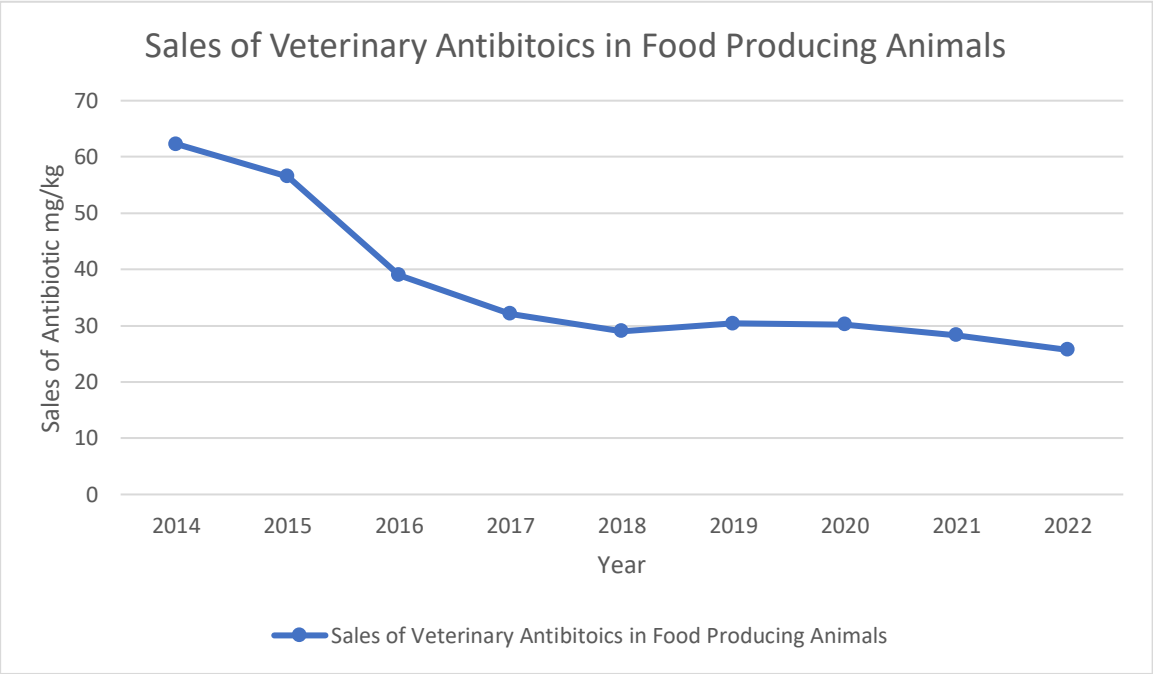
VETERINARY POLICY RESEARCH FOUNDATION

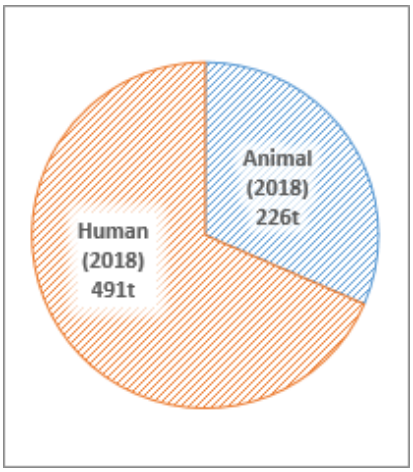
Antimicrobial Usage and Resistance Fact File

Current Usage in the UK

Animal antibiotic usage targets for 2018, set by the Government commissioned O'Neill report of 50mg/kg, were met two years early. Overall usage in food producing animals dropped by 59% (to 25.7mg/kg) from 2014 to 2022, these are the lowest ever recorded[169] .In people antibiotic use per kg bodyweight reduced by 9% from 2013-17 (from 135mg/kg to 123mg/kg) and declined by a further 15.1% from 2017-2022[170]. Use of antibiotics as growth promoters in Europe (including the UK) has been banned since 2006. Antibiotics used in animals must be dispensed by a vet for an animal 'under their care'.

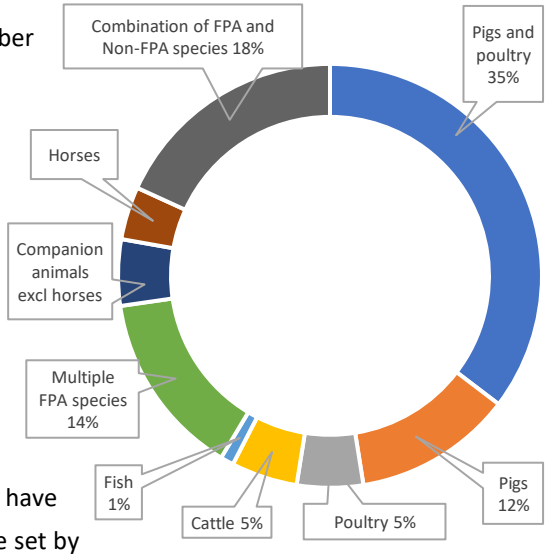


Most antibiotics sold in the UK (measured in tonnes of active ingredient) are for human use (see chart). There are also differences in the types of antibiotics used in humans and animals. In animals the most common active ingredients are tetracyclines (32%), penicillins (28%) and aminoglycosides (12%), accounting for 72% of those sold [169] . In humans, 72.1% of antibiotics are prescribed in NHS GPs, with penicillins accounting for 45.2% of NHS GP prescriptions [170] .The World Health Organisation's Highest-Priority Critically Important Antibiotics account for 0.5% of total antibiotic sales for animals and sit below the targets set by the EU (see section 6.2).



The UK has the 5th lowest level of antibiotic consumption in food-producing animals out of 31 European countries reporting this data (2018).

FIGURE 2 - ANTIBIOTIC DISPENSED FOR HUMAN AND ANIMAL USE IN THE UK (TONNES)



Species specific usage of antibiotics are difficult to calculate for a number of reasons:

- Sales are routinely recorded although there has been good uptake of voluntary usage recording schemes in pigs, poultry (inc eggs), salmon and trout farming.
- Sales data for products licensed for use in multiple species cannot be further differentiated and sales may vary from actual usage (pers comms, NOAH).
- Records of actual antibiotic usage may be measured in different ways in difference sectors (see section 6).

RUMA (Responsible Use of Medicines in Agriculture Alliance) have established an industry targets task force, with targets for reduced use set by leading vets and farmers from beef, dairy, egg, fish, gamebird, pig, poultry and sheep sectors.

UK Antibiotic Usage and Resistance: Fact File

Last updated November 2023

About the Veterinary Policy Research Foundation (VPRF)

The VPRF is a not-for-profit organisation set up by Lord Trees with the purpose of employing a veterinary surgeon as an intern/researcher to facilitate Lord Trees' activities in the House of Lords.

Declarations by the authors

The authors are veterinary surgeons and support action to combat antibiotic resistance that balances the need to maintain the health and welfare of both humans and animals.

Professor the Lord Trees is a veterinary surgeon and a crossbench peer. Catrina Prince, Dr Gabrielle Laing, Anthony Ridge and Fiona Shuttleworth are veterinary surgeons, who have held the role of Parliamentary Veterinary Intern. The Parliamentary Veterinary Internship is funded by The Veterinary Policy Research Foundation that receives sponsorship from several veterinary organisations, professional bodies and universities. Further information on the VPRF can be found on our website: https://vprf.wordpress.com/

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Aims and Objectives

The purpose of this document is to provide an unbiased and factual summary of mainly quantitative information relating to antibiotic usage and antibiotic resistance in the UK in animals and humans. The report primarily focuses on *Campylobacter spp, Salmonella spp and E. coli* which are commonly found in animals and capable of transmitting to and causing disease in humans. The report also brings together information on current activities being undertaken by the UK Government, human and veterinary healthcare professions and the animal industries to combat the negative impacts of antibiotic resistance on human and animal health.

This report does not consider drug resistance in viruses, fungi, protozoa or helminths.

We have **not** attempted a comprehensive review or analysis of research examining the **transfer** of antibiotic resistant bacteria from animals to humans and from humans to animals.

This report provides a summary of the data and information relating to antibiotic usage and resistance known to the authors at the time of publication. The authors aim to update this report as new relevant information becomes available. The date of the latest update is displayed on the cover page. The authors welcome any constructive feedback on additional data to include or ways to further improve this document. These will be considered in future updates.

IMPORTANT NOTE FROM THE AUTHORS ON GLOBAL CONTEXT

Whilst this document largely focuses on the UK for practical reasons, it is important to recognise that antibiotic resistance is a global problem. In contrast to the UK, many countries have no or limited legal controls on the use of antibiotics in humans and animals. These countries also tend to have high populations of both humans and animals, with close contact between the two. Antibiotic resistance which arises anywhere in the world can very quickly spread to many other countries by human carriage of bacteria as a result of the massive and rapid global movement of people. The movement of animals and food products can also contribute. It is thus essential that the problem is addressed globally as recommended in the Review on Antimicrobial Resistance commissioned by the UK Government. Whatever is done in the UK will not solve the global problem, nor will it eliminate the risks associated with antibiotic resistance in the UK.

1. Introduction

1.1 Antibiotic resistance is now well recognised as a major international threat to society.[1]

1.2 The ability to treat bacterial infections with antibiotics is a crucial element of both human and animal healthcare.

1.3 Antibiotic usage selects for the development of antibiotic resistance in bacterial populations.[2]

1.4 Resistance to antibiotics that are crucial for the treatment of certain diseases and particularly the development of simultaneous resistance to several antibiotics (multi-drug resistance) can severely restrict our ability to treat infections.

1.5 The development of new types of antibiotics helps to overcome existing resistance. However, in the last 30 years almost no new classes of antibiotics have been discovered.[3]

1.6 Increased usage of antibiotics combined with greater movement of people are major contributors to the development and global spread of antibiotic resistant bacteria.[4]

1.7 Resistance mechanisms can potentially spread through bacterial populations including from animals to humans (e.g. from direct contact, the environment and/or via the food chain[5]) and from humans to animals[6].

1.8 The use of antibiotics in animals has been linked to increases in certain types of antibiotic resistance in humans.[7] However, ceasing use of the antibiotic where resistance has developed has not necessarily resulted in a return bacterial susceptibility to the antibiotic (see Box 3, section 7.2).

1.9 Genetic studies have the capacity to expand our understanding of the origin and spread of antibiotic resistance genes. There has been evidence of transference of antibiotic-resistant bacteria from animals to humans between pigs and a pig-farm worker, however, genetic, population level studies of antibiotic resistant zoonotic bacteria causing disease in humans have been found to be genetically distinct from isolates from livestock or meat product (see section 7.2).

2. Summary of key facts

2.1 Antibiotic usage in the UK

2.1.1 There are limitations in the availability of accurate data on antibiotic usage in humans and animals and currently (November 2023) no centralised system for data collection across all species in the UK.

2.1.2 Total antibiotic usage in humans has decreased from 521 in 2013 to 491 tonnes in 2017. These figures, however, do not include private prescriptions, estimated to increase the total figure by around 10%. In 2015 usage reduced significantly across the whole human healthcare system for the first time. Approximately 80% of total human antibiotic usage in the UK arises from community usage such as GP prescriptions and 20% from usage in hospitals. (Figure 6).[160]

2.1.3 Total antibiotic usages in all animals have decreased from 447 tonnes in 2014 to 193 tonnes in 2022.[169]

2.1.4 Total antibiotic usage across humans and animals reduced by 28% i.e. from 986.0 tonnes in 2014 to 706.3 tonnes in 2019. As of 2019, the animal sector consumed 32% of antibiotics, down from a 44% consumption share in 2014.[193]

2.1.5 Overall, antibiotic use has fallen by 18% in humans and 51% in animals between 2014-2019.[193]

2.1.6 Furthermore, 2019 UK data shows that one third of all UK antibiotics were used in animals, and two thirds in humans. This is important, as global data (whereby animal use may be higher is certain countries) is often incorrectly extrapolated to the UK.[193]

2.1.7 Antibiotic use in trout farms has increased by 130% since 2017. The British Trout Association are carrying out a survey to investigate this increase but predict the unprecedented levels of antibiotic use may be due to outbreaks of *Aeromas salmonicida.* They expect levels will fall below 2017 values and below industry targets by next year.[*169*]

2.1.8 Sector specific targets for agricultural antibiotic use were agreed at RUMA Conference 2017 (Responsible Use of Medicines in Agriculture). Antibiotic usage for growth promotion in animals has been banned in the UK and across the EU since 2006.[8]

2.1.9 In the UK, antibiotics for use in animals must be prescribed by a veterinary surgeon. The majority of antibiotics prescribe din humans need to be prescribed by a qualified health professional (doctor, dentist, nurses with suitable qualifications etc). However, some antibiotics are available to purchase over the counter.

2.1.10 The European Medicines Agency (EMA) has, on request from the European Commission, identified the most Highest Priority Critically Important Antibiotics (HP-CIAs) based on degree of risk to human health due to antimicrobial resistance development, following use in animals. It has concluded that the Highest Priority Critically Important Antibiotics are **fluoroquinolones**, **3rd and 4th generation cephalosporins** and **colistin.**[9]

2.1.11 Compared to other European countries, the UK has below average antibiotic use in the human sector; with the third lowest use of fluoroquinolones in humans (0.5 DDDs per 1000 inhabitants per day). During 2013-2017 there was no statistically significant change in human consumption of antibiotics across Europe[161], but since 2022 some classes of antibiotics have a statistically

significant reduced consumption (tetracyclines, macrolides, cephalosporins etc.), notably not broad-spectrum penicillins.[171]

2.1.12 When comparing amounts of active ingredient used for animals and humans, the largest proportion of HP-CIAs was prescribed for use in humans in 2017[160]. Figure 5 shows Fluoroquinolones and 3rd and 4th generation cephalosporins are used more heavily in humans than in animals.

2.1.13 Between 2013-2022 animal sales of fluoroquinolones reduced by 71%, 3rd and 4th generation cephalosporins by 89% and colistin by 100%[169]. Overall, total sales (mg/PCU) of HP-CIA antibiotics in animals decreased by 81% from 2014 to 2022. They currently represent 0.5% of total veterinary antibiotic sales.[169]

2.1.14 In cats, the HP-CIA 3rd generation cephalosporin was the most sold active ingredient antibiotic in 2022, making up 42% of sales.[169]

2.1.15 Antibiotics of last resort in human medicine are piperacillin/tazobactam, carbapenems and colistin.[170]

2.1.15.1 Use of colistin in secondary care increased between 2016-2020, and then dropped by 15.1% in 2021.

2.1.15.1.1 In 2020 there were significant increases in colistin prescribing in all trust types apart from acute multi-service trusts.

2.1.15.2 Use of carbapenems has fallen across all trust types over the past 5 years. There was a notable large increase in 2020 due to their inclusion within NICE hospital-acquired-pneumonia guidelines during the COVID-19 pandemic.

2.1.15.3 Use of piperacillin/tazobactam significantly reduced in 2017 due to shortages; impacting the use of other alternative antibiotics.[158] and has been increasing from 2017-2020 after being included in multiple guidelines for pneumonia treatment in hospital. Since 2020, use has been reducing across all trust types.[170]

2.1.15.4 In 2019, the human health sector consumed 93% of all HP-CIAs when comparing percentage consumption in tonnes between humans and animals.[193]

2.1.16 There are no piperacillin/tazobactam or carbapenem containing drugs licensed for use in animals in the UK[10]

2.1.17 Colistin is a last resort antibiotic used in human medicine in the UK for the treatment of drug resistant infections (Box 1). Widespread use of colistin in Chinese pig farms has been implicated in the development and spread of colistin resistant bacteria. [11]

2.1.18 In animals, colistin sales in the UK is one of the lowest in Europe (0.01mg/PCU[159]) and below the recently recommended target set by the European Medicines Agency (1 mg/PCU) (Box 1) and the European Country mean in 2018 (3.4mg/PCU, data from 31 countries).

2.1.19 A voluntary restriction on colistin usage in UK farm animals was agreed in December 2015.[12]

2.1.20 Since 2021, colistin has not been sold in the UK for use in animals.[169]

2.2 Antibiotic resistance in the UK

2.2.1 *E. coli*, *Salmonella* and *Campylobacter* are zoonotic organisms easily transmitted from animals to humans including via the food chain. *E. coli* is considered an indicator organism for monitoring

antibiotic resistance levels in animal populations and along with *Salmonella* and *Campylobacter* are primary causes of food poisoning in the UK.[13]

2.2.2 New surveillance from the Veterinary Medicines Directorate (VMD) 2022 includes 3 new species of bacteria[169]

2.2.2.1 Campylobacter coli:

2.2.2.1.1 Added to the surveillance panel as they often are more antibiotic resistant than *C. jejuni* and can possibly transfer resistant genes to *C. jejuni.*

2.2.2.2 Enterococcus faecalis

2.2.2.3 Enterococcus faecium

2.2.2.3.1 The addition of *Enterococcus* allows the detection of vancomycin resistant enterococci (VRE) and detecting antimicrobial resistance in general in gram-positive bacteria.

2.2.2.3.2 No VRE was detected in any of the 2022 isolates.[169]

2.2.3 Comparable data on antibiotic resistance levels in bacterial populations from humans and animals are limited.[14]

2.2.4 In humans, antibiotic resistant gram-negative infections are responsible for the majority of clinically significant cases of resistance. Resistance of *E. Coli, Klebsiella pneumoniae, Klebsiella oxytoca* and *Pseudomonas spp.* remained broadly stable between 2013 and 2017[158] . However, E.coli resistant to piperacillin/tazobactam (the most frequently used antibiotic for the treatment of sepsis) and carbapenems increased significantly between 2017-2021.[170] Similarly, non-susceptibility of Klebsiella pneumoniae to ciprofloxacin, 3rd generation celphalosporins and piperacillin/tazobactam also statistically increased during this period.

2.2.5 Resistance to key antibiotics (excluding penicillin) has increased over the previous 5 years (from 2022) within invasive group A Streptococcus infections – implications for treatment regimes for patients allergic to penicillin.

2.2.6 Using currently available data, the percentage of *E. coli*, *Salmonella* and *Campylobacter* bacterial isolates showing antibiotic resistance to the antibiotics that are most critical for human health are generally lower in animals than in humans.[160]

2.2.7 Similar patterns of resistance are seen in *Campylobacter species* from chickens, chicken meat and in humans, which is consistent with possible resistance transmission routes through the human food chain. However, *E.coli* and *Salmonella spp*. exhibit more variation in resistance patterns between animals and humans, and it is likely that resistance in animals is not a driver of resistance of these bacteria in humans.[193]

2.2.8 Since 2020, the proportion of human bloodstream infections caused by resistant bacteria has reduced due to the reduction of E.coli infections, likely due to multifactorial effects from the COVID-19 pandemic.[170]

2.2.8.1 However E.coli blood stream infection resistance to co-amoxyclauv remains high in 2021 at 41.2%.[170]

2.2.9 Carbapenem resistance in human bloodstream infections remains low (0.2% *E. coli 2020) (* 0.3% *K. Oxytoca* and 0.8%% *K. pneumoniae in 2017*)[170]

2.2.10 Vancomycin resistance in human bloodstream infections caused by *Enterococcus spp.* increased from 10% to 16% between 2011 and 2015.[15] Since 2017, vancomycin resistance has remained stable at approximately 20% resistant isolates.[170]

2.2.11 Several bacterial species including the causative agents of tuberculosis and gonorrhoea in humans show significant levels of antibiotic resistance but are not reported or treated in animals.

3. Definitions

Antimicrobial resistance (AMR):

Antimicrobial resistance occurs when microorganisms such as bacteria, viruses, fungi, and parasites change in ways that render the medications used to cure the infections they cause ineffective.[16]

Note: Whilst there are significant resistance problems associated with antiviral drugs (e.g. HIV treatments) and anti-parasitic drugs (e.g anti-malarials) this document is concerned primarily with antibiotic resistance.

Antibiotic resistance:

Antibiotic resistance is the ability of bacteria to resist the effects of an antibiotic. Antibiotic resistance occurs when bacteria change in a way that reduces the effectiveness of drugs, chemicals, or other agents designed to cure or prevent infections.[17]

There are different methods of defining resistance so, to allow comparison with human data, the veterinary data in this document have been presented using human clinical breakpoints (CBP) wherever possible (Tables 4 and 5) (i.e. resistance is defined as being present if the resistance level in the bacteria would likely be clinically significant in humans). Epidemiological cut-off values are an alternative method to define resistance often used in reference laboratories.[18]

Antibiotic sensitivity testing (AST):

Several methods may be used to test which antibiotics specific bacterial populations are sensitive to. The majority of these methods involve growing populations of the bacteria in the lab and observing the effects of specific antibiotics on these populations. Testing usually takes place in a laboratory and, depending on the method used, can take between 3.5 and 18 hours.[19] The use of whole genome sequencing has been investigated as a novel method for antimicrobial susceptibility. A larger evidence base is needed for it to become routine but price for the technology is decreasing.[20]

Critically Important Antibiotics (CIAs):

The World Health Organisation (WHO) has defined antibiotics that are of critical importance to human health based on two major criteria[21]:

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 to be the highest priority critically important antibiotics for human health. These are: macrolides, 3rd and 4th generation cephalosporins, quinolones and glycopeptides.

