



HM Government

UK One Health Report

Joint report on antibiotic use and antibiotic resistance, 2013–2017

Published: 31 January 2019





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Executive summary

Antibiotic Use and Resistance in Animals and People 2013–2017

Key points

Antibiotic use

*In mg/kg**

- Based on use per 'bodyweight', there was a reduction of 40% in food-producing animals (from 62 mg/kg to 37 mg/kg) and 9% in people (from 135 mg/kg to 123 mg/kg).

By weight of active ingredient

- Total use/sales in tonnes dropped by 19% from 957 to 773 tonnes.
- In 2017, use in people was 491 tonnes and sales for use in animals (food-producing animals**, horses and pets) were 282 tonnes.
- Use in people represented 55% of all use/sales in 2013 and 64% in 2017.
- Overall, 89% (17 tonnes) of highest priority critically important antibiotics (HP-CIAs) were used in people. Their use increased in people by 8% and decreased in animals by 51%.

Antibiotic resistance

- For food-producing animals, no resistance was detected in *Escherichia coli* or *Salmonella* spp. to colistin, and very low*** or no resistance was detected respectively to 3rd generation cephalosporins. There was low resistance level to fluoroquinolones for *E. coli* and only very low resistance for *Salmonella* spp.
- For people, resistance level to 3rd generation cephalosporins and to fluoroquinolones was moderate for *E. coli*, and was low and moderate respectively for *Salmonella* spp. Resistance level to colistin was low in both *E. coli* and *Salmonella* spp.
- For people, retail chicken meat and food-producing animals, resistance level to fluoroquinolones was high for *Campylobacter jejuni*. Resistance to erythromycin was low in *C. jejuni* isolates from people and retail chicken meat and very low in isolates from food-producing animals.

Note:

* mg/kg: is the milligrams of active ingredient of antibiotics sold/used per kilogram of bodyweight of food-producing animals or people in the UK.

** Food-producing animals include pigs, chickens and turkey for *E. coli*, chickens and turkeys for *C. jejuni* and pigs, broilers, layer chickens and turkeys for *Salmonella* spp.

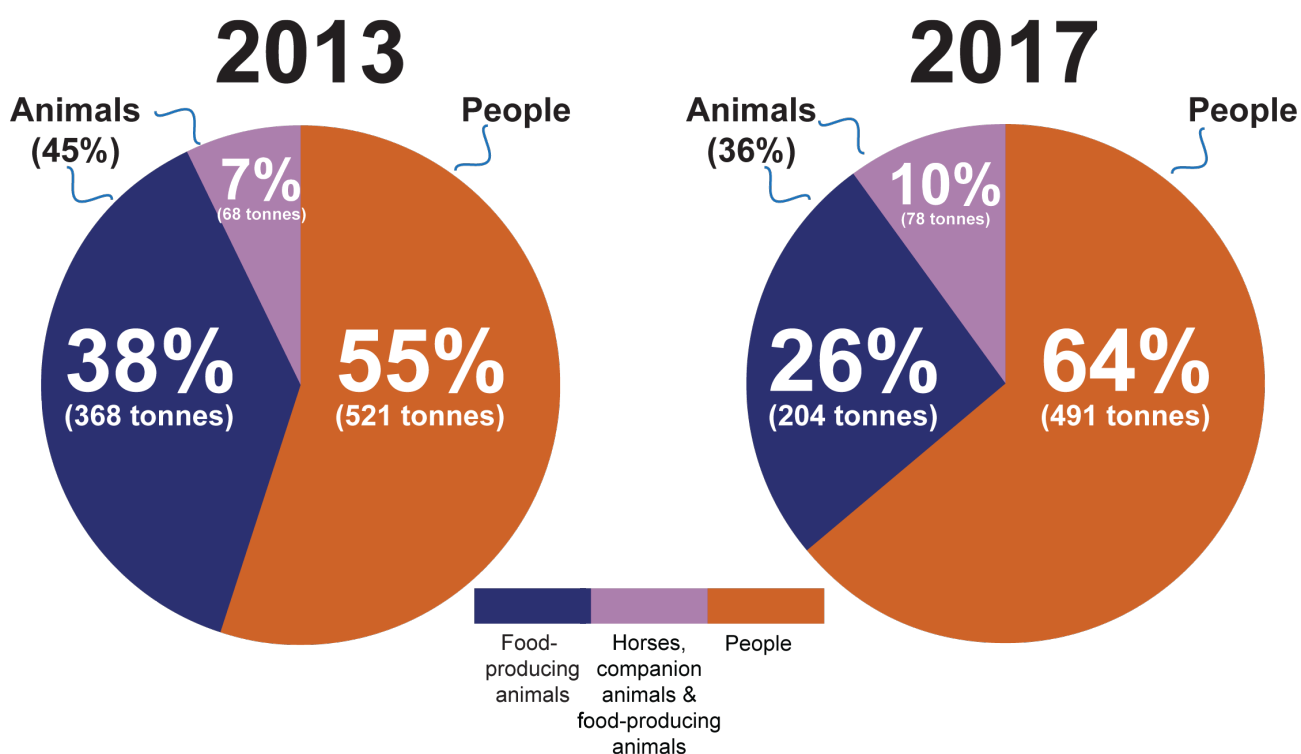
*** Resistance levels are classified according to the classification in the European Union summary reports on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food, as published by the European Food Safety Authority. The classification is as follows: <0.1 rare; 0.1–1.0 very low; >1.0–10.0 low; >10.0–20.0 moderate; >20.0–50.0 high; >50.0–70.0 very high; >70.0 extremely high.

Antibiotic Use

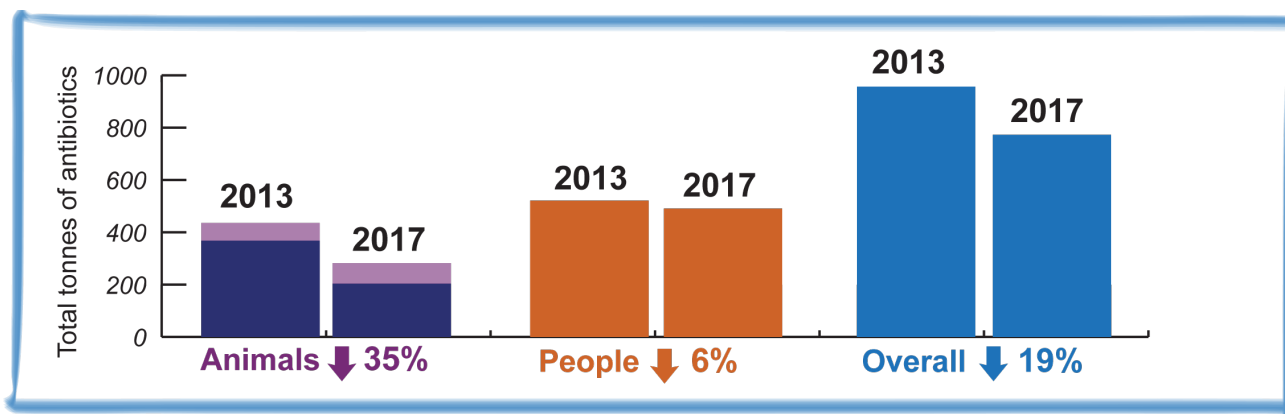
Reductions in total tonnes between 2013 and 2017

In 2017, a total of 773 tonnes¹ of antibiotic active ingredients was dispensed in the UK for use in people and animals. This represents an overall reduction of 19% between 2013 and 2017. Tonnage used dropped by 6% in people (521 to 491¹ tonnes; excluding private prescriptions) and by 35% in animals (436 to 282 tonnes) over this period.

Of the 773 tonnes, 64% was for use in people, 26% for use in food-producing animals only and 10% for use in companion animals and horses, but also in food-producing animals. Of the 64% prescribed for human use, approximately 80% was used in the community and 20% in hospitals. Of the 36% sold for use in animals, 72% was for use in food-producing animals only and 28% for use in horses, companion animals and also allowed for food-producing animals.

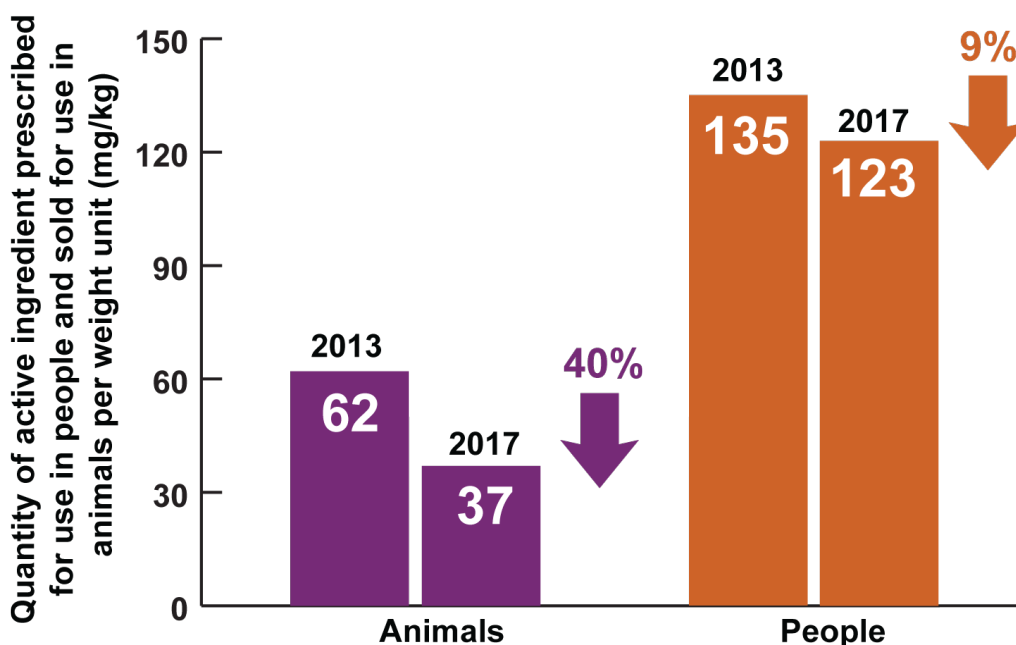


¹ For the human sector, use data include all publicly funded prescriptions in primary and secondary care, but not from the private sector. Therefore, this figure does not cover all human use as there is no method to collect private prescriptions.



Reductions in mg/kg between 2013 and 2017

When the tonnage is corrected for bodyweight and population size of humans and animals at the likely time of treatment, the amount used in people was 123 mg/kg and the amount used in food-producing animals was 37 mg/kg. This represents a reduction of 9% and 40% respectively when compared to 2013 levels.

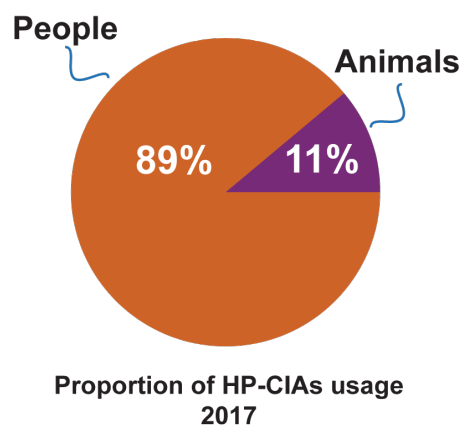
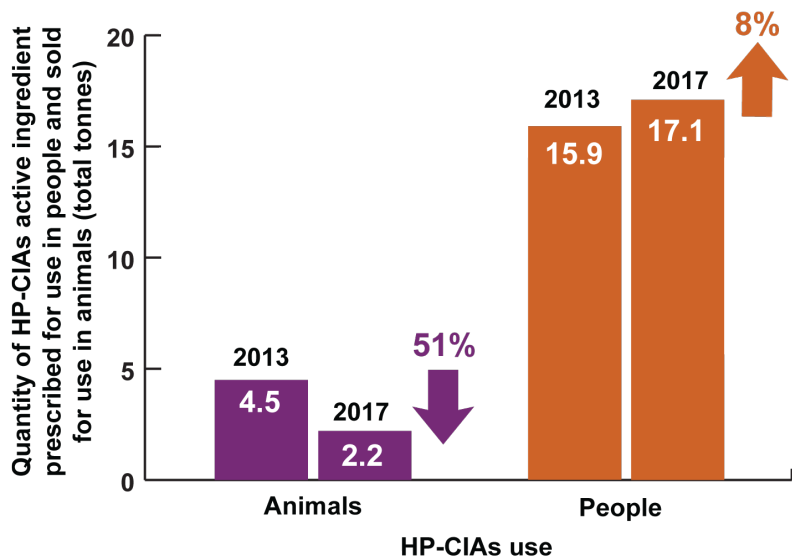


Total tonnes of HP-CIAs used between 2013 and 2017

Overall, 19.3 tonnes of antibiotics (2.5% of total UK use) classed as HP-CIAs² were prescribed or sold for use in humans and animals of which 89% was used in people and 11% in animals.

Sales of HP-CIAs for use in animals was 2.2 tonnes (0.8% of total sales for use in animals); a drop of 51% compared to 2013. In people, HP-CIAs use was estimated at 17.1 tonnes (3.5% of total human use); an increase of 8% compared to 2013.

² HP-CIAs include the following three classes: 3rd and 4th generation cephalosporins, fluoroquinolones and colistin.

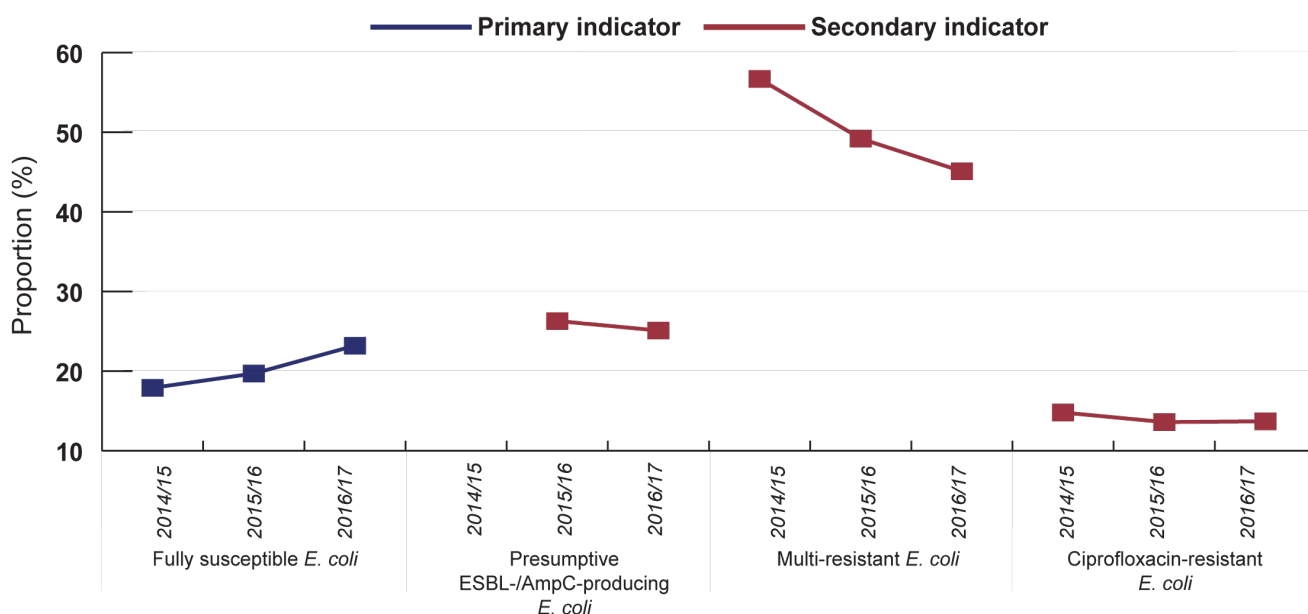


Antibiotic Resistance

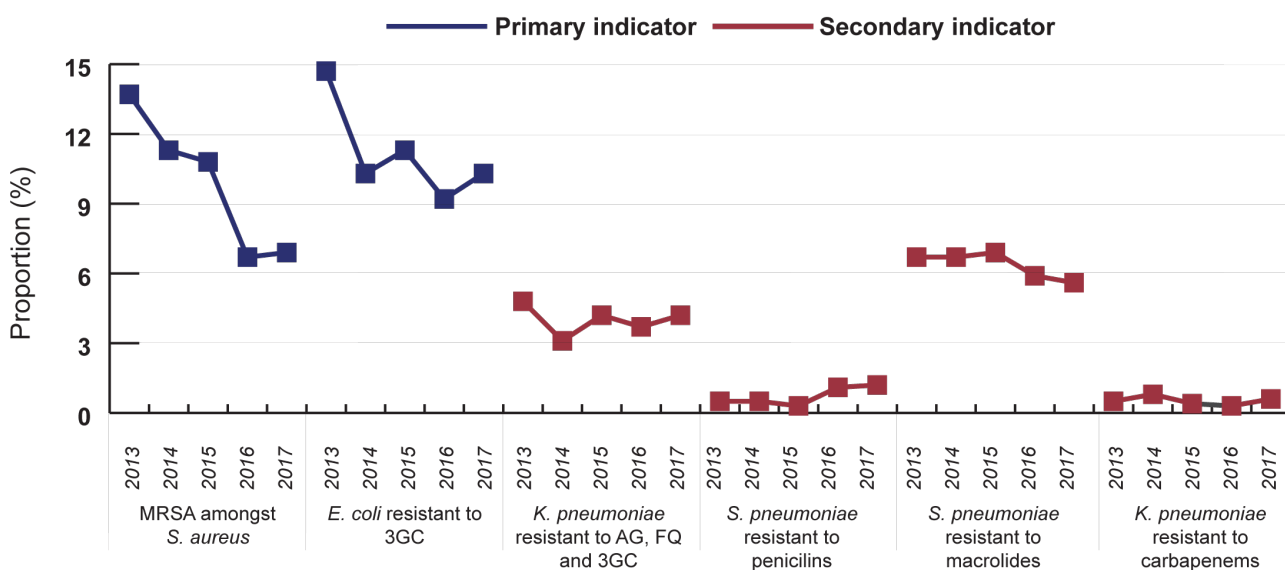
EU harmonised key outcome indicators for AMR

The European Centre for Disease Prevention and Control, the European Food Safety Authority and the European Medicines Agency have published a recommended set of harmonised primary and secondary key outcome indicators for monitoring antibiotic resistance in food-producing animals and humans in the European Union Member States. In the UK, the majority of indicators have either reduced or were stable between 2013 and 2017.

Indicators for resistance in bacterial isolates from **food-producing animals**



Indicators for resistance in bacterial isolates from **people**



E. coli – *Escherichia coli*
S. aureus – *Staphylococcus aureus*
K. pneumoniae – *Klebsiella pneumoniae*

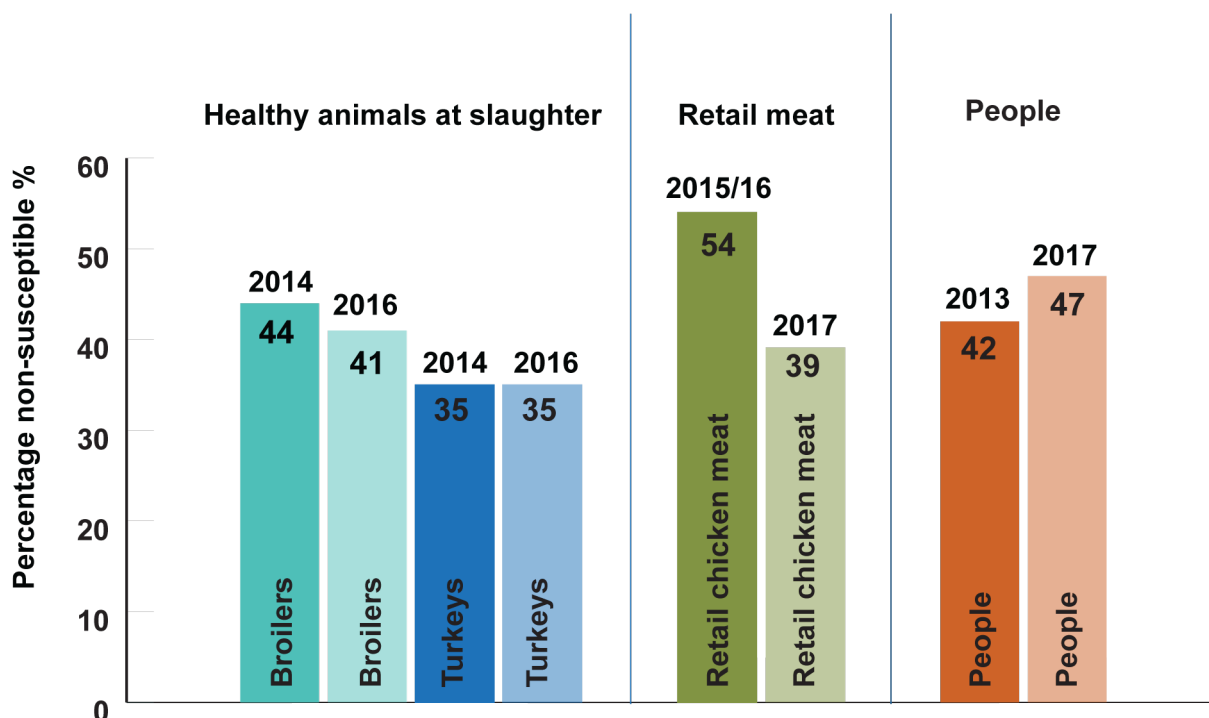
S. pneumoniae – *Streptococcus pneumoniae*
 3GC – 3rd generation cephalosporins
 AG, FQ – aminoglycosides, fluoroquinolones

Campylobacter jejuni

Ciprofloxacin

In isolates from broilers and turkeys at slaughter and chicken meat at retail, the level of resistance to ciprofloxacin decreased or remained stable between the two study years, whereas it increased in people.

Campylobacter jejuni isolates non-susceptible to ciprofloxacin



Erythromycin

All *Campylobacter jejuni* isolates obtained from healthy broiler and turkey samples from the abattoir showed <1% resistance to erythromycin in both year one and two of sampling.

The level of decreased-susceptibility in *C. jejuni* isolates obtained from retail chicken meat samples increased from 0% in 2015/2016 to 7.6% in 2017.

In human *C. jejuni* isolates, non-susceptibility to erythromycin increased from 2.5% in 2015 to 3.4% in 2017.

Note: Results from healthy animals at slaughter are interpreted using EUCAST human Clinical Breakpoints (CBP); those from retail meat are interpreted using EUCAST Epidemiological Cut-off values (ECOFF); and results from humans are interpreted using CBP.

Salmonella spp.

Resistance levels in non-typhoidal *Salmonella* spp. isolates to HP-CIAs were low (<2%) or not detected in samples from poultry farms (broilers, layer hens, turkeys) in 2016.

The proportion of human *Salmonella* spp. isolates tested that were non-susceptible (intermediate and resistant) to HP-CIAs decreased for colistin (from 6% to 3%), but increased for ciprofloxacin (from 4% to 14%), cefotaxime (from 1% to 2%) and ceftazidime (from 0% to 4%) between 2013 and 2017. However, this may result from the changes in serovars identified in humans between 2014 and 2017, as well as the change in susceptibility testing practice over this time.

Escherichia coli

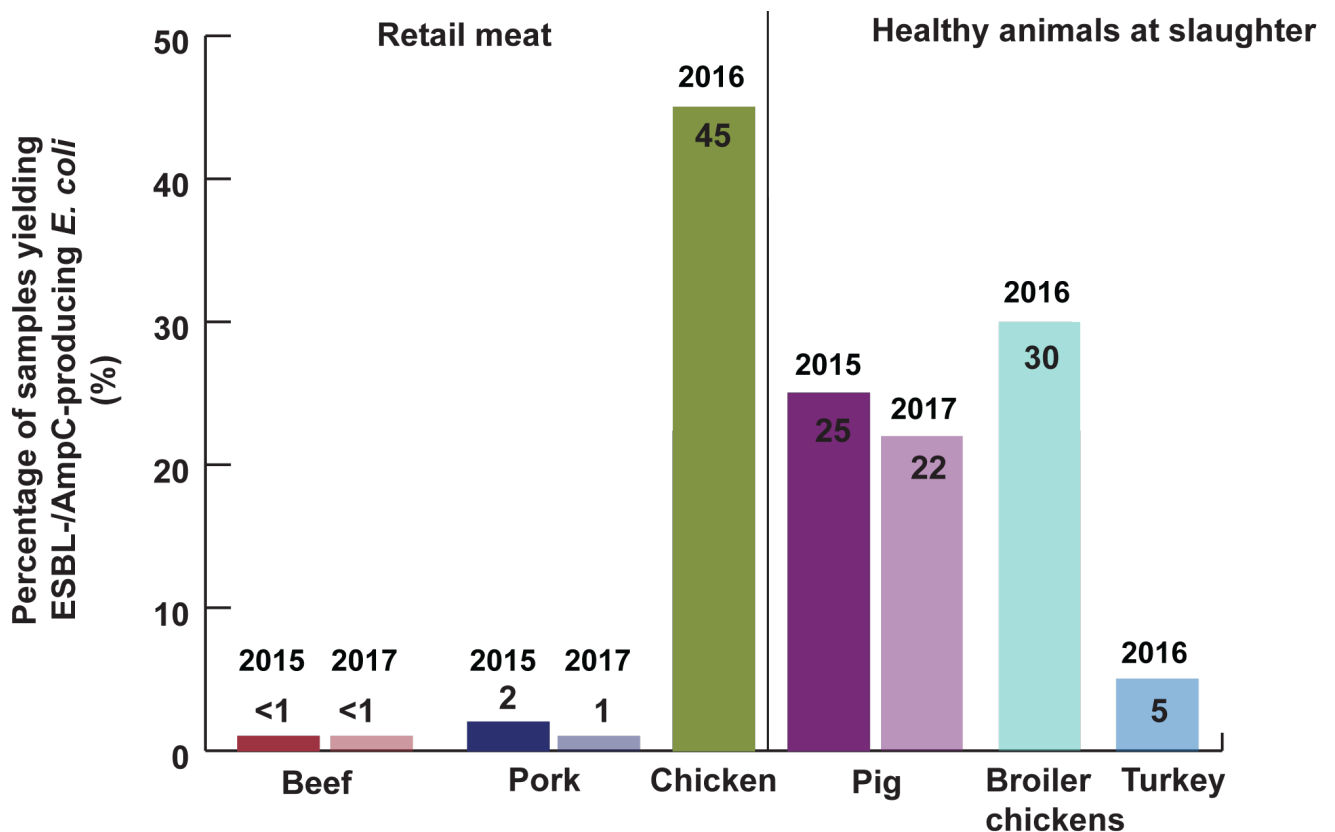
Between 2014 and 2017, no resistance to the HP-CIAs colistin, cefotaxime and ceftazidime was detected in *E. coli* isolates from broilers, turkeys and pigs at slaughter. Resistance levels to HP-CIA ciprofloxacin were low (<7%) in *E. coli* isolates from broilers, turkeys and pigs.

In 2017, 1% of human *E. coli* blood isolates were non-susceptible to colistin, 20% to ciprofloxacin, and 12% to 3rd generation cephalosporins.

ESBL-/AmpC-/carbapenemase-producing *E. coli*

Samples from animals at slaughter and meat at retail were tested for presence of extended-spectrum β -lactamase (ESBL-) and AmpC β -lactamase (AmpC-) producing *E. coli*. Between 22%-25% of pig, 30% of broiler and 5% of turkey samples collected at slaughter yielded ESBL-/AmpC-producing *E. coli*. Samples from beef and pork at retail yielded 1-2% ESBL-/AmpC-producing *E. coli*; for chicken meat, this was 45%.

None of the *E. coli* isolates from pigs, broilers and turkeys were presumptive carbapenemase-producers.



Chapter 1: Introduction

Antimicrobial or antibiotic resistance (AMR) is a major cause of concern for human and animal health, and no single action will provide an adequate solution. Resistant bacteria from animals, humans and food can be cross-transmitted and environmental reservoirs are a potentially important source for the mobilisation and transfer of resistance genes. Thus an integrated One Health approach to AMR surveillance and public health action is needed.

In 2013, the government of the United Kingdom (UK) published the 'UK five year AMR strategy 2013 to 2018', setting out actions to slow the development and spread of AMR following a One Health approach¹. In 2016, the Review on Antimicrobial Resistance, commissioned by the UK government, published its final report and presented ten recommendations to tackle AMR, including actions on infection prevention and control and reduction of antibiotic use in animals and humans². In 2017, the European Commission (EC) published its 'European One Health Action Plan against AMR'³.

This is the second UK One Health Report and it includes, in addition to antibiotic use data from food-producing animals and humans and data on AMR in bacterial isolates from animals and humans, comparative data on AMR in isolates from retail meat. The aims of the report are to:

- Assess occurrence of resistance along the food chain;
- 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.

The report presents the results of AMR monitoring for key zoonotic and indicator bacterial pathogens for animals and humans: *Campylobacter* spp., non-typhoidal *Salmonella* spp., *Escherichia coli* and livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA). It gives an overview of available data in the context of the One Health approach. Data included in this report have been presented in more detail in separate annual veterinary and human surveillance reports, which are referred to in the relevant text.

Certain antibiotic classes are categorised by the World Health Organization (WHO) as critically important antibiotics for human use. Based on the need to preserve these antibiotics, there are important 'One Health' and antibiotic stewardship considerations for the veterinary sector to take into account. Therefore, this report focuses on the Highest Priority Critically Important Antibiotics (HP-CIAs) classified as such by the Antimicrobial Advice *ad hoc* Expert Group (AMEG) from the European Medicines Agency (EMA)^{4,5}, who based their classification on importance to both human and veterinary medicine. These HP-CIAs are: colistin, fluoroquinolones and 3rd and 4th generation cephalosporins (see also Annex I).

The previous One Health Report presented ten recommendations (see Annex D)⁶; progress on these recommendations is addressed in text boxes throughout this report. Chapter 2 presents data on antibiotic use in food-producing animals and in humans. Resistance data from bacterial isolates from food-producing animals, retail meat and humans are presented in Chapter 3. An introduction to antibiotics and resistance in the environment is included in Chapter 4. A discussion of the data from a One Health perspective concludes the report in Chapter 5. Technical and background information can be found in the Annexes.

