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Ireland

One Health Report on Antimicrobial Use & Antimicrobial Resistance

Ireland's first One Health Report on Antimicrobial Use and Antimicrobial Resistance 2016

January 2019

This Report was developed on behalf of Ireland's National Interdepartmental AMR Consultative Committee.

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Interdepartmental Antimicrobial Resistance (AMR) Consultative Committee Foreword

Dr Tony Holohan
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As joint chairs of the National Interdepartmental AMR Consultative Committee we welcome the publication of Ireland's first *One Health Report on Antimicrobial Use and Antimicrobial Resistance*. This Committee, which was jointly established by both our Departments, recognises the growing need for a 'One Health' approach to tackling healthcare associated infection and antimicrobial resistance, as recommended by the World Health Organisation and the European Commission.

The Committee oversaw the development and publication of Ireland's first *National Action Plan on Antimicrobial Resistance 2017 – 2020*, (iNAP), which was published in October 2017. The development of this Report was one of the strategic objectives of iNAP. This Report was produced through a collaborative process involving professionals working in the human and animal health sectors in Ireland.

We believe that this Report will further encourage joint working between the human and animal health sectors, in terms of identifying emerging and current antimicrobial resistance challenges in both populations, as well as identifying differences in surveillance methodology and data gaps. We also expect that this, and future reports, will allow evaluation of available data from humans and animals side by side, and begin to assess the relationship between antibiotic sales, use and resistance across the two sectors.

Within the context of 'One Health' this report seeks to raise public and professional awareness in both the health and agricultural sectors of the human and animal health threat of AMR, and the repercussions for human health, and the agricultural and food industry.

We thank the members of the Interdepartmental Antimicrobial Resistance Consultative Committee for their leadership in the development of this report, in particular the report authors for their commitment to completing this task.

We are confident that this first joint surveillance report emphasises that cross-sectoral cooperation at all levels is the only approach to effectively tackle AMR and will progress understanding and inform future evidence based intersectoral policy and decisions in relation to the issue of AMR.

Dr. Tony Holohan CMO

Dr. Martin Blake CVO

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Glossary

Antibacterials
Antibacterials are substances that destroy *bacteria* or suppress bacterial growth or reproduction.

Antimicrobials
Antimicrobials are substances that destroy *microorganisms* or suppress microbial growth or reproduction. They are used to prevent and treat bacterial, viral, fungal and protozoal infections in humans and animals (where they may be known respectively as antibacterials, antivirals, antifungals and antiprotozoals).

The terms 'antimicrobial' and 'antibiotic' are frequently used. While antibiotics are produced naturally (from biological materials e.g. moulds or bacteria), antimicrobials may be produced from synthetic or biological material. Therefore the term 'antimicrobial' is technically more accurate to describe substances of non-biological origin that destroy microorganisms.

Antimicrobial Resistance (AMR)
Antimicrobial resistance (AMR) refers to a microorganism's ability to grow and reproduce or to survive exposure to an antimicrobial. AMR occurs when an antimicrobial that was previously effective is no longer effective to treat an infection or disease caused by a microorganism.
AMR is exacerbated by human factors such as inappropriate use of antimicrobials in human and veterinary medicine, poor hygiene conditions and practices in healthcare settings or in the food chain facilitating the transmission of resistant microorganisms. Over time, this makes antimicrobials less effective and ultimately useless.

Antimicrobial Stewardship
Antimicrobial stewardship is a systematic approach to optimising antimicrobial therapy. It includes not only limiting inappropriate use but also optimising antimicrobial selection, dosing, route and duration of therapy to maximise clinical cure while limiting unintended consequences, such as the emergence of antimicrobial resistance, adverse drug events and cost.

Bacteria
Bacteria are one of the major groups of microorganisms or microbes, some of which can infect and cause disease in humans and animals. A range of descriptive terms are used. Bacteria cultivated in a laboratory are referred to as isolates, those capable of causing disease as pathogens (pathogens that are transmissible between animals and humans are zoonotic), and those that are normally resident on or in humans/animals without causing disease as commensals or colonisers.