In 2013, the European Medicines Agency (EMA) reviewed these antibiotics to assess which antibiotics, used in veterinary medicine, contribute the greatest risk to development of antibiotic resistance in humans. They identified two classes: **3rd and 4th generation cephalosporins** and **fluoroquinolones.[22]** In 2016 **colistin,** an antibiotic from the polymixin class, was added to this list (see Box 1).[23]

In this document "Critically Important Antibiotics" refers to the EMA definition.

Broad/Narrow spectrum antibiotics:

An antibiotic that is effective at killing or preventing the replication of a wide range of disease-causing bacteria is termed broad spectrum in contrast to narrow-spectrum antibiotics which are only effective against specific types of bacteria.

Gram staining (gram positive/gram negative bacteria):

Gram staining is a method of classification of bacteria into two classes (gram positive and gram negative) according to differences in the structure of the bacterial cell wall. Gram positive bacteria include *Staphylococci* spp. (e.g. MRSA), *Streptococci* spp. Gram negative bacteria include *E. coli*, *Klebsiella* spp., *Salmonella* spp., and *Campylobacter* spp. Antibiotics vary in their capacity to treat infections caused by different gram positive or gram negative bacteria. Gram negative bacteria often show greater degrees of antibiotic resistance than gram positive bacteria.[24]

Veterinary cascade:[25]

If there is no medicine authorised in the UK for a specific condition, the veterinary surgeon responsible for treating the animal(s) may, in order to mitigate unacceptable suffering, treat the animal(s) in accordance with the following sequence:

(a) a veterinary medicine authorised in the UK for use in another animal species or for a different condition in the same species; or, if there is no such product;
(b) either:
    (i) a medicine authorised in the UK for human use, or
    (ii) in accordance with a Special Import Certificate from the Veterinary Medicines Directorate (VMD), a veterinary medicine from another Member State; or, if there is no such product;
(c) a medicine prepared extemporaneously, by a vet, pharmacist or a person holding an appropriate manufacturer's authorisation.

Population Correction Unit (PCU)[26]

The mg/PCU is a unit of measurement developed by the European Medicines Agency to monitor antibiotic use and sales in animals across Europe. The Population Correction Unit is the standardised average weight in kilograms (kg) of all animals at time of treatment multiplied by the number of animals based on national statistics (live and/or slaughter).

Defined Daily Doses (DDD)

In humans, antimicrobial usage is expressed as the number of defined daily doses per 1,000 inhabitants per day. This provides an estimation of the proportion of the populations treated with a particular drug every day.

Defined Daily Doses Vet (DDDVet)

In companion animals, antimicrobial usage can be expressed as the average number of days that each cat/dog in the UK has received an antibiotic throughout the year. These methods of drug usage comparisons account for differences in dose rates of different drugs, and the length of activity of long-acting products.[169]

4. Categories of antibiotics

There are currently over 20 different classes of antibiotic[27]. The list below is not an exhaustive but represents the most commonly used antibiotic classes in the UK.[28]

Antibiotics class Critical antibiotics for human health in red * = WHO definition only ** = EMA definition only	Examples	Examples of UK human usage[29]	Examples of UK animal usage[30]
Penicillins	Penicillin Amoxicillin Ampicillin Flucloxacillin	Widely used to treat a variety of infections, including skin, airway and urinary tract infections.	Used in a wide variety of farm animal and pet species for a broad range of diseases including mastitis, lung infections, urinary tract infections.
Tetracyclines	Doxycycline Lymecycline Oxytetracycline	Used as an alternative to penicillins for airway infections. Commonly used to treat moderate to severe acne and rosacea	Commonly used particularly for the treatment of lung infections in farm animals.
Macrolides*	Erythromycin Azithromycin Clarithromycin Tylosin Tilmicosin	Can be particularly useful for treating lung infections, or an alternative for people with a penicillin allergy or to treat penicillin-resistant strains of bacteria	Often considered as an alternative to penicillins. Used for lung and udder infections in cattle and respiratory infections in poultry and pigs.
TMPS	Trimethoprim/ sulfamethoxazole	Can be used for a wide variety of infections including urinary tract infections.	Used in a wide variety of species for a broad range of diseases including lung infections, urinary tract infections and diarrhoea.
Lincosamides	Clindamycin Lincomycin	Not frequently used due to high degree of side effects. Sometimes used for drug-resistant infections.	Used in dogs and cats for the treatment of dental infections and abscesses. Also used in cattle and pigs including in feed treatment of diarrhoea and lung infections.
Aminoglycosides	Streptomycin Gentamicin Neomycin Spectinomycin	Tend to only be used to treat very serious illnesses such as blood infections (septicaemia), as they can cause serious side effects, including hearing loss and kidney damage; usually given by injection. Also used via inhalation for treatment of serious lung infections.	Used by injection for treatment of lung infections in horses. In feed and in water preparations used to treat diarrhoea in pigs and lung infections in poultry. Used in eye and ear drops in pet animals.

Cephalosporins **1st/2nd generation** **3rd/4th generation**	Cephalexin Cefaclor Cefuroxime Ceftriaxone Cefotaxime Ceftiofur	Used to treat a wide range of infections, but are also effective for treating more serious infections, such as pneumonia, septicaemia, meningitis and gonorrhoea	Used for skin and urinary tract infections in pet animals. Used for treatment of udder, reproductive tract and skin (foot) infections in cattle.
Fluoroquinolones	Ciprofloxacin (Humans) Enrofloxacin (Animals) Marbofloxacin	Broad-spectrum antibiotics used to treat a wide range of infections (e.g. airway and urinary tract infections).	Authorised for use in many species. Used to treat a very wide variety of infections but now no longer recommended as first line treatment due to risk of development of resistance.
Polymyxins	**Colistin **** (Polymyxin E) Polymyxin B	Colistin is a last resort antibiotic for serious multidrug resistant gram-negative infections. Given by injection. High risk of kidneys and nerve damage. Polymyxin B is used topically to treat eye and ear infections.	Colistin is infrequently used in animals in the UK. It can be used for treatment of gut infections in pigs, poultry and cattle. Polymyxin B used topically to treat ear infections (e.g. dogs)
Glycopeptides	Vancomycin	Given by injection as last resort in serious drug resistant infections (e.g. MRSA)	Not used in the UK. Avoparcin was historically used as growth promoter in Europe before being banned in 1997.
Phenicols	Chloramphenicol Florfenicol	Eye drops used for treatment of eye infections.	Used for treatment of airway infections in cattle, sheep and pigs. Eye drops used under the cascade for treatment of eye infections in dogs and cats. Used in Salmon for treatment of furunculosis.

5. Legal Environment – Antibiotic use in animals

5.1 The use of antibiotics for growth promotion in animals in the European Union (EU) (including the UK) has been banned since 2006.[31]

5.2 In the UK the Veterinary Medicines Regulations 2013 implement the European Veterinary Medicines Products Directive [2001/82/EC] regulating manufacture, authorisation, marketing, distribution and post-authorisation surveillance of all veterinary medicinal products including antibiotics.

5.3 The European law is currently under review. Draft proposal for EU Regulations on "Veterinary Medicines" and "Medicated Feed" were published in September 2014. Two pieces of legislation are proposed:

5.3.1 Veterinary medicines proposal: Proposes to introduce options to restrict or ban veterinary usage of certain antibiotics critical for human medicine. Aims to stimulate innovation of new veterinary medical products and improve data collection on antimicrobial usage.

5.3.2 Medicated feed proposal: Proposes to tighten the rules for prescribing medicated feed (stopping prophylactic use and with additional requirement for the prescriber to examine animals and diagnose disease before prescription). Allows the use of medicated feed for pets.

5.3.3 As of June 2018, new regulations for administering of medicated feed have been approved by the European Parliament. These regulations limit the use of prophylactic and metaphylactic use of medicated feed for cases where there is a high risk of spread of infection when one animal is already infected and when there is no appropriate alternative. Furthermore, a veterinarian will have to carry out a physical examination and diagnosis in order to prescribe antibiotic-medicated feed.[32]

5.3.4 Since January 2022, The Veterinary Medicinal Products Regulation (Reg EU 2019/6) became applicable. It contains measures to support the availability and safety of veterinary medicines and strengthen and enhance EU action against AMR. They advocate for responsible antimicrobial use in animals and reserve certain antimicrobials solely for treating infections in humans.[175] The regulation bans the routine use of antibiotics and restricts preventative antibiotics to exceptional treatment needs of individual animals.[190]

5.3.5 In June 2023, the Council of the EU has adopted the recommendation to strengthen EU action against AMR.[192]

5.3.5.1 They encourage members states to[192]:

5.3.5.1.1 Improve health and welfare of FPAs → to decrease occurrence and transmission of infectious disease → to reduce the requirement for antimicrobials.

5.3.5.1.2 Reduce the overall EU sales of antimicrobials in farmed animals and aquaculture by 50% by 2030.

5.3.5.1.3 To develop effective evidence-based alternatives to the use of antimicrobials and vaccinations for animal health

5.4 EU ambassadors agreed on EU Council's Animal Medicine package in December 2017.This regulation aims to protect some CIAs for humans only and restrict some antibiotic prescribing. The regulation was adopted by the Council on 26th November 2018 has been operational since 2021.

5.5 In the UK the Royal College of Veterinary Surgeons provides a Professional Code of Conduct for veterinary surgeons that states that:

> *The responsible use of veterinary medicines for therapeutic and prophylactic purposes is one of the major skills of a veterinary surgeon and crucial to animal welfare and the maintenance of public health.*
>
> *The development and spread of antibiotic resistance is a global public health problem that is affected by use of these medicinal products in both humans and animals. Veterinary surgeons must be seen to ensure that when using antibiotics they do so responsibly, and be accountable for the choices made in such use.*

Failure of a veterinary surgeon to follow this Code of Conduct can result in disciplinary action and could result in the veterinary surgeon being disqualified.

5.6 As part of the UK Government's 5 year action plan for AMR 2019 commits to 'implement similar provisions' to EU regulations.[190]

5.7 In January 2023, the UK Government announced plans to strengthen the law on unnecessary antibiotic prescribing in animals by making changes to the Veterinary Medicines Regulations 2013. Currently a full consultation is being prepared with legislation excepted to be laid out in 2023.[190]

5.8 Support and guidance for veterinary surgeons on responsible usage of antibiotics is available from many sources including the Responsible Use of Medicines in Agriculture Alliance (RUMA)[33], British Veterinary Association (BVA)[34] and BVA's specialist divisions providing practical advice to vets working in different veterinary sectors (e.g. pigs, poultry, cattle, sheep, companion animals and horses). A list of guidance documents compiled by the Veterinary Medicines Directorate is available online.[35]

6. UK Antibiotic Usage Data

6.1 Methods and limitations of data collection

6.1.1 Human

6.1.1.1 The usage of antibiotics in the UK is calculated by combining data from prescriptions of antibiotics. The data presented below have been sourced by combining data on prescriptions sourced from primary care (e.g. GPs) and secondary care (e.g. hospitals) databases in England, Northern Ireland, Scotland and Wales. The largest percentage of animals used in humans are prescribed in primary care settings (6.2 a) pie chart).

6.1.1.2 Data in this report may be an underestimate of usage as it does not include private prescriptions dispensed in the community or at private hospitals.

6.1.1.3 Data on usage in humans is normally recorded as a defined daily dose (DDD) which is the internationally recognised unit of measurement of medicine consumption, recommended by the World Health Organisation (WHO).

6.1.1.4 The DDD is the assumed average maintenance dose per day for a medicine used for its main indication in adults. The DDD accounts for differences in drug potency (i.e. the same weight of antibiotic may offer 20 doses of Antibiotic A but 100 doses of antibiotic B).

6.1.1.5 This unit of measurement allows data from different classes of antibiotic to be grouped together and for meaningful comparisons of antibiotic usage to be made over time and between countries. European data are collected by the European Centre for Disease control (ECDC) to form the European Surveillance of Antimicrobial Consumption network (ESAC-Net).

6.1.1.6 Data on the number of prescription items is also collected which can be used to infer whether changes in DDD are due to a change in the number of prescriptions or changes in the nature of prescriptions (e.g. dosage or length of prescription)

6.1.1.7 In this report, we have presented data on human usage in tonnes of active ingredients, as calculated for the UK One Health Report 2013-2017 (Published in January 2019) This is to allow direct comparison with animal data. As of November 2023, there has not been another One-Health Report published, and therefore current data used in the report is likely outdated.

6.1.2 Animal

6.1.2.1 Total Antibiotic sales data are collected from Marketing Authorisation Holders (MAHs) via the Veterinary Medicines Directorate (VMD). This has been a legal requirement since 2005.[36]

6.1.2.2 Data are reported annually in the UK Veterinary Antibiotic Resistance and Sales Surveillance Report (VARSS) by the VMD.

6.1.2.3 Since 2010, the European Medicines Agency has compiled data from EU/EEA countries (including the UK) to form an annual European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) report.

6.1.2.4 The size and demographic of food animal populations can vary year on year due to market conditions so, to allow trends to be analysed between years and between European countries, the total quantity of antibiotics sold (mg of active ingredient) is divided by the likely total weight of

food producing animals at the time of treatment (PCU) to obtain an estimate of antibiotic usage in mg/PCU [37]. The PCU (Population Correct Unit) is calculated as the number of live and/or slaughtered food animals multiplied by the estimated weight at time of treatment.[38]

6.1.2.5 Sales data are likely an overestimate of the amount of antibiotics used in animals as not all antibiotics sold will be used (e.g. due to wastage or expiry). Sales data may also not reflect antibiotic usage as they do not consider import and export of antibiotics.

6.1.2.6 Sales data offer limited information on the species treated. All antibiotics sold are authorised for use in specific species but many antibiotics are authorised for use in more than one species (e.g. pigs and poultry). In addition, antibiotics may be used in species other than those for which they are licenced (under the cascade).

6.1.2.7 The UK lacks a centralised system that accurately records usage of antibiotics by animal species although these systems are currently under development. Data from the poultry meat industry are reported annually by the British Poultry Council and, data from the pig meat industry is currently collected via an online system (eMB Pigs). More recently, the Agriculture and Horticulture Development Board (AHDB) has developed the 'Medicine Hub', which helps dairy, beef and sheep producers monitor and compare antibiotic use, and helps tackle resistance.

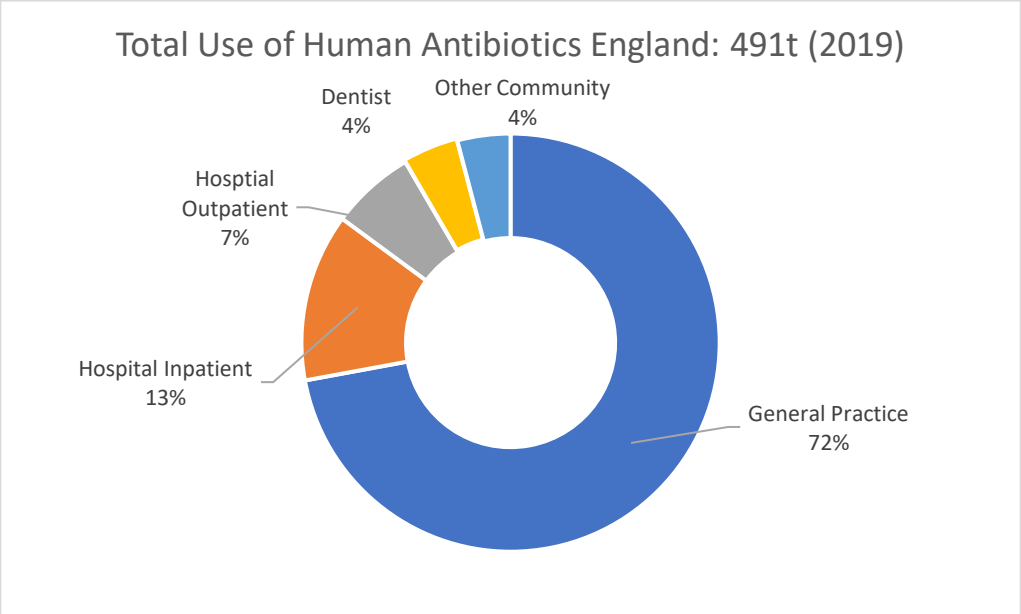
6.1.2.8 Current antibiotic usage data in animals do not allow determination of how appropriately antibiotics are being used as they do not tell us whether they were used following a specific diagnosis or the dose or duration of treatment. These are all important factors in the development of antibiotic resistance.

6.1.2.9 The standardisation of data collection using units of measurement comparable to human defined daily doses (defined daily dose for animals (DDDvet) and defined course dose for animals (DCDvet)) has been developed by the European Medicines Agency for pigs, cattle and broilers (meat chickens). It has also been adopted by the FSA for companion animals (dogs/cats) and horses.[169] These units of measurement take into account differences in dosing, pharmaceutical form and route of administration for different species and are intended to allow more accurate estimation of animal exposure to veterinary antimicrobials.[39]

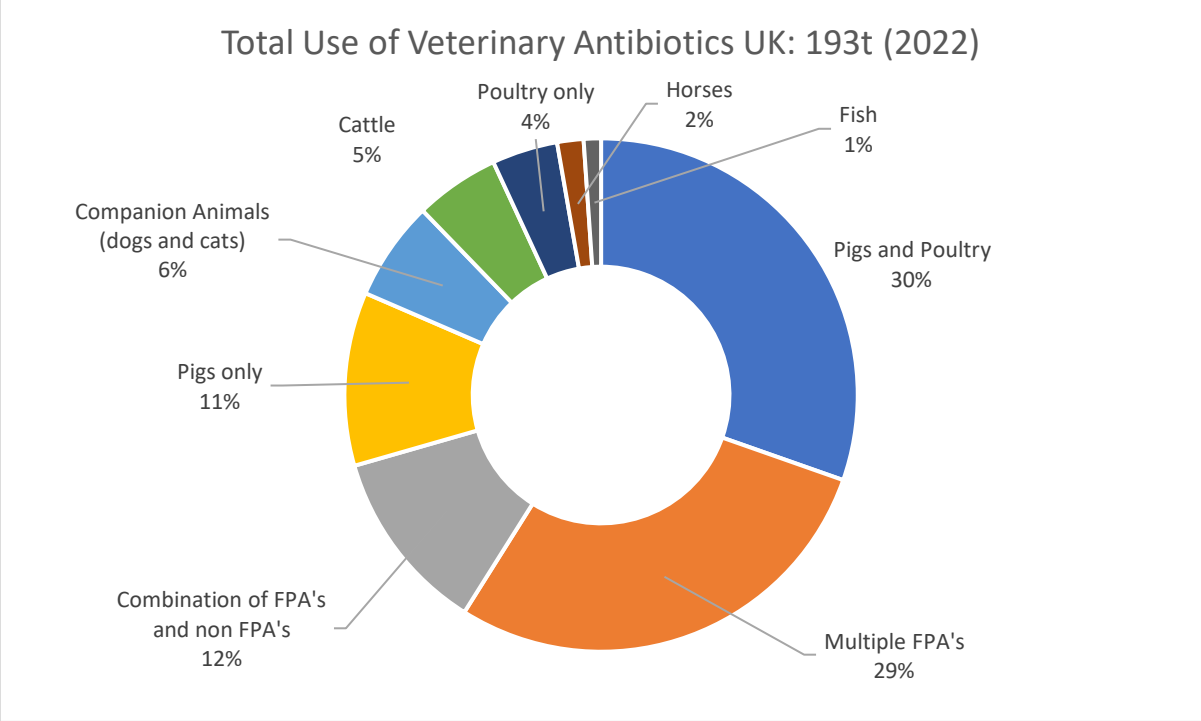
6.2 Results of Data Collection

FIGURE 1: **a) HUMAN PRESCRIPTIONS (BY SECTOR) 2017 (TONNES)** [160, 161, 170]
b) TOTAL UK ANIMAL ANTIBIOTIC SALES BY SPECIES 2022[169]

a)



b)



*FPA – Food Producing Animal

Note: The breakdown for human data has been estimated by applying the proportions of usage (measured in DDD) in England (2017) as published in the 2021 ESPUAR to the data on total UK human usage of antibiotics from the One Health Report (2013-2017) published in January 2019. There has been no further report since the time of writing (November 2023), and therefore these figures remain, despite likely being outdated. Animal sales data as reported in VARSS 2022 report by species licenced for but may have been used in other species under the cascade. Furthermore, the data collected for cattle and sheep was of poor representation and cannot be extrapolated to the entire of the UK. Human usage data do NOT include private prescriptions and are therefore an underestimate. Actual usage is likely to be approximately 10% higher (source: One Health Report 2013)

FIGURE 2:

a) POPULATION ADJUSTED ANTIBIOTIC CONSUMPTION IN HUMANS AND ANIMALS[193]. ACCOUNTS FOR THE VARIATION IN BODYWEIGHT AND SIZE OF ANIMALS AND HUMANS EXPRESSED IN MG/KG OF ACTIVE INGREDIENT ADJUSTED FOR POPULATION SIZE.[193]