The importance of a One Health approach: colistin resistance in bacterial isolates from animals, humans and meat

Colistin is used as a last resort antibiotic in human medicine, and used widely in livestock in parts of the world. In November 2015, the discovery of the plasmid mediated colistin resistance gene *mcr-1* in China was published⁷; since then other similar genes have been discovered (e.g. *mcr-2*, *mcr-3*)⁸. The AMEG, reconvened by the EMA in response to a request by the EC, recommended that colistin should be added to the AMEG category 2 (higher risk critically important antimicrobials; see Annex I).

Public Health England's (PHE) Antimicrobial Resistance and Healthcare Associated Infections (AMRHAI) Reference Unit analysed archived whole-genome sequences of ~24,000 bacterial isolates submitted to PHE between 2013 and 2015. It identified 15 *mcr-1*-positive isolates, consisting of ten human *Salmonella enterica* and three human *Escherichia coli* isolates, as well as two *Salmonella* Paratyphi B var Java isolates from poultry meat imported in 2014⁹. Since starting screening in 2016, AMRHAI has identified three additional *mcr-1*-positive strains among referred human colistin-resistant isolates. In the period since the last report (2014 to 2017), there has been a total of 302 colistin-resistant non-typhoidal *Salmonella* spp. or *E. coli* isolates from humans reported, and 32 non-typhoidal *Salmonella* spp. with plasmid-mediated resistance gene *mcr-1* identified.

In response to the discovery of the *mcr-1* gene, overall colistin use in food-producing animals in the UK decreased by 99% between 2015 and 2017 to 0.001 mg/kg¹⁰. This was the result of various livestock sectors voluntarily stopping or restricting the use of colistin. Based on the electronic Medicine Book Pigs (eMB Pigs), colistin use in pigs was 0.01 mg/kg in 2017, a 99% decrease from 2015¹⁰. According to data from the British Poultry Council (BPC), colistin use in meat poultry in the UK reduced from 40 kg in 2015 to 8 kg in 2016, after which they voluntarily stopped its use in this livestock sector^{11, 12}.

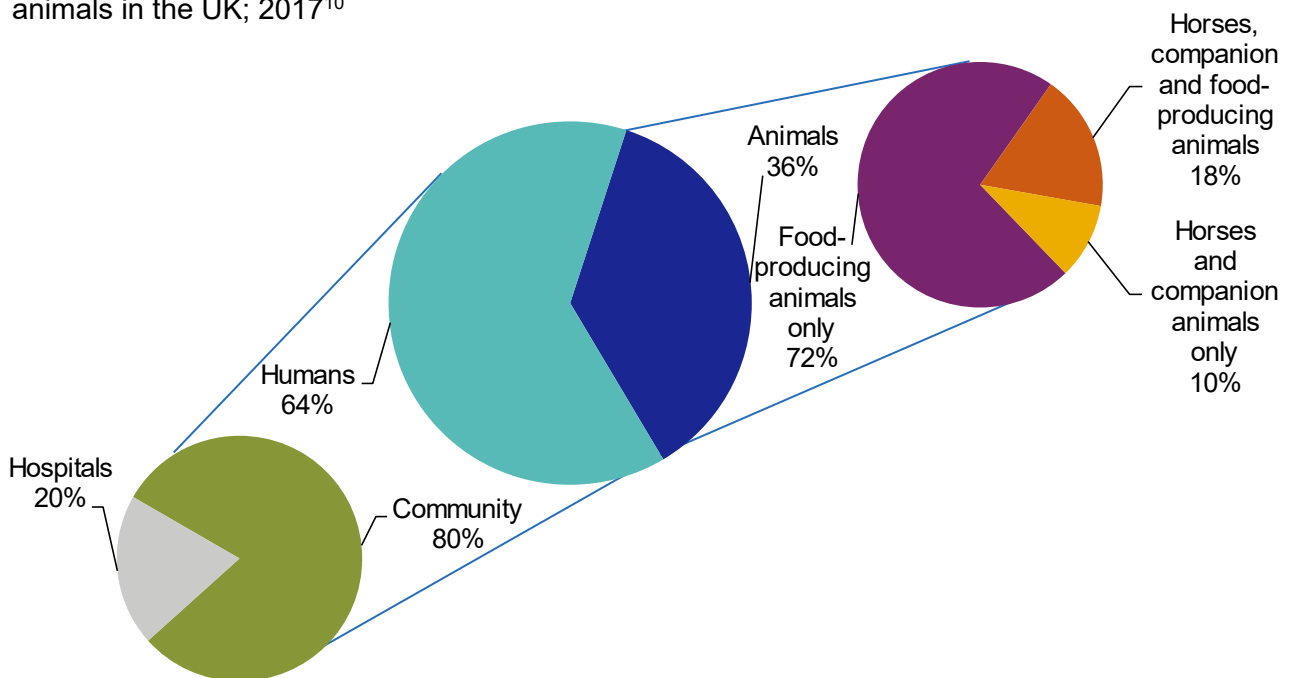
All *E. coli* and *Salmonella* spp. isolated from food-producing animals under the framework of the EU harmonised AMR monitoring are tested for susceptibility to colistin. Since 2016, the Animal and Plant Health Agency (APHA) also performs enhanced colistin resistance testing on these *E. coli* isolates from England, Scotland and Wales, through additional selective culture methods. Between 2014 and 2017, no resistance to colistin was detected in the bacterial (*Salmonella* spp. and *E. coli*) isolates obtained and tested under the EU monitoring from healthy broiler chickens, turkeys or pigs at slaughter, and pork and broiler meat at retail.

Chapter 2: Antibiotic use

2.1 Sales in veterinary and usage in human medicine

In 2017, the total UK antibiotic consumption in humans and animals was 773 tonnes of active ingredient. Of this total, 282 tonnes (36%) were antibiotics sold for use in animals; 204 tonnes (26% of the total UK antibiotic consumption) were antibiotics authorised for use in food-producing animals only (72% of total animal use), 51 tonnes (7%) for use in food-producing animals, companion animals and horses, and 27 tonnes (3%) for use in companion animals and horses only (Figure 1). The other 491 tonnes (not including all data from the private sector^c; 64%) were antibiotics prescribed for humans: 80% was prescribed in the community and 20% in the hospital sector. This represents an average 19% reduction in total tonnes of antibiotic active ingredient sold for use in animals and prescribed for humans in the UK between 2013 and 2017 with a 35% reduction in animal and a 6% reduction in human sectors over this time period (Table 1).

Figure 1: Proportion of tonnes of active ingredient prescribed for humans and sold for use in animals in the UK; 2017¹⁰



Antibiotic usage data by species are being collected by some animal production sectors and these data are voluntarily provided for inclusion in the annual UK-VARSS reports¹⁰. However, usage data is not available for all sectors and production coverage is variable. For the purpose of this One Health Report the sales data of antibiotics for use in veterinary medicine are provided, which cover all animals in the UK. These data have been published annually since 1998, and are used to monitor trends in use and to inform policy on AMR.

Human health surveillance in the UK does not collect sales data for antibiotics used in human medicine; its antibiotic use data warehouse is a repository for national antibiotic prescribing data collated from primary and secondary care. This allows PHE to monitor trends in antibiotic use and

^c This includes data from all publicly funded prescriptions in primary and secondary care but not all from the private sector (private community or solely private hospitals). Therefore, this figure does not cover all human use as there is no method to collect private prescriptions. In the previous Report use from the private sector was estimated to add around 10% on top of human consumption data, but it is not possible to confirm that it is still the same proportion for 2017.

publish prescribing indicators at an increasing level of data granularity. The published indicators are being used by healthcare staff, commissioners, academics and the public to measure and evaluate the impact of National Health Service (NHS) quality initiatives, develop local AMR action plans, inform antibiotic stewardship activities and/or to compare antibiotic usage between peer groups, for example GP surgeries or NHS Trusts.

The antibiotic groups most sold for use in animals are tetracyclines, followed by penicillins, and trimethoprim/sulphonamide combinations (Table 1). The biggest percentage reductions in sales between 2013 and 2017 were for colistin (99% reduction), fluoroquinolones (50%), trimethoprim/sulphonamides (49%), lincosamides (47%), tetracyclines (46%) and macrolides (42%). An increase of 89% was seen for sales of amphenicols (from 2.6 to 4.9 tonnes) between 2013 and 2017, which may be a result of replacement of HP-CIAs with, for example, florfenicol. However, this antibiotic class accounted only for <2% of total sales in 2017. The overall reduction between 2013 and 2017 for sales of antibiotics for veterinary use was 35%. Another increase (46%) was seen for sales of aminoglycosides.

Table 1: Total systemic antibiotics prescribed in humans from primary and secondary care and quantity of antibiotics sold for use in food-producing animals in the UK, expressed in tonnes active ingredient and percentage of the total; 2013–2017¹⁰

Antibiotic group	Antibiotics prescribed in humans ^a (tonnes (%))		Antibiotics sold for use in animals ^b (tonnes (%))	
	2013	2017	2013	2017
Penicillins	339.1 (65)	330.2 (67)	87.5 (20)	72.5 (26)
Tetracyclines	54.6 (10)	48.2 (10)	194 (44)	104.9 (37)
Macrolides	54.5 (10)	43.5 (9)	40.3 (9)	23.3 (8)
Trimethoprim/sulphonamides	24.0 (5)	17.4 (4)	60.7 (14)	31.0 (11)
1 st and 2 nd generation cephalosporins	17.4 (3)	13.3 (3)	4.9 (1)	4.1 (1)
Fluoroquinolones	12.1 (2)	12.0 (2)	2.6 (0.6)	1.3 (0.5)
Other antibacterials**	7.9 (2)	10.4 (2)	20.4 (5)	13.7 (5)
3 rd and 4 th generation cephalosporins	3.4 (0.7)	4.5 (0.9)	1.2 (0.3)	0.9 (0.3)
Monobactams, carbapenems [‡]	3.4 (0.7)	4.0 (0.8)	0 (0)	0 (0)
Lincosamides	2.3 (0.4)	3.1 (0.6)	6.2 (1)	3.3 (1)
Glycopeptides [‡]	1.4 (0.3)	1.9 (0.4)	0 (0)	0 (0)
Aminoglycosides	0.9 (0.2)	0.8 (0.2)	14.8 (3)	21.6 (8)
Polymyxins (incl. colistin)	0.4 (0.1)	0.6 (0.1)	0.7 (0.2)	0.007 (0)
Amphenicols	0.1 (0)	0.1 (0)	2.6 (0.6)	4.9 (2)
Other quinolones [‡]	0.0 (0)	0.0 (0)	0 (0)	0 (0)
TOTAL	521.4 (100)	491.0 (100)	436.0 (100)	281.6 (100)

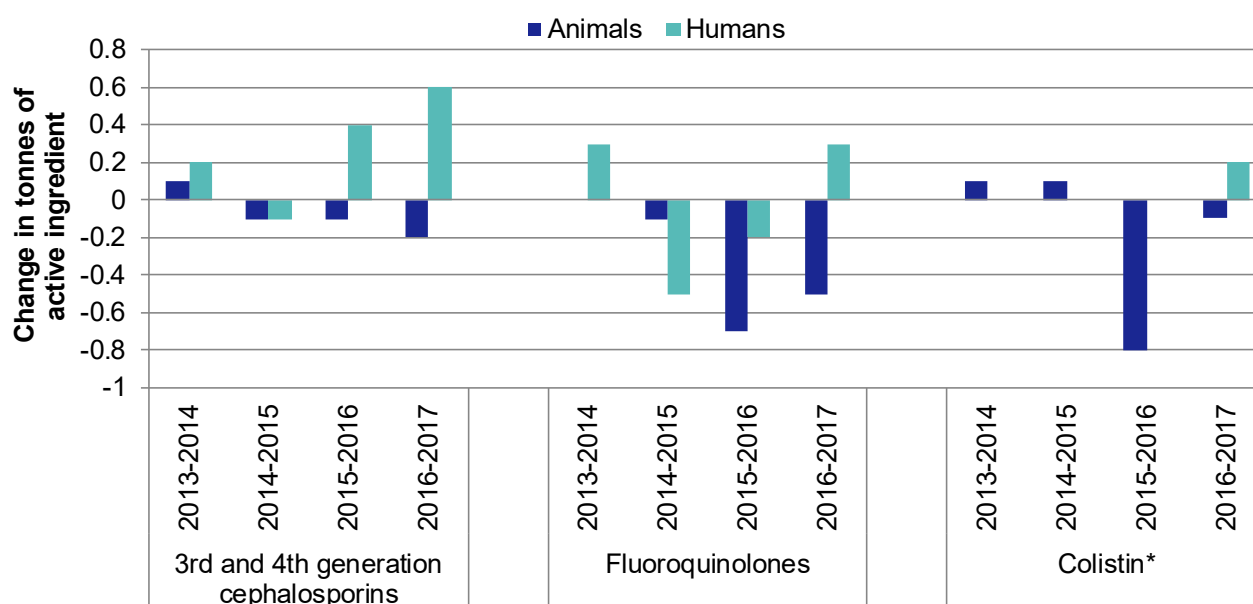
^a ERRATUM: Please note that an error was identified in the figures published for total systemic antibiotics prescribed in humans from primary and secondary care in the UK One Health report 2015. The translation of colistin from Defined Daily Doses to weight was calculated incorrectly and revision of the ATC index meant changes to units which were applied to the retrospective figures calculated for this year's report. Please take this into account when comparing antibiotic consumption data for humans presented in the 2015 One Health Report with the 2019 report; ^b Figures differ from the previous One Health Report as the methodology has been adapted to the ESVAC methodology; historical figures have been retrospectively calculated following the same method; * Other (humans): nitrofurantoin, fusidic acid, metronidazole, fosfomicin, methenamine/hippurate, linezolid. Additionally, two oral agents outside the 'J01' group (fidaxomicin [A07AA12], vancomycin [A07AA09]) which are used to treat *Clostridium difficile* infections were included; [‡] Other (animals): bacitracin, fosfomicin, furaltadone, metronidazole, novobiocin, paromomycin, rifaximin; [‡] There are no authorised veterinary medicines which contain antibiotics from these classes.

The combined primary and secondary care consumption of systemic antibiotics (ATC groups J01, A07AA) was 491 tonnes active ingredient in the human sector in the UK in 2017, a decline of 30 tonnes (6%) since 2013. The breakdown by antibiotic groups is shown in Table 1. In terms of tonnes of active ingredient, the antibiotic group most prescribed in humans are the penicillins (around two thirds of the total weight of drugs consumed), followed by tetracyclines and macrolides (Table 1). Total consumption decreased for penicillins, tetracyclines, macrolides, trimethoprim/sulphonamides, 1st and 2nd generation cephalosporins and fluoroquinolones, but increased for antibiotics grouped as ‘other’ (see for definition Table 1), colistin, 3rd and 4th generation cephalosporins, lincosamides and glycopeptides in the UK between 2013 and 2017.

Caution is advised in interpreting these data as the Defined Daily Dose (DDD) of any given drug varies considerably and thus weight may not accurately reflect the prevalent consumption of a particular drug. For more detailed information on antibiotic consumption trends in the UK human sector please consult the national reports for England¹³, Wales¹⁴, Northern Ireland¹⁵ and Scotland¹⁶.

Figure 2 shows the year-over-year changes in tonnage of the HP-CIAs prescribed/sold in the human and veterinary sector respectively in the UK between 2013 and 2017. The tonnage of active ingredient sold for use in food-producing animals has mostly reduced over the period 2013–2017, whereas the tonnage used in the human sectors fluctuated over the same period. When comparing tonnes of active ingredient of 3rd and 4th generation cephalosporins, fluoroquinolones and colistin, the majority (89%) is prescribed for humans, although more colistin was sold for use in animals in 2013 (Table 1). Overall, the use of HP-CIAs increased by 8% in humans and decreased by 51% in animals between 2013 and 2017.

Figure 2: Year-over-year change in tonnes of active ingredient of HP-CIAs prescribed for humans and sold for use in animals in the UK; 2013–2017



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

To enable comparisons across human and animal data, the weight of the total UK human population was calculated, using the methodology described in Annex H. A similar measure was calculated for the biomass of the food-producing animal species. As only food-producing animals are included in this measure, the corresponding mass of active ingredient was calculated including only antibiotics authorised for use in these species. The calculated mass of active ingredient was

then converted to milligrams per kilogram estimated biomass for both populations. In 2017, consumption of antibiotics in food-producing animals was 37 mg/kg (down 40% from 62 mg/kg in 2013) and consumption of systemic and intestinal antibiotics in humans equated 123 mg/kg (down 9% from 135 mg/kg in 2013).

Monitoring of antibiotic residues in meat

Council Directive 96/23/EC^d requires each European Union Member State (MS) to carry out an annual surveillance programme (National Residues Control Plan). Of all bovine, porcine, ovine, caprine and equine animals, 0.4% must be tested – this equates to approximately 30,000 samples per annum. Annexes I and II of 96/23/EC set out the groups of veterinary residues that MSs are obliged to test for: 0.25% is apportioned to unauthorised substances, with the remaining 0.15% covering veterinary drugs and contaminants; antibiotics fall under this particular remit. The total number of tests to be taken for antibiotics from the 0.15% figure varies according to species (outlined in 96/23/EC). Over 30 different antibiotic substances are tested for in the plan throughout the calendar year. Each analysed test undergoes a screening and confirmatory process at the National Reference Laboratories (NRL), Fera and the Agri-Food and Biosciences Institute (AFBI). The procedures adopted at the NRL for the validation of both confirmatory and screening methods of antibiotics and all other substances are set out in accordance with Commission Decision 2002/657/EC^e.

In 2017, 6,399 samples were analysed for antibiotic residues, 19 (0.3%) of which were non-compliant (covering a range of antibiotics, for example tetracyclines, macrolides and amphenicols, but no HP-CIAs). Findings on the causality of non-compliant results are published on a bi-monthly basis at <https://www.gov.uk/government/collections/residues-statutory-and-non-statutory-surveillance-results>.

2.2 Antibiotic usage – international picture

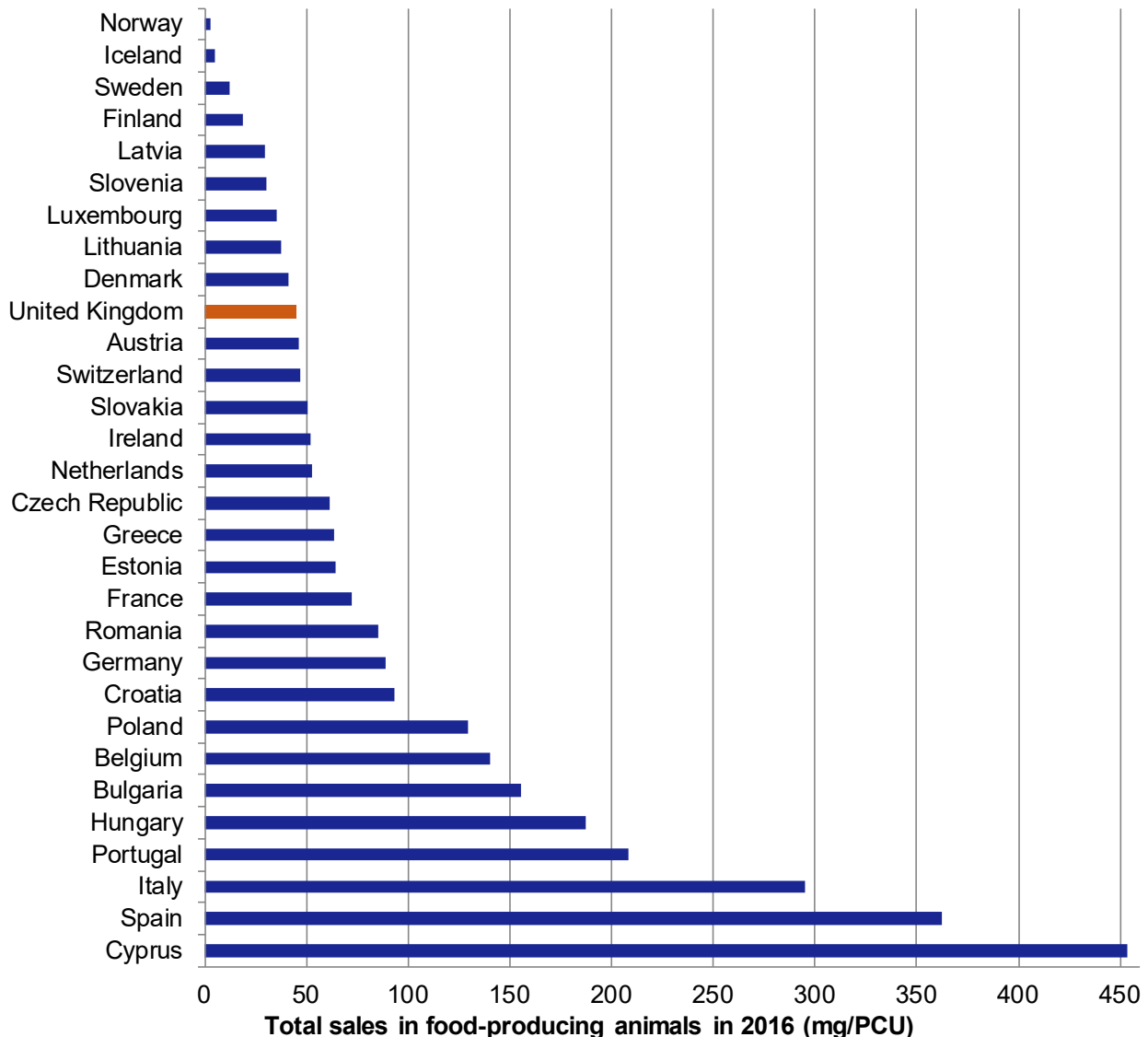
An overview of antibiotic consumption in food-producing animals for all participating European countries can be found in the annual European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) reports on the EMA's website¹⁷. The European Surveillance of Antimicrobial Consumption Network (ESAC-Net) publishes annual reports on antimicrobial consumption data for the community and for the hospital sector provided by EU MSs and two EEA countries¹⁸.

Figure 3 is derived from the most recent ESVAC report and shows the total amount of antibiotics sold for use in food-producing animals in Europe in 2016, expressed in milligrams/Population Correction Unit (mg/PCU)¹⁷. In comparison with other ESVAC participating countries, the UK is ranked 10th of 30 (1 being lowest usage) within Europe. The total sales of antibiotics for food-producing animals were 45 mg/PCU in 2016. In 2017, the total sales for food-producing animals in the UK had further reduced to 37 mg/PCU.

^d <https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A31996L0023>

^e <https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A32002D0657>

Figure 3: Quantity of antibiotics sold for use in food-producing animals for 30 European countries as reported by ESVAC; mg active substance sold per population correction unit (mg/PCU); 2016¹⁷



Progress on recommendation 8 of the 2015 report

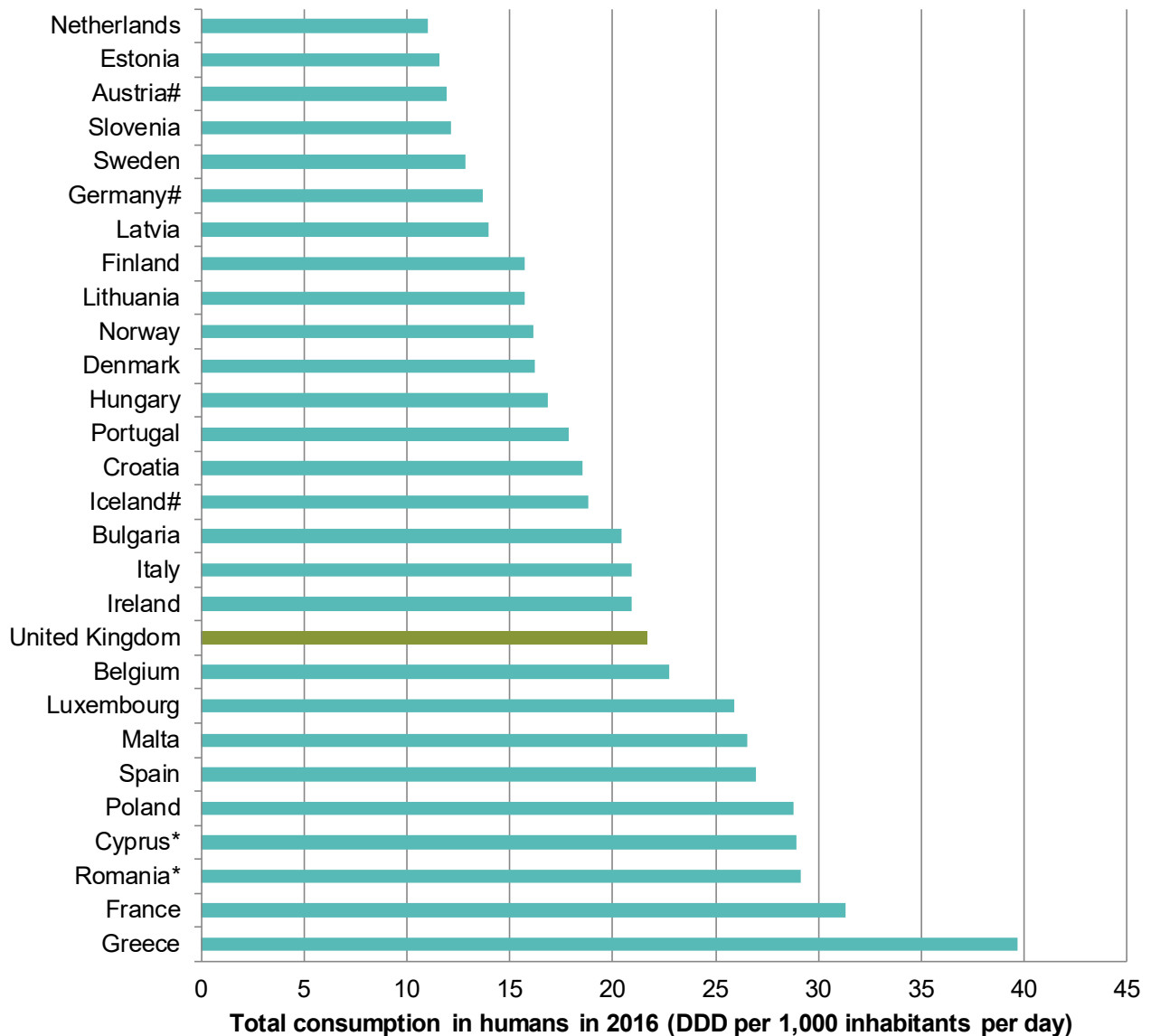
“VMD will participate in the protocol development of the European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) project to collect farm level data from the pig sector; and investigate and facilitate options for collecting accurate antimicrobial consumption data at an individual farm level.”

During 2014–2015, the VMD participated in a trial for collecting data on use of antibiotics in pigs for the ESVAC project of the EMA. Furthermore, a representative for the VMD acts as member of the ESVAC ‘by species’ Expert Advisory Group, which drafted guidance on the collection of antibiotic use data by species¹⁹.

In addition, the VMD supports the development of datasets on antibiotic usage in a growing number of animal production sectors. These data are voluntarily provided by the animal production sectors for inclusion in the annual UK – Veterinary Antimicrobial Resistance and Sales Surveillance (UK-VARSS) reports¹⁰.

Figure 4 shows the data as presented by the most recent ESAC-Net report for consumption of antibiotics for systemic use in the community and hospital sector in Europe in 2017. The combined rate (expressed as DDD per 1,000 inhabitants per day) of antibiotic consumption in the UK in 2017 was 21.7; this ranged between 11.0 and 39.7 for all countries¹⁸. In comparison with other ESAC-Net participating countries, this puts the UK at 19th of 28 (1 being lowest usage) within Europe. However, caution is needed in interpreting this information as comparison is made against other countries and not a benchmark.

Figure 4: Consumption of antibiotics for systemic use (ATC group J01) in the community and hospital sector in Europe as reported by ESAC-Net; 2017¹⁸



* Country only provided total care data; # country provided no hospital data

2.3 EU harmonised indicators for use

September 2017 saw the publication by the European Centre for Disease Prevention and Control (ECDC), European Food Safety Authority (EFSA) and EMA of a recommended set of harmonised key outcome indicators for monitoring antibiotic consumption in the EU MSs. The rationale for the selection of these indicators is described in more detail in the joint working group paper²⁰. Results for the UK are presented in this chapter.

2.3.1 Animals

The EU harmonised primary outcome indicator for antibiotic consumption in food-producing animals is:

- Overall sales of veterinary antibiotics in milligrams of active substance per kilogram of estimated weight at treatment of livestock and of slaughtered animals in a country (mg/PCU).

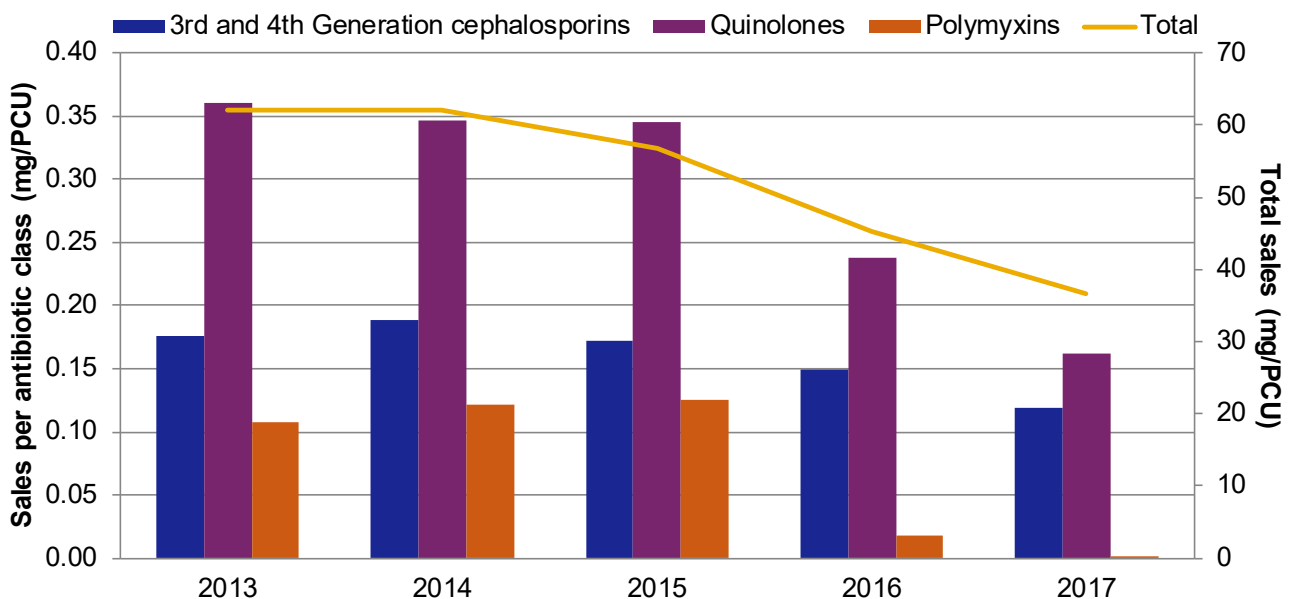
The secondary indicators are:

- Sales in mg/PCU for 3rd and 4th generation cephalosporins;
- Sales in mg/PCU quinolones (and percentage of fluoroquinolones);
- Sales in mg/PCU for polymyxins.