Critically Important Antimicrobials
Critically important antimicrobials are antimicrobials of last resort for treatment of human infection.

Empiric treatment
Treatment given without confirmation of the cause of the disease and based on clinical judgement. Sometimes urgency dictates empiric treatment (for example, when a significant infection by an unknown organism is treated with a broad spectrum antimicrobial while results of bacterial culture and other tests are awaited).

Enterobacteriaceae*
A family of Gram-negative bacteria found in the bowel of humans and animals (e.g. *E. coli*, *Klebsiella pneumoniae*, *Salmonella* spp). Occasionally, they escape the bowel, causing infection elsewhere in the body.
[*term changed in 2018 to *Enterobacteriales*]

Microorganisms or microbes
Microorganisms or microbes are microscopic living organisms. Examples include bacteria, viruses, protozoa, and some fungi and parasites. They are widespread in nature and are vital to the sustainability of ecosystems. Many are essential to human and animal health. Some may cause illness.

One Health
A concept promoting a 'whole of society' approach which recognises that the health of people is connected to the health of animals and the environment.

Surveillance
Surveillance means collecting, collating, analysing data and communicating information to those who need to know. It involves the generation and timely provision of information that can inform appropriate decision making and action.

Susceptibility testing
Susceptibility testing is used to determine if a microorganism is susceptible or not to a selection of antimicrobial agents.

Zoonoses
Zoonoses are infections that are transmissible between animals and people.

Abbreviations and Acronyms

AHI	Animal Health Ireland
AMP	Ampicillin
AMS	Antimicrobial Stewardship
AMR	Antimicrobial Resistance
AMU	Antimicrobial Use
ATC	Anatomical Therapeutic Chemical (ATC) Classification System
AST	Antimicrobial Susceptibility Testing
AZI	Azithromycin
BSI	Bloodstream infections
CAZ	Ceftazidime
CHL	Chloramphenicol
CIAs	Critically Important Antimicrobials
CIDR	Computerised Infectious Disease Reporting
CIP	Ciprofloxacin
CIR	Crude Incidence Rate
CIT	Cork Institute of Technology
COL	Colistin
CPE	Carbapenemase Producing *Enterobacteriaceae*
CRE	Carbapenem Resistant *Enterobacteriaceae*
CTX	Cefotaxime
DAFM	Department of Agriculture, Food & the Marine
DDD	Defined Daily Dose
DoH	Department of Health
EARS-Net	European Antimicrobial Resistance Surveillance Network
ECDC	European Centre for Disease Control
E. coli	*Escherichia coli*
EFSA	European Food Safety Authority
EMA	European Medicines Agency
EPA	Environmental Protection Agency
ESAC-Net	European Surveillance of Antimicrobial Consumption Network
ESBL	Extended spectrum beta lactamase
ESVAC	European Surveillance of Veterinary Antimicrobial Consumption
EU	European Union
EURL	European Reference Laboratory
EUCAST	European Committee on Antimicrobial Susceptibility Testing
FAO	Food and Agriculture Organisation
FSAI	Food Safety Authority of Ireland
GEN	Gentamycin
HALT	Healthcare Associated Infections and Antimicrobial use in LTCFs
HCAI	Healthcare Associated Infection
HIQA	Health Information and Quality Authority
HPRA	Health Products Regulatory Authority
HPSC	Health Protection Surveillance Centre
HSE	Health Service Executive
ID	Infectious Disease
***i*NAP**	Ireland's National Action Plan on Antimicrobial Resistance 2017-2020
JIACRA	Joint Interagency Antimicrobial Consumption and Resistance Analysis
KP	*Klebsiella pneumonia*
KPI	Key Performance Indicator
LTCF	Long term care facility
MDR	Multi-drug resistance
MDRO	Multi-drug resistance organism
MER	Meropenem
MRSA	Methicillin resistant *Staphylococcus aureus*
MS	Member States
NAL	Nalidixic acid
NCPERLS	National CPE Reference Laboratory
NRL	National Reference Laboratory
OIE	World Organisation for Animal Health
OPAT	Outpatient Parenteral Antimicrobial Therapy
PCR	Polymerase Chain Reaction
PCRS	Primary Care Reimbursement Service
PHL	Public Health Laboratory
PNPS	Penicillin non-susceptible *S. pneumoniae*
PPS	Point Prevalence Survey
PPS	Point Prevalence Study
PVP	Private Veterinary Practitioner
RVL	Regional Veterinary Laboratory
S. aureus	*Staphyloccus aureus*
SHX	Sulphamethoxazole
STI	Sexually Transmitted Infection
TET	Tetracycline
THP	Trimethoprim
TIG	Tigecycline
UCD	University College Dublin
UTI	Urinary Tract Infection
VRE	Vancomycin-resistant enterococci
WGS	Whole Genome Sequencing
WHO	World Health Organisation

