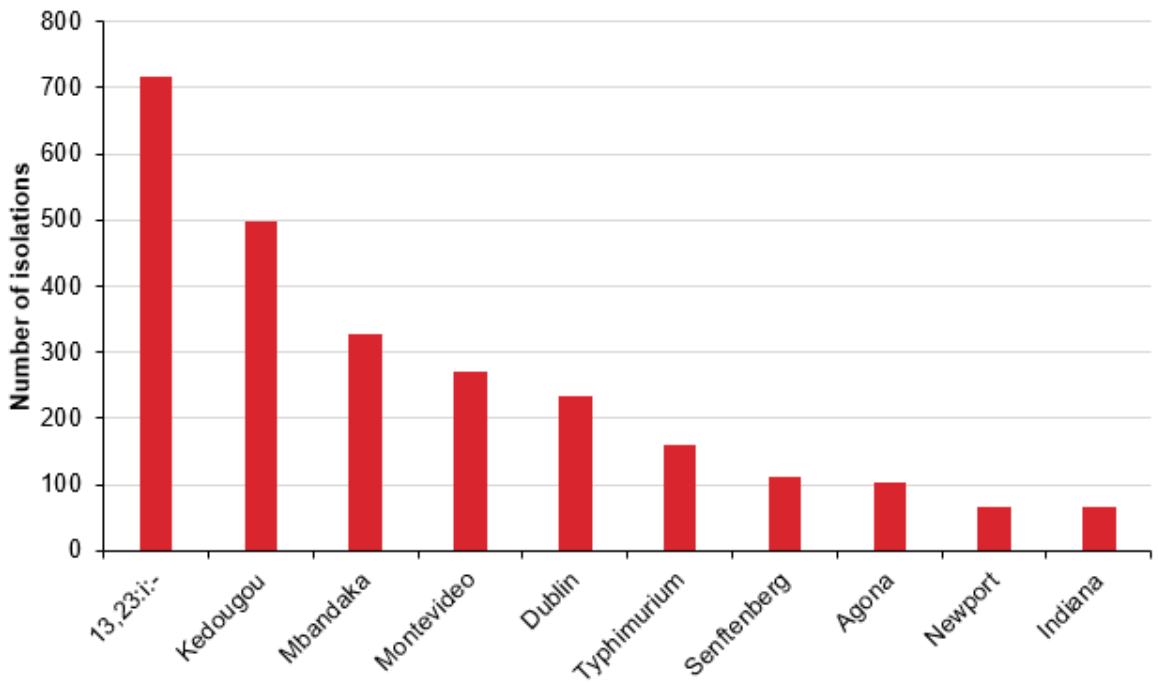
Turkeys - There was no resistance observed the HP-CIAs ceftazidime, cefotaxime or ciprofloxacin. The highest levels of resistance were to streptomycin (42%), tetracyclines and sulphonamide (33%), ampicillin (31%) and trimethoprim/sulphonamides (18%).

4.3.6.2 Top ten *Salmonella* serovars in 2020

Some serovars can have characteristic patterns of resistance, so knowledge of the most frequently isolated serovars can be of benefit when considering trends in resistance. The ten most frequently detected serovars of non-typhoidal *Salmonella* isolates recovered from cattle, pigs, sheep, chickens and turkeys in Great Britain in 2020 are presented in **Figure 4.20**. In 2020, the most consistently isolated serovar was 13,23:i:- (n=716), followed by *S*. Kedougou (n=499), *S*. Mbandaka (n=326) and *S*. Montevideo (n=270).

Details of commonly recovered serovars in Northern Ireland and Scotland are provided in Tables S4.8.10 and S4.8.11 of the supplementary material.

Figure 4.20: Top ten most isolated *Salmonella* serovars from livestock in Great Britain during 2020.



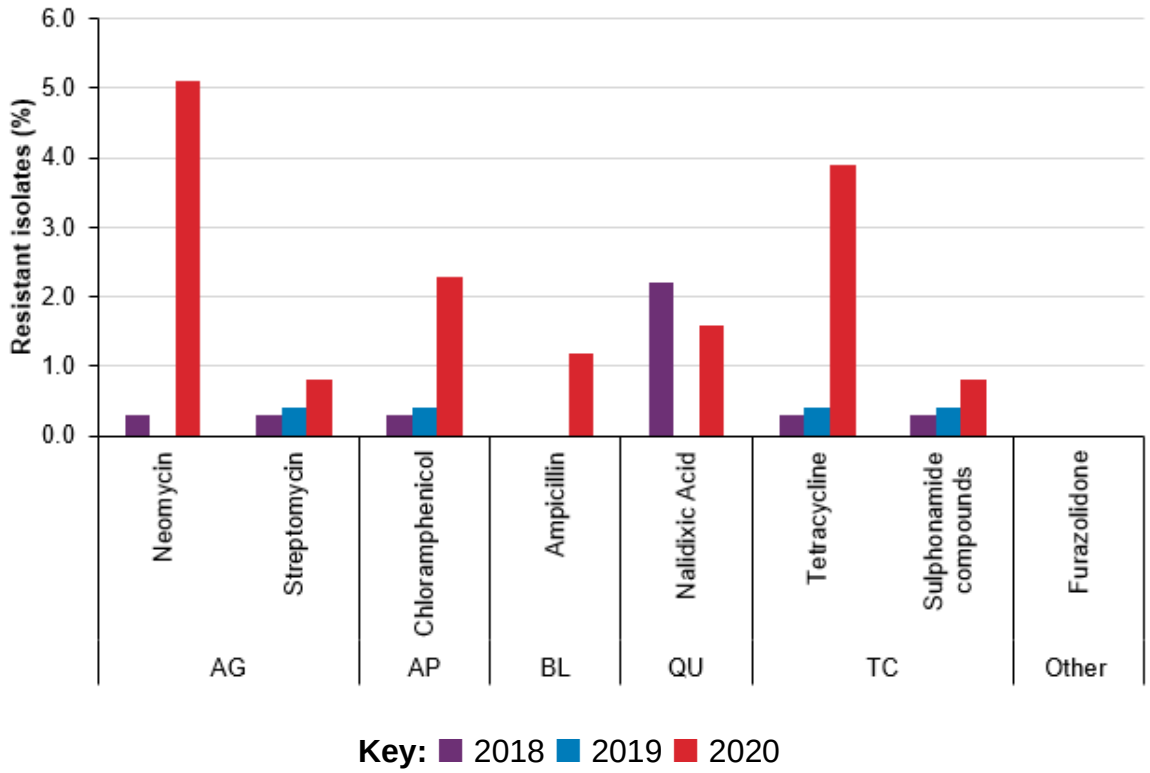
4.3.6.3 *Salmonella* Dublin

Of the 256 *Salmonella* Dublin cultures tested during 2020, 89% were susceptible to all 16 antibiotics, which is a decrease compared to 99.6% in 2019. The majority of *S.* Dublin

isolates have been sensitive to all 16 antibiotics since records began in 1971, and the percentage of fully susceptible isolates has shown only slight fluctuations between 2006 and 2019. However, in 2020, an increase in the proportion of resistant isolates was observed (**Figure 4.21**). This decrease in susceptibility was mostly due to an increase in *S.* Dublin resistant to neomycin and/or chloramphenicol, representing a change in the sensitivity trends relating to this serovar.

