HM Government

Third UK One Health Report

Joint report on antibiotic use, antibiotic sales, and antibiotic resistance

Published November 2023

This publication is available at www.gov.uk/government/publications.

Suggested citation: Veterinary Medicines Directorate (2023). *Third UK One Health Report - Joint report on antibiotic use, antibiotic sales and antibiotic resistance.* New Haw, Addlestone: Veterinary Medicines Directorate.

Front cover images credits: Getty; photographers Naumoid, Shaun Taylor, Environment Agency, UKHSA, Unsplash.com

Any enquiries or correspondence regarding this publication should be sent to us at: postmaster@vmd.gov.uk.

Published 29th November 2023

Lead Authors

Veterinary Medicines Directorate

- Fraser Broadfoot
- Tamsin Dewé
- Kitty Healey
- Anju Kirby
- Daisy Neale
- Alexandra Pickering
- Catrina Prince
- Max Renton
- Sophie Spalding

UK Health Security Agency

- Colin Brown
- Emma Carter
- Yung-Wai Chan
- Holly Fountain
- Sarah Gerver
- Gauri Godbole
- Rebecca Guy
- Hannah Higgins
- Jamie Rudman

Contributors

England and Wales

Veterinary Medicines Directorate

Aisling Glennie, Kate Agami, Naomi Bull, Jen Dow, Klara Saville, Sannah Malik

UK Health Security Agency

Alicia Demirjian, Diane Ashiru-Oredope, Katie Hopkins, Berit Muller-Pebody, Jordan Charlesworth, Mariyam Mirfenderesky, Bruno Pichon, Katherine Henderson, Nicola Naylor

Animal and Plant Health Agency

Chris Teale, Muna Anjum, Francesca Martelli, Roderick Card

Centre for Environment Fisheries and Aquaculture Science

David Verner-Jefferys
Edel Light

Environment Agency

Alwyn Hart
Ian Martin
Sarah Rustage
Wiebke Schmidt

Food Standards Agency

Bobby Kainth
Kirsten Stone
Paul Cook

IDEXX Laboratories Ltd

Larry Roberts
Matthew Jones

NationWide Laboratories

Stephen Steen

Natural Resource Wales

Thomaz Andrade

NHS Wales

Eleri Davies
Maggie Heginbothom
Robin Howe

The Mid Yorkshire Hospitals NHS Trust

Jayanta Sarma

University of Bristol

Fernando Sánchez-Vizcaíno

University of Liverpool

Alan D. Radford
David A. Singleton
Dorina Timofte
Genever Morgan
Gina L. Pinchbeck
Kate Baker
Nicola J. Williams
Pisut Pongchaikul
P-J.M Noble
Rebecca J. Bengtsson
Shirley Smith
Susan Dawson
Vanessa Schmidt

Welsh Government

Andrew Gill
Gavin Watkins
Geraint Hamer
Sian Timms

Welsh Lamb and Beef Producers

Don Thomas
Iestyn Jones

Scotland

Edinburgh Napier University

Donald Morrison

NHS Scotland

Dominic Mellor
Julie Wilson
Pauline Dunlop

Scotland's Rural College

Geoff Foster

Scottish Environment Protection Agency

Alan Hern | Brian O'Keefe | Dan Merckel
David Findlay | John Redshaw

Scottish Government

Vivienne McKinnon

Northern Ireland

Agri-Food and Bioscience Institute

Anegla Lahuerta-Marin | Catherine Couzens

Department of Agriculture, Environment and Rural Affairs Northern Ireland

Hilary Glasgow | Ray Thomas

Department of Health Northern Ireland

Alasdair MacInnes | Anna Morrison

Table of contents

Foreword

Antimicrobial resistance (AMR) continues to be a global threat to human and animal health. Bacteria carrying resistance genes are present in, and spread between, people, animals, food, and the environment and so a One Health approach to tackling AMR is needed, with all sectors working together to affect change. This third publication of the One Health Report brings together antibiotic resistance and consumption data from humans and animals, combined with data on antibiotic resistance in food and antimicrobial substances in the environment. The data presented here is from 2014 to 2019, the last calendar year before the COVID-19 pandemic, which resulted in delays to publication.

Much of this data has already been published separately. The value of this report is that by bringing together existing data, it allows us to better interpret the usage and resistance patterns across all sectors: humans, animals, food, and the environment. This in turn helps us better understand the drivers of AMR in different sectors and how they may interact, allowing us to prioritise the public health risks and areas for intervention. In this report, there are some new additions highlighting emerging areas of work in companion animals and the environment, which are needed to develop our understanding of AMR transmission between people and animals.

Tackling AMR has been a UK priority for many years and, since 2013, has taken a One Health approach through the UK's five-year strategy (2013 to 2018) and five-year national action plan (2019 to 2024) on AMR. A key goal has been to drive down inappropriate use of antibiotics across all sectors, which is crucial to slowing the development of antibiotic resistance. It is therefore encouraging that since this approach has been adopted, antibiotic use has fallen by 18% in people and 51% in animals between 2014 to 2019.

Certain antibiotics used in human and veterinary medicine are classed as highest-priority, critically important antibiotics (HP-CIAs) for use in people, and the animal sector has tried to minimise their use to ensure they continue to be effective for as long as possible in human medicine. It is reassuring to see the 74% reduction in the use of these HP-CIAs to a very low level in the animal health sector. This action, where one sector implements changes primarily intended for the benefit of another sector, crystallises the One Health approach.

In 2019, approximately one third of all UK antibiotic medicines were used in animals and two thirds in humans. It is interesting to see these figures side by side, particularly as there are some sources that report that antibiotic use in animals, globally, is higher than in people. That is clearly not the case in the UK. Since much animal antibiotic use is in farm animals, which are typically young animals, it is appropriate that use in animals is lower than use in people.

The picture of AMR across humans and animals is more complicated as it depends on bacterial species and host factors. However, the data shows some key similarities and differences between humans and animals which help us consider possible AMR transmission routes. For example, the similar patterns of AMR seen in *Campylobacter*

species from chickens, chicken meat and people are consistent with strong linkages through the food chain. This contrasts with AMR trends in *Salmonella* spp. and *E. coli,* which show much more variation, and suggest that in these bacteria, resistance in animals is not a major driver of AMR in people. We know there are also AMR transmission routes through the environment both from animals to people and from people to animals, but these are currently far less well understood and characterised. Nevertheless, understanding and tackling human-to-animal transmission routes – both direct and through the environment – is important for understanding the scope for animals to act as a reservoir of resistance passed to them from people.

As we develop the UK's next five-year action plan on AMR, this report provides an important reminder of the value of integrated surveillance. It is essential that we continue to expand our surveillance of AMR across people, animals, food, and the environment and enhance our capability to interpret the data, to inform interventions across the One Health spectrum that mitigate the threat of AMR.

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

Dr Colin Brown
Director (Interim): Clinical and Emerging Infections & Deputy Director: HCAI, Fungal, AMR, AMU, & Sepsis Division Clinical & Public Health Group

Introduction

This report presents data on antimicrobial use (AMU) in human and animal health, the presence of antibiotics in the natural environment, and antimicrobial resistance (AMR) in people, animals, food, and the environment across the UK from 2018 to 2019.

What is AMR?

AMR refers to the ability of any microbes (bacteria, as well as viruses, fungi, and protozoa) to resist treatment with drugs designed to kill them or stop their growth. This is a problem wherever these drugs are needed to control disease. Antibiotics are medicines used to specifically treat or prevent bacterial infections, and antibiotic resistance occurs when bacteria develop the ability to resist treatment with antibiotics. This report focuses almost exclusively on antibiotic resistance (though there are other antimicrobial agents used to treat viruses, fungi and parasites), and so the term 'AMR' is used interchangeably with 'antibiotic resistance' unless otherwise indicated.

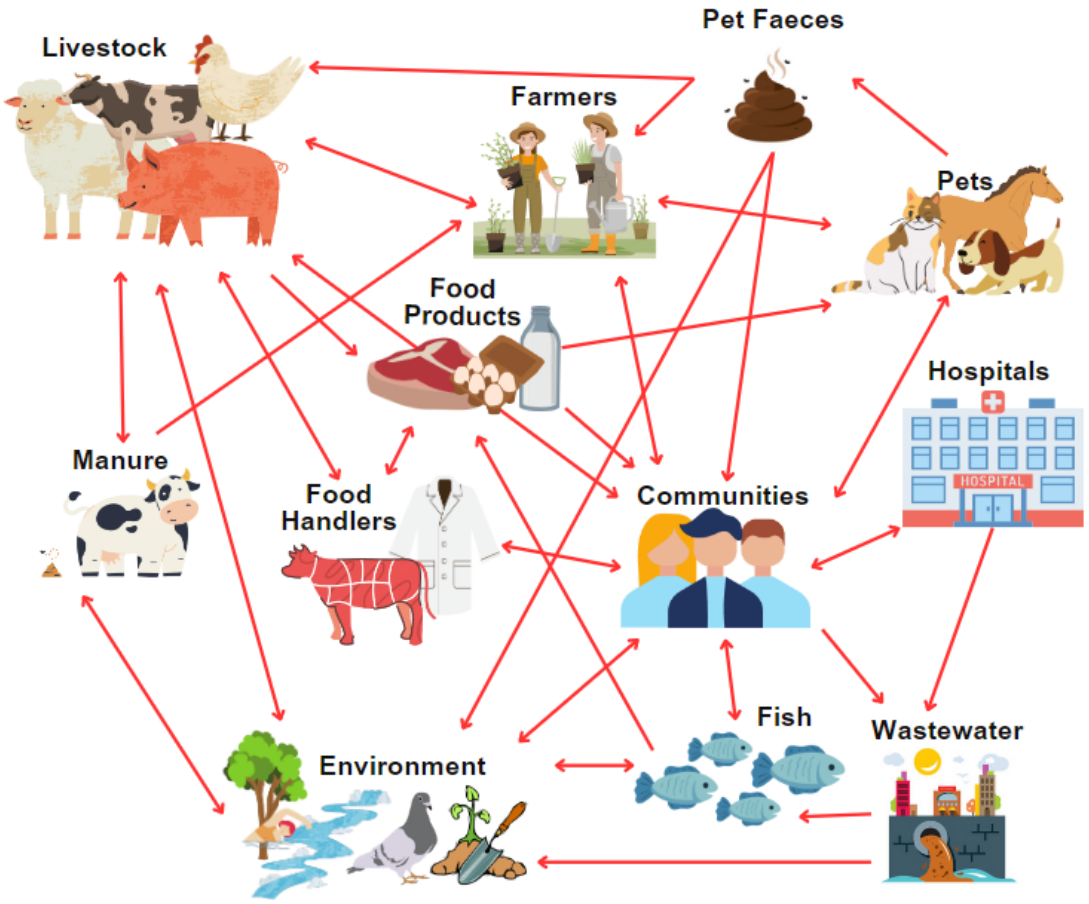
Bacteria can develop resistance through genetic mutation or transfer of resistance genes from other bacteria. Antibiotic resistance can occur naturally, however, exposing bacteria to antibiotics (when they are used in humans and animals, or are present in environments such as wastewater) creates a selection pressure that favours resistant bacteria. This selection pressure increases the rate at which antibiotic resistance develops and spreads and can even lead to multi-drug resistant (MDR) bacteria, which are resistant to multiple antibiotic treatments. Some bacteria are becoming totally-drug resistance, meaning there are no available treatment options). Antibiotic resistance genes are spread when bacteria reproduce but can also be transferred directly to different bacterial strains or species.

What is 'One Health' and why does it include AMR?

One Health is an integrated, unifying approach that aims to sustainably balance and optimize the health of people, animals, and ecosystems. It recognizes the health of humans, domestic and wild animals, plants, and the wider environment are closely linked and inter-dependent (**Figure 1**).

AMR epitomises a One Health issue because bacteria carrying resistant genes are present in people, animals, food, and the environment. Recognising the interconnectedness of these domains is key to understanding the development, transmission, and persistence of AMR. For example, resistance genes in bacteria excreted from the human gut end up in sewage, which comes into contact with the natural environment. From here, they can be transmitted to other people or animals via water courses or wild birds. Resistant bacteria in animals can enter the food chain; resistance can also spread from animals to people, or from people to animals, through direct contact, for example via companion animals, veterinary practices, or animal husbandry. Resistance genes can also transfer from commensal bacteria (those that are part of the normal gut flora) to pathogens that cause disease.

Figure 1: Potential One Health transmission pathways of antimicrobial resistance.



What kind of surveillance do we do for AMR in the UK and why?

Because antibiotic use is such a strong driver of AMR, it is important to understand which antibiotics are being used, where, why, and for how long. Measuring and monitoring the consumption of antibiotics in the UK has several benefits. It enables identification of antibiotic consumption trends and risk factors, allows us to assess the impact of interventions to encourage appropriate use, and facilitates comparison between settings and countries. Additionally, it allows prescribers (human healthcare professionals and veterinary surgeons) and users of antibiotics (such as farmers) to benchmark their consumption against others, which can optimise antibiotic use. Antibiotic consumption data is available for both human and animal health sectors in the UK. There are currently no antibiotics authorised as plant protection products in the UK, effectively prohibiting their use. Antifungal products are used on UK plants, and can contribute to antifungal resistance, but this is not the focus of this report.

Equally, surveillance is essential to measure the presence of AMR in the UK and to help understand the transmission and interactions of AMR in humans, animals, food, and the environment. Across the UK, representative surveillance of AMR in indicator organisms and foodborne pathogens in livestock, and their meat, is conducted every year. This allows us to monitor the background level of AMR in major food-producing animal species and evaluate the risks to consumers, identify trends, and assess the impact of interventions. Surveillance of AMR in human clinical patients is different, as it largely focuses on measuring AMR in bacteria causing clinical disease or colonising patients in healthcare settings and is thus

representative of a select demographic (people accessing care for ill health), rather than the general UK population.

There are some challenges to bringing together data from different sectors and disparate surveillance programmes: AMU data requires settling on a suitable metric that is meaningful in both human and veterinary medicine, including choice of antibiotics; and AMR results from animal and food sectors cannot at present be directly compared to human data, due to differences in the sampling and testing methodologies.

Why are we publishing this report?

The complexities of AMR evolution and transmission mean that AMR is a problem that cannot be addressed in isolation within individual sectors. This report is intended to promote One Health thinking by global veterinary and public health professionals, policymakers, academics, and other interested parties. In particular, we would like to encourage specialist readers to think outside of their own individual sector and engage with partners in other areas.

What's in this report?

In the Third UK One Health Report, we are bringing together antibiotic consumption (**Chapter 1**) and antibiotic resistance (**Chapter 2**) surveillance data from animal, food, and human sectors, from all four nations of the UK, in a new way. Most of these results have already been published separately for individual sectors, but by presenting them together in this report, we facilitate comparisons between the different settings. We also highlight new AMR research and monitoring results in two emerging areas: the environment (**Chapter 3**) and companion animals (dogs, cats, and horses, **Chapter 4**).

The data presented in **Chapter 1** to **Chapter 3** stretch from 2014, our baseline year, to 2019, the last calendar year before the COVID-19 pandemic. AMU and AMR data from 2020 onwards will be presented in the next AMR One Health Report. This report also contains updates on governmental and stakeholder efforts to contain and control AMR between 2019 and 2023, many of which are ongoing. Finally, **Chapter 5** includes details of stewardship initiatives, new surveillance activities, and our cross-government system for responding to AMR threats. A glossary of the terms used throughout the report can be found in **Annex A**.

Table 1: Descriptions of percentage resistance levels referenced in this report using the EFSA definitions.

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%

Table 2: Antibiotics referred to throughout the report grouped by antibiotic class.

Antibiotic class	Antibiotic
Aminoglycosides	Gentamicin, kanamycin, neomycin
Amphenicols	Florfenicol
Beta-lactams: Third-generation cephalosporins	Cefotaxime, ceftazidime, cefovecin
Beta-lactams: Carbapenems	Ertapenem, meropenem
Beta-lactams: Penicillins	Amoxicillin, amoxicillin/clavulanate, ampicillin
Glycylcyclines	Tigecycline
Lincosamide	Lincomycin, clindamycin,
Macrolides	Azithromycin, clarithromycin, erythromycin, spiramycin, tylosin
Polymyxins	Colistin
Quinolones	Ciprofloxacin, enrofloxacin, marbofloxacin
Tetracyclines	Doxycycline, oxytetracycline, tetracycline
Trimethoprim/sulphonamides	Sulfamethoxazole, trimethoprim

Chapter 1: Antibiotic consumption

What's in this chapter?

Antibiotic use is the major driver of antimicrobial resistance (AMR). This chapter presents the total, and population-adjusted antibiotic consumption across and between the human and animal health sectors in the United Kingdom between 2014 and 2019. It also presents antibiotic consumption broken down into different animal and human health sub-sectors.

Classes of antibiotics vary in the proportions in which they are used in human medicine and veterinary medicine. Data on antibiotic consumption by class in both the human and food-producing animal sectors are therefore also presented.

Background

Antibiotics used in animals in the UK must be prescribed by a veterinary surgeon. The use of antibiotics in livestock feed for growth promotion has been illegal in the UK since 2006. Most antibiotics administered to people need to be prescribed by a qualified health professional, such as a doctor or dentist, or certain qualified prescribing nurses and pharmacists. For humans, certain antibiotics are available to purchase over the counter, for example in topical preparations. The largest percentage of antibiotics used in humans are prescribed in primary care settings, such as by general practitioners (GPs), rather than in hospitals (secondary or tertiary care settings). The relative proportion of antibiotic classes used will also vary between settings in human and veterinary medicine.

Measuring antibiotic consumption

Monitoring the consumption of antibiotics gives us an indication of the strength of selection pressure on AMR. It also informs the development of targeted interventions to reduce the use of unnecessary antibiotics and allows progress to be monitored.

Consumption data may be expressed using different technical units of measurements and at varying level of granularity. This means that when viewing human and animal consumption data together, it is important to use a metric that allows comparison of different species, such as tonnes or 'mg/kg'. The 'mg/kg' measurement presents the total volume of active ingredient consumed by weight, adjusted for the population at risk of treatment. This takes into consideration variations in bodyweight and size of animal and human populations over time. The resulting metric is milligrams (mg) of antibiotic active ingredient per population kilogram (kg). See **Annex B** for more detail on antibiotic consumption data collected and the metrics used.

Antibiotic class categorisation and highest-priority critically important antibiotics (HP-CIAs)

Antibiotics can be categorised according to the risk that their consumption in animals and humans presents to human health. The categorisation of antibiotics is informed by available scientific evidence and expert opinion and has several benefits. For example, it can help inform prescribing decisions, be a tool for the preparation of treatment guidelines, and can help prioritise interventions at local and national level. Human health and animal health sectors have developed similar but separate antibiotic use categorisation methods (see **Annex C** for details), which are informed by the likely public health risk of AMR arising from use within each sector.

Categorisation tools in human and animal health therefore prioritise different 'top-level' antibiotics as key targets of stewardship programmes and monitoring. In human health, these are termed 'Reserve' or the lower risk but important to monitor 'Watch' antibiotics under the 'AWaRE' categorisation. In animal health, higher risk antibiotic classes are the 'highest-priority critically important antibiotics (HP-CIAs)' according to the categorisation framework are published here.

This report presents the use in both humans and animals of antibiotics classed as HP-CIAs. We highlight the use of HP-CIAs because the effect on AMR in humans arising from their use in animals has been assessed from both a human and animal health perspective, in a 'One Health' way. The HP-CIAs are fluoroquinolones, third- and fourth-generation cephalosporins, and colistin. In humans, only polymyxins are on the 'Reserve' list, whilst third- and fourth-generation cephalosporins and fluroquinolones are on the lower risk 'Watch' list. It is therefore important to note that the HP-CIA use in the human sector is presented below for information purposes only and, is unlikely to be a useful indicator for the success of stewardship initiatives specific to the human health sector. In fact, one of the reasons for limiting HP-CIA use in animals is so that these antibiotic classes can be available if needed to treat serious human disease.

Antibiotic consumption in the UK, 2014 to 2019

Population-adjusted antibiotic consumption

Population-adjusted antibiotic consumption is a measure of antibiotic consumption that accounts for the variations in bodyweight and size of animal and human populations over time. It can be presented to understand antibiotic consumption within animal and human populations. Consumption data may be expressed using different technical units of measurements and at varying level of granularity. This means that when comparing human and animal consumption data, it is important to use a metric that allows comparison of different species, such as tonnes or mg/kg.

Between 2014 and 2019, the magnitude of the decrease in population-adjusted antibiotic consumption varied between years (**Figure 1.1A**) and overall, decreased by 51% in animals (from 62.3 mg/kg to 30.4 mg/kg) and 18% in humans (from 124.5 mg/kg to 102.7 mg/kg) (**Figure 1.1B**).

Figure 1.1A: Active ingredient adjusted for population size (mg/kg) of antibiotic consumption in animals and in humans, 2014 to 2019.

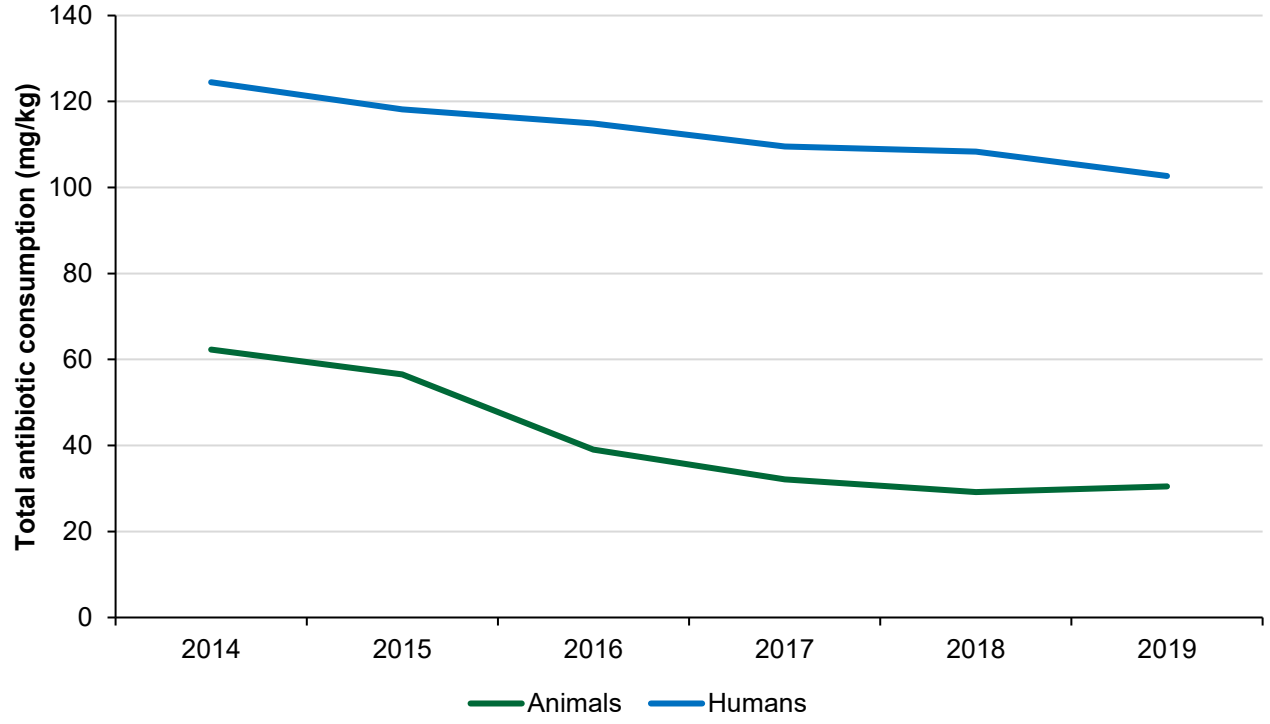
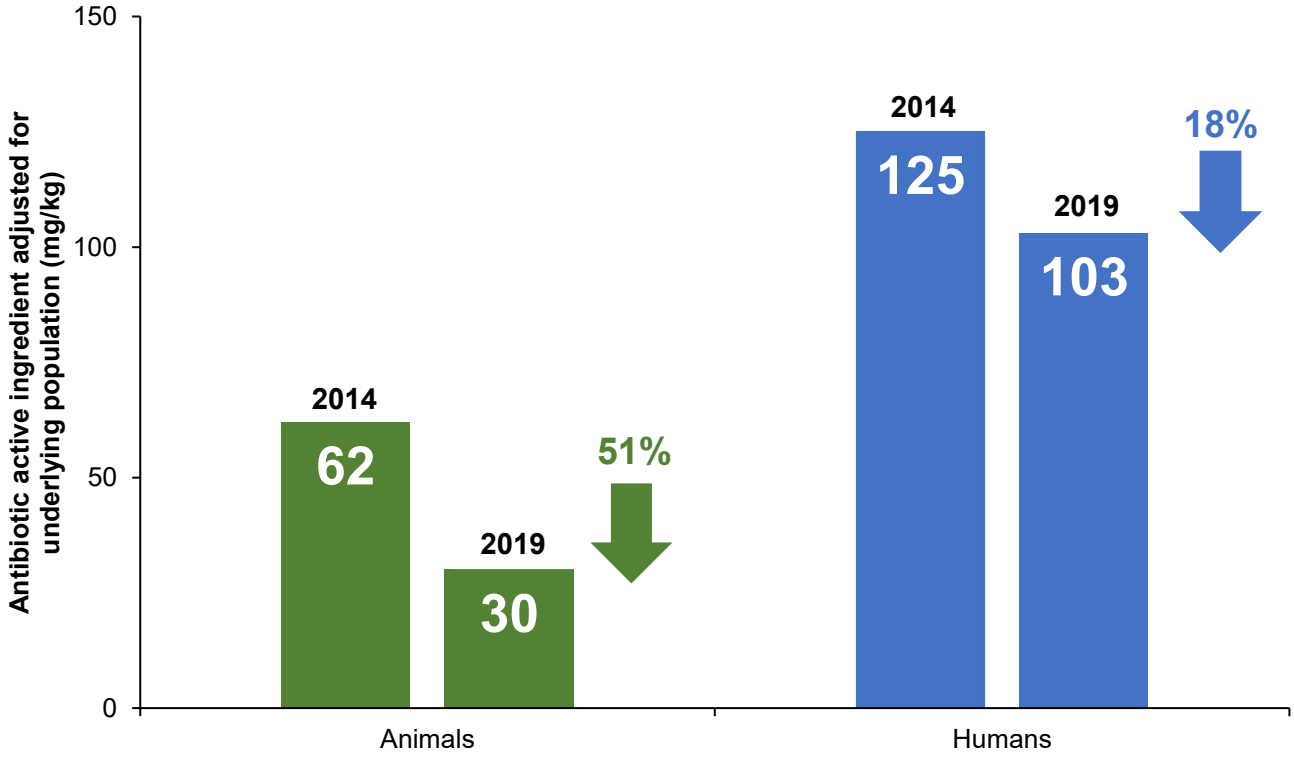
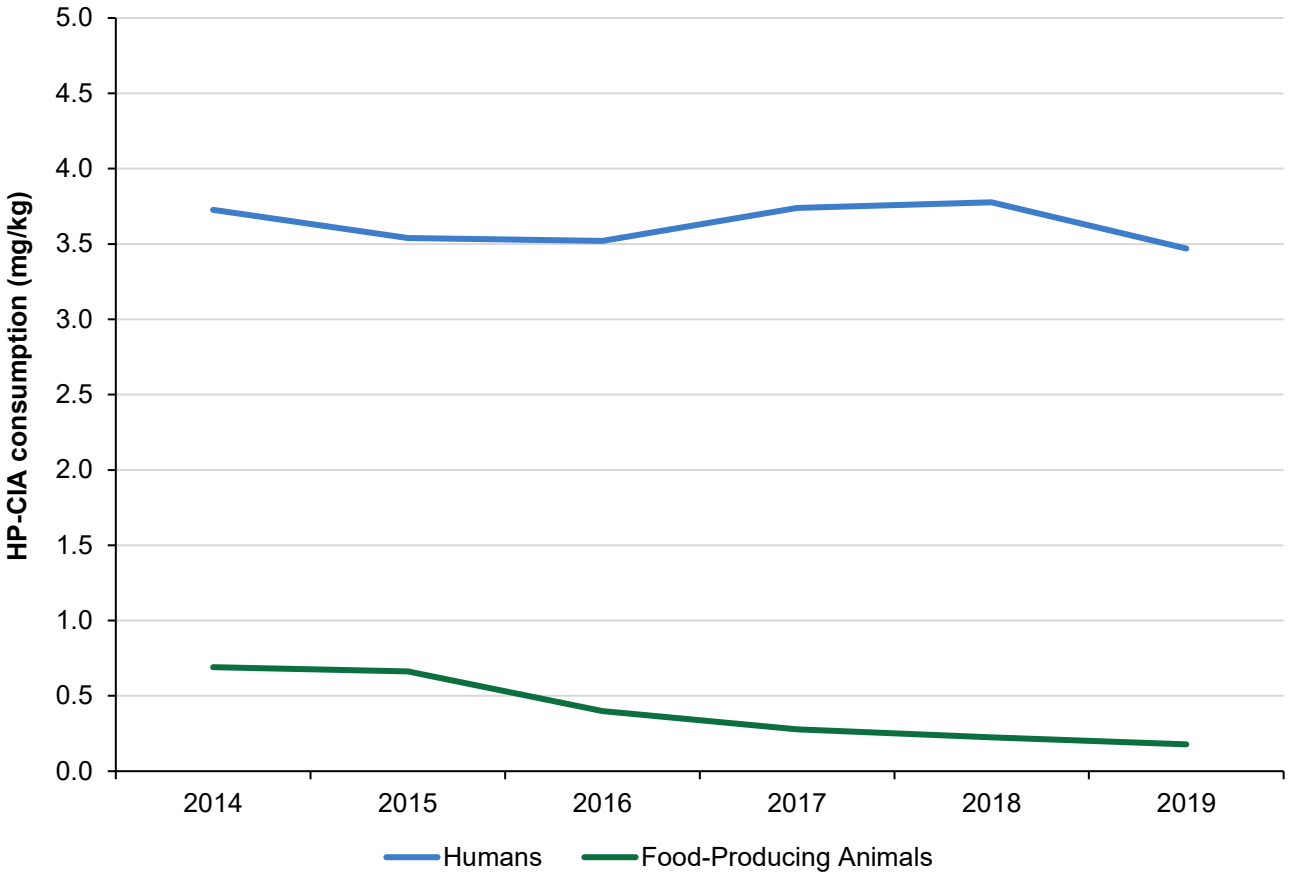


Figure 1.1B: Antibiotic active ingredient adjusted for underlying population (mg/kg) in animals and humans in 2014 and 2019.