In the UK all quinolones sold for use in food-producing animals are fluoroquinolones.

Figure 5 shows the outcome indicators for antimicrobial consumption in food-producing animals in the UK over the period 2013–2017. All indicators showed a reduction between 2013 and 2017. Total sales reduced by 40% (from 62 mg/PCU to 37 mg/PCU). Sales of 3rd and 4th generation cephalosporins decreased by 32% (from 0.18 mg/PCU to 0.12 mg/PCU), sales of quinolones decreased by 55% (from 0.36 mg/PCU to 0.16 mg/PCU) and sales of colistin decreased by 99% (from 0.11 mg/PCU to 0.001 mg/PCU).

Figure 5: EU harmonised primary (total sales of veterinary antibiotics in mg/PCU) and secondary (sales in mg/PCU for 3rd and 4th generation cephalosporins, quinolones and polymyxins) outcome indicators for antibiotic consumption in food-producing animal species in the UK; 2013–2017



2.3.2 Humans

For the human sector, the primary and secondary indicators listed below have been recommended jointly by ECDC, EFSA and EMA to assess progress in reducing the use of antibiotics. The indicators aim to capture the selective pressure of specific antibiotic classes on the development of antibiotic resistance, facilitate monitoring the use of critically important antibiotics and the effect of antibiotic stewardship initiatives.

Primary indicator:

- Total consumption of antibiotics for systemic use (ATC group J01) – in hospitals and the community – expressed as defined daily doses (DDD) per 1,000 inhabitants and per day.

Secondary indicators:

- Ratio of consumption of broad-spectrum penicillins, cephalosporins, macrolides (except erythromycin) and fluoroquinolones to the consumption of narrow-spectrum penicillins, cephalosporins and erythromycin in the community;
- Proportion of total hospital consumption of glycopeptides, 3rd and 4th generation cephalosporins, monobactams, carbapenems, fluoroquinolones, polymyxins, piperacillin and enzyme inhibitor, linezolid, tedizolid and daptomycin.

Total consumption of systemic antibiotics has fallen (5.2%) in the UK between 2013 and 2017 from 22.9 to 21.7 DDD per 1000 population per day (Figure 6). Over the same time period the ratio of broad-spectrum antibiotic consumption compared to narrow-spectrum antibiotic consumption changed from 0.42 to 0.46 in the community and the consumption of broad-spectrum antibiotics in hospitals, measured as a proportion of the total hospital consumption, increased from 15.1% until 2016 (16.6%) followed by a decrease to 15.7% in 2017 (Figure 7).

Figure 6: EU harmonised primary indicator: total consumption of antibiotics for systemic use in humans (DDD per 1,000 inhabitants and per day) in the UK; 2013–2017

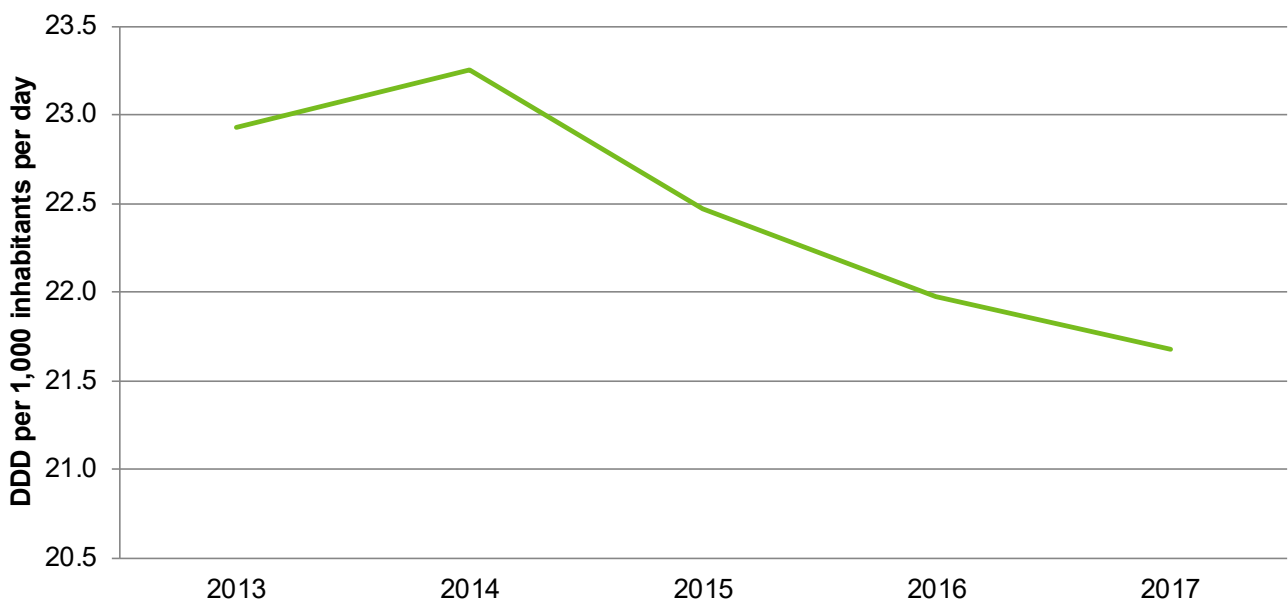
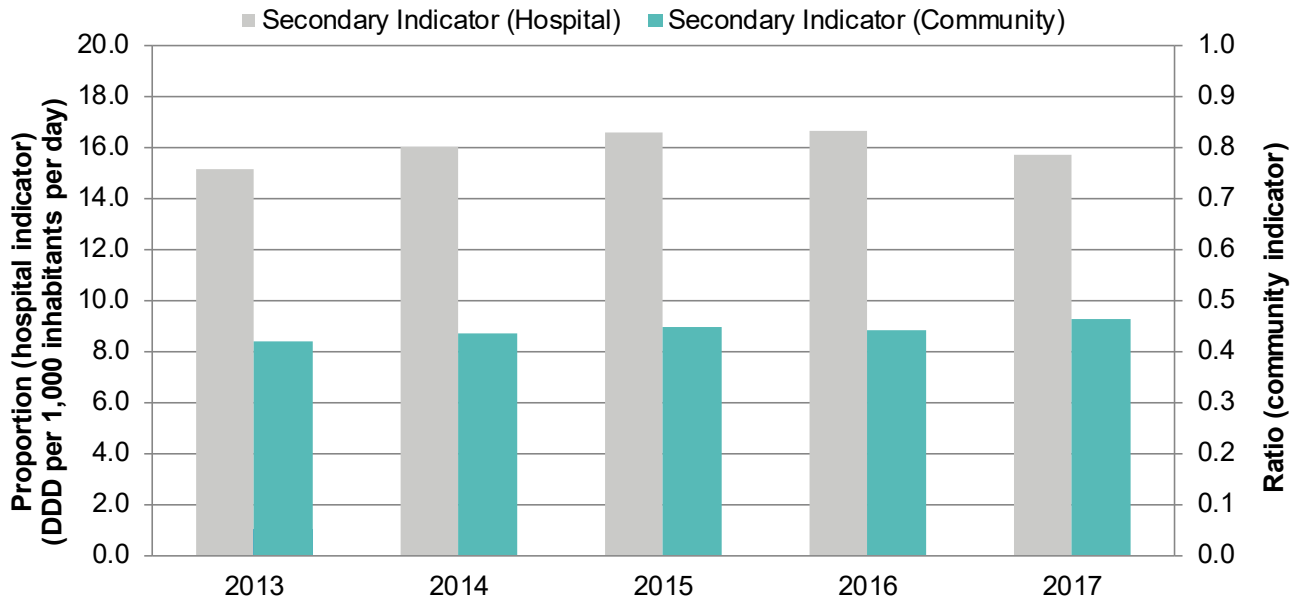


Figure 7: EU harmonised secondary indicators: ratio of the community consumption of broad-spectrum penicillins, cephalosporins, macrolides (except erythromycin) and fluoroquinolones to the consumption of narrow-spectrum penicillins, cephalosporins and erythromycin, and proportion of total hospital antibiotic consumption that are glycopeptides, 3rd and 4th generation cephalosporins, monobactams, carbapenems, fluoroquinolones, polymyxins, piperacillin and enzyme inhibitor, linezolid, tedizolid and daptomycin (DDD per 1,000 inhabitants per day) in the UK; 2013–2017



2.4 Concluding remarks

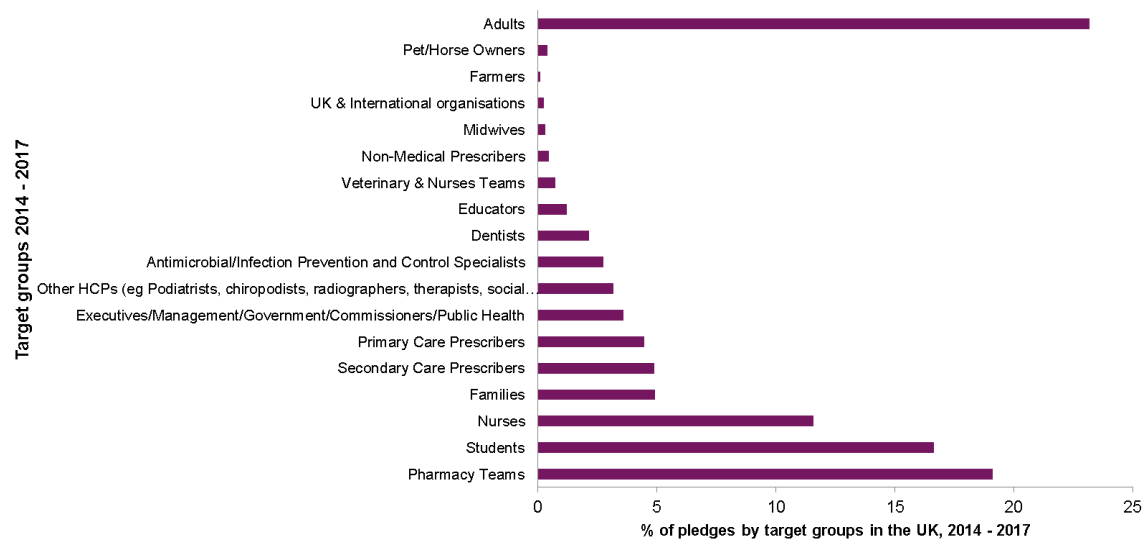
There was a large decrease in sales of veterinary antibiotics between 2013 and 2017, ranging between 16% and 99% for each antibiotic class with 35% reduction overall. Sales of HP-CIAs for use in animals were very low in 2017, and have decreased by 51% since 2013. Prescriptions for use of antibiotics in humans also showed an overall decrease (6%), with decreases in use for most antibiotic classes. Use of HP-CIAs is low in humans. When comparing amounts of active ingredient used for animals and for humans, the largest proportion of HP-CIAs was prescribed for use in humans in 2017. Compared to other European countries, the UK has below average antibiotic use in both the animal and human sector.

Antibiotic stewardship from a One Health perspective

Since 2014, PHE has worked in collaboration with the VMD on the Antibiotic Guardian campaign, which is a pledge-based behaviour change strategy. Since the start of the Antibiotic Guardian campaign, the website has been visited 470,968 times. This has translated into over 55,000 pledges (see figure below).

Case studies of antibiotic stewardship activities in human and animal health which were shortlisted entries for the Antibiotic Guardian Awards following peer review are available through the shared learning platform (www.antibioticguardian.com/shared-learning). The awards celebrate the work of healthcare professionals across England in tackling antibiotic resistance and protecting antibiotic usage. At the [Antibiotic Guardian's gala event](#) held in London in June 2018, awards were presented, among others, to Bristol Veterinary School (Agriculture and Food category), RUMA (Responsible Use of Medicines in Agriculture Alliance; Community Communications and Prescribing & Stewardship categories), NHS Sunderland CCG (Diagnostic Stewardship category), and King's College London (Student of the Year category), reflecting the 'One Health' approach of the Antibiotic Guardian campaign.

Antibiotic Guardian pledges (%) by target group in the UK, 2014–2017



Chapter 3: Antibiotic resistance

3.1 EU harmonised indicators for AMR

The ECDC, EFSA and EMA have published a recommended set of harmonised key outcome indicators for monitoring antibiotic resistance in the EU MSs. The rationale for the selection of these indicators is described in more detail in the joint working group paper²⁰. Results for the UK are presented in this chapter.

3.1.1 Animals

The primary summary indicator for AMR in food-producing animals in a country is:

- Proportion of indicator *E. coli* isolates from broilers, fattening turkeys, fattening pigs and calves (as collected under the framework of Commission Implementing Decision 2013/652/EU^f), weighted by the size (expressed in PCU) of the four animal populations, that are fully susceptible to the entire panel of antibiotics defined in the Decision.

The secondary indicators are:

- Proportion of indicator *E. coli* isolates from broilers, fattening turkeys, fattening pigs and calves, weighted by PCU, that shows decreased-susceptibility to at least three antibiotics from different classes from the predefined panel of antibiotics;
- Proportion of indicator *E. coli* isolates from broilers, fattening turkeys, fattening pigs and calves, weighted by PCU, that are microbiologically resistant to ciprofloxacin;
- Proportion of samples identified as positive for presumptive ESBL-/AmpC-producing indicator *E. coli* in the framework of the specific monitoring for ESBL-/AmpC-/carbapenemase-producing indicator *E. coli* from broilers, fattening turkeys, fattening pigs and calves, weighted by PCU.

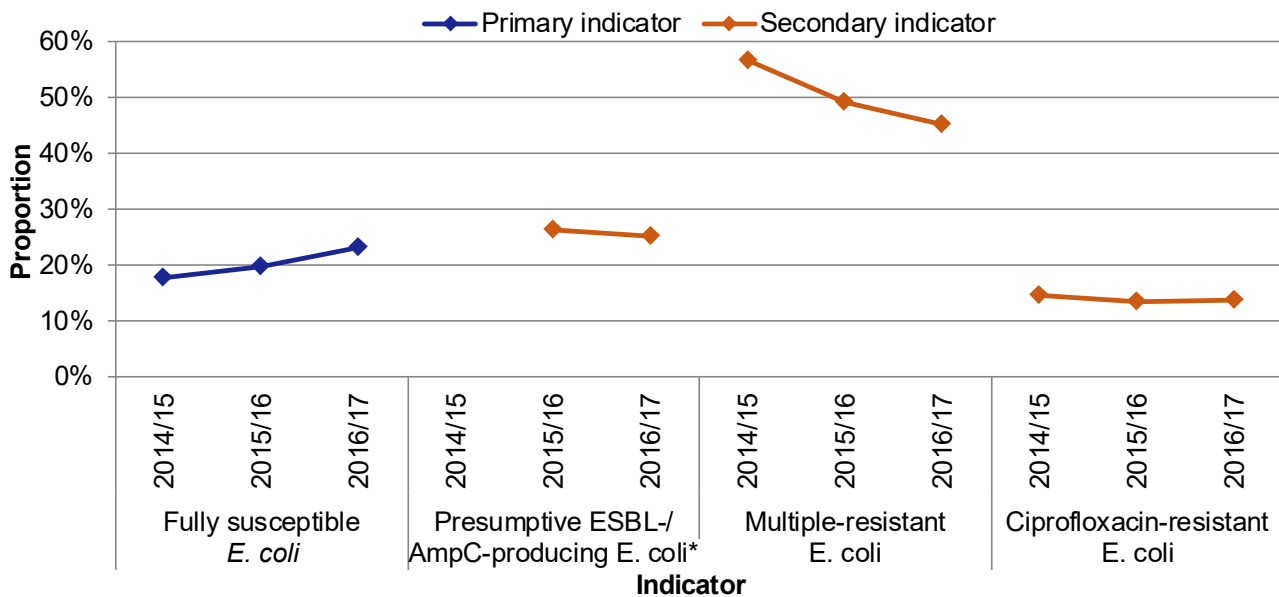
In the UK, the veal industry does not reach the threshold of 10,000 tonnes of meat produced per year, and therefore is excluded for the EU AMR monitoring programme. Due to the sampling schedule the indicators can only be expressed for any combination of two consecutive calendar years.

The primary indicator for the UK showed that the proportion of fully susceptible *E. coli* increased by 30% between 2014/2015 and 2016/2017, from 18% to 23%, indicating there was an increase in the level of susceptibility in relation to the biomass of food-producing animals (Figure 8).

The secondary indicators also showed an increase in the level of susceptibility (Figure 8). The proportion of indicator *E. coli* isolates that shows decreased-susceptibility to at least three antibiotics from different classes from the predefined panel of antibiotics decreased by 20% from 57% to 45%. The proportion of indicator *E. coli* isolates that are microbiologically resistant to ciprofloxacin showed a 7% reduction from 15% to 14%. Lastly, the proportion of samples identified as positive for presumptive ESBL-/AmpC-producing indicator *E. coli* decreased by 5% between 2015/2016 and 2016/2017, from 26% to 25%.

^f <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32013D0652>

Figure 8: Recommended primary (proportion of fully susceptible *E. coli* isolates) and secondary indicators (proportion of presumptive ESBL-/AmpC-producing *E. coli* isolates, proportion of multiple-resistant *E. coli* isolates and proportion of *E. coli* isolates microbiologically resistant to ciprofloxacin) for the animal AMR monitoring in the UK; 2014–2017



* Data not available for 2014/2015

3.1.2 Humans

In humans the primary antibiotic resistance indicators are:

- Proportion of methicillin-resistant *Staphylococcus aureus* among *S. aureus* isolates;
- Proportion of 3rd generation cephalosporin-resistant *E. coli*.

The primary indicators for the UK showed that the proportion of *E. coli* resistant to 3rd generation cephalosporins decreased between 2013 and 2017 from 15% to 10% (30% reduction), and a 50% reduction in proportion of MRSA in humans was seen over the same time period, from 14% to 7% (Figure 9).

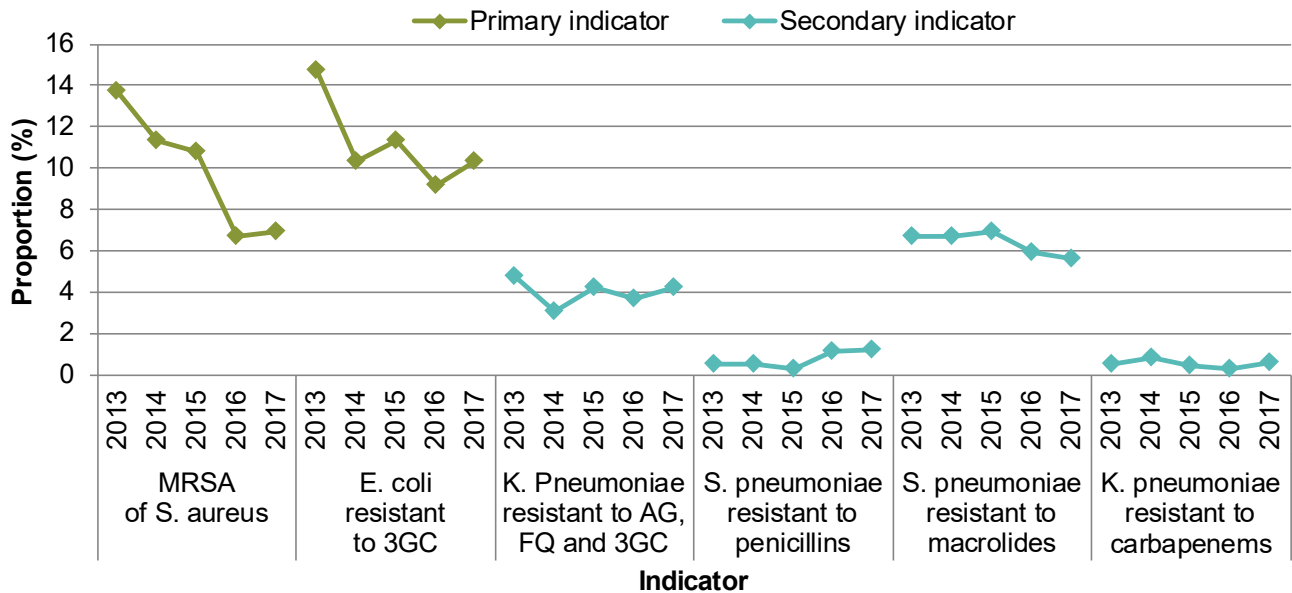
The secondary antibiotic resistance indicators for human surveillance reflect key areas for monitoring in the international as well as domestic hospital and community sectors; these are:

- Proportion of *Klebsiella pneumoniae* resistant to aminoglycosides, fluoroquinolones and 3rd generation cephalosporins;
- Proportion of *K. pneumoniae* resistant to carbapenems;
- Proportion of *Streptococcus pneumoniae* resistant to macrolides;
- Proportion of *S. pneumoniae* resistant to penicillins.

There was a reduction in resistance in two of the secondary indicators between 2013 and 2017. The proportion of *K. pneumoniae* resistant to aminoglycosides, fluoroquinolones and 3rd generation cephalosporins reduced by 13% between 2013 and 2017, from 4.8% to 4.2%, and the proportion of *Streptococcus pneumoniae* resistant to macrolides reduced from 6.7% to 5.6%, a 16% reduction.

The other two secondary indicators increased slightly over the same time period, but remain ≤1% resistant: the proportion of *S. pneumoniae* resistant to penicillins was 1% in 2017, and the proportion of *K. pneumoniae* resistant to carbapenems was <1% (Figure 9).

Figure 9: Recommended primary (proportion of 3rd generation cephalosporin-resistant *E. coli* isolates and proportion of MRSA among *S. aureus* isolates) and secondary indicators (proportion of *K. pneumoniae* resistant to fluoroquinolones, 3rd generation cephalosporins and aminoglycosides, proportion of *K. pneumoniae* resistant to carbapenems, proportion of *S. pneumoniae* resistant to penicillins and proportion of *S. pneumoniae* resistant to macrolides) for the human health AMR monitoring in the UK; 2013–2017*



* Data are taken from the ECDC Surveillance Atlas – Antimicrobial Resistance and reflect UK data as reported through the EARS-Net surveillance programme. This surveillance does not include all laboratories within the UK; AG = aminoglycosides; FQ = fluoroquinolones; 3GC = 3rd generation cephalosporins

3.2 Resistance in selected bacteria common to animals and humans

3.2.1 *Campylobacter* spp.

3.2.1.1 Background

Campylobacter are commensal bacteria which are common in poultry and pigs, and a zoonotic pathogen. They are the most common cause of human foodborne bacterial disease in the UK, estimated to cause more than 280,000 cases each year²¹. Handling, preparation and consumption of contaminated broiler meat has been identified as one of the main sources of human infection. In humans, the symptoms usually occur two to five days after infection and are often mild and self-limiting. Antibiotic treatment is not usually required but severe cases may be treated with a macrolide antibiotic (e.g. clarithromycin, azithromycin, erythromycin) with a move away from using ciprofloxacin, as resistance to quinolones is now considered to be too high for these antibiotics to be used for empirical treatment²².

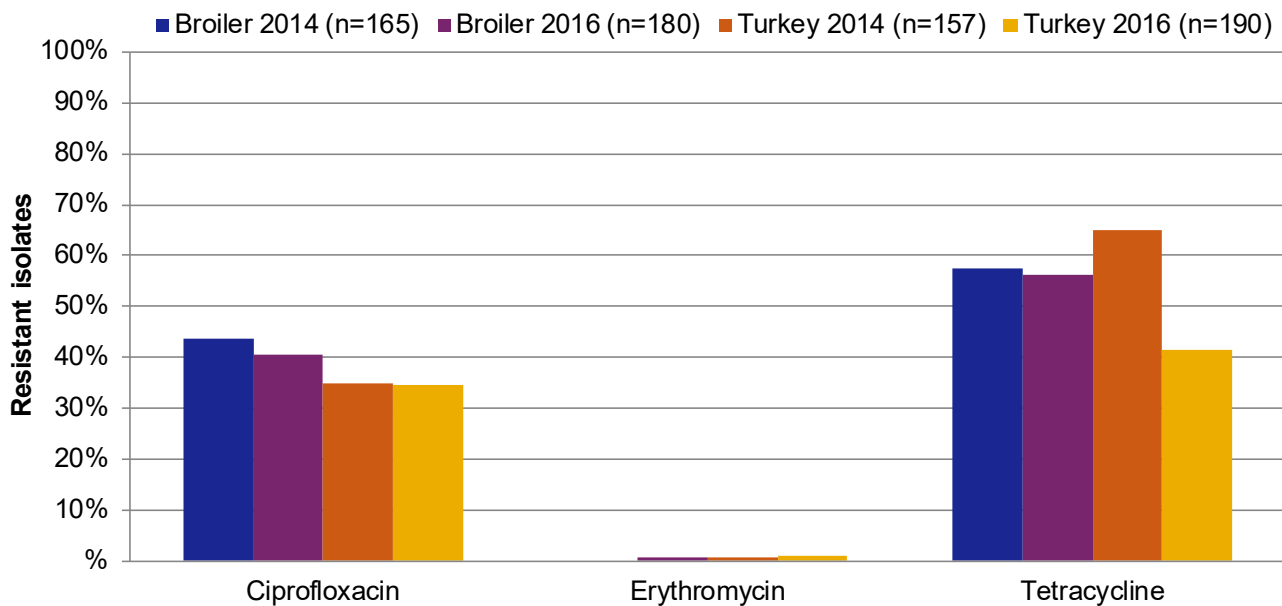
3.2.1.2 Resistance – food-producing animals

Compared to 2014, in 2016 the percentage of resistance (interpreted using European Committee for Antimicrobial Susceptibility Testing – EUCAST – human clinical breakpoints; CBPs) in *Campylobacter jejuni* isolated from broiler caecal samples (collected at slaughter under the EU AMR monitoring scheme, see Annex F) slightly decreased for ciprofloxacin (from 44% to 41%) and

remained very low for erythromycin (<1%); ciprofloxacin was a previously recommended treatment option for severe cases of campylobacteriosis in human medicine.

A similar pattern was seen in *C. jejuni* isolates obtained from turkey caecal samples in 2014 and 2016, with a stable level of resistance to ciprofloxacin (35%) and very low resistance to erythromycin ($\leq 1\%$) (Figure 10).

Figure 10: Percentage resistance (interpreted using EUCAST human CBPs) in *C. jejuni* isolates from caecal samples taken at slaughter from broiler chickens and turkeys in the UK (EU harmonised monitoring); 2014 and 2016¹¹



Other antibiotics were included in the panel for susceptibility testing in accordance with Decision 2013/652/EU, which based the prioritisation on whether the antimicrobial was considered to be relevant for human therapeutic use and/or epidemiologically relevant to be able to monitor and/or detect new resistance mechanisms of public health importance²³.

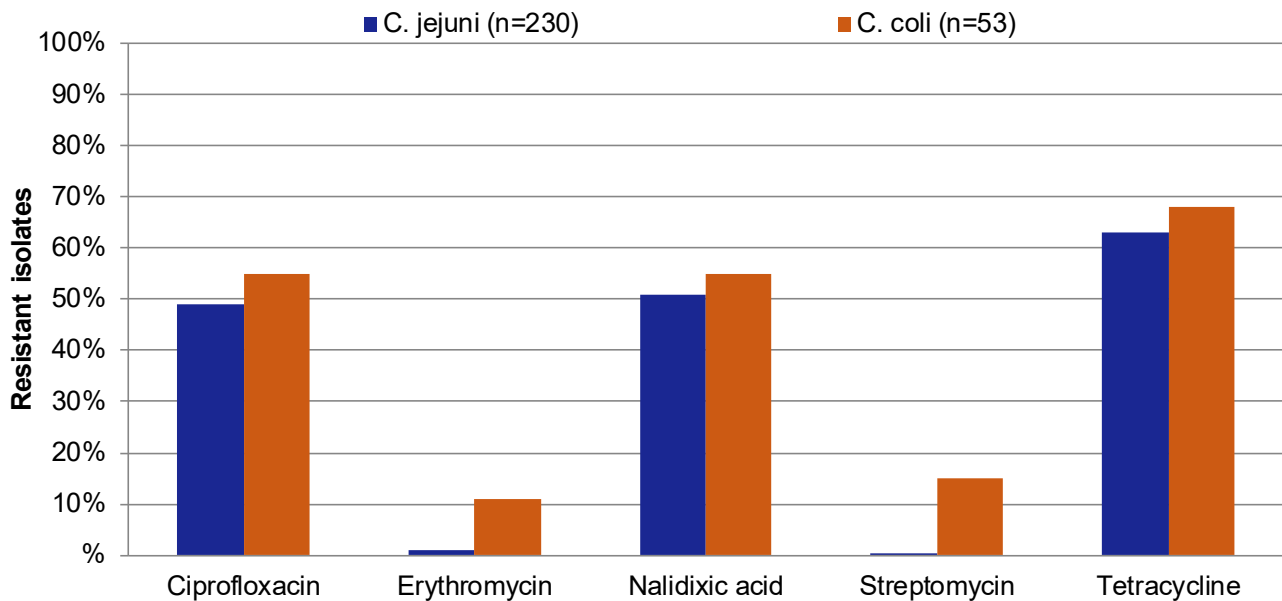
The percentage of broiler isolates showing resistance to tetracycline in 2016 was similar to 2014 (58% in 2014 compared to 56% in 2016). The proportion of broiler isolates showing decreased-susceptibility (interpreted using EUCAST epidemiological cut-off values; ECOFFs) to nalidixic acid was lower in 2016 compared to 2014 but still high (from 44% in 2014 to 41% in 2016). Decreased-susceptibility to gentamicin and streptomycin was not detected, or was low, in broiler isolates from both years ($\leq 1\%$). In turkey isolates, there was less resistance to tetracycline in 2016 compared to 2014 (42% and 65%, respectively). The level of decreased-susceptibility to nalidixic acid was high in both years (35% and 33%). There were low levels of decreased-susceptibility to gentamicin ($\leq 1\%$) and streptomycin (<2%) in turkey isolates for both years (Figure 10).