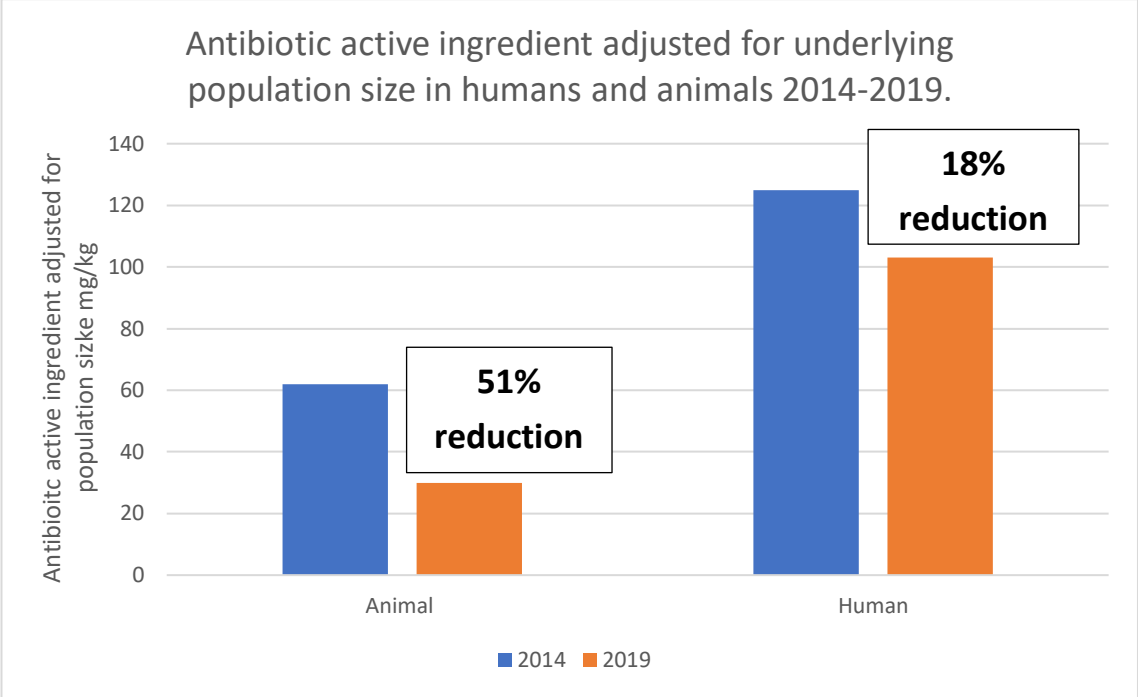


FIGURE 3: UK HUMAN ANTIBIOTIC PRESCRIPTIONS IN PERCENTAGE BY CLASS 2022[170]

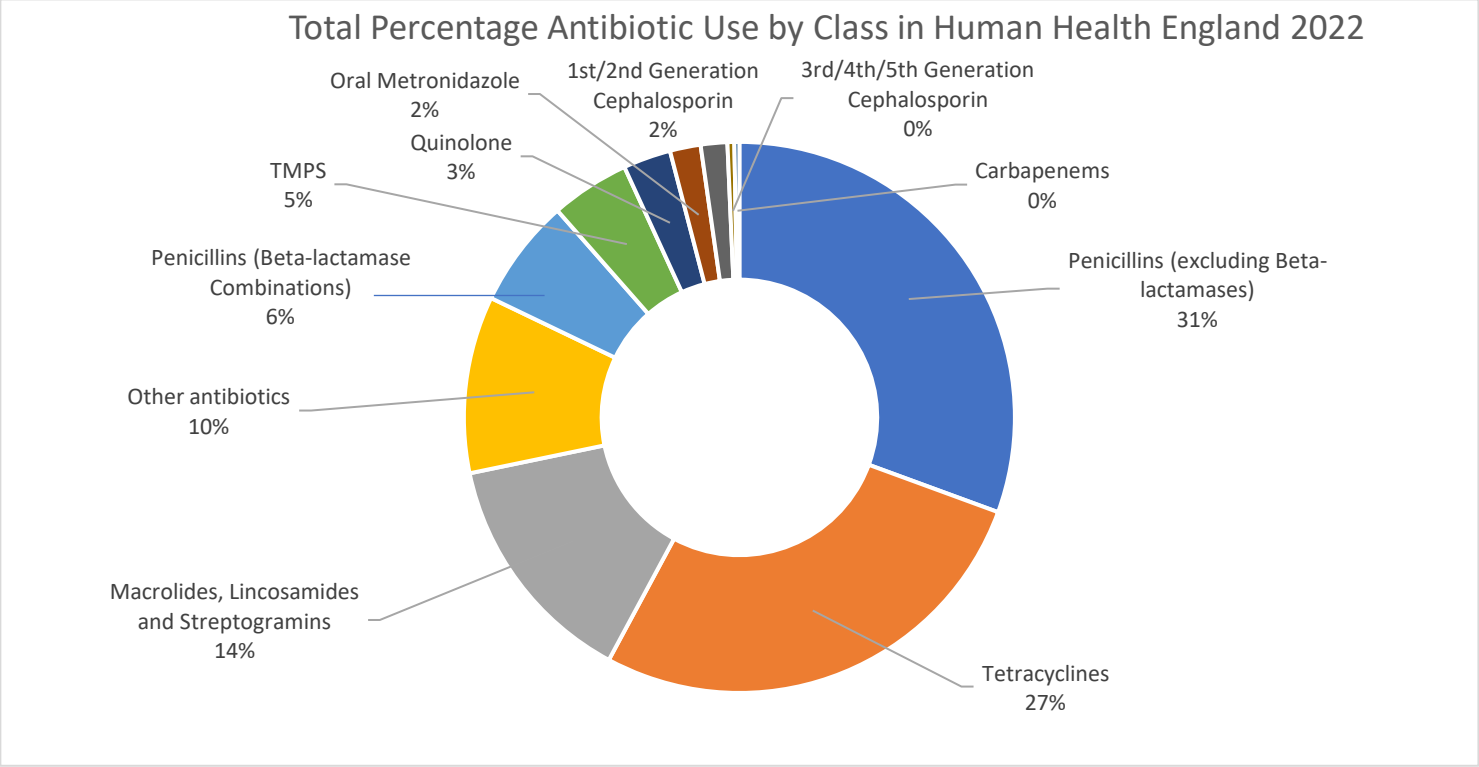


FIGURE 4: UK ANTIBIOTICS SOLD IN FPAs IN PERCENTAGE BY CLASS 2022[1]

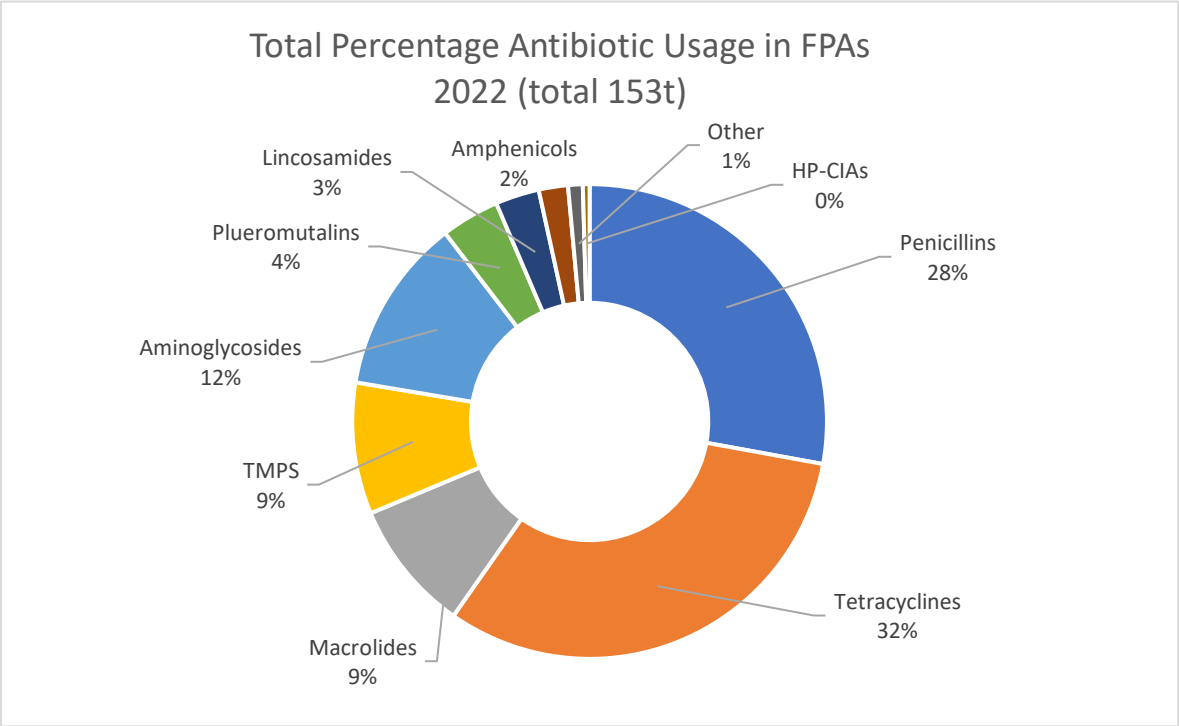
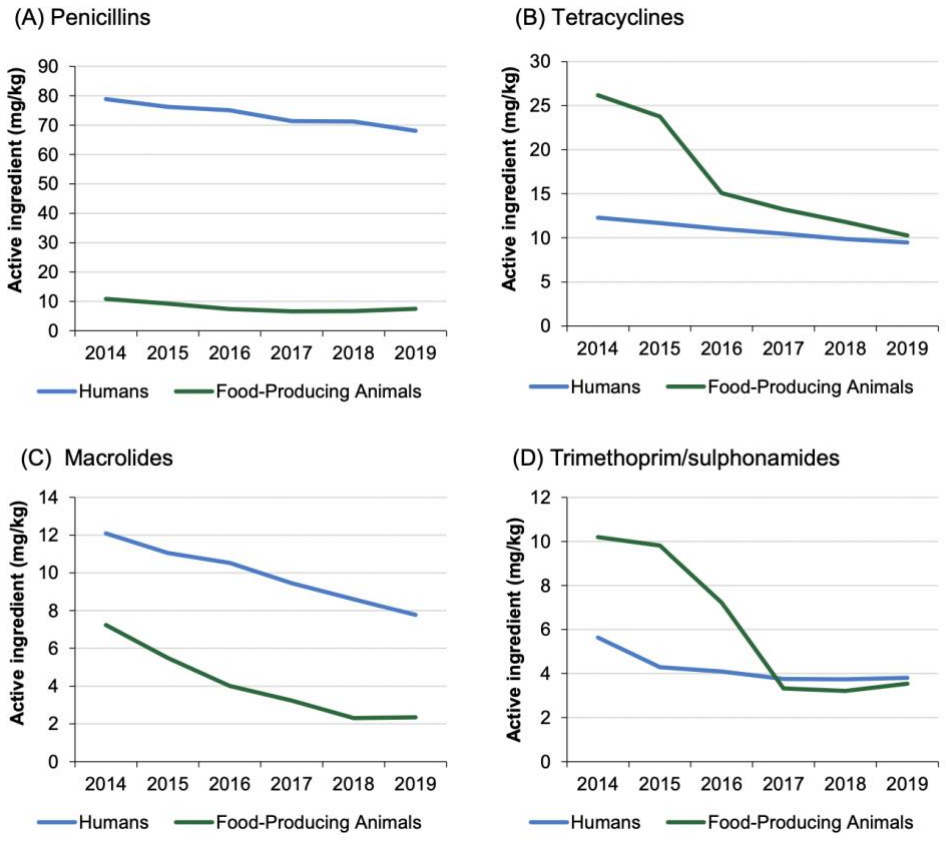


FIGURE 5: VARIATION IN FOUR MAIN ANTIBTIOIC CLASS CONSUMPTION BETWEEN HUMANS AND FOOD PRODUCING ANIMALS 2014-2019, WITH ADJUSMENT OF POPULATION SIZE.[193]



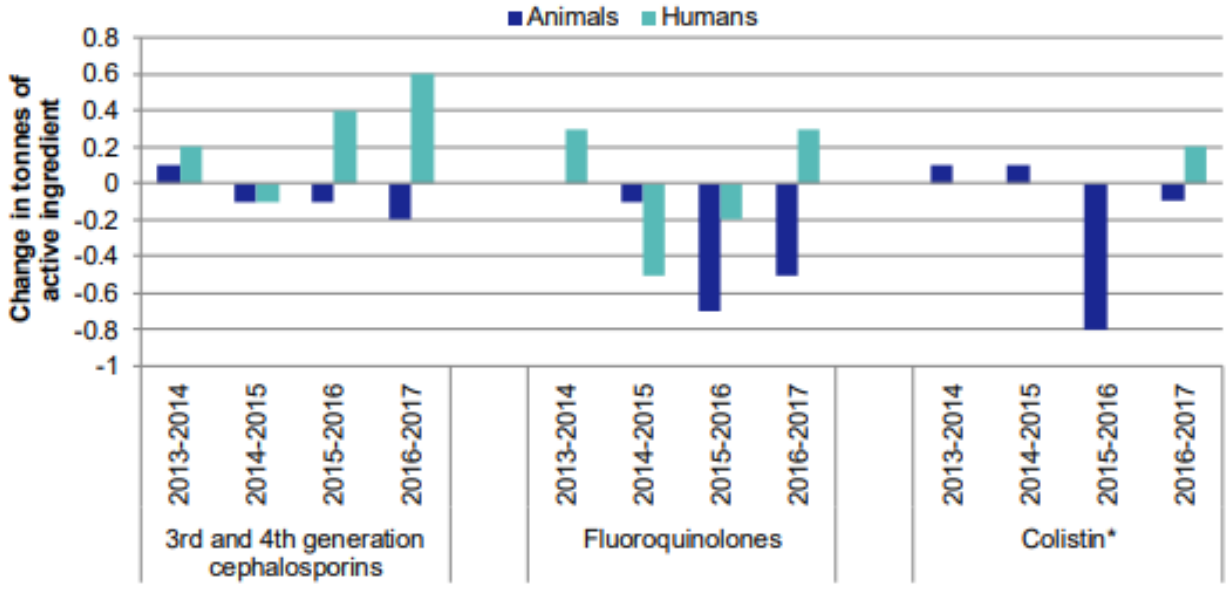
Between 2014-2019, figure 5.a shows a 14% and 35% reduction in human and food producing animal (FPA) consumption of penicillin, respectively. Tetracycline consumption (figure 5.b) is near identical between humans and FPAs in 2019, but there was a 61% reduction and 23% reduction in usage in FPAs and humans between 2014-2019, respectively. This is largely thought to be due to a reduction of in-feed use of tetracyclines in pigs and poultry. Furthermore, figure 5.c shows a steady reduction in macrolide consumption in both humans and FPAs, by 36% and 68% respectively between 2014-2019. This reduction in humans might be attested to the reduction in antibiotic prescribing for infections of presumed viral aetiology. The 2019 population-adjusted consumption of trimethoprim/sulphonamides (TMPS) is similar in humans and FPAs, 3.8mg/kg and 3.5mg/kg respectively (figure 5.d). In FPAs, there was a decrease of 67% between 2014-2017, again likely due to reduction of in-feed use in pigs. In humans, consumption decreased by 32% between 2014-2019 where TMPS is largely used for prophylaxis in immunosuppressed patients in secondary care settings.[193]

TABLE 1: ESTIMATED UK HUMAN AND ANIMAL ANTIBIOTIC USAGE 2013, 2017[160]AND 2019[193]

Antibiotic class	Antibiotics prescribed in humans (tonnes (%))			Antibiotics sold for use in animals (tonnes (%))		
	2013	2017	2019	2013	2017	2019
Penicillins	339.1 (65)	330.2 (67)	316.8 (69)	87.5 (20)	72.5 (26)	59 (27.5)
Tetracyclines	54.6 (10)	48.2 (10)	44.1 (9.4)	194 (44)	104.9 (37)	72.8 (34)
Macrolides	54.5 (10)	43.5 (9)	36.2 (8.0)	40.3 (9)	23.3 (8)	16.7 (8)
TMPS	24.0 (5)	17.4 (4)	17.7 (3.8)	60.7 (14)	31.0 (11)	25.1 (12)
1st and 2nd generation cephalosporins	17.4 (3)	13.3 (3)	12.2 (2.6)	4.9 (1)	4.1 (1)	3.9 (1.8)
Flouroquinolones	12.1 (2)	12.0 (2)	10.8 (2.3)	2.6 (0.6)	1.3 (0.5)	1 (0.4)
Other antibacterials	7.9 (2)	10.4 (2)	9.9 (2.1)	20.4 (5)	13.7 (5)	0.1 (0.1)
3rd and 4th generation cephalsporins	3.4 (0.7)	4.5 (0.9)	4.9 (1)	1.2 (0.3)	0.9 (0.3)	0.2 (0.1)
Monobactems, carbapenems	3.4 (0.7)	4.0 (0.8)	3.8 (0.8)	0 (0)	0 (0)	0(0)
Lincosamides	2.3 (0.4)	3.1 (0.6)	3.1 (0.7)	6.2 (1)	3.3 (1)	4.8 (2.3)
Glycopeptides	1.4 (0.3)	1.9 (0.4)	n/a	0 (0)	0 (0)	n/a
Aminoglycosides	0.9 (0.2)	0.8 (0.2)	0.9 (0.2)	14.8 (3)	21.6 (8)	23.9 (11.6)
Polymixins (incl. colistin)	0.4 (0.1)	0.6 (0.1)	0.5 (0.1)	0.7 (0.2)	0.007 (0)	0.01 (0)
Amphenicols	0.1 (0)	0.1 (0)	0.1 (0)	2.6 (0.6)	4.9 (2)	4.3 (2)
Other quinolones	0 (0)	0 (0)	0 (0)	0 (0)	0 (0)	0(0)
Total	**521.4 (100)**	**491.0 (100)**	**461 (100)**	**436.0 (100)**	**281.6 (100)**	**211.81 (100)**

IMPORTANT NOTE: **In 2017 there was a shortage of piperacillin/tazobactam, leading to the need to use alternative antibiotics, some of which were 3rd and 4th generation cephalosporins and contributes to their increase from 2013-2017.**

FIGURE 5: YEAR-OVER-YEAR CHANGE IN TONNES OF ACTIVE INGREDIENT HP-CIAs PRESCRIBED FOR HUMANS COMPARED TO THOSE SOLD FOR USE IN ANIMALS IN UK; 2013-17[160] (2017 data)



* No changes in amount of colistin prescribed for use in human medicine between 2013 and 2016

BOX 1: COLISTIN - THE EMERGENCE OF PLASMID-MEDIATED RESISTANCE

Colistin is a relatively old antibiotic from the polymyxin class that has been used widely in veterinary medicine over the last 50 years particularly in the pig, poultry and cattle industries. In the UK, there has been no colistin usage in animals for the past 2 years (since 2020)[169]. Across Europe colistin is used more heavily in animals than in the UK, particularly in Italy, Spain, Portugal and Germany, and it is the fifth most used antibiotic in European food producing animals.[40]

In human medicine, colistin is a last resort antibiotic used against gram-negative bacterial infections that are resistant to other antibiotics. Use of colistin is associated with severe side effects in humans including kidney toxicity but its use has increased in recent years (e.g. to treat lung infections in patients with cystic fibrosis). Human colistin usage in the UK is the second highest in Europe.[41]

The emergence of a colistin resistance gene (*mcr-1*) in bacteria from healthy Chinese pigs, food and humans in China was reported in November 2015.[42] The resistant gene was located on a plasmid which is a mobile piece of DNA capable of spreading directly between bacteria. The *mcr-1* gene has been found predominantly in *E. coli* bacteria from several food producing species (pigs, poultry and cattle) and in humans across several continents including Asia, Europe and North America.[43] The gene has also been identified in bacteria isolated from food products and environmental samples. In July 2016 an additional plasmid-mediated colistin resistance gene (*mcr-2*) was identified in *E. coli* from cattle and pigs.[44] In September 2016, a possible case of transmission of mcr-1–harbouring *E. coli* between a companion animal and a human was reported in a pet shop worker in China.[45] The emergence of plasmid mediated colistin resistance mechanisms has raised concerns that colistin resistance may quickly spread to other bacteria important to human health and compromise the ability for these infections to be treated with currently available antibiotic classes.

In December 2015, after discussion with the pig, poultry and cattle industry, the Responsible Use of Medicines in Agriculture Alliance (RUMA) announced a voluntary restriction on colistin usage in UK agriculture. This recommends that colistin is only used as a last resort and only after the results of culture and sensitivity testing.[46]

The VMD conducted a review of *E. coli* bacterial samples from 105 pig herds and discovered *mcr-1* positive samples in two herds. A separate screening of bacterial samples collected from a representative group of pigs slaughtered in the UK detected 2/313 (0.6%) prevalence of the *mcr-1* gene.[47]

The European Medicines Agency (EMA) stated in 2013 that there was no evidence that the use of colistin in food producing animals resulted in widespread colistin resistance and its transfer to humans. The EMA reviewed this position in the light of the finding of plasmid mediated resistance to colistin stating that "the larger abundance of the MCR-1 gene in veterinary isolates compared to human isolates, together with the much higher use of colistin in livestock compared to human medicine, and the finding of the *mcr-1* gene along with genetic determinants typically seen in animal environments, has been considered suggestive of a flow from animals to humans". [48] In May 2016 the EMA made recommendations for Member States to reduce colistin usage to a maximum of 5mg/PCU (population correct unit) and ideally to below 1mg/PCU[49] The UK currently has one of the lowest animal usage of polymyxins in Europe (the class that contains colistin) with no usage since 2020.