Most *S.* Dublin isolates (85%) originated from cattle in 2020 and this was similar to the situation recorded in previous years. *S.* Dublin isolates from species other than cattle in 2020, included 13 isolates from sheep, 13 from dogs, one from a goat, and 11 from animal feed (mainly feed for pets).

Figure 4.21: Resistant *Salmonella* Dublin isolates from 2018 to 2020.



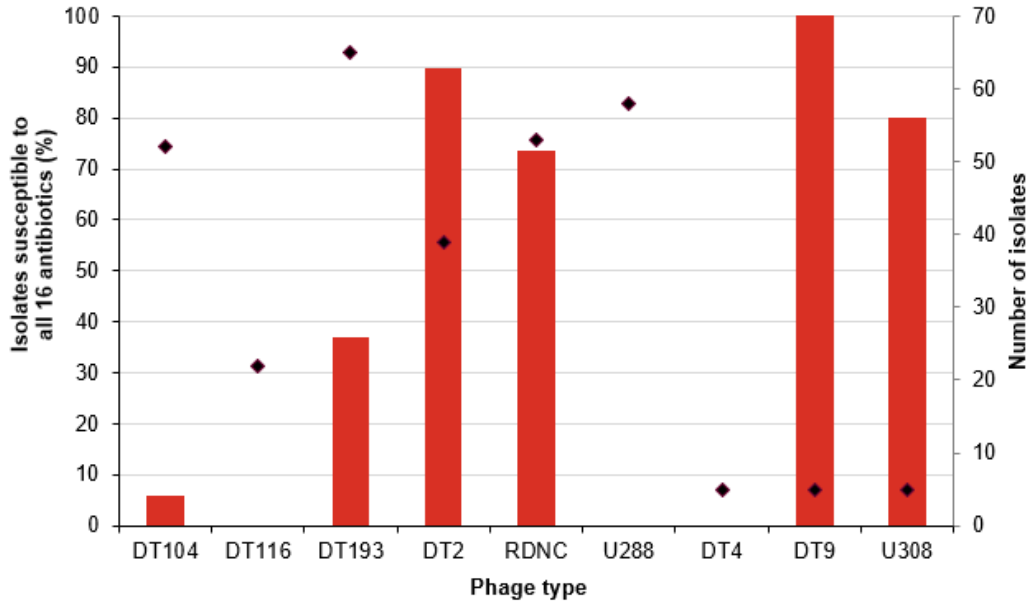
AG: aminoglycoside, AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

4.3.6.4 *Salmonella* Typhimurium

The number of isolates of *Salmonella* Typhimurium tested in 2020 was 340. Resistance varies widely between phage types; the nine most frequent definitive or undefined phage types subjected to susceptibility testing at APHA are given in **Figure 4.22.** The percentage of *S.* Typhimurium isolates that were sensitive to all antibiotics tested was 40%, which is a

decrease from the 2019 (49%), and 2018 figures (54%), but higher than the figures reported in 2017 (34%).

Figure 4.22: Fully susceptible isolates of *S*. Typhimurium (and number tested) of eight most frequent definitive or undefined types subjected to susceptibility testing at APHA; 2020



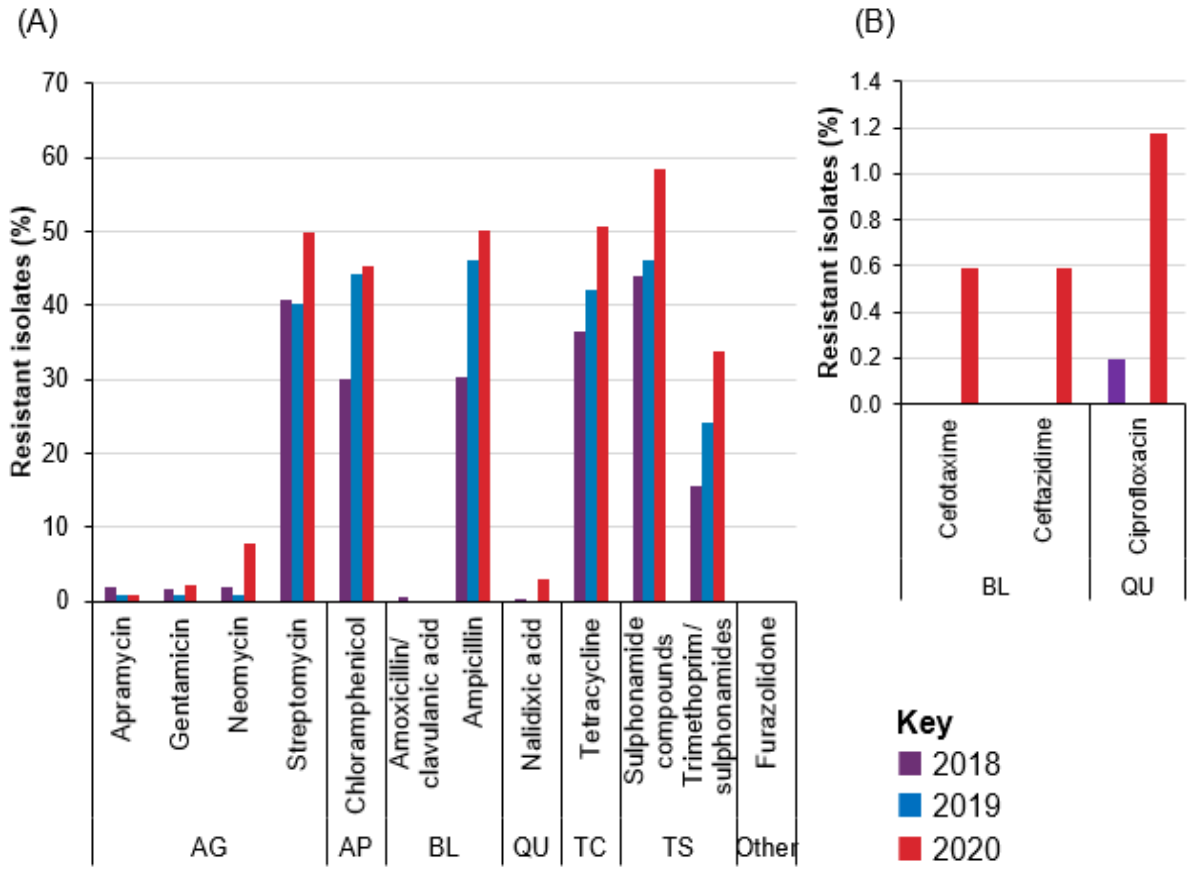
Key: ◆ number of isolates tested ■ percentage susceptibility

Figure 4.23 (and Table S4.8.8 of the supplementary material) presents an overview of percentage resistance in *S*. Typhimurium to the antibiotics tested between 2018 and 2020. The generally high level of resistance of *S.* Typhimurium isolates observed in recent years has partly been a reflection of the contribution of DT104 and its variants DT104B and U302 which have comprised more than a quarter of isolates in some years in the previous decade.

Only three of the 52 DT104 isolates tested in 2020 were sensitive to all antibiotics tested. All remaining DT104 and all the U302 isolates (n=2) were resistant to at least one of the 16 antibiotics tested. The proportion of *S.* Typhimurium isolates comprising DT104 and its variants, which had shown a general decline between 2007 and 2014, showed a resurgence in between 2015 and 2017 but was at a lower level in 2020 (16%). The typical pentavalent resistance pattern AmCSSuT (ampicillin, chloramphenicol, streptomycin, sulphonamides, tetracycline) was the most common resistance pattern seen in *S.* Typhimurium DT104, occurring in 62% (33 out of 52) of isolates. A resurgence of pentavalent (AmCSSuT) *S.* Typhimurium DT104 begun in 2017. This was mainly due to an increased number of incidents of this *Salmonella* in cattle and sheep in North Wales and related areas. In 2020, incidents of this phenotype were still identified, but at lower levels than 2017.