3.2.1.3 Resistance – retail meat

A survey of whole, UK-produced fresh chicken at retail during the period February 2014 to March 2015 tested 4,011 samples; 73% of the samples yielded *Campylobacter* spp.²⁴. A subset of the *C. jejuni* (n=230) and *C. coli* (n=53) isolates were tested to determine the antibiotic resistance profiles (interpreted using breakpoints, see Annex F for methodology).

Resistance to ciprofloxacin was detected in 49% of the *C. jejuni* isolates and 55% of the *C. coli* isolates tested. Resistance to erythromycin was higher in *C. coli* isolates (11%) than in *C. jejuni* isolates (<1%) (Figure 11).

Figure 11: Percentage resistance (interpreted using breakpoints) in *C. jejuni* and *C. coli* isolates from retail chicken meat in the UK; 2014–2015^{24,25}



A high level of resistance to nalidixic acid and tetracycline was detected in isolates from both *Campylobacter* species (51%–68%). All isolates were susceptible to gentamicin, neomycin and kanamycin (results not shown), and 24% of *C. jejuni* and 28% of *C. coli* isolates were susceptible to all antibiotics tested.

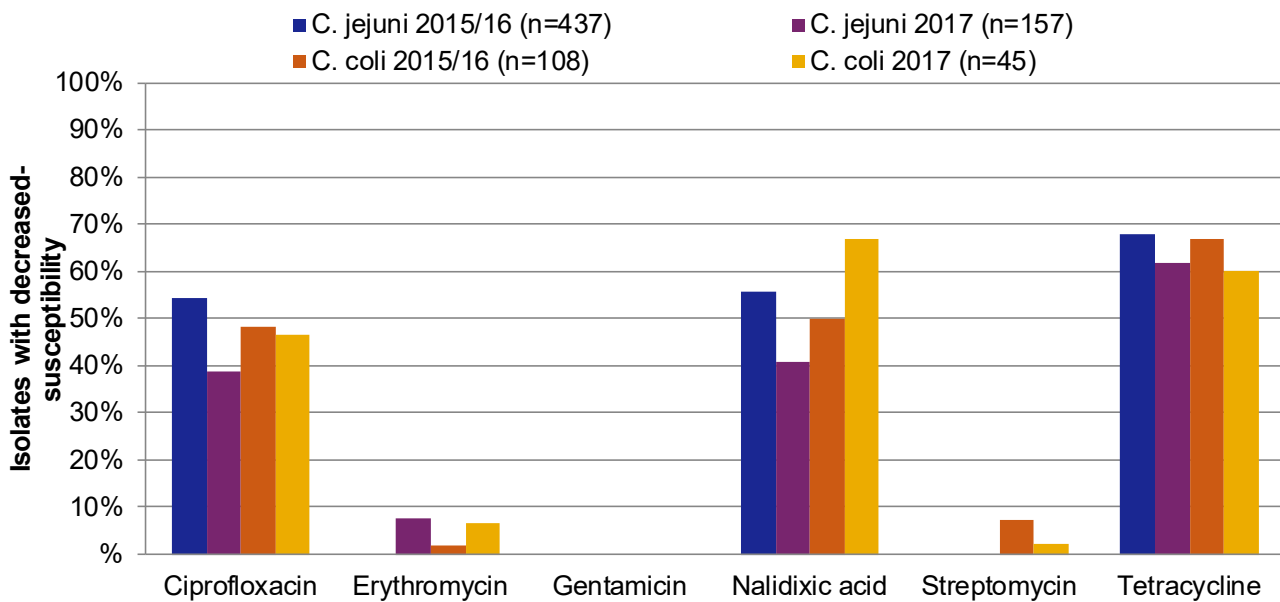
A subsequent study determined antibiotic susceptibility in 437 *C. jejuni* and 108 *C. coli* isolates from 2,998 samples from whole, UK-produced fresh chicken at retail during the period July 2015 to May 2016²⁶. During September and October 2017, 157 *C. jejuni* and 45 *C. coli* isolates obtained from 79 samples of fresh or frozen raw chicken (whole and portioned), collected at retail, were tested for antibiotic susceptibility²⁷.

A smaller proportion of *C. jejuni* and *C. coli* isolates showed decreased-susceptibility to ciprofloxacin in 2017 (39% and 47%, respectively) than in 2015/16 (54% and 48%, respectively), but the proportion increased for erythromycin (7% and 8%, respectively, in 2017 vs. 0 and 2%, respectively, in 2015/16) (Figure 12).

The 2017 *C. coli* isolates also showed a larger proportion (67%) of decreased-susceptibility to nalidixic acid than the 2015/16 isolates (50%). For the other antibiotics tested, the proportions of isolates with decreased-susceptibility were smaller in 2017 than in 2015/16 (see Figure 12).

Differences in the levels of susceptibility to ciprofloxacin and tetracycline between isolates from standard and organic birds were examined for the 2015/2016 data. No significant differences were found, however the small sample size, especially for organic chickens (18 organic, 76 free range and 454 standard chicken samples), may have limited the ability to detect important differences where they may exist.

Figure 12: Percentage isolates with decreased-susceptibility (interpreted using EUCAST ECOFFs) in *C. jejuni* and *C. coli* strains isolated from retail chicken meat in the UK; 2015–2017^{26, 27}



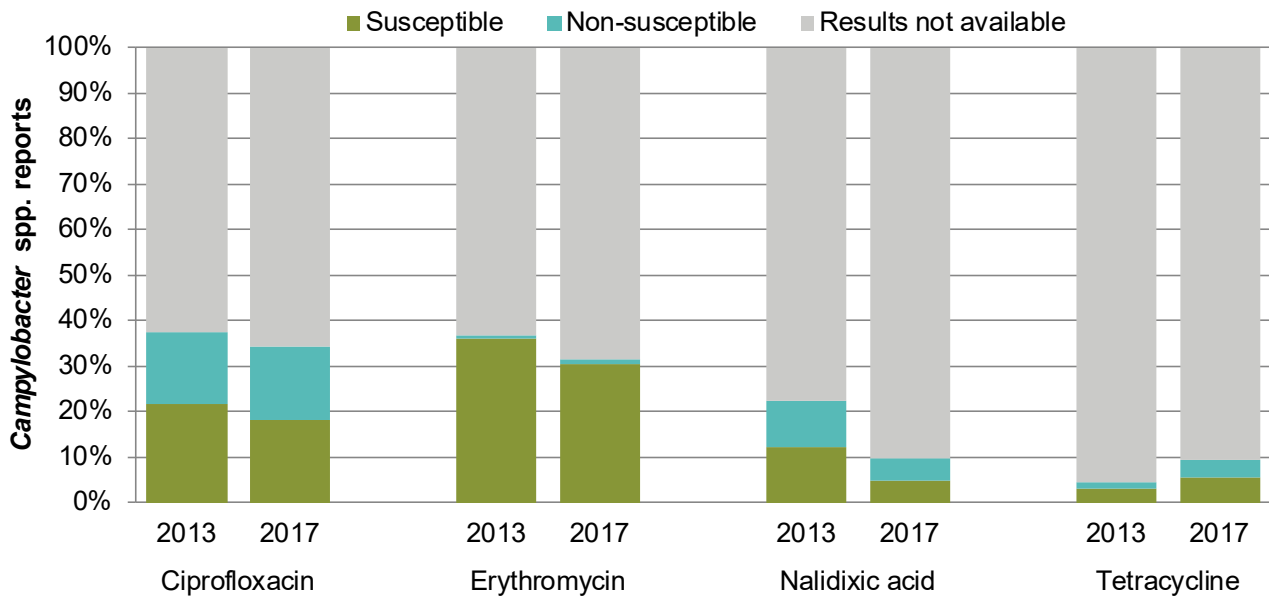
3.2.1.4 Resistance – humans

The number of *Campylobacter* spp. isolates reported through routine laboratory surveillance from humans in the UK in 2017 was 60,408, a 7% decrease from the 64,764 isolates reported in 2013. Laboratory guidance does not currently recommend identification of *Campylobacter* spp. to species level unless clinically indicated. As such, only 23% of *Campylobacter* spp. isolates reported via this surveillance were identified to species level in 2017; 91% of those with species information recorded were *C. jejuni*²⁸.

The level of *Campylobacter* spp. susceptibility testing in 2017 remained low for all antibiotics included in the surveillance, with the most frequently tested antibiotic being ciprofloxacin (35%). This low level of susceptibility testing may reflect the fact that the majority of cases do not require treatment.

The proportion of *Campylobacter* spp. isolates that were non-susceptible (resistant and intermediate) increased between 2013 and 2017 for ciprofloxacin (from 42% to 47%) and stayed low for erythromycin (3%) (Figure 13). A similar pattern was seen for isolates identified to species level in 2017 with *C. jejuni* isolates non-susceptible to ciprofloxacin at 44% and 43% in *C. coli* isolates, and erythromycin non-susceptibility at 4% in *C. jejuni* isolates and 12% in *C. coli* in 2017 (data not shown). The proportion of non-susceptible *Campylobacter* spp. isolates also increased between 2013 and 2017 for nalidixic acid (from 45% to 51%) and tetracycline (from 33% to 39%).

Figure 13: Percentage susceptibility (interpreted using human EUCAST CBPs; non-susceptible: resistant and intermediate) in routine laboratory surveillance reports of human *Campylobacter* spp. isolates in the UK; 2013 (n=64,764) and 2017 (n=60,408)



3.2.1.5 Control measures in place to reduce risk of transmission

Antibiotic resistant zoonotic organisms present in animals, such as *Campylobacter* spp., can be transmitted to humans²⁹. Human *Campylobacter* infection is often caused by consumption and handling of raw or undercooked meat, especially poultry meat.

The surveys on retail chicken meat provide evidence that *Campylobacter* spp. isolates can be obtained from chicken meat sold at retail in the UK; insufficient data are available to draw conclusions regarding differences between *Campylobacter* spp. contamination rates in meat from different countries of origin. Proportions of isolates with ciprofloxacin and tetracycline resistance from food were similar to those causing human clinical infection and much higher than the proportions seen in animals at slaughter. Control measures along the food chain as well as domestic cooking procedures eliminate or reduce the risk of infection. In the UK, guidance is provided by the BPC to reduce the prevalence of *Campylobacter* spp. through different control measures along the poultry food chain; interventions focus for example on on-farm biosecurity, bird catching practices, washing practices at the slaughterhouse and packaging³⁰.

The National Health Service (NHS) provides advice on how to prevent *Campylobacter* poisoning: “cover and chill raw chicken, don’t wash raw chicken, wash used utensils and cook chicken thoroughly”; the Food Standards Agency (FSA) adds the advice to wash hands thoroughly with soap and warm water after handling raw chicken^{31, 32}.

Food poisoning is a notifiable disease in England and Wales according to the Public Health (Control of Disease) Act 1984^g, and *Campylobacter* spp. as a causative pathogen according to the Health Protection (Notification) Regulations 2010^h. Surveillance of notifications is an important means to identify and manage situations on campylobacteriosis and other enteric pathogens in early stages to prevent further spread.

^g <https://www.legislation.gov.uk/ukpga/1984/22>

^h <http://www.legislation.gov.uk/ukxi/2010/659/contents/made>

3.2.1.6 International picture

A full overview for all participating European countries can be found in the EU summary reports on antibiotic resistance in zoonotic and indicator bacteria from humans, animals and food in 2014–2016³³⁻³⁵. Results below on isolates from animals are interpreted using EUCAST ECOFF values which means that results are not directly comparable to those based on EUCAST human CBP values.

The harmonised monitoring of antibiotic resistance in human *Campylobacter* spp. isolates within the EU includes testing for susceptibility to ciprofloxacin, erythromycin, gentamicin (invasive isolates only) and tetracycline³⁶. The same antibiotics are also tested in the EU harmonised monitoring of resistance in *C. jejuni* isolated from broiler chickens and turkeys at slaughter.

Compared to the other European MSs, the level of decreased-susceptibility in the UK is generally lower. The UK was among the EU MSs with the lowest level of decreased-susceptibility to erythromycin in broiler *C. jejuni* isolates in 2014 (0%; average for EU MSs: 6%) and 2016 (0.6%; average for EU MSs: 1.3%). Decreased-susceptibility to ciprofloxacin was also lower than average in 2014 (44%; average for EU MSs: 70%) and 2016 (41%; average for EU MSs: 67%).

Regarding *C. jejuni* isolates from turkey, decreased-susceptibility to erythromycin was also lower than average in 2014 (0.7%; average for EU MSs: 3%), but it was around the average in 2016 (1.1%; average for EU MSs: 1.0%). The level of decreased-susceptibility to ciprofloxacin in turkey isolates was the lowest of the 10 EU MSs providing data in 2014 (35% vs. 70% on average) and 9 MSs providing data in 2016 (35% vs. 76%).

The UK was one of the three countries reporting the lowest levels of resistance found in *C. jejuni* isolated from humans in 2016 to gentamicin, ciprofloxacin, and tetracycline (out of 17 EU MSs), with erythromycin resistance being lower than the average. Compared with the position in 2013, the ranking for resistance in human isolates remained similar for all antibiotics tested, the only exception was for tetracycline where the UK improved, from 6th (out of 14 EU MSs) to 3rd in 2016³⁵.

3.2.1.7 Concluding remarks

The data suggest that resistance to erythromycin (one of the antibiotics classed by the WHO as highest priority critically important antibiotics for human medicine (HP-CIA; see Annex I for detail) remains (very) low in *Campylobacter* spp. isolates from broilers and turkeys at slaughter as well as from human clinical infections, but decreased-susceptibility was detected in around 7% of *Campylobacter* spp. isolates from retail chicken meat in 2017.

In line with recent EFSA data on *Campylobacter* spp. isolates from broiler meat, voluntarily provided by seven EU MSs, decreased-susceptibility to the HP-CIA ciprofloxacin was common in *Campylobacter* spp. isolates from UK retail meat^{33, 35}. Decreased-susceptibility and resistance to ciprofloxacin is also a concern in *C. jejuni* isolated from healthy poultry and in human *Campylobacter* spp. isolates, where levels of ciprofloxacin resistance continue to be high.

Susceptibility testing on *Campylobacter* spp. isolates prior to treating with erythromycin or ciprofloxacin would therefore be recommended, as these antibiotics are two of the treatment options available (for severe cases).

Progress on recommendation 2 of the 2015 report – Sentinel *Campylobacter* study

*“Public health organisations should scope the development of a national sentinel surveillance system for *Campylobacter* spp. isolates collected from human infections. In addition, public health organisations should highlight the importance of identifying *Campylobacter* to a species rather than genus level, as different species have different antibiotic profiles.”*

PHE’s Gastrointestinal Bacteria Reference Unit (GBRU) started the process of routinely collecting human *Campylobacter* spp. isolates from a selection of laboratories in England in 2017 in addition to the small number of isolates that are received for further characterisation during outbreak investigations; with the intention to develop this into a sentinel surveillance system. The sites chosen are regional specialist PHE laboratories based in various parts of England. This will enable detailed data collection on a more representative sample of *Campylobacter* spp. isolates and allow greater understanding of AMR trends at species level. The *Campylobacter* spp. isolates currently referred to GBRU from these sentinel sites (Leeds, Southampton, Cambridge and Birmingham) and from two other sites (Oxford and Newcastle) as part of a three-year FSA funded surveillance project (combined total of 1,914 isolates from all six sites between January–December 2017), represents a 4% sample of the total number of cases (n=53,068) which were reported in England in 2017.

3.2.2 Non-typhoidal *Salmonella* spp.

3.2.2.1 Background

Salmonella are a major cause of foodborne illness in humans and animals. There are more than 2,500 serovars, all of which can cause food poisoning in humans, though fewer than 100 serovars account for most human infections. Salmonellosis in humans is generally contracted through the consumption of contaminated animal products, such as eggs, (poultry) meat, and milk³⁷. Gastrointestinal symptoms caused by *Salmonella* spp. usually do not require treatment with antibiotics but severe cases and patients at risk of invasive disease are treated according to antibiotic susceptibility results (most commonly with ciprofloxacin, azithromycin or 3rd generation cephalosporins³⁸).

3.2.2.2 Resistance – food-producing animals

Non-typhoidal *Salmonella* spp. isolates from poultry farms

The results shown in this section from the EU harmonised AMR monitoring scheme for *Salmonella* spp. in poultry are from isolates taken from boot swabs, dust samples or composite faecal samples, collected on broiler chicken, layer chicken and fattening turkey farms under the framework of the National Control Plans (according to EU Regulations (EC) No 2160/2003ⁱ and No 2073/2005^j; see Annex F for more details).

ⁱ <https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX:32003R2160>

^j <https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A32005R2073>

Three (<1%) of 761 *Salmonella* spp. isolates from poultry farms, sampled in 2014 and 2016, had detectable resistance to colistin based on EUCAST human CBPs – all three isolates were from layer farms and isolated in 2014, and none of the 761 isolates were resistant to cefotaxime or ceftazidime. No or very low (<1%) resistance was detected to ciprofloxacin in broiler, layer or turkey isolates (Figure 14 and Figure 15).

Figure 14: Percentage resistance (interpreted using EUCAST human CBPs) in *Salmonella* spp. obtained from broiler and layer chicken farms in the UK (National Control Plan/EU harmonised AMR monitoring); 2014 and 2016¹¹

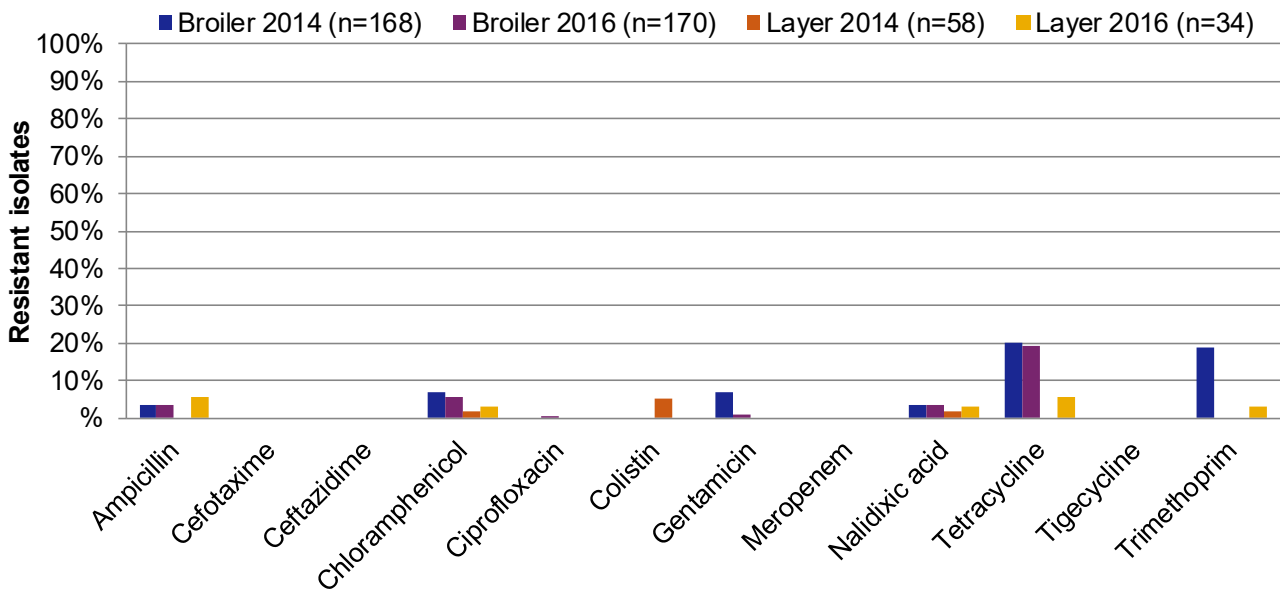
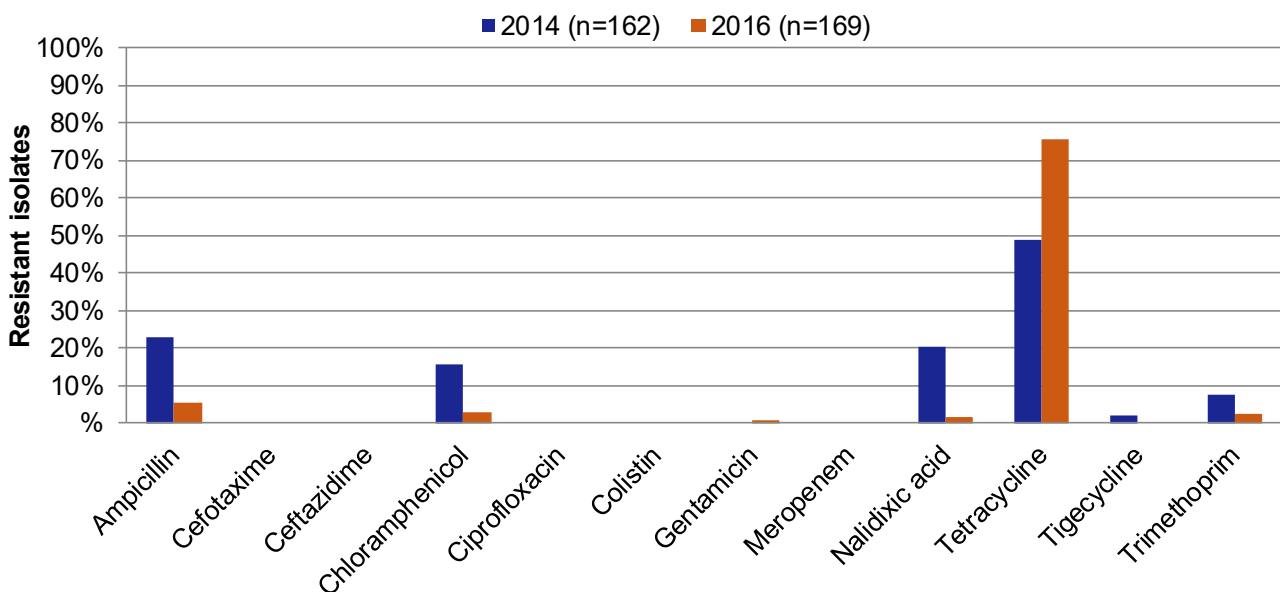


Figure 15: Percentage resistance (interpreted using EUCAST human CBPs) in *Salmonella* spp. obtained from turkey farms in the UK (National Control Plan/EU harmonised AMR monitoring); 2014 and 2016¹¹



Low resistance was observed to nalidixic acid (2%–4%) for broiler and layer isolates, and in turkey isolates resistance went from 20% in 2014 to 2% in 2016. No *Salmonella* spp. isolates from broiler and layer samples showed resistance to meropenem or tigecycline, and resistance to tigecycline in turkey isolates decreased from 2% to 0% while resistance to gentamicin remained very low (<1%).

In isolates from broiler farms, a large decrease was detected between 2014 and 2016 in the proportion of isolates resistant to trimethoprim and gentamicin (Figure 14). Resistance in *Salmonella* spp. isolates from layer farms remained low for all antibiotics tested. In *Salmonella* spp. isolates from turkey farms, resistance to ampicillin decreased from 23% to 5% and resistance to trimethoprim from 7% to 2% (Figure 15). In contrast, resistance to tetracycline increased in turkey isolates (from 49% to 76%) between 2014 and 2016.

***Salmonella* spp. isolates from broilers and pigs at slaughter**

Salmonella spp. isolates from neck skin samples from broilers and isolates from pig carcass swabs at slaughter were provided by food business operators under the Zoonoses Order 1989^k and the EC Regulation 2073/2005 on microbiological criteria for foodstuff (process hygiene criteria only).

In 2016, 17 *Salmonella* spp. isolates from broiler neck skin samples were tested for susceptibility, under the EU harmonised monitoring programme. Based on EUCAST ECOFFs, no decreased-susceptibility was observed to the HP-CIAs (cefotaxime, ceftazidime, ciprofloxacin and colistin) and the majority of other antibiotics tested (ampicillin, chloramphenicol, gentamicin, meropenem, nalidixic acid and tigecycline). Two isolates showed decreased-susceptibility to sulphamethoxazole, two to trimethoprim and one to tetracycline³⁵.

For pigs, a limited number of isolates were available. Of the nine *Salmonella* spp. isolates tested in 2015 from samples from healthy pigs, all were susceptible to the HP-CIAs cefotaxime, ceftazidime, ciprofloxacin and colistin, and to meropenem or tigecycline. Three isolates showed resistance to ampicillin and three to tetracycline (based on EUCAST human CBPs). In 2017, four *Salmonella* spp. isolates were tested, of which all were susceptible to the HP-CIAs cefotaxime, ceftazidime, ciprofloxacin and colistin. Two isolates were resistant to ampicillin and two to tetracycline.

Resistance in *Salmonella* Typhimurium isolates

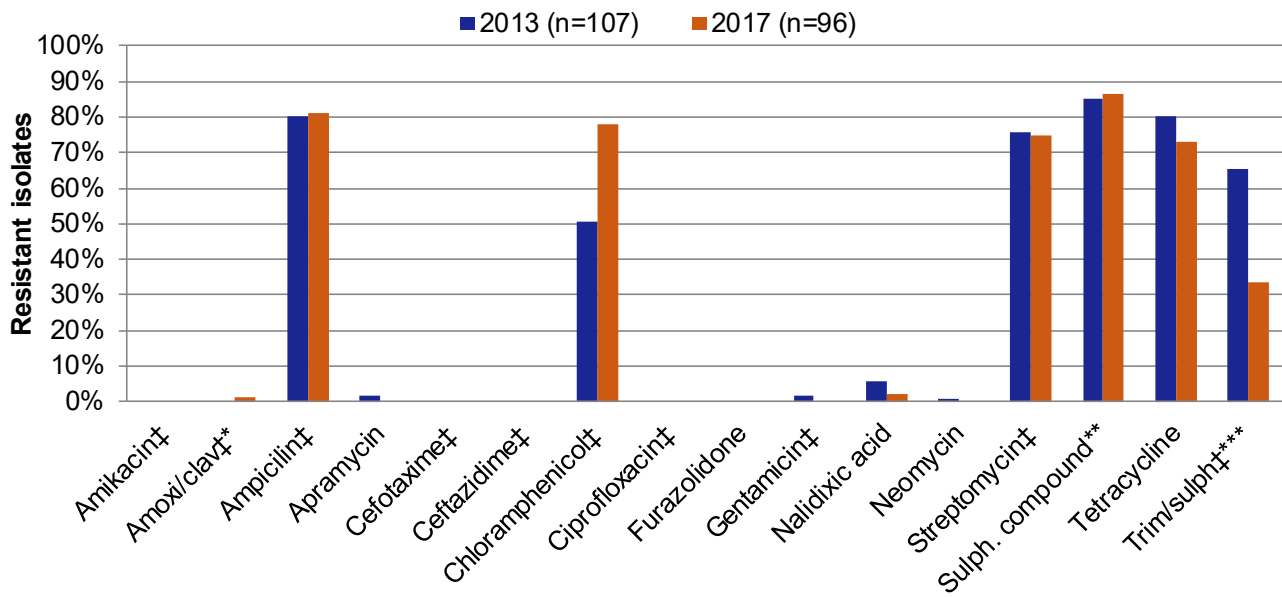
Results on AMR in *Salmonella* Typhimurium isolates are presented in addition to the data for all *Salmonella* spp. since this serovar is also common in humans. Figure 16 shows the resistance observed in *Salmonella* Typhimurium isolated from livestock in England and Wales in 2013 and 2017, tested under the clinical surveillance programme (see Annex F for detail).

It should be noted that these isolates were obtained from samples from healthy poultry flocks as well as samples from clinical cases in cattle, pigs and chickens. In the latter case, samples were tested for diagnostic purposes, but it is unknown whether these samples were collected pre- or post-antibiotic treatment, or how many isolations and incidents were represented in the data included. Therefore, the results may not be representative and should be interpreted with caution.

With regard to HP-CIAs, none of the isolates from cattle, pigs or chickens were resistant to cefotaxime, ceftazidime, or ciprofloxacin in 2013 and 2017 (Figure 16). Resistance to nalidixic acid appears to have more than halved (from 6% in 2013 to 2% in 2017). The majority of isolates in 2017 were resistant to ampicillin, chloramphenicol, streptomycin, tetracycline and sulphonamide compound (73–86%). An apparent increase (from 50% in 2013 to 78% in 2017) in resistance to chloramphenicol and decrease (from 65% in 2013 to 33% in 2017) in resistance to trimethoprim/sulphonamide can be seen in Figure 16.