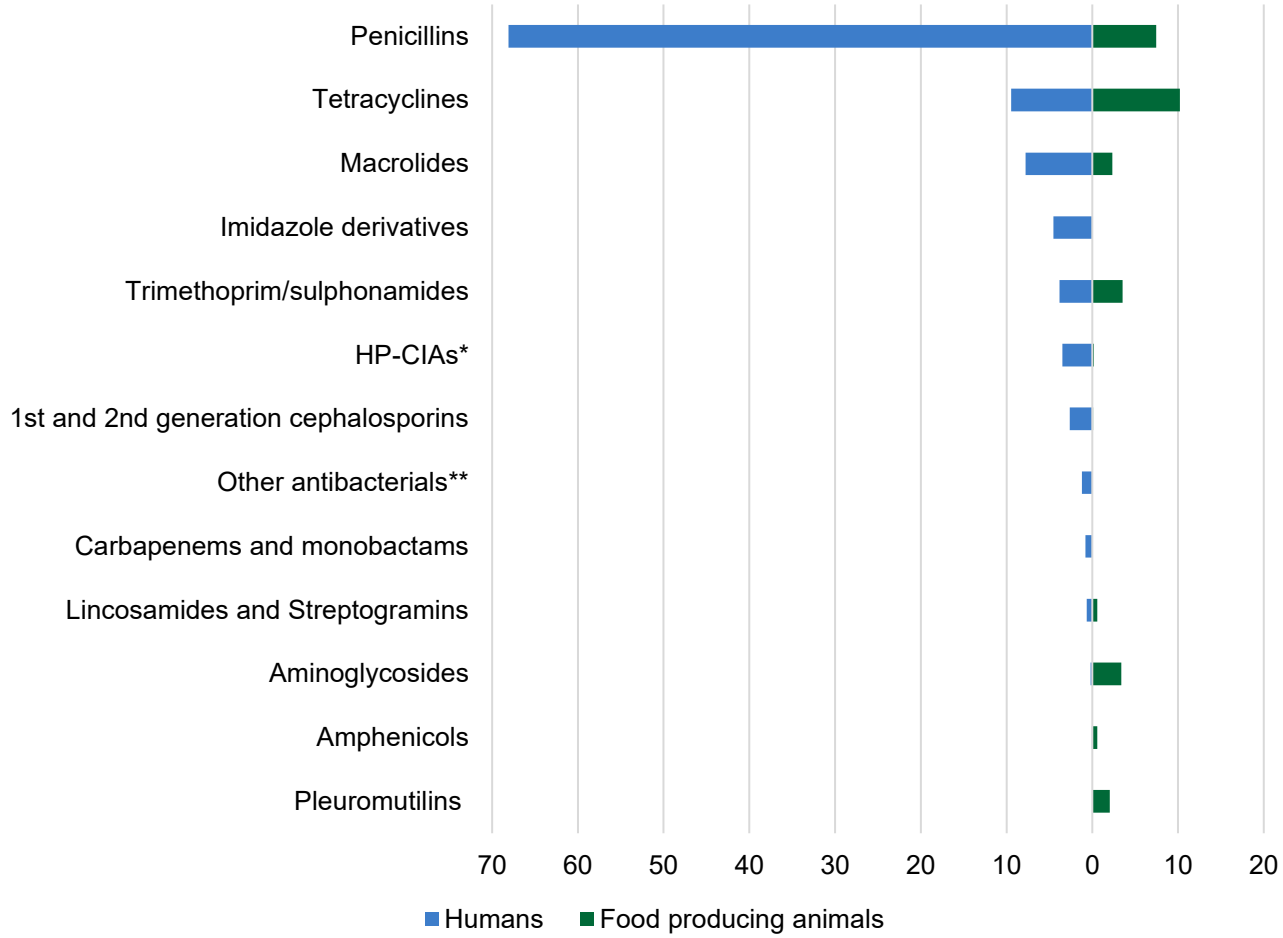
Between 2014 and 2019, HP-CIAs in animals decreased by 75% (from 0.67 mg/kg to 0.17 mg/kg) (**Figure 1.2**), reflecting the fact that a reduction in HP-CIAs has been a key focus in antibiotic stewardship initiatives in animals. Between 2014 and 2019, consumption of antibiotics classed as HP-CIAs in humans decreased by 7% (from 3.73 mg/kg to 3.47 mg/kg). A lesser HP-CIA decrease in humans is an unsurprising finding, because, in proportion to relative public health risk, the antibiotic classes for which stewardship efforts are most focussed in the human sector are different to those in animals and, as many HP-CIAs are already reserved for more serious infections in humans, may be harder to decrease.

Figure 1.2: Highest-priority critically important antibiotic (HP-CIA) consumption adjusted for population (mg/kg) in food-producing animals and in humans, 2014 to 2019.



The relative consumption of different antibiotic classes within human and food-producing animal health sectors in 2019 is shown in **Figure 1.3**. Penicillins (which includes amoxicillin and other penicillins) were the most prescribed antibiotic class, representing two thirds (66%) of total human antibiotic use. The next most consumed antibiotic classes in people were tetracyclines (9%) and macrolides (8%). In animals, tetracyclines were the most sold antibiotic class, representing 34% of total antibiotics sold in animals, followed by penicillins (24%), trimethoprim/sulphonamides (12%) and aminoglycosides (11%).

Figure 1.3: Antimicrobial classes consumed in humans and food-producing animals (mg/kg), 2019.



* Antibiotics are considered highest-priority critically important antibiotics (HP-CIAs) if they are within 'Category B' in the Antimicrobial Expert Group (AMEG) report, which includes third- and fourth-generation cephalosporins, polymyxins, and quinolones/fluoroquinolones.
** The class 'other antibacterials' includes: in animals - aminocoumarins; in humans - glycopeptide antibacterials, steroid antibacterials, nitrofuran derivatives, oral vancomycin and fidaxomicin, oral and rectal metronidazole and tinidazole, other cephalosporins and penems and other antibacterials.

Between 2014 and 2019, four antibiotic classes represented 86% of total (human and food-producing animal) consumption by weight of active ingredient and so these classes were selected for further analysis. **Figure 1.4** shows how the consumption of these antibiotic classes has varied between 2014 and 2019.

Overall, in food-producing animals, consumption of the four classes (penicillins, tetracyclines, macrolides, and trimethoprim/sulphonamides) reduced during this time period. This was a direct result of industry stewardship initiatives, including the British Poultry Council Stewardship (formed in 2011), the National Pig Association Pig Industry Antibiotic Stewardship Programme (launched in 2016) and the Responsible Use of Medicine in Agriculture Alliance (RUMA) Sector Targets (published in 2017). Similarly, consumption of these drugs in humans has also decreased, which is likely due to national initiatives such as the UK 5-Year Antimicrobial Resistance Strategy 2013 to 2018 of which one of the aims was to conserve and steward the effectiveness of antimicrobials in current use. See **Annex D** for more detail on the antibiotic consumption by antibiotic class for humans and animals

from 2014 to 2019.

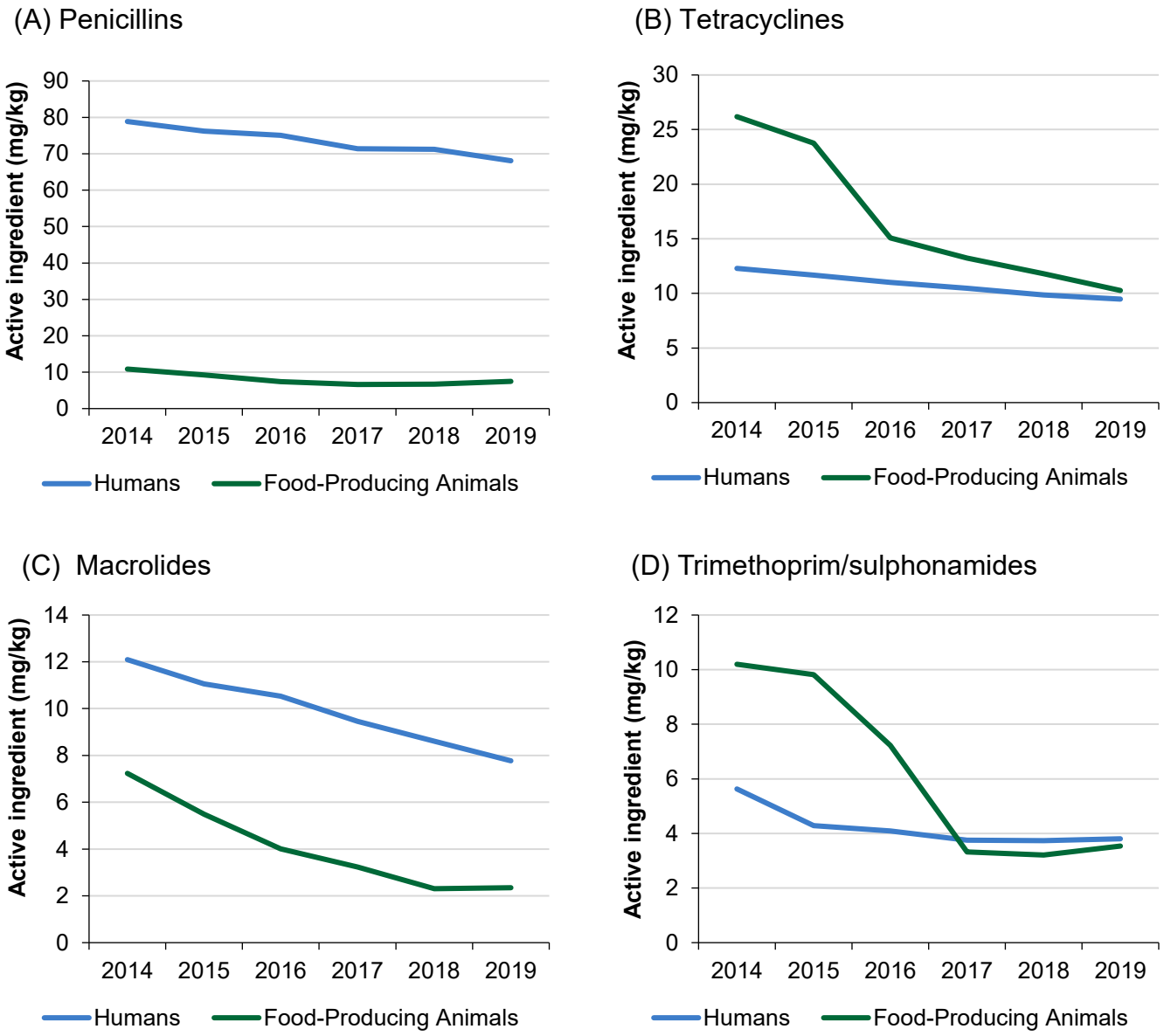
Penicillin consumption between 2014 to 2019 decreased in both humans and animals between 2014 and 2019 (**Figure 1.4A**). There was a gradual reduction (-14%) in human consumption of penicillins (from 78.9 mg/kg to 68.1 mg/kg) and a reduction (-35%) in animal consumption of penicillins (from 11.4 mg/kg to 7.5 mg/kg).

Consumption of tetracyclines, when adjusted for population, was roughly equivalent in the two sectors in 2019. Consumption of tetracyclines (**Figure 1.4B**) has reduced in humans by 23% (2.8 mg/kg) and in food-producing animals by 61% (15.8 mg/kg) between 2014 and 2019. In food-producing animals, sales of tetracyclines dramatically reduced between 2015 and 2016 by 37% (8.6 mg/kg). This decrease is largely due to a reduction of in-feed use in pigs and meat poultry.

Consumption of macrolides, when adjusted for population, was more than double in humans (7.8 mg/kg) than in food-producing animals (2.3 mg/kg) in 2019. Macrolide consumption (**Figure 1.4C**) has steadily decreased in both humans and in food-producing animals since 2014, by 36% (4.3 mg/kg) and 68% (4.9 mg/kg), respectively. In human health, there has been an increasing push for more appropriate prescribing to help combat resistance, especially for respiratory tract infections, where considerable efforts have been focused on reducing prescriptions for infections of presumed viral aetiology, which could help explain the steeper decrease of macrolide use.

The population-adjusted consumption of trimethoprim/sulphonamides was similar in people (3.8 mg/kg) and food-producing animals (3.5 mg/kg) in 2019. Trimethoprim/sulphonamide consumption (**Figure 1.4D**) in food-producing animals rapidly decreased by 67% (6.8 mg/kg) between 2014 and 2017, largely due to a reduction of in-feed use in pigs. Between 2017 and 2019, consumption remained relatively steady. Consumption in humans has fallen by 32% between 2014 and 2019 and is largely used for prophylaxis in immunocompromised patients with treatment mainly taking place in secondary care facilities.

Figure 1.4: The four most consumed antimicrobial classes across both humans and animals from 2014 to 2019, split by human and food-producing animals (mg/kg): (A) penicillins (B) tetracyclines (C) macrolides (D) trimethoprim/sulphonamides.



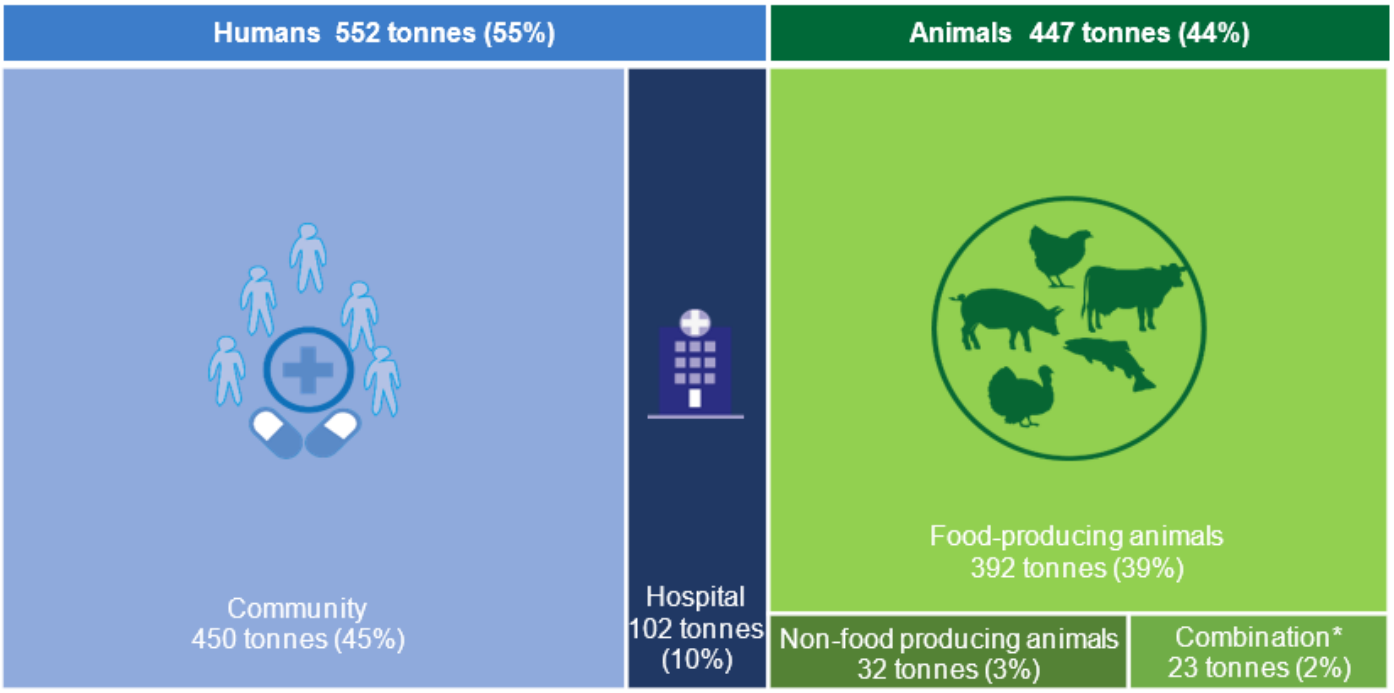
Antibiotic consumption by sector

The weight (tonnes) of antibiotics consumed can be presented to understand levels of consumption across human and animal sectors and sub-sectors.

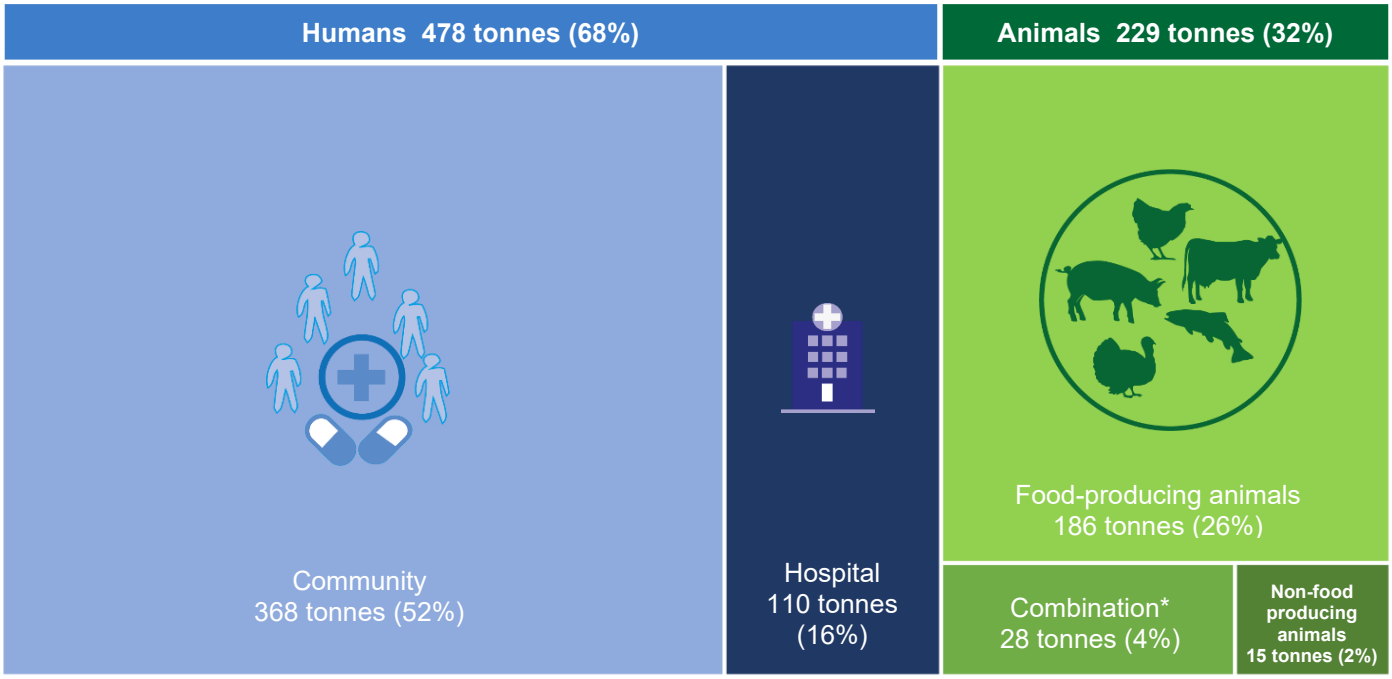
Between 2014 and 2019, the total antibiotic consumption by weight, across humans and animals, decreased by 28%, from 986.0 tonnes to 706.3 tonnes. Of this, the relative percentage consumed by the animal sector has decreased from 44% in 2014 to 32% in 2019 [see **Figure 1.5** In the human health sector, community consumption reduced by 18% (from 450 tonnes to 368 tonnes) in that time, whereas in-hospital consumption increased by 8% (from 102 to 110 tonnes)].

Figure 1.5: Percentage of active ingredient (tonnes) dispensed for humans and sold for use in all animal species in the UK during (A) 2014 and (B) 2019 by sector. Note each percentage figure has been rounded to the nearest integer and therefore totals may not be equal to 100%.

A) 2014



B) 2019



* Combination of food-producing and companion animals

Percentage of antibiotic classes consumed in the animal and human sectors, by total weight in tonnes

When looking at the percentage consumption in tonnes, between humans and food-producing animals, within each antibiotic class in 2019 (see **Annex D** for data presented graphically), the human health sector consumed all (100%) carbapenems and monobactams and 93% of HP-CIAs. The relative lower consumption of HP-CIAs in the food-producing animal sector (7%) reflects the target to restrict the use of HP-CIAs in animals to help retain their efficacy in human medicine. The human sector consumed 84% of penicillins and 93% those classed as 'other antibacterials' and approximately three quarters of first- and second- generation cephalosporins (76%); and around two thirds (68%) of macrolides. The animal sector accounted for all (100%) pleuromutilin consumption, and almost all amphenicol (98%) and aminoglycoside (96%) consumption. Within the classes tetracyclines, lincosamides and streptogramins, and trimethoprim/sulphonamides there was a more balanced percentage consumption across the human and the animal sector, with around 40% of these antibiotic classes consumed in the human sector, and around 60% consumed in the animal sector.

International picture

The UK contributes surveillance data to global databases to enable analysis and communication of information and ultimately to learn lessons and change practices in relation to antimicrobial use. Antibiotic use in animals is submitted to the World Organisation for Animal Health ANIMUSE database. UKHSA currently report human health data on AMR and AMU to the WHO via its Central Asian and European Surveillance of Antimicrobial Resistance network (CAESAR).

An overview of antibiotic consumption in food-producing animals for all participating European countries can be found in the annual European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) reports. Similarly, the European Surveillance of Antimicrobial Consumption Network (ESAC-Net) publishes annual reports on antimicrobial consumption data for the community and for the hospital sector provided by European Union (EU) Member States and two European Economic Area (EEA) countries. Caution is needed in interpreting this information as countries may vary in their method of data collection, and, for animals, in the type and size of production systems.
For people in EU Member States and two EEA countries in 2019, the combined rate of antibiotic consumption reported was 19.4 Daily Defined Doses (DDDs) per 1,000 inhabitants per day; this ranged between 9.5 and 34.1 for all countries. For 2019, the UK reported 18.2 DDDs per 1,000 inhabitants per day; in comparison with the other ESAC-Net reporting countries the UK was the 14th lowest of 30 countries within Europe. In the same year, the population-adjusted consumption of antibiotics in food-producing animals in the EU overall was 30.5 mg/kg with a range of between 2.3 mg/kg and 399.7 mg/kg between the 31 countries reported. The UK was the 7th lowest of the reporting countries.

Summary

Between 2014 and 2019 antibiotic consumption reduced by over one half (51%) in animals and by just under one fifth in humans (18%), and HP-CIA consumption in food-producing animals has reduced by 75%, accounting for 5% of total HP-CIA use in 2019. Combined, these reductions reflect the significant efforts across and within the UK human and animal sectors to improve responsible antimicrobial use. **Chapter 5** contains further details on responsible use initiatives in humans and animals, as well as stewardship initiatives in human health. The considerable achievements so far also highlight the value of collecting and collating antibiotic consumption data to show us how antibiotics are used and help to define targeted interventions to keep antibiotics working.

Continuing to collect more granular or detailed information on how antibiotics are used in different sectors is important as it allows more targeted interventions to be developed. Targeted interventions are generally more effective at optimising antibiotic use and tackling AMR and so the collection of more granular data is crucial to develop these for both the human and animal health sectors. For humans, the key ambition, with work underway, is to analyse and produce insights into patient-level prescribing data understanding the reason for treatment in both primary and secondary care settings and links with AMR detection. Current findings and planned activity are detailed annually in the ESPAUR report In England and SONAAR report in Scotland. In animals, a key collaborative focus will continue to be expanding the collection and collation of data for companion animal species and to all major livestock sectors. This will allow an improved understanding of use in specific species, enable evaluation of stewardship initiatives, and better evidence interpretation of AMR findings. Currently, most of the major livestock industries voluntarily collect and submit antibiotic use data to their industry body, which is then shared with the government in an anonymised, aggregated form, and published annually in the UK-VARSS report.

Chapter 2 - Antibiotic resistance

What's in this chapter?