Of the 52 DT104 isolates, four (originating from animal feed or related samples, especially raw meat pet food) were resistant to nalidixic acid and five isolates (originating from pigs) were resistant to trimethoprim/sulphonamides. No isolates of DT104 were recovered from turkeys between 2012 and 2020.

Figure 4.23: Resistance to non-HP-CIAs (A) and HP- CIAs (B) of *Salmonella* Typhimurium isolates. Note scale differs between graphs.



AG: aminoglycoside, AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

S. Typhimurium U288 and DT193 from pigs accounted for 16% and 8.5% of the total numbers of *S.* Typhimurium isolates respectively; none of the U288 and only one out of 29 DT193 isolates from pigs were fully susceptible in 2020.

Considering all definitive types of *S.* Typhimurium, resistance to trimethoprim/sulphonamides has fluctuated markedly in recent years between 16% and 34%. In 2020, resistance was 34%. It has been predominantly isolates from pigs that have accounted for these fluctuations; a high proportion of many definitive types of *S.*

Typhimurium isolated from pigs are resistant to trimethoprim/sulphonamides. The definitive and undefined phage types of *S.* Typhimurium resistant to trimethoprim/sulphonamides and recovered from pigs in 2020 included contributions primarily from isolates of two phage types DT193 and U288. AmCSSuTTm (ampicillin, chloramphenicol, streptomycin, sulphonamides, tetracycline, trimethoprim/sulphonamides) was the most common resistance pattern observed in both DT193 isolates (12 isolates) and U288 isolates (26 isolates) from pigs.

In 2020, resistance to apramycin was 0.9%. Two *S.* Typhimurium isolates in 2020 were resistant to amikacin, two to cefotaxime and ceftazidime, four to ciprofloxacin and ten to nalidixic acid.

Multiple antibiotic resistance (defined as resistance to four or more antibiotic agents in the panel of 16) was detected in definitive and undefined phage types DT104 (from cattle, pig, dog, feed [especially pet food] and sheep), DT115 (dog), DT116 (cattle, horse, feed), DT193 (pig, chicken, cattle, feed, horse), DT2 (pigeon), DT204b (pigeon), DT4 (pig), DT288 (pig, feed), U302 (cattle, feed), U308 (pig), U323 (pig), and from isolates which did not react to phages or did not belong to a definitive or undefined type (pig, feed, cattle, turkey). Nine different phage types (namely DT1, DT126, DT189, DT194, DT40, DT41, DT41b, DT9, DT320), several of which are mainly associated with wildlife, were susceptible to all of the antibiotics in the test panel.

4.3.6.5 Monophasic *Salmonella* serotypes

Sixty-one isolates of *Salmonella* 4,12:i:- were tested, belonging to definitive phage types DT193 (55), DT194 (1); three isolates were not typable and for two isolates a PT could not be determined. Most isolates were from pigs (54%) with feed, especially raw meat pet food, and related samples being the next most common source of origin (31%). The most common pattern of resistance observed was AmSSuT (ampicillin, streptomycin, sulphonamides, tetracycline) which occurred in 20 out of 55 of DT193 isolates. Considering the DT193 isolates, 44 out of 55 (80%) had the AmSSuT resistance pattern alone or with one or more additional resistances.

A total of 107 isolates of *Salmonella* 4,5,12:i:- were tested, including phage types DT193 (n=93), DT104 (n=7), U311 (n=2), two isolates that were untypable and three isolates for which no PT could be determined. The most common resistance pattern in DT193 isolates was AmSSuT, occurring in 43% of isolates (40 out of 93). Most isolates of monophasic *Salmonella* 4,5,12:i:- DT193 were from pigs (47%).

Considering the aminoglycosides other than streptomycin, apramycin resistance was detected in 36% and neomycin resistance in 24% of *S.* 4,12:i:- from pigs (n=33). Resistance to neomycin and apramycin was observed in 5.3% of *S.* 4,12:i:- isolates from feed, especially raw meat pet food, or feed constituents (n=19). Apramycin resistance was detected in 35% and neomycin resistance in 31% of *S.* 4,5,12:i:- from pigs (n=48). Resistance to apramycin was also observed in 10.5% of *S.* 4,5,12:i:- isolates from feed or

feed constituents, and resistance to neomycin was present in 21% of these isolates (n=19). Resistance to the aminoglycosides apramycin and neomycin was therefore detected in monophasic *S.* Typhimurium isolates from both pigs and feed/raw meat pet food in 2020.

4.3.6.6 *Salmonella* other than Dublin and Typhimurium

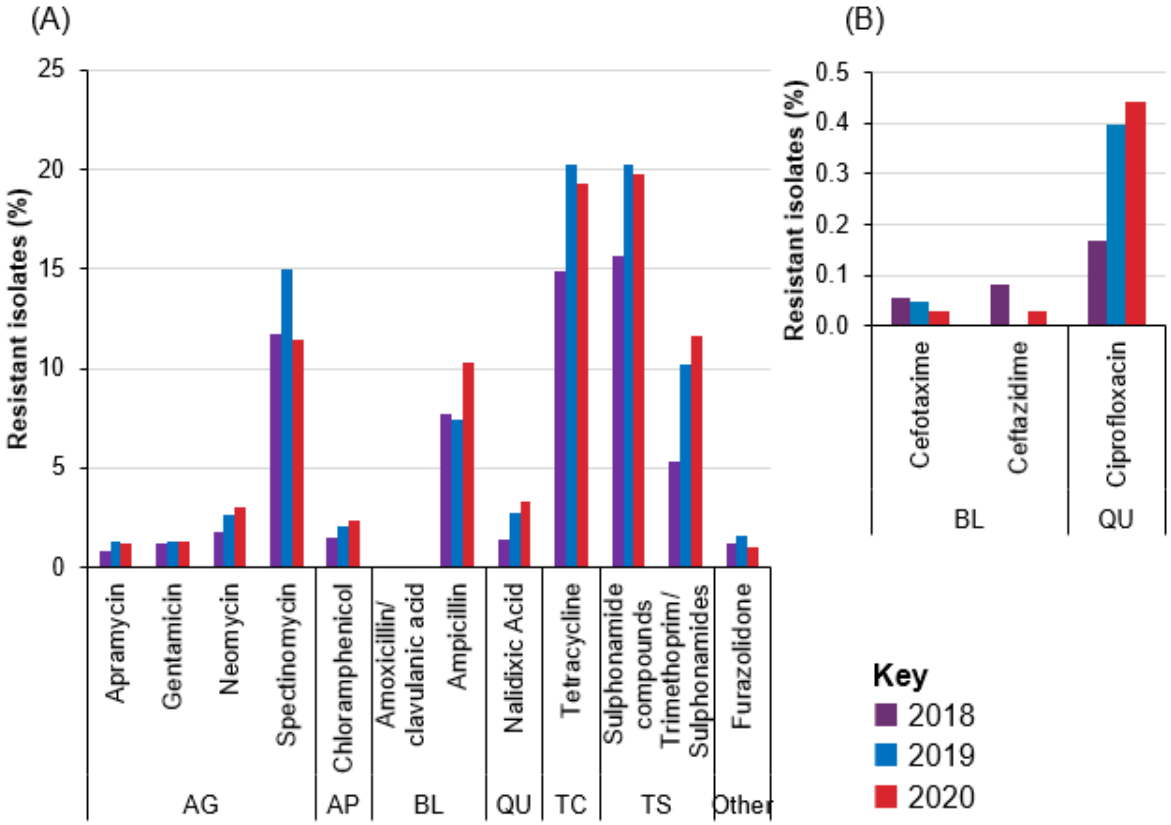
Of the 3617 isolates of serovars other than *S.* Dublin and *S.* Typhimurium tested, 70% were sensitive to all the antibiotics in the test panel, a slight decrease since 2019, when 72% were fully sensitive (**Figure 4.24**). 75 isolates (2.1% of the total) were *S.* Enteritidis, of which 67 (89%) were fully susceptible. Three isolates were resistant to nalidixic acid: two phage type 3a isolates, both from chickens and one PT8 from a snake.