^k <http://www.legislation.gov.uk/uksi/1989/285/made>

Figure 16: Percentage resistance (interpreted using British Society for Antimicrobial Chemotherapy (BSAC) human clinical break points where available, indicated with ‡) to selected antibiotics in *Salmonella* Typhimurium isolates collected under the clinical surveillance programme from cattle, pigs and chickens in England and Wales; 2013 and 2017^{10, 39}



‡ Interpreted using BSAC human CBPs; * Amoxicillin/clavulanate; ** Sulphonamide compound; *** Trimethoprim/sulphonamide

Most commonly isolated *Salmonella* serovars

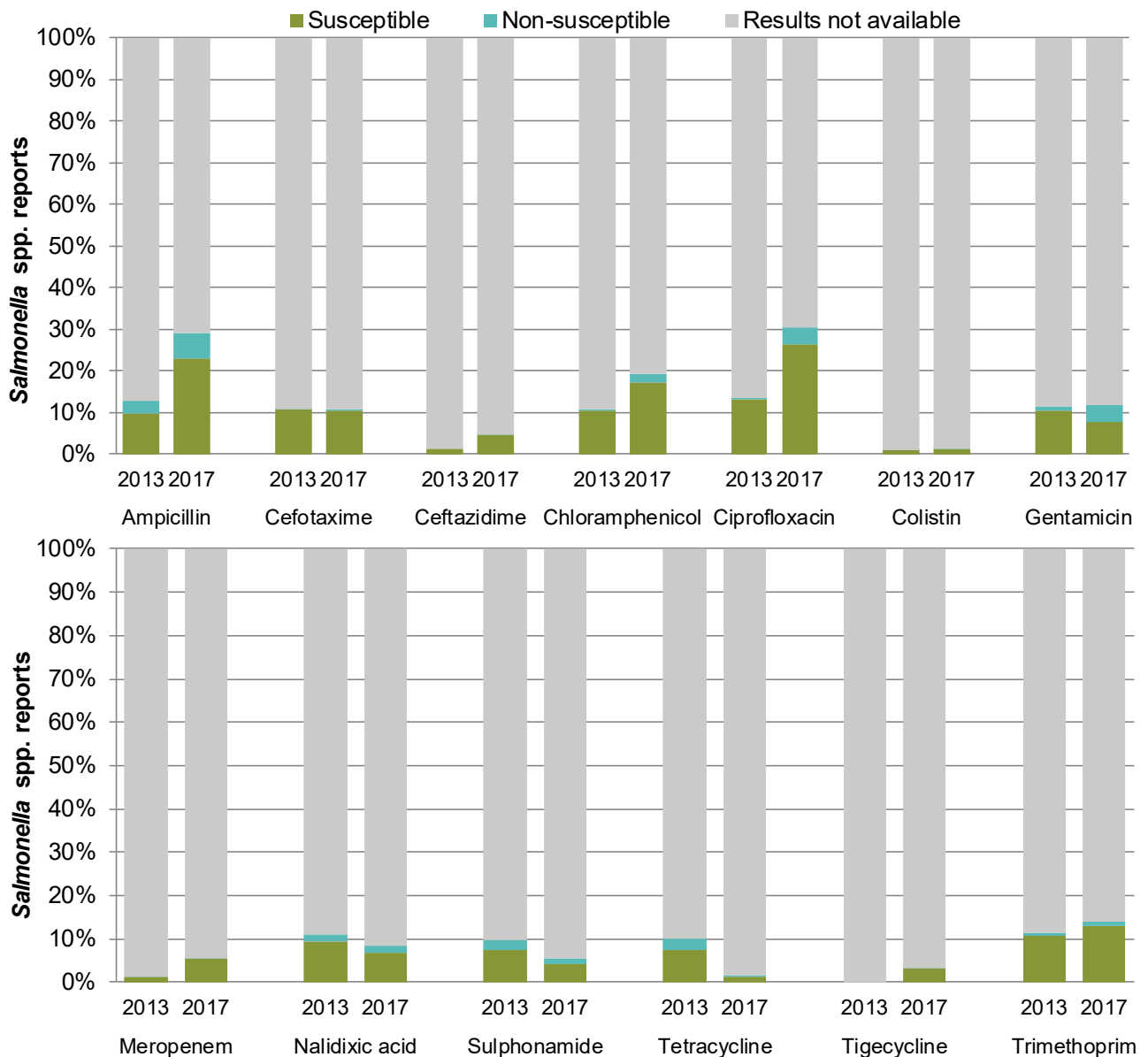
In 2017, serovar Dublin (475 isolates) represented the largest proportion of *Salmonella* serovars among isolates recovered from food-producing animals (cattle, pigs, sheep, chickens, turkeys and ducks) in the UK (both statutory and non-statutory samples), followed by Derby (373 isolates), Mbandaka (317 isolates), Senftenberg (260 isolates) and Kedougou (211 isolates)^{40, 41}. In 2013 the top five serovars in England, Wales and Scotland consisted of Dublin (458 isolates), Mbandaka (294 isolates), Montevideo (248 isolates), Senftenberg (206 isolates) and Kedougou (192 isolates) (see Annex C for the top ten most isolated serovars from animal samples in 2013 and 2017)⁴⁰.

3.2.2.3 Resistance – humans

Non-typhoidal *Salmonella* spp. isolates from human samples

There were 16,911 (non-typhoidal) *Salmonella* spp. faecal isolates recorded via routine laboratory surveillance in 2017; susceptibility information was recorded for between 1% (colistin) and 31% (ciprofloxacin) of isolates (Figure 17). The proportion of *Salmonella* spp. isolates tested that were non-susceptible (intermediate and resistant) to HP-CIAs decreased for colistin (from 6% to 3%), but increased for ciprofloxacin (from 4% to 14%), cefotaxime (from 1% to 2%) and ceftazidime (from 0% to 4%).

Figure 17: Percentage susceptible and non-susceptible (intermediate and resistant) isolates (interpreted using CBPs) in non-typhoidal *Salmonella* spp. from human faecal isolates (routine laboratory surveillance reports) in the UK; 2013 (n=7,933) and 2017 (n=16,911)

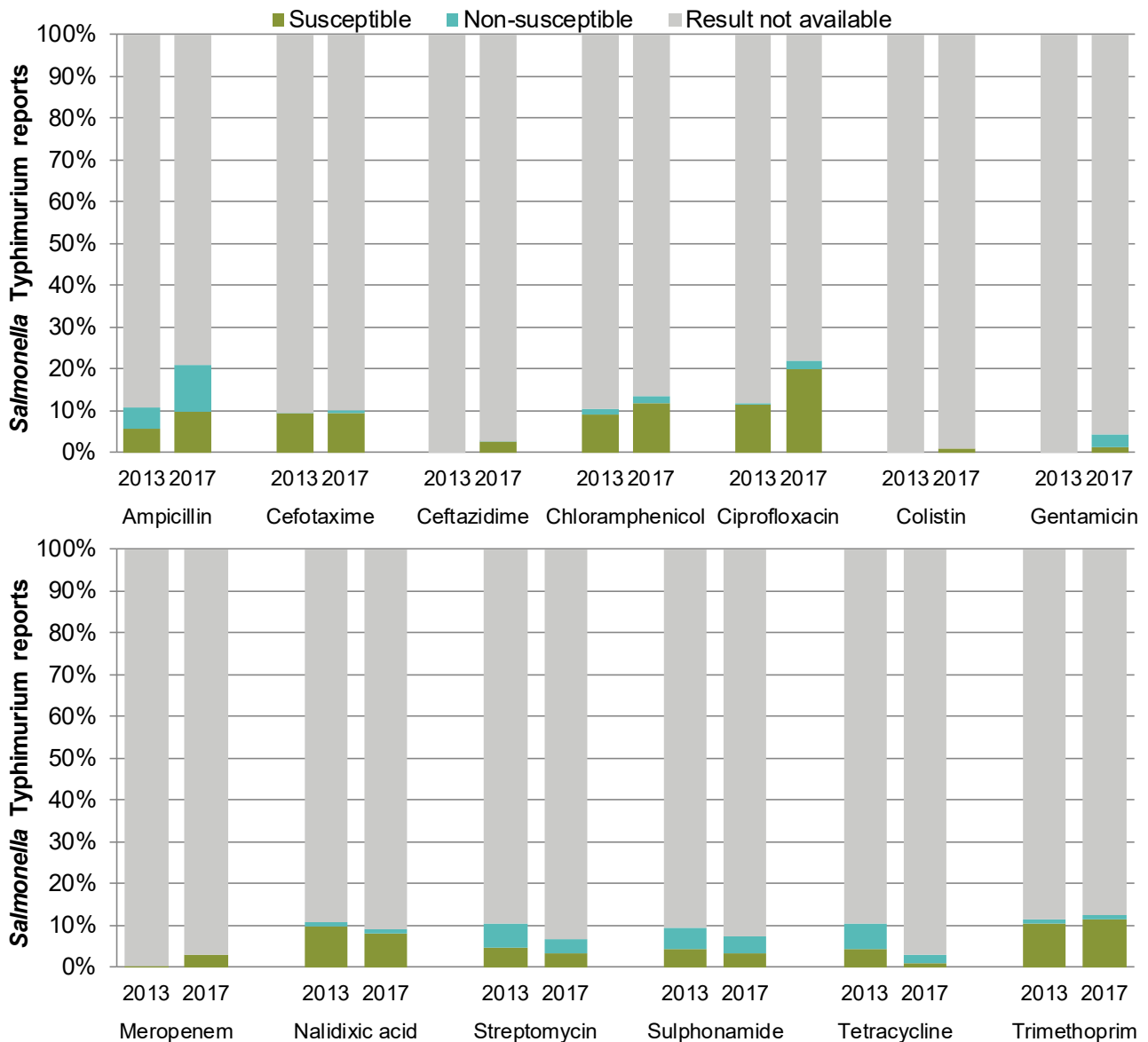


With regard to the other antibiotics tested, the proportion of *Salmonella* isolates that were non-susceptible increased for chloramphenicol (from 5% to 10%), gentamicin (from 11% to 34%), nalidixic acid (from 16% to 19%) and tetracycline (from 28% to 35%) between 2013 and 2017 (Figure 17). However, susceptibility testing in routine surveillance remains low (1%–14% in 2013, 1%–31% in 2017).

Resistance in *Salmonella* Typhimurium isolates

Data on AMR in *Salmonella* Typhimurium isolated from human faecal specimens are presented in addition to the data for all *Salmonella* spp. since this serovar is also common in animals. In both 2013 and 2017, susceptibility patterns from human *Salmonella* Typhimurium isolates are similar to those seen in isolates from animals and their environment (Figure 16). Of the isolates tested in 2017 a small proportion was non-susceptible to cefotaxime (4%), ceftazidime (7%) or ciprofloxacin (10%), and there was no non-susceptibility detected to colistin.

Figure 18: Percentage resistance (interpreted using CBPs) in *S. Typhimurium* isolates from humans reported through routine laboratory surveillance in England and Wales; 2013 (n=1,652) and 2017 (n=2,424)



With regard to the other antibiotics, a large proportion was non-susceptible to ampicillin (53%), streptomycin (49%), gentamicin (66%), sulphonamide compound (56%) or tetracycline (63%), see Figure 18. Reports of susceptibility testing have been consistent between 2013 and 2017, however they remain low (between 0% and 22% tested for each antibiotic), and as such these results should be interpreted with caution.

Most commonly isolated non-typhoidal *Salmonella* serovars

Salmonella Enteritidis and *Salmonella* Typhimurium continue to be the dominant non-typhoidal *Salmonella* serovars identified in gastrointestinal disease reference isolates in the UK in 2017, representing 27% (n=2,459) and 16% (n=1,423) of referrals, respectively. Compared to the previous report there were some changes in the top ten identified serovars between 2013 and 2017: the monophasic variant of *Salmonella* Typhimurium is now listed as the third most frequently reported serovar in 2017 (7%; in 2013 *S. Infantis* was third) and *Salmonella* Montevideo has fallen from 10th in 2013 to 25th most frequently reported serotype in 2017 (see Annex C).

***Salmonella* reference laboratory data and genotypic resistance**

In 2017, 9,131 non-typhoidal *Salmonella* isolates were referred to GBRU, PHE for confirmation. Whole genome sequencing (WGS) is routinely being used to type non-typhoidal *Salmonella* isolates since April 2014. An earlier evaluation of the prediction of phenotypic resistance from genotypic profiles, in isolates received at GBRU between April 2014 and March 2015, identified that 98% of the isolates were concordant, and the largest number of discrepant results were associated with streptomycin⁴². WGS has proven to be extremely valuable in rapid screening of bacterial isolates for emerging resistance mechanisms especially to critical antibiotics⁹. Between 2014 and 2017, WGS identified 32 non-typhoidal *Salmonella* isolates with transmissible colistin resistance gene *mcr-1* (17/32 had history of recent travel abroad) and one carbapenemase gene *bla*_{OXA48} acquired abroad.

APHA is considering validating the *Salmonella* WGS pipeline to be able to provide information on presence of AMR genes in relation to the presence of phenotypic resistance to selected antibiotics. This process is likely to start after the validation of the serogenotyping platform, which will be ready for implementation in 2020.

3.2.2.4 Control measures in place to reduce risk of transmission

The UK Zoonoses Order 1989 lists the animal species from which *Salmonella* spp. isolations should be reported to a Veterinary Investigation Officer of one of the Veterinary Investigation Centres of APHA⁴⁰. At a European level, Directive (EC) No. 2003/99^l sets out the requirements for monitoring of zoonoses and zoonotic agents in the EU.

Great Britain also implements National Control Programmes (NCP) for *Salmonella* in commercial chicken and turkey sectors. Under the framework of these NCPs, all commercial egg laying holdings with 350 or more birds, adult breeding flocks with more than 250 birds, all commercial broiler flocks, breeding turkey holdings with more than 250 adult birds and fattening turkey flocks with more than 500 birds should be sampled at defined times and intervals (varying by type of bird (e.g. breeding, laying, meat) and poultry species) by the food business operator or an official control, taking boot/sock swabs and/or composite faecal or dust samples according to a strict protocol set out by the respective NCPs and Commission Regulations (e.g. No. 584/2008^m for turkeys). Boot/sock swabs cover the feet of the person sampling, and this person will walk around the poultry house, making sure to collect material from the floor on the 'socks'. The protocols describe how many pairs of swabs should be taken, in which area, and the area covered per poultry house.

Samples are sent to a government-approved laboratory and subsequently tested for presence of *Salmonella* spp. When tested positive for *Salmonella*, the producer is required to contact the veterinarian for advice on biosecurity measures to prevent transmission. If the test is positive for *Salmonella* Enteritidis or *Salmonella* Typhimurium, the holding must be cleaned and disinfected,

^l <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX:32003L0099>

^m <https://eur-lex.europa.eu/legal-content/EN/ALL/?uri=CELEX%3A32008R0584>

after which an official will take samples of the next flock. If again positive, cleaning and disinfection will need to be performed again and movement on and off the holding will be restricted.

All *Salmonella* spp. isolates (except some food and feed isolates) identified in England and Wales are required to be sent to APHA for serotyping and antibiotic susceptibility testing. The majority of poultry samples taken in Scotland are sent to APHA and all mammalian samples are tested at SRUC Consulting Veterinary Services and serotype confirmed at the Scottish *Salmonella*, *Shigella* and *Clostridium difficile* Reference Laboratory.

As with campylobacteriosis prevention, people are recommended to handle animal products in food production in a hygienic manner and to ensure that meat is cooked thoroughly. Surveillance of notifications of food poisoning caused by *Salmonella* spp. are an important means to identify and manage situations on salmonellosis in early stages to prevent further spread. Information on local level incidence of non-typhoidal *Salmonella* are published routinely (England and Wales only), via the weekly notification reportsⁿ and (England only) via the Health Protection profile on the Fingertips Website^o.

3.2.2.5 International picture

A full overview for all participating European countries can be found in the EU summary reports on antibiotic resistance in zoonotic and indicator bacteria from humans, animals and food in 2014–2016³³⁻³⁵. Results below on isolates from animals are interpreted using EUCAST ECOFF values, which may explain some of the discrepancies when compared with results interpreted based on CBP values.

When comparing the degrees of susceptibility seen in *Salmonella* spp. isolates from UK broilers and turkeys in 2014 and 2016 to that of other EU MSs, it can be concluded that the UK is among the countries with the lowest levels of decreased-susceptibility to HP-CIAs^{33, 35}. No decreased-susceptibility was detected in isolates from broiler flocks to cefotaxime (0% vs. 0.8% for average of EU MSs), ceftazidime (0% vs. 0.6% for average of EU MSs) and colistin (0% vs. 2% for average of EU MSs) and the level of decreased-susceptibility to ciprofloxacin was far below average (9% vs. 54% for average of EU MSs) in 2016.

No decreased-susceptibility was detected in isolates from fattening turkey flocks to cefotaxime (0% vs. 0.9% for average of EU MSs), ceftazidime (0% vs. 0.2% for average of EU MSs) and colistin (0% vs. 0.3% for average of EU MSs) and the level of decreased-susceptibility to ciprofloxacin was far below average (2% vs. 51% for average of EU MSs) in 2016.

In addition, no decreased-susceptibility was detected in isolates from laying hen flocks to cefotaxime (0% vs. 0.1% for average of EU MSs) and ceftazidime (0% vs. 0% for average of EU MSs). The level of decreased-susceptibility to colistin (0% vs. 6% for average of EU MSs) and to ciprofloxacin (9% vs. 17% for average of EU MSs) was below average in 2016.

The UK was also among the countries with the lowest resistance to cefotaxime (0% vs. 1% for average of EU MSs), ceftazidime (0% vs. 1% for average of EU MSs) and colistin (0% vs. 1% for average of EU MSs) in *Salmonella* spp. isolated in 2015 from pigs³⁴.

Resistance in *Salmonella* spp. isolated from humans in the UK in 2016 showed that the UK was among the countries with lower than average resistance to HP-CIAs, with the exception of ceftazidime where the UK has the 18th lowest resistance (out of 21 European MSs)^{35, 43}.

ⁿ <https://www.gov.uk/government/collections/notifications-of-infectious-diseases-noids>

^o <https://fingertips.phe.org.uk>

Progress on recommendation 1 of the 2015 report

“Public health organisations should work with clinical laboratory colleagues to ensure that all *Salmonella* species are sent to the relevant reference laboratories for speciation and antimicrobial susceptibility testing. The referral form should include data on foreign travel, including countries visited, in the previous four weeks.”

The additional field on travel has been completed for greater than 50% of non-typhoidal *Salmonella* referrals in 2014 and 63% in 2015. In 2016 (January to March), 56% of referrals included information on recent travel, with 48% (831/1,719) of them indicating no (n=752) or unknown (n=10) recent travel or travel to an unknown destination (n=69). Of those where travel was indicated (n=888), seven (<1%) travelled within the UK and an additional 159 (18%) travelled elsewhere in Europe, 406 (46%) travelled to Asia, 163 (18%) travelled to Africa, 118 (13%) to North America and 24 (3%) to the South Americas. A recent study indicated that there was no difference in likelihood of non-typhoidal *Salmonella* bacteraemia (severity) between those who had travel indication and those who did not⁴⁴. Further analyses into the differences in serovars and resistances between travel and non-travel associated *Salmonella* are being undertaken.

3.2.2.6 Concluding remarks

The data show low resistance to the majority of the HP-CIAs in *Salmonella* spp. isolates from food-producing animals: there was no resistance to colistin or 3rd generation cephalosporins in isolates obtained from broiler chicken, layer chicken or turkey farms in 2016 or from pig carcass swabs in 2017, and resistance to ciprofloxacin was very low.

In *Salmonella* spp. from human isolates, resistance to HP-CIAs appears to have increased, which is of concern when considering treatment options. However, it is hard to draw conclusions from this given the changes in serovars identified in humans between 2014 and 2017, as well as the change in susceptibility testing practice over this time. Further analysis by serovar would be beneficial.

In 2016, the highest levels of resistance in isolates from poultry farms were to tetracycline, especially in turkeys. The highest levels of resistance in human isolates from 2017 were found to ampicillin, ciprofloxacin and gentamicin. Different *Salmonella* spp. serovars dominate in the human and animal populations. Since resistance patterns are related to the *Salmonella* serovar, this should be a consideration when comparing general *Salmonella* spp. data between humans and animals. For *S. Typhimurium*, a serovar commonly identified in both animal and human sectors, susceptibility patterns appear similar between animal isolates and human isolates, with the exception of lower degrees of susceptibility to chloramphenicol and trimethoprim/sulphonamide in isolates from animals.

Relative to other European countries, the UK has an average or lower than average resistance to HP-CIAs in isolates from animals. With regard to human isolates, the UK has lower than average resistance to HP-CIAs, with the exception of resistance to ceftazidime.

Progress on recommendation 3 of the 2015 report

"Public health organisations should support the work of professional organisations to transition UK clinical laboratories to a single standardised nationally agreed methodology for routine antimicrobial testing in 2016."

In 2016, the BSAC published support for the EUCAST method, aligning their breakpoints and withdrawing support for the BSAC methodology⁴⁵. BSAC also offered training workshops and support to assist in the transfer of laboratories from the BSAC to the EUCAST method^p. A review in 2017 found that only 12% of laboratories were still exclusively using the BSAC methodology for disk diffusion susceptibility testing^q.

3.2.3 *Escherichia coli*, including ESBL-, AmpC- and carbapenemase-producers

3.2.3.1 Background

Escherichia coli are frequently found in intestines of humans and animals; mostly as commensals. Since they harbour and potentially transfer genes conferring antibiotic resistance to other bacteria in the gut, *E. coli* are indicator bacteria for antibiotic resistance levels in Gram-negative bacteria and used for AMR surveillance in humans and food-producing animals. There are many different strain types and some strains can cause a range of infections, such as urinary and intestinal tract infections. When localised infections spread to the blood, *E. coli* bacteraemia (bloodstream infection) may occur. *E. coli* was the most common bacterial cause of bloodstream infections in people 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.

Extended-spectrum β -lactamase (ESBL-) and AmpC β -lactamase (AmpC-) producing *E. coli* are of particular concern since these enzymes convey resistance to a wide range of β -lactam antibiotics, including penicillins and 3rd generation cephalosporins, and therefore pose a serious therapeutic challenge to clinicians and veterinarians due to the limited treatment options.

3.2.3.2 Resistance – food-producing animals

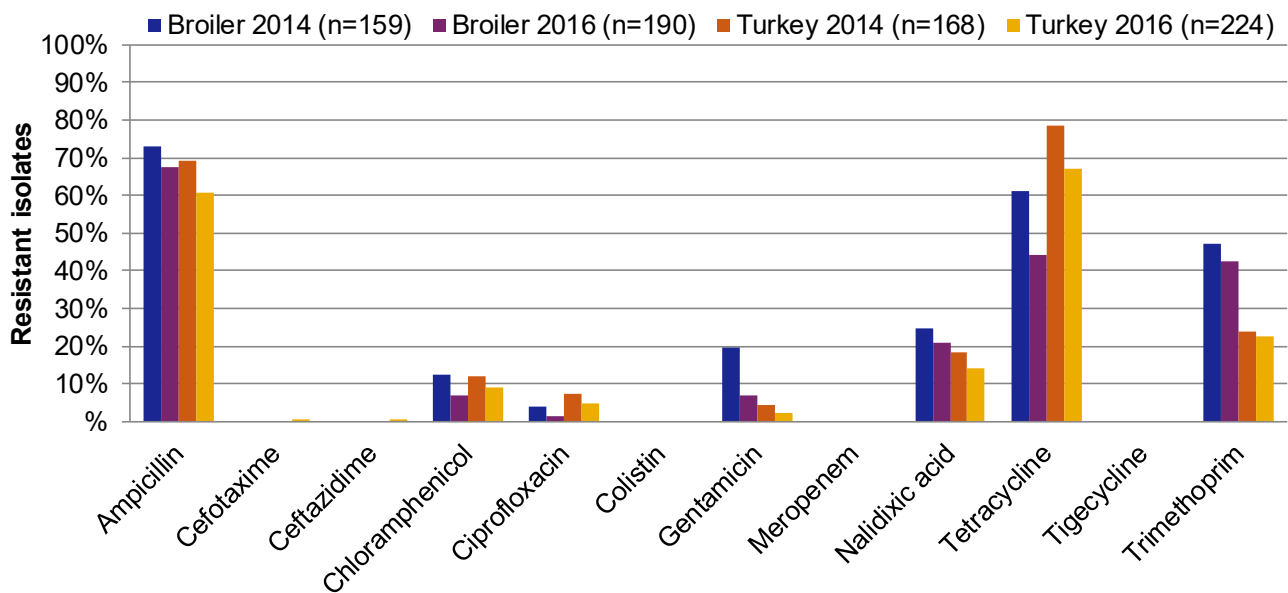
Antibiotic susceptibilities were determined for *E. coli* isolated from caecal samples from healthy broiler chickens and turkeys at slaughter, collected for the EU harmonised AMR monitoring scheme in 2014 and 2016 (see Annex F).

No resistance (interpreted using EUCAST human CBPs) was found in *E. coli* isolates from broilers to the HP-CIAs cefotaxime, ceftazidime and colistin in 2014 or 2016. A decrease was notable in resistance to ciprofloxacin (from 4% to 2%). In turkey isolates, a small decrease was notable between 2014 and 2016 in resistance to ciprofloxacin (from 7% to 5%). Resistance to cefotaxime and ceftazidime remained very low (<1%); no resistance to colistin was detected (Figure 19).

^p <http://bsac.org.uk/bsac-to-actively-support-the-eucast-disc-diffusion-method-for-antimicrobial-susceptibility-testing-in-preference-to-the-current-bsac-disc-diffusion-method/>

^q <https://www.gov.uk/government/publications/uk-smi-report-on-survey-into-susceptibility-testing-methodology/report-on-survey-into-susceptibility-testing-methodology>

Figure 19: Percentage resistance (interpreted using EUCAST human CBPs) in *E. coli* isolated from broiler chickens and turkeys in the UK (EU harmonised monitoring); 2014 and 2016

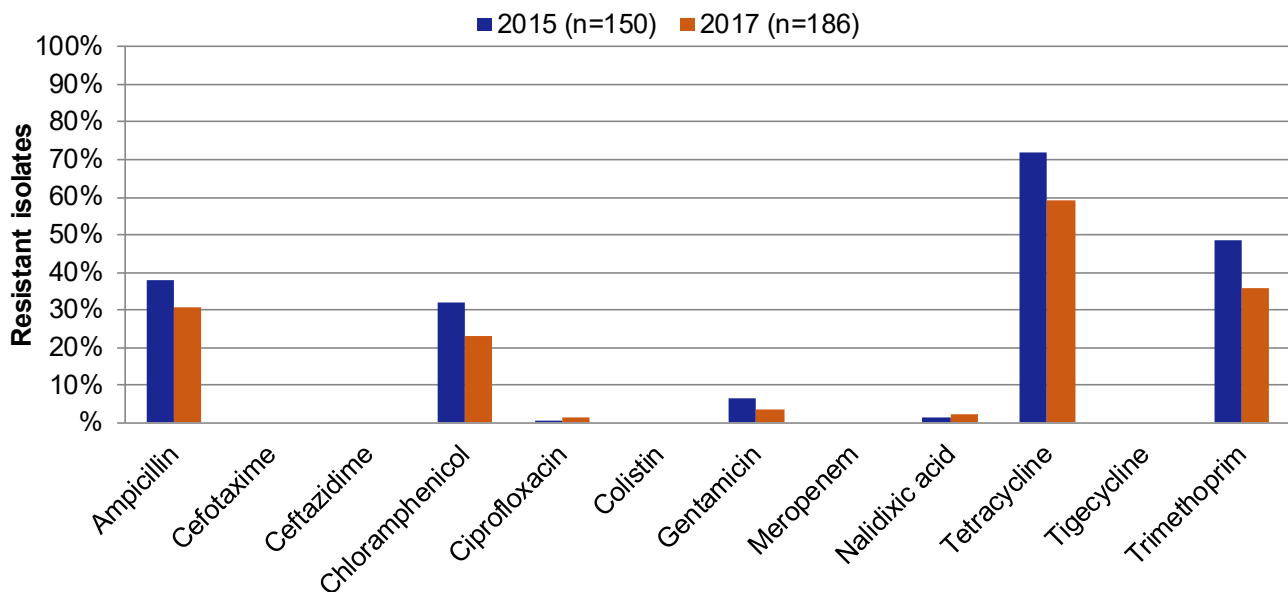


None of the *E. coli* isolates from broiler chickens showed resistance to meropenem or tigecycline. Resistance to tetracycline, gentamicin and chloramphenicol showed the largest decrease (from 61% to 44%, 20% to 7% and 13% to 7%, respectively). Resistance to nalidixic acid decreased from 25% to 21%.

None of the isolates from turkey showed resistance to meropenem or tigecycline. The largest absolute decrease in resistance was for tetracycline (from 79% to 67%), ampicillin (69% to 61%) and nalidixic acid (from 19% to 14%; Figure 19).

No resistance was observed in the *E. coli* isolated from caecal samples from healthy pigs to the HP-CIAs cefotaxime, ceftazidime and colistin, and low resistance was detected to ciprofloxacin (<2%) in both 2015 and 2017 (Figure 20).

Figure 20: Percentage resistance (interpreted using EUCAST human CBPs) in *E. coli* isolated from pigs in the UK (EU harmonised monitoring); 2015 and 2017



None of the isolates were resistant to meropenem or tigecycline. The highest level of resistance in *E. coli* isolates from caecal samples from healthy pigs at slaughter for each year (2015 and 2017) was to tetracycline (72% in 2015 and 59% in 2017), trimethoprim (49% in 2015 and 36% in 2017) ampicillin (38% in 2015 and 31% in 2017) and chloramphenicol (32% in 2015 and 23% in 2017), but decreased for nearly all antibiotics between 2015 and 2017.

The EU harmonised AMR monitoring requires specific testing for presence of ESBL-, AmpC- and carbapenemase-production in *E. coli* from pig, broiler and turkey caecal samples at slaughter, as well as from fresh chicken, pig and bovine meat at retail (see Annex F for methodology). Carbapenems are not authorised for use in food-producing animal species; however, they are included to monitor emergence or risk of resistance to those antibiotics in bacteria in man.

Under this selective method, 25% and 22% of the pig samples yielded *E. coli* resistant to cefotaxime (1 mg/L) in 2015 and 2017, respectively. For samples from broiler chickens and turkeys in 2016, this was 30% and 5%, respectively (Table 2). The majority of these resistant isolates had an ESBL-phenotype and around a third had an AmpC-phenotype. Only a few samples had a combined ESBL/AmpC- phenotype. None of these *E. coli* isolates from pigs, broiler chickens and turkeys were presumptive carbapenemase-producers.