Antimicrobial resistance (AMR) is found in many bacteria, including disease causing organisms found in animals and humans. Some AMR bacteria are specific to either human or animal hosts, whilst others can affect both humans and animals. This means that AMR can impact animal species as well as humans, individually. Routine surveillance of AMR in animals focuses on bacterial species that are relevant to both human and animal hosts, due to their relevance across sectors.

This chapter brings together data on AMR in key bacteria that are applicable across both human and animal species. These key bacteria are routinely monitored in healthy food-producing animals at slaughter, meat sold at retail, and human patients with clinical infection (and in some cases colonisation) attending healthcare settings across the UK. These bacteria are gastrointestinal organisms that can spread between animals and people and can cause disease: *Salmonella*, *Campylobacter* species (ssp.) and *Escherichia coli*. We also highlight AMR in other bacteria which are not routinely monitored across sectors but illustrate the importance of a One Health approach to AMR.

Background

Commensal bacteria are those that are present in the normal microflora of a host but have the capability to cause disease. *Salmonella* and *Campylobacter* spp. are commensal bacteria found in the gut of healthy animals. These bacteria are a major cause of foodborne disease in humans. *Campylobacter* spp. and *Salmonella* spp. were the two most-reported zoonotic diseases in Europe in 2019. In the UK, *Campylobacter* spp. are the leading cause of foodborne bacterial disease. The improper handling and preparation of raw chicken as well as the consumption of chicken are identified as important risk factors for *Campylobacter* infections. It is estimated that there are 500,000 human cases of campylobacteriosis in the UK annually, with *C. jejuni* accounting for approximately 90% of infections. *Campylobacter* infection usually causes self-limiting gastroenteritis in humans, although it is rarely associated with complications such as sepsis, and chronic carriage in immunocompromised individuals.

Escherichia coli is a commensal organism of the gastrointestinal tract (GIT); commonly carried in the GIT of healthy animals and people. There are some pathogenic strains which can cause gastrointestinal and other diseases in humans or animal species. In humans, *E. coli* is the principal cause of urinary tract infections (UTIs) and Gram-negative bloodstream infections (BSIs).

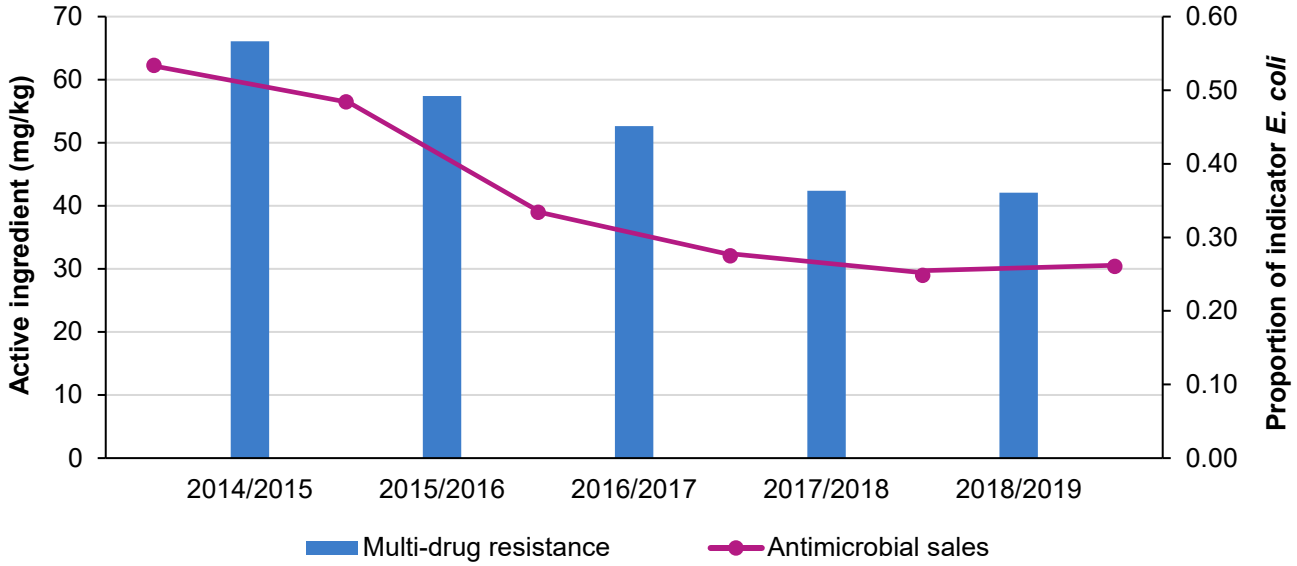
Measuring antibiotic resistance

Monitoring AMR in non-typhoidal *Salmonella* spp. and *Campylobacter* spp. in healthy animals, and in meat sold to consumers, helps us understand the levels of AMR in bacteria that could enter the food chain and cause disease in people. Monitoring AMR in *E. coli* provides us with an internationally recognised indicator of resistance in livestock and livestock products. Between 2014 and 2019, this data was obtained as part of the EU's Harmonised Monitoring Programme for AMR. This programme was originally developed to harmonise monitoring and reporting of AMR in the food chain across Europe and focused on major food-producing sectors. The panel of antibiotics tested spans different antibiotic classes and includes those of relevance to public health and epidemiological relevance, as well as those of increasing importance in the management of Gram-negative infections in people. AMR, often associated with infections, is also monitored in people generally through passive surveillance utilising patients' clinical samples.

The figures presented here show the results of AMR surveillance in 2014 to 2019 in *Salmonella* and *Campylobacter* spp. in chickens, chicken meat, and people; and AMR in *E. coli* from chickens, pigs, their meat, and people. Results from AMR monitoring in animals and food are not directly comparable to those presented for humans, due to differences in sampling and laboratory methodology (see **Annex F** for further details). Susceptibility of bacteria to antibiotics is assessed using either epidemiological cut-off values (ECOFF) or clinical break points (CBP). ECOFFs denote the highest minimum inhibitory concentration (MIC) value that results in susceptibility, whilst CBP denotes resistance associated with the likelihood that treatment would fail. Both ECOFF and CBP are used throughout this report, because CBPs are the favoured method in human medicine, as they related directly to patient treatment, whilst ECOFFs are used in surveillance schemes across animals, food and humans when no clinical correlates exist. Animal and food data is representative of the livestock population entering the food chain across the UK, whilst human data is collected largely through passive surveillance from diagnostic and reference laboratories that isolate bacteria from patients' clinical samples.

Despite these limitations, it is nonetheless useful to examine trends in resistance in animals, people, and food, as this may help identify links between and appropriate interventions across sectors. For example, the substantial reductions in antibiotic use achieved by the livestock sectors and veterinary profession are likely to be behind the decreasing levels of multi-drug resistance (MDR: resistance to three or more antibiotic classes) we are seeing (**Figure 2.1**).

Figure 2.1: Proportion of multi-drug resistance in *Escherichia coli* from broiler chickens, fattening turkeys and fattening pigs weighted by Population Correction Unit, averaged over two years against active ingredient adjusted for population (mg/kg) of antibiotics sold for use in food-producing animals.



Antibiotic resistance in the UK, 2014 to 2019

This section presents the results of AMR monitoring for pigs and poultry at slaughter, their meat, and in human patients, from 2014 until 2019, as available. This data is published on an annual basis for individual sectors in the UK-VARSS report (animals), FSA Retail Meat Survey (food) and EARS-Net reports (people).

We examine the presence of resistance in each of the key bacteria (*E. coli, Salmonella,* and *Campylobacter*). Results show the percentage of bacteria resistant to any antibiotic within each antibiotic class. The antibiotic classes shown are those that are commonly recorded across human and animal health settings and divided into highest-priority critically important antimicrobials (HP-CIAs) and non-HP-CIAs. Note that the data has been interpreted using the 2019 Antimicrobial Expert Group (AMEG) categories (**Annex C**).

Salmonella enterica ssp. *enterica*

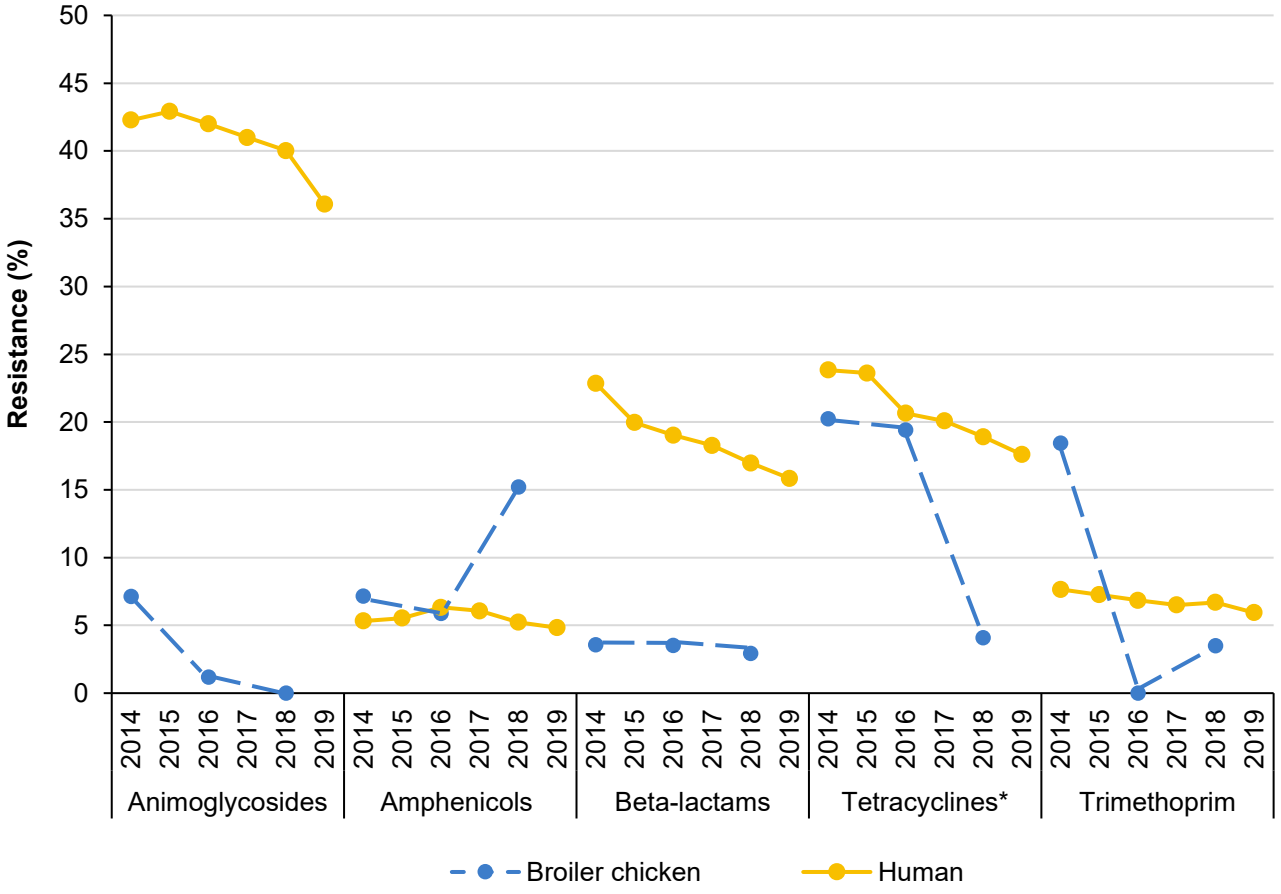
There is a large disparity in resistance prevalence in *Salmonella* spp. between humans and animals. In humans *Salmonella* spp. can cause food poisoning which is usually self-limiting and treated with fluids and rest, however if antibiotic treatment is needed, the most commonly prescribed treatments for Salmonellosis infections in humans are fluoroquinolones (e.g., ciprofloxacin) or third-generation cephalosporins (e.g., cefotaxime). Cases of Salmonellosis in animals are not treated with antibiotics. Non-typhoidal *Salmonella* contains many different serovars, which vary widely in their resistance levels. Different serovars also have different patterns of infection in individual host species and are affected by a number of factors unrelated to antibiotic use. In animals, these factors include biosecurity and the ability of different serovars to persist in the environment. In people, they include foreign travel, underlying health conditions, colonisation with multi-drug resistant (MDR: resistance to three or more antibiotic classes) bacteria, and environmental exposures.

Non-HP-CIAs

Resistance to non-HP-CIAs in *Salmonella* spp. from broiler chickens in 2014-2019 differed markedly from resistance in people (**Figure 2.2**). Resistance to all antibiotic classes shown, with the exception of amphenicols, was higher in *Salmonella* isolated from human patients than in chickens entering the food chain. The highest levels of resistance observed were to aminoglycosides, with 36% of non-typhoidal *Salmonella* isolated from people in 2019 being resistant to this antibiotic class.

Trends in AMR show some large reductions in resistance to tetracyclines (-79.7%) and trimethoprim (-81.1%) in broiler chickens between 2014 and 2018. Less dramatic, but noticeable, reductions in resistance to aminoglycosides (-14.7%), beta-lactams (-31.0%), tetracyclines (-26.1%), and trimethoprim (-23.4%) were recorded in *Salmonella* from human patients. The sharp decrease in tetracycline resistance in *Salmonella* isolated from chickens may be attributable to the significant reduction in tetracycline use, which fell by 61% between 2014 and 2018.

Figure 2.2: Resistance to non-highest-priority critically important antibiotics (non-HP-CIAs) in *Salmonella* spp. isolates from broiler chickens and humans.



Resistance to non-HP-CIAs in *Salmonella* spp. from broiler chicken flock National Control Programme (NCP) samples and humans (infections acquired within UK and abroad) through routine laboratory surveillance. Broiler chicken results were interpreted using EUCAST clinical breakpoints (CBPs) unless otherwise indicated and human results were inferred from presence of resistance determinants using whole genome sequencing (WGS) data.

* Broiler chicken data interpreted using EUCAST epidemiological cut-off (ECOFF) values

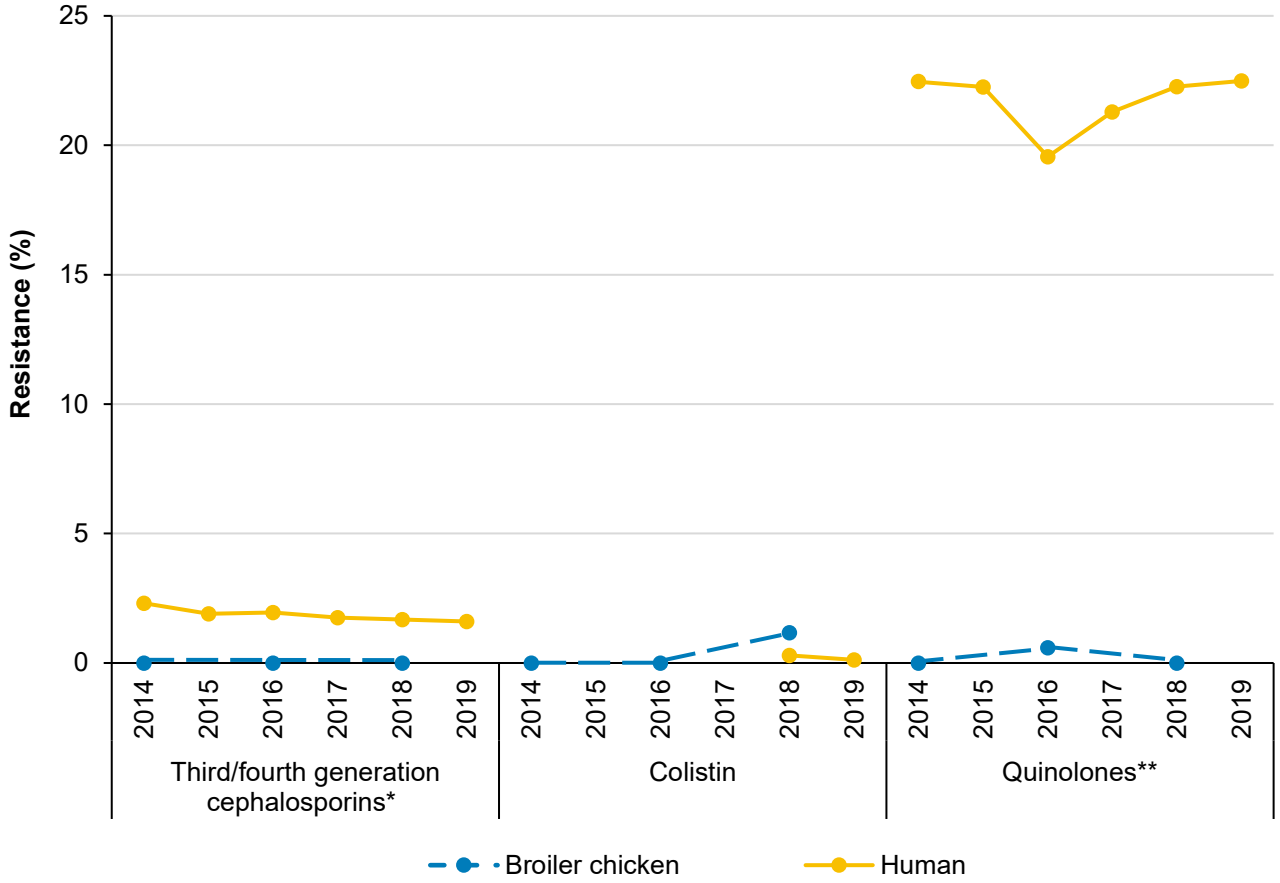
HP-CIAs

Resistance to HP-CIAs third- and fourth-generation cephalosporins, and colistin in *Salmonella* spp., was very low in both broiler chickens and human patients in 2018 and 2019 (<2% in all cases). Resistance to trimethoprim was low (<10%) for both humans and broiler chickens in 2018 and 2019, whilst resistance to beta-lactams varied; low in broiler chickens (2.9%) and moderate in humans (17.0%). Testing for colistin resistance in *Salmonella* from human patients is limited; in clinical practice testing is recommended where there is extensive drug resistance and complicated by the need for specialist testing using broth micro-dilution. There was no recorded resistance to fluoroquinolones (ciprofloxacin) in broiler chickens. Resistance figures for *Salmonella* in human patients were only available for the entire quinolone class, not fluoroquinolones specifically, and was 22.5% in 2019. Quinolones are an important treatment option for Salmonellosis in people.

Trends in *Salmonella* resistance to third- and fourth-generation cephalosporins and quinolones (in people) or fluoroquinolones (in chickens) appear flat (**Figure 2.3**). Trends for colistin resistance are difficult to interpret for both chickens and people due to limited data points.

Undetectable levels of resistance to third- and fourth-generation cephalosporins in meat poultry in *Salmonella* is consistent with these antibiotics not being used in this sector since 2012. The presence of colistin resistance in *Salmonella* spp. in broiler chickens in 2018 is attributable to two *S.* Enteritidis isolates recovered from healthy chickens on farms. This *Salmonella* serovar may show a degree of intrinsic, or naturally occurring, resistance to colistin, independent of antibiotic use. No colistin has been used in meat poultry since 2016.

Figure 2.3: Resistance to highest-priority critically important antibiotics (HP-CIAs) in *Salmonella* spp. isolates from broiler chickens and humans.



Resistance to HP-CIAs in *Salmonella* spp. isolated from broiler chicken flock National Control Programme (NCP) samples and humans through routine laboratory surveillance. Broiler chicken results were interpreted using EUCAST clinical breakpoints (CBPs) and human results were inferred from presence of resistance determinants using whole genome sequencing (WGS) data.
* For broiler chickens, only third-generation cephalosporin resistance is shown
** For broiler chickens, only ciprofloxacin resistance is shown

Campylobacter spp.

Campylobacter is the most common cause of food poisoning in humans in the UK. A vast majority of human *Campylobacter* infections are acquired from food, direct contact with animals or environmental cross-contamination. Antibiotic treatment is rarely indicated except in invasive infections or the immunocompromised. In cases that require treatment, antibiotics prescribed include macrolides such as erythromycin, and fluroquinolones such as ciprofloxacin.

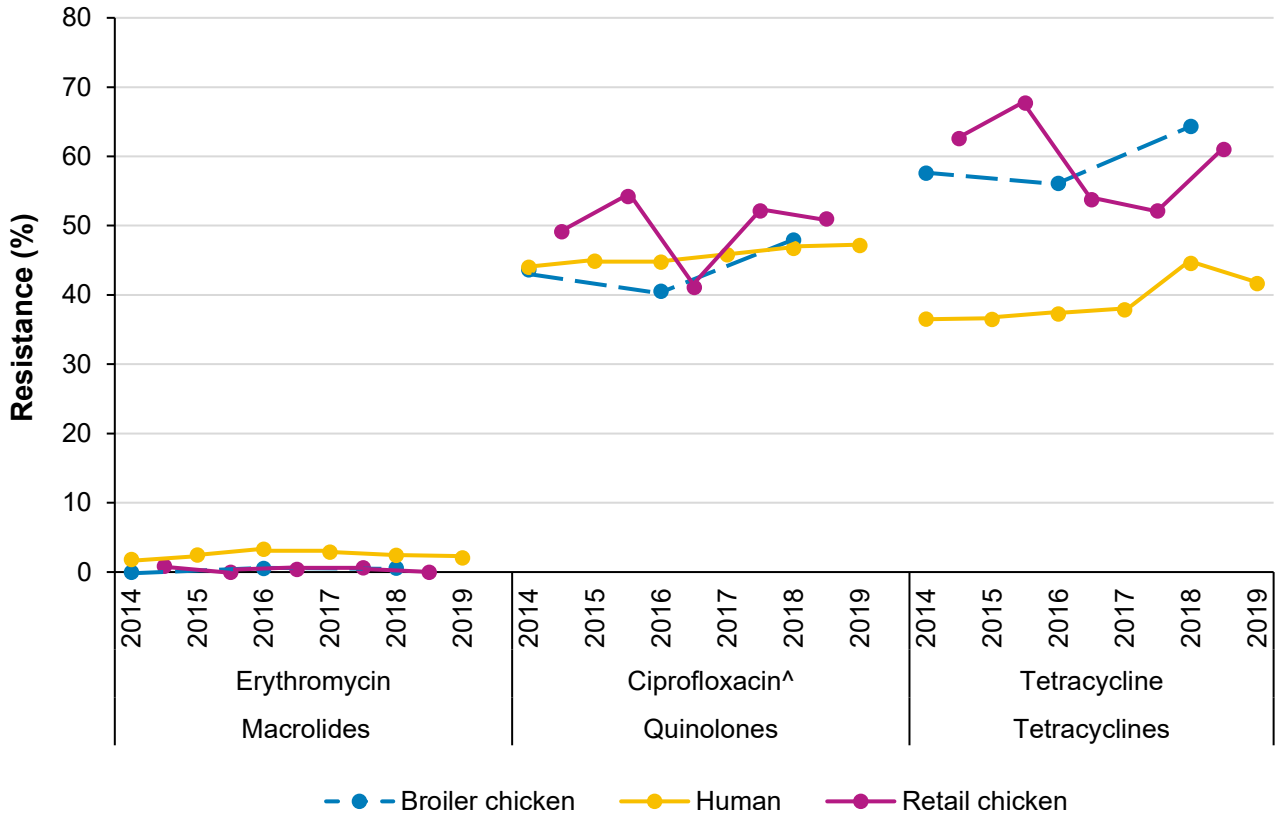
Results in this section focus on three antibiotics: erythromycin, tetracycline, and ciprofloxacin (an HP-CIA). Results include resistance in *C. jejuni* from broiler chickens, chicken meat sold at retail, and human patients, and in *C. coli* from chicken meat and human patients. AMR in *C. coli* from broiler chickens was not monitored during 2014-2019, in accordance with EU protocols.

Campylobacter jejuni

Resistance in *C. jejuni* is similar between broiler chickens, chicken meat, and human patients (**Figure 2.4**). Resistance to erythromycin is low (<3%) and very low in broiler chickens (<1%). Resistance to ciprofloxacin is high (>40%) across the broiler chicken and human sectors and very high (>50%) in chicken meat. Resistance to tetracycline was higher in both chickens (64.3%) and retail chicken meat (61.1%) than in human patients (41.7%) in 2019. Trends in resistance to erythromycin, tetracycline, and ciprofloxacin also appear broadly aligned between sectors. Resistance to ciprofloxacin appears to have gradually increased between 2014 and 2019.

Recent research shows that ciprofloxacin resistance in *C. jejuni* from chicken caecal samples, whole carcasses, and retail meat portions are not significantly different. Fluoroquinolone resistance has persisted in *C. jejuni* in broiler chickens in the UK, despite very low use of these antibiotics. Several other countries in Europe have reported persistently high resistance to fluoroquinolones in *Campylobacter* spp., and scientists have been working hard to understand why this is happening. Resistance to fluoroquinolones is primarily caused by mutations in the *gyrA* gene and can spread rapidly through bacterial reproduction. It is reassuring that resistance to erythromycin remains low in *C. jejuni,* due to the importance of this antibiotic as a treatment option in human medicine.

Figure 2.4: Resistance in *Campylobacter jejuni* isolates from broiler chickens, chicken meat and human patients to selected antibiotics (HP-CIAs and non-HP-CIAs).