TABLE 2: UK IN-FEED AND IN-WATER VETERINARY ANTIBIOTIC PRODUCTS FOR ANTIBIOTICS CRITICALLY IMPORTANT FOR HUMAN MEDICINE (EMA DEFINITION)[50]

Class/antibiotic	In-feed medications	In-water medications (No. products)
Fluoroquinolones	Not available	Enrofloxacin *chickens, turkeys and rabbits (2); chickens and turkeys (3); chickens and rabbits (1); cattle (2); pigs (2)*
3rd and 4th Generation cephalosporins	Not available	Not available
Colistin	Colistin sulphate *pigs(1)*	Colistin sulphate *cattle, chickens, pigs, sheep and turkeys (3); cattle, chickens, pig and sheep (1); chickens (1)*

Note: Antibiotics from many other antibiotic classes are also available for in-feed and in-water use in animals in the UK. This list only includes antibiotics whose use in animals contributes the greatest risk to development of antibiotic resistance in humans as defined by the European Medicines Agency.[51]

6.2.1 In-feed and in-water products have been used in agriculture to administer antibiotics to groups of animals.

6.2.2 This may be given therapeutically (to treat animals affected by disease), metaphylactically (to reduce the risk of a specific diagnosed disease spreading through a population) or prophylactically (to reduce the risk of outbreaks of disease in high-risk populations). Prophylactic use of antibiotics are discouraged.

6.2.3 In 2022, 31% of all antibiotics sold for use in animals were sold for administration via medicated feed (59.8 tonnes). There has been a reduction in premixed antibiotic sales of 16% between 2021-2022.[169]

6.2.4 There are no in-feed fluoroquinolone or 3rd/4th generation cephalosporin containing products authorised for animal use in the UK.

6.2.5 There are nine in-water fluoroquinolone containing products authorised for use in animals. These are not authorised for prophylactic use.

6.2.6 There are four in-water and two oral solution colistin containing products in the UK authorised for use in livestock. These are not authorised for prophylactic use.

6.2.7 In 2018 the European Parliament agreed on tighter regulations of medicated feed, banning all prophylactic and metaphylactic use, as well as restricting veterinary prescription of antimicrobials. These were implemented under Regulation (EU) 2019/4 (see section 5.3).

6.2.7.1 Companion Animal Data

6.2.7.1.1 Dogs and Cats

Data is collected from mandatory pharmaceutical sales data, reported by marketing authorisation holders to the Veterinary Medicines Directorate. This data therefore doesn't directly correspond to actual consumption of antibiotics in dogs and cats in the UK. Furthermore, antibiotic use data is presented using daily defined doses (DDDVet) – the average number of days an animals receives an antibiotic dose per animal per year. This due to the long-acting nature of several antibiotic formulations in companion animal medicine, for example cefovecin (3rd generation cephalosporin) whereby a single injection lasts 2 weeks and therefore isn't adequately represented in the mg/kg metric[193]. In order to extrapolate antibiotics licenced for multiple species into usage per species, the VMD used stratification data from marketing holder authorisations which estimated the percentage of the sales of each product was administered to each species the drug was licenced for.

In 2022, sales of antibiotic products in dogs was 2.6 DDDVet (the same as in 2020), decreasing by 15% since 2021 and by 41% since 2014[169]. Furthermore, data in cats reveals a similar picture; in 2022 sales were 2.1 DDDVet, decreasing by 13% from the previous year and by 14% since 2014[169]. Between 2014-2019, sale of antibiotic products reduced by 33% and 8% in dogs and cats respectively, and by 42% and 13% of HP-CIA sales in dogs and cats respectively, over the same period[193]. The more gradual reduction in cat antibiotic sales is likely due to the high usage of the 3rd generation cephalosporin – cefovecin. A 2016 study found that cefovecin was the most commonly prescribed antibiotic in cats, making up 36.2% of antibiotic prescriptions[193]. They looked at electronic health records of cats prescribed Convenia (cefovecin) in first opinion practice totalling 1,148 entries. In most cases cefovecin was prescribed when owners are unable to orally medicate their cats (55.8%), and is often used first line, with only 16.8% of entries recording a microbiological evaluation before prescription[199]. Ideally, the use of this antibiotic should be justified by culture and sensitivity testing and only used in cases where first line antibiotic treatment is inappropriate or ineffective[193].

6.2.7.1.2 Horses

A 2022 study investigated the use of antibiotics in over 64,000 horses under the active care of 39 UK veterinary practices in 2018[200]. They found 19.5% of horses were prescribed systemic antibiotics, with potentiated sulphonamides and tetracyclines accounting for 83.7% of the antibiotic courses prescribed. HP-CIAs were prescribed in only 8.9% of antibiotic courses, but in 71.7% of these cases the antibiotic was used as a first line therapy[200]. They were commonly prescribed to treat urogenital (31.1%), skin (25.2%)

and respiratory (15.9%) conditions in animals <1 years old, thoroughbreds and racehorses[200]. Only 1 in 5 of HP-CIAs prescribed were as a result of culture and sensitivity testing[200].

6.3 Trends in usage data

Sales of antibiotics for animal use in 2022 were the lowest since recording began (1993), with 193 tonnes sold (Figure 6) a decrease of 57% since 2014.[169]. The number of daily doses prescribed for human use has declined over the last 5 years (Figure 6), but the vast majority occurs in General Practice.

FIGURE 6: UK ANIMAL ANTIBIOTIC SALES 2014-2022 (Tonnes)[169]

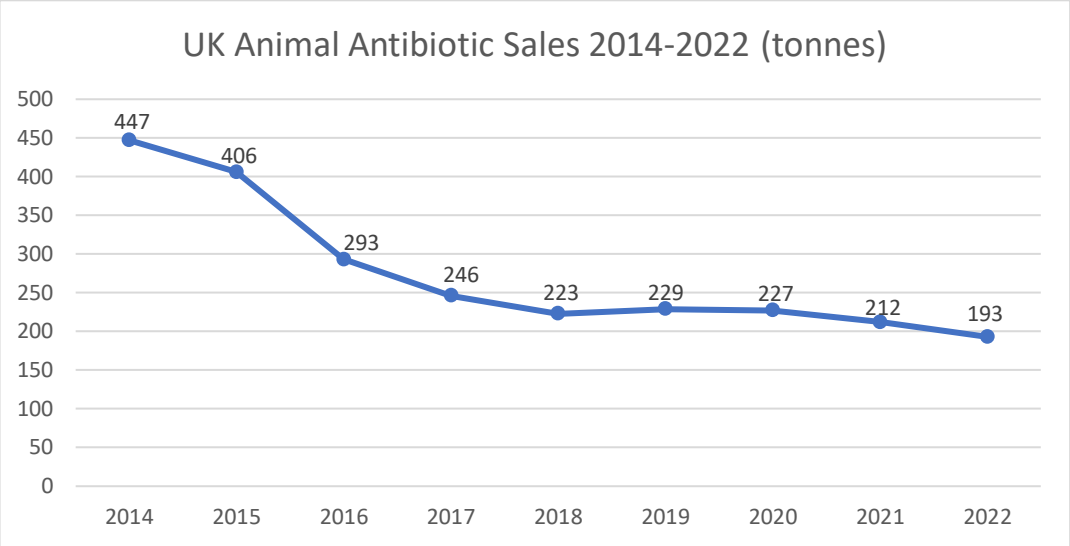
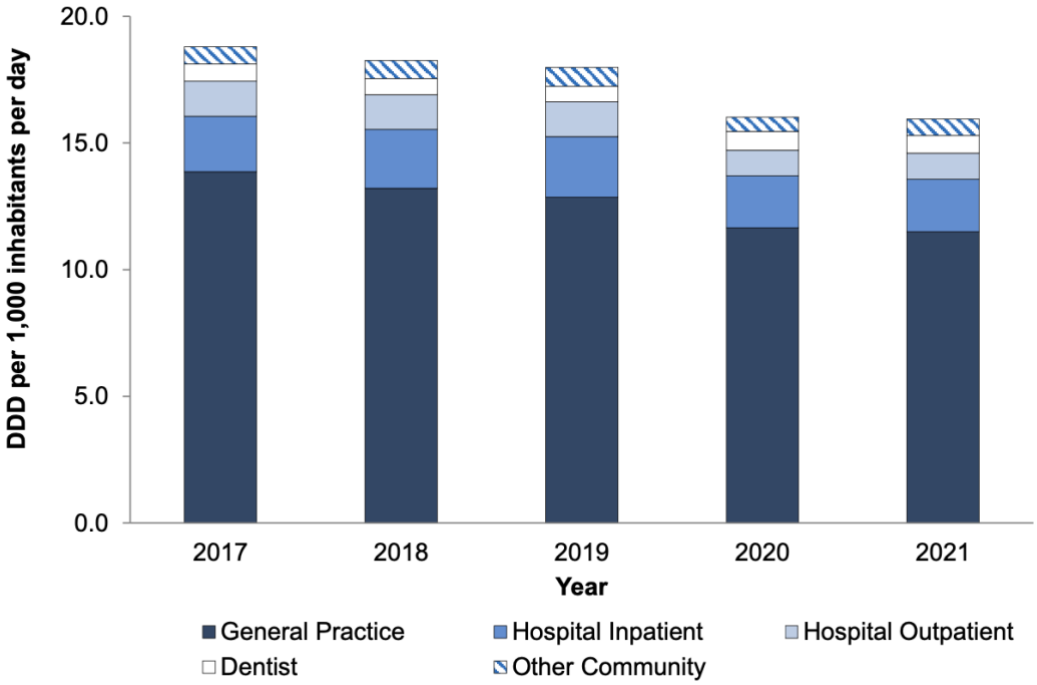


FIGURE 7: ANTIBIOTIC ITEMS IN HUMAN PRIMARY CARE BY PRESCRIBER GROUP, EXPRESSED AS ITEMS PER 1000 INHABITANTS PER DAY 2017-21[170]

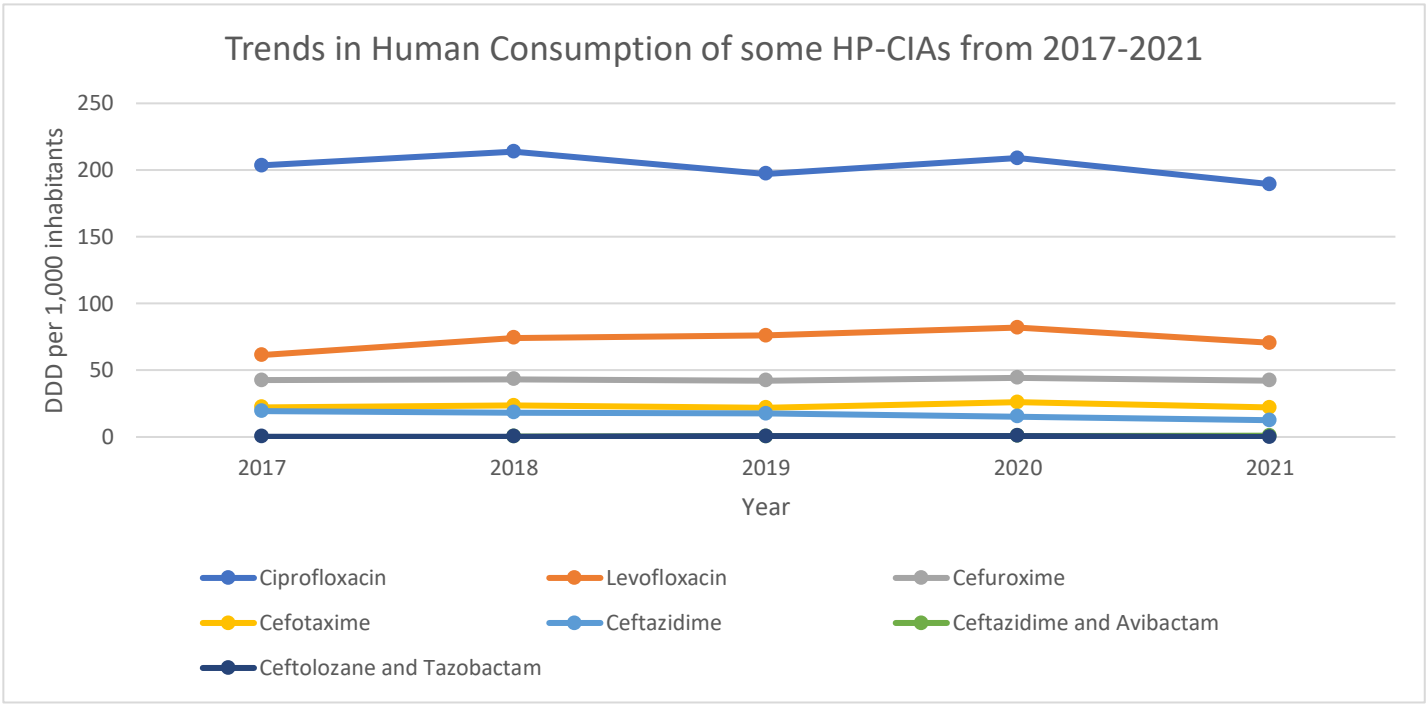


IMPORTANT NOTE: There are large differences in scale between individual graphs in Figure 6,7. The purpose of these figures is to present trends in usage (humans) and sales (animals) of individual drug classes and not for direct cross comparison between classes. Figure 7 only shows the primary care prescriber groups and does not include data from secondary care groups. Antibiotic consumption in secondary care in England decreased by 10.4% in 2021, compared to 2022, from 4,881 to 4,372 DDDs per 1000 admissions.

Data collected for the English surveillance programme (ESPAUR) for 2022[170] showed first and second-generation cephalosporin usage increased by 4.3% between 2021 and 2022. Human antibiotic consumption of 3rd, 4th and 5th generation cephalosporins increased from 0.063 DDDs per 1000 inhabitants per day in 2017 to 0.065 in 2022; the majority of this consumption came from hospital inpatient settings. This reflects their use as alternative antibiotics to piperacillin/tazobactam during the piperacillin/tazobactam shortage in 2017 and the licensing of cetazidine/avibactam combination in 2018. In August 2022, NICE published guidelines which recommends the treatment of severe, drug-resistant infections caused by gram negative bacteria with cetazidine and avibactam combinations.[189]

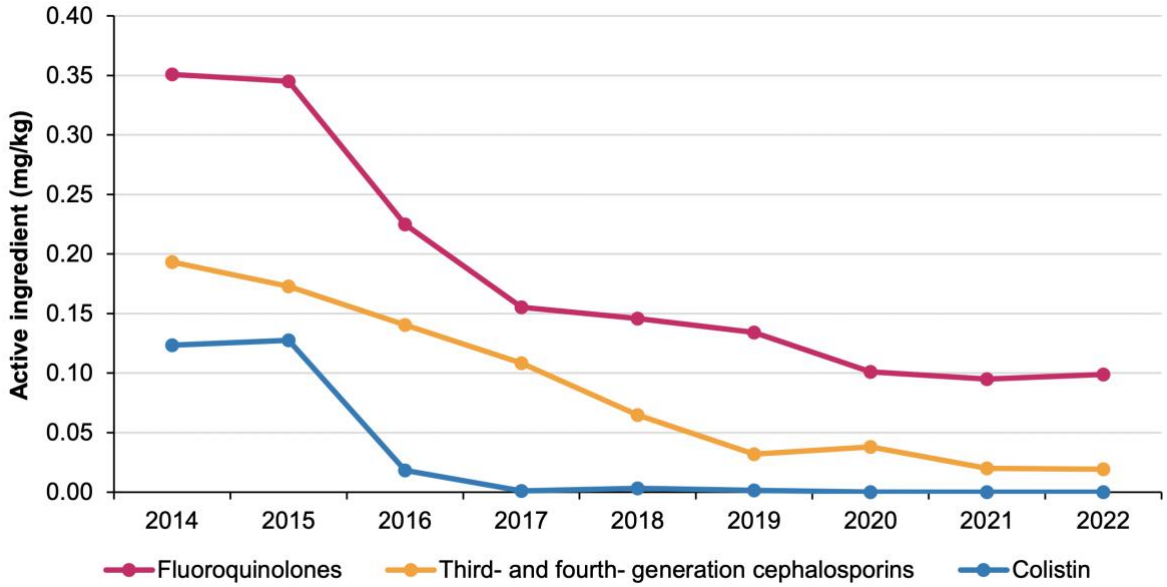
Quinolone consumption has slowly reduced in humans between 2017 and 2021; amounting to a DDD per 1000 inhabitants per day of 0.442 in 2021, down from 0.531 in 2017. GP quinolone consumption has also decreased (-26.6%) over this time period. Ciprofloxacin accounted for 78.1% of total quinolone use in 2017. Ciprofloxacin, norfloxacin and ofloxacin prescriptions have all declined from 2013 to 2017, but levofloxacin consumption has increased by 98% over this period.

FIGURE 8: QUINOLONE AND 3rd GENERATION CEPHALOSPORIN (Cefuroxime, Cefotaxime, Ceftazidime) ANTIBIOTIC USE IN TRUSTS AS DDDs PER 1,000 ADMISSIONS ENGLAND (2017-2021)[170]



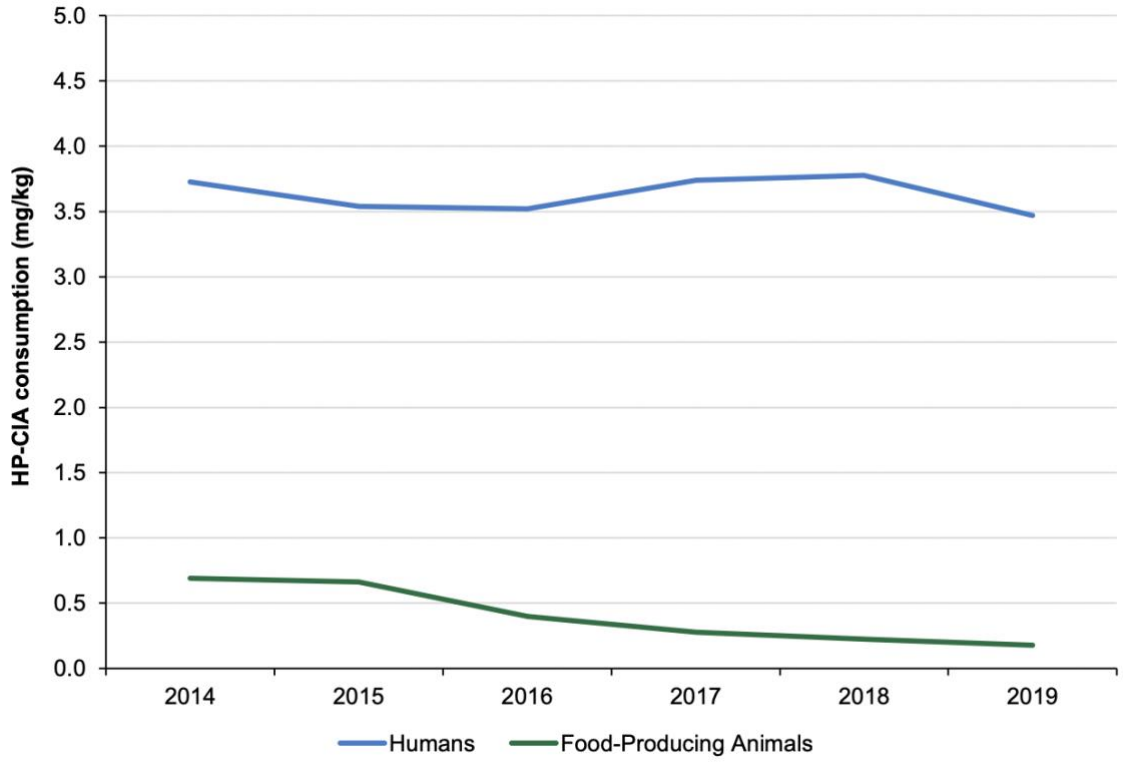
Colistin use has increased in a secondary care setting between 2017-2020 from 21.4 to 31.9 DDD per 1,000 admissions. In 2021, usage dropped by 15.1% to 27.1 DDD per 1,000 admissions compared to 2020. Consumption decreased in GPs in 2013-2017, reflecting a switch from GPs to specialised centres prescribing nebulising colistin. The prescribing rate is highest among acute specialist trusts (83.7 DDD per 1,000 admissions) with paediatric departments prescribing the most colistin.[170]

FIGURE 9: TRENDS IN UK ANIMAL SALES OF CRITICALLY IMPORTANT ANTIBIOTICS FROM 2014-2022 [169]



Note – different scales between use of HP-CIAs in Human vs Animal Consumption. The data is taken from different data sets, and therefore cannot be compared, but do provide an idea of the trends within human and animal medicine of the use of HP-CIAs.