Neomycin resistant *Salmonella* isolates originated mainly from pigs (21% of 131 isolates), cattle (12% of 126 isolates), ducks (5.3% of 170 isolates), feed/pet food or feed constituents (3.8% of 1026 isolates), and chickens (0.4% of 1631 isolates). *Salmonella* Indiana is typically isolated from ducks and was the main serovar showing resistance to neomycin (8 out of 60 isolates resistant); the *S.* Indiana isolates from ducks were also frequently resistant to furazolidone (12 out of 60 isolates) and this was similar to the situation observed in 2019.

For pigs in 2020, 58% were resistant to streptomycin, 60% to sulphonamides and 61% to tetracyclines. Lower levels of resistance to these antibiotics were seen in turkeys (41%, 33% and 33% respectively), cattle (17%, 17% and 21% respectively) and chickens (6.0%, 23% and 16% respectively).

In 2020, the proportion of *Salmonella* isolates originating from feed or related samples (29%) was similar to 2018 (24%) but the proportion of fully susceptible isolates from feed decreased from 75% to 68%.

Figure 4.24: Resistance to non-HP-CIAs (A) and HP-CIAs (B) of *Salmonella* other than Dublin and Typhimurium isolates. Note scale differs between graphs.



AG: aminoglycoside, AP: amphenicols, BL: beta-lactams, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

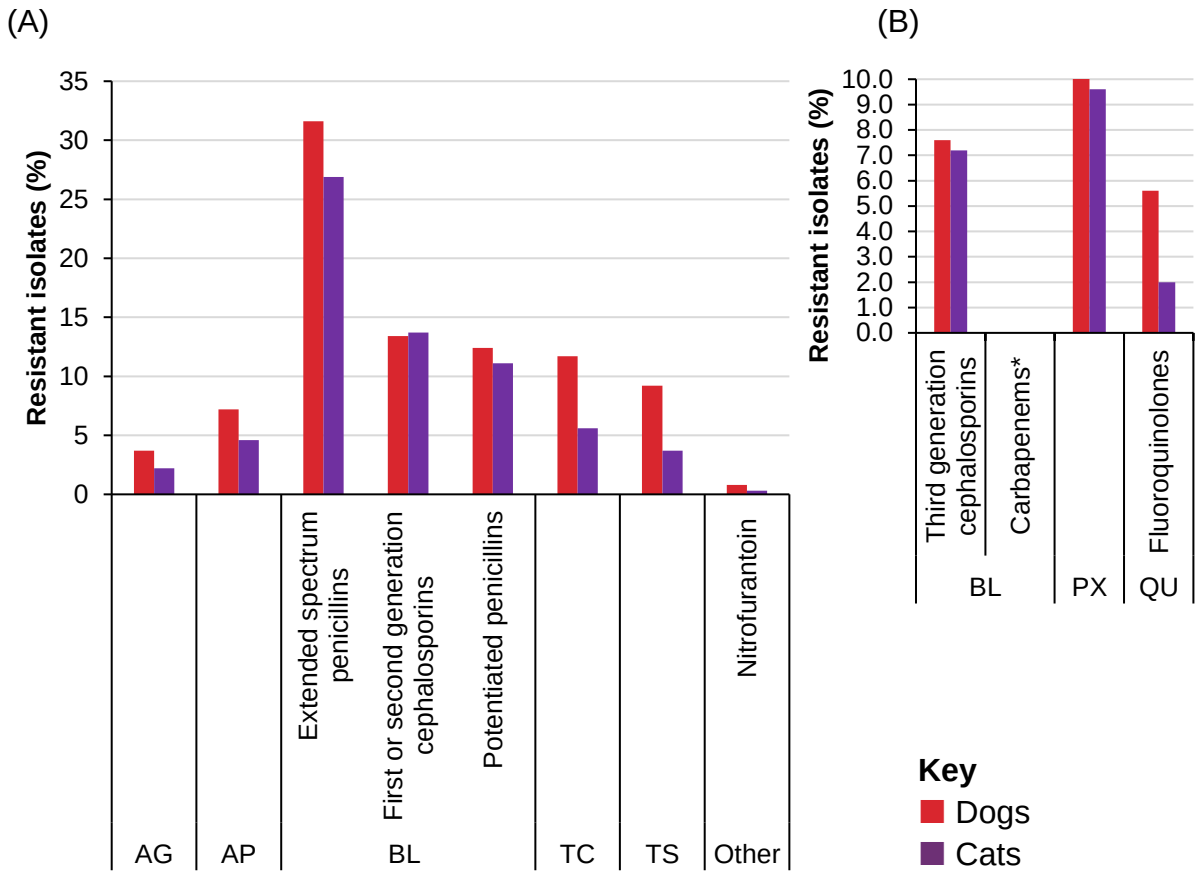
4.3.7 AMR in dogs and cats

A project undertaken by the Small Animal Veterinary Surveillance Network (SAVSNET), looked at antibiotic prescriptions (see **Chapter 2** for details) and AMR trends in dogs and cats in the UK. Data from clinical AST from diagnostic laboratories between 2016 and 2020 were analysed, covering submissions from just under 60% of RCVS registered veterinary practice sites in the UK. Presented below (**Figure 4.25**, **Figure 4.26** and **Figure 4.27** are the results for resistance levels against antibiotic classes (see Annex B for class abbreviation explanations) for three key bacterial species commonly associated with clinical infection in people and their pets: *Escherichia coli*, *Staphylococcus pseudintermedius,* and *Pseudomonas aeruginosa*. Methods applied and details on the number of tests conducted are presented in Table S4.1.4 and section S4.9 of the supplementary material.

Data shown in this section are subject to the same limitations as the rest of the clinical surveillance chapter: subject to biases, and should not be considered representative of the UK population. Additionally, data collected from different private laboratories is often not

directly comparable: the number of bacterial isolates tested against the different antibiotic classes varies (see section S4.9 of the supplementary material), and participating laboratories varied in their approach to AST both in terms of methodology and interpretation. This limits the ability to firmly draw conclusions on clinical AMR in dogs and cats; nonetheless, collating this data is an important step towards AMR surveillance in these animals.

Figure 4.25: Resistance to non-HP-CIA classes (A) and HP-CIA sub-classes (B) of total *E. coli* from dogs and cats isolated from clinical samples collected by private veterinary surgeons between 2016 and 2020. Note scale differs between graphs.