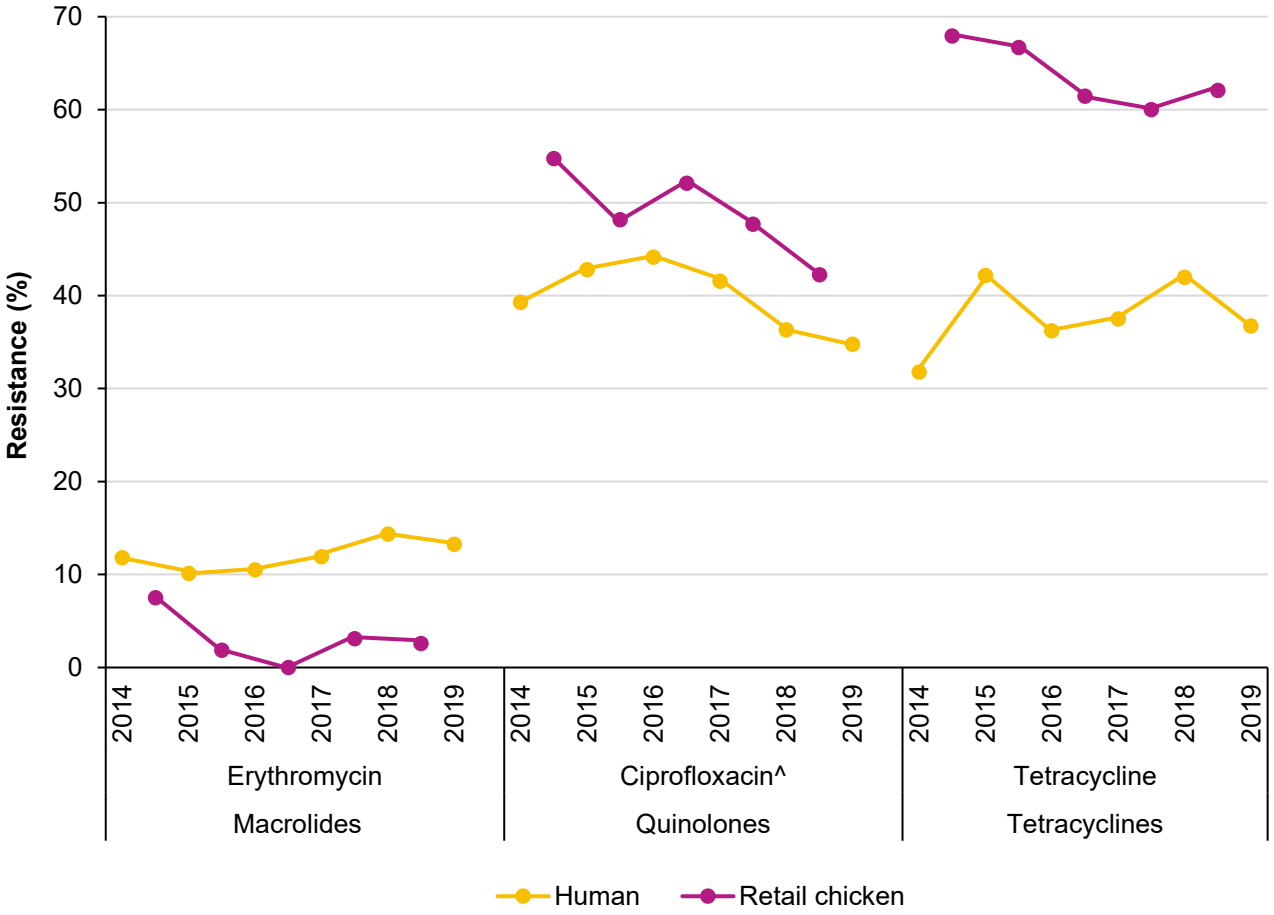


Resistance to highest-priority critically important antibiotics (HP-CIAs) and non-HP-CIAs in *Campylobacter jejuni* isolated from broiler chickens at slaughter, fresh whole retail chicken and humans through routine laboratory surveillance. Broiler chicken and human results were interpreted using EUCAST clinical breakpoints (CBPs). Retail chicken results were interpreted using EUCAST epidemiological cut-off (ECOFF) values from 2014 to 2018 and predicted from whole genome sequencing (WGS) data from 2018 to 2019.
^ HP-CIA

Campylobacter coli

Across all sectors, erythromycin resistance in *C. coli* was higher than in *C. jejuni*. Like in *C. jejuni,* similar levels of resistance to erythromycin and ciprofloxacin were recorded in *C. coli* from chicken meat sold at retail and human patients between 2014-2019 (**Figure 2.5**). However, resistance to erythromycin in *C. coli* tended to be higher in humans (13.3% in 2019) than in retail chicken meat (2.6% in 2018/2019), whereas resistance to tetracycline (62.1%) and ciprofloxacin (42.2%) were both higher in meat.

Figure 2.5: Resistance in *Campylobacter coli* isolates from chicken meat and human patients to selected antibiotics (HP-CIAs and non-HP-CIAs).



Resistance to highest-priority critically important antibiotics (HP-CIAs) and non-HP-CIAs in *Campylobacter coli* isolated from fresh whole retail chicken and humans through routine laboratory surveillance. Human results were interpreted using EUCAST clinical breakpoints (CBPs). Retail chicken results were interpreted using EUCAST epidemiological cut-off (ECOFF) values from 2014 to 2018 and predicted from whole genome sequencing (WGS) data from 2018 to 2019.
^ HP-CIA

In terms of trends, resistance to erythromycin in *C. coli* declined in retail chicken meat by 65.3% between 2014/2015 and 2018/2019, whereas it appears to have remained stable in people. Resistance to ciprofloxacin declined by 22.9% in *C. coli* isolated from chicken meat and 11.5% in those from human patients. Resistance to erythromycin in *C. coli* from human patients has remained stable despite usage reducing by 40.7% between 2013 and 2017, as treatment choices have moved towards other macrolides (clarithromycin and azithromycin), due to dosing issues and side effects.

Escherichia coli

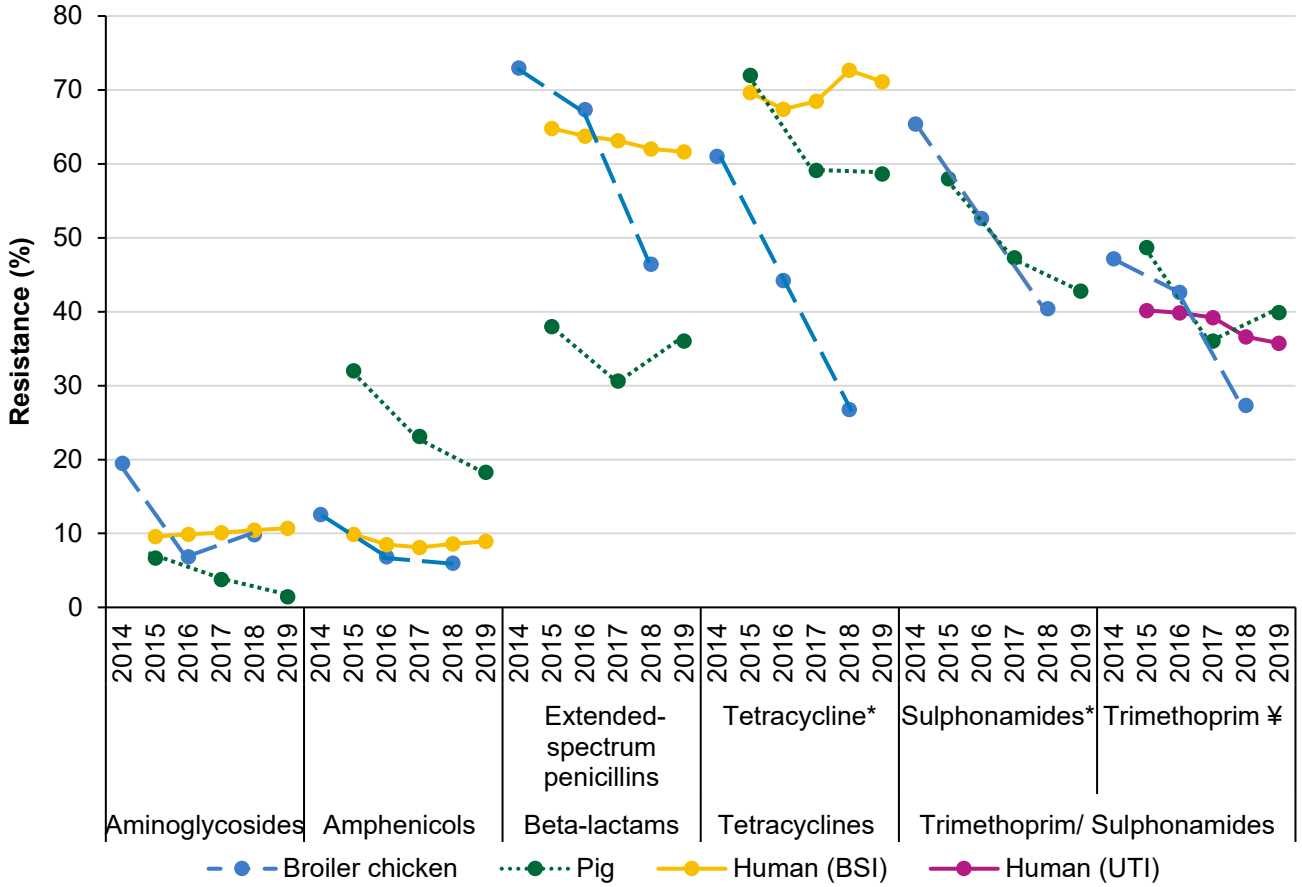
Non-HP-CIAs

Resistance to non-HP-CIAs in *E. coli* presents a complicated picture, with both levels and trends varying by antibiotic class, and between sectors (**Figure 2.6**). However, the highest levels of resistance in 2019 were recorded against the most used antibiotic classes (beta-lactams, tetracyclines, and trimethoprim-sulphonamides) in both veterinary and human medicine (**Figure 1.4**), and the levels of AMR in animals in 2019 was lower than, or similar to, those reported in people.

In terms of trends, resistance to non-HP-CIAs in *E. coli* isolated from human patients was mostly flat over 2014-2019, although downwards trends are observable for resistance to beta-lactams in BSIs (-4.3%), and to trimethoprim in UTIs (-11.2%). Resistance in *E. coli* from animals has decreased for all antibiotic classes over the same time period. Particularly dramatic reductions in *E. coli* resistant to non-HP-CIAs were observed in chickens, including a 56.1% reduction in tetracycline resistance, and a 36.4% reduction in beta-lactam resistance.

Some of these results mirror those seen in AMU data (**Chapter 1**). For example, trimethoprim is the second most used in-feed antibiotic in pigs, and is often used to treat UTIs in humans. Higher levels of resistance to amphenicols in pigs could be attributed to more of these antibiotics being used in animals; this class is very rarely used in humans, used only for topical preparations or very serious systemic infections. The decline in AMR in healthy pigs and chickens at slaughter is consistent with reductions in antibiotic consumption observed in livestock since 2014 (see UK-VARSS, **Chapter 2**). Conversely, some results are less closely related to AMU. For example, tetracycline use in human medicine has decreased by 23% (2.8 mg/kg) between 2014 and 2019, but resistance to the tetracycline class has remained stable over the same period.

Figure 2.6: Resistance to non-highest-priority critically important antibiotics (non-HP-CIAs) in *Escherichia coli* isolates from pigs, broiler chickens, and humans.



Resistance to non-HP-CIAs in *E. coli* isolated from the gut contents of healthy pigs and broiler chickens at slaughter, and human blood-stream infections (BSIs) and urinary tract infections (UTIs). Results are interpreted using EUCAST clinical breakpoints (CBPs) unless otherwise indicated.
* Interpretated using EUCAST epidemiological cut-off (ECOFF) values; human data are based on a testing rate of <20% specimens and are likely selecting for resistant results in both Tetracyclines and Sulphonamides.
¥ Trimethoprim testing in human BSI specimens is low, with only 40% *E. coli* tested in 2019. CBP is only available for uncomplicated UTI for *E. coli* and trimethoprim.

HP-CIAs

Resistance to HP-CIAs in *E. coli* isolated from gut contents of healthy pigs and chickens at slaughter between 2014 to 2019 was considerably lower than in those isolated from human BSIs; there is no systematic data available on *E. coli* carriage in healthy human gut contents, so these are not directly comparable.

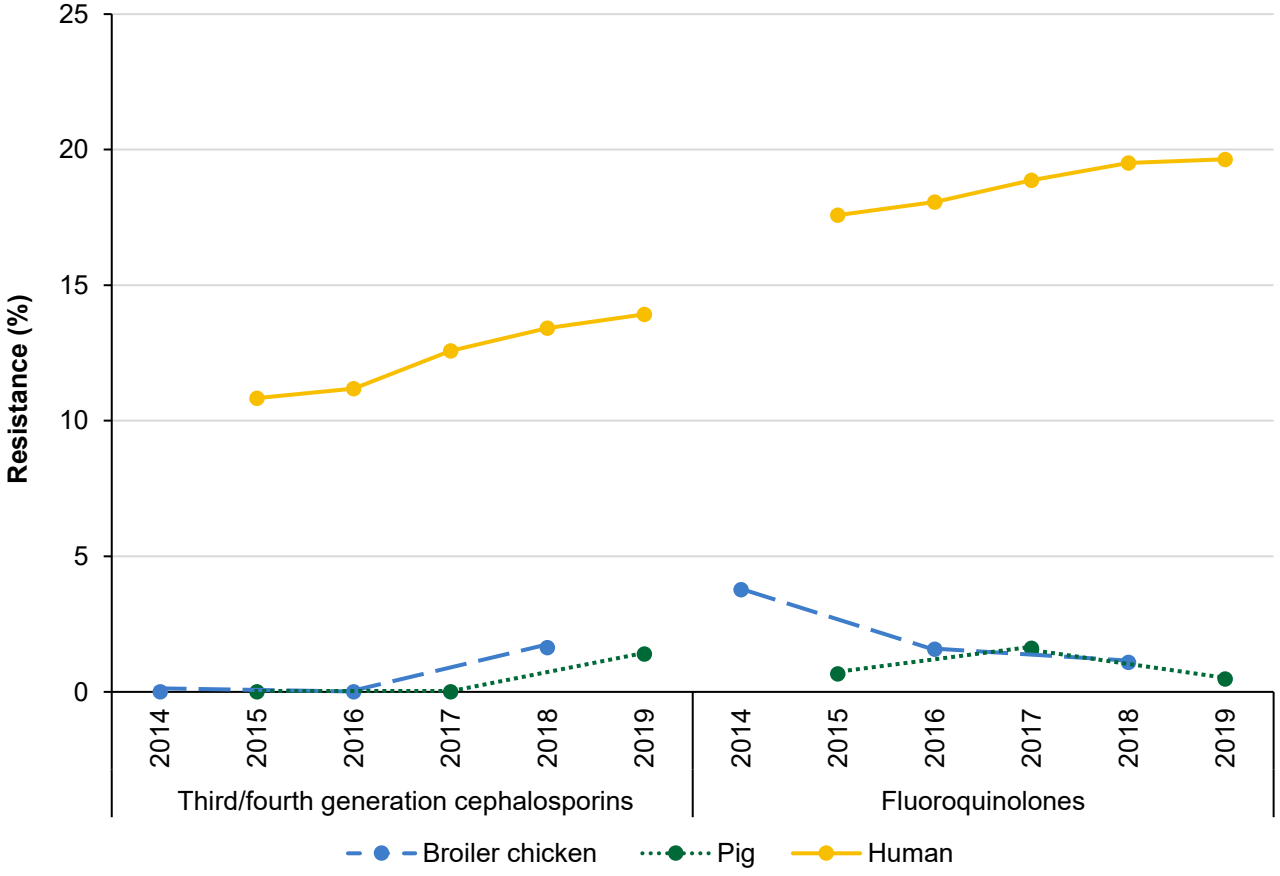
Resistance to third- and fourth-generation cephalosporins was <2% in healthy chickens and pigs, and over 10% in human BSIs (**Figure 2.7**). Resistance to fluoroquinolones in chickens and pigs was even lower, although it was moderate in people (17.6%). No resistance to colistin was detected in healthy pigs, chickens, or turkeys between 2014-2019. This reflects the extremely low use of colistin in food-producing animals. Colistin has not been used in the poultry industry since 2017, and usage has declined by 99.8% in pigs (0.002 mg/kg in 2019).

While trends in resistance to third- and fourth-generation cephalosporins remained fairly flat in animals over the 2014 to 2019 period, resistance to both has increased in human BSIs;

between 2015 and 2019 resistance has increased in human *E. coli* BSIs by 28.7%, and to fluoroquinolones by 11.36%.

Higher levels of resistance to HP-CIAs in human patients with illness (BSI or UTI), compared to healthy animals, is likely to reflect selection of drug-resistant pathogens causing invasive disease and higher usage of HP-CIAs in healthcare settings. Cephalosporins and quinolones are uncommonly used in primary medical care (less than 3.5% of total antibiotic use in primary care) but selection of drug resistant bacteria causing invasive disease is associated with the higher use of penicillins or trimethoprim. By contrast, HP-CIAs are rarely used in pigs and poultry, having reduced considerably since 2014 (**Figure 1.1**). Third- and fourth-generation cephalosporins were not used at all in broiler chickens in 2019. In people, the increase in resistance to third- and fourth-generation cephalosporins in *E. coli* isolated from BSIs between 2016 and 2018 could be associated with a significant increase in usage in secondary care of this antibiotic class as an alternative treatment to piperacillin-tazobactam, which was in short supply in late 2016 and early 2017.

Figure 2.7: Resistance to highest-priority critically important antibiotics (HP-CIAs) in *Escherichia coli* isolates from pigs, broiler chickens, and humans.



Resistance to HP-CIAs in *E. coli* isolated from the gut contents of healthy pigs and broiler chickens at slaughter, and human blood-stream infections (BSIs). Results are interpreted using EUCAST clinical breakpoints (CBPs).

Extended-spectrum beta-lactamase (ESBL)- and AmpC-producing *E. coli*

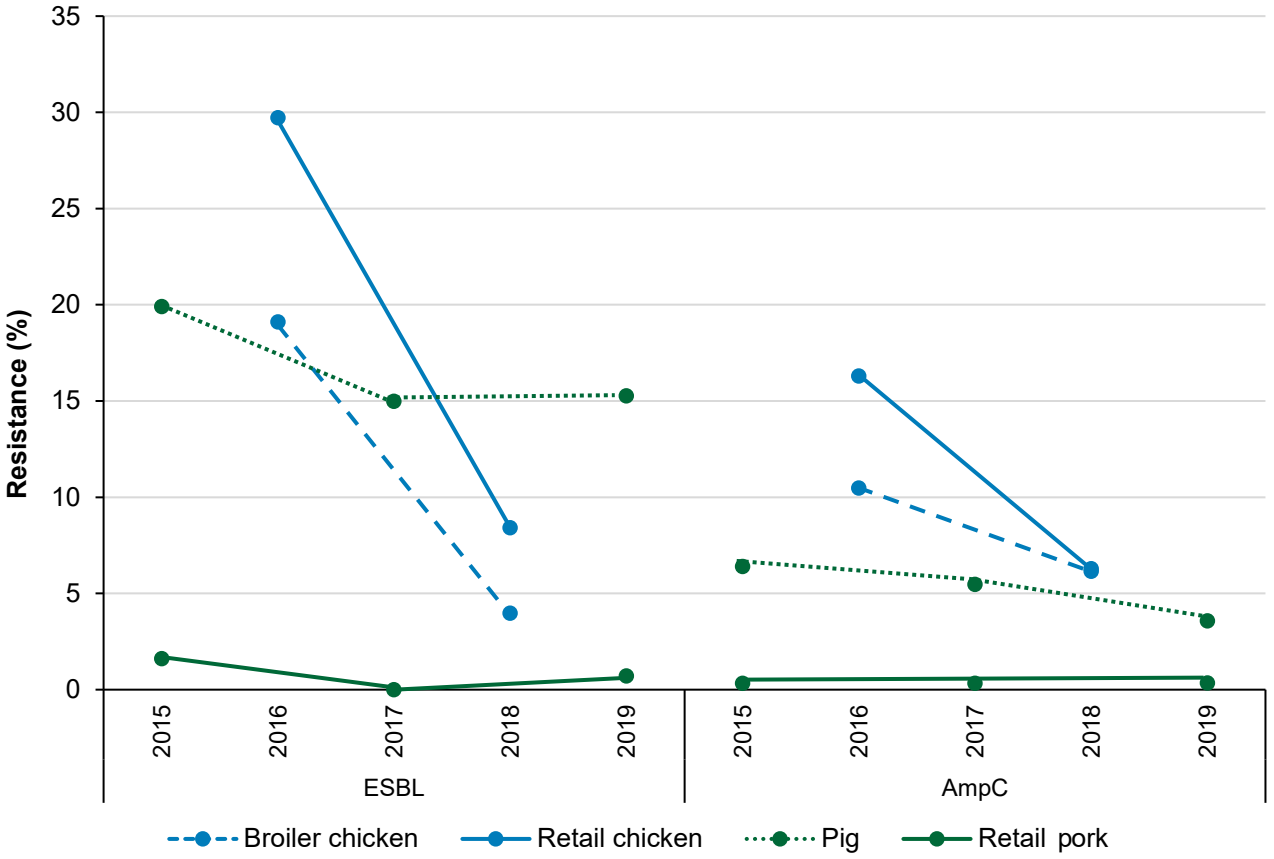
AMR monitoring in livestock and meat includes additional testing for ESBL/AmpC-producing *E. coli*, because these genes confer resistance to HP-CIAs third- and fourth-generation cephalosporins, as well as other beta-lactams. This testing is done using selective media, which is a technique used to detect the presence of these organisms even when they are present in very small numbers and would otherwise be masked by other gut organisms. The results give us the percentage of animals, or meat bought at retail, that carry any of these organisms. It is important to note that this is a different measure to what is presented in the previous section, which gives us the percentage of bacteria resistant to different antibiotic classes, and so these results cannot be compared.

These results show that pigs are more likely to carry ESBL-producing *E. coli* amongst their gut contents (15.8% in 2019) than chickens (**Figure 2.8**). However, less than 1% of pork bought at retail is contaminated with these resistant bacteria. Levels of ESBL-producing *E. coli* in healthy chickens at slaughter (4.0%) and in chicken meat are more closely aligned.

Between 2015 and 2019, the proportion of pigs and pork carrying ESBL- and AmpC-producing *E. coli* remained stable. Between 2016 and 2018, there was a substantial reduction in chickens (-79.1%) and chicken meat (-71.7%) carrying ESBL-producing *E. coli*. The percentage of retail chicken meat carrying AmpC-producing *E. coli* also reduced.

The difference between carriage in pigs and pig meat indicates that slaughter-line processes for pigs are effective at reducing contamination of carcasses. Ensuring proper cooking of meat is required to remove residual risk. The closer alignment in results for chicken reflect the challenges to reducing faecal contamination of poultry carcasses within abattoirs. The substantial reductions in carriage of ESBL- and AmpC-producing *E. coli* observed in chicken and chicken meat is most likely linked to decreased use of antibiotics in the meat poultry sector.

Figure 2.8: ESBL-/AmpC- producing *Escherichia coli* in broiler chickens, pigs, chicken meat and pork.



E. coli samples from the gut contents of healthy pigs and broiler chickens at slaughter and fresh meat of pig and broiler chickens at retail were cultured on MacConkey agar plates supplemented with a third generation cephalosporin in order to determine presence of ESBL/AmpC-producing *E. coli*.

Enterococci

Enterococci are other enteric bacteria that reside in the intestine of nearly all people and animals. In some cases, enterococci can cause disease, which in people is treated with antibiotics such as amoxicillin or vancomycin. Vancomycin is used to treat Gram-positive infections. Vancomycin-resistant enterococci (VRE) are of particular concern, as they are associated with complex treatment regimens with higher mortality rates than infections caused by vancomycin sensitive enterococci (VSE).

There was previously thought to be a direct connection between VRE in livestock and humans, attributable to the historic use of avoparcin, an antibiotic with chemical similarity to vancomycin, as a feed additive for livestock (see papers here and here). As a result, avoparcin use was banned across Europe in 1997. This led to a decrease in VRE prevalence in livestock. In humans, there is no published prevalence from the GI tract; the prevalence of resistance in BSIs was 17% in 2021.

Box 2.1: One Health research into vancomycin-resistant enterococci

A 2018 study funded by the Department of Health and Social Care (DHSC) and the Wellcome Trust analysed *Enterococcus faecium* isolates from livestock, retail meat, wastewater treatment plants and human patients with BSIs. The majority of human and livestock isolates, and the AMR genes in these isolates, were found to be genetically very different to one another, indicating limited overlap between animal strains and those causing BSIs in people. *E. faecium* was frequently detected on farms, but no vancomycin-resistant *E. faecium* (VREfm) isolates were found on farms. However, VREfm was ubiquitous in wastewater treatment plant samples.

Further research in 2019 detected VREfm in 20 wastewater treatment plants in the East of England, and at much higher levels in untreated wastewater from catchments that received sewage discharge from hospitals, than those that did not. Genetic analyses demonstrated a close relationship between some VREfm isolates from wastewater and BSIs in hospital patients. The researchers also found that processing watewater using secondary and tertiary treatment methods (such as activated sludge, or sand filtration, respectively), were ineffective at preventing environmental contamination by VREfm. No VREfm was detected in plants that used an additional treatment step of terminal ultraviolet light.

Box 2.2: Vancomycin-resistant *Enterococcus faecium* in Scotland

Scotland has one of the highest proportions of VREfm in human patients in Europe, with 41.8% of human *E. faecium* bacteraemia isolates reported as non-susceptible to vancomycin in the 2019 SONAAR report. The recently published EARS-Net report describes a significant increase in vancomycin resistance across Europe with only Lithuania (56.6%) reporting higher resistance than Scotland. It is not clear why Scotland has a higher level of VREfm compared to other countries in the UK. Although there are a number of factors known to increase the risk of VREfm in hospitals, less is known outside of the healthcare setting: for example the carriage of VREfm by healthy people, and the role of the environment as a reservoir and vector for transmission. The SONAAR programme is commencing a new One Health research project to better understand the epidemiology, clonal diversity and risk factors associated with VREfm infection.

Other resistant organisms

Monitoring AMR in major GIT organisms across the One Health spectrum is important for tracking the impact of interventions and understanding AMR transmission pathways, including through the environment and healthy human populations. However, there are other organisms relevant to public and animal health that are not routinely monitored in all sectors, but nonetheless provide insight into AMR transmission and evolution.

Klebsiella pneumoniae

K. pneumoniae is commonly found in the human intestine and the environment but can also cause a range of healthcare-associated infections such as pneumonia and bloodstream infections. There has been mandatory reporting of *Klebsiella* spp. BSI in England for enhanced surveillance of community- and healthcare-associated infections since 2017. In terrestrial livestock, *K. pneumoniae* can cause bovine pneumonia, metritis, and mastitis, however, the annual number of detections through clinical surveillance in England and Wales is consistently low (<20 isolates). *K. pneumoniae* has also been detected in avian species at low levels.

K. pneumoniae is a member of the *Enterobacterales* family of Gram-negative bacteria, in which there has been a notable increase in the occurrence of carbapenemases. These are enzymes that inhibit the action of carbapenem antibiotics and are produced by specific genes. Carbapenems are critical 'last resort' antimicrobials for treating disease caused by *Enterobacterales* and are not used in livestock. Carbapenem usage in human medicine can lead to the evolution and carriage of carbapenem resistance genes in the human gut, which when excreted, can enter the environment through sewage (**see Chapter 3, Box 3.1**).

Livestock-associated methicillin resistant *Staphylococcus aureus* (LA-MRSA)

Methicillin is a beta-lactam antibiotic, related to penicillin. Methicillin-resistant *Staphylococcus aureus* (MRSA) is usually also resistant to other antibiotics that could be used to treat infections caused by *S. aureus*. MRSA can be categorised into healthcare-associated MRSA (HA-MRSA) and community-associated MRSA (CA-MRSA), both of which spread from person to person. In the UK, we have more limited differences between HA-MRSA and CA-MRSA in people, compared to other countries such as the USA. Over the past 12 years, national strategies have been hugely successful at decreasing rates of MRSA BSIs in human patients and has reduced the proportion of *Staphylococcus aureus* BSI resistant to methicillin from approximately 50% to 5%.

Livestock-associated MRSA, or LA-MRSA, is an MRSA strain prevalent in livestock and can infect humans. It is thought that LA-MRSA clonal complex (CC) 398 – the most common type of LA-MRSA globally – was a strain that originated in people, but transferred to livestock and eventually acquired methicillin resistance genes. LA-MRSA was first discovered in pigs in mainland Europe in 2004 and was shown to colonise people in rural settings. It was also detected in cities surrounded by dense farming. LA-MRSA is different from other types of MRSA found in humans, and is prevalent in livestock globally.

All LA-MRSA in livestock identified by government and partner laboratories are reported in the UK-VARSS report. The first animal cases in the UK were reported in southeast England in 2008. Between 2013 and 2019, LA-MRSA was identified in 28 cases in livestock in the UK, mainly in pigs (21 cases) but also in cattle (three), poultry (three) and pheasants (one). However, a recent study conducted in a small number of UK abattoirs isolated LA-MRSA from over 40% of batches of pigs sent to slaughter in the six investigated abattoirs. LA-MRSA has been reported at low or moderate prevalence in animal products bought at retail in the UK, including bulk milk and retail meat. Approximately 60% of meat sold in the UK is

imported from European countries with higher levels of LA-MRSA.