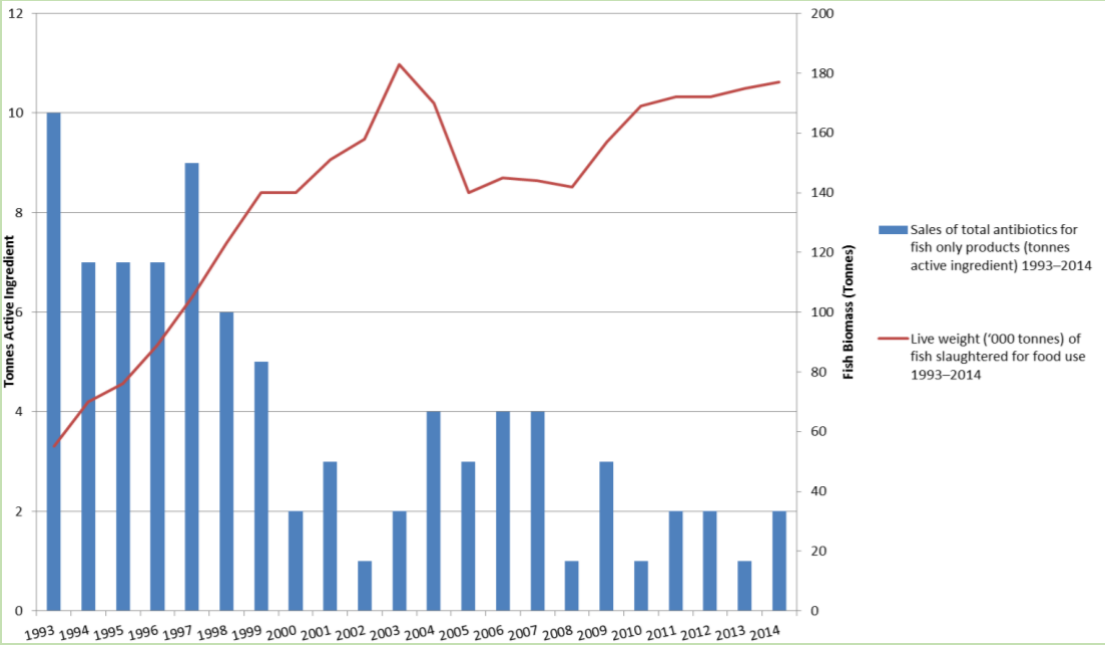
FIGURE 10: HP-CIAS CONSUMPTION ADJUSTED FOR POPULATION (MG/KG) IN FOOD PRODUCING ANIMALS AND HUMANS, 2014-2019.[193]



BOX 2: AQUACULTURE

Fish farming (aquaculture) is the most rapidly growing global form of animal food production.[52] Scotland are the largest producers of Atlantic salmon in the EU and the third largest globally. In the UK, the use of antibiotics in aquaculture has decreased significantly despite increases in production (see below). This has been associated with widespread use of vaccinations (e.g. furunculosis vaccines in Salmon).[53]

Current usage of antibiotics in aquaculture in 2022 was 3.61 tonnes according to sales data [169]. This is very small in comparison to the total usage of antibiotics in animals (193 tonnes). However, it is the only category of species in which there has been an increase in sales of antibiotics between 2013-2022. The sales of antibiotics for fish has over quadrupled from 0.8 tonnes in 2013 to 3.61 tonnes in 2022[169]. There is now a need to focus on the health of the cleaner fish, which are used for a biological control of sea lice on farmed fish.



7. UK Antibiotic Resistance Data

7.1 Methods and limitations of data collection

There are two types of surveillance used for monitoring antibiotic resistance: clinical "scanning" surveillance and structured surveillance.

Clinical surveillance

This is a passive form of surveillance whereby data are collated on antibiotic sensitivity in samples collected by doctors and vets during clinical work. It is used primarily to identify rare or emerging resistance profiles. Reporting bias means that this type of sampling may not provide accurate data on the prevalence of antibiotic resistance and cannot be used to reliably monitor year on year trends.

Structured surveillance

For structured surveillance of antibiotic resistance data on antibiotic resistance are collected from a representative sample of a certain bacterial population. Standardised testing methods are used to allow more reliable indication of resistance levels and more meaningful comparison between years and between countries. In the UK, the primary example of this type of surveillance is EU harmonised surveillance of antibiotic resistance levels in animals. This data are submitted annually to the European Food Standards Agency and published as part of an EU-wide summary report on antimicrobial resistance.[54]

7.1.1 Humans

7.1.1.1 Clinical human surveillance

Voluntary submissions of data are collated on national databases from a wide range of clinical microbiological laboratories. Public Health England (PHE) launched a web-based surveillance system in 2014 to facilitate this with 95% of English NHS hospitals routinely submitting AST data and 50% producing daily automated reports. There are several mandatory surveillance schemes in the NHS that enhance and centralise data collection e.g. for blood stream infections involving *Staphylococcus aureus* (e.g. MRSA) and *Escherichia coli* and for faecal samples containing *Clostridium difficile*. [55] In May 2015, PHE launched an online surveillance network for bacteria resistant to carbapenem antibiotics (*E. coli* and *Klebsiella* spp.) which was further enhanced in 2016. The UK currently participates (2017) in the European Antimicrobial Surveillance System (EARS-Net), a pan-European survey managed by the European Centre for Disease Control and conducted under WHO guidance. Data are compiled annually and published in atlas of Infectious Disease.[56]

The method of testing used at different laboratories varies (including the types of antibiotic resistance tested for and the criteria used to define resistance) so combined results for the UK must be interpreted with caution. For some types of infection (e.g. *Neisseria gonorrhoea*) centralised surveillance programmes are run to complement the data available from routine clinical surveillance. This involves collection of samples from sentinel laboratories across the UK and testing using them in a single laboratory thereby helping to highlight geographic and temporal trends in antibiotic resistance.

7.1.1.2 Structured human surveillance

The British Society for Antimicrobial Chemotherapy (BSAC) resistance surveillance project has been running for over 15 years and regularly collects and tests bacterial samples from human cases of respiratory (airway) disease and bacteraemia (bloodstream). Isolates are collected from a large number of clinical centres according to a defined collection protocol that aims to collect a representative sample of bacteria present in UK human cases of respiratory disease and bacteraemia.[57]

7.1.2 Animals

7.1.2.1 Clinical veterinary surveillance

Voluntary submissions of animal material and bacterial swab samples collected by veterinarians and farmers are made to the Animal and Plant Health Agency (APHA), Scotland's Rural College (SRUC) and the Agri-Food Biosciences Institute (AFBI) for diagnostics that can include antibiotic sensitivity testing. Under the Zoonoses Order (1989) all UK laboratories that isolate *Salmonella* from a food producing animal must report this to APHA and these samples may be requested for antibiotic susceptibility testing.

7.1.2.2 Structured (EU Harmonised) surveillance

A systematic and structured surveillance programme is in place to monitor levels of antibiotic resistance in zoonotic bacteria from healthy animals that are of key concern for human health (2003/99/EC, 2007/516/EC and 2013/652/EU). The testing requirements were expanded in 2014 and a summary of the current testing regime (harmonised across the EU) is presented in Annex I. In the UK the programme requires regular collection of a representative sample of bacteria from healthy pigs and poultry (e.g. UK National Control Programme for *Salmonella*). The bacteria are tested for resistance against antibiotics that are relevant to human health including 3rd and 4th generation cephalosporins and fluoroquinolones. Standardised testing methods are used to allow trends to be monitored within the UK and across the EU. The UK Veterinary Antibiotic Resistance and Sales Surveillance Reports (VARSS) is published by the Veterinary Medicines Directorate and monitors the usage of antibiotics (including HP-CIAs) across a host of livestock species and includes resistance surveillance in key indicator bacteria, and those with high public health risk; *E.coli*, *Salmonella spp*, *Campylobacter spp*. (recently including *Campylobacter coli*), and as of 2022 including *Enterococcus faecalis* and *faecium.*

7.2 Antibiotic resistance data in key zoonotic bacteria

Zoonotic bacteria are bacteria that can pass from animals to humans and capable of causing disease in humans, and back again. The transfer of such bacteria between animals and humans (e.g. via the food chain, environment and/or direct contact) presents a possible route for the transfer of antibiotic resistance from animals to humans. Key bacteria to consider include *Campylobacter, Salmonella, E. coli* and *Enterococcus*

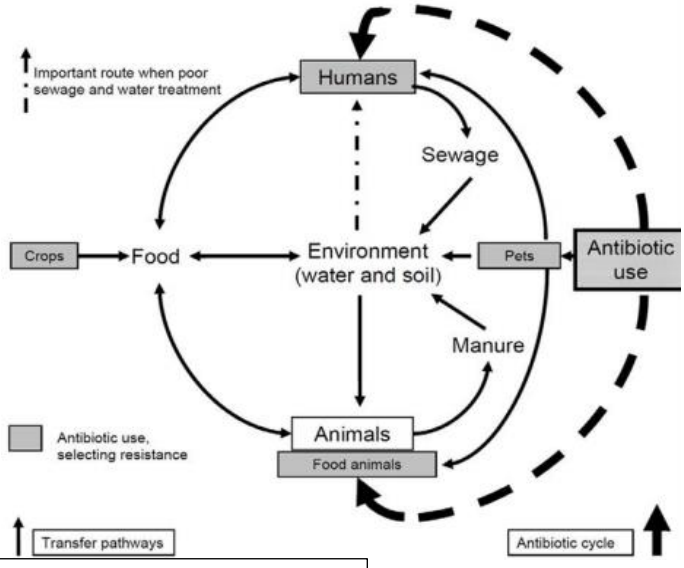


FIGURE 11: TRANSMISSION PATHWAYS OF ANTIBIOTIC RESISTANCE BETWEEN HUMANS, ANIMALS AND THE ENVIRONMENT

spp. (see below). It is important to recognise that there are many other bacterial species in which resistance poses a threat to humans and/or animal health and that there is also a complex network of pathways through which bacteria (including those carrying antibiotic resistance) may transfer between animals, humans and the environment (Figure 9). Monitoring antibiotic resistance in these bacteria from healthy animals, and in food products helps gain and understanding of the possible transmission route of antibiotic resistance between animals and humans, possibly via the food chain. Results from antibiotic resistance data between humans and animals is not directly comparable due to differences in sampling and laboratory methodology.[193]

Resistance to antibiotics can occur in bacteria naturally via random genetic mutation of the bacteria genome. However exposing bacteria to antibiotics, applies a selection pressure to the bacterium which favours those bacteria which are naturally resistant to that antibiotic. The non-resistance bacteria will die because of the antibiotic, leaving the resistant bacterium able to survive and proliferate. Furthermore, these resistant genes can spread between bacteria of the same, or different species, via horizontal gene transfer – whereby resistance genes are passed from one bacterium to another.

7.2.1 Evidence for transference of AMR bacteria from animals to humans and vice versa.

There is evidence for and against the transference of AMR genes between bacteria present in animals to humans.

An example demonstrating transference of AMR bacteria between animals and human is presence of MRSA in pigs and pig workers. Livestock-associated MRSA (LA-MRSA) is a zoonotic MRSA strain that is prevalent in livestock globally. The most common type of LA-MRSA, clonal complex 398 (ST 398), is thought to initially have arisen in humans but transferred to livestock and acquired resistance to methicillin[193]. The same strains of LA-MRSA have been demonstrated to be isolated from pigs and pig workers; pig workers can be consistent carriers of livestock MRSA but these strains are rarely transmitted human-to-human.[165,166,167,]. A study in Australia showed isolated two strains of MRSA from pig workers and pigs (ST93 and ST398)[168]. ST398 is less virulent and less transmissible in humans than ST93 but carries drug-resistance traits to many antimicrobials used in human and veterinary medicine. If a pig or human became infected with both strains simultaneously, this could lead to the drug resistance traits in the less virulent strain (ST398) transferring to the more virulent strain (ST93) and multi-drug resistant ST93 could be a serious public health concern. This appears to have occurred, resulting in the emergence of multidrug resistant ST93 MRSA strain but the public health risk to those not in contact with pig farms is unknown[168].

In the early 2000's, the strain was first detected in livestock in mainland Europe. People who has prolonged and repeated contact with livestock has an increased risk of acquiring the infection, and therefore it is more commonly found to colonise gastrointestinal tracts of people in rural settings, or those in cities surrounded by farmland[194]. Human transmission is associated with occupational exposure, but circulation in healthcare settings has been reported. In the UK, the first livestock case was detected in 2008. Between 2013 and 2019 28 cases have been identified in the UK; 21 cases in pigs, 3 in cattle, 3 in poultry and 1 in pheasants[193]. However, a recent study conducted across 6 UK abattoirs isolated the pathogen from 43.8% of pigs[195]. It has also been reported at low/moderate prevalence in animal products for sale in the UK i.e. retail meat.

Approximately 60% of imported meat from the EU is imported from countries with higher levels of LA-MRSA[193]. The first UK human case was in 2007 – with no apparent link to livestock, however human cases are rare. On average, 4,500 MRSA isolates are typed at a national reference laboratory annually (collected in a voluntary referral service) of which >0.2% are the 398 LA-MRSA pathogen[193].

The first hospital setting outbreak of LA-MRSA ST398 occurred in 2020 in a regional burns centre[196]. In total, 22 isolates were recovered from 12 patients over 6 months. Whole genome sequencing (WGS) showed all isolates were genetically similar implying spread between people within the hospital, possibly by asymptomatic carriers. Furthermore, there is evidence to support resistance genes being acquired throughout the outbreak within the hospital. 16 isolates were resistant to mupirocin, the main antibiotic used in MRSA hospital infections. WGS showed mupirocin resistance was associated with another gene linked to reduced susceptibility to chlorhexidine, a common antiseptic and surgical disinfectant used in hospitals. The outbreak was contained via infection control measures including deep cleaning, decolonisation of staff, and increased personal protective equipment and hasn't been detected in the hospital since. The outbreak highlights the transmission potential of the pathogen over months, despite installing strict control measures and active surveillance[196].

A different study looked at over 100 Ampicillin and Tetracycline resistant E.coli isolates in 44 clusters in Tanzania where humans and cattle lived in close proximity. They found indistinguishable pulse field-gel electrophoresis band patterns between livestock and humans in 52% clusters. They suggest the homology resulted from frequent transfer of faecal microorganisms between cattle, humans and the soil and risk factors for transference may include poor husbandry practices and living near animals.[174]

7.2.2 Evidence that AMR bacteria in humans is not directly linked to those in animals

Emerging research using molecular typing of zoonotic bacteria for antibiotic-resitance genes in samples collected from humans and animals suggests they are mostly genetically distinct populations. Samples of *E.coli*[58] and Vancomycin-resistant *Enterococcus faecium*[59] bacteria were shown to hold different genetic codes for resistance in samples taken from humans and livestock or meat. This suggests there was no direct spread of AMR bacteria from livestock or meat-products in cases of serious infections in people. A similar study looking at *E.coli* (drug resistant and sensitive) isolates from livestock and retail meat in Eastern England found genetically distinct isolates between livestock and *E.coli* in humans. They suggest that serious human *E.coli* infections were not caused my AMR transfer between livestock, whereas, they find highly similar isolates from the same species on different farms, suggesting livestock transfer isolates amongst themselves [172]. A large scale study in Northern Italy concerning 15 *Klebsiella* species from humans, animals and the environment, concluded that 'direct transmission from the multiple non-human (animal and environmental) sources… …accounts for <1% of hospital disease, with the vast majority of clinical cases originating from other humans.'[173] Another large scale study of *Salmonella* isolates from humans and animals in Scotland found distinct populations of multidrug-resistant *Salmonella typhimurium* DT104 bacteria in humans and animals. Bacteria from human and animal sources had different resistance genes and antibiotic resistance profile suggesting low levels of transmission of antibiotic resistant bacteria between animals and humans or vice versa. [60,61]

BOX 3:

A FAILURE TO RETURN TO SUSCEPTIBILITY AFTER ANTIBIOTIC USE STOPPED

Fluoroquinolones in poultry and people

Fluoroquinolones became licensed for use in poultry in the US between 1995 and 1996. In the late 1990s, prevalence of fluoroquinolone-resistant *Campylobacter* infections in people rapidly increased. Enrofloxacin (a fluoroquinolone) was withdrawn from use in US poultry in 2005, however the prevalence of fluoroquinolone resistant human *Campylobacter* infections has continued to increase, questioning the extent to which interventions in agriculture can reduce prevalence of resistant infections in humans[163]. Use of fluoroquinolones to treat food-borne diarrhoeal disease in humans could be maintaining the high rate of resistance in humans. Since stopping the use of enrofloxacin the prevalence of resistant *Campylobacter* in chickens has remained the same, indicating that once the microbe has developed resistance, this resistance can persist in the absence of the antimicrobial[164].

Taken from POSTNOTE "Reservoirs of Antimicrobial Resistance", Published Tuesday 19th February 2019 to which The Professor Lord Trees contributed.

7.2.2.1 Campylobacter

Campylobacter are the leading zoonotic bacterial cause of human gut infection (gastroenteritis), estimated to cause more than 280,000 cases per year.[160] The bacteria are commonly found in the digestive system of healthy animals (commensal bacteria) and may be found on raw or incompletely cooked meat. They rarely cause clinical disease in animals. The majority of human infections are transmitted from contaminated food/environment and direct contact with animals.[169] A Food Standards Agency Survey (published in 2021) found campylobacter contamination in 59.6% of non-major retail chickens during the one-year survey period August 2019-October 2020.[162, 176] Most cases of campylobacteriosis in humans resolve without the need for antibiotic treatment, but occasionally the disease may be severe or even life threatening. In these cases, the most commonly prescribed antibiotics are macrolides, tetracyclines and fluroquinolones.[62] The two most common species of *Campylobacter* involved in cases of human food poisoning are *Campylobacter jejuni* (90% of infections)[193] and *Campylobacter coli*. Meat chickens (broilers) are usually considered a major source of *C. jejuni* infection in cases of human food poisoning. *C. coli* was added to the AMR surveillance programme of the VMD led UK VARSS Report in 2022 due to its increasing resistance to numerous antimicrobials that *C. jejuni* isn't resistant to, and therefore poses a risk of horizontal gene transfer of resistant genes to the *C.jejuni*.[169] Table 3 shows resistance data across human and animal cases using multiple collection methods.

TABLE 3: UK ANTIBIOTIC RESISTANCE IN *CAMPYLOBACTER SPP.*

Antibiotic	Human antibiotic resistance Clinical surveillance			Animal antibiotic resistance EU harmonised surveillance* (n=no. of isolates)				
	2013[63] **(85% are *C. jejuni*)**	**2017**[160] **(Only 21% identified, of these 91% *C.jejuni*)**	**2019**	**2013**[64]	**2014**[65]	**2016**	**2017**[160]**	**2022**[169]
Fluoroquinolones (ciprofloxacin)	**42%** (n=23,425)	**All *Campylobacter spp* 47%** (n=60,408) **_C.jejuni_ 44%** (n=42,328) ***C. Coli* 12%^** (n=unknown)	***C jejuni* >40%** ***C.coli* 35%**	***C. jejuni***				
				31% Chickens (n=61)	**44% Chickens** (n=165) **35% Turkeys** (n=157)	**41% Broilers** (n=180) **35% Chickens** (n=190)	**39% Chickens** (n=157)	**59% Broilers** (n = 180) **26% Turkeys** (n = 136)
				C. coli				
				13% Pigs (n=141) **42% Chickens** (n=33)			**47% Chickens** (n=45)	**27% Broilers** (n = 59) **45% Turkeys** (n = 110)
Macrolides (erythromycin)	**2.5%** (n=23,137)	***C. jejuni* 4%** (n=42,328) **C. coli 12%** (n=unknown)	***C. jejuni* 3%** ***C.coli* 13.3%**	***C. jejuni***				
				0% Chickens (n=61)	**0% Chickens** (n=165) **0.6% Turkeys** (n=157)	**0.6% Chickens** (n=180) **1.1% Turkeys** (n=190)	**7% Chickens** (n=157)	**2.8% Broilers** (n = 180)
				C. coli				
				28% Pigs (n=141) **3% Chickens** (n=33)			**8% Chickens** (n=45)	**3.8% Broilers** (n = 59)
Tetracyclines	**33%** (n=2,929)	**39%** (n= 60, 408)	***C. jejuni* 41.7%** ***C.coli* 38%**	***C. jejuni***				
				48% Chickens (n=61)	**59% Chickens** (n=165) **65% Turkeys** (n=157)	**56.1% Chickens** (n=180) **43.2% Turkeys** (n=190)	**61% Chickens** (n=45)	**66% Broilers** (n = 180) **43% Turkeys** (n = 136)
				C. coli				
				79% Pigs (n=141) **55% Chickens** (n=33)			**60% chickens** (n-60)	**48% Broilers** (n = 59) **66% Turkeys** (n = 110)
Ertapenem (Carbapenem)***	**No data**			***C. jejuni***				
				No data* **				**13% Broilers** (n = 180) **17% Turkeys** (n =136)
				C. coli				
				No data* **				**22% Broilers** (n = 59) **63% Turkeys** (n =110)

*Human clinical breakpoint data not available so figures are presented using epidemiological cut-off values to define resistance

***2017 data was for Campylobacter* resistance in animals was not reported in the VARSS 2017 report (as is normally the case. Data was instead taken from the UK One Health Report 2013-2017 with a smaller sample size of retail chicken meat.