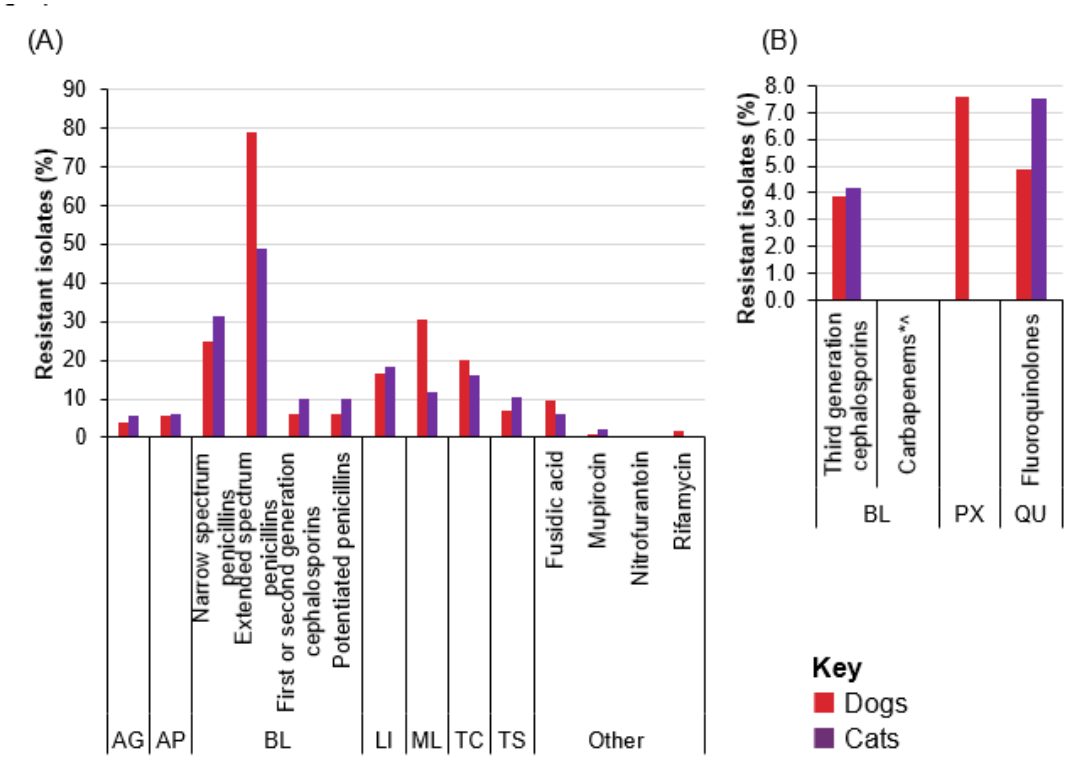


* Less than 20 isolates tested in cats
AG: aminoglycoside, AP: amphenicols BL: beta-lactams, PX: polymyxins, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

Figure 4.25 shows the percentage resistance of the total number of *E. coli* collected from dogs (n= 46,458) and cats (n=16,483) during the period 2016 to 2020, largely originating from samples collected from the urinary tract or anal region. Of these isolates, 35% from dogs and 30% from cats were resistant to at least one antibiotic class. The most frequently reported non-susceptibility in both species was to beta-lactams (31% and 28% in dogs and cats respectively). By contrast, resistance to HP-CIAs was relatively low: resistance to third generation cephalosporins was detected in 7.6% and 7.2% of isolates from dogs and cats, respectively; resistance to fluoroquinolones was 5.6% and 2.0%, respectively. Multi-drug

resistance (MDR) in *E. coli* was more frequently reported from dogs (6.3%) than cats (2.3%).

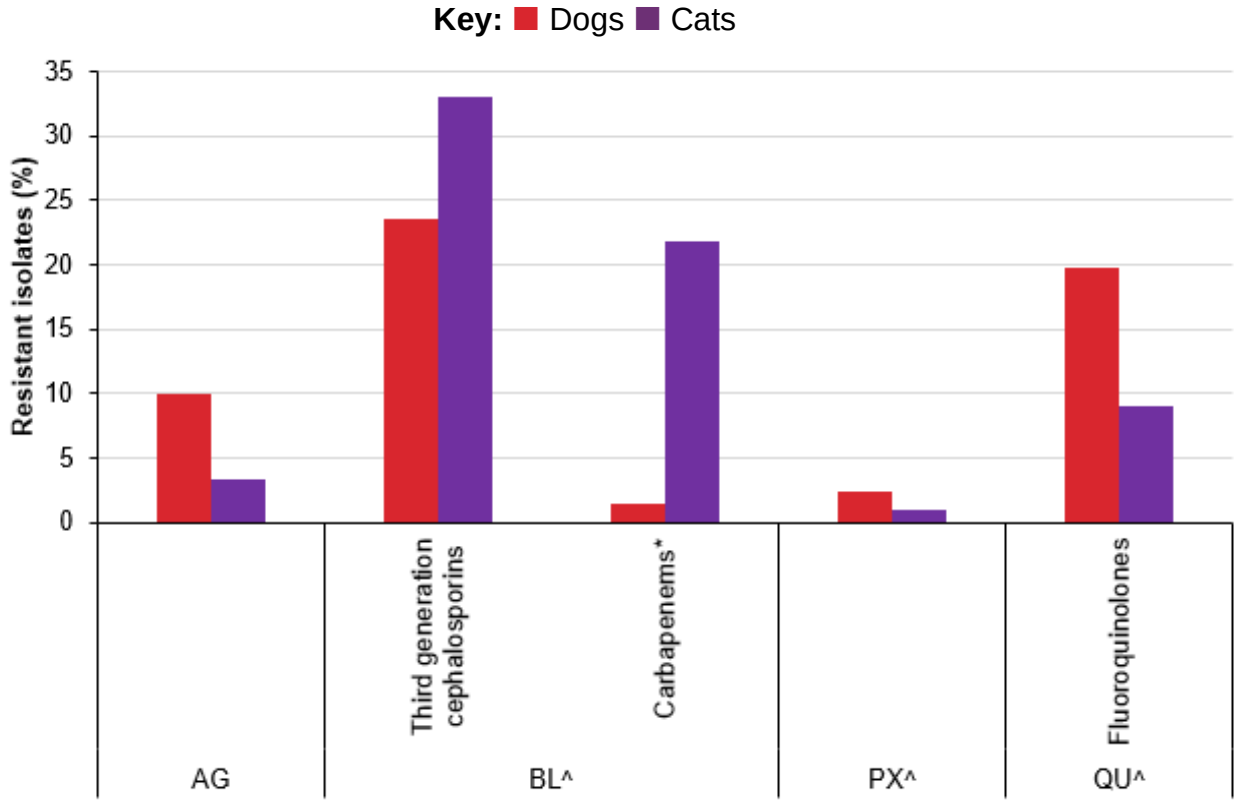
Figure 4.26: Resistance to non-HP-CIA classes (A) and HP-CIA sub-classes (B) of total *S. pseudintermedius* isolates from dogs and cats isolated from clinical samples collected by private veterinary surgeons between 2016 and 2020. Note scale differs between graphs.