The first human cases of LA-MRSA in the UK were detected in 2007 in Scotland, with no apparent link to livestock. Transmission to humans is largely associated with occupational activities (see guidance here for those who work with livestock), however circulation of ST398 LA-MRSA within healthcare settings has been reported (see **Box 2.3**). Local surveillance of MRSA is key to control the intrusion of LA-MRSA into healthcare settings and to monitor its impact on public health. Currently, there is no data publicly available on the prevalence of sequence type (ST) 398 LA-MRSA in humans in England. Based on voluntary referrals of MRSA isolates to the *Staphylococcus* and *Streptococcus* Reference Service (SRSS) laboratory at UKHSA, human cases of ST398 LA-MRSA are rare. On average, 4,500 MRSA isolates are typed at the national reference laboratory per year, of which less than 0.2% are ST398 LA-MRSA. Half of these isolates originate from skin and soft tissue infections (SSTI), and a quarter each from BSIs or screening.

Box 2.3: First hospital outbreak of ST398 livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) in the UK.

The first hospital outbreak of ST398 LA-MRSA in the UK occurred in a burns unit in 2020. The index case was a chicken farmer; however, this is thought to be a coincidence, as they tested negative for LA-MRSA when they were admitted to hospital. In total, 22 LA-MRSA isolates were recovered from 12 burns patients over a six-month period. Whole genome sequencing (WGS) showed that all 22 isolates were closely related, indicating that the bacteria had spread between people within the hospital. It is possible that the LA-MRSA was carried asymptomatically by staff and transmitted to patients.

Investigation showed that the AMR patterns of the LA-MRSA changed during the outbreak. Mupirocin is the main antibiotic used for MRSA decolonisation in hospitals. 16 isolates were resistant to mupirocin, which to our knowledge, is the first time that mupirocin resistance has been reported in an ST398 LA-MRSA isolate. Whole genome sequencing (WGS) showed that the mupirocin resistance gene was acquired within the hospital and was associated with another gene linked to reduced susceptibility to chlorhexidine, a common antiseptic and disinfectant used in human healthcare settings.

The outbreak was contained by thorough infection control measures which consisted of deep cleaning of rooms, and decolonisation of staff. The strain has not been detected since these heightened control measures were implemented in the unit.

Streptococcus suis

Streptococcus suis is a bacterial pathogen found in pigs that can also causes invasive infections in humans. Clinical presentations of *S. suis* infection in pigs include arthritis, meningitis, pneumonia, sepsis, and other systemic illnesses, and in humans include meningitis and BSIs. *S. suis* is a possible reservoir of AMR genes on mobile genetic elements; however, in the UK, resistance to commonly used treatment options (beta-lactam antibiotics) remains rare.

In the veterinary sector, between 63 and 115 isolates of *S. suis* have been isolated from pigs each year since 2014. In 2019, extremely high levels of resistance were seen to tetracyclines (87.0%), with high resistance to lincomycin (41.7%) and tylosin (47.0%). One isolate detected in 2018 was resistant to penicillin. The low prevalence of penicillin resistance is reassuring given that this is the first-line treatment in people.

Between 2014 and 2019 there were 17 reported episodes of *S. suis* bacteraemia in people. Of these 17 human cases, around 50% had antibiotic susceptibility testing (AST) information. Only one of these isolates was resistant to penicillin. None of the reported cases were resistant to more than two antibiotics.

International picture

An overview of antibiotic resistance in zoonotic and indicator bacteria from humans, animals and food in all participating European countries can be found in the EU summary reports. These are produced annually by the European Food Safety Authority and European Centre for Disease Prevention and Control EFSA/ECDC. These results show that the UK is performing well compared to other European countries, particularly in key indicators of resistance, such as presumptive ESBL-/AmpC-/carbapenemase-producing *E. coli.* Post EU-exit, UK-wide results for these key indicators in animals will continue to be published in Chapter 3 of the UK-VARSS report.

Results for AMR monitoring in humans are published annually for England, in the ESPAUR report. Human monitoring data for Scotland is published in the SONAAR report, whilst health data from Wales is published in numerous reports by the HARP team. In Northern Ireland, results from AMR surveillance in humans is published by the Public Health Agency in their annual report. AMR in food is reported from routine surveillance activity conducted by the FSA.

Summary

The AMR data presented here reveal distinct similarities and differences between resistance levels in bacteria within animals and humans, depending on the bacterial species monitored. For example, AMR in S*almonella* spp. varies widely across the animal and human sectors. This is due to the differing patterns of AMR between different S*almonella* serovars and also different host factors affecting humans and animals. Conversely, similar patterns of AMR in *Campylobacter* spp. are reported across chickens, chicken meat, and human patients, suggesting strong linkages through the food chain. In *E. coli*, the picture changes again, with similarities and differences in AMR between the sectors varying by antibiotic class.

These results demonstrate the complexities of monitoring AMR in different sectors and interpreting the data. While causation cannot be determined from these results, they do indicate that AMR in *Salmonella* and *E. coli* carried by pigs and chickens is unlikely to be the main driver of resistance in human patients. The same does not appear to be true for AMR in *Campylobacter* spp. carried by broiler chickens, which are a major source of this foodborne infection. This clearer link between resistance in *Campylobacter* in people and in animals has driven the poultry sector's stewardship initiatives (**Chapter 1**).

Regular surveillance is important to measure trends in resistance and assess the impact of interventions, ideally harmonising collection methodologies between settings. It is also a means of detecting novel or emerging resistances. Without regular surveillance, the transmission of AMR between sectors is even more difficult to understand. Joining up AMR data from animals, food, people, and the environment, especially using whole genome sequencing (WGS), will be essential to unpicking transmission pathways in detail.

To be effective, AMR surveillance needs to continuously evolve and expand. Monitoring AMR in *C. coli* and enterococci was introduced for UK livestock in 2022. Results will be published in subsequent UK-VARSS reports. Additional programmes contributing to the development of AMR surveillance, such as PATH-SAFE and the Private Laboratories Initiative, are outlined in **Chapter 5**. Ideas to improve and integrate AMR surveillance are actively considered by cross-governmental experts within the One Health Integrated Surveillance (OHIS) subgroup of the Defra Antimicrobial Resistance Co-ordination (DARC) group.

Chapter 3 – The natural environment: an emerging area

What's in this chapter?

In this chapter we present results of monitoring programmes for antimicrobial substances in UK water bodies in 2018 to 2019. We also introduce some new research that has been conducted on antimicrobial resistance (AMR) in the natural environment since then.

Background

AMR exists in natural environments (e.g., air, water, soil), however, human activities can increase its prevalence, posing a potential risk to human animal and ecosystem health. The spread and impact of AMR in the environment between and among humans and animals remains poorly understood and there is no established ongoing surveillance programme for AMR in the environment in the UK.

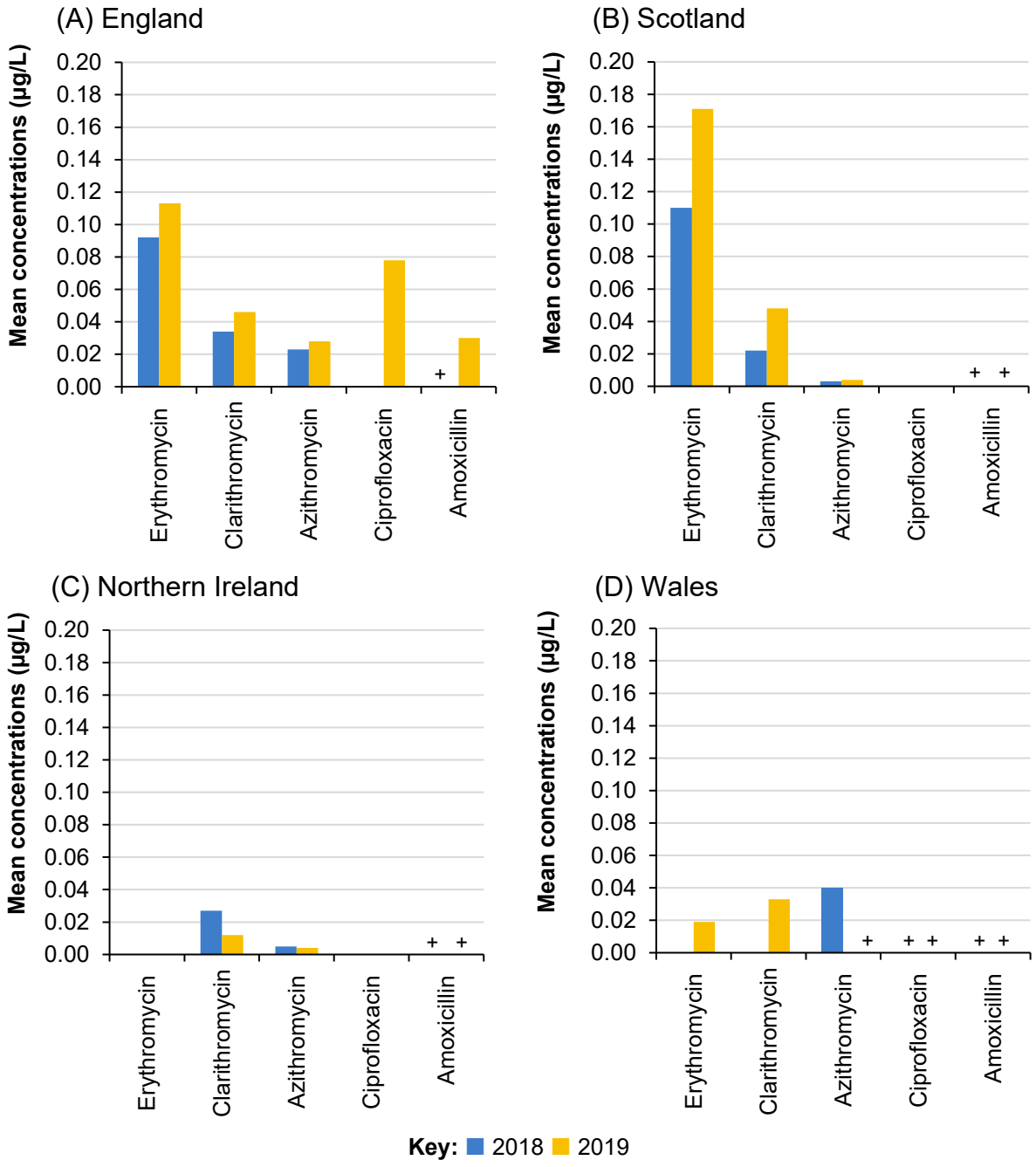
The UK 5-year AMR National Action Plan (NAP) acknowledges the need to improve the evidence base on antibiotics and AMR in the environment, to identify and assess the sources and pathways of AMR, and resultant risks. Work in this area is being developed across the UK.

Measuring antimicrobial substances in the environment

The Watch List of the EU Water Framework Directive was created to provide monitoring data for chemicals of potential concern in the aquatic environment. It includes the following antibiotic categories: macrolides, erythromycin, clarithromycin and azithromycin, the fluoroquinolone ciprofloxacin, and the beta-lactam amoxicillin. Monitoring the presence of these antibiotics in surface waters was undertaken across the UK in 2018 and 2019 (**Figure 3.1**). For England, Scotland and Wales, where data was available, an increase in mean concentrations of antibiotics was seen over the monitoring period. For Northern Ireland, mean concentrations either decrease or remained stable.

Antibiotics in the environment in the UK, 2018 to 2019

Figure 3.1: Mean concentrations of antibiotics in surface waters for 2018 and 2019 across the four nations, monitored under the EU Water Framework Directive; (A) England^, (B), Scotland^, (C) Northern Ireland^ and (D) Wales.



^All analysis using Liquid chromatography–mass spectrometry (LC-MS), except for amoxicillin in England. Any < Limit of Detection (LOD) results from LC-MS analysis were excluded in the calculation of mean (min-max), as the method is considered semi-quantitative and the LODs given were indicative only.
+ No data available

The UK Water Industry Research (UKWIR) Chemicals Investigation Programme (CIP) is the UK water Industry's response to current and emerging legislation on trace substances in the water environment. The phase, known as CIP2 ran from 2015 to 2020. Samples from over

600 UK sewage treatment plants and samples of effluent were analysed for 74 substances. The sewage treatment plant samples included river water upstream and downstream of the plant discharge. Preliminary findings suggest certain antibiotics found in water are of potential concern. Furthermore, findings showed high variability in the removal of active pharmaceutical ingredients between and within plants. For example, macrolides were among the substances less substantially reduced in concentration during treatment. They were present in effluent samples at a higher concentration than the estimated Predicted No-Effect Concentration (PNEC: the concentration of a chemical below which no adverse effects of exposure in an ecosystem are measured). Under Phase 3 of the CIP, which ran from 2020 to 2022, remaining knowledge gaps in understanding AMR in the wastewater treatment process are being investigated.

In England in 2018, the British Geological Survey assessed emerging substances in groundwater for the Environment Agency (EA). Nine fungicides, namely epoxiconazole, propiconazole, boscalid, carbendazim, azoxystrobin, tebuconazole, fluopicolide, thiamethoxam and the transformational product prothioconazole-desthio, were detected in English groundwater. Antifungal resistance, antifungal usage, fungal resistance mechanisms, and potential testing methods are currently being investigated by the EA.

Antimicrobial resistance in the environment

In Scotland, Antimicrobial Resistance and Healthcare Associated Infection (ARHAI) Scotland, the Scottish Environment Protection Agency (SEPA), Scotland's Rural College, and Edinburgh Napier University have investigated *E. coli* cefotaxime resistance in human bacteriaemia isolates, heathy animal isolates and bathing water isolates (SONAAR Report 2020). Cefotaxime-resistant *E. coli* were detected (using a 4 mg/L cefotaxime screening protocol) at least once during the bathing water season at 58%, 78% and 39% of bathing water sites in 2018, 2019 and 2021 respectively. SEPA has also tested cefotaxime-resistant *E. coli* isolates from 12 bathing water sites for resistance to 12 clinically important antibiotics and detected multi-drug resistance at all sites. SEPA has also been piloting testing of vancomycin resistance in enterococci (VRE) for 2022 bathing water samples and is contributing to an ARHAI Scotland led project on One Health surveillance of VRE in human, animal, and bathing water isolates (see **Chapter 2**).

The Welsh Government has been liaising with Dŵr Cymru Welsh Water and the University of South Wales, who undertook pilot studies in the River Wye. Results indicate antimicrobial resistance genes (ARGs) of clinical relevance and faecal contamination were present. The presence of many metals and chemicals were correlated with ARGs, suggesting a common source or co-selection.

In England, the EA collated evidence on AMR in air, highlighting knowledge gaps and potential future research through its recent report 'Review of airborne antimicrobial resistance'. Furthermore, existing datasets relating to AMR have been identified and described to set out a framework for understanding AMR in the environment.

Wildlife, such as badgers and foxes, are potential reservoirs of AMR. However, because they are not treated with antibiotics, they also act as sentinels mirroring the presence of AMR in the environment. Recent research conducted in 2018 and 2019 by the Department

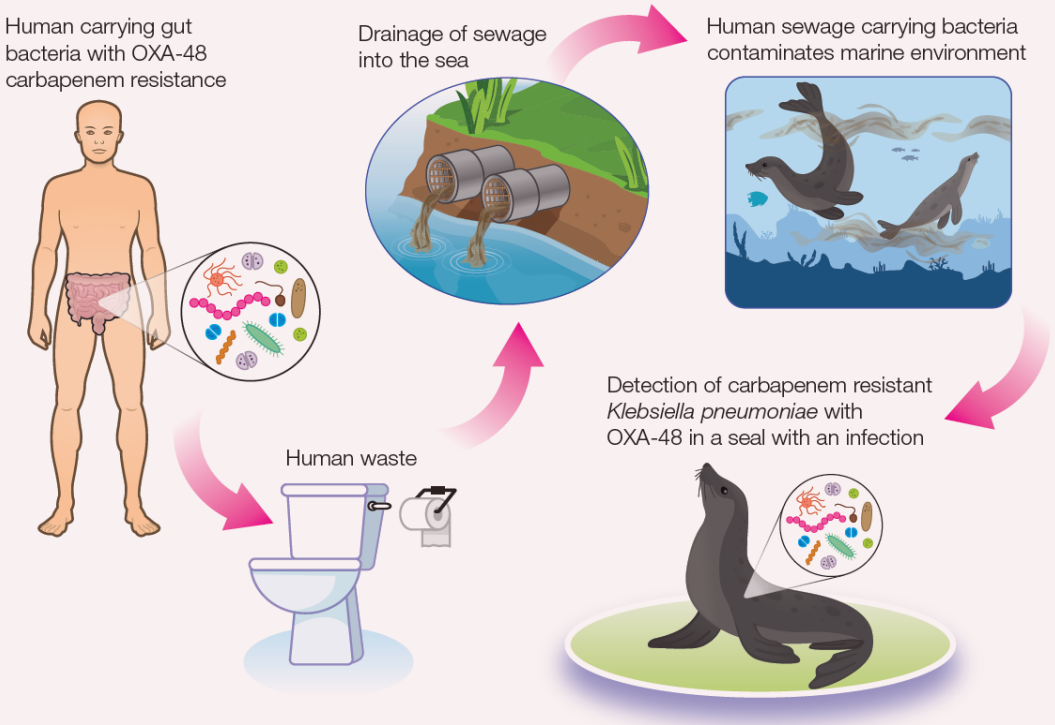
of Agriculture, Environment and Rural Affairs (DAERA) in Northern Ireland estimated the prevalence of resistance to extended-spectrum beta-lactamases (ESBL)-producing *E. coli* and *Salmonella* spp. in badgers (8.9% and 9.6%, respectively) and foxes (11.5% for ESBL *E. coli*). These findings provide an important baseline for further research exploring the origin of the detected resistances, such as farm animal and human related origins.

Box 3.1: Human sewage discharge into the environment is a likely origin of carbapenem-resistant bacteria in a seal.

This case study illustrates the One Health nature of AMR. It demonstrates the likely transmission of AMR from people to a wild seal, via the environment. The *bla*$_{\text{OXA-48}}$ gene confers resistance to carbapenems, a group of antibiotics that are not used in livestock due to their importance in human medicine (see *K. pneumoniae* section of **Chapter 2**). Carbapenem usage can lead to the evolution and carriage of carbapenem resistance genes (such as *bla*$_{\text{OXA-48}}$) in the human gut which, when excreted, can enter the environment through sewage.

In 2017, a clinically unwell seal rescued from a beach in England was found to be infected with *K. pneumoniae* carrying the *bla*$_{\text{OXA-48}}$ gene, along with other AMR genes. Whole genome sequencing (WGS) showed that the *bla*$_{\text{OXA-48}}$ gene was carried on a plasmid (a mobile genetic element), which can transfer between *Enterobacterales,* and which was genetically similar to *bla*$_{\text{OXA-48}}$ plasmids detected in humans. Antibiotics are not administered to wild animals, and the seal was collected from a beach approximately 8km from a major sewage outlet. Given these findings, it is likely that the *bla*$_{\text{OXA-48}}$ gene conferring carbapenem resistance, and its carrier plasmid, was spread in human waste and was acquired by the seal through sewage pollution of the marine environment (**Figure 3.2**).

Figure 3.2: Infographic showing the transmission pathway of antibiotic-resistant bacteria to the marine environment and wildlife.



Antimicrobial resistance in shellfish

There are growing concerns that aquatic environments represent hotspots for the evolution, retention, and dissemination of AMR (see here and here). However, prevalence data for AMR in aquatic environments is limited. Filter-feeding shellfish present a good model for addressing this gap as they naturally concentrate bacterial contamination from the environment and are already examined in the UK and Europe for faecal contamination as part of National Food Hygiene Regulations.

A pilot study jointly carried out between the Centre for Environment, Fisheries and Aquaculture Science (Cefas) and the Animal and Plant Health Agency (APHA), examined 106 *E. coli* isolates originally collected between 2017 and 2018 as part of the Food Safety Scotland (FSS) shellfish monitoring programme and UK research projects. Species sampled included cockles, oysters, mussels, and clams. Isolates underwent antibiotic susceptibility testing (AST) according to UK and EU protocols, and WGS.

Results showed considerable genetic diversity in the *E. coli*, with 65 different sequence types (STs) identified. Of the 106 isolates analysed, 85 were fully sensitive to all 14 antibiotics tested and harboured no known AMR genes. No isolates were resistant to the HP-CIA colistin, or meropenem, gentamicin, or tigecycline, which are of importance to human health. The most common resistances were to tetracycline (15%), ampicillin (12%) and sulfamethoxazole (9%). The most prevalent (approximately 10%) ARGs identified included the *tet*, *sul*, and bla_{TEM} genes. Seven isolates (6%) were multi-drug resistant (MDR: resistant to three or more antimicrobial classes), of which two were ESBL producers resistant to the third-generation cephalosporins cefotaxime and ceftazidime. One of these harboured the $bla_{CTXM-27}$ gene and was ST131, a human pandemic clone. The other was ST449 and carried the bla_{CTXM-}15 gene.

This pilot study has shown that shellfish provide an informative and readily available surveillance target for monitoring AMR in the aquatic environment and its potential to enter the human food chain.

Chapter 4 – Companion animals: an emerging area

What's in this chapter?

In this chapter, we focus on major companion animal species in the UK: dogs, cats, and horses. Antimicrobial usage (AMU) in dogs and cats, estimated from pharmaceutical sales data reported to the Veterinary Medicines Directorate (VMD), is presented. This chapter also includes results of some recent scientific studies on AMU and antimicrobial resistance (AMR) in companion animals and in pet food.

Background

Companion animals are animals which are kept as pets. This includes dogs, cats, horses, lagomorphs (e.g., rabbits), amphibians, reptiles, fish, and birds. Cats and dogs make up most of the companion animals in the UK. In 2019, the PDSA Animal Wellbeing (PAW) Report stated that almost half of UK adults owned a pet including 10.9 million cats, 9.9 million dogs and 0.9 million rabbits.

Sales data on veterinary antibiotics licensed for use in companion animals are routinely collected by the VMD, however there is no routine surveillance system to monitor the prevalence of AMR in companion animals. There is, however, increasing interest in this area due to the close contact between companion animals and humans, and potential for transfer of AMR.

Measuring antibiotic consumption in dogs, cats and horses

The total amount of antibiotics consumed by dogs and cats in the UK in any given year can be estimated from information the VMD obtains annually from Marketing Authorisation Holders (MAHs) regarding the sales of products containing antibiotics.

Population-adjusted antibiotic consumption in dogs and cats is presented in mg/kg, to align with metrics developed for UK food-producing animals. Additionally, HP-CIAs are presented using a different metric, the Daily Defined Doses (DDDVet) which represents average number of defined antibiotic doses received per animal per year. This is because the third-generation cephalosporin cefovecin is used as a single injection which lasts for 14 days, especially in cats, and therefore is not correctly represented in a mg/kg metric. The methodology behind these calculations can be found in **Annex I**.

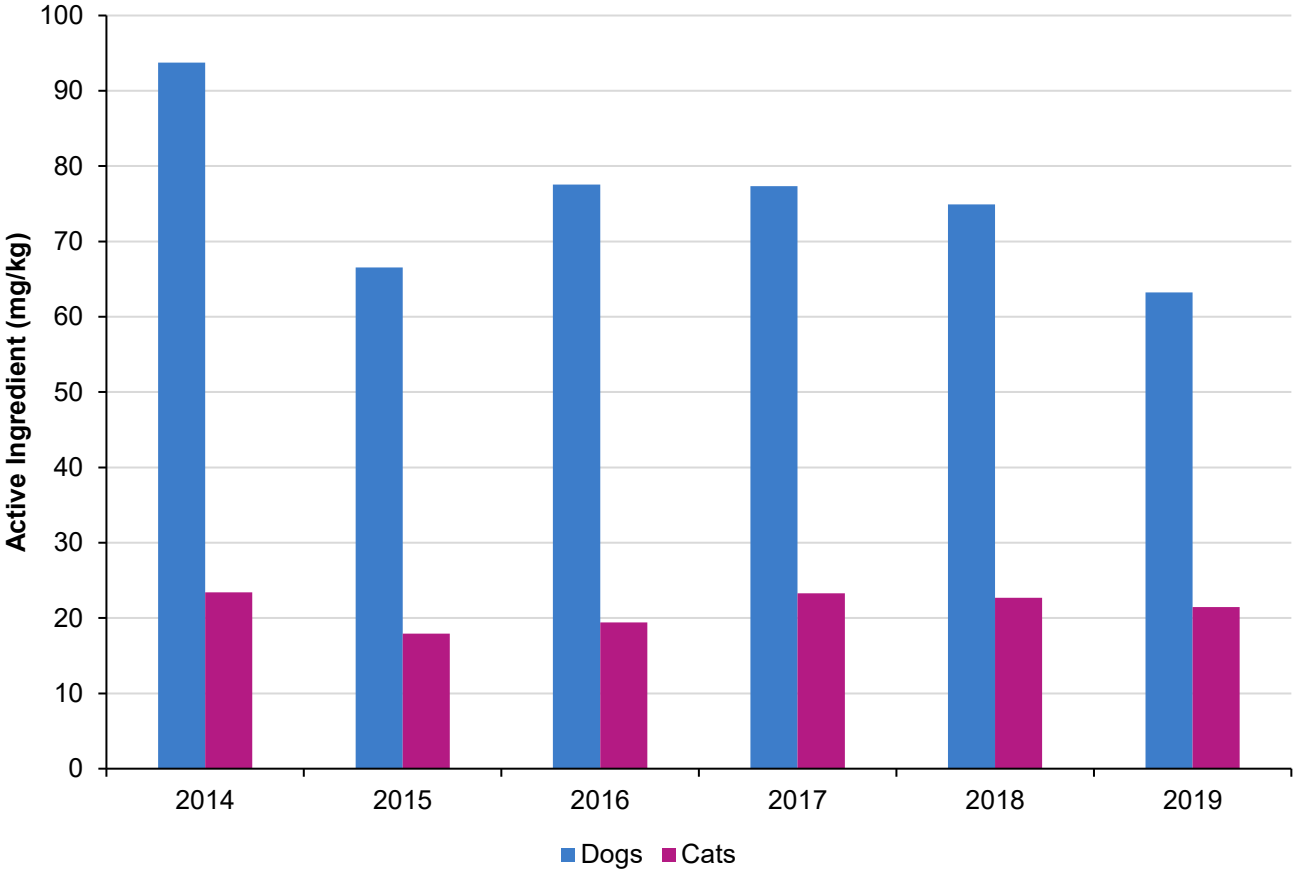
Antibiotic consumption in dogs and cats in the UK

Using the mg/kg metric, in 2019, the total amount of systemic (oral and injectable) antibiotics sold adjusted for the population was 63.2 mg/kg in dogs and 21.5 mg/kg in cats.

Highest-priority critically important antibiotic (HP-CIA) use in dogs and cats in 2019 was 0.53 mg/kg in dogs and 0.93 mg/kg in cats.