^91% of campylobacter identified to species level was C. jejuni, did not state what the other 9% was.

***included in the VARSS report for the first time in 2022, as a last resort antibiotic for human health and is used in some countries to treat invasive *Campylobacter* infection

7.2.2.1.1 C. jejuni – 2019[193]

Resistance to ciprofloxacin remains high in human isolates, which is a pubic health concern as fluroquinolones are of the main antibiotic classes used when *Campylobacter* infections require antibiotic treatment[169]. As mentioned in Box 3, Table 3 highlights how fluroquinolone resistance has persisted in broiler chickens despite very low use of this antibiotic class in poultry. This is a pattern repeated in several other European countries. Fluroquinolone resistance is primarily causes by a mutation in gyrA gene which is spread rapidly through bacterial reproduction. Scientists are yet to fully understand and evaluate the persistence of Campylobacter resistant to fluroquinolones once the selection pressure of applying the antibiotics is removed.[193] The 2023 One Health Report (using data between 2014-2019) shows that overall, prevalence of resistant *C.jejuni* is **similar** between broiler chickens, chicken meat, and human infections[193]. They include chicken meat within their data collection in order to understand between possible transmission pathways of resistant bacteria between animals to humans via the food chain. All groups show low resistance to erythromycin and high resistance to ciprofloxacin (similar to Table 3) which was found in >40% in broilers and humans and >50% in chicken meat for retail. In addition, tetracycline resistant bacteria were found in higher quantities on broilers and chicken meat (64.3% and 61.1% respectively), compared to in human infections of 41.7% in 2019[193].

7.2.2.1.2 *C.col* - 2019i[193]

Using the same UK One Health Report data, and Table 3, there are significantly higher levels of erythromycin resistance in all *C.coli* populations, hence its recent inclusion in the VARSS report 2022. Erythromycin is the first-line antibiotic used to treat Campylobacter infections in humans[193].

7.2.2.2 Salmonella

Salmonella can be a cause of food poisoning via meat, eggs, and dairy products or sometimes via fruit and vegetables that have been contaminated with animal faeces. In humans, the bacteria can infect the gut and cause severe diarrhoea (gastroenteritis). *Salmonella* can also cause typhoid fever which is a more severe disease but usually spreads between humans rather than from animals to humans. In the UK, human cases of non-thyphoidal S*almonella* is the second most commonly reported pathogen causing gastroenteritis[177] .Cases have been steadily decreasing from around 14,000 cases in 2004 to around 8,000 in 2013[66] and just over 5,000 in 2022[177] .In 2014, methods of laboratory reporting changed and are thought to be mostly responsible for the apparent increase in Salmonella cases between 2014 (8,078) and 2016 (10,341) in England ~15 per 100,000. There are thousands of types (serovars) of S*almonella* although *Salmonella enteritidis* and *Salmonella typhimurium* are the most common serovars involved in gastroenteritis in humans. As with *Campylobacter*, most cases resolve without antibiotic treatment but in severe cases fluoroquinolones such as ciprofloxacin or third-generation cephalosporins such as cefotaxime are the most commonly prescribed antibiotics[67]. In animals, *Salmonella* infections are not treated with antibiotics. It is rare for human serovars of *Salmonella* to be isolated from animals, and antibiotic resistance profiles vary markedly between serovars making a meaningful comparison of human and animal data difficult.[68] Table 4 shows resistance data for HP-CIAs and Aminoglycoside antibiotic classes across human and animal cases using multiple collection methods. Note – the undetectable level of 3rd/4th generation cephalosporin resistance in broilers in 2016 onwards is attested to the use of these antibiotics being stopped in this sector in 2012[193]. No colistin has been used in meat poultry since 2016[193].

TABLE 4: UK ANTIBIOTIC RESISTANCE IN *SALMONELLA SPP.*

Antibiotic	Human antibiotic resistance Clinical surveillance (n=no. of isolates)			Animal antibiotic resistance								
				Clinical surveillance ((n=no. of isolates))					EU harmonised surveillance (n=no. of isolates)			
	2013[69]	2017**	2019[193]	2013[70]	2014[71]	2015[72]	2016	2017	2013[73]	2016	2017***	2022[169]
Fluoroquinolones (ciprofloxacin)	**16%** (n=8,459)	**14%** (n=16,911)	**22.5% (entire quinolne class)**	**0% Pigs; Cattle; Sheep** (n=214; 775; 140) **1% Chickens** (n=899) **7% Turkeys** (n=248)	**0% Pigs; Cattle; Sheep** (n=204; 427; 59) **1% Chickens** (n=525) **11% Turkeys** (n=143)	**0% Pigs; Sheep** (n=172, 57) **<1% Cattle** (n=346) **<1% Chickens** (n=768) **6% Turkeys** (n=251)	**0% Pigs; Cattle, Sheep** (n=160, 336, 91) **0.9% Chickens** (n= 696) **Turkeys 1.8%** (n=111)	**0% Pigs, Cattle, Sheep** (n=158; 392; 104) **0.5% Chicken** (n=873) **0.6% Turkeys** (n=180)	**0% Pigs** (n=147) **0% Chickens; Turkeys** (n=226; 170)	**8.8% Broilers** (n=170) **0.9% Layers** (n= 34) **<0.01% Turkeys** (n=169)	**0% Cattle, Pigs, Chickens** (n=96)	**2.5% Broilers** (n = 170) **1.8% Layers** (n = 56) **9.2% Turkeys** (n = 119)
3rd gen cephalosporin (cefotaxime/ ceftazidime)	**2%** (n=8,459)	**1-4%** (n= 16,911)	**2%**	**<1% Pigs** (n=214) **0% Cattle; Sheep Chickens; Turkeys;** (n=775; 140; 899; 248)	**0% Pigs; Cattle; Sheep; Chickens; Turkeys;** (n=204; 427; 59; 525; 143)	**<1% Pigs** (n=172) **0% Cattle; Sheep; Chickens; Turkeys** (n= 346; 57;768; 251)	**0% Pigs, Cattle, Sheep, Chickens, Turkeys** (n=160; 3,369; 768; 111)	**0% Pigs, Cattle Sheep, Turkeys** (n=158, 392 140, 180) **<1% Chickens** (n=696)	**2% Pigs** (n=147) **0% Chickens; Turkeys** (n=226; 170)	**0% Broilers** (n=170) **0.03% Layers** (n= 34) **0% Turkeys** (n=169)	**0% Cattle, Pigs, Chickens** (n=96)	**None in Broilers, Layers and Turkeys**

Aminoglycosides (gentamicin)	**5%** (n=8,459)	**34%** (n=16,911)	**36%**	**8% Pigs** (n=214) **<1% Cattle** (n=775) **<1% Sheep** (n=140) **3% Chickens** (n=899) **<1% Turkeys** (n=248)	**9% Pigs** (n=204) **0% Cattle** (n=427) **2% Sheep** (n=59) **3% Chickens** (n=525) **0% Turkeys** (n=143)	**28% Pigs** (n=172) **0% Cattle; Sheep** (n=346; 57) **2% Chickens** (n=768) **<1% Turkeys** (n=251)	**0% Cattle, Sheep** (n=336, 91) **21.9% Pigs** (n=160) **2.3% Chickens** (n=768) **<1% Turkeys** (n=251)	**0% Cattle, Sheep, Turkeys** (n=392, 104, 111) **24.1% Pigs** (n=38) **1% Chickens** (n=696)	**16% Pigs** (n=147) **5% Broilers** (n=170) **0% Layers** (n=56) **0% Turkeys** (n=170)		**0% Cattle, Pigs, Chickens** (n-96)	**None in Broilers, Layers** **2% Turkeys** (n = 119)

** Interpreted using the British Society for Antimicrobial Chemotherapy (BSAC) human clinical breakpoints where available*
** Non-typhoidal *salmonella* isolates
*** Only *S. Typhimurium*

Data from 2014-2019 showed how Salmonella spp. resistance levels in broiler chickens to non-HP-CIAs differed significantly from resistance exhibited in humans – with resistance levels being markedly higher in humans than in chickens entering the food chain.[193] Overall, there has been a significant reduction in resistance of Salmonella spp. to tetracyclines (-79.9%) and trimethoprim (-81.1%) in broiler chickens between 2014-2018. This is likely due to the significant reduction in tetracycline usage in FPAs during this period (-61%). Human resistance reductions are less dramatic but have still shown an improvement over the same time period with reductions of resistance in aminoglycosides (-14.7), beta-lactams(-31%), tetracyclines (-26.1%) and trimethoprim (-23.4)[193].

7.2.2.3 Escherichia coli

Escherichia coli are bacteria commonly found in human and animal faeces and are used as an indicator organism for antibiotic resistance.[74] Certain serotypes can cause serious disease in humans. *E. coli* was the most common cause of bloodstream infections in the UK in 2017 which led to the UK Government's ambition to halve the number of healthcare-associated gram-negative bloodstream infections by March 2021[160]. As of November 2023, hospital onset *E.coli* blood stream infections remain largely similar to cases in 2017, dropping from 7,888 in 2016-2017 to 7,881 2022-2023[178] . Antibiotics are very important for the treatment of this condition. *E. coli* are also a common cause of urinary tract infection (cystitis) in humans for which antibiotics are commonly prescribed. Penicillins, aminoglycosides, 3rd generation cephalosporins, fluoroquinolones, and carbapenems are commonly used for treatment of *E. coli* in humans.[75] Shigella Toxin producing E. Coli O157 (STECO157) is a less common cause of gastroenteritis (but the most common type of E.Coli 0157) and can have serious complications with reservoirs in cattle and other ruminants[76]. Transmission of STEC to humans is primarily through ingestion of faecal-contaminated food and water[179]. Antibiotic treatment of STEC0157 is not recommended in humans in the UK[77] and yet there is evidence of resistance profiles[78]. Research into how this is the case is ongoing, but it could possibly be related to antimicrobial use within domestic animals. In 2016 there were 962 cases (~1 per 100,000)[79] but there is no routine surveillance of STEC0157 in animals or recommended treatment for it as it is an asymptomatic infection[80]. Table 5 shows resistance data across human and animal cases using multiple collection methods. The vast majority of animal clinical surveillance data for *E.coli* are from very young animals and antibiotic resistance appears to be more common in this group compared with older animals.

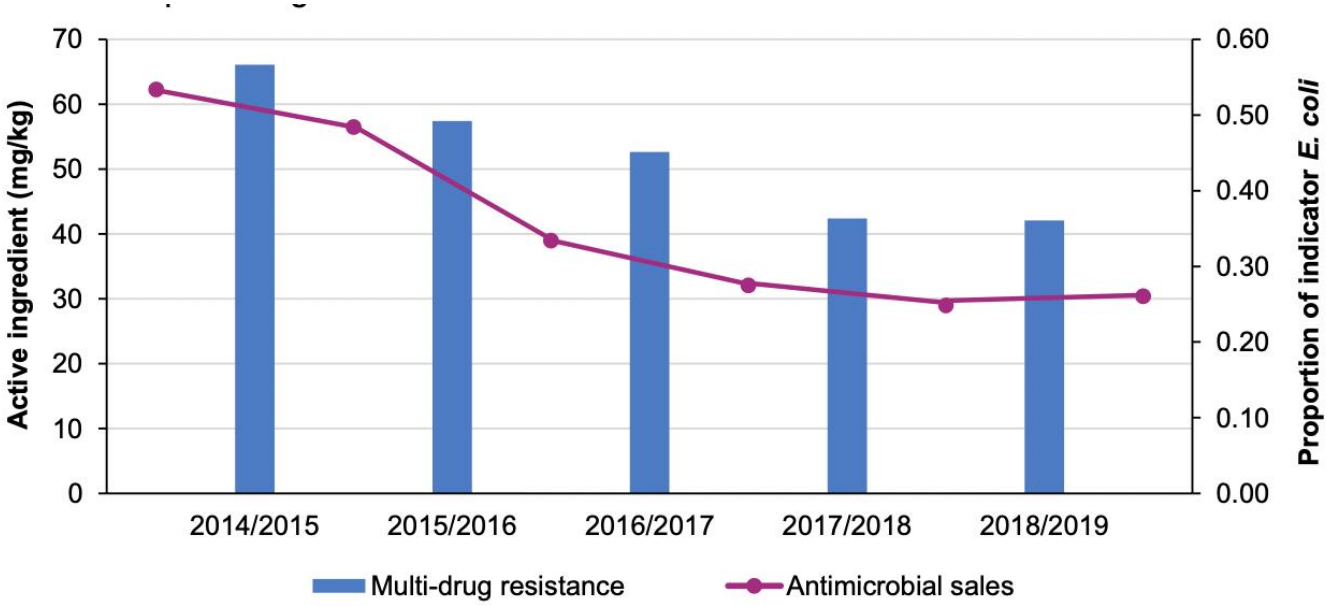
TABLE 5: UK ANTIBIOTIC RESISTANCE IN *ESCHERICHIA COLI*

Antibiotic	Human antibiotic resistance				Animal antibiotic resistance								
	Clinical surveillance				Clinical surveillance*[81]			EU harmonised surveillance					
	2013[82]	2016	2017	2019	2014	2015	2017	2013[83]	2014[84]	2015[85]	2016[160]	2017	2022[169]
Fluoroquinolones (ciprofloxacin /enrofloxacin)	**18%** (n=28,882)	**19 %**	**20%** (n=41,891)	**19.6%**	**8%** (n=1,144)	**11%** (n=1,101)	**6%** (n=810)	**1%** Pigs (n=157)	**4% Chickens** (n=159) **7% Turkeys** (n=168)	**3% Pigs** (n=150)	**2% Broilers** (n=190) **5% Turkeys** (n=224)	**3% Pigs** (n=186)	**11% Broilers** (n = 170) **8.5% Turkeys** (n = 168)
3rd gen cephalosporins (cefotaxime/ ceftazidime)	**10%** (n=23.982)	**12%**	**12%** (n=41,891)	**14%**	**7-14%** (n=593)	**7-9%** (n= 526)	**9-14%** (n=469)	**1%** Pigs (n=157)	**0% Chickens** (n=159) **0% Turkeys** (n=168)	**0% Pigs** (n=150)	**0% Broilers** (n=190) **<1% Turkeys** (n=224)	**0% Pigs** (n=186)	**1.8% Broilers** (n = 170) **0.6% Turkeys** (n = 168)

Aminoglycosides (Gentamicin)	**9%** (n=30,539)	**10%**	**11%** (n=41,891)	**11%**	No data**	No data**	**No data****	**3%** Pigs (n=157)	**20% Chickens** (n=159) **4% Turkeys** (n=168)	**7% Pigs** (n=150)	**7% Chickens** (n=190) **2% Turkeys** (n=224)	**4% Pigs** (n=186)	

* Combined results for *E. coli* from cattle, sheep, pigs, broilers (meat chickens) and turkeys
** Gentamicin was not included in clinical surveillance of veterinary samples but was included in EU harmonised surveillance.

FIGURE 10: PROPORTION OF MULTI-DRUG RESISTANT E.COLI FROM BROILER CHICKENS, FATTENING TURKEYS AND FATTENING PIGS ADJUSTED FOR POPULATION SIZE AND AVERAGED OVER 2 YEARS AGAINST ACTIVE INGREDIENT ADJUSTED FOR POPULATION (MG/KG) OF ANTIBITOICS SOLD FOR USE IN FPAs



7.2.2.3.1 *E.coli* resistance to HP-CIAs

E.coli resistant to HP-CIAs were found to be significantly lower in isolates from the gastrointestinal tract of animals compared to isolates from blood stream infections in humans between 2014-2019. However, this data is hard to directly compare as there is currently no baseline data for the normal level of *E.coli* in a humans microbiome. Human origin *E.coli* showed higher overall resistant to both fluroquinolones and 3rd and 4th generation cephalosporins when compared to broiler chickens and pigs in 2019[193]. Concerningly, human resistance to 3rd and 4th generation cephalosporins increased by 28.7% and to fluroquinolones by 11.36% in *E.coli* isolates, this is likely a reflection of selection of drug-resistant bacteria from the higher usage of HP-CIAs in a human clinical setting and the piperacillin-tazobactam shortage in 2016/2017[193].

In the 2022 VARSS report, resistance to the fluroquinolone, ciprofloxacin, was observed in 77% of *E.coli* isolates (compared to 38% in 2020) with either AmpC or ESBL phenotype (which confer resistance to cephalosporin and beta-lactam antibiotics, respectively). Furthermore, high level ciprofloxacin resistance was detected in 31% of ESBL/AmpC producing *E.coli*. This demonstrates co-resistance of 2 classes of HP-CIAs increasing in predominance in *E.coli* animal populations in the UK.[169] In the 2019 One Health Report, *E.coli* isolates from pig gastro-intestinal tracts showed a 15.8% resistance in these genes, however <1% of pork at retail is contaminated with these resistant bacteria. Conversely, the 4% of chickens at slaughter who possess this resistnt gene align more closely with the percentage of resistant isolates found in chicken

meat at retail[193]. Between 2015 and 2019, the proportion of pigs and pork carrying ESBL- and AmpC-producing *E. coli* remained stable – possibly indicating that pig slaughter processes are highly effective in reducing bacterial contamination of carcasses. Between 2016 and 2018, there was a substantial reduction in chickens (-79.1%) and chicken meat (-71.7%) carrying ESBL-producing *E. coli*, and the percentage of retail chicken meat carrying AmpC-producing *E. coli* also reduced. These results are likely due to reduced use of antiobitcs in the poultry meat sector[193].

7.2.2.3.2 *E.coli* resistance in non-HP-CIAs

The 2019 One Health report found that the highest levels of antibiotic resistance in *E.coli* were found with the most commonly used antibiotics to treat *E.coli* infections in human and animal species – beta lactams, tetracyclines and TMPS[193]. In humans, between 2014-2019, there was very little change in *E.coli* resistant bacteria, with a slight reduction in beta lactam resistance found in blood stream infections (-4/3%) and in TMPS used for urinary tract infections (-11.2%). Despite tetracycline usage reducing by 23% in this period, *E.coli* resistance levels have remained stable and therefore is doesn't seem that resistance correlated with antibiotic usage for tetracyclines and E.coli bacteria. In broilers, E.coli resistance has reduced over all antibiotic classes monitored (Table 1). There have been dramatic reduction in resistance to tetracyclines (-51.6%) and beta-lactam antibiotics (-36.4%).[193] This is largely attributed to the significant reduction of antibiotics used in FPAs since 2014, and in this case, levels of resistance in E.coli populations seem to be correlated with antibiotic usage.[169]

A study in 2019 analysed 20 wastewater treatment plants in east England, testing both treated and untreated water facilities for *E.coli* lineages[198]. Half of the treatment plants were a direct recipient of hospital waste. They found that all samples tested positive for E.coli, and all but one were positive for beta-lactam resistance E.coli isolates. Furthermore, they found that the most rigorous wastewater treatment methods (UV light) did not eradicate the resistant E.coli in 66% of cases. They found more *E.coli* isolates in untreated water systems receiving sewage from hospitals which were found to be genetically similar to those found in the human blood stream infections from the hospitals feeding into the wastewater[198].

7.2.2.4 Enterococcus spp.

Enterococcus faecalis and faecium are new additions to the AMR surveillance programme in the VARSS report 2022. They are commensal gut bacteria in both humans and animals, although in some instance they can cause disease. The most commonly used antibiotics to treat *Enterococcus* infections are amoxicillin (penicillin class) or vancomycin (glycopeptide antibiotic) and therefore vancomycin-resistance enterococci (VRE) are a public health concern due to the higher mortality rates associated with resistant infection. Furthermore, they are often used as indicator species for resistance in Gram positive bacteria.

Previously, there was believed to be a direct correlation between livestock VRE and humans which was attributed to the historic use of avoparcin as a feed additive for livestock which is chemically similar to vancomycin. Avoparcin use was therefore banned in Europe in 1997, leading to a decrease in VRE prevalence in livestock[193]. No vancomycin resistance was detected in either *Enterococcus* species in 2022[169]. In 2021, the prevalence of VRE causing blood stream infections in humans was 17%[193]. In 2018, *Enterococcus faecium* isolates were analysed from livestock, retail meat, wastewater treatment plants and human blood stream infections as part of a one health study to discern the possible transmission pathways of VRE[197]. The majority of isolates from livestock and humans were genetically dissimilar. They found no VRE on farms, but the bacteria were ubiquitous in wastewater treatment samples[197].