* Less than 20 isolates tested in dogs
^ No isolates tested in cats
AG: aminoglycoside, AP: amphenicols, BL: beta-lactams, LI: lincosamides, ML macrolides, PX: polymyxins, QU: quinolones, TC: tetracyclines, TS: trimethoprim/sulphonamides

Figure 4.26 shows the percentage resistance of the total number of *S. pseudintermedius* collected from dogs (n = 62,387) and cats (n = 1,049) during the period 2016 to 2020, largely originating from samples collected from skin and ears. Of these isolates, 47% from dogs and 45% from cats were resistant to at least one antibiotic class. Beta-lactam resistance was again detected most frequently in both species (32% and 36% in dogs and cats, respectively). Resistance to polymyxins was detected in dogs (7.6%) but not in cats (although very few isolates were tested from this species). Of the HP-CIAs, resistance to third generation cephalosporins was low (3.9% and 4.2% in dogs and cats, respectively) and resistance to fluoroquinolones was detected in a higher proportion in cats (7.5%) than dogs (4.9%). MDR in *S. pseudintermedius* was more frequently reported in cats (10%) than dogs (6.7%).

Figure 4.27: Resistance (to both non-HPCIAs and HP-CIAs) of *P. aeruginosa* isolates from dogs and cats isolated from clinical samples collected by private veterinary surgeons between 2016 and 2020.



^ HP-CIA
* Less than 20 isolates tested in cats
AG: aminoglycoside, BL: beta-lactams, PX: polymyxins, QU: quinolones

Figure 4.27 shows the percentage resistance of the total number of *P. aeruginosa* isolated from dogs (n=40,503, largely originating from ears) and cats (n=1844, largely oronasopharyngeal samples) during the period 2016 to 2020. Of these isolates, 26% from dogs and 12% from cats were resistant to one antibiotic class. Aminoglycoside resistance was reported more frequently in dogs (9.9%) than cats (3.4%), as was resistance to polymyxins (2.4% in dogs and 1.0% in cats). There was a similar pattern of resistance to fluoroquinolones (20% in dogs and 9% in cats); however, the proportion of third generation cephalosporin resistance was higher in cats (33%) than in dogs (24%). MDR was detected in 1.4% and 0.2% of canine and feline *P. aeruginosa* respectively. Carbapenem resistance was tested in only a small number of *P. aeruginosa* isolates and was detected in 1.4% of isolates from dogs (68 isolates tested) and 22% of isolates from cats (9 isolates tested). Carbapenems are often included on standard laboratory AST profiles, however rarely reported to the veterinary clinician. These antibiotics are invaluable for the treatment of infections due to multi-resistant Gram-negative bacteria in humans.

The usefulness of this data is constrained by the limitations outlined above, however, these results do highlight some areas that warrant further investigation. For example, resistance to beta-lactams was the most frequently reported resistance in all three bacterial species isolated from dogs and cats. This is consistent with prescribing patterns: as noted in Section 2.3.7.2, between 2014 and 2020, beta lactams accounted for 74% of prescriptions for dogs and 89% in cats. However, penicillins are also the most frequently prescribed antibiotics in people[44], and the dynamics of resistance transmission between people and their pets are not well understood. Conversely, despite third generation cephalosporins being the most frequently prescribed antibiotics in cats, resistance to these compounds in *E. coli* and *S. pseudintermedius* collected from cats remains fairly low. It is unclear whether calculating antibiotic usage in percentage of prescriptions over-states third generation cephalosporin use compared to the mg/kg metric, or whether other factors are contributing to this apparent discrepancy. High rates of resistance to HP-CIAs in *P. aeruginosa* isolated from dogs and cats is also of concern, particularly given the close contact between people and their pets. Further genomic and epidemiological analysis would be useful to elucidate the evolution and transmission of resistance within households and between human and pet populations.

The detection of MDR in isolates of *E. coli*, *S. pseudintermedius*, and *P. aeruginosa*, while at relatively low levels, has obvious ramifications for antibiotic treatment options and ultimately, animal health and welfare. MDR was more prevalent in isolates originating from referral practices or those employing RCVS-accredited specialists (data not shown), possibly reflecting prior antibiotic use. The SAVSNET team noted that a history of antibiotic usage was rarely provided on AST submission forms, which is a clear area for improvement which would be of benefit both to clinical practice and to AMR surveillance. Detection of AMR, and consequently, optimisation of treatment choices could be facilitated by vets through increased and prompt use of AST in cases with a suspected bacterial infection, and by private veterinary laboratories through harmonisation and standardisation of AST methodologies.

[44] ESPAUR report 2019 to 2020 (publishing.service.gov.uk)

Annexes

Annex A: Glossary of terms

Active ingredient	The part of an antibiotic medicine that acts against the bacterial infection. Alternatively called ‘active substance’.
AMEG	Antimicrobial Advice *ad hoc* Expert Group; AMEG is an *ad hoc* group established by the European Medicines Agency jointly under the Committee for Medicinal Products for Veterinary Use (CVMP) and the Committee for Medicinal Products for Human Use (CHMP). The AMEG was set up to provide guidance on the impact on public health and animal health of the use of antibiotics in animals, and on the measures to manage the possible risk to humans.
ATC vet	Anatomical Therapeutic Chemical classification system for veterinary medicinal products
AHDB	Agriculture and Horticulture Development Board
Antibiotic	A large group of antibacterial substances capable of destroying or inhibiting the growth of bacteria, used for treatment or prevention of bacterial infections.
Antimicrobial	Naturally occurring, semi-synthetic or synthetic substances that exhibit antimicrobial activity (kill or inhibit the growth of micro-organisms). Used for treatment or prevention of infections. Antimicrobials include antibacterials (antibiotics), antivirals, antifungals and antiprotozoals.
Antibiotic/antimicrobial resistance	The ability of a bacterium/micro-organism to grow or survive in the presence of an antibiotic at a concentration that is usually sufficient to inhibit or kill bacteria/micro-organisms of the same species.
BPC	British Poultry Council
Broiler	A broiler is any chicken that is bred and raised specifically for meat production
CBP	Clinical Break Point: relates the laboratory results to the likelihood of clinical treatment success or failure.
CHAWG	Cattle Health and Welfare Group

Critically Important Antibiotics	These are antibiotic classes, which are the sole or one of limited available therapies, to treat serious bacterial infections in people and are used to treat infections caused by bacteria that may be transmitted to humans from non-human sources or, bacteria that may acquire resistance genes from non-human sources (WHO definition).
HP-CIAs	Highest Priority Critically Important Antibiotics. In this report the classification according to the AMEG has been used; therefore the following classes of antibiotics are included under HP-CIAs: fluoroquinolones; third and fourth generation cephalosporins and polymyxins (including colistin).
Defra	Department for Environment, Food and Rural Affairs
ECOFF	Epidemiological cut-off value: represents the point at which bacteria have developed a higher level of resistance to an antibiotic than the background level of resistance that exists naturally for that bacterial species. A 'resistant' (or 'non-susceptible') ECOFF does not necessarily imply a level of resistance which would correspond with clinical treatment failure.
EMA	European Medicines Agency
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
Food-producing animal (species)	Animals used for food production including (but not limited to): cattle, sheep, pigs, poultry, salmon, trout and bees.
Injectable product	A product which is administered to animals via injection.
Intramammary product	A product which is administered into the udder.
Medicated feeding stuff	Feeding stuffs that contain a veterinary medicine and that are intended for feeding to animals without further processing.
MIC	Minimum Inhibitory Concentration: the lowest concentration of an antibiotic that inhibits visible growth of a bacterium after overnight incubation.
Non-food-producing animal (species)	Animals not reared for food. These are mainly companion animals including (but not limited to): dogs, cats, horses, small mammals, rabbits and birds.
PHWC	Pig Health and Welfare Council