Between 2014 and 2019, sales of antibiotic products used in dogs reduced by 33% (from 93.7 to 63.2 mg/kg) (**Figure 4.1**). Over the same period, a less pronounced decrease was seen in the sale of antibiotics used in cats, with a reduction of 8% (from 23.4 to 21.5 mg/kg) (**Figure 4.1**). For information on the use of different antibiotic classes in cats and dogs, please see the UK-VARSS report 2021.

Figure 4.1: Amount of active ingredient (mg/kg) of total antibiotics sold for use in dogs and in cats each year between 2014 to 2019.



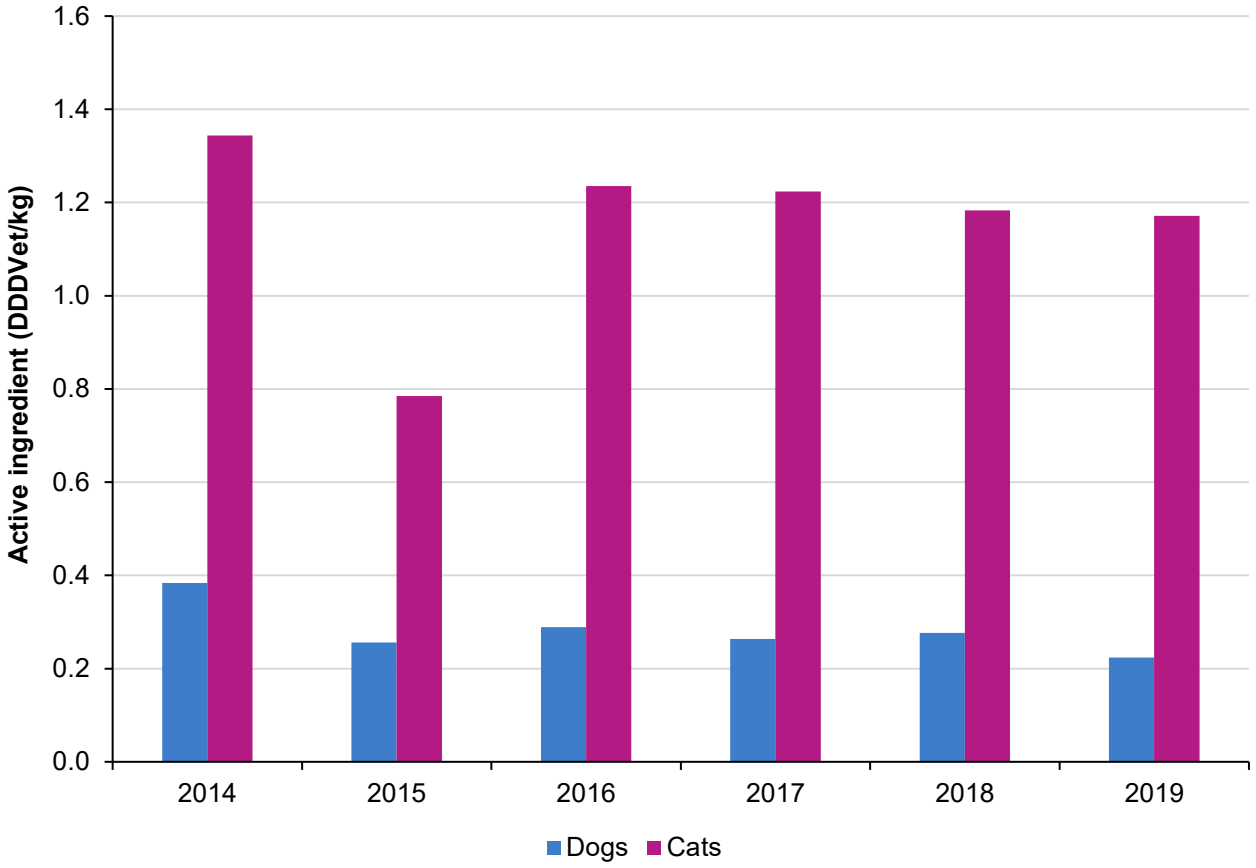
HP-CIAs

Using the DDDVet metric, sales of antibiotics classed as HP-CIAs sold for consumption in dogs reduced by 42% between 2014 and 2019 and by 13% in cats (**Figure 4.2**).The data demonstrate some encouraging trends, with both use of all antibiotics and use of HP-CIAs decreasing between 2014 and 2019. However, overall, HP-CIA use remains high, particularly in cats. It is not known why HP-CIA use in cats in 2015 is lower than in other years. In a study carried out by Small Animal Veterinary Surveillance Network (SAVSNET) looking at antibiotic prescription patterns from 457 veterinary premises between 2014 and 2016, antibiotics were prescribed in almost half of all consultations involving sick cats. In addition, the most frequently prescribed systemic antibiotic (36.2% of antibiotic prescriptions) was cefovecin, a third-generation cephalosporin and an HP-CIA. A separate study conducted between September 2012 and September 2013, found that almost half

(48.2%) of cefovecin prescriptions in cats were to treat skin disease.

Cefovecin is not authorised for use in humans. Cefovecin is licensed for use in dogs and cats as a long-acting injectable and the most cited reason for prescribing was the inability of owners' to orally medicate their pet at home. Relevant product information sheets state that cefovecin should be reserved for clinical conditions which have responded poorly, or are expected to respond poorly, to other classes of antimicrobial agents. The British Small Animal Veterinary Association (BSAVA) advises that HP-CIAs in dogs and cats should only be used when "first-line antibacterials are inappropriate or ineffective" and, where possible, be based on culture and sensitivity testing.

Figure 4.2: Amount of active ingredient (DDDVet/kg) of total antibiotics classified as highest-priority critically important antimicrobials (HP-CIAs) sold for use in dogs and cats each year between 2014 to 2019.



Reasons for antibiotic use in horses in the UK

A 2022 study, funded by the VMD and carried out by the Royal Veterinary College (RVC), explored use of antibiotics in 64,322 horses under the active care of 39 UK veterinary practices in 2018. The study found that 19.5% were prescribed a systemic antibiotic, with potentiated sulphonamides and tetracyclines accounting for 77% of antibiotic courses prescribed. However, HP-CIAs were prescribed for 8.9% of antimicrobial courses (and in 71.7% of these as a first-line therapy), with culture and sensitivity informing antibiotic choice in just 1 in 5 of HP-CIA prescription cases. The use of HP-CIAs was particularly high in youngstock (<1-year olds), and thoroughbreds and racehorses, and the top conditions

treated with HP-CIAs were urogenital (31.1% of cases), skin (25.2% cases) and respiratory conditions (15.9% cases).

This study highlights that the empirical use of HP-CIAs in horses remains commonplace, despite industry advice that HP-CIAs should be protected. HP-CIAs should not be considered first-line antimicrobials, and use of HP-CIAs in horses should be based on the results of culture and susceptibility testing.

Antibiotic resistance in companion animals

Box 4.1: Unusual AMR findings in companion animals

UKHSA's Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit occasionally investigates bacterial isolates with unusual AMR that veterinary diagnostic laboratories have obtained from companion animals. Analysis of these isolates demonstrates that there is evidence of AMR transmission from human-animal and vice versa.

In 2018, four linezolid-resistant *Enterococcus faecalis* isolates from dogs and cats were referred to the AMRHAI Reference Unit for investigation. Molecular characterisation revealed the linezolid resistance was due to *optrA,* a plasmid-mediated gene that confers resistance to oxazolidones and phenicols. Linezolid is an important antibiotic for use in resistant Gram-positive infections in humans, including methicillin-resistant *Staphylococcus aureus* (MRSA) and vancomycin-resistant enterococcus (VRE). Although linezolid is not licensed for use in the UK for companion animals, the *optrA* gene also confers resistance to florfenicol, an antibiotic used in animals. This is the first report of *optrA*-positive enterococci from companion animals. Dog food has been reported as a source of *optrA*-positive *E. faecalis* in Portugal, suggesting this may be a potential route of infection for both companion animals and their owners.

In 2021, an *E. coli* was isolated from a canine wound and submitted to the AMRHAI Reference Unit to be screened for acquired carbapenemase genes. Carbapenems are not licenced for use in animals in the UK. The isolate harboured a bla_{NDM-5} gene (the most common bla_{NDM} variant identified). This was most likely acquired from people as NDM-positive Enterobacterales accounted for the largest percentage (35.5%) of carbapenemase-producing Enterobacterales (CPE) isolated from humans according to the AMRHAI in 2021.

Raw pet food – an antimicrobial resistance One Health risk

Raw pet food (RPF), which is made from raw meat and offal, is becoming an increasingly popular choice amongst UK pet owners. Dogs and people can pick up bacteria directly through eating or handling uncooked food, or via contact with food bowls or other equipment used for raw feeding (**Figure 4.3**). People can also become infected through

contact with their dog's faeces. Recent research[1] shows that resistant bacteria are more prevalent in RPF than in conventional pet food, which goes through a heat-treatment step designed to kill microorganisms.

In one VMD-funded study by the University of Liverpool, the most popular raw food brands were determined through a pet owner questionnaire[2]. Packs of RPF from these brands were bought at retail outlets and online, directly from manufacturers. Of 110 total samples, up to 60% of samples tested per brand had *E. coli* counts higher than the level deemed acceptable by animal by-product regulations. In 39% of RPF samples, *E. coli* isolates were resistant to at least one antibiotic class. Of these, 16% of samples were positive for extended-spectrum beta-lactamases (ESBL)-producing *E. coli* (i.e., resistant to HP-CIAs third- and fourth-generation cephalosporins), and 8% were multi-drug resistant (MDR: resistance to three or more classes of antibiotics). This included resistance to additional HP-CIAs, as 5.5% of the ESBL-producing *E. coli* were also resistant to the fluoroquinolone ciprofloxacin. All six RPF samples yielding isolates with dual HP-CIA resistance contained red meat products as a constituent component. Two samples also contained offal, one contained game and one additionally contained chicken.

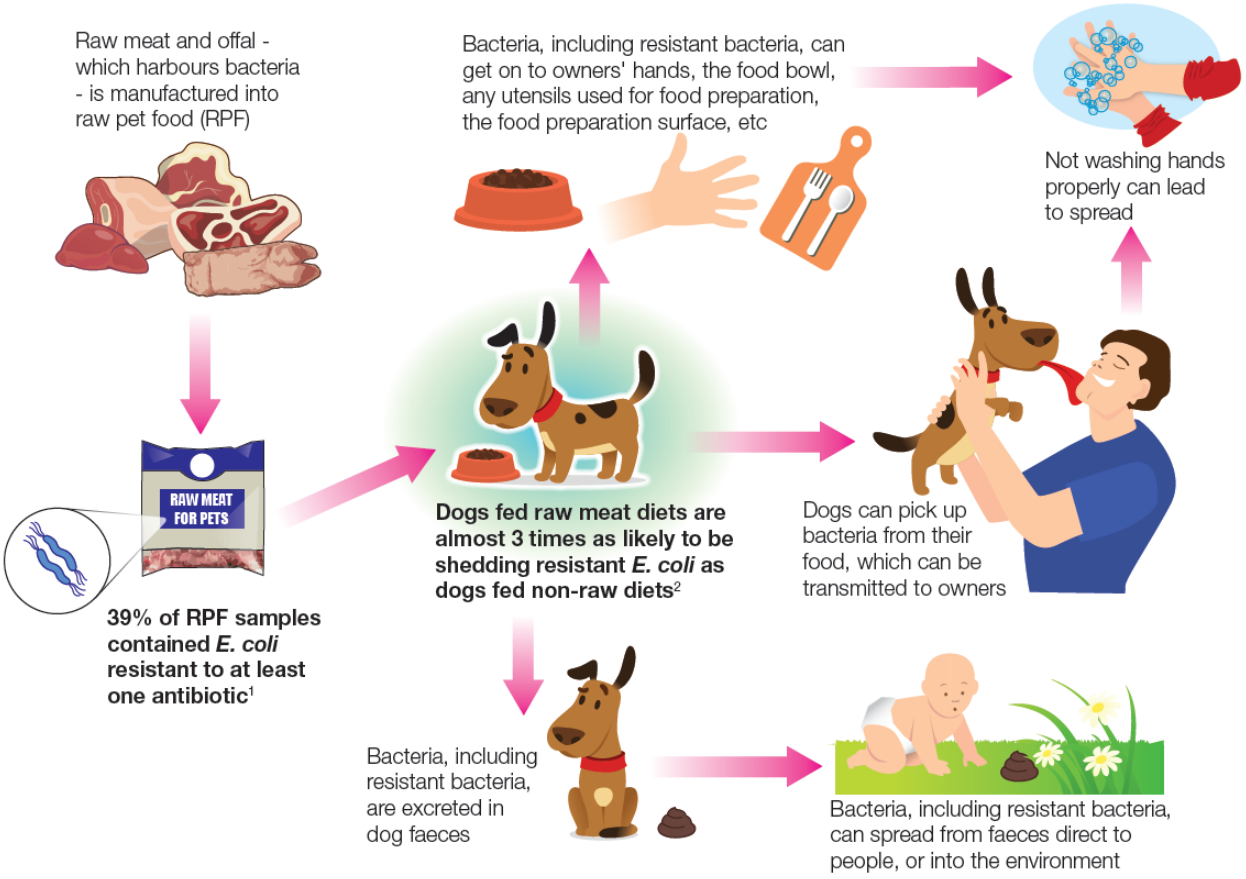
A study also measured the presence of AMR in dog faeces and found that dogs fed raw diets were 23% more likely to excrete ESBL-producing *E. coli* and 15% more likely to excrete MDR *E. coli* in their faeces than dogs fed non-raw diets[1]. A study performed by the University of Bristol showed a person's antibiotic-resistant urinary tract infection (UTI) may have been linked to a fluoroquinolone-resistant *E. coli* detected in a puppy. This work also found that the only significant risk factor for 16-week-old puppies shedding resistant *E. coli* (including fluoroquinolone-resistant *E. coli*) in their faeces was being fed RPF. In a second study by the same group, raw meat feeding was shown to be significantly associated with the excretion of CTX-M-producing *E. coli*.

Another factor that can contribute to the higher prevalence of AMR in RPF is the mixing together of raw meat and offal from different sources, including products imported from countries with higher rates of AMR. One example of this was highlighted in a 2020 ResAlert (resistant alert; see **Chapter 5**), when a *Salmonella* Java harbouring the transferable colistin resistance gene *mcr-9.1* was isolated in RPF sampled at a UK manufacturer. The likely explanation for this exotic detection was cross-contamination from imported RPF ingredients in the manufacturing plant.

In summary, the research conducted through various studies highlights the bacterial risks associated with RPF in the UK and that raw feeding may pose a risk to animal and human health.

[1] Morgan, G., Pinchbeck, G., Schmidt, V., Williams, N. A cross-sectional study of the prevalence of antimicrobial-resistant *E. coli* carriage in dogs fed raw and non-raw diets in the UK [abstract]. In: Proceedings of the 16th International Symposium of Veterinary Epidemiology and Economics; 2022 Aug 7-12; Halifax, Nova Scotia, Canada. Abstract nr 339.
[2] Morgan, G., Williams, N., Schmidt, V., Pinchbeck, G. Antimicrobial resistance and the presence of *E. coli*, *Salmonella* spp. and Enterobacter spp. in raw meat diets fed to dogs in the UK [abstract]. In: BSAVA Congress Proceedings; 2022 Mar 24-26; Manchester, UK. Abstract nr 50.

Figure 4.3: Potential transmission pathways of antibiotic resistance via raw pet food.



[1]Morgan, G., Williams, N., Schmidt, V., Pinchbeck, G. Antimicrobial resistance and the presence of *E. coli*, *Salmonella* spp. and Enterobacter spp. in raw meat diets fed to dogs in the UK [abstract]. In: BSAVA Congress Proceedings; 2022 Mar 24-26; Manchester, UK. Abstract nr 50.

[2]Morgan, G., Pinchbeck, G., Schmidt, V., Williams, N. A cross-sectional study of the prevalence of antimicrobial-resistant *E. coli* carriage in dogs fed raw and non-raw diets in the UK [abstract]. In: Proceedings of the 16th International Symposium of Veterinary Epidemiology and Economics; 2022 Aug 7-12; Halifax, Nova Scotia, Canada. Abstract nr 339.

Chapter 5 – Control measures and new initiatives

What's in this chapter?

In this chapter we highlight current antimicrobial resistance (AMR) control measures, including our ResAlert system, which ensures a UK-wide coordinated response to resistant bacterial isolates that are potentially high risk to human and/or animal health. We also provide examples of new initiatives in antibiotic stewardship and antimicrobial use (AMU) and AMR surveillance that have been implemented since 2014.

ResAlert – the One Health approach to antimicrobial resistance risk management

ResAlert (resistant alert) is recognised internationally as amongst best practice in AMR control. The ResAlert response is triggered following isolation of a resistant bacterial isolate from animals (or their environment, animal feed, or food of animal origin) that is considered potentially high risk to human and/or animal health. This system was initiated in early 2015 due to the detection of livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) on a pig premise.

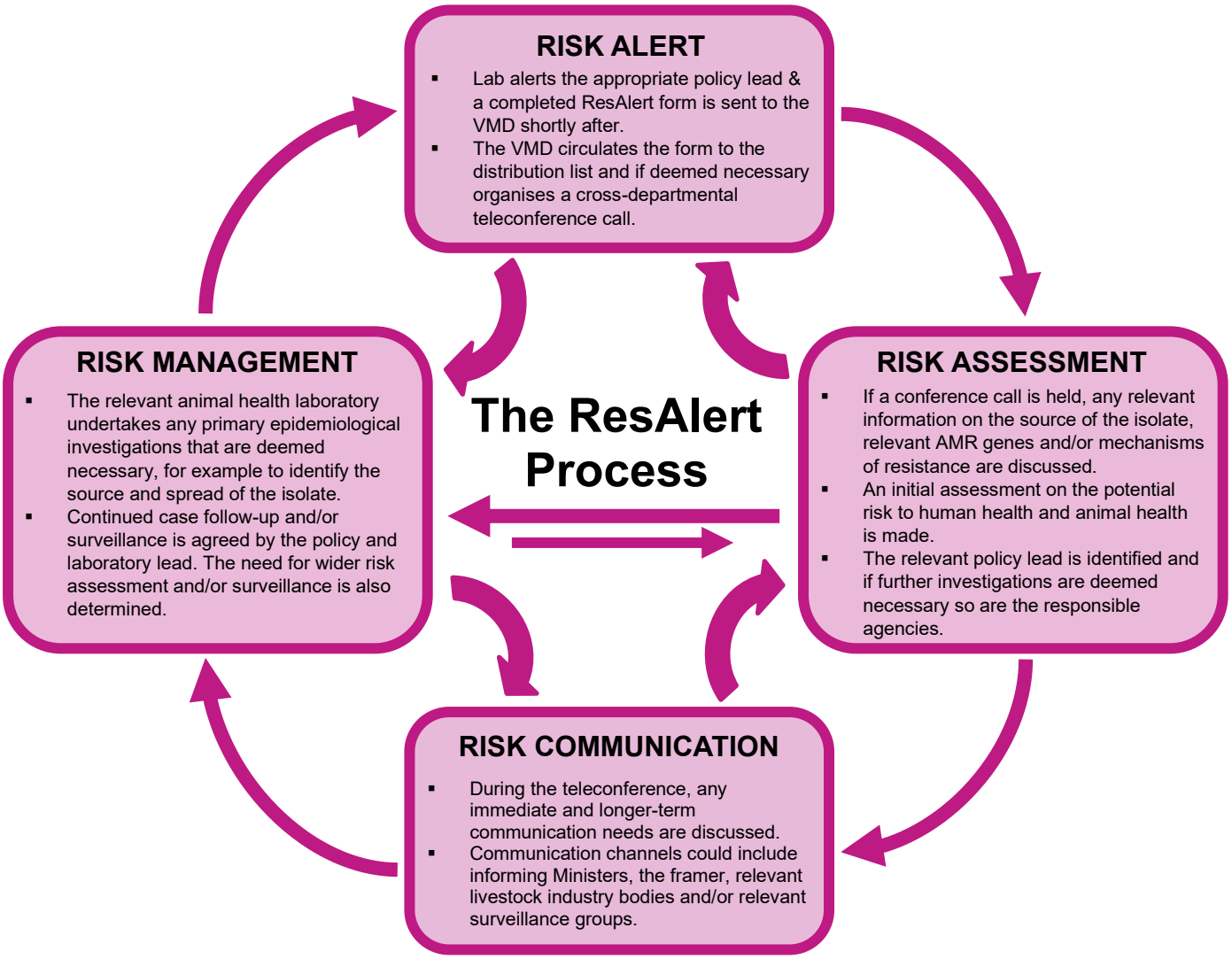
The Veterinary Medicines Directorate (VMD) coordinates the ResAlert process and group, which includes experts from human and animal health, food safety, the environment, and the Devolved Administrations. ResAlerts processed between 2018 and 2019 are listed in **Table 5.1**.

Table 5.1: ResAlerts raised between 2018 and 2019.

Microorganism	Source
Carbapenem-resistant *E. coli*	Seal
Penicillin-resistant *Streptococcus suis*	Pig
Methicillin-resistant *Staphylococcus pseudintermedius*	Otter
Tetracycline sensitive MRSA positive for *mecA*	Bovine
LA-MRSA	Bovine
LA-MRSA	Pig
LA-MRSA	Pig
LA-MRSA	Turkey
ESBL-producing *Klebsiella pneumoniae*	Tortoise
CTX-M-producing *E. coli*	Pig

The ResAlert process consists of four components; the 'alert', where the membership is made aware of the detection, the risk assessment to determine the risk to human and animal health, and risk management and communication components which are used to determine next steps. An overview of the four components can be found in **Figure 5.1**. Actions from each may take place simultaneously and may be revisited or ongoing. Risk communication is a continuous process.

Figure 5.1: Infographic illustrating the ResAlert process.



While not equivalent, the UK Public Health Antibiotic Resistance Alerts System, hosted by the UK Health Security Agency (UKHSA), disseminates AMR findings of particular concern throughout the medical laboratory network. This group includes microbiological expertise from the Animal and Plant Health Agency (APHA), to assess the veterinary impact of any findings.

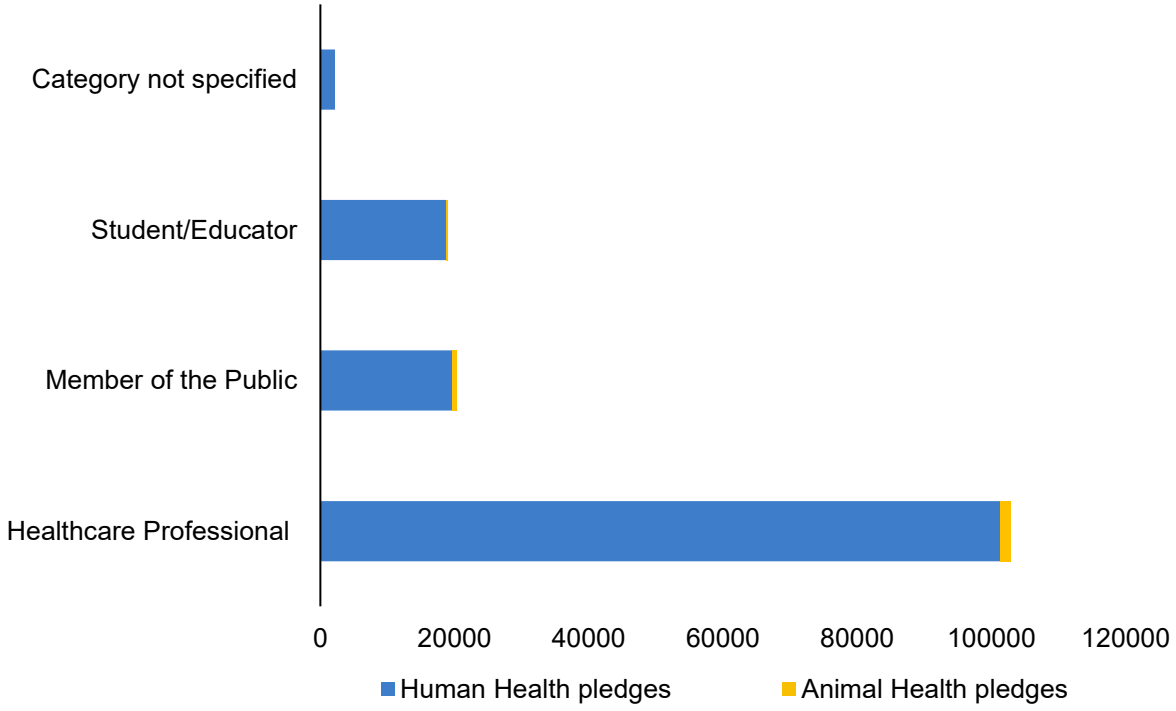
New initiatives in antibiotic stewardship

Below are updates on existing initiatives or examples of new initiatives that have been implemented in antibiotic stewardship since the last One Health Report was published in 2019.

Antibiotic Guardian

A pledge-based Antibiotic Guardian campaign, with the aim of transitioning from raising awareness to increasing engagement with antibiotic stewardship across sectors, was launched by Public Health England (PHE), now UKHSA, in 2014. The campaign uses an online pledge-based approach among human and animal health professionals, scientists and educators and the public. Note there are over 100 times the number of health and social care workers (over 3 million) compared to the number of practicing veterinary surgeons (30 thousand) in the UK. Antibiotic Guardians can select from a range of pre-determined pledges or choose to write their own pledge.

Figure 5.2: Number of antibiotic stewardship pledges made on the Antibiotic Guardian website from initiation of the scheme to end of 2021.



From initiation to the end of 2021, a total of 144,445 pledges were made. The 'Pharmacy Teams' sub-category within the category 'Healthcare Professional' recorded the highest number of pledges overall (68,192) representing 47% of the total pledges made across all categories and sectors by the end of 2021. Examples of pledges can be found on the Antibiotic Guardian website.

Antibiotic Guardian Shared Learning & Awards Event: Animal health, agriculture and food supply

The Antibiotic Guardian Shared Learning & Awards (AGSLA) event has run annually from 2016 until 2020. The event took a pause in 2021 and returned in 2023. The event receives approximately 80 submissions each year from across animal and human health sectors. The winning and highly commended entries can be viewed here.

Antibiotic Amnesty

In November 2022, the veterinary profession came together alongside pharmacists in the National Health Service (NHS) to hold an Antibiotic Amnesty. The aim was to encourage the pet-owning public to return any unused or out of date veterinary antibiotics so they could be disposed of safely by their pharmacy or veterinary practice. Safe disposal of unused or leftover antibiotics is important to avoid the health risks associated with inappropriate use and environmental pollution that could increase AMR.

This initiative was supported by many major veterinary organisations including the British Small Animal Veterinary Association (BSAVA), the National Office for Animal Health (NOAH), the VMD, the British Veterinary Association (BVA), the Royal College of Veterinary Surgeons (RCVS), RCVS Knowledge, RUMA Companion Animal & Equine (RUMA CA&E) and the Bella Moss foundation, as well as several veterinary corporates and independent practices. An additional Amnesty is underway for 2023.

The 2022 Antibiotic Amnesty saw pet owners return for safe disposal over 750 antibiotic tablets, 12-part boxes of tablets, 53 bottles of antibiotic ear drops or ointments and 17 antibiotic injections. A range of antibiotic classes, including highest-priority critically important antibiotics (HP-CIAs), were among the returns. Additionally, a survey of pet owners (n=139) suggests that antibiotics were left over in around one quarter of veterinary prescription (24%), which is higher than previously reported in human patients (17%). Survey respondents reported moderate awareness (72%) of safe routes for antibiotic disposal.