TABLE 6: UK ANIMAL ANTIBIOTIC RESISTANCE IN *ENTEROCOCCUS Spp.*

Antibiotic	Animal Antibiotic Resistance EU harmonised surveillance (n=no. of isolates) 2022[169]
Macrolides (Erythromycin)	***E. faecalis***
	49% Broilers (n = 74) **63% Turkeys** (n = 100)
	E. faecium
	32% Broilers (n = 166) **58% Turkeys** (n = 181)
Tetracyclines	***E. faecalis***
	62% Broilers (n = 74) **86% Turkeys** (n = 100)
	E. faecium
	55% Broilers (n = 166) **72% Turkeys** (n = 181)
Penicillins (Ampicillin)	***E. faecalis***
	None
	E. faecium
	5.4% Broilers (n = 166)
Fluroquinolone	***E. faecalis***
	None
	E. faecium

	6% Broilers (n = 166) **5% Turkeys** (n = 181)

7.2.2.4 Antibiotic Resistance in Companion Animals

Linezolid is an antibiotic commonly used to treat resistance Gram-positive bacterial infections in humans, including VRE and MRSA[193]. In 2018, four linezolid-resistance *Enterococcus faecalis* isolated form dogs and cats were found. Molecular analysis attributes the resistance to optrA, a plasmid-mediated gene, which also confers resistance to phenicols i.e. florfenicol[193]. Linezolid is not licenced for use in companion animals in the UK, by florfenicol is an antibiotic used in animals, and could be source of the resistant gene in *E. faecalis* in the UK[193]. Furthermore, raw dog food has been reported as a possible transmission route and source of optrA-positive *E.faecalis* in Portugal[201].

In 2021, a case of carbapenem resistant *E.coli* was isolated from a dog wound. Carbapenems are not licenced for use in animals in the UK, and it is believed resistance was likely acquired in the dog from people, as the variant found in the dog wound ($bla_{NDM)}$ is the most common variant (35.5% of cases) reported in humans.[202]

Recent research shows resistance bacteria are more prevalent in raw dog food compared to conventional food which is heat-treat to kill microorganisms.[193] In one study of 110 raw food samples, up to 60% tested has *E.coli* levels higher than acceptable levels by animal by-product regulations, and in 39% of samples, they were resistant to at least one class of antibiotic. They found that 8% of samples were multidrug resistant and 5.5% of extended-spectrum, beta-lactamases (ESBL) producing *E.coli* were also resistant to the fluroquinolone, ciprofloxacin[193]. Furthermore, another study found that dogs fed raw diets were 23% more likely to excrete ESBL-producing *E.coli,* and 15% to shed multidrug resistance E.coli in their faeces compared to dogs fed non raw diets[193]. Furthermore, in 2020 a ResAlert found *Salmonella spp.* with transferable colistin resistance isolated from raw pet food sampled at a UK manufacturer[193]. It is believed to have originated from cross contamination from imported raw feed ingredients in countries with higher rates of AMR compared to the UK[193]. Overall, there are increased risks of bacterial infection, and resistance bacterial infection, associated with raw pet food which may be a public health and an animal health risk.

7.2.2.5 Other important examples of antibiotic resistance in humans and animals

There are many other bacteria not considered in this report in which antibiotic resistance is of important clinical relevance to humans particularly causative agents of bloodstream infections (e.g. *Klebsiella pneumonia,* methicillin resistant *Staphylococcus aureus*), urinary tract infections, gonorrhoea and tuberculosis. There are also several bacteria where resistance is of clinical relevance in animals including a causative agent of diarrhoea in pigs (e.g. *Brachyspira hyodysenteriae*), the causative agents of lung infections in several species including farm animals (e.g. *Pasteurella multocida*), and many of the causative agents of udder infections in cattle (e.g. *E. coli*, *Staphylococcus aureus* and *Streptococcus spp*). Some taxa such as the causative agents of tuberculosis and gonorrhoea show significant degrees of antimicrobial resistance but are either not found (gonorrhoea) or not treated with antibiotics (tuberculosis) in animals.

Table 7 (below) lists the bacterial species for which UK antibiotic resistance data are cited for both humans and animals in the three major reports on UK antibiotic resistance levels (humans: ESPAUR Report from Public Health England (annual), animals: UK-VARSS report from the Veterinary Medicines Directorate and the UK One Health Report from the Veterinary Medicines Directorate and UK Health Security Agency). It is

notable that of the eighteen bacterial taxa cited only six are cited by both 2018 reports suggesting that to a large extent the bacterial taxa demonstrating antibiotic resistance differ between humans and animals. However, some bacteria can infect both humans and animals and therefore resistance genes can spread to humans from animals and vice versa.

TABLE 7: BACTERIAL TAXA DEMONSTRATING ANTIBIOTIC RESISTANCE IN HUMANS AND ANIMALS IN THE UK FOR WHICH DATA IS CITED

Bacterium	Human UK antibiotic resistance data cited in ESPAUR report 2018[159]	Human UK antibiotic resistance data One Health Report 2019	Animal Antibiotic Resistance Data in the One-Health Report 2019	Animal UK antibiotic resistance data cited in UK-VARSS report 2018[159]	Animal UK antibiotic resistance data cited in UK-VARSS report 2022[169]
Acinetobacter spp.	✓				
Actinobacillus pleuropnuemoniae				✓	
Brachyspira hyodysenteriae				✓	
Campylobacter spp.	✓	✓	✓	✓	✓
*Corynebacterium pseudotuberculosis**				✓	
Enterococcus spp.	✓	✓	✓	✓	✓
Erysipelothrix rhusiopathiae				✓	
*Escherichia coli**	✓	✓	✓	✓	✓
Histophilus somni				✓	
Klebsiella oxytoca	✓				
*Klebsiella pneumoniae**	✓	✓	✓	✓	
Listeria spp.				✓	
Mannheimia haemolytica				✓	
Mycobacterium tuberculosis (TB)	✓				
Neisseria gonorrhoeae	✓				

Pasteurella multocida				✓▪	
Bibersterinia (Pasturella) trehalose				✓▪	
Pseudomonas spp.	✓▪			✓▪	
Salmonella spp.	✓▪	✓▪	✓▪	✓▪	✓▪
Staphylococcus aureus (e.g. MRSA)*	✓▪	✓▪	✓▪	✓▪	
Streptococcus dysgalactiae				✓▪	
Streptococcus pneumoniae	✓▪				
*Streptococcus suis**				✓▪	
Streptococcus uberis				✓▪	
Trueprella (Arcanobacterium) pypogenes				✓▪	
*Yersinia spp.**				✓▪	

Klebsiella pneumoniae is a Gram-negative bacteria which is a member of the enterobacteriaceae family. Increasingly, *K. pneumoniae* are found to be resistant to the HP-CIA carbapenem antibiotic class through the acquisition of carbapenases, an enzyme that have the ability to breakdown these antibiotics. Notably, this antibiotic class is not used in animals (Table 1). The use of carbapenens in human medicine can lead to the evolution of resultant bacteria within the human gastrointestinal tract which are excreted in faeces and enter the environment via sewage systems[193].

Streptococcus suis is a bacterial pathogen that causes arthritis and. Pneumonia in pigs as well as meningitis and sepsis in pigs and humans. It is a possible reservoir of antibiotic resistant genes found on mobile genetic elements which can be transferred between different bacteria. In 2019 there were high levels of resistance against tetracycline (87%), lincomycin (41.7%) and tylosin (47%) found in animals[193]. [[look up resistance papers]] However, in the UK *S.suis* resistance to commonly used first line in human treatments (beta-lactam antibiotics) is rare in both animals and humans.

7.2.2.6 Overall UK Resistance picture

Overall, it is difficult to interpret causation of resistance from the data available, due to the huge complexity in extrapolation and standardisation of results from different sectors using different collection methods. The resistance data shows different patterns of resistance between humans and animals depending on the bacterial species involves. There seems to be a clearer correlation between *Campylobacter* resistant

transmission from broiler chickens into the human food chain via contaminated retail chicken meat[193]. This clearer link between resistance transmission pathways is a testament to the poultry sectors antibiotics stewardship initiatives. Furthermore the same isn't true of *Salmonella* or *E.coli*, whereby isolates vary widely across human and animal sectors, particularly in *Salmonella* where different serovars show different resistant patterns[193]. There is a requirement for regular, harmonised surveillance across human, animal, and environmental sectors to measure trends in resistance, assess impact of interventions, improve understanding of resistance transmission pathways and enable easy data collection and analysis.

8 What is being done?

What follows is not an exhaustive list. This section gives details of what the authors considered (at the time of publication) to be the most significant non-legislative actions being taken at UK, European and Global level to reduce the risks associated with antibiotic resistance in humans and animals. Changes to EU legislation on veterinary medicinal products and medicated feed are outlined in Section 5.

8.2 UK

8.2.2 Public sector

In the Annual Report of the Chief Medical Officer 2018 (Health 2040- Better Health Within Reach) the UK Chief Medical Officer Dame Sally Davies highlighted the certainty that, without significantly changing how we use antimicrobials, AMR will have a devastating effect on future health care. It recognised the need for research and innovation for new drugs such as antibiotics, vaccines and phages, better and more appropriate use of existing drugs and improved infection control. It also highlighted the critical requirement of coordinated policy interventions across countries and through international organisations, due to the ability of both resistant and non-resistant pathogens to travel across national borders. It discussed the increasing evidence of farm animals exposed to a high usage of antibiotics developing resistant bacteria, which then make their way into the food-chain. There was also reference to social movements in the US which have led to some food companies taking steps to limit the use of antibiotics in their supply chains.

8.1.2.1 Review documents on AMR – July 2014

Review on Antimicrobial Resistance announced by the Prime Minister July 2014 chaired by the economist Lord O'Neill and published nine review documents on antimicrobial resistance. Note: Antimicrobial resistance encompasses resistance to viruses (e.g. HIV) and protozoa (e.g. Malaria).

1. Antimicrobial Resistance: Tackling a crisis for the health and wealth of nations (published 11th December 2014)
2. Tackling a global health crisis: Initial steps (published 5th February 2015)
3. Securing New Drugs for Future Generations – the Pipeline of Antibiotics (published 14th May 2015)
4. Rapid Diagnostics: Stopping unnecessary use of antibiotics (published 23rd October 2015)
5. Safe, Secure and Controlled: Managing the Supply Chain of Antimicrobials (published 20th November 2015)
6. Antimicrobials in agriculture and the environment: reducing unnecessary use and waste (published 8th December 2015)

    Recommendations:

    - Set global targets to reduce antibiotic use in agriculture (e.g. 50mg/kg of livestock/fish within the next 10 years)
    - Allow individual countries to decide how to meet these targets
        - E.g. Antibiotic taxation, subsidies to support transition of farmers to alternative husbandry methods or regulations on usage
        - Support use and development of vaccinations and better diagnostic tools
        - Improve public awareness including labelling "antibiotic free" produce

        - Improve surveillance of antibiotic usage and resistance
    - Agree a harmonised global approach to identify antibiotics critical for human health (within the next year) with possibility to restrict or ban usage of these antibiotics in agriculture.
    - Seek international agreements for minimum standards for antibiotic manufacturing waste disposal in the environment
7. Vaccines and alternative approaches: reducing our dependence on antimicrobials (published 11th February 2016)
8. Infection prevention, control and surveillance: Limiting the development and spread of drug-resistance (published 22 March 2016)
9. Tackling Drug-Resistant Infections Globally: final report and recommendations (published 19th May 2016)

    Recommendations:
    - A massive public awareness campaign
    - Improve hygiene and prevent spread of disease
    - Reduce unnecessary use of antimicrobials in agriculture and their dissemination into the environment
        - 2018: Introduce 10 year targets to reduce agricultural antibiotic use
        - Restrict usage of antibiotics that are critically important for human health
        - Improve transparency from food producers to enable consumers to make better informed purchase decisions
        - Set minimum standards for regulators for treatment and release of manufacturing waste from antimicrobial production
    - Improve global surveillance of drug resistance and antimicrobial consumption in humans and animals
    - Promote new, rapid diagnostics to cut unnecessary use of antibiotics
    - Promote development and use of vaccines and alternatives
    - Improve the numbers, pay and recognition of people working in infectious diseases
    - Establish a Global Innovation fund for early-stage and non-commercial research
    - Better incentives to promote investment for new drugs and improving existing ones
    - Build a global coalition for real action – via the G20 and the UN

8.1.2.2 Government Targets – September 2016

Government response to review on antimicrobial resistance – The UK government responded to the O'Neill report in September 2016 "warmly welcoming" the final report and setting targets to:

- **Reduce healthcare associated gram-negative bloodstream infections in England by 50% by 2020** (humans)
- **Reduce inappropriate antibiotic prescribing by 50%, with the aim of being a world leader in reducing prescribing by 2020** (humans)
- **Reduce antibiotic use in livestock and fish farmed for food to a multi-species average of 50mg/kg by 2018 using methodology harmonised across other countries in Europe**.

- Set agreed animal sector specific reduction targets by 2017

8.2.2.4 5-year Action Plan – 2013-2018

UK Five Year Antimicrobial Resistance Strategy (2013-2018) – Sets out seven key areas for action in combating AMR including strategies to:

- "Prevent" – improve infection prevention measures to reduce need for antimicrobials,
- "Protect" – optimise responsible use of antimicrobials and
- "Promote" – encourage development of new diagnostic (e.g. to detect resistance and help select appropriate antibiotic choices) and treatment methods (e.g. novel drugs).

8.2.2.5 5-year Action Plan – 2019-2024

Tackling antimicrobial resistance 2019-2024: The UK's five-year national action plan - this reports builds upon the Government's previous Five Year Antimicrobial Resistance Strategy (2013-2018) and aims to ensure progress towards the Government's 20 -year vision on AMR. It focuses heavily on the One Health and coordinated approach required to address AMR. It outlines key areas to tackling AMR:

- **Reducing the need for, and unintentional exposure to, antimicrobials** to be achieved by:
  - Lowering burden of human and animal infection
  - Greater global access to clean water and sanitation
  - Minimise spread of AMR through the environment
  - Better food safety
- **Optimising use of antimicrobials** to be achieved by:
  - Optimal use of antimicrobials in humans, animals and agriculture
  - Stronger laboratory capacity and surveillance of AMR in humans and animals
- **Investing in innovation, supply and access** to be achieved by:
  - Sustainable investment in basic research
  - Development of, and access to, therapeutics for those who need them
  - Development of, and access to, diagnostics and vaccines
  - Better quality assurance of AMR health products

The plan also sets out measures of success to ensure progress towards the 20 year vision which include targets to:

- Reduce UK antibiotic use in food-producing animals by 25% between 2016 and 2020
- Reduce UK antimicrobial use in humans by 15% by 2024
- Halve healthcare associated Gram-negative blood stream infections

In May 2021, the One Health Integrated Surveillance (OHIS) subgroup of the Defra Antimicrobial Resistance Coordination (DARC) group was formed. It aims to develop and integrate AMR surveillance across human, animal food and environmental health sectors. The findings will advise the next UK AMR National Action Plan and other cross government initiatives i.e. PATH-SAFE.

8.2.2.6 UK 20-year Vision for AMR – January 2019

Contained and Controlled: The UK's 20-year vision for antimicrobial resistance – Published January 2019. A report detailing how the UK will aim to achieve its vision in 2040 of a world in which antimicrobial

resistance is effectively contained, controlled and mitigated. It focuses on the local, national and global One-Health approach required and collaborations both nationally and internationally. The UK will contribute to global effort through:

- **A lower burden of infection, better treatment of resistant infections and minimised transmission in communities, the NHS, farms, the environment and other settings.**
- **Optimal use of antimicrobials and good stewardship across all sectors, including access to safe and effective medicines manufactured responsibly.**
- **New diagnostics, therapies, vaccines and interventions in use and research and development in the pipeline for antimicrobials, alternatives, diagnostics, vaccines and infection prevention across all sectors.**
- **Encourage antimicrobial stewardship through international collaboration and intervention plants to mitigate the risks of global spread of AMR across humans, animals, the environment and food.**

It discusses the UK's nine ambitions for change which are as follows:

1. Continue to be a good global partner
2. Drive innovation
3. Minimise infection
4. Provide safe and effective care to patients
5. Protect animal health and welfare
6. Minimise environmental spread
7. Support sustainable supply and access
8. Demonstrate appropriate use of antimicrobials
9. Engage the public on AMR

8.2.2.7 Other UK Reports

- One Health Reports:
  - Last published November 2023
  - UK Health Security Agency (formerly Public Health England - an executive agency of the Department of Health) produces a cross-government report presenting antibiotic use data from FPA's and humans, data on AMR in bacterial isolates from animals and humans and comparative data on AMR in isolates from retail meat.
  - It aims to assess occurrence of resistance along the food chain and to add context to the surveillance data by providing information on control measures in place to reduce the risk of transmission of the bacteria monitored and policy decisions that have been taken to tackle AMR.
  - UK Health Security Agency and Veterinary Medicines Directorate: UK One Health Report (2023)
  - Public Health England and Veterinary Medicines Directorate: UK One Health Report (2019)
  - Public Health England and Veterinary Medicines Directorate: UK One Health Report (2013)
- Veterinary Medicines Directorate (VMD) AMR and Sales Reports:
  - Last published November 2023
  - The VMD (an executive agency of DEFRA) produce an annual report reviewing the available data on veterinary antibiotic sales and resistance levels – Veterinary Antibiotic Resistance and Sales Surveillance (VARSS)

  - VMD: VARSS Report 2022
  - VMD: VARSS Report 2017
- Public Health England AMR Reports:
  - Last published November 2022
  - PHE produces as annual report reviewing antimicrobial usage and resistance levels in humans in England.
  - PHE: ESPAUR 2021-2022
  - PHE ESPAUR 2017-2018

8.2.2.8 Public sector engagement

- eBug learning courses:
  - Developed by UKHSA, all materials are accredited by Association for Science Education.
  - Aims to educate young people (aged 3-16 years) with information, activities and discussion points to build knowledge around microbes, disease, hygiene, vaccination and AMR.
  - Students learn about food safety, farm hygiene and interplay of public and animal health.
  - In 2022, education packs were sent to over 20,000 schools in England in collaboration with NHS England and NHS Improvement.
- TARGET antibiotics toolkit:
  - Includes resources intended for primary car providers for tailor-made antimicrobial stewardship interventions and improve antibiotic prescribing. Leaflets can be sent online to patients covering advice on common infections, including UTIs.
  - Resources are developed by the UKHSA, the Royal College of General Practitioners and the Antimicrobial Stewardship in Primary Care Group.
  - TARGET antibiotic checklist collects data from >8,000 pharmacists in England and provides information on >210,000 patients collecting antibiotic prescriptions. The checklist aims to support pharmacists to ensure safety of patients and public education on responsible antimicrobial use and managing common infections.

8.2.3 UK Animal sector

Responsible Use of Medicines in Agriculture Alliance (RUMA) (Est. 1997)

- Independent alliance of farming, animal health industry, food retailing and associated groups aiming to produce a co-ordinated and integrated approach to best practice in animal medicine use.
- Offers best practice guidelines to veterinarians and farmers, supports training for farmers and provides briefings for government to inform policy decisions as well as setting voluntary sector targets for improving antibiotic use in eight key livestock species. (http://www.ruma.org.uk/).
- Targets for 2021-2024 – RUMA Targets Task Force 2
- Latest report – November 2023; RUMA Targets Task Force 2 – 3 years on

British Poultry Council Antibiotic Stewardship Programme (Est. 2011)

- Represents 90% of commercial meat poultry production (note: this does not currently include egg or game bird producers but does include turkeys and ducks)
- Reported an 79.5% reduction in total antibiotic use since 2012 despite suspected increase (~5%) in poultry population. This has been attributed to the availability of better-quality feed in 2014. [180,86]

- Implemented an industry ban on use of 3rd and 4th generation cephalosporins in 2012
- Reported no fluroquinolone used in chicken meat production in 2022, as well as a 98.7% reduction in HP-CIAs since 2012.[180]
- Has made voluntary submission of data on antibiotic usage to the VMD.
- Voluntary commitment to stop colistin usage in all British poultry in the stewardship scheme (2016)
- Latest report – November 2023; BPC Antibiotic Stewardship Scheme 2023

Pig Health and Welfare Council Antimicrobial Usage Sub-Group

- Developed the electronic medicines book for pigs (eMB-Pigs) with funding via Industry Levy (AHDB-Pork) and VMD to collect data on antibiotic usage. The online hub launched in April 2016.
    - Farmers can submit and monitor antibiotic usage over time and compare their data with anonymous data from other pig farmers
    - Participation will help farmers to meet obligations of quality assurance schemes to record antibiotic usage.
    - In the future may be expanded to include other species.
- eMB-Pigs reviews and analyses data from 95% of the pigs produced in the UK[181]
- Figures released by the Pig Health and Welfare Council showed a 20% reduction in antibiotic usage between 2021-2022, reaching their 2024 target 2 years early[181]
- Latest report – November 20222; PHWC Biennial Report 2021-2022

Cattle health and welfare group

- Established a Cattle Antimicrobial Usage Data Collection Steering Group
- Several individual initiatives present through veterinary practices, data collection companies, universities and milk recording schemes but lack of a centralised hub to combine data.
- Proposals developed for a data capture system focusing on collecting vet prescription data should be operational by 2017.[87]
- The Medicine Hub was launched in 2021 to encourage data collection of antibiotic use for dairy, beef and sheep producers in the UK.
- Similary, the welsh lamb and beef producers antimicrobial usage calculator went live in n2021 allowing standarisation and therefore comparison of farm-;evel antibiotic use.