Oral/water product	A product that is administered to animals orally. In this report this includes boluses, topdressings, powders, dissolvable powders, solutions.
Population Correction Unit (PCU)	This is a technical unit of measurement which is used to represent the estimated weight at treatment of livestock and slaughtered animals. It takes into account a country's animal population over a year, along with the estimated weight of each particular species at the time of treatment with antibiotics. 1 PCU = 1 kg of different categories of livestock and slaughtered animals.
Premix	Veterinary medicinal products intended for incorporation into medicated feeding stuffs.
Prodrug	Ingredient that after administration is metabolized (that is to say, converted within the body) into the pharmacologically active drug.
PSUR	Periodic Safety Update Report. Pharmacovigilance documents submitted by marketing authorisation holders (MAHs) at defined time points post-authorisation. These documents are intended to provide a safety update resulting in an evaluation of impact of the reports on the risk-benefit of a medicinal product.
TRACES	The 'TRAde Control and Expert System' (TRACES) is the European Commission's online management tool for all sanitary requirements on intra-EU trade and importation of animals, semen and embryo, food, feed and plants.
VMD	Veterinary Medicines Directorate, an Executive Agency of the Department for Environment, Food and Rural Affairs (Defra).
WHO	World Health Organization

Annex B: Descriptions of resistance levels

Table A1: Descriptions of percentage resistance levels referenced in this report (Chapters 3 and 4)[45]

Description of resistance level	Equivalent percentage resistance range
Rare	<0.1%
Very low	0.1% to 1%
Low	>1% to 10%
Moderate	>10% to 20%
High	>20% to 50%
Very high	>50% to 70%
Extremely high	>70%

[45] Annex A of European Union Summary Report on Antimicrobial Resistance in Zoonotic and Indicator Bacteria from Humans, Animals and Food in 2018/2019 | Zenodo

Annex C: List of figures

Annex D: List of tables

Annex E: Data background and limitations

Antibiotic sales data

- Sales data do not permit accurate analysis of antibiotic consumption by animal species or production category. Some formulations of antibiotics are authorised with indications for use in more than one species, for example pigs and poultry. It is not possible to ascertain from sales data in which species the product was used.
- A given quantity of antibiotic may represent many doses in small animals or few doses in large animals. It is not possible to predict the number of doses represented by the quantity sold.
- Changes in quantities of veterinary antibiotics sold should be considered in parallel with changes in the UK animal population over the corresponding time period. The populations of animal species are an important denominator and may vary quite markedly from year to year depending on market conditions for animal derived food. Similarly variations in the size of the animals being treated should be taken into consideration as larger animals will require a larger relative quantity of antibiotics over a treatment period.
- To try and address the variation in animal populations and demographics, over time and between countries, the ESVAC project has developed a Population Correction Unit (PCU), a calculation that estimates the weight of the animal (or group of animals) receiving an antibiotic at the most likely time of administration. This unit is now used across EU Member States and is currently the best approximation of consumption. We have used this form of analysis in this report.
- Sales data in general over-estimate use, as not all antibiotics sold will be used. There is natural wastage resulting from pack sizes that do not meet dose need, and from drug expiry. In addition, a product could be sold one year and used, for example, the next year.
- Some products may be sold to UK feed mills for inclusion in feed which is then exported outside of the UK; currently there is no method for separating these sales from the total UK sales data, resulting in an over-estimate of use in UK feed.
- Some products may be imported into the UK on a Special Import Certificate; currently there is no method for including these data in the total UK sales data, resulting in an under-estimate of use in the UK.
- Medication sold for use in humans may be used in animals under certain circumstances, according to the prescribing Cascade; figures on such use are not included in the data presented. Further information on Cascade prescribing can be found in section S1.4 of the supplementary material.

Resistance data, harmonised monitoring scheme

- The sampling size and strategy are designed to provide a sample which is representative of the wider population for each combination of bacteria and animal species.
- The organisms monitored such as *Salmonella* spp. and *E. coli*, are of direct relevance to human health. Antibiotics are considered HP-CIAs if they are within "Category B" in the Antimicrobial Expert Group (AMEG) report[46]; these have been included in the panel of antibiotics against which these organisms are tested. These include third and fourth generation cephalosporins and fluoroquinolones.
- The sampling methodology used is standardised and harmonised to produce comparable and robust susceptibility data for a representative proportion of food-producing animals and food products. However, pigs and poultry are monitored on alternating years, therefore not providing annual data.
- EUCAST human clinical break points (CBPs) and epidemiological cut-off values (ECOFFs) and are used to interpret susceptibility to antibiotics. This will enable the comparison of animal resistance data with similar data generated for human health, within the UK. Minimum inhibitory concentrations (MICs) are also recorded and will enable any future changes in CBPs or ECOFFs to be taken into account.
- It should be noted that when using selective culture methods, the occurrence of ESBL-, AmpC- or carbapenemase-producing *E. coli* is assessed with much greater sensitivity than when using non-selective culture methods. The difference is most likely explained by the fact that the population of ESBL-, AmpC- or carbapenemase-producing *E. coli* may be a minority among the *E. coli* populations in the gut flora of these food-producing animals, so the probability of randomly picking a resistance phenotype from a non-selective agar plate is low for most samples tested. Therefore, these selective methods are not able to quantify the risk which these bacteria may potentially pose to human or animal health. Selective methods are used to detect low numbers of resistant *E. coli* which may be present as a minor component of the total flora.

Resistance data, clinical surveillance (including MIC testing of veterinary pathogens)

There are a number of limitations associated with the antibiotic resistance data and they should be borne in mind when interpreting results from the veterinary clinical surveillance programme. This is a biased population and cannot be considered to accurately reflect the bacterial populations present within the general animal population in the UK. To note, the respiratory veterinary pathogen samples that undergo MIC testing are the same of those that undergo disc diffusion testing in the clinical surveillance program. Therefore, the same sampling limitations as those listed for the clinical surveillance program apply here.

[46] AMEG 2018 - Categorisation of AMs (europa.eu)

Scanning surveillance limitations:

- Veterinary surgeons have the option to submit samples to private laboratories rather than Government laboratories/Veterinary Investigation Centres. The proportion of samples that Government laboratories test compared to other laboratories is not known, and therefore we cannot know how representative the samples processed by APHA, SRUC Veterinary Services and AFBI are of total diagnostic submissions.
- Furthermore, geographical proximity of a farm or veterinary practice to a Government diagnostic laboratory may have an impact on the submission rate of samples; clinical surveillance may therefore, naturally, over-represent the animal populations within certain geographical areas.
- Other factors can also influence the submission rate of samples to veterinary diagnostic laboratories. These can include for example the severity of disease, impact on production or the value of the animals involved.
- The clinical surveillance performed on chickens includes a range of types of bird (layers, broilers, breeders and others) as well as both commercial and backyard flocks. The occurrence of resistance can be influenced by a number of factors, including the types of chickens examined, degree of epidemic spread of resistant bacterial clones the emergence, dissemination and transfer of resistance determinants between and amongst bacteria as well as by the selective pressure exerted by the use of antibiotics.
- The levels of resistance demonstrated by the clinical surveillance isolates presented in this report may be higher than those seen in the wider bacterial populations present within animals in England and Wales. This is because samples from diseased animals may be submitted from animals that have been unresponsive to initial antibiotic therapy, and thus the isolates recovered may have already been exposed to antibiotic pressure(s).
- APHA does not provide a veterinary diagnostic service for companion animals. Therefore, bacteria from these animal groups are under-represented in this report.
- The veterinary clinical surveillance data detail the number of bacterial isolates that underwent sensitivity testing, but not the numbers of animals for which samples were submitted for examination. Several bacteria may have been cultured from an individual animal or from a group of animals on the same farm. This type of clustering is not accounted for in the report, though since only low numbers of bacteria are usually subjected to susceptibility testing from the same outbreak of disease, its importance is probably limited.
- The diagnostic tests performed on any sample received through the clinical surveillance programme are dependent on the individual case; that is to say, isolates of the same bacterial species are not always tested against the same panel of antibiotics. Therefore, if resistance is not detected in one isolate, it may not mean that resistance is not present, but that it was not tested for. This is especially true of commensal organisms.
- Criteria for the susceptibility testing of some veterinary pathogens are not well-established; this document presents the data which have been collected and