The Responsible Use of Medicine in Agriculture Alliance Targets

The Responsible Use of Medicine in Agriculture Alliance (RUMA) have facilitated a Targets Task Force Group, comprising of a vet and a farmer from each sector, to work with their sector stewardship group(s) and agree voluntary sector targets for improving stewardship and reducing antibiotic use for eight key livestock sectors. The targets are tailored to the specific circumstances and features of each sector, but all are based on the principle that “prevention is better than cure”. Delivering on these targets, combined with better disease control and improved data on antibiotic use (which can be used to inform interventions) has catalysed sustainable and meaningful change not only in antibiotic use but also to animal health and welfare.

Sector-specific antimicrobial use and stewardship groups are active for the cattle (beef, dairy and calves), sheep, poultry, pigs, gamebirds and salmon sectors, and more recently

for companion animals (pets and horses) through the RUMA CA&E Group. Each group meets regularly and consists of, for example, industry experts, animal health professionals, farmers, assurance scheme/ retail representatives and the VMD.

Development of eBug learning courses

The eBug programme, developed by UKHSA, seeks to reach and equip those who work with or support children and young people (aged 3-16 years) with the information, activities and discussion points to build knowledge around microbes, disease, hygiene, vaccination and AMR. The programme has recently been reviewed, updated, and expanded. All materials have been accredited by the Association for Science Education and included as supporting resources for the updated UKHSA guidance 'Health protection in education and childcare settings'. Students learn about the linkages between animal and human health, including preventing infection in farm animals, and food safety.

- Educational packs were disseminated to every maintained school and academy across England (over 20,000 schools), in collaboration with NHS England and NHS Improvement (NHSEI) in January 2022.
- All resources can be accessed for free on the e-Bug website, www.e-Bug.eu.

Two further e-Bug e-Learning courses aimed at educators and childcare practitioners can be accessed through FutureLearn. Both courses were developed with the British Society for Antimicrobial Chemotherapy (BSAC) and are accredited by the Royal College of Pathologists.

- The e-Bug Health Educator training is designed to support educators to teach students about the spread, prevention, and treatment of infections and antibiotic use. The course has 730 users (56% active); 96% of learners stated the course improved their knowledge, and it has been accessed across 95 countries.
- The Preventing and Managing Infections in Childcare and Pre-school course is designed to support individuals working in these settings to prevent and manage infections. The course includes information on microbes, the importance of hygiene in a childcare environment, controlling outbreaks and immunity. The course has 981 users (70% active). Most learners agreed that the course improved their knowledge (93%), and it has been accessed across 93 countries.

Farm Vet Champions (RCVS Knowledge) and Arwain Vet Cymru

Alongside the Arwain Defnydd Gwrthfaicrobaidd Cyfrifol (ArwainDGC) national veterinary 'Prescribing Champions' network in Wales, which originated from the Arwain Vet Cymru project, RCVS Knowledge are leading a project with funding from the VMD to engage individual farm animal vets as Farm Vet Champions. The project delivers over 20 hours of high quality, free, continuing professional development (CPD) training for veterinary surgeons to build capacity, capability, and confidence when engaging with their clients in the application of good antibiotic stewardship in a range of farm animal sectors. Topics include antimicrobial stewardship, infection prevention and control, behavioural change and optimising prescribing practices.

Treat Antibiotics Responsibly Guidance Education Tools (TARGET)

The TARGET Antibiotics Toolkit includes free resources and learning materials that can be used by primary care providers to tailor antimicrobial stewardship interventions in their practices and improve antibiotic prescribing. This includes the TARGET Antibiotic Checklist interactive workshops and slide decks, leaflets to use with patients, audit toolkits, antibiotic and diagnostic quick reference tools and other training resources. TARGET resources were developed by the UKHSA, the Royal College of General Practitioners (RCGP) and the Antimicrobial Stewardship in Primary Care (ASPIC) Group.

In 2021, the TARGET treating your infection leaflets were published in HTML allowing easier patient access to information, particularly during remote primary care consultations. The content and wording of six SMS template messages to share TARGET leaflets covering advice on respiratory tract infections (RTIs) and urinary tract infections (UTIs) was created in collaboration with prescribers. From July 2021 to April 2022, 5,487 leaflets have been shared through SMS templates, with the leaflet covering UTIs for women under 65 consistently used the most each month, making up 46% of all the leaflets sent.

The TARGET Antibiotics: Prescribing in Primary Care e-learning course, developed in collaboration with the BSAC, is a free course hosted on FutureLearn. It consists of modules aimed at Health Care Professionals (HCPs) and covers antibiotic stewardship topics related to management of common infections. To date, 170 users have actively participated in the course and content updates are planned for 2023.

The TARGET Antibiotic Checklist supports community pharmacy staff to ensure the safety of patients and educate the public on appropriate antibiotic use and managing common infections. Data was collected from 8,374 pharmacists in England providing information on 213,105 patients collecting an antibiotic prescription.

Farm Vet Champions Specific Measurable Attainable Realistic Time-bound (SMART) goals (RCVS Knowledge)

Launched in May 2022, the second phase of the Farm Vet Champions initiative allows Farm Vet Champions to set SMART goals on antibiotic stewardship at an individual and at a practice level. The goals will allow Farm Vet Champions to use the training received on the Farm Vet Champions platform into practice. They will be able to track progress towards these goals via an online platform, share experiences across a network of other Farm Vet Champions, and bring in other veterinary team members to achieve shared goals.

Equine and pets - VetTeam AMR (RCVS Knowledge)

VetTeam AMR focuses on antibiotic prescribing in equine and companion animals in veterinary teams. This major collaborative project has developed an auditing and benchmarking tool which allows vet teams to measure and track changes in antimicrobial use. It supports the continuous improvement in prescribing habits at the point of care, provides access to free online education and will provide a means for veterinary teams to network and share lessons on a national scale.

Companion animals - Interventions in veterinary practice to reduce use of HP-CIAs

There is evidence to show that strategies to improve antibiotic stewardship in companion animal practice are effective in improving responsible prescribing. In a randomised control trial, veterinary practices in which stewardship interventions were implemented to target HP-CIA prescribing showed a 39% reduction in feline HP-CIA prescriptions over the 6-month study period. Stewardship interventions employed during the trial included: the Practice Clinical Lead being informed by letter the practice was a higher-than-average user alongside a detailed benchmarking report, signposting to BSAVA PROTECT and corporate AMR policy, the provision of training videos, participation in a reflection and education programme delivered by a senior vet, and practice-wide meetings on stewardship.

Knowledge and attitudes about antibiotics and antibiotic resistance – Findings from a survey of 2,404 UK healthcare workers

A recent survey conducted throughout the European Union (EU) aimed to ascertain multidisciplinary healthcare workers' (HCWs') knowledge, attitudes and behaviours towards antibiotics, antibiotic use and antibiotic resistance. In total, 2,404 UK participants responded. HCWs correctly answered that antibiotics are not effective against viruses (97%), they have associated side effects (97%), unnecessary use makes antibiotics ineffective (97%) and healthy people can carry antibiotic-resistant bacteria (90%). However, fewer than 80% correctly answered that using antibiotics increases a patient's risk of antimicrobial resistant infection or that resistant bacteria can spread from person to person. Only 31% of participants correctly identified the use of antibiotics to stimulate growth in farm animals is illegal in the EU.

Whilst the majority of HCWs (81%) agreed there is a connection between their antibiotic prescribing behaviour and the spread of antibiotic-resistant bacteria, only 64% felt that they have a key role in controlling antibiotic resistance. The top three barriers to providing advice or resources were lack of resources (19%), insufficient time (11%) and the patient being uninterested in the information (7%). Approximately 35% of UK respondents who were prescribers prescribed an antibiotic at least once in the week previous to responding to the survey due to a fear of patient deterioration or complications.

These findings highlight that a multifaceted One Health approach to tackling the barriers to prudent antibiotic use in the UK is required and provides evidence for guiding targeted policy, intervention development and future research. Education and training should focus on patient communication, information on spreading resistant bacteria and increased risk for individuals. All materials should, where relevant, reinforce a One Health approach to AMR and AMU.

New initiatives in antimicrobial usage surveillance

Below are updates on existing initiatives or examples of new initiatives that have been implemented in AMU since the last One Health Report was published in 2019.

Medicine Hub

Until recently, there was no central industry surveillance system in place for the ruminant industry to collate antibiotic use data to enable national surveillance and farm-level benchmarking in the UK beef, sheep, and dairy sectors. A UK-wide industry-led voluntary industry initiative, Medicine Hub, was launched in 2021 and is hosted by the Agricultural and Horticultural Development Board (AHDB). Medicine Hub enables dairy, beef, and sheep farmers to collate antibiotic use data in a standardised way. This will allow on-farm benchmarking which is important for farmers and vets to understand antibiotic use and stewardship within on their farms. Medicine Hub will also allow the industry to calculate an aggregated, annual antimicrobial use figure for each sector across the UK, to evidence changes and show trends in antimicrobial use. Being transparent around antimicrobial use will also bring reputational benefits to the industries.

The Welsh Lamb and Beef Producers antimicrobial usage calculator

The Welsh Lamb & Beef Producers (WLBP) AMU Calculator went live in 2021 and allows WLBP members to calculate farm-level antibiotic use in a standardised way, allowing vets and farmers to better understand their own antibiotic use and to see how they compare to similar farm types. From July 2022, members of the Farm Assured Welsh Livestock (FAWL) scheme are required to have their antibiotic use calculated on the platform during the annual health and welfare review with the vet and, so far, over 2700 beef, sheep and dairy farms have added data. Data from WLBP will form part of the national picture through the centralised UK antibiotic data collection platform, Medicine Hub.

New initiatives in antimicrobial resistance surveillance

Below are examples of new initiatives that have been implemented in AMR surveillance since the last One Health Report was published in 2019.

One Health Integrated Surveillance

In May 2021, the One Health Integrated Surveillance (OHIS) subgroup of the Defra Antimicrobial Resistance Coordination (DARC) group was formed. The purpose of this subgroup is to develop a strategy for the integration of AMR surveillance across animal and human health, food, and the environment, and all four UK nations. The group identified evidence gaps relating to AMU and AMR surveillance across the One Health spectrum and identified necessary steps to address these. The outputs from the group are feeding into the next UK AMR national action plan (NAP) development and cross-government One Health initiatives such as Pathogen Surveillance in Agriculture, Food and the Environment (PATH-SAFE, see below) and the National Biosurveillance Network (NBN).

Pathogen Surveillance in Agriculture, Food and Environment (PATH-SAFE)

PATH-SAFE is a cross-governmental, UK-wide programme running from March 2021-March 2024. It has been funded to a value of £19.2m by phase two of the Shared

Outcomes Fund through Her Majesty's Treasury (HMT) and is led by Food Standards Agency (FSA). The PATH-SAFE project aims to develop a model national genomic surveillance network, using innovative tools such as state-of-the-art DNA-sequencing technology and environmental sampling, to improve the detection and tracking of foodborne pathogens and AMR throughout agri-food systems.

A key element of the PATH-SAFE project is to build upon existing initiatives and utilise expertise from academia, industry, and government along with advanced genomic and microbiological techniques to progress surveillance of foodborne disease and AMR. PATH-SAFE core members include Department for Environment, Food and Rural Affairs (Defra), Department of Health and Social Care (DHSC), Environment Agency (EA), Food Standards Scotland (FSS), UK Health Security Agency (UKHSA), and the VMD, with several delivery partners across government, academia, and industry. Specific AMR surveillance pilots include measuring AMR in sheep, beef and dairy cattle, livestock feed, and the natural environment.

Private Laboratories Initiative

The Private Labs Initiative (PLI) is a collaborative project between VMD and APHA. Private veterinarians send a range of clinical samples to private veterinary laboratories, as well as government laboratories, to aid diagnosis and treatment. However, results generated by most private veterinary laboratories do not feed into centralised AMR surveillance activities. This project explores how AMR data from private laboratories could be collected and processed to enhance routine AMR surveillance in animals undertaken by VMD. Early outputs from the proof-of-concept phase were published in UK-VARSS 2020. The project aims to produce outputs that are of value to private veterinary laboratories, veterinarians, and the wider livestock industries, as well as to AMR surveillance and One Health practitioners.

New initiatives in the environment sector

Measuring antibiotic residues in the environment

The Northern Ireland Environment Agency, an agency within the Department of Agriculture, Environment and Rural Affairs (DAERA), completed a baseline study of antibiotic residues in the aquatic environment between 2019 and 2020. Discharges from wastewater treatment works employing different treatment technologies and servicing a range of Population Equivalents (a measure of the size of the population that each work services) were studied along with sites downstream of these discharges. Sites downstream of large pig and poultry farms and farms to which pig and poultry waste had been exported, downstream of fish farms and consented discharges from care homes were also targeted by this study. It is hoped that this work will resume in 2023.

The One Health Breakthrough Partnership (OHBP) has been working to reduce pharmaceutical pollution of Scotland's water environment through sustainable One Health innovation. It has been trialling upstream interventions to reduce the use of medicines in healthcare and their unintended discharge to the water environment. It has conducted

research on the removal of pharmaceuticals from wastewater and has conducted a baseline review of the amounts and potential ecotoxicological and AMR risks of pharmaceuticals in Scotland's surface waters. Clarithromycin, erythromycin, and ciprofloxacin have been found to present a higher AMR risk. The OHBP has also produced and published 'Pharmaceuticals in the Water Environment', the first open access interactive tool in the UK to combine national environmental and prescribing data. With data for 60 medicines detected in river water, raw wastewater, and treated wastewater, this tool is designed to help researchers, academics, health professionals and environmental scientists develop a better understanding of the link between medicine use and the presence of pharmaceuticals in the environment.

Measuring antimicrobial resistance in the environment

The Welsh Government commissioned the UK Centre for Ecology and Hydrology to conduct a review on AMR in rural water in Wales. Following the recommendations from this review, work has been undertaken to compile data on AMR in the environment and its sources. The data has informed the creation of hazard maps investigating the effects of catchment-scale pollution on AMR in Welsh river environments. The hazard maps will help guide future environmental AMR monitoring efforts in Wales. Among other things, the report recommends establishing surveillance of direct and indirect drivers of AMR in the environment. This would help to establish a baseline for quantifying the success of future mitigation measures.

International activities

The UK plays a pivotal and practical role in supporting efforts to curb AMR across the globe using a One Health approach. The UK's 20-Year Vision to contain and control AMR encourages best practice for antibiotic use through international collaboration with global partners and outlines plans to ensure impactful interventions to mitigate the global risks of spread of AMR across humans, animals, the environment, and food.

The UK government works to advocate for AMR across many international forums including the G7 and G20, the Codex Alimentarius Commission, Quadripartite initiatives, the Transatlantic Task Force on AMR (TATFAR) and Professor Dame Sally Davies represents the UK at the Global Leaders' Group in her role as UK Special Envoy on AMR.

The UK's commitment to sustained international cooperation on AMR has secured important steps forward in the past year. Through the UK's leadership, AMR took centre stage under the UK's G7 presidency in 2021 with ambitious commitments made across multiple ministerial tracks to support innovation, access, and stewardship for antimicrobials. The UK actively participated in the discussions of the intergovernmental Codex Alimentarius Task Force on AMR (TFAMR) to revise the Code of Practice to Minimize and Contain Foodborne Antimicrobial Resistance and the Guidelines on integrated monitoring and surveillance of foodborne AMR. These revised texts were adopted by the Codex Alimentarius Commission in Nov 2021.

The UK contributes surveillance data to global databases to enable analysis and communication of information and ultimately to learn lessons and change practices in

relation to antimicrobial use. Antibiotic use in animals is submitted to the World Organisation for Animal Health ANIMUSE database. UKHSA currently report human health data on AMR and AMU to the WHO via its Central Asian and European Surveillance of Antimicrobial Resistance network (CAESAR).

Food and Agriculture Organisation (FAO)

The FAO has collectively designated the AMR expertise across the VMD, APHA and Cefas as an AMR Reference Centre (the UK was the first in the world to receive this recognition). Through this we provide support to (but not exclusively) low- and middle- income countries to build their capabilities in tackling AMR by improving their AMR and AMU surveillance and approaches in veterinary medicine residues monitoring and policy. Similarly, the UKHSA's Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit has been designated a World Health Organisation (WHO) Collaborating Centre for Reference and Research on AMR and Healthcare Associated Infections. In this role, AMRHAI supports the WHO in providing reference laboratory services for antimicrobial susceptibility testing of bacteria and detection of AMR mechanisms, and in capacity building activities via developing and supporting implementation of laboratory standards and procedures for AMR-related laboratory services. AMRHAI also works with the FAO AMR Reference Centre as part of the One Health AMR Reference Centre Cooperative to facilitate a One Health approach to tackling AMR.

Fleming Fund

The Fleming Fund is a UK aid programme partnering with 25 countries across Asia and Africa to tackle antimicrobial resistance, with One Health as a core principle. It is the world's single largest investment in global AMR surveillance, and an additional £210 million has been announced at the G20 meeting in India in 2023. The Fund is managed by the Department of Health and Social Care (DHSC) and invests in strengthening surveillance systems through a portfolio of country and regional grants, global projects and fellowship schemes. These surveillance systems contribute high quality, robust data, informing local, regional, and national policies and changing practices in both human and animal health.

Muscat Manifesto

The Muscat Manifesto declaration commits countries to a comprehensive set of ambitions targeted at tackling AMR, with One Health at its centre. The UK welcomed the manifesto as an approach that has put antimicrobial resistance at the top of global agendas. The manifesto commitments complement the UK's objectives in our UK National AMR Action Plan as well as the ambitions in our 20 -Year Vision for AMR, and the UK, alongside 46 other countries across the globe, have endorsed the Manifesto.

Looking to the future the Muscat Manifesto will help inform conversations in political leadership and action on AMR in the upcoming UN General Assembly AMR High Level Meeting (UNGA HLM) in 2024. This meeting brings together all 193 member states and presents a rare opportunity to tackle AMR on a truly global scale and across One Health sectors. We are looking forward to working with international partners to achieve an ambitious declaration to contain and control AMR across all sectors.

Annexes

Annex A: Glossary of terms

AMR	Antimicrobial Resistance
AGSLA	Antibiotic Guardian Shared Learning & Awards
AHDB	Agriculture and Horticulture Development Board
AMEG	Antimicrobial ad-hoc Expert Group
AMRHAI	Antimicrobial Resistance and Healthcare Associated Infections
AMU	Antimicrobial Use
APHA	Animal and Plant Health Agency
ARGs	Antimicrobial Resistance Genes
ARHAI	Antimicrobial Resistance and Healthcare Associated Infection
Arwain DCG	Arwain Defnydd Gwrthfaicrobaidd Cyfrifol (Responsible Antimicrobial Use)
ASPIC	Antimicrobial Stewardship in Primary Care
AST	Antimicrobial Susceptibility Testing
BPC	British Poultry Council
BSAC	British Society for Antimicrobial Chemotherapy
BSAVA	British Small Animal Veterinary Association
BSI	Bloodstream infection
BVA	British Veterinary Association
CA-MRSA	Community-Associated Methicillin-Resistant *Staphylococcus aureus*
CBPs	Clinical breakpoints
CC	Clonal complex
CIP	Chemicals Investigation Programme
CPD	Continuous professional development
DAERA	Department of Agriculture, Environment and Rural Affairs (Northern Ireland)
DARC	Defra's Antimicrobial Resistance Coordination group
DDDVet	Daily Defined Doses
Defra	Department for Environment, Food & Rural Affairs

DH	Department of Health
DHSC	Department of Health and Social Care
EA	Environmental Agency
EAAD	European Antibiotic Awareness Day
EARS-Net	European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Prevention and Control
ECOFF values	EUCAST epidemiological cut-off values
EEA	European Economic Area
EFSA	European Food Safety Authority
EMA	European Medicines Agency
eMB	Electronic Medicines Book
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESBL	Extended-Spectrum Beta-Lactamase
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	European Union
EUCAST	European Committee on Antimicrobial Susceptibility Testing
EURL	EU Reference Laboratories
FAO	Food and Agriculture Organisation of the United Nations
FAWL	Farm Assured Welsh Livestock
Food-producing	In the UK food-producing animals include cattle, chickens, duck, turkeys, gamebirds, goats, pigs, sheep and fish
FSA	Food Standards Agency
FSS	Food Safety Scotland
GIT	Gastrointestinal tract
GP	General Practitioner
HA-MRSA	Healthcare-Associated Methicillin-Resistant *Staphylococcus aureus*
HCP	Healthcare professional
HCW	Healthcare worker
HP-CIA	Highest-priority critically important antibiotics
HTML	Hypertext Markup Language
LA-MRSA	Livestock-Associated Methicillin-Resistant *Staphylococcus aureus*

LC-MS	Liquid chromatography-mass spectrometry
LOD	Limit of Detection
MAHs	Marketing Authorisation Holders
MDR	Multi-drug resistant
NAP	National Action Plan
NCP	National Control Programme
NDM	New-Delhi metallo beta-lactamase enzyme
NHSEI	NHS England and NHS Improvement
NOAH	National Office for Animal Health
OHBP	One Health Breakthrough Partnership
OHIS	One Health Integrated Surveillance group
PATH-SAFE	Pathogen Surveillance in Agriculture, Food and Environment
PAW	PDSA Animal Wellbeing
PDSA	People's Dispensary for Sick Animals
PHE	Public Health England (now UKHSA)
PLI	Private Labs Initiative
PNEC	Predicted No-Effect Concentration
RCGP	Royal College of General Practitioners
RCVS	Royal College of Veterinary Surgeons
RPF	Raw pet food
RTI	Respiratory tract infection
ResAlert	Resistant alert
RUMA	Responsible Use of Medicines in Agriculture Alliance
RUMA CA&E	RUMA Companion Animal & Equine
RVC	Royal Veterinary College
SAVSNET	Small Animal Veterinary Surveillance Network
SCC	Staphylococcal cassette chromosome
SEPA	Scottish Environment Protection Agency
SMART goals	Specific Measurable Attainable Realistic Time-bound goals
SMS	Short Messaging Service
SONAAR	Scottish One Health Antimicrobial Use and Antimicrobial Resistance report
STs	Sequence Types
TARGET	Treat Antibiotics Responsibly Guidance Education Tools
TFAMR	Task Force on AMR

UK	United Kingdom
UKHSA	United Kingdom Health Security Agency
UK-VARSS report	United Kingdom Veterinary Antimicrobial Resistance and Sales Surveillance report
UTI	Urinary tract infection
VMD	Veterinary Medicines Directorate
VRE	Vancomycin Resistance in enterococci
VREfm	Vancomycin-resistant *Enterococcus faecium*
VSE	Vancomycin-sensitive enterococci
WBLP	Welsh Lamb & Beef Producers
WGS	Whole genome sequencing
WHO	World Health Organisation

Annex B: Methods – Antibiotic consumption chapter

Data on antibiotic sales for UK animals, is collected annually by the Veterinary Medicine Directorate from Marketing Authorisation Holders (pharmaceutical companies). The antibiotic products sold can be categorised based on which one or more species the products were licensed to be used in (e.g., if they were licensed for food-producing animals, for companion animals, or for a combination of both). In humans, antibiotic dispensing data is collected differently in each of the four Nations. In England dispensing data has been aggregated to provide a total from all NHS-funded community pharmacies submitted for renumeration via the NHS Business Service authority and via IQVIAs Hospital Pharmacy Audit data for secondary care. There is no method to collect private sector prescriptions.

Table A.1: Data included under the term 'antibiotic consumption' in Chapter 1.

	Data	Definition	Data provider	Data source
Animals	Antibiotic Sales	Amounts of antibiotics sold intended for use in animals.	Marketing Authorisation Holders (pharmaceutical companies).	Sales records, for example, to veterinary practices, feed mills and/or wholesalers.
Humans	Antibiotic Prescriptions	Amounts of publicly funded antibiotics dispensed for use in humans.	Publicly funded (GPs and other community settings such as out of hours centres) and secondary and tertiary care (hospitals, acute and specialist) settings. European Antimicrobial Consumption Surveillance Network (ESAC-Net)	Primary care prescription data are available at a patient-level in Scotland, Wales and Northern Ireland and aggregated at a General Practice level in England. Hospital data are aggregated dispensed data to wards and patients.

Human antibiotic consumption was from data submitted by the UK to the European Antimicrobial Consumption Surveillance Network (ESAC-Net) for 2019. Data was collected for community (primary care) and hospital (secondary care and tertiary care) as the number of Daily Defined Doses (DDDs) per the WHO's Anatomical Therapeutic Chemical (ATC) classification substance and route of administration. Briefly, DDDs are the average

maintenance dose per day for a medicine for its main indication in adults. DDDs are only produced for medicines with an Anatomical Therapeutic Chemical (ATC) code. Rates, rather than total DDDs, are often used to assess consumption in humans and these are expressed as DDDs per 1,000 population per day (DIDs). For this report, antibiotics for systemic use (ATC group J01) and locally active intestinal antibiotics (ATC group A07AA) were included. Primary care data are available at a patient-level in Scotland, Wales and Northern Ireland and aggregated at a General Practice level in England. Hospital data are aggregated dispensed data to wards and patients.

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. Note that data presented in mg/kg for food-producing animals (which equals mg/PCU) do not include tablets or topicals, as, in line with the ESVAC methodology, these are assumed to be exclusively administered to companion animals.

Milligram per Population kilogram

Trends in sales of antibiotics over time are determined by taking into consideration variations in the size and number of the animal and human population. To achieve this, sales data for food-producing animals were analysed using the Population Correction Unit (PCU), which was formulated by the European Medicines Agency and represents the weight of the food-producing animal population (in kg) at risk by using standardised weights that represent the average weight at time of treatment. 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. Full technical details on PCU methodology can be found in the 2011 ESVAC report. Within the AMU sections of this One Health report, all references to mg/kg for food-producing animals equate to mg/PCU.

Data on antibiotic consumption by people was converted into milligram (mg) per population kilogram (kg). The World Health Organisation's (WHO) ATC classification system was used to convert DDDs to weight of active ingredient in milligrams. The estimated weight of the UK population was calculated using data from the Health Survey for England 2019.

Annex C: Categorisation of antibiotic classes

The World Health Organisation (WHO) ranks antimicrobials that are of critical importance to human health based on the risk that use in animals poses to the development of antimicrobial resistance issues in people. This looks at two major criteria:

1. The antibiotic agent is the sole or one of limited available therapies to treat serious human disease.
2. The antibiotic agent is used to treat disease caused by:
    a. a zoonotic organism (that can pass from non-human to human) or,
    b. an organism that can obtain resistance genes from non-human sources

Four antibiotic classes fulfil all these criteria and are considered the 'highest-priority critically important antibiotics' for human health. These are: macrolides, third- and fourth-generation cephalosporins, quinolones and glycopeptides.

European Medicines Agency's (EMA) Ad-hoc Antimicrobial Expert Group reviewed all critically important antibiotics identified by the World Health Organisation in 2013, to assess which antibiotics used in veterinary medicine contribute the greatest risk to development of antibiotic resistance in humans. They identified two classes as highest risk, or 'highest-priority critically important': third- and fourth-generation cephalosporins and fluoroquinolones.