Table 2: ESBL-/AmpC-producing *E. coli* in pig, broiler chickens and turkey caecal samples at slaughter following selective culture in the UK; 2015–2017³⁴

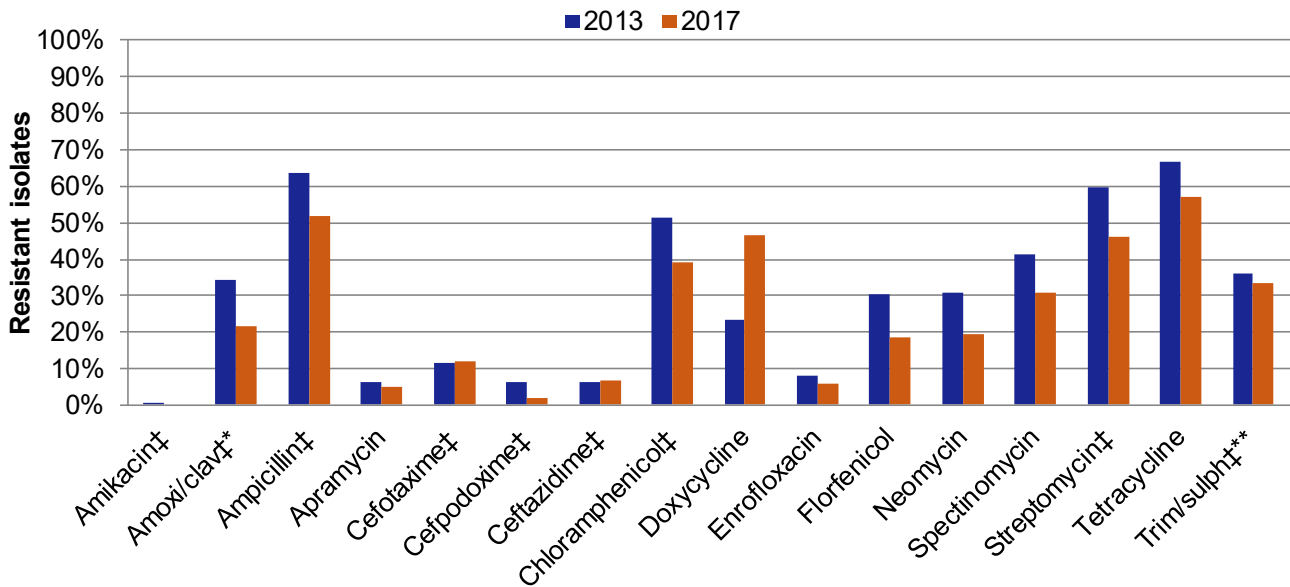
Species	Pig		Broiler chicken	Turkey
	2015*	2017*	2016*	2016**
No. of samples tested	327	347	382	362
No. of samples yielding <i>E. coli</i> microbiologically resistant to 1mg/L cefotaxime (%)	82 (25)	75 (22)	113 (30)	17 (5)
No. of isolates with ESBL-phenotype (%)	65 (22)	56 (16)	73 (19)	12 (3)
No. of isolates with AmpC-phenotype (%)	21 (7)	23 (7)	40 (10)	5 (1)
No. of isolates with combined ESBL/AmpC-phenotype (%)***	4 (1)	4 (1)	2 (<1)	0

* Data from the UK; ** Data from Great Britain; *** Isolates are also included in the ESBL and AmpC data.

Combined results on resistance in *E. coli* isolated from cattle, pigs, sheep, chickens and turkeys from the clinical surveillance programme, where field samples are collected and tested for diagnostic purposes, are shown in Figure 21. Those samples are tested for diagnostic purposes, generally isolated from sick animals. In addition, it is unknown whether these samples are collected pre- or post-antibiotic treatment. Therefore, these results should be interpreted with caution as they may not be representative of the prevalence in the general population.

In 2017, resistance levels to the HP-CIAs cefotaxime and ceftazidime were similar to those in 2013 (11%/6% in 2013 and 12%/7% in 2017, respectively), whereas a slight decrease was found for resistance to cefpodoxime (from 6% to 2%) and enrofloxacin (from 8% to 6%). Resistance to amoxicillin/clavulanate decreased between 2013 and 2017, from 34% to 21%. Other large decreases from 2013 to 2017 were seen for resistance to florfenicol, neomycin, chloramphenicol, ampicillin, streptomycin, tetracycline and spectinomycin, but an increase was detected for resistance to doxycycline (23% to 47%).

Figure 21: Percentage resistance (interpreted using BSAC breakpoints where available; indicated by ‡) in *E. coli*/coliform isolates collected under the clinical surveillance programme from cattle, pigs, sheep, chickens and turkey in England and Wales; 2013 (n=1,400) and 2017 (n=810)



‡ Interpreted by BSAC human CBPs; * Amoxicillin/clavulanate; ** Trimethoprim/sulphonamide

Progress on recommendation 7 of the 2015 report

“The Veterinary Medicines Directorate (VMD) will conduct carbapenem resistance monitoring (as part of the EU monitoring and reporting of antimicrobial resistance in zoonotic and commensal bacteria in accordance with the EU legislation, Commission Decision 2013/652/EU), a year earlier than mandated.”

Carbapenemases are enzymes that hydrolyse (destroy) carbapenems and other β -lactam antibiotics, especially in members of the Enterobacteriaceae family. They are considered an emerging threat worldwide as in many cases carbapenems are the last effective antibiotic in human medicine against multidrug resistant Gram-negative bacterial infections. Carbapenems are not used in food-producing animals but considering the importance in human medicine and the potential dissemination from humans to animals directly or through environmental routes, resistance to carbapenems is monitored³³.

Monitoring for carbapenemase-producing *E. coli* commenced in 2015. For 2015, 2016 and 2017, none of the samples collected from broiler chickens, turkey and pigs, and in parallel none of the samples from pork, beef and broiler meat, yielded carbapenemase-producing *E. coli*.

3.2.3.3 Resistance – retail meat

Under the EU harmonised AMR monitoring scheme, meat samples are tested on an agar selecting for cefotaxime-resistant *E. coli*, which gives insight into the number of samples potentially showing ESBL- or AmpC-phenotypes. These phenotypes convey resistance to antibiotics that are important for treating human infections.

A total of 312 beef and 312 pork samples were tested in 2015⁴⁶, and 314 beef and 310 pork samples in 2017⁴⁷. The majority of the tested samples originated from the UK, but a small proportion originated from other EU countries. Both in 2015 and 2017, two (0.6%) beef samples yielded *E. coli* microbiologically resistant to 1mg/L cefotaxime (interpreted using EUCAST ECOFFs), but in 2017 a smaller proportion of pork samples (0.3%) yielded 1mg/L cefotaxime-resistant *E. coli* than in 2015 (2%) (Table 3).

Overall, about 1% of retail beef and pork samples in the UK that were tested in 2015 and 2017 were positive for AmpC- or ESBL-producing *E. coli*; all positive isolates originated from the UK. Two of the 2015 isolates (one beef, one pork) and two of the 2017 isolates (one beef, one pork) had an AmpC-phenotype; the other isolates (2015: one beef, five pork; 2017: one beef) had an ESBL-phenotype (Table 3).

Two isolates showed decreased-susceptibility to ciprofloxacin; none of the isolates showed decreased-susceptibility to colistin. All of the isolates were susceptible to the last resort carbapenems imipenem, ertapenem, or meropenem (results not shown)^{46,47}.

Of 313 chicken samples tested in 2016, 141 (45%) yielded *E. coli* with decreased-susceptibility (interpreted based on ECOFFs) to 1mg/L cefotaxime⁴⁸. Of the 141 isolates resistant to 1mg/L cefotaxime, 93 had an ESBL-phenotype. Forty-eight of the 141 isolates had an AmpC-phenotype (Table 3).

Table 3: *E. coli* resistance in retail beef and pork^{46,47}, and retail chicken⁴⁸ in the UK; 2015–2017

Retail meat	Beef		Pork		Chicken
	2015	2017	2015	2017	2016
No. of samples tested	312	314	312	310	313
No. of positive samples yielding <i>E. coli</i> microbiologically resistant to 1mg/L cefotaxime (%)	2 (<1)	2 (<1)	6 (2)	1 (<1)	141 (45)
No. of isolates with ESBL-phenotype (%)	1 (<1)	1 (<1)	5 (2)	0	93 (30)
No. of isolates with AmpC-phenotype (%)	1 (<1)	1 (<1)	1 (<1)	1 (<1)	48 (15)
No. of isolates with combined ESBL/AmpC-phenotype (%)*	0	0	0	0	2 (<1)

* These isolates are also included in the ESBL and AmpC data

None of the 141 isolates resistant to 1 mg/L cefotaxime showed decreased-susceptibility to the carbapenem antibiotics ertapenem, imipenem and meropenem or to colistin. Additionally, none of the isolates showed decreased-susceptibility to the antibiotics azithromycin, temocillin and tigecycline. As expected, all isolates had decreased-susceptibility to the β -lactam antibiotic ampicillin. All of the isolates designated as ESBL-phenotype showed decreased-susceptibility to the cephalosporin antibiotics cefepime and ceftazidime, and all but one isolate showed decreased-susceptibility to cefotaxime. All of the isolates designated as AmpC-producers showed decreased-susceptibility to ceftazidime, cefotaxime and ceftazidime (results not shown)⁴⁸.

Overall, 30% and 15% of retail chicken samples were positive for ESBL- or AmpC-producing *E. coli* respectively. There was a decrease in the proportion of samples positive for ESBL-producing *E. coli* compared to a previous (2013–2014) UK study, which reported that 65% of 159 retail chicken samples were positive for ESBL-producing *E. coli*⁴⁹.

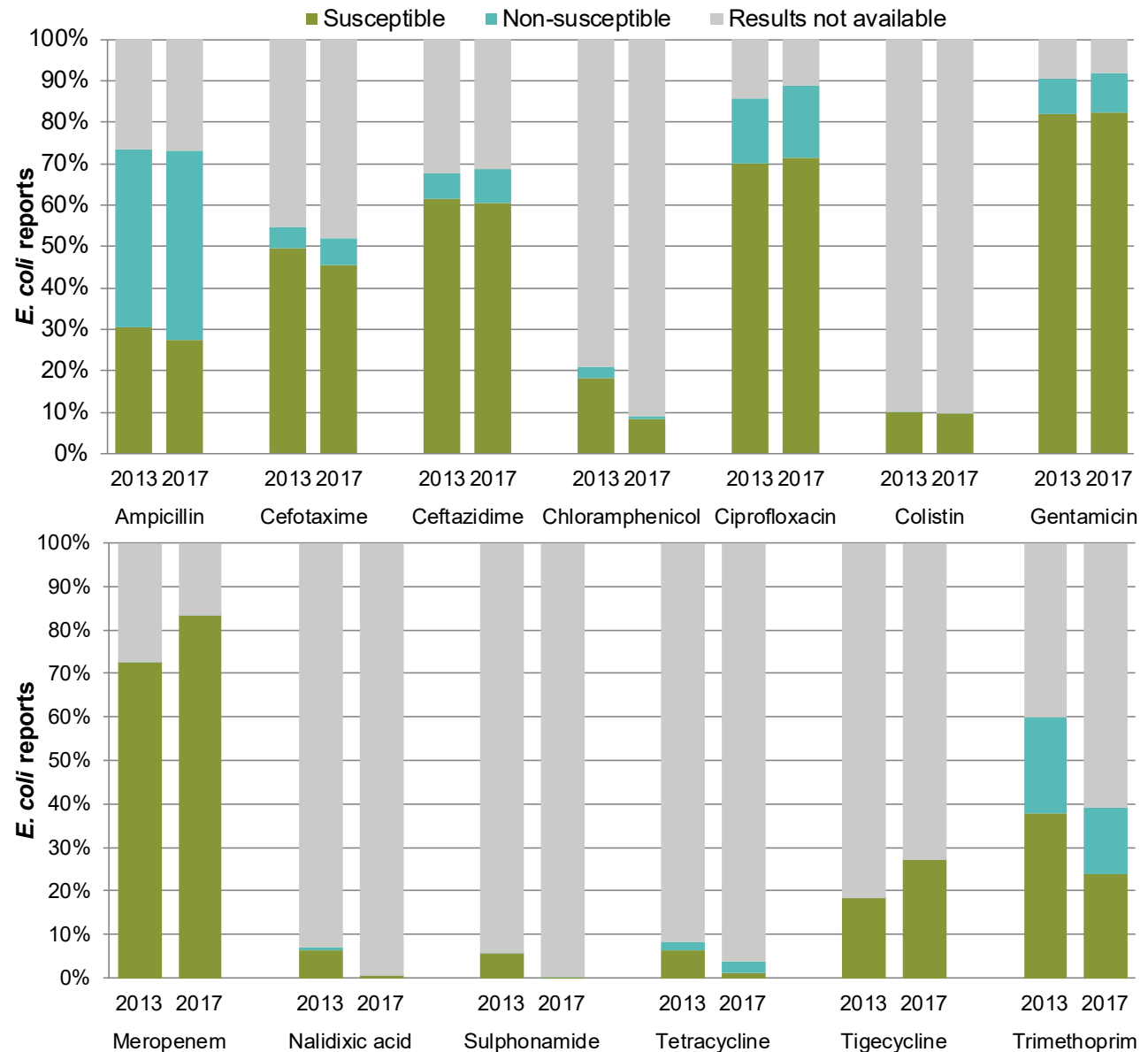
3.2.3.4 Resistance – humans

In 2017, 41,891 *E. coli* bloodstream infections in humans were reported in the UK through routine laboratory surveillance. The degree of susceptibility testing varied by antibiotic, with those

recommended for clinical use being tested more frequently and with a higher frequency in specimens from normally sterile sites.

Since the last One Health report, the level of antibiotic susceptibility testing and non-susceptibility (intermediate and resistant) of *E. coli* blood samples has been varied (Figure 22).

Figure 22: Percentage susceptible and non-susceptible* isolates (interpreted using CBPs) in human *E. coli* blood isolates in the UK; 2013 (n=35,357) and 2017 (n=41,891)



* Including both resistant and intermediate susceptibility results

The key antibiotics for treatment of Gram-negative infections/bloodstream infections (covered by the UK Five Year AMR Strategy 2013–2018¹) presented in Figure 22 indicate that the percentage non-susceptibility has stayed the same or decreased within the UK between 2013 and 2017. Non-susceptibility remained moderate in *E. coli* isolates to ciprofloxacin (20%) and 3rd generation cephalosporins (cefotaxime and ceftazidime, both 12%) in 2017. Non-susceptibility to colistin was detected in 1% of isolates tested.

Non-susceptibility also remained very high to ampicillin (63%) and high to trimethoprim (39%), whereas lower levels of non-susceptibility were recorded for gentamicin (11%) and meropenem (0%). Some local laboratories undertake selective testing/screening of ESBL presence and record

this via routine surveillance⁵⁰. In 2017, 23,402 *E. coli* urine isolates (2%) were reported as being tested for ESBL presence, of which 16,452 (70%) yielded ESBLs, a higher proportion as those tested in 2013 (59%; 5,578/9,532). Eight percent of *E. coli* blood isolates were tested for ESBL presence in 2017; of those tested, 40% recorded the presence of an ESBL.

The PHE reference laboratory, AMRHAI, stopped providing a molecular service for detection of acquired AmpC genes a few years ago. However, similar to the ESBL testing, some local clinical laboratories do undertake selective testing/screening of AmpC presence and record this via routine surveillance. In 2017, 5,138 *E. coli* urine isolates (<1%) were reported as being tested for AmpC presence, of which 2,002 (38%) yielded AmpC, the same proportion as those tested in 2013 (38%; 485/1,262). Eight percent of *E. coli* blood isolates were tested for AmpC presence in 2017; of those tested, 2.5% recorded the presence of an acquired AmpC. The low level of testing for AmpC suggests limited capacity as well as the high likelihood for selection bias, possibly based on presence of cephalosporin or carbapenem resistance.

In 2017, the AMRHAI Reference Unit received 3,000 Enterobacteriaceae isolates that were confirmed positive for at least one carbapenemase, with most of the isolates indicating colonisation rather than infection¹³. The 'big 5' carbapenemase families (KPC, OXA-48-like, NDM, VIM and IMP), and combinations thereof, accounted for >99% of isolates. Carbapenemases belonging to the OXA-48-like family continue to be the most frequently identified, accounting for 48.5% of confirmed carbapenemase-producing Enterobacteriaceae (CPE) in 2017, followed by NDM (24.4%), KPC (15.1%), IMP (4.7%) and VIM (2.4%). Since the majority of CPE referred to AMRHAI in 2017 were from sites suggesting colonisation, minimum inhibitory concentrations (MICs) were not determined. However, AMRHAI's MIC data for 700 confirmed CPE isolates indicated that, as in previous years, CPE isolates were not only resistant to carbapenems but also to multiple other classes of antibiotics.

3.2.3.5 Control measures in place to reduce risk of transmission

E. coli is commonly found in the lower intestine of humans and livestock. Most strains are harmless and are opportunistic pathogens whereas some strains, such as Vero cytotoxin-producing *E. coli* (VTEC), also known as Shiga toxin-producing *E. coli* (STEC), can cause serious food-poisoning. These strains are transmitted to humans through contact with contaminated water and the environment, and through consumption of contaminated foods (raw or undercooked meat products). VTEC are destroyed by thoroughly cooking of foods until all parts reach a temperature of 70°C.

Guidance documents to aid in reducing transmission of, and infection by, VTEC are available from the UK government website⁵¹. Most measures are related to handling, storing and preparing of food products. In addition, it is important to wash hands thoroughly after using the toilet, handling raw meat, before meals and after contact with animals. Furthermore, guidance is provided around farm and petting zoo visits (such as: avoid putting fingers in mouths while on the farm, wash hands thoroughly, do not eat or drink while touching animals).

Study on ESBL-producing *E. coli* in animals, people and food

A recent UK study examined different sources of ESBL-producing *E. coli*, including human faeces, sewage, farm slurry, livestock, raw meats, fruit and vegetables in order to understand the contribution of non-human sources of ESBL-producing *E. coli* to the burden of human gut colonisation/infections.

From >20,000 human faeces samples tested, the study estimated that 11% of the UK population have gut colonisation by ESBL-producing *E. coli*. Approximately 65% (n=159) of retail chicken, 3% of pork (n=79) and 1% of beef (n=159) samples, and 28% of farm slurry samples (n=97) were positive for ESBL-producing *E. coli*, but all tested fruit and vegetable samples (n=400) were negative⁴⁹.

Different strains of ESBL-producing *E. coli* were identified, with ST131 (an internationally-recognised 'high-risk' clone of *E. coli*) dominant, accounting for over one-third (35%) of all ESBL-producing *E. coli* from human faeces and almost a fifth (18%) of ESBL-producing *E. coli* from sewage samples. ST131 also dominated among bloodstream ESBL-producing *E. coli* included within the study, accounting for almost two-thirds (64%) of isolates recovered. By contrast, only two (0.9%) livestock or food ST131 isolates were found in this study (one from chicken meat and one from a chicken) but both could be distinguished from ST131 from humans.

After excluding ST131, the next *E. coli* type in rank, overall and in each of the human sources, was ST38 (9% in sewage isolates, 8% in human faeces and 6% in human bacteraemia isolates), but no ST38 isolates were found in the meat, slurry or livestock surveillance isolates, suggesting that it is a 'human-adapted' strain.

The dominant ESBLs also differed between sources, with CTX-M-15 most commonly identified in the human group, accounting for 77% of ESBL-producing *E. coli* isolates from human bacteraemia, 71% from human faeces and 54% from sewage, but in only 7% of isolates from meat and farm slurry. In contrast, CTX-M-1 dominated in isolates from non-human sources, accounting for 56% of isolates from raw meat, livestock and farm slurry, but just 5% of ESBL-producing *E. coli* from blood or human faeces, and 10% from sewage.

The study showed that most human infections and colonisations with ESBL-producing *E. coli* are attributable to a very small number of successful strains (especially a clone known as ST131), which may be spread from person to person through poor hygiene or from the environment to individuals in home, community and healthcare settings. During the study period (2013–14), non-human reservoirs of ESBL-producing *E. coli* in the UK had only a limited role in contributing to the major burden of human disease. Some infected or colonised people may acquire an ESBL-producing *E. coli* strain from a non-human source, but evidence from this study indicates that this is a small minority (<10%).

In support of the UK Government's ambitions to reduce healthcare associated Gram-negative bloodstream infections by 50% by 2021 – with an initial focus on *E. coli* – PHE, along with professional and partner organisations, have co-produced resources to help health and social care economies achieve these reductions by strengthening infection prevention and improved antibiotic prescribing. Toolkits for the early detection, management and control of CPE have been developed for acute trusts as well as health and residential settings in the community and initiatives such as the TARGET antibiotic toolkit, which provides diverse resources to support health professionals and educate patients in appropriate use of antibiotics, have helped embed stewardship programmes.

3.2.3.6 International picture

Results below on isolates from animals are interpreted using EUCAST ECOFF values, which means that results are not directly comparable to those interpreted using CBP values.

The UK is consistently among the EU MSs with the lowest level of decreased-susceptibility to HP-CIAs in *E. coli* isolated from broilers and turkeys in 2014 and 2016^{33, 35}. In 2016, there was full susceptibility to cefotaxime, ceftazidime and colistin (average decreased-susceptibility for EU MSs: 4%, 4% and 2%, respectively) and to ciprofloxacin there was decreased-susceptibility in 22% (average for EU MSs: 64%). In 2015, in comparison to other EU MSs, the UK had the lowest observed level of decreased-susceptibility to cefotaxime and ceftazidime (0% vs. average of 1% for EU MSs), lower than average decreased-susceptibility to ciprofloxacin (2% vs. average of 11% for EU MSs) and only a marginally higher level of decreased-susceptibility to colistin (0.6% vs. average of 0.4% for EU MSs) in *E. coli* isolated from pigs³⁴.

With regard to EU harmonised monitoring for presumptive ESBL-/AmpC-/carbapenemase-producing *E. coli*, the UK had a lower than average prevalence for ESBL- and AmpC-producing *E. coli* isolated from fattening pigs in 2015 (22% and 7% for ESBL- and AmpC-phenotype, respectively, vs. 32% and 10% on average for EU MSs), from turkeys in 2016 (3% and 1% for ESBL- and AmpC-phenotype, respectively, vs. 37% and 7% on average for EU MSs) and from broilers in 2016 (19% and 11% for ESBL- and AmpC-phenotype, respectively, vs. 35% and 24% on average for EU MSs). The UK also had a lower than average prevalence for ESBL- or AmpC-producing *E. coli* isolated from pork samples in 2015 (2% and 0.4% for ESBL- and AmpC-phenotype, respectively, vs. 7% and 2% on average for EU MSs). Similar results were seen for *E. coli* isolates from beef (1% and 1% for ESBL- and AmpC-phenotype, respectively, vs. 5% and 2% on average for EU MSs) and broiler meat samples (30% and 16% for ESBL- and AmpC-phenotype, respectively, vs. 36% and 27% on average for EU MSs) in 2016.

The UK data reported to the European Antimicrobial Resistance Surveillance Network (EARS-Net) showed lower than average resistance in *E. coli* bacteraemia samples isolated from humans to fluoroquinolones and 3rd generation cephalosporins but slightly higher resistance to carbapenems when compared to other EU MSs⁵².

3.2.3.7 Concluding remarks

Under the EU AMR monitoring scheme, very low levels of resistance were found in broiler and turkey isolates to 3rd generation cephalosporins (<1%), low resistance to ciprofloxacin (<4% for broilers and ≤7% for turkeys) and no resistance to colistin. Resistance decreased between 2014 and 2016 to nearly all tested antibiotics in both poultry species. In pig isolates no resistance was found to 3rd generation cephalosporins or colistin, and low resistance to ciprofloxacin (<2%).

In broilers and pigs, specific testing for ESBL- and AmpC-producing *E. coli* yielded a high prevalence (22-30%) with the majority of isolates showing the ESBL-phenotype. In turkeys

prevalence was around 5%. Prevalence in retail meat was consistently low for pork and beef (<2%) whereas in chicken meat the prevalence was 45%, with twice as many ESBL-phenotype isolates being observed than AmpC-phenotype isolates. No carbapenemase-producing *E. coli* were found in animal or retail meat samples tested under the EU AMR monitoring scheme during 2015–2017.

E. coli isolates from humans showed high levels of resistance to ampicillin and trimethoprim. The limited surveillance data available on ESBL-/AmpC-/carbapenemase-producing *E. coli* in humans, is largely based on selective testing. Based on data from local laboratories, 38% of *E. coli* urine isolates tested showed AmpC presence in 2017, whereas this was 8% for *E. coli* blood isolates. In the same year, 40% of *E. coli* bacteraemia isolates tested showed an ESBL-phenotype. This is higher than the 8.7% ESBL-positive observed in BSAC UK Bacteraemia Surveillance samples (n=38/437)^r. BSAC tests up to 20 consecutive *E. coli* bacteraemia isolates each year from 25 centres with good geographical spread throughout the UK and Ireland. The higher proportion of ESBL-positive isolates observed in the routine surveillance compared to the representative BSAC sample suggests that testing for presence of ESBLs in *E. coli* samples is biased in the routinely reported data towards testing of resistant organisms. A study in England in 2014 indicated that CTX-M ESBL colonisation was established in the general population and that an estimated 0.1% of the population were colonised with a CPE⁵³. In 2017 3,000 referred Enterobacteriaceae (primarily colonisation) isolates were positive for at least one carbapenemase, indicating low prevalence, but a concerning increase over time.

Progress on recommendation 9 of the 2015 report

“Public and professional One Health activities should be enhanced through engagement with the European Antimicrobial Awareness Day (EAAD) campaign and aligning training programmes for human and animal health professionals.”

Infographics, posters, key messages, tweets, articles, and more material were produced in collaboration with other government departments, the animal industry and charity organisations for European Antibiotic Awareness Day and subsequently for World Antibiotic Awareness Week in the past 5 years. This promoted responsible use of antibiotics in animals, optimal prescribing practice in humans and animals, best husbandry practices; furthermore, *ad hoc* surveys were ran and informed the public on some misunderstood facts. Training material is available for various health professionals and students; more is being developed for the farming industry.

Engagement during World Antibiotic Awareness Week will continue, to highlight the importance of tackling antibiotic resistance together.

3.2.4 LA-MRSA

3.2.4.1 Background

The term livestock-associated methicillin-resistant *Staphylococcus aureus* (LA-MRSA) was coined following the identification of a novel MRSA lineage in pigs, pig farmers and their families in the Netherlands and France in the early 2000s. LA-MRSA belonging to multi-locus sequence type clonal complex 398 (CC398) has subsequently been identified in diverse livestock species (such

^r <http://www.bsacsurv.org/reports/bacteraemia#results>

as pigs, veal calves, poultry, horses and dairy cows) in Europe and worldwide. In most instances, LA-MRSA is found in the nose or on the skin of livestock without causing clinical signs of infection.

In humans, LA-MRSA is predominantly identified in those in direct contact with LA-MRSA positive animals. Such individuals can become colonised, with LA-MRSA being found asymptotically in the nose or on the skin. However, as with other types of MRSA such as healthcare- and community-associated MRSA, if LA-MRSA enters the body through breaches in the skin, it can cause a local skin infection or, more rarely, invasive disease such as pneumonia or bacteraemia.

LA-MRSA varies widely in their susceptibility to antibiotics, with some displaying resistance to multiple classes⁵⁴⁻⁵⁷, though various therapeutic options remain available.

3.2.4.2 Resistance – livestock and other animal species

In 2008, a survey was undertaken to determine the prevalence of LA-MRSA positive pig herds in EU MSs⁵⁸. Breeding pig holdings in the UK were tested; none of 258 holdings were positive for CC398 LA-MRSA or for other MRSA.

Subsequently, there have been occasional reports of CC398 LA-MRSA in the UK from livestock and other animal species. Some have been identified in healthy animals as a result of research/surveillance studies and others as a result of clinical investigations (Table 4).

Table 4: Published case studies of LA-MRSA from livestock and other animal species in the UK

Origin	Animal species	No. positive animals in study	LA-MRSA lineage (MLST-CC)	No. MDR*	Reason for sampling	Year(s) reported	References
England	Horse	2	CC398	2	Screen (n=1) Clinical (n=1)	2009	59
	Poultry	1	CC398	1	Clinical	2013	57, 60
	Pig	4	CC398	4	Clinical & research	2014–2017	57, 60, 61
	Beef cattle	1	CC398	1	Clinical	2016	57, 60
Northern Ireland	Pig	7	CC398	7	Clinical	2014–2017	60, 62
	Pig	3	CC30	0	Clinical	2015	63
	Dairy cattle	1	CC398	1	Clinical	2015	60
Scotland	Pheasant	1	CC398	1	Clinical	2017	60, 64
UK (Equine hospital)	Horse	12	CC398	11**	Research	2017	65
UK (Zoo)	Mongoose	3	CC398	3	Clinical & research	2017	66

* Multi-drug resistant; resistant to ≥ 2 clinically relevant antibiotic classes in addition to β -lactams. All were resistant to penicillin, oxacillin/cefoxitin and tetracycline; resistance to gentamicin, trimethoprim, erythromycin, clindamycin, ciprofloxacin \pm chloramphenicol was variable; ** Susceptibility data available for 11 isolates; not stated for one isolate.

Associated genomic studies highlight marked genetic diversity indicating multiple independent incursions rather than expansion of a single CC398 LA-MRSA clone within UK livestock.

To date, all CC398 LA-MRSA from livestock in the UK have been multidrug resistant (MDR; resistant to ≥ 2 antibiotic classes in addition to β -lactams), commonly displaying resistance to penicillin, oxacillin/cefoxitin, tetracycline, erythromycin, clindamycin and trimethoprim. Genetic markers associated with resistance to heavy metals (zinc and cadmium) and decreased susceptibility to biocides were also present in some strains.

Of note, resistance to linezolid has been recorded in two CC398 LA-MRSA isolates from breeding pigs in Belgium³⁵.

3.2.4.3 Resistance - retail meat and animal products

In mainland European countries where LA-MRSA is prevalent in food-producing animals, LA-MRSA has been detected in up to 45% of raw meat samples³⁵. Variable CC398 LA-MRSA rates have been recorded from raw pork, chicken and turkey meat at retail in the UK (Table 5), with meat samples originating from the UK and from other European countries.

Table 5: Published reports of LA-MRSA from retail meat and animal products in the UK

Sample type	No. samples	No. (%) LA-MRSA positive	Spa type(s)	LA-MRSA lineage (MLST-CC)	No. (%) MDR*	Year study conducted	Reference
Raw chicken	30	1 (3)	t1939	CC9	1 (100)	2011	55
Raw chicken	50	4 (8)	t011, t034, t899	CC398	4 (100)	2015	56
Raw chicken	51	0	-	-	-	2015	67
Raw turkey	11	2 (18)	t011, t034	CC398	1 (50)	2015	56
Raw pork	30	0	-	-	-	2011	55
Raw pork	63	3 (5)	t011, t034	CC398	2 (67)	2015	56
Raw pork	52	2 (4)	t011, t034	CC398	2 (100)	2015	67
Raw beef	30	0	-	-	-	2011	55
Bulk tank milk	~1500	7** (~0.5%)	t011, t2346	CC398	7 (100)	2012	68

* Multi-drug resistant; resistant to ≥ 2 clinically relevant antibiotic classes in addition to β -lactams. All were resistant to penicillin, oxacillin/cefoxitin and tetracycline; resistance to trimethoprim, erythromycin, clindamycin \pm ciprofloxacin was variable; ** Recovered from 5 geographically dispersed farms.