acknowledges their limitations and shortcomings. Resistances of particular importance or significance are wherever possible subject to confirmatory testing. The disc diffusion test can be regarded as a screening test, enabling the rapid testing of large numbers of isolates in a cost-effective way and providing a timely result for veterinarians which can assist them in the selection of antimicrobial chemotherapy.

- The breakpoints used for determining resistance for isolates recovered under the veterinary clinical surveillance programme in GB are those recommended by BSAC. These breakpoints were originally determined for human medicine and their use in veterinary medicine is based on the assumption that the concentration of antibiotic at the site of infection is approximately the same in animals as it is in humans. Currently it is not known if this assumption is always correct, especially as different dosing regimens may be used in different animals and pharmacokinetics may vary between species. Currently, there is insufficient data available to apply animal species specific breakpoints to all organism/ antibiotic combinations where these are required.
- Different antibiotic susceptibility testing methodologies are used in England and Wales (APHA), Scotland (SRUC Veterinary Services), and Northern Ireland (AFBI). APHA and SRUC Veterinary Services use BSAC methodology to determine resistance/susceptibility based on human clinical breakpoints, whilst AFBI use CLSI. **In light of the different methodologies and breakpoints used, the amalgamated results of UK wide monitoring should be interpreted with caution.**
- For antibiotic susceptibility testing done by APHA, in the case of some veterinary drug-bug combinations a BSAC CBP value may not exist. In this case, APHA may have derived a tentative or suggested breakpoint or the historical veterinary breakpoint (zone size cut-off of resistant: ≤13 mm) may have been used to define resistance. The breakpoints used are set out in S4.1 of the supplementary material.

Laboratory methodology:

- *E. coli* isolates are not collected from routine samples from healthy livestock in Northern Ireland. Only clinical cases submitted for post-mortem investigation of colibacillosis, or similar diseases, will proceed to isolate pathogenic *E. coli*. AMR testing on *E. coli* isolates is mainly performed if samples are coming from less than 2-week old calves and animals with bovine mastitis.
- With regards to *E. coli*, each organisation in the UK sets their own criteria for testing AMR in *E. coli* from clinically sick animals and these criteria are not uniform. This is pertinent to highlight as the selection of isolates for susceptibility testing based on age or other criteria can influence the result obtained. Bacterial isolates recovered from young animals can often be more resistant than those from older animals and this relates to the fact that antibiotics are in general more frequently administered to young animals than to older animals.
- The disc diffusion methodology used to date for assessing susceptibility of veterinary pathogens from scanning surveillance are limited in the availability of

breakpoints for all relevant antibiotic and organism combinations. Assessing the susceptibility of veterinary pathogens by determination of the MIC using a standardised broth microdilution method provides a higher quality, internationally-recognised output, which is comparable with other monitoring programmes.

Annex F: Sources for reporting of sales data

To enable calculation of sold quantities of active ingredient of antibiotics, data were supplied by:

Marketing Authorisation Holders (MAHs)
It is mandatory for Marketing Authorisation Holders of manufactured antibiotics to provide the Veterinary Medicines Directorate with total annual sales data for each antibiotic product sold within the UK. Data were collected, verified and analysed to calculate the total weight, in tonnes, of each active ingredient sold for each antibiotic. Antibiotic sales data are collected as a proxy for antibiotic use.

Periodic Safety Update Reports (PSURs)
Sales figures submitted by MAHs in PSURs, for the purpose of Pharmacovigilance, were used to validate sales data published in this report. Where a PSUR had been returned to the VMD Pharmacovigilance team in the 2019 calendar year, reported sales were compared to those returned to the AMR team and any discrepancies were queried.

To enable calculation of the Population Correction Unit, data were supplied by:

Defra Statistics division
The live weights of animals slaughtered for food are calculated by Defra. The population numbers of food-producing animals were supplied by Defra via the ‘Agriculture in the UK’ report.

CEFAS
The annual live weight of fish at slaughter for the UK was supplied by CEFAS (Centre for Environment, Fisheries and Aquaculture Science).

TRACES
Import and export figures obtained from TRACES were provided by the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project and used in the calculation of the PCU.

Annex G: Contributors

Compiled by the Veterinary Medicines Directorate

Contributing Pharmaceutical Companies and Other Marketing Authorisation Holders

- Alfamed
- Alfasan Nederland B.V.
- Alivira Animal Health
- Andres Pintaluba S.A.
- Animalcare Limited
- aniMedica GmbH
- Audevard
- Avimedical B.V.
- Bela-Pharm GmbH & Co. KG
- Bimeda Animal Health Ltd
- Boehringer Ingelheim Animal Health Ltd
- Ceva Animal Health Ltd
- Ceva Sante Animale
- Chanelle Animal Health Ltd
- CP Pharma Handelsgesellschaft
- Cross Vetpharm Group Ltd
- Dechra Ltd
- Divasa Farmavic S.A.
- Dopharma Research B.V.
- ECO Animal Health
- Ecuphar N.V
- Ecuphar Veterinaria S.L.U.
- Eli Lilly & Company Ltd
- Elanco Europe Ltd
- Emdoka bvba
- Eurovet Animal Health B.V.
- Fatro S.P.A.
- Franklin Pharmaceuticals Ltd
- Global Vet Health S.L.
- Harkers Ltd
- Huvepharma N.V.
- Huvepharma SA
- I.C.F. Sri Industria Chimica Fine
- Industrial Veterinaria S.A.
- Intervet Ltd,
- Kela N.V.
- Kernfarm B.V.
- Krka Dd
- Labiana Life Sciences
- Laboratorios e Industrias IVEN S.A.
- Laboratorios Calier S.A.
- Laboratorios Hipra S.A.
- Laboratorios Karizoo S.A.
- Laboratorios Maymo S.A.
- Laboratorios SYVA S.A.U
- Lavet Pharmaceuticals Ltd
- Le Vet Beheer B.V.
- Livisto Int.'I.S.L
- Lohmann Pharma
- Nimrod Veterinary Products Ltd
- Norbrook Laboratories Ltd
- Orion Corporation
- Oropharma N.V.
- Pharmaq Ltd
- Pharmsure International Ltd
- Phibro Animal Health S.A.
- Richter Pharma AG
- SP Veterinaria S.A.
- TVM UK
- Univet Ltd
- Vetcare Oy
- Vétoquinol UK Ltd
- Vétoquinol SA
- Vetpharma Animal Health S.L.
- Virbac S.A.
- VMD N.V.
- Zoetis UK Ltd