Companion animals (pets)

- The British Small Animal Veterinary Association (BSAVA) promotes the responsible use of antimicrobials by companion animal vets (predominantly dogs and cats) through the PROTECT ME campaign.[88] [182] This encourages companion animal veterinary practices to develop practice protocols for antimicrobial usage with emphasis on reducing unnecessary usage and reducing usage of antibiotics important for human health.
- SAVSNET[89] and VetCompass[90] – Voluntary systems for submitting anonymous information from veterinary laboratories and/or veterinary practices. The VMD has funded projects to use these data to gain better understanding of antimicrobial usage and resistance levels in UK pets.
- Idexx Pet Resist[91] – Idexx veterinary laboratories provide a quarterly surveillance reports on antibiotic resistance trends in small animals. This uses the data available from the testing of samples submitted to their laboratory network from UK pets.

British Equine Veterinary Association (BEVA)

- Developed a PROTECT-ME toolkit for use by equine veterinary practices based.[92] This is based on the PROTECT model used in companion animals and encourages veterinarians to develop and implement practice protocols for responsible antibiotic use. It also incorporates monitoring of usage and resistance levels and education of team members and clients. In May 2016 BEVA received a highly commended award at the Antibiotic Guardian Awards for their contribution to antibiotic stewardship.[93]
- BEVA runs an "Antibiotic Champion Award" which encourages submission of antibiotic sales data.

Animal Welfare Foundation

- Funding research into social aspects of client compliance using motivational interviewing techniques. The study has shown vets to take a more parental approach which uses directive language, rather than a mutualistic and relationship-centred communication approach. The latter approach has now been recommended for vets to use to help motivate and change behaviours of owners which could be particularly useful in farming sectors when it comes to cutting down on antibiotic use.[94]

ResAlert System

- An international response system initiated in 2015 to alert healthcare professionals of new resistant bacteria (considered a potential high risk to animal or human health) and generate risk analysis used for their control.
- In the UK, this is coordinated by the VMD.

Antibiotic Guardian Campaign

- Launched in 2014 by the then PHE, it aims to create a transition from raising awareness of AMR to increasing engagement across human and animal health sectors, including healthcare professionals, members of the public and students and educators.
- Between 2014-2021 a total of 144,445 pledges were made to improve antibiotic guardianship.

Antibiotic amnesty

- Formed in 2022, it aims to encourage pet owners to return any unused or out of date veterinary antibiotics for safe disposal by the veterinary practice or a registered pharmacy in order to reduce environmental pollution and avoid health risks associated with inappropriate usage of antimicrobials to reduce AMR.
- Supported by the BVA, RCVS, NOAH, RUMA, VMD etc.
- Another initiative is running in 2023.

RCVS Farm Vet Champions

- Supported by RCVS knowledge and funded by the VMD it provide over 20 hours of free CPD for veterinary surgeons to build confidence and ability when engaging with clients in application of good antimicrobial stewardship.
- In 2022, the scheme launched SMART goals for farm vet champions to be set at an induvial or practice level. This allows training to be put into practice to broaden the benefits and develop leaders. Progress is tracked online.

PATH-SAFE

- Cross-governmental UK-wide programme since 2021, funded to £19.2million through His Majesty's Treasury and is led by the Food Standards Agency.
- It aims to develop model national genomic surveillance network using DNA sequencing, environmental sampling to improve the monitoring and surveillance of tracking food borne pathogens and AMR throughout all stages of the food chain.

8.2.4 UK Human sector

Antibiotic Guardian Initiative:

- Launched by PHE in September 2014 to encourage health professionals, patients and the public to pledge to use antibiotics responsibly. Over 194,000 pledges received so far (November 2023).
- Antibiotic Guardian Initiative

Other:

- The TARGET (Treat antibiotics Responsibly, Guidance, Education Tools) antibiotic toolkit, hosted by the Royal College of General Practitioners, is a key source of guidance for responsible antibiotic prescribing in primary care (e.g. GPs).
- An Antimicrobial Stewardship Toolkit for English Hospitals "Start Smart, Then Focus" was published in 2011 and updated in 2015. It provides and evidence based framework for responsible prescription of antibiotics in human hospitals.
- Public Health England published a more complete list of resources to promote responsible human antimicrobial prescribing.
- In April 2015 Public Health England made local surveillance data on antimicrobial resistance publicly available via the Fingertips data portal.
- The British Society for Antimicrobial Chemotherapy (BSAC) is an inter-professional organisation that aims to combat antimicrobial resistance by supporting antimicrobial education (funds Antibiotic Action which is a global public awareness initiative on drug resistance and also co-created a Massive Open Online Course (MOOC) in antimicrobial stewardship with the University of Dundee), surveillance (undertakes structured surveillance of antibiotic resistance in UK human cases of respiratory disease and bacteraemia) and research (Journal of Antimicrobial Chemotherapy).
- The National Institute for Health and Care Excellence (NICE) have produced a quality standard on infection prevention and control. Improved standards of hygiene in hospitals have been linked to large reductions in hospital acquired bacterial infections including MRSA.[95]
- Cochrane Systematic review of the use of delayed prescriptions for respiratory infections found no difference in most clinical outcomes when using no or delayed prescribing rather than immediate antibiotic prescription with similar patient satisfaction across the groups.[96]

8.3 Europe

European Antibiotic Awareness Day is held on 18th November each year to promote public awareness of antibiotic resistance.

8.3.2 Human sector

The European Centre for Disease Prevention and Control (ECDC) collates data on human antibiotic consumption and resistance levels across Europe (EU and EAA countries). This is reported in two annual reports and the data can also be viewed via online interactive databases:

ESAC-Net report[97] is a Europe-wide network of national surveillance systems, providing European reference data on antimicrobial consumption from both the community and hospital sector. The reports of the database are provided through the European Surveillance System (TESSy). Latest data available is for 2016. Note – countries may vary their data collection methods and therefore not all results can be directly extrapolated and compared to one another.

EARS-Net report 2016 (published November 2017) shows data for antibiotic resistance levels in seven bacterial groups of key importance to human health: *Escherichia coli, Klebsiella pneumoniae, Pseudomonas aeruginosa, Acinetobacter* species*, Streptococcus pneumoniae, Staphylococcus aureus,* and *Enterococci*.[98]

8.3.3 Animal sector

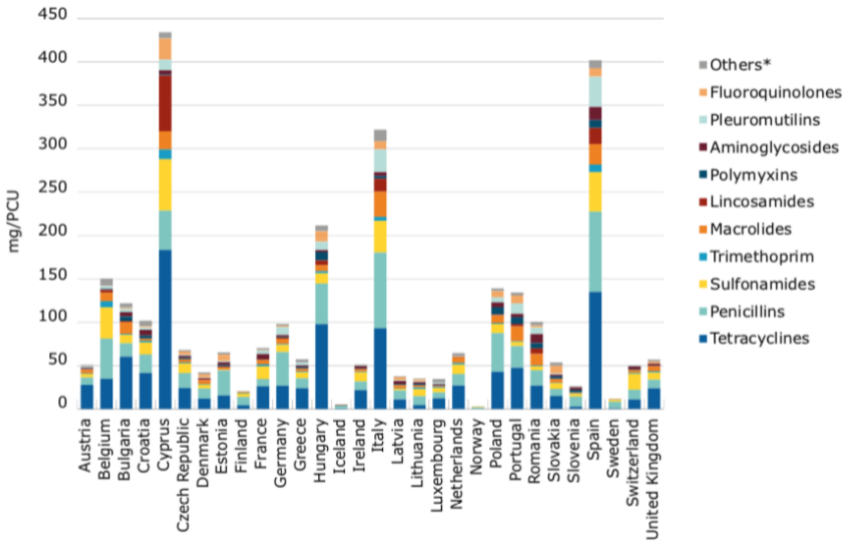


FIGURE 10: EU/EEC ANIMAL ANTIBIOTIC SALES IN FOOD PRODUCING SPECIES (mg/PCU, 2015) [99]

*Note: Polymyxin usage may be used as a rough guide to **colistin** usage.*
Differences between countries can be partly explained by differences in animal demographics, in the selection of antimicrobial agents in dosing regimes, in type of data sources, and veterinarians prescribing habits and prices.

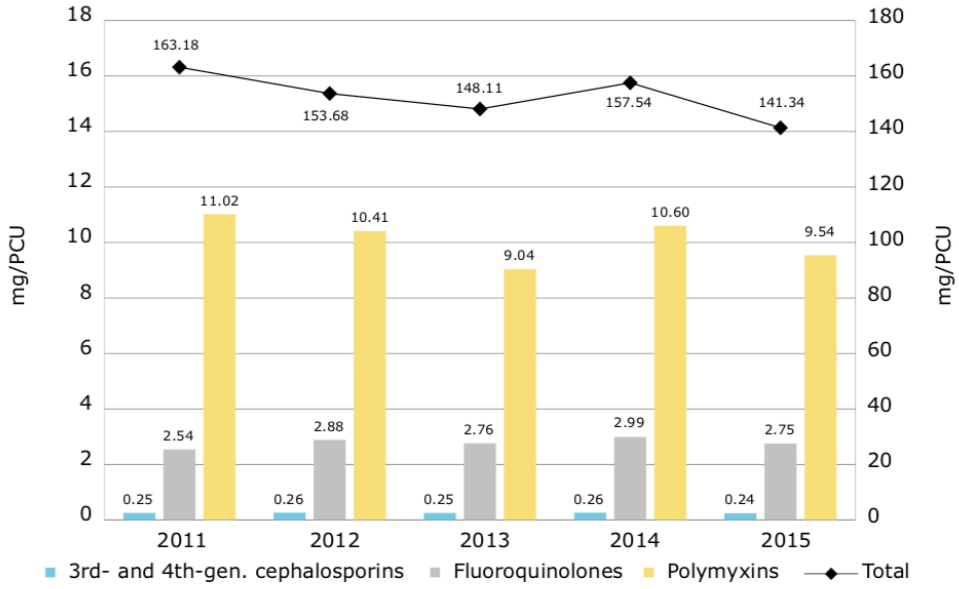


FIGURE 11: TOTAL AND FLUOROQUINOLONE + 3RD/4TH GENERATION CEPHALOSPORIN ANTIBIOTIC SALES EU 25 2011-2015 *Note: Different scales on the vertical axis. Larger scale on the right refers to total usage. The apparent increase in total sales in 2014 can be explained by a change in the sales data collecting system in Spain.*[100]

The European Medicines Agency commissioned the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project in 2010 to collate the available data on antimicrobial sales in Europe (EU/EEA countries). ESVAC currently has three work-streams for 2016-2020 focusing on collection of overall sales data, development of systems for collection of data on consumption by animal species and establishment of technical units of measurement.[101] The sixth ESVAC report published in October 2016 reported an overall 2.4% decrease in total antimicrobial sales for food producing species over the four year period 2011-2014.[102] In February 2018, EMA published guidance on reporting antimicrobial consumption data by animal species with supporting rationale document for the recommendations.[103] Since the UK has left the EU, there has been no inclusion of comparable data since 2020. Despite this, caution is required when interpreting this data due to differences in data collection methods between countries and the differences in type and size of animal production systems. The total level of fluoroquinolone and 3rd/4th generation cephalosporin used in food producing animals has remained constant 2011-15 (Figure 11).

The Committee for Medicinal Products for Veterinary Use (CVMP) is responsible for preparing the European Medicines Agency's (EMA) opinions on all questions concerning veterinary medicines (including antibiotics). In July 2011 the committee's strategy for veterinary antimicrobial use in Europe 2011-2015 was adopted.[104] In November 2015 the committee released a draft of the strategy for veterinary antimicrobial use in Europe 2016-2020. This calls for an evidence based, global, one health approach.[105]

The EMA has made several recommendations to the European Commission on usage of antimicrobials in animals.[106] They have recently (June 2023) adopted to 'strengthen EU action against AMR'.

In January 2015 the ECDC, EMA and the European Food Safety Authority (EFSA) published the first integrated analysis of antimicrobial usage and resistance data from humans and food producing animals in Europe.[107]

In 2015 the European Commission requested a joint report from EMA and EFSA on measures to reduce the need to use antimicrobial agents in animal husbandry in the European Union, and the resulting impacts on food safety. The report is due for publication by December 2016.[108] In June 2018 the EU commission released its new AMR One Health Action Plan. In July 2018, the Codex Alimentarius Commission approved reopening of the AMR task force to look at developing guidance on integrated AMR surveillance and updating its code of practice on minimising the risk of AMR in the food chain.

Since 2014, the EU funding programmes (Horizon 2014-2020 and Horizon Europe 2021-2027) have invested over £600 million to support research and development in AMR. In the first 2 years of Horizon Europe, they have committed over £25 million on 13 research projects relating to tackling AMR.[192]

8.4 Global

8.4.2 World Antibiotic Awareness Week (18-24 November 2023).

8.4.3 Global consumption of antibiotics is on the increase with a 40% rise between 2000 and 2010.[109] Over the same period the world population increased by 13%.[110]

8.4.4 Projections by the Organization for Economic Cooperation and Development (OECD) indicate an anticipated twofold increase in resistance to last-resort antibiotics by 2035 when compared to 2005 levels.[191]

8.4.5 The Global WHO Antimicrobial Resistance Action Plan (2015) reinforced by resolutions from the World Organisation for Animal Health (OIE) and the United Nations Food and Agriculture Organization (FAO) recommends that:

8.4.5.4 Countries should develop national action plans to combat antimicrobial resistance

8.4.5.5 Surveillance systems for antibiotic usage and resistance in animals and people should be improved.

8.4.6 WHO Guidelines released in November 2017 use a different definition of CIA to the European Medicines Agency (used by the UK and Europe) because they identify the degree of risk to human health should antimicrobial resistance develop after use in animals.

8.4.7 In March 2018 the international Inter-Agency Coordination Group was launched to take forward the commitments of the Global AMR Action Plan (2015) and the UN General Assembly AMR Declaration (2016).. More recently, the G7 Chief Veterinary Officers Forum produced a consensus paper on agreed terms for definitions of terms relating to AMR to help international discussions take place using a common language.

8.4.8 The Transatlantic Task Force on Antimicrobial Resistance (TATFAR) was set up in 2009 to promote collaboration between the EU and the US on issues related to antimicrobial resistance including promotion of responsible antimicrobial use by human and veterinary healthcare professionals, infection prevention in humans and stimulating the development of new antimicrobials.[111] The secretariat for the taskforce transferred from the ECDC (European) to the CDC (American) in January 2014. In October, 2015, TATFAR revised its work plan and identified 20 actions for continued collaboration through 2020 and shown on their website.

8.4.9 UK government initiated the Fleming Fund in February 2015 to improve surveillance of drug resistant infections across 25 low and middle-income countries to improve policy at local, regional and national levels. It secured £210 million in funding at the G20 meeting in India 2023[193]. Aims over 5 years (2015-2020) to build a global network of laboratories in partnership with the Wellcome Trust, the Bill and Melinda Gates Foundation, the Institut Pasteur International Network and others.[112]

8.4.10 In October 2015, the UK Prime Minister and the Chinese President, Xi Jinping, announced the intention to create a Global AMR Innovation Fund. The aim of the fund is to increase investment to stimulate global research in AMR. The UK has committed £50m to set-up this Global AMR Innovation Fund to target and coordinate investment globally.[113]

8.4.11 G20 summit (China, September 2016): International leaders called for action on antimicrobial resistance including a call for the WHO, FAO, OIE and OECD to report back in 2017 with options to address all AMR aspects, including the economic aspects.[114]

8.4.12 The United Nations (UN) held a high level meeting on antimicrobial resistance on 21st September 2016. Members acknowledged that "Within the broader context of AMR, resistance to antibiotics [...] is the greatest and most urgent global risk that requires increased attention and coherence at the international, regional, and national levels" and called for "the Secretary-General to establish, […]an ad hoc interagency coordination group, […]drawing, where necessary,

on expertise from relevant stakeholders, to provide practical guidance for approaches needed to ensure sustained effective global action to address AMR."[115]

8.4.13 European Medicines Agency, the Japanese Pharmaceutical and Medical Devices Agency and the United States Food and Drug Administration reached an agreement in 2017 to align data requirements for certain aspects of the clinical development of new antibiotics. The aim of this collaboration is to facilitate a single development programme for new antibacterials that can satisfy the regulatory requirements of each of the three agencies.[116]

8.4.14 WHO runs the global initiative on AMR - Global Antimicrobial Surveillance System – which standardises collection and analysis of data. It shares data related to AMR (including within the food chain) to inform decision making at local, national and global levels. Every year they produce a report on AMR.[192]

8.4.15 The Muscat Manifesto commits 46 countries to targets which aim to tackle AMR.

ANNEX I: SUMMARY OF ANIMAL EU ANTIMICROBIAL RESISTANCE MONITORING REQUIREMENTS (2013/652/EU)[1]

	Sampling Year						
	2014	2015	2016	2017	2018	2019	2020
Salmonella spp. - Broilers	x		x		x		x
Salmonella spp. - Layers	x		x		x		x
Salmonella spp. - Fattening Turkeys	x		x		x		x
Salmonella spp. - Broiler Carcases	x		x		x		x
Salmonella spp. - Fattening Turkey Carcases	x		x		x		x
Salmonella spp. - Pig Carcases		x		x		x	
Campylobacter jejuni - Broilers	x		x		x		x
Campylobacter jejuni - Fattening Turkeys	x		x		x		x
E. coli - Broiler Caeca	x		x		x		x
E. coli - Turkey Caeca	x		x		x		x
E. coli - Pig Caeca		x		x		x	
ESBL, AmpC and Carbapenemase producing *E. coli* - Broiler Caeca	x		x		x		x
ESBL, AmpC and Carbapenemase producing *E. coli* - Turkey Caeca	x		x		x		x
ESBL, AmpC and Carbapenemase producing *E. coli* - Pig Caeca		x		x		x	
ESBL, AmpC and Carbapenemase producing *E. coli* - Fresh broiler meat, pig meat and bovine meat gathered at retail	x	x	x	x	x	x	x
Campylobacter coli - Broilers	x		x		x		x
Campylobacter coli - Pigs		x		x		x	
E. faecium and *E. faecalis* - Broilers, Fattening Turkeys, Fattening Pigs, Bovines <1yr age	x	x	x	x	x	x	x

Key:
x = Mandatory
x = Voluntary
Pig and Bovine
Poultry

Note: The UK is exempt from the monitoring of resistance in isolates of bovine origin as we do not meet the cattle (<1 year of age) slaughter throughput as specified in the legislation.

[1] Callum Harris, Veterinary Medicines Directorate, UK VARSS Report 2014

ANNEXE III UK EQUINE SECTOR ANTIBIOTIC USAGE AND RESISTANCE

Last updated: 21 June 2017

1. Antibiotic usage

1.1. In 2016, 29 tonnes of 337 (8.6%) of antibiotic sold for use in animals was for use in horses[117]. Antibiotic sales cannot be used to reliable determined antibiotic use in horses as many products are licensed for other species and there is higher use of off-label products.[169]

1.2. A study covering 15% of the UK equine population found that the DDDvet/animal for horses reduced by 10% from 2012 to 2022.[169]

1.3. There are 28 antibiotic products licenced for use in horses in the UK (see Table 1)

Table 1: Antibiotic products licensed in the UK for use in horses (correct on 21 June 2017)[118]

Antibiotic	Number of products
Potentiated sulphonamides	10
Penicillin family	10 (4 with *Streptomycin* and 1 with *Neomycin*)
Tetracyclines	
- *Oxytetracycline*	2
Third/fourth generation cephalosporins:	
- *Ceftiofur*	2
- *Cefquinome*	1
Aminoglycosides	
- *Streptomycin*	1
- *Gentamicin*	1
Thiamphenicol	1

Source: VMD Product Information Database

1.4. Actual usage in horses is difficult as sales data may not directly equate to usage

1.4.1. many products licensed for use in horses are also licenced for use in other species

1.4.2. antibiotics not licenced for use in horses may be used under the Cascade

1.5. A survey of antibiotic prescribing in UK equine veterinary practices (Hughes et al. 2013)[119] found that:

- potentiated sulphonamides where the most commonly prescribed antibiotic
- 11 % of prescriptions were for antimicrobials not licenced for use in horses
- fluoroquinolones and 3rd/4th generation cephalosporins accounted for 1% and 3% of prescriptions respectively
- < 1% of equine veterinary practices had antimicrobial use guidelines

2. Antibiotic resistance

2.1. As horses are not considered food animals in UK risk of transfer of antibiotic resistant bacteria via the food chain is low. However, use of horses as companion animals and working animals creates opportunities for transmission due to close contact with people.

2.2. Horses are known to be able to carry Methicillin Resistant Staphylococcus Aureus (MRSA)

2.2.1. Studies in North America and Europe have identified MRSA carriage in 0-10.9% of healthy horses and on some farms over 50% of horses may carry MRSA.[120]

2.2.2. Zoonotic transmission of MRSA from horse to humans has been reported

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Note: There are a large number of repeated references in this list. This has been done to facilitate future updates.

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