A single report of CC9 LA-MRSA (a lineage prevalent in livestock and retail meat in Asia) has been identified in British chicken meat in the UK. The majority of LA-MRSA recovered from retail meat was MDR with genomic studies highlighting genotypic diversity, so not indicative of a common source. One study conducted in the UK reported that the level of LA-MRSA present in the meat tested was low (<20 CFU/g raw meat)⁵⁶. CC398 LA-MRSA has also been identified in bulk milk from dairy cattle in five geographically dispersed farms in the UK⁶⁸.

3.2.4.4 Resistance - humans

Varying LA-MRSA colonisation rates have been reported among those with occupational exposure to livestock in mainland Europe, with rates of up to 86% in pig farmers, 37% in poultry farmers, 37% in cattle farmers, 45% in veterinarians and 6% in slaughterhouse workers³⁵.

To date, there have been reports of CC398 LA-MRSA from 13 patients in the UK (Table 6). Although the context and sampling strategies differed in the various studies, all isolates were from screening/carriage sites or superficial infections. None reported occupational exposure as a known risk factor. Most isolates (9; 69%) were MDR. A one-year prospective study of all MRSA recovered from humans in the East of England highlighted a low LA-MRSA rate; just one of 2,283 (<0.01%) isolates was identified as CC398 LA-MRSA⁶⁹.

During 2015/2016, a collaboration between two PHE teams (Healthcare Associated Infections and Antimicrobial Resistance [HCAI and AMR] and Emerging Infections and Zoonoses [EIZ]) and the VMD, aimed to estimate the LA-MRSA carriage rate in an "at risk" UK population. The study screened adult volunteers with frequent occupational or recreational contact with animals, attending two national Veterinary shows and a Pig and Poultry Fair, for LA-MRSA carriage. The results will be published shortly.

Table 6: Reported cases of CC398 LA-MRSA from humans in the UK

Year of isolation	Country	Specimen type	Spa type	Phenotype	MDR	Reference
2009	Scotland	Swab	t011	PEN, OXA CIP, TET	Yes	70
2010	Scotland	Swab	t011	PEN, OXA, ERY, CLIND, CIP, TET, GENT	Yes	70
2011	Scotland	Swab (umbilicus)	t011	PEN, OXA	No	70
2011	Scotland	Swab	t899	PEN, OXA, CLIND, TRIM, TET	Yes	70
2011	Scotland	Swab (umbilicus)	t011	PEN, OXA	No	70
2011	Scotland	Swab (umbilicus)	t899	PEN, OXA, TRIM, TET	Yes	70
2010	England	Wound swab	t011	PEN, OXA, TET	No	71
2011	England	Wound swab	t011	PEN, OXA, FUS, CIP, ERY, CLIND, GENT, TET, TRIM	Yes	71
2011	England	Wound swab	t011	PEN, OXA, GENT, TET, TRIM	Yes	71
2013	England	Wound swab	t011	PEN, OXA, TET	No	72
2013	England	Sputum	t011	PEN, OXA, CIP, CLIND, ERY, GENT, TET, TRIM	Yes	72
2013	England	Sputum	t899	PEN, OXA, CIP, ERY, TET, TRIM	Yes	72
2013	England	Screen swab	NS	PEN, OXA, ERY, CLIND, TET	Yes	69

PEN = penicillin; OXA = oxacillin/cefoxitin; TET = tetracycline; TRIM = trimethoprim; CLIND = clindamycin; ERY = erythromycin; CIP = ciprofloxacin; FUS = fusidic acid; GENT = gentamicin; MDR = multi-drug resistant; NS = not stated

3.2.4.5 Control measures in place to reduce risk of transmission

The UK government has published two leaflets which provide information and guidance on LA-MRSA for those who work with livestock or in abattoirs, available at: <https://www.gov.uk/government/publications/la-mrsa-information-for-people-who-work-with-livestock>.

The FSA has published a risk assessment of MRSA in the UK food chain with particular focus on LA-MRSA. FSA advice regarding LA-MRSA was “*that raw food should be stored appropriately, handled hygienically and cooked thoroughly. In combination, these measures should be sufficient to ensure that any harmful bacteria present are destroyed.*”

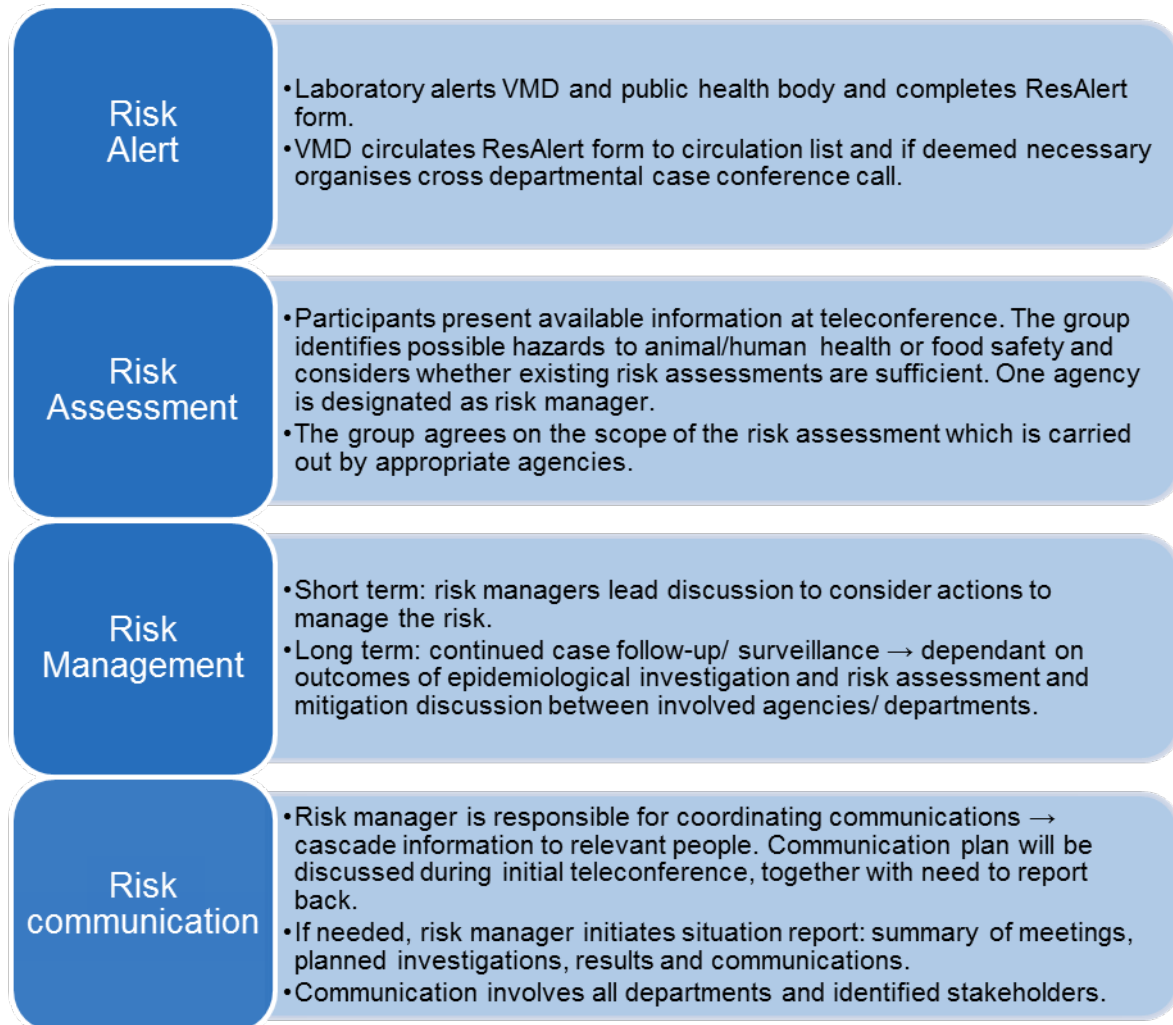
PHE and its predecessor organisation the Health Protection Agency have issued alerts to improve awareness of LA-MRSA by diagnostic laboratories⁷³. Sharing of WGS data from UK government agencies has been initiated to identify possible sources and/or transmission events involving CC398 LA-MRSA across the One Health landscape.

3.2.4.6 Concluding remarks

Currently, insufficient data are available to establish detailed prevalence of LA-MRSA in the various domains (e.g. livestock, food, humans) in the UK. Occasional reports of CC398 LA-MRSA across multiple animal species combined with its detection in the food chain and in humans, suggest it is present in the different populations; however further monitoring activities will be needed to establish the extent of its dissemination within and between populations.

ResAlert – One Health approach to AMR risk management

ResAlert refers to the coordinated UK-wide response to the identification of a resistant bacterial isolate from an animal, considered to present a high risk for human and/or animal health. This system was initiated in early 2015. An overview of the four pillars of the response can be found below. The actions from each pillar do not necessarily take place in a linear fashion; in particular risk communication, which is a continuous process. The VMD coordinates the ResAlerts, in collaboration with governmental agencies covering human and animal health, food safety, and the Devolved Administrations. ResAlerts processed during 2015–2017 are listed in the table below.



Micro-organism	Source (no. of ResAlerts 2015–2017)
Carbapenem-resistant <i>Klebsiella pneumoniae</i>	Seal (1)
ESBL-producing <i>E. coli</i>	Chicken (1)
LA-MRSA	Pig (7); pheasant (1); bovine (1); turkey (1)*
Ciprofloxacin-resistant <i>Salmonella</i> Kentucky	Broiler chicken (1); raw pet food (1)
<i>Salmonella</i> Infantis (risk due to persistence)	Laying hen (1)
Colistin-resistant <i>Salmonella</i> Typhimurium var Copenhagen	Pig (1)
ESBL-phenotype <i>Salmonella</i> Oslo	Horse (1)

* These results differ from Table 4 due to the tables representing a different time period.

Chapter 4: Antibiotics and AMR in the environment

The UK Five Year AMR Strategy 2013–2018 acknowledged the need for more research to increase understanding of the significance of the different resistance transmission pathways between the environment, humans and animals¹.

There is no structural, statutory surveillance dedicated to assessing the level of AMR in the environment in the UK. However, the following initiatives provide useful insight into the issue:

- The EU Water Framework Directive includes a list of potential water pollutants that must be carefully monitored in surface waters by the EU MSs to determine the risk they pose to the aquatic environment. This Watch List of substances includes the macrolides erythromycin, clarithromycin and azithromycin, the β -lactam amoxicillin and the fluoroquinolone ciprofloxacin. Monitoring for presence of antibiotics in surface waters will provide valuable data for future research of AMR in the environment.
- In England there is the Reduction and Prevention of Agricultural Diffuse Pollution (England) Regulations 2018, intended to reduce and prevent the pollution of waters from diffuse agricultural sources. Although this regulation is not specifically intended to reduce AMR levels in water, this may be a side effect if there is a reduction in pollution of water from agricultural sources potentially containing antibiotic residues or AMR determinants.
- Some of the work performed to increase understanding of antibiotic residues and AMR determinants in the environment includes the UK Water Industry Research's (UKWIR) Chemicals Investigation Programme Phase 2 (CIP2), which runs from 2015 until 2020. CIP2 samples over 600 UK sewage treatment plants, including samples of river water upstream and downstream of the plant discharge as well as samples of effluent, covering 74 substances. Preliminary findings of the programme mention that data from CIP2 suggest some antibiotics found in water are of potential concern^{u,74}. Findings from the first phase of the CIP showed a high variability in the removal of active pharmaceutical ingredients between and within plants. Among the substances which were less substantially reduced in concentration were macrolide antibiotics, which were present in effluents at a higher concentration than the estimated 'predicted no effect concentrations'. Phase 3 of CIP is now being planned and will focus on various aspects of AMR across water treatment works following on from the previous phases.

In terms of future work, in 2018 a network comprising 23 partners (including the UK Government agencies APHA, Cefas, Environment Agency, PHE and VMD) from 15 countries (including Low and Middle Income Countries) was awarded funding from the Joint Programming Initiative on AMR. The network aims to identify robust, measurable surveillance indicators and methodologies for assessing environmental AMR levels^v.

As part of the next UK AMR National Action Plan, developing an improved evidence base on AMR in the environment will be an area of importance for the UK over the next five years.

^s <https://eur-lex.europa.eu/legal-content/EN/TXT/?uri=CELEX%3A32018D0840>

^t <http://www.legislation.gov.uk/ukxi/2018/151/contents/made>

^u <https://ukwir.org/the-chemicals-investigation-programme-phase-2,-2015-2020>

^v <https://www.jpamr.eu/supportedprojects/7th-call-results/>

Chapter 5: Discussion

The One Health Report presents data on antibiotic use in human and veterinary medicine, and on antibiotic resistance in key pathogens isolated from food-producing animals, retail meat and humans, with a view to assess the occurrence of resistance along the food chain. In addition, it adds context to the presented 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.

The report shows that substantial reductions have been achieved in antibiotic use in 2017 across the animal and human sector since the publication of the first UK One Health Report in 2013, with 35% reduction in total sales (in tonnes) of antibiotics for use in animals (in food-producing animals, the reduction in mg/kg is 40%), and 6% reduction in antibiotics prescribed in human medicine.

The reductions in the animal sector highlight how the food-producing animal sectors, including producers, their representative bodies and veterinarians, have taken robust action to address the threat of AMR. Actions have included improvements with regard to animal health and welfare plans, focusing on disease prevention (e.g. through vaccination), biosecurity, husbandry, cleaning and disinfection, nutrition and promoting responsible antibiotic use. In addition, animal livestock sectors have shown willingness to accept change, seek innovation and share best practice. In addition, several animal sectors (e.g. cattle, sheep, meat poultry, laying hens, pigs) have voluntarily banned or severely limited the use of HP-CIAs¹⁰.

In the human sector, the reduction in antibiotic use reflects improved focus on antibiotic stewardship activities and the impact of national quality improvement schemes, as well as professional training and public engagement.

Since the publication of the previous One Health Report, a lot of activities have taken place under the umbrella of the One Health approach. There is continuing close collaboration between the animal and human health domains, for example through research into ESBL-producing *E. coli* in animals, humans and food (see text box on p.45), the response to the discovery of *mcr-1*-mediated colistin resistance (see text box on p.10), and the coordinated UK-wide response to the identification of resistant bacterial isolates from animals considered to present a high risk for human and/or animal health (ResAlert; see text box on p.51). In addition, harmonised surveillance indicators developed by ECDC, EFSA and EMA have been used for this report, showing progress in reducing antibiotic use and AMR in both food-producing animals and people.

The previous years have also seen joint presentations at conferences and shared workshops on antibiotic use and resistance. Cross-government agencies continued to be actively involved in promoting antibiotic stewardship across domains, for example through the Antibiotic Guardian campaign and coordinated actions to raise awareness during European Antibiotic Awareness Day and World Antibiotic Awareness Week (see text box on p.20). Governmental organisations from both the animal and human domains are involved in international work, for example through the One Health European Joint Programme, the Joint Programming Initiative on AMR and the Fleming Fund.

However, there is also room for improvement and further enhancements to the One Health approach in order to tackle the issue of AMR. The UK AMR Strategy 2013–2018 included as one of the key areas for future action in its UK Commitment to Action “*better access to and use of surveillance data in human and animal sectors through new arrangements that facilitate greater consistency and standardisation of the data collected across the system and encourage improved data linkage*”. Despite efforts to harmonise and standardise methodology across domains, this has not happened to the extent needed to draw relevant conclusions from the data currently available.

Recording of data that allow comparison is recommended, in addition to identifying drug-bug combinations of importance to both veterinary and human medicine.

Harmonisation is lacking in various ways. For example, laboratory methodologies vary between UK countries and domains, data on AMR are not routinely collected across different sectors (for example, currently there are no routine surveillance data available on *Salmonella* spp. and *Campylobacter* spp. in retail meat, nor is routine surveillance implemented on AMR in the environment), and the panel of antibiotics for which resistance is tested differs between isolates obtained from animals, humans and food. Improved integration of surveillance on AMR should take place at all levels and cover not only data collection but also data analysis, interpretation and reporting of results. Communication between the various organisations involved in the UK surveillance on antibiotic use and resistance (such as government departments, laboratories, competent authorities) needs to be further strengthened.

As highlighted above, data on AMR included in this report are not fully comparable across domains, mainly due to differences in methodologies used for assessing susceptibility to antibiotics. It is clear though that the level of bacterial resistance has reduced between 2013 and 2017 for the majority of antibiotics tested in bacteria from healthy food-producing animals at slaughter. The level of decreased antibiotic susceptibility in bacterial isolates obtained from meat at retail appears higher than the levels reported in animals at slaughter. This may indicate that cross-contamination occurs during processing of meat, leading to greater resistance prevalence and highlighting the importance of campaigns on safe food preparation both at home and in restaurants.

The data included in this report show that the level of antibiotic use in food-producing animals and humans has decreased over recent years. The decrease in the levels of resistance in bacterial isolates obtained from healthy animals at slaughter coincides with the decrease of antibiotic use, while antibiotic resistance in human medicine has remained generally stable. A systems map was developed by DHSC and Defra, outlining the links between the various domains and highlighting the complexities behind AMR (Figure 23). The lack of harmonisation and integration across systems hampers the understanding of the complexity of AMR and the factors influencing the development and spread of resistance. More work is needed to improve the understanding of the relative contribution of the different sectors as well as the routes and pathways to the development, transmission and persistence of resistance within and between domains. This would enable the development of evidence-based targeted interventions aiming at tackling the issue of AMR as part of a One Health approach.

Data quality needs to be improved in all sectors, for example in terms of coverage, granularity and validation. Future One Health Reports should seek to include estimates on the number of people and animals treated each year. To obtain these estimates, more insight would be needed into dosing and treatment duration, which would need to come from animal/patient-level prescription data. Preferably, integrated, meaningful indicators to monitor progress on AMR and antibiotic use across domains should be developed. Ideally, future One Health Reports should also include data on antibiotic use and resistance in companion animals and horses. It should be explored what data are available on antibiotic use in companion animals and horses and whether a standardised national denominator could be established so that data from companion animals and horses could be analysed to the same level as data from food-producing animals.

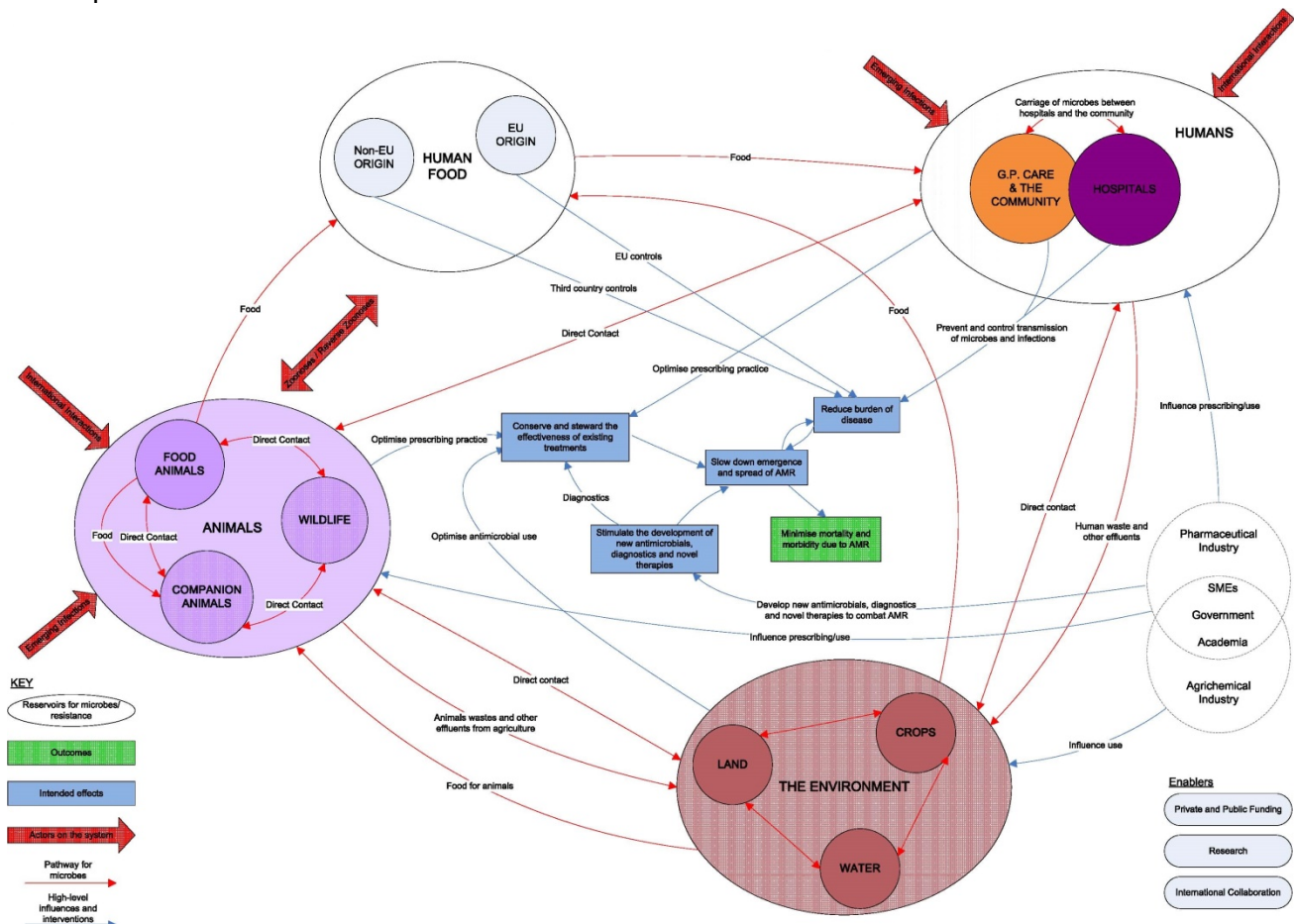
The need for including data on AMR from a wider range of bacteria (such as bacteria included in the WHO priority list that are of relevance to animal health) should also be explored. Joint horizon scanning and response to emerging risks from AMR should be a continuous process to review and revise the surveillance needs across domains. New tools and methodologies (such as whole

genome sequencing) are becoming increasingly available, which will add to the knowledge base as they provide new insights into resistance, resistance relatedness and provenance, and resistance mechanisms.

The years following the publication of the UK Five Year AMR Strategy 2013–2018¹ have provided a preview of what can be achieved when a cross-government One Health approach is applied in the fight against AMR. This work needs to be continued and further expanded, and the One Health approach needs to be further strengthened, specifically by connecting environment, food, animals and humans with contributions from the different government departments, as well as counterparts from the Devolved Administrations to work together in the fight against AMR. In January 2019, the UK Government published a new five-year National Action Plan to tackle AMR⁷⁵ alongside its twenty-year Vision in which AMR is contained and controlled by 2040⁷⁶. Building on the considerable achievements made during the previous UK AMR Strategy, the plan sets out challenging ambitions and actions for the next five-years taking a One Health approach for delivery.

In order to combat AMR appropriately and effectively, concerted collaborative efforts are necessary across the human health, veterinary medicine, food and environment sectors. A truly One Health approach must involve partnerships between those working at the interface of multiple related disciplines and will be crucial to ensuring a robust response to the threat of AMR at local, regional and global level. These approaches will bring future improvements and actions that will result in further progress against the threat of antimicrobial resistance.

Figure 23: AMR systems map: influences on the development of AMR at top level, taken from ‘Antimicrobial Resistance (AMR) Systems Map Overview of the factors influencing the development of AMR and the interactions between them’⁷⁷



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Annex C *Salmonella* serovars

Annex Table C1: Top ten most isolated *Salmonella* serovars in the UK in humans and animals (cattle, sheep, pigs, chickens, turkeys and ducks), 2013 and 2017⁴⁰.

Humans*			Animals		
Rank	2013	2017	Rank	2013**	2017
1.	Enteritidis	Enteritidis	1.	Dublin	Dublin
2.	Typhimurium	Typhimurium	2.	Mbandaka	Derby***
3.	Infantis	Typhimurium – monophasic	3.	Montevideo	Mbandaka
4.	Newport	Newport	4.	Senftenberg	Senftenberg
5.	Virchow	Infantis	5.	Kedougou	Kedougou
6.	Kentucky	Agona	6.	Derby***	13,23:i:-
7.	Stanley	Stanley	7.	Indiana	Typhimurium
8.	Agona	Kentucky	8.	13,23:i:-	Montevideo
9.	Java	Virchow	9.	Typhimurium	Indiana
10.	Montevideo	Java	10.	Orion	Give var. 15+

* All isolates: blood, urine and faecal; ** Isolates from England, Wales and Scotland only; *** Includes presumptive *S. Derby*.

Annex D Recommendations 2015 UK One Health report

Recommendation 1

Public health organisations should work with clinical laboratory colleagues to ensure that all *Salmonella* species are sent to the relevant reference laboratories for speciation and antibiotic susceptibility testing. The referral form should include data on foreign travel, including countries visited, in the previous four weeks.

Recommendation 2

Public health organisations should scope the development of a national sentinel surveillance system for *Campylobacter* isolates collected from human infections. In addition, public health organisations should highlight the importance of identifying *Campylobacter* to a species rather than genus level, as different species have different antibiotic profiles.

Recommendation 3

Public health organisations should support the work of professional organisations to transition UK clinical laboratories to a single standardised nationally agreed methodology for routine antibiotic testing in 2016.

Recommendation 4

Public health organisations should work with professional organisations to develop guidance related to recommended antibiotic and bacterial combinations, which should be tested and reported by clinical laboratories for key One Health pathogens. Animal health organisations should review the antibiotics tested from clinical veterinarian samples and through the EU harmonised monitoring in animals to align with key antibiotics required for human treatment.

Recommendation 5

Human public health reference laboratories should follow the EU protocol for harmonised monitoring of antibiotic resistance in human *Salmonella* and *Campylobacter* isolates.

Recommendation 6

Public health organisations should explore data available on human sales of antibiotics from manufacturers and holders of human antibiotic marketing authorisations.

Recommendation 7

The Veterinary Medicines Directorate (VMD) will conduct carbapenem resistance monitoring (as part of the EU monitoring and reporting of antibiotic resistance in zoonotic and commensal bacteria in accordance with the EU legislation, Commission Decision 2013/652/EU), a year earlier than mandated.

Recommendation 8

VMD will participate in the protocol development of the European Surveillance Veterinary Antibiotic Consumption (ESVAC) project to collect farm level data from the pig sector; and investigate and facilitate options for collecting accurate antibiotic consumption data at an individual farm level.

Recommendation 9

Public and professional One Health activities should be enhanced through engagement with the European Antibiotic Awareness Day (EAAD) campaign and aligning training programmes for human and animal health professionals.

Recommendation 10

The human and animal surveillance bodies should produce a further report in two years, encompassing robust data collected by the Food Standards Agency (FSA) on the burden of AMR in imported food animals.

Annex E Sources and caveats/limitations of consumption data

Human data

Human antibiotic prescribing is based on the data submitted by the UK to the [European Antimicrobial Consumption Surveillance Network \(ESAC-Net\)](#). Data were collected for community (primary care) and hospital (secondary care and tertiary care) as the number of Daily Defined Doses (DDD) per the WHO's [Anatomical Therapeutic Chemical \(ATC\)](#) classification substance and route of administration. For the purpose of this report, antibiotics for systemic use and intestinal antibiotics ([ATC] groups J01, A07AA) were included, expressed as tonnes of active compound. Data were not available from private prescriptions dispensed in the community and private hospitals. Primary care data are available at a patient level in Scotland, Wales and Northern Ireland and aggregated at a General Practice level in England. Hospital data are aggregated dispensed data to wards and patients.

The WHO's ATC classification system was also used for assigning weights of active ingredient.

Animal data

Annual sales data of all authorised antibiotic veterinary medicinal products are provided to VMD by the marketing authorisation holders, in accordance with the Veterinary Medicines Regulations 2013 (S. I. 2013 No. 2033), schedule 1, paragraph 31 (3a). The weight of active substance sold is an exact measurement following from the quantitative composition of active ingredient for each product and the number of units sold. For the purpose of this report, antibiotics of ATCvet groups QJ01, QJ51 and QA07AA were included. Sales of dermatological preparations and preparations for sensory organs are not included.

It is not possible to calculate accurate data on antibiotic sales at the animal species level or production category from the overall sales data, as antibiotic veterinary products often are authorised for use in more than one animal species and therefore it is not possible to know in which species the product sold was used.

Use based on sales data is often over estimated as for example not all antibiotics sold will be used (due to natural wastage, or reaching expiry date), or some products are sold to UK feed mills which exports the feed after adding those products.

Medicinal products sold for use in humans but used in animals according to the prescribing cascade are not included in the overall sales data.

Annex F Methodology AMR data

Human data

Human clinical specimens tested in clinical diagnostic laboratories are grouped into 14 day-patient-organism episodes, where follow-up specimens (where the same organism is identified) within 14 days are excluded. Antibiotic susceptibility tests are collated and the most resistant result for an antibiotic within that 14 day episode is retained. Clinical diagnostic laboratories use clinical breakpoints to determine a susceptibility result of 'susceptible', 'intermediate' or 'resistant', as determined according to test method and published breakpoints (EUCAST, BSAC or CLSI), manual laboratory methods (e.g. disc diffusion) or automated diagnostic systems (e.g. Vitek). Results are presented as 'non-susceptible' which is the sum of those that are resistant and those that are reported as intermediate.

The reference laboratories assess resistance according to clinical breakpoint, as well as using epidemiological cut offs (ECOFF). Harmonised monitoring of *Salmonella* and *Campylobacter* spp. from human samples within the EU determines which breakpoints are used for international publication.^w

UK reports to ECDC for the annual zoonoses report used within the international comparison summaries are made by the reference laboratory. Data for the harmonised indicators were obtained from the ECDC Surveillance Atlas reflecting UK data through the Ears-Net surveillance programmes. This surveillance does not include all laboratories within the UK.