In 2016 colistin, an antibiotic from the polymyxin class, was added to this list. In 2019, the EMA updated this list and published the updated AMEG categorisation of antibiotics which includes new classes of antibiotics and takes account of the need to use antibiotics in animals versus the risk of antimicrobial resistance to public health.

There are now four categories of antibiotics:

1. Category A ("Avoid") includes antibiotics currently not authorised for veterinary use. These medicines cannot be used in food-producing animals and should only be given to pets under exceptional circumstances.
2. Category B ("Restrict") refers to quinolones, third- and fourth-generation cephalosporins and polymyxins. These are critically important in human medicine and their use in animals should be restricted only to those cases when there are no antibiotics in categories C or D that could be clinically effective and use should be based on antimicrobial susceptibility testing, wherever possible.
3. Category C ("Caution") covers antibiotics for which alternatives for human use generally exist, but only few alternatives are available in certain veterinary indications. They should only be used when there are no suitable antibiotics in category D that could be clinically effective.
4. Category D ("Prudence") covers antibiotics that should be used as first-line treatments, wherever possible but, as always, should be used prudently and only when medically needed.

The AWaRe Classification of antibiotics was developed in 2017 by the WHO Expert Committee on Selection and Use of Essential Medicines as a tool to support antibiotic stewardship efforts in people at local, national, and global levels. Antibiotics were classified

into three groups, Access, Watch and Reserve, considering the impact of different antibiotics and antibiotic classes on antimicrobial resistance, to emphasize the importance of their appropriate use. In 2021, the AWaRe classification was updated to include an additional 78 antibiotics not previously classified, bringing the total to 258.

Annex D: Antibiotic consumption by antibiotic class, 2014 to 2029

Table A.2: Active ingredient in mg/kg of antibiotics consumed for humans from 2014 to 2019.

Antibiotic Class	2014	2015	2016	2017	2018	2019
Amoxicillin	40.8	38.8	37.9	36.4	35.7	33.8
Other Penicillins*	38.1	37.4	37.2	35.0	35.5	34.3
Tetracyclines	12.3	11.7	11.0	10.5	9.9	9.5
Macrolides	12.1	11.1	10.5	9.5	8.6	7.8
Imidazole derivatives	4.5	4.3	3.9	3.9	3.8	3.6
Sulphonamides and Trimethoprim	5.6	4.3	4.1	3.8	3.7	3.8
HP-CIAs**	3.7	3.5	3.5	3.7	3.8	3.5
First- and second-generation cephalosporins	3.8	3.3	3.0	2.9	2.7	2.6
Other antibacterials***	1.9	2.1	2.3	2.2	2.9	2.1
Carbapenems, monobactams	0.9	0.9	0.8	0.9	0.8	0.8
Lincosamides and Streptogramins	0.6	0.6	0.5	0.7	0.7	0.7
Aminoglycosides	0.2	0.2	0.2	0.2	0.2	0.2
Amphenicols	0.03	0.03	0.03	0.03	0.02	0.02
Total	**124.5**	**118.2**	**114.9**	**109.6**	**108.4**	**102.7**

* Includes all penicillins excluding amoxicillin

** Antibiotics are considered HP-CIAs if they are within the 'category B' in the Antimicrobial Expert Group (AMEG) report, which includes, third- and fourth-generation cephalosporins, polymyxins, and quinolones/fluoroquinolones.

*** Other antibacterials glycopeptide antibacterials, steroid antibacterials, nitrofuran derivatives, oral vancomycin and fidaxomicin, oral and rectal metronidazole and tinidazole, other cephalosporins and penems and other antibacterials.

Table A.3: Active ingredient in mg/kg of antibiotics consumed for animals from 2014 to 2019.

Antibiotic Class	2014	2015	2016	2017	2018	2019
Tetracyclines	26.1	23.6	15.0	13.1	11.7	10.2
Amoxicillin	9.7	8.4	6.1	5.5	5.4	6.3
Sulphonamides and Trimethoprim	10.0	9.7	7.0	3.3	3.2	3.5
Aminoglycosides	3.6	3.5	2.2	2.5	2.7	3.4
Macrolides	7.2	5.5	4.0	3.2	2.3	2.3
Pleuromutilins	1.8	2.2	1.4	1.4	1.2	2.1
Other Penicillins	1.7	1.4	1.8	1.8	1.3	1.2
Amphenicols	0.4	0.4	0.6	0.6	0.6	0.6
Lincosamides and Streptogramins	1.0	0.9	0.5	0.3	0.4	0.6
HP-CIAs*	0.7	0.6	0.4	0.3	0.2	0.2
First- and second-generation cephalosporins	0.1	0.1	0.1	0.1	0.1	0.1
Other antibacterials**	0.03	0.03	0.02	0.02	0.02	0.02
Imidazole derivatives	0	0	0	0	0	0.005
Total	**62.3**	**56.5**	**39.0**	**32.1**	**29.2**	**30.4**

* Includes all penicillins excluding amoxicillin

** Antibiotics are considered HP-CIAs if they are within the 'category B' in the Antimicrobial Expert Group (AMEG) report, which includes, third- and fourth-generation cephalosporins, polymyxins, and quinolones/fluoroquinolones.

Table A.4: Active ingredient by class in tonnes of antibiotics consumed in animal and human sectors in 2019.

Antibiotic Class	Animals	Humans
First- and second-generation cephalosporins	3.9	12.2
Aminoglycosides	23.9	0.9
Amphenicols	4.3	0.1
Carbapenems and monobactams	0	3.8
Imidazole derivatives	2.0	16.8
Lincosamides and Streptogramins	4.8	3.1
Macrolides	16.7	36.2
Other**	0.1	9.9
Penicillins	59.0	316.8
Pleuromutilins	14.6	0
Tetracyclines	72.8	44.1
Trimethoprim/sulphonamides	25.1	17.7
Third- and fourth-generation cephalosporins*	0.2	4.9
Fluoroquinolones*	1.0	10.8
Polymyxins*	0.01	0.5
Total	**228.5**	**477.8**

* Antibiotics are considered HP-CIAs if they are within the 'category B' in the Antimicrobial Expert Group (AMEG) report, which includes, third- and fourth-generation cephalosporins, polymyxins, and quinolones/fluoroquinolones.

** Other antibacterial includes: in animals - aminocoumarins; in humans - includes glycopeptide antibacterials, steroid antibacterials, nitrofuran derivatives, oral vancomycin and fidaxomicin, oral and rectal metronidazole and tinidazole, other cephalosporins and penems and other antibacterials.

Table A.5: Percentage of weight (tonnes) active ingredient consumed in animal and human sector.

Antibiotic Class	Animals (%)	Humans (%)
Carbapenems and monobactams	0	100
HP-CIAs*	7	93
Other antibacterials**	7	93
Penicillins	16	84
First- and second-generation cephalosporins	24	76
Macrolides	32	68
Trimethoprim/sulphonamides	59	41
Lincosamides and streptogramins	61	39
Tetracyclines	63	37
Aminoglycosides	96	4
Amphenicols	98	2
Pluromutilins	100	0

* Antibiotics are considered HP-CIAs if they are within the 'Category B' in the Antimicrobial Expert Group (AMEG) report, which includes, third- and fourth-generation cephalosporins, polymyxins, and quinolones/fluoroquinolones.

** The category "other antibacterials" includes: in animals - aminocoumarins; in humans - includes glycopeptide antibacterials, steroid antibacterials, imidazole derivatives, nitrofuran derivatives, oral vancomycin and fidaxomicin, oral and rectal metronidazole and tinidazole, other cephalosporins and penems and other antibacterials.

Annex E: Examples of standards on the use of highest-priority critically important antibiotics (HP-CIAs) in UK food assurance schemes

Cattle and sheep

Red Tractor, Farm Assured Welsh Livestock Beef and Lamb Scheme (FAWL) and Quality Meat Scotland (QMS) require an annual review of HP-CIA use in cattle and sheep. Under Red Tractor vets also need to provide a statement outlining the justification for use of an HP-CIA, including sensitivity testing and/or diagnostics.

Pigs

QMS Scotland stipulate that HP-CIAs should only be used when there is no suitable alternative, or where sensitivity tests have been completed beforehand. Their use must be justified in the Veterinary Health and Welfare Plan and an antibiotic reduction plan must be in place to prevent recurrent use. Under Red Tractor vets also need to provide a statement outlining the justification for use of an HP-CIA, including sensitivity testing and/or diagnostics.

Poultry

The use of third- and fourth-generation cephalosporins, glycopeptides and colistin are not permitted in poultry farms under Red Tractor and the use of macrolides and fluoroquinolones must only be as a last resort, under veterinary direction. In the laying hen sector, the use of fluoroquinolones in day old chicks and the use of third- and fourth-generation cephalosporins is prohibited under the British Lion Code.

Annex F: Data sources – Antibiotic resistance chapter

Livestock

This surveillance is conducted in major food-producing animal species (pigs, broiler chickens, layer chickens and fattening turkeys). The Veterinary Medicines Directorate (VMD) co-ordinates this surveillance in the UK. Sampling is designed to cover over 60% of abattoir throughput. It is randomised, stratified, and weighted by slaughter throughput of healthy animals (full methods available here). Harmonised monitoring surveillance co-ordinated by the VMD and the *Salmonella* poultry National Control Programme include data from all UK countries. Clinical surveillance includes data contributed by GB, Scotland, and Northern Ireland. Data for all UK countries are published in the UK-VARSS report, however due to methodological differences, data from Scotland and Northern Ireland are published in the UK-VARSS supplementary material.

The VMD contracts the Food Standards Agency (FSA) to collect samples from abattoirs in England, Scotland, and Wales; DAERA co-ordinate caecal sampling in Northern Ireland. The Animal and Plant Health Agency (APHA) then conduct laboratory analysis on samples collected in England, Scotland, and Wales, whilst the Agri-Food and Biosciences Institute (AFBI) conducts analysis for Northern Ireland. UK retail meat surveys are also conducted by the FSA to quantify AMR in meat products on sale to the public, to assess immediate consumer risks. Only surveillance data from pigs, broilers and retail pork and chicken are included in this report as these link directly to FSA retail meat surveys to better assess AMR across the agrifood chain for comparison with human data. Data for all animals monitored are published annually in the UK-VARSS report.

In 2018 and 2019, samples were taken from healthy broilers, pigs and turkeys at slaughter by FSA personnel, in accordance with Decision 2013/652/EU20. This standardised the monitoring and reporting of AMR in the food chain across Europe. Post EU-exit, since January 2020, the UK continue to largely operate in accordance with the EU decision, with some enhancements to ensure continuity of data outputs from this programme and facilitate data comparability across Europe. In the UK, key livestock species are monitored in alternating years (poultry in even years, pigs in odd years). *Salmonella* spp. isolates from poultry are collected within the National Control Programme (NCP). When interpreting results, susceptibility is interpreted using EUCAST human clinical break point (CBP) values and EUCAST epidemiological cut-off values (ECOFFs) which also allow data to be compared internationally.

Routine AMR surveillance monitors the presence of ESBL/AmpC-producing *E. coli* in healthy pig and broiler chicken caecal samples at slaughter, as well as from fresh chicken and pig meat at retail through the harmonised monitoring programme. Surveillance also covers laying hens and fattening turkeys however these are not included in this report. Selective media is used to culture ESBL/AmpC-producing *E. coli* as this ensures that if any are present in a sample, they will be detected as these are important resistances to monitor due to public health relevance. This means that we have data from livestock and retail meat to compare for ESBL-producing *E. coli* (**Figure 2.8**).

Human

AMR in humans is not fully quantified because a vast majority of infections are self-limiting and not confirmed by laboratory testing. Only a small percentage of human strains have antibiotic susceptibility testing especially after introduction of molecular testing for detection of food pathogens and gastrointestinal bacteria. Therefore, caution should be taken when interpreting the results presented here as it is difficult to make meaningful comparisons between trends of antibiotic resistance profiles in human and food isolates.

Human data is collected largely through passive surveillance from diagnostic and reference laboratories. Human non-typhoidal *Salmonella* spp. isolates presented in this report are from faeces and sterile sites from patients, whilst *E. coli* isolates from humans are from blood samples as a proxy for invasive infection. *E. coli* BSI data are from England, Scotland, and Northern Ireland. Human *Campylobacter* spp. isolates included in the chapter are from sterile sites or/and faecal samples.

Note that the testing of certain bacteria-antibiotic combinations from human clinical samples is not always comprehensive; this means there can be a bias towards resistant bacteria for antibiotics reserved for use in secondary care in these results. Samples from primary care may be more likely to be tested in general where primary treatment (often without culture) has failed or for more complex, treatment-experienced patients.

Annex G: Description of resistance levels

Table A.6: Descriptions of percentage resistance levels referenced in this report using the EFSA definitions.

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%

Annex H: List of bacterial species monitored for antibiotic resistance in the UK as of 2019

Bacterium	Human	Animal
Acinetobacter spp.	X	
Brachyspira hyodysenteriae		X
Campylobacter spp.	X	X
Citrobacter spp.	X	
Enterococcus spp.	X	
Escherichia coli	X	X
Haemophilus influenzae	X	
Klebsiella oxytoca	X	
Klebsiella pneumoniae	X	X
Mannheimia haemolytica		X
Morganella spp.	X	
Mycobacterium tuberculosis (TB)	X	
Neisseria gonorrhoeae	X	
Pasteurella multocida		X
Pseudomonas spp.	X	X
Proteus spp.	X	
Providencia spp.	X	
Salmonella spp.	X	X
Serratia spp.	X	
Staphylococcus aureus (e.g. MRSA)	X	X
Stenotrophomonas spp.	X	
Streptococcus dysgalactiae		X
Streptococcus pneumoniae	X	
Streptocuccus suis		X
Streptococcus uberis		X

Data cited for both humans and animals are from the two major annual reports on UK antibiotic resistance levels in humans (EPSAUR Report 2020-2021) from UKHSA and animals (2020 UK-VARSS Report) from the Veterinary Medicines Directorate

Annex I: Companion animals and public health

The mg/kg metric for dogs and cat AMU

To ensure that only antimicrobial products certainly or very likely to have been used in dogs and/or cats were included in the analysis, only products licensed for the following species were analysed; dogs only, cats only, a combination of dogs and cats only, and products licenced for dogs and/or cats alongside other animal species commonly seen in small animal practice (rabbits, reptiles, ornamental birds and rodents). Products licensed for dogs and/or cats in combination with horses and/or food-producing animals were not included in the analysis.

Calculating the mg/kg metric

The combined weight of the dog/or cat population at risk of being treated with antibiotics in any given year was calculated as follows:

Total number of animals in the UK x mean weight of one animal (kg) = estimated animal biomass (kg) at risk of antibiotic treatment

Animal population numbers in the UK each year were taken from annual PAW Report survey data, which is a survey representative of the UK pet-owning population. The average weight in kilograms for cats and dogs in each year was estimated by calculating the aggregated mean weight for all adult cats and all adult dogs registered at veterinary practices participating in the Small Animal Veterinary Surveillance Network (SAVSNET) for each respective year. This includes data from 1,049,449 dogs and 542,324 cats from just under 300 veterinary practices. In 2019, the average weight of dogs was calculated to be 18.2 kg and the average weight for cats was calculated to be 4.5 kg.

The main limitation with using mg/kg for trend monitoring is that this metric tends to underestimate products which have lower dose rates (such as many HP-CIAs) and long-acting antibiotic products. Conversely, some products have higher dose rates so tend to be relatively over-represented with the mg/kg metric.

The DDDVet/kg metric for dog and cat AMU

To overcome the above limitations, analysis of companion animal sales data for systemic antibiotics is also presented using the 'average number of Daily Defined Doses (nDDDVet) per animal per year' which accounts for the dose rate of each antibiotic product and represents the average number of days (or daily doses) that each animal across the UK has been exposed to an antibiotic.

To overcome this you can calculate a metric [Average number of Defined Daily Doses per animal (nDDDVet/animal)] that takes into account dose rates and course lengths and represents the average number of days (or daily doses) that each animal across the UK has been exposed to an antibiotic. This is calculated by the following calculation (for each active ingredient/route of administration and for both dogs and cats):

Average number of DDDvet/animal (nDDDVet/animal) =

$$\frac{\textit{Total amount of active ingredient (mg)}}{\textit{Daily dose rate (DDDVet) in mg/kg * Total weight of population (kg)}}$$

The results are then added together to get the total figure.

The DDDVet figures used can be found below and have been obtained by looking at the dose rates used for each product on their Summary of Product Characteristics. If there is a dose range, then the lowest dose was chosen, and where the dose rate varies between products with the same active ingredient or route of administration, then the median dose rate was selected. For long-acting products, the DDDVet is calculated by dividing the daily dose rate with the length of activity for that product.

The metrics described here have been developed alongside, and with support of, the RUMA Companion Animal and Equine group.

Table A.7: DDDVet/kg metric for dogs

Ingredient	Formulation	Length of activity	Average daily dose rate	DDD (mg/kg)
Amoxicillin*	Tablets/ Oral Solution	1.0	20.0	20.0
Ampicillin	Tablets	1.0	20.0	20.0
Cephalexin	Tablets	1.0	30.0	30.0
Cefovecin	Injection	14.0	8.0	0.6
Clindamycin	Tablets/ Oral Solution	1.0	11.0	11.0
Doxycycline	Tablets	1.0	10.0	10.0
Enrofloxacin	Tablets/ Injection	1.0	5.0	5.0
Marbofloxacin	Tablets/ Injection	1.0	2.0	2.0
Metronidazole	Tablets	1.0	50.0	50.0
Metronidazole-spiramycin	Tablets	1.0	35.9	35.9
Oxytetracycline	Tablets	1.0	50	50
Pradofloxacin	Tablets	1.0	3.0	3.0
Trimethoprim-sulphadiazine	Tablets/ Injection	1.0	30.0	30.0

* Includes those in combination with clavulanic acid, although clavulanic acid is not counted as an active ingredient

Table A.8: DDDVet/kg metric for cats

Ingredient	Formulation	Length of activity	Average daily dose rate	DDD (mg/kg)
Amoxicillin*	Tablets/ Oral Solution	1.0	20.0	20.0
Cephalexin	Tablets	1.0	30.0	30.0
Cefovecin	Injection	14.0	8.0	0.6
Clindamycin	Tablets/ Oral Solution	1.0	11.0	11.0
Doxycycline	Tablets	1.0	10.0	10.0
Enrofloxacin	Tablets/ Injection	1.0	5.0	5.0
Marbofloxacin	Tablets/ Injection	1.0	2.0	2.0
Metronidazole	Tablets/ Oral Solution	1.0	50.0	50.0
Metronidazole-spiramycin	Tablets	1.0	35.9	35.9
Pradofloxacin	Tablets	1.0	3.0	3.0
Pradofloxacin	Oral Solution	1.0	5.0	5.0
Trimethoprim-sulphadiazine	Tablets/ Injection	1.0	30.0	30.0

* Includes those in combination with clavulanic acid – although clavulanic acid is not counted as an active ingredient)

Annex J: Update on the recommendation of the 2015 UK One Health Report

Recommendation 1: *"Public health organisations should work with clinical laboratory colleagues to ensure that all* Salmonella *species are sent to the relevant reference laboratories for speciation and testing. The referral form should include data on travel abroad, including countries, in the previous four weeks. This will allow accurate epidemiological data to be collected on species, AST, the ability to review differences in isolates that were more likely acquired in the UK versus abroad, improved comparisons across Europe and focussed treatment based on likely country of origin in the future."*

Complete: The Diagnostic laboratories send at least one *Salmonella* spp. isolate per patient episode to the reference laboratory for confirmation of identification and AMR surveillance. The referral forms have been updated to collect data on foreign travel in the preceding 4 weeks.

Recommendation 2: *"Public health organisations should scope the development of a national sentinel surveillance system for* Campylobacter *isolates collected from human infections. In addition, public health organisations should highlight the importance of identifying* Campylobacter *to a species rather than genus level. This would allow national data on species, AST and travel history to be collected on a robust sampling frame to determine antibiotic resistance and impact of travel on* Campylobacter *resistance in human campylobacteriosis. It would also ensure that treatment, where necessary, is based on robust epidemiological data."*

In progress: UKHSA are working with national laboratory standards to improve the identification, speciation and AMR testing on a representative number of isolates. The national sentinel sites are being approached with roll out of faecal molecular assays across regional public health laboratories in England.

Recommendation 3: *"Public health organisations should support the work of the BSAC to transition clinical laboratories to EUCAST methodology and breakpoints in 2016. This will allow more robust, reliable and comparable data to be collected using the national passive surveillance systems."*

Complete: BSAC published support for the EUCAST method in 2016, aligning their breakpoints and withdrawing support for the BSAC methodology.

Recommendation 4: *"Public health organisations should work with BSAC and the UK Standards for Microbiology Investigations to develop guidance related to recommended antibiotic and bacterial combinations, which should be tested and reported by human clinical laboratories for key One Health pathogens. Clinical laboratories should continue to report all notifiable diseases and AST results to the national surveillance organisation. Animal health organisations should review the antibiotics tested against isolates from clinical veterinarian samples and through the EU harmonised monitoring in animals. This would reduce the variability in testing and reporting that currently is evident across clinical*

laboratories and would improve the robustness of the current passive surveillance systems. It would also allow the early ascertainment of emerging threats, the development of risk assessments and interventions to minimise the spread of antibiotic resistance."

Complete: In the harmonised monitoring programme, certain active ingredients are included in the antibiotic testing panel which are not authorised for use in food-producing animals. These are included to monitor resistances of concern to public health (for example, carbapenem resistance). Additionally, transition to gold-standard minimum inhibitory concentration (MIC) testing of veterinary pathogens from clinical diagnostic samples was initiated in 2021 by the VMD in collaboration with APHA. The antibiotics chosen for inclusion in the panel were selected according to their clinical importance and licensing in the UK and across Europe, as well as their suitability as representatives of resistance to a given class. Although the focus is on veterinary antibiotics, to support vets' prescribing choices, the panel includes some antibiotics that are key to human and animal health, such as doxycycline and amoxicillin/clavulanate.

Recommendation 5: *"Human public health reference laboratories should follow the EU protocol for harmonised monitoring of antimicrobial resistance in human* Salmonella *and* Campylobacter *isolates. This includes speciation, typing, AST using quantitative methodology on recommended antibiotic panels, specific testing for antibiotic-resistant enzymes and whole genome sequencing. Where current resources are inadequate scoping of requirements should occur. This will improve the comparison of trends in the occurrence of antibiotic resistance of human* Salmonella *and* Campylobacter *infections, including comparison with food/animal isolates and provide information of the genetic determinants of resistance that are important for public health recognition of cross-border threats in Europe."*

Complete: AMR profiles were determined using the epidemiological cut-off (ECOFF) values as recommended in the EURL/EUCAST protocol for harmonising monitoring of AMR in human *Salmonella* spp. and *Campylobacter* spp. isolates.

Recommendation 6: *"Public health organisations should explore data available on human sales of antibiotics, from manufacturers and holders of human marketing authorisations. This will allow a determination of data gaps in current surveillance in humans and improve the comparability of data across humans and animals."*

Complete: There is no single data source containing all sales of antibiotics for use in people in the UK. UKHSA and DHSC have prioritised establishing surveillance of individual-level prescribing data, to give a more accurate measure of antibiotic usage.

Recommendation 7: *"VMD should conduct carbapenem resistance monitoring (as part of the EU harmonised monitoring of key bacteria from the 01 January 2014 in accordance with the legislation, Commission Decision 2013/652/EU on the 'monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria'), a year earlier than mandated. This legislation details the requirements to monitor antimicrobial resistance in* Salmonella *spp.,* Campylobacter *spp., and* E. coli *in various livestock populations at slaughter, as well as meat products at retail. In 2016, 2018 and 2020 isolates of* E. coli,

Campylobacter *and* Salmonella *from broilers and turkeys will be examined for resistance, while in 2015, 2017 and 2019 isolates of* E. coli *and* Salmonella *from pigs UK One Health Report 40 will be examined. The* E. coli *from pigs will be screened for carbapenem resistance a year ahead of schedule."*

Complete: Monitoring for carbapenemase-producing *E. coli* was not able to commence a year earlier than mandated, however, has been in place since 2015. As mentioned in the previous One Health Report, between 2015 and 2017 no carbapenemase-producing *E. coli* were detected in samples collected from broiler chickens, turkeys, or pigs at slaughter as well as pork, beef, or broiler meat at retail. This trend continued for 2018 and 2019. Of note in human health, from 1 October 2020, all diagnostic laboratories in England have a duty to notify all acquired carbapenemase-producing Gram-negative bacteria identified in human samples, alongside the results of any antimicrobial susceptibility test and carbapenem any resistance mechanism in any of the causative agents listed in Schedule 2 of the Health Protection (Notifications) Regulations 2010.

Recommendation 8: *"The VMD should participate in the protocol development of the ESVAC project to collect farm level data from the pig sector. This programme will be extended in 2015, further rolled out to look at antibiotic consumption in the poultry and cattle sectors over the next three years. The VMD will investigate and facilitate options for collecting accurate antibiotic consumption data at an individual farm level. This will improve the antibiotic use data available in animals and allow improved farm level and species level ecological analysis and its relationship to antibiotic resistance to be defined."*

Complete: In 2016, the electronic Medicines Book (eMB) for pigs was launched by the UK pig farming industry. The eMB is administered by the Agriculture and Horticulture Development Board (AHDB) and acts as a central database to enable UK pig producers to record and benchmark their antibiotic use. Since 2016, the farm assurance schemes Red Tractor and Quality Meat Scotland have required members to record antibiotic use quarterly on the eMB. Over 95% of UK pig producers are part of Red Tractor and almost 100% of Scottish pig producers are part of QMS. An anonymised, aggregated annual figure reflecting UK antibiotic use in pigs is provided by the sector for the inclusion in the annual UK-Veterinary Antimicrobial Resistance and Sales Surveillance (UK-VARSS) report.

Recommendation 9: *"The One Health approach should be enhanced in public and professional activities through engagement with EAAD campaign and aligning and integrating this approach to training programmes for human and animal health professionals. This is a crucial component to develop cross-sectoral understanding and improved working in the future."*

Complete: UKHSA launched the One Health pledge-based Antibiotic Guardian campaign in 2014, with the aim of transitioning from raising awareness to increasing engagement. The campaign uses an online pledge-based approach among human and animal health professionals, scientists and educators and the public. Annually, the World Antimicrobial Awareness Week and EAAD activities provide a focused

opportunity to raise awareness and increase engagement. The national toolkit is available via https://www.gov.uk/government/publications/european-antibiotic-awareness-day-resources-toolkit-for-healthcare-professionals-in-england.

Recommendation 10: *"The human and animal surveillance bodies should produce a further report in two years. Future work must include detailed data from the Food Standards Agency to improve knowledge on antibiotic resistance detected in UK and imported food sold in supermarkets and other outlets. This will ensure that progress with these recommendations is reported and surveillance developments in support of the UK AMR strategy occur."*

Complete: VMD and UKHSA colleagues have worked hard to coordinate and produce this year's One Health Report despite the pressures associated with the COVID-19 pandemic. Due to this pressure, this report has been produced with reduced personnel and resource and was necessarily delayed. Nonetheless, data on AMR in retail meat collected by the FSA has been included in this year's report and presented together with AMR surveillance data from human patients, and food-producing animals, for the first time.