England

Data on microorganism and antibiotic susceptibility for England were obtained for routine diagnostic specimens from the PHE national communicable disease and antibiotic resistance reporting system SGSS (Second Generation Surveillance System)⁷⁸. Data on blood (*Campylobacter* spp. and *E. coli*) and faecal (*Salmonella* spp. and *Campylobacter* spp.) specimens were obtained from the communicable disease reporting (CDR) module of SGSS. Additional *Campylobacter* and *Salmonella* information was obtained from the PHE Gastrointestinal Bacteria Reference Unit (GBRU) based on samples referred to the Unit.

Campylobacter isolates are sent to the reference laboratory when there is a public health response to a potential outbreak or where the clinical laboratory wishes to identify at species level and confirm antibiotic susceptibilities. Less than 1% of clinical *Campylobacter* isolates are sent to the reference laboratory.

Scotland

Microorganism and antibiotic susceptibility testing data were obtained from all clinical diagnostic laboratories in Scotland and participating reference laboratories via ECOSS (Electronic Communication of Surveillance in Scotland), an electronic data link from microbiology laboratories to Health Protection Scotland (HPS).

Faecal samples are not routinely received by HPS, sample size is therefore very small and susceptibility data are not representative of national data. During 2016 ampicillin susceptibility testing changed to the combination ampicillin/amoxicillin

^w <https://ecdc.europa.eu/sites/portal/files/media/en/publications/Publications/antimicrobial-resistance-Salmonella-Campylobacter-harmonised-monitoring.pdf>

For *Salmonella* blood samples, the only cephalosporin tested is cefotaxime, and no carbapenem (meropenem/imipenem) is tested.

Northern Ireland

Northern Ireland microorganism and antibiotic susceptibility data were retrieved from CoSurv, the electronic system by which all clinical diagnostic laboratories in Northern Ireland reported voluntarily to the Public Health Agency from their own laboratory information systems.

E. coli blood isolate susceptibility information is only available for ciprofloxacin and gentamicin

Wales

Microorganism and antibiotic susceptibility data for Wales were retrieved from the Welsh DataStore systems. DataStore collects all data stored on the hospital information systems and maps into a pseudo-anonymised standardised format.

Salmonella information was obtained from the PHE GBRU based on samples referred to the Unit. Susceptibility information for faecal isolates in 2017 was not available at time of compilation.

Animal data

EU harmonised AMR monitoring

In accordance with the EU harmonised AMR monitoring (as set out in Commission Implementing Decision 2013/652/EU) the UK government monitors antibiotic resistance in zoonotic and commensal bacteria from healthy food-producing animals at slaughter and fresh meat at retail. Samples are collected at alternating years for poultry (turkey and broilers) and pig populations. This is a programme carried out in the UK and data collected through this programme are considered to be more relevant to public health and better reflect the potential exposure of humans to AMR from animals and food.

VMD is the national competent authority for AMR in animals and therefore coordinates the EU harmonised monitoring for the UK. FSA personnel collect the samples for monitoring *E. coli* and *C. jejuni* at the slaughterhouse for England, Scotland and Wales and at retail for the UK; DAERA coordinates the caecal sample collection in Northern Ireland. Samples are subsequently tested and analysed by APHA for England, Scotland and Wales and by AFBI for Northern Island. Retail samples obtained for specific monitoring of ESBL-/AmpC-/carbapenemase-producing *E. coli* are tested by APHA for the UK, *Campylobacter* spp. isolated from retail meat were tested by PHE laboratories.

E. coli are isolated (n = 170 for each animal species) from caecal samples at slaughter. In addition, specific samples from caecal contents at slaughter and fresh meat at retail (n = 300 for each animal species and type of sample) are tested for presence of ESBL-/AmpC-/carbapenemase-producing *E. coli*. *C. jejuni* are isolated (n = 170 for each animal species) from caecal samples from broilers and fattening turkeys.

Susceptibility testing is performed against a panel of antibiotics defined by the EU and using a standardised broth microdilution method. In addition, samples collected for specific ESBL-/AmpC-/carbapenemase-producing *E. coli* monitoring are cultured on MacConkey agar + 1 mg/L cefotaxime to isolate ESBL-/AmpC-/carbapenemase-producing *E. coli*, on CHROMagar to isolate ESBL-producing *E. coli*, and onto chromID CARBA and chromID OXA-48 agars to isolate carbapenemase-producing *E. coli*. *E. coli* isolates from samples collected in GB are also cultured on MacConkey agar + 2 mg/L colistin.

Salmonella isolates are obtained from boot swabs/dust samples collected on farm for each population of laying hens, broilers and fattening turkeys under the National Control Plan and sent to APHA for further testing. In addition, carcass neck skin samples of broilers and fattening turkeys and carcass swabs from pigs are taken by food business operators at slaughter. Private laboratories perform bacteriological culture on these samples for presence of *Salmonella* and are asked to submit isolates to APHA for serotyping and antibiotic susceptibility testing.

Susceptibility is interpreted using EUCAST human clinical break point (CBP) values and EUCAST epidemiological cut-off values (ECOFFs).

Clinical surveillance

In addition to the EU harmonised AMR monitoring, the UK performs passive surveillance which evaluates AMR in veterinary pathogens isolated from diagnostic samples from field cases of clinical disease undergoing investigation. The samples are submitted by private veterinary surgeons to APHA veterinary laboratories in England and Wales for identification of a potential bacterial pathogen and subsequent susceptibility testing to provide the veterinarian with relevant information for treatment. Similar programmes are conducted in Scotland (SRUC Veterinary Services) and Northern Ireland (AFBI). This surveillance programme also includes susceptibility testing of *Salmonella* isolates recovered from animals and their environment in GB, as part of the UK Zoonoses Order 1989.

In principle, susceptibility testing is performed using a disc diffusion method on Iso-Sensitest Agar (Oxoid) with appropriate media supplementation, where necessary, for fastidious organisms, following guidelines by the British Society for Antibiotic Chemotherapy (BSAC). Resistance is determined using BSAC human clinical breaking points. When no published BSAC breakpoints are available, historical APHA veterinary breakpoints are used. Clinical isolates obtained under the framework of the clinical surveillance programme are tested for resistance using a disc diffusion method; since 2016 APHA routinely implements a pre-diffusion method to test for colistin resistance.

Food data

EU harmonised AMR monitoring in retail meat

The European Commission has set-up a 7-year mandatory Member State surveillance (2014-2020) for antibiotic resistance in specific pathogens in food-production animals within slaughterhouse environments. The FSA is leading on an additional component of this survey by analysing retail meats (beef, pork and poultry) in the UK for ESBL-, AmpC- and carbapenemase-producing *E. coli*. Testing for colistin resistance and the colistin resistance genes (*mcr-1*, *mcr-2*) has also been included since January 2016. As the FSA is undertaking this survey on behalf of the EC, the Commission's Decision in relation to scope, sampling methodology, analytical methods and reporting of data must be adhered to.

Although the survey commenced in 2014, there was no requirement to take retail samples for AMR in the first year. The sampling regimes are outlined below:

- 300 beef and 300 pork retail samples to be collected/tested in 2015, 2017 and 2019.
- 300 poultry meat retail samples to be collected/tested in 2016, 2018 and 2020.

Sampling represents 80% retail market share and 80% population coverage of the four countries of the UK; sampled proportionally throughout the full year. Analysis requires initial isolation and enrichment of *E. coli* from all meat samples, prior to testing for AMR *E. coli*. Analysis is performed in a step-wise process against a two-tier panel of antibiotic agents depending on the presence of positive isolates. Data collected by the testing facility is submitted to the EFSA on an annual basis

in May following each year of completion; aggregated to UK datasets with no identification of retail names or product brands.

AMR *Campylobacter* Retail Chicken Survey

The FSA has carried out several microbiological surveys of *Campylobacter* contamination in fresh whole UK-produced chilled chickens at retail sale. As part of this survey, a subset of the *Campylobacter* isolates collected has been tested for their resistance to a range of antibiotic agents.

A first overall survey tested 4,011 samples of whole, UK-produced fresh chicken during the period February 2014 to March 2015 (Year 1). The samples were evenly distributed throughout the year and the UK (in proportion to population size of each country), and testing was performed by six laboratory sites. Retailers were sampled in proportion to their market share, according to available data, with their share of free range, organic and standards chickens taken into account.

A subset (283) of the *Campylobacter* isolates was tested for antibiotic resistance. These were selected as every tenth isolate (or next viable isolate) but selection was adjusted to ensure adequate representation of producer premises and retailers. All recoverable organic and free range chicken isolates were included. The objective of the AMR analysis was to establish the proportion of *C. jejuni* and *C. coli* strains isolated from Year 1 of the retail chicken survey that were resistant to a range of antibiotic agents relevant to public health.

To determine resistance, Iso-Sensitest Agar with the addition of 5% horse blood containing specified breakpoint concentrations of antibiotics was used. An isolate suspension was made in brain heart infusion broth to McFarland 0.5 turbidity and was inoculated onto the surface of each of the antibiotic containing agars. An isolate was considered resistant if it grew on the agar and scored susceptible if there was no growth, and the corresponding antibiotic free plate showed pure growth from the suspension. AMR profiles were determined using the following antibiotics and concentrations as described in ²⁵:

Chloramphenicol	8 mg/L, 16 mg/L
Ciprofloxacin	1 mg/L (CpL), 5 mg/L (CpH)
Erythromycin	4 mg/L (EryL), 16 mg/L (EryH)
Gentamicin	1 mg/L, 2 mg/L, 4 mg/L (GH)
Kanamycin	16 mg/L (K)
Nalidixic acid	16 mg/L (NalL), 32 mg/L (NalH)
Neomycin	8 mg/L (Ne)
Streptomycin	2 mg/L (SL), 4 mg/L (SH)
Tetracycline	2 mg/L (TetL), 8 mg/L (TetH), 128 mg/L (TetH)
Trimethoprim	2 mg/L

A second survey (Year 2) tested 2,998 samples of whole, UK-produced fresh chicken during the period July 2015 to March 2016. A pilot study was also carried out from April 2016 to July 2016 to assess a new sampling methodology. Approximately 416 chilled chickens were sampled and tested during this pilot period. The samples for the main survey were evenly distributed throughout the year and the UK, and retailers were sampled with their share of free-range, organic and standard chickens taken into account.

A subset (548) of the *Campylobacter* isolates was tested for antibiotic resistance. These were selected as every tenth isolate (or next viable isolate) but selection was adjusted to ensure adequate representation of producer premises and retailers. All recoverable organic and a high proportion of free range chicken isolates were included.

To determine resistance, Muller Hinton Agar with the addition of 5% horse blood containing specified breakpoint concentrations of antibiotics was used. An isolate suspension was made in

sterile saline to McFarland 0.5 turbidity and was inoculated onto the surface of each of the antibiotic containing agars. An isolate was considered resistant if it grew on the agar and scored susceptible if there was no growth, and the corresponding antibiotic free plate showed pure growth from the suspension. AMR profiles were determined using the epidemiological cut-off (ECOFF) values as recommended in the ECDC EU protocol for harmonising monitoring of AMR in human *Salmonella* and *Campylobacter* isolates³³

Annex G Caveats/limitations of AMR data

Human data

The four UK health administrations have similar methods for data collection of antibiotic resistance in human isolates, although there are differences in how these are managed. For the majority of bacteria resistance is collected through passive surveillance systems, collecting microbiology results from clinical laboratories. Additional information is collected through reference laboratory surveillance. Over 70% of *E. coli* bacteraemia and *Salmonella* infections have antibiotic susceptibility testing results available. However, less than 50% of *Campylobacter* isolates have susceptibility testing and where this is performed it is predominantly limited to erythromycin and ciprofloxacin. Less than 1% of *Campylobacter* isolates are sent to the Reference laboratory, where they are tested against a wide array of antibiotics.

Different antibiotic susceptibility testing methodologies are used in England and Wales, Scotland, and Northern Ireland. England, Wales and Scotland utilise the BSAC/EUCAST methodology to determine resistance/susceptibility to an antibiotic based on human clinical breakpoints, whilst in Northern Ireland, an accredited CLSI method utilising different antibiotic concentrations is used for testing. The amalgamated results of such UK wide monitoring should be interpreted with caution. There was a phased transition by the Scottish diagnostic laboratories from CLSI to EUCAST breakpoints in 2012 – 2013. In Wales, all microbiology laboratories are currently moving to EUCAST AST methodology and previously used BSAC methodology.

Testing for presence of ESBL and/or AmpC is not routinely undertaken in clinical laboratories, but rather some laboratories with capacity will test for presence if key criteria have been met (such as patient risk factors and phenotypic resistance profile of the specimen). This selective testing increases the likelihood of ESBL and/or AmpC presence in the subset tested.

Campylobacter AMR from human samples presented within this report combines faecal and blood isolate reports. AMR in *Salmonella* isolates from human samples presented in this report are from faecal samples only. Resistance summaries in *E. coli* human isolates use blood samples only. Additional detail on specimen type and antimicrobial are available in Annex Tables F1–2.

Annex Table F1: Antimicrobial susceptibility test data by sample type and pathogen by devolved administration (England [E]; Northern Ireland [NI]; Scotland [S]; Wales [W])

	<i>Campylobacter</i> sp.								<i>Campylobacter coli</i>								<i>Campylobacter jejuni</i>							
	Blood				Faecal				Blood				Faecal				Blood				Faecal			
	E	NI	S	W	E	NI	S	W	E	NI	S	W	E	NI	S	W	E	NI	S	W	E	NI	S	W
Ciprofloxacin	*	*	*		*	*	*						*	*	*					*	*	*		
Nalidixic acid	*		*		*	*	*						*	*	*					*	*	*		
Erythromycin	*	*	*		*	*	*						*	*	*					*	*	*		
Gentamicin	*		*		*	*	*						*	*	*					*	*	*		
Streptomycin	*		*		*	*	*						*	*	*					*	*	*		
Chloramphenicol	*		*		*	*	*						*	*	*					*	*	*		
Tetracyclines	*		*		*	*	*						*	*	*					*	*	*		

Annex Table F2: Antimicrobial susceptibility test data by sample type and pathogen by devolved administration (England [E]; Northern Ireland [NI]; Scotland [S]; Wales [W])

	<i>Salmonella</i> spp.								<i>Escherichia coli</i>							
	Blood				Faecal				Blood				Faecal			
	E	NI	S	W	E	NI	S	W	E	NI	S	W	E	NI	S	W
Amikacin					*	*										
Ampicillin					*	*	*		*		*					
Cefotaxime					*	*	*		*		*					
Cefoxitin					*	*										
Ceftazidime					*	*			*		*					
Chloramphenicol					*	*	*		*		*					
Ciprofloxacin					*	*	*		*	*	*					
Colistin					*	*			*		*					
Ertapenem					*	*										
Erythromycin					*	*			*		*					
Gentamicin					*	*	*		*		*					
Meropenem					*	*			*		*					
Nalidixic acid					*	*	*		*		*					
Neomycin					*	*										
Streptomycin					*	*	*									
Sulphonamides					*	*	*		*		*					
Tetracycline					*	*	*		*		*					
Tigecycline					*	*			*		*					
Tobramycin					*	*										
Trimethoprim					*	*	*		*		*					

Animal data

The ECOFF represents the value where bacteria have developed a higher level of resistance to that antibiotic than the background level of resistance that exists naturally for that bacterial species; this does not necessarily correspond with likelihood of clinical treatment failure.

The use of selective culture methods leads to a greater sensitivity for assessing occurrence of ESBL-, AmpC- and carbapenemase-producing *E. coli* than the use of non-selective culture methods. Selective methods are used to detect low numbers of resistant *E. coli*, but do not permit quantitation

Only small numbers of *Salmonella* isolates originating from neck skin samples taken by food business operators are tested for susceptibility, and these results are not likely to be representative and should be interpreted with caution.

Sampling performed under the clinical (passive) surveillance system, is not considered representative for the general livestock population and results should be interpreted with caution. It should be noted that these *E. coli* are isolated from samples from field cases and tested for diagnostic purposes, meaning that these are most often isolated from sick animals. It is unknown whether these samples are collected pre- or post-treatment, and these results should be interpreted with caution. This is a biased population and cannot be considered to accurately reflect the bacterial populations present within the general animal population in the UK. Further, veterinary surgeons have the option to submit samples to private laboratories. The proportion of samples that

Government laboratories test compared to other laboratories is not known, and therefore representativeness of the samples processed by APHA, SRUCVS, and AFBI is unknown.

Geographical proximity of a farm or veterinary practice to a Government diagnostic laboratory has an impact on the submission rate of samples; clinical surveillance may therefore over-represent the animal populations within certain geographical areas.

The levels of resistance demonstrated by the clinical surveillance isolates presented in this report may be higher than those seen in the wider bacterial populations present within animals in England and Wales. This is because samples from diseased animals may be submitted from animals that have been unresponsive to initial antibiotic therapy, and thus the isolates recovered may have already been exposed to antibiotic pressure(s). Isolates from companion animals, which are submitted to APHA are only investigated for antibiotic resistance if there is a public health concern, and therefore bacteria from these animal groups are under-represented in this report. The veterinary clinical surveillance data detail the number of bacterial isolates that underwent susceptibility testing, but not the numbers of animals for which samples were submitted for examination. Several bacteria may have been cultured from an individual animal or from a group of animals on the same farm. This type of clustering is not accounted for in the report, though since only low numbers of bacteria are usually subjected to susceptibility testing from the same outbreak of disease, its importance is probably limited.

The diagnostic tests performed on any sample received through the clinical surveillance programme are dependent on the individual case; i.e. isolates of the same bacterial species are not always tested against the same panel of antibiotics. Therefore, if resistance is not detected in one isolate, it may not mean that resistance is not present, just that it was not tested for. This is especially true of commensal organisms.

The breakpoints used for determining resistance for isolates recovered under the veterinary clinical surveillance programme in GB are those as recommended by BSAC. These breakpoints were originally determined for human medicine and their use in veterinary medicine is based on the assumption that the concentration of antibiotic at the site of infection is approximately the same in animals as it is in humans. Currently it is not known if this assumption is always correct.

Different antibiotic susceptibility testing methodologies are used in England & Wales (APHA), Scotland (SRUCVS), and Northern Ireland (AFBI). APHA and SRUCVS use BSAC methodology to determine resistance/susceptibility based on human clinical breakpoints, whilst AFBI use CLSI. In light of the different methodologies and breakpoints used, the amalgamated results of UK wide monitoring should be interpreted with caution.

For AST testing done by APHA, in the case of some veterinary drug/bug combinations a BSAC cut-off may not exist. In this case, APHA may have derived a tentative or suggested breakpoint or the historical veterinary breakpoint (zone size cut-off of resistant ≤ 13 mm) may have been used to define resistance.

E. coli isolates are not collected from routine samples from healthy livestock in Northern Ireland. Only clinical cases submitted for post-mortem investigation when colibacillosis, or similar diseases, will proceed to isolate pathogenic *E. coli*. AMR testing on *E. coli* isolates is mainly performed if samples are coming from less than 2-week old calves and animals with bovine mastitis.

With regards to *E. coli*, each organisation in the United Kingdom sets their own criteria for testing AMR in *E. coli* from clinically sick animals and these criteria are not uniform. This is pertinent to highlight as the selection of isolates for susceptibility testing based on age or other criteria can influence the result obtained.

Annex H Human biomass and Population Correction Unit

Human biomass

Data on the UK human population were taken from Population Estimates Summary for the UK, mid-2017, Office for National Statistics. The following body weights were used to estimate human biomass⁷⁹: a body weight of 70 kg was used for adults aged above 18 years, a body weight of 40 kg was used for children aged 4-17 years, a body weight of 12 kg for children aged 1-3 years and a body weight of 5 kg was used for infants aged 0- 12 months.

Population correction unit (PCU)

Trends in sales of antibiotics over time are determined by taking into consideration variations in the size and number of the animal population. This is achieved by using a population correction unit (PCU). The PCU is a technical unit of measurement formulated by the EMA and adopted by the ESVAC project to standardise sales data against an animal population denominator.

The PCU is calculated by multiplying a standardised average weight at time of treatment with the associated annual animal/slaughter numbers. The calculation also takes into account animals exported from the UK to EU countries for slaughter and imported from EU countries to the UK for fattening. These data are provided by ESVAC and obtained from Eurostat (statistical office of the EU) and TRACES (Trade Control and Expert System of the EU) and validated by reports supplied by Defra and Cefas. For more information on the calculation and the PCU, please see the document provided on the UK Government's website:

<https://www.gov.uk/government/publications/understanding-the-mgpcu-calculation-used-for-antibiotic-monitoring-in-food-producing-animals> and the ESVAC website:

<https://www.ema.europa.eu/en/veterinary-regulatory/overview/antimicrobial-resistance/european-surveillance-veterinary-antimicrobial-consumption-esvac#population>.

Annex I Highest Priority Critically Important Antibiotics for human and veterinary medicine

WHO – critically important antibiotics for human medicine

The WHO has developed criteria and subsequently applied these to rank antibiotic classes according to their importance in human medicine. The criteria are⁸⁰:

- *“The antimicrobial class is the sole, or one of limited available therapies, to treat serious bacterial infections in people.”*
- *“The antimicrobial class is used to treat infections in people caused by either: (1) bacteria that may be transmitted to humans from nonhuman sources, or (2) bacteria that may acquire resistance genes from nonhuman sources.”*

Antibiotic classes meeting both criteria are classified as critically important antibiotics for human medicine. Within this category certain antibiotics are subsequently classified as highest priority, and these are included in Annex Table I1.

AMEG – category 2

The Antimicrobial Advice *ad hoc* Expert Group (AMEG) of the EMA provided guidance on the impact on public health and animal health of the use of antibiotics in animals, and on the measures to manage the possible risk to humans. As part of this guidance the AMEG ranked the antibiotics classified by WHO as CIAs according to the degree of risk to man due to resistance development following use in animals, thereby taking a One Health approach^{4, 5}. If that risk was estimated to be higher, antibiotics were classed as category 2 (with category 1 being low or limited risk). These antibiotic classes are included in Annex Table I1. In this report the classification according to AMEG is used.

Annex Table I1: Overview of antibiotic classes classified as Highest Priority Critically Important Antibiotics (HP-CIAs) for human medicine by WHO and category 2 by the AMEG

WHO – HP-CIA	AMEG – category 2
Colistin	Colistin
Fluoroquinolones	Fluoroquinolones
Quinolones	
3 rd and 4 th generation cephalosporins	3 rd and 4 th generation cephalosporins
5 th generation cephalosporins	
Macrolides	
Ketolides	
Other polymyxins	
Glycopeptides	

WHO/England – AWaRE categories

The WHO recently updated the Essential Medicines List (EML) and classified key antibiotics into three categories (AWaRe): to improve access (Access), to monitor important antibiotics (Watch) and to preserve effectiveness of ‘last resort’ antibiotics (Reserve).

Adaptation of the AWaRe list for England was achieved using expert elicitation for the antibiotics that were not in the EML categories. In addition, given a national priority to reduce use of piperacillin/tazobactam and carbapenems, these were moved from Access into Watch and

Reserve categories respectively. In total, the status of 38 antibiotics was changed between the WHO AWaRe list and the adapted list for England (Annex Figure I1).

Annex Figure I1: Overview of antibiotic substances categorized according to AWaRE (Access, Watch, Reserve) according to WHO and PHE⁸¹

ATCname	ATC code	AWaRe WHO	AWaRe England	
amikacin	J01GB06	Access	Watch	Access
amoxicillin and enzyme inhibitor	J01CR02	Access	Watch	Watch
ampicillin combinations	J01CA51	Other	Access	Access
cefaclor	J01DC04	Other	Watch	Watch
cefadroxil	J01DB05	Other	Watch	Watch
cefalexin	J01DB01	Access	Watch	Watch
cefamandole	J01DC03	Other	Watch	Watch
cefazolin	J01DB04	Access	Watch	Watch
cefoxitin	J01DC01	Other	Watch	Watch
cefprozil	J01DC10	Other	Watch	Watch
cefradine	J01DB09	Other	Watch	Watch
ceftazidime and beta-lactamase inhibitor	J01DD52	Watch	Reserve	Reserve
cefuroxime	J01DC02	Other	Watch	Watch
chloramphenicol	J01BA01	Access	Watch	Watch
clindamycin	J01FF01	Access	Watch	Watch
doripenem	J01DH04	Watch	Reserve	Reserve
ertapenem	J01DH03	Watch	Reserve	Reserve
fosfomycin (oral)	J01XX01	Other	Access	Access
fusidic_acid	J01XC01	Other	Reserve	Reserve
imipenem	J01DH51	Watch	Reserve	Reserve
lymecycline	J01AA04	Other	Watch	Watch
meropenem	J01DH02	Watch	Reserve	Reserve
minocycline	J01AA08	Other	Watch	Watch
nalidixic_acid	J01MB02	Other	Watch	Watch
neomycin	J01GB05	Other	Access	Access
ofloxacin	J01MA01	Other	Watch	Watch
oxytetracycline	J01AA06	Other	Watch	Watch
piperacillin	J01CA12	Other	Access	Access
pivmecillinam	J01CA08	Other	Watch	Watch
pristinamycin	J01FG01	Other	Watch	Watch
quinupristin	J01FG02	Other	Watch	Watch
sodium_fusidate	J01XC01	Other	Access	Access
temocillin	J01CA17	Other	Watch	Watch
tetracycline	J01AA07	Other	Access	Access
ticarcillin	J01CA13	Other	Watch	Watch
tobramycin	J01GB01	Other	Watch	Watch
trimethoprim	J01EA01	Other	Access	Access
tetracycline combinations	J01AA20	Other	Watch	Watch

Annex J Glossary of terms

Active ingredient	The part of an antibiotic medicine that acts against the bacterial infection. Alternatively called 'active substance'.
AFBI	Agri-Food and Biosciences Institute, Northern Ireland
AMEG	Antimicrobial Advice <i>ad hoc</i> Expert Group; AMEG is an ad hoc group established by the European Medicines Agency jointly under the Committee for Medicinal Products for Veterinary Use (CVMP) and the Committee for Medicinal Products for Human Use (CHMP). The AMEG was set up to provide guidance on the impact on public health and animal health of the use of antibiotics in animals, and on the measures to manage the possible risk to humans.
AMR	Antibiotic Resistance/Antimicrobial Resistance
AMRHAI	Antimicrobial Resistance and Healthcare Associated Infections Reference Unit
APHA	Animal and Plant Health Agency; an executive agency for Defra, the Scottish Government and the Welsh Government.
ATC	Anatomical Therapeutic Chemical Classification System
ATCvet	Anatomical Therapeutic Chemical Classification System for veterinary medicinal products
Antibiotic	A large group of antibacterial substances capable of destroying or inhibiting the growth of bacteria, used for treatment or prevention of bacterial infections.
Antimicrobial	Naturally occurring, semi-synthetic or synthetic substances that exhibit antimicrobial activity (kill or inhibit the growth of micro-organisms). Used for treatment or prevention of infections. Antimicrobials include antibacterials (antibiotics), antivirals, antifungals and antiprotozoals.
Antibiotic/antimicrobial resistance	The ability of a micro-organism/bacterium to grow or survive in the presence of an antimicrobial that is usually sufficient to inhibit or kill micro-organisms of the same species.
Antibiotic Stewardship	Antibiotic stewardship is a key component of a multifaceted approach to preventing emergence of antibiotic resistance. Good antibiotic stewardship involves selecting an appropriate drug and optimising its dose and duration to cure an infection while minimising toxicity and conditions for selection of resistant bacterial strains.
AST	Antibiotic susceptibility testing: using laboratory methods to determine whether a bacterium is susceptible to a drug <i>in vitro</i> .
Bacteraemia	The presence of bacteria in the bloodstream.
BPC	British Poultry Council
BSAC	British Society for Antibiotic Chemotherapy
CBP	Clinical Break Point: relates the laboratory results to the likelihood of clinical treatment success or failure.
Cefas	Centre for Environment, Fisheries and Aquaculture Science
Critically Important Antibiotics	These are antibiotic classes, which are the sole or one of limited available therapies, to treat serious bacterial infections in people and are used to treat infections caused by bacteria that may be transmitted to humans from non-human sources or, bacteria that may acquire resistance genes from non-human sources (WHO definition).
DAERA	Department of Agriculture, Environment and Rural Affairs, Northern Ireland

DHSC	Department of Health and Social Care
Defra	Department for Environment, Food and Rural Affairs
ECDC	European Centre for Disease Prevention and Control
ECOFF	Epidemiological cut-off value: represents the point at which bacteria have developed a higher level of resistance to an antibiotic than the background level of resistance that exists naturally for that bacterial species. A 'resistant' (or 'non-susceptible') ECOFF does not necessarily imply a level of resistance which would correspond with clinical treatment failure.
EFSA	European Food Safety Authority
EMA	European Medicines Agency
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EUCAST	European Committee on Antimicrobial Susceptibility Testing
Eurostat	Eurostat is the statistical office of the European Union
Food-producing animal (species)	Animals used for food production including (but not limited to): cattle, sheep, pigs, poultry, salmon, trout and bees.
FSA	Food Standards Agency
HP-CIA	Highest Priority Critically Important Antibiotics. In this report the classification according to the AMEG has been used; therefore the following classes of antibiotics are included under HP-CIAs: fluoroquinolones, 3rd and 4th generation cephalosporins and colistin.
HPS	Health Protection Scotland
MIC	Minimum Inhibitory Concentration: the lowest concentration of an antibiotic that inhibits visible growth of a bacterium after overnight incubation.
Non-food-producing animal (species)	Animals not reared for food. These are mainly companion animals including (but not limited to): dogs, cats, horses, small mammals, rabbits and birds.
NRL	National Reference Laboratory
OIE	World Organisation for Animal Health
PHE	Public Health England
Population Correction Unit (PCU)	This is a technical unit of measurement which is used to represent the estimated weight at treatment of livestock and slaughtered animals. It takes into account a country's animal population over a year, along with the estimated weight of each particular species at the time of treatment with antibiotics. 1 PCU = 1 kg of different categories of livestock and slaughtered animals.
SG	Scottish Government
TARGET	Treat Antibiotics Responsibly, Guidance, Education, Tools
TRACES	The 'TRAde Control and Expert System' (TRACES) is the European Commission's online management tool for all sanitary requirements on intra-EU trade and importation of animals, semen and embryo, food, feed and plants.
VMD	Veterinary Medicines Directorate, an Executive Agency of Defra.
WG	Welsh Government
WHO	World Health Organization