Summary

Antimicrobials are medicines, mostly antibiotics, used to treat and prevent bacterial infections or disease in humans and animals. Antimicrobial resistance (AMR) occurs when antimicrobials that were previously effective are no longer so. AMR is an urgent and growing problem worldwide, mainly due to antimicrobial overuse.

A One Health approach is needed to tackle the problem. Human, animal and environmental health is interconnected. The human health, agriculture and environment sectors must work together.

This One Health AMR Surveillance Report is Ireland's first cross-sectoral report on antimicrobial use (AMU) and AMR in humans and animals.

Antimicrobial Use (AMU)

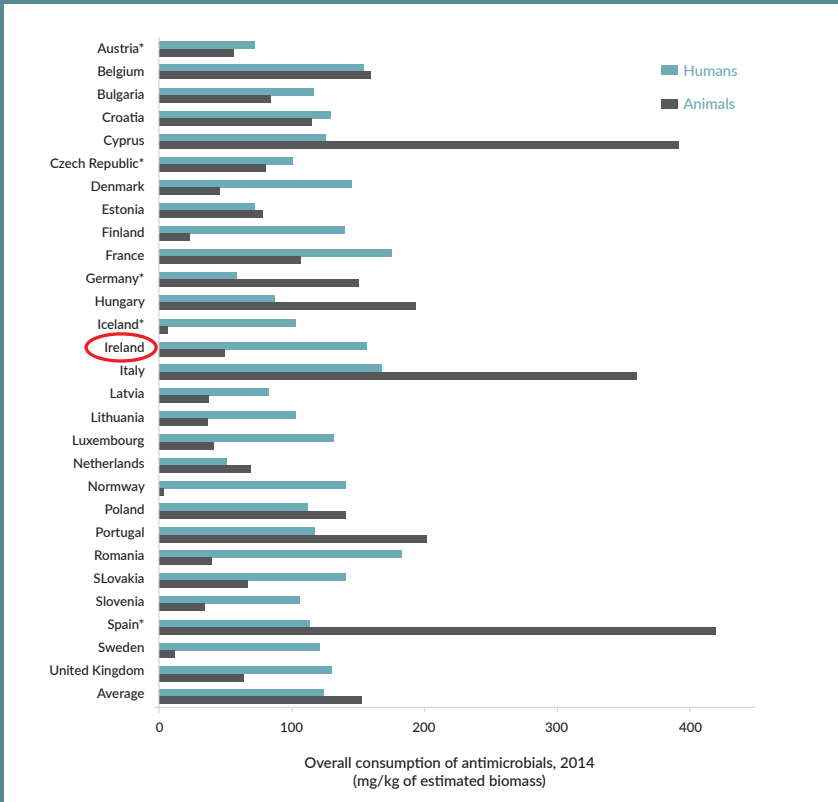
AMU in Humans and Animals

In most EU/EEA Member States (18 out of 28 countries studied, including Ireland), reported antimicrobial use is *'lower or much lower'* per unit of biomass in food-producing animals than in humans.

AMU in Ireland

- Humans 155.6 mg/kg of estimated biomass/yr
- Animals 48.0 mg/kg of estimated biomass/yr

From:
Joint Interagency Antimicrobial Consumption and Resistance Analysis (JIACRA) Report
JIACRA Report 2017 (2014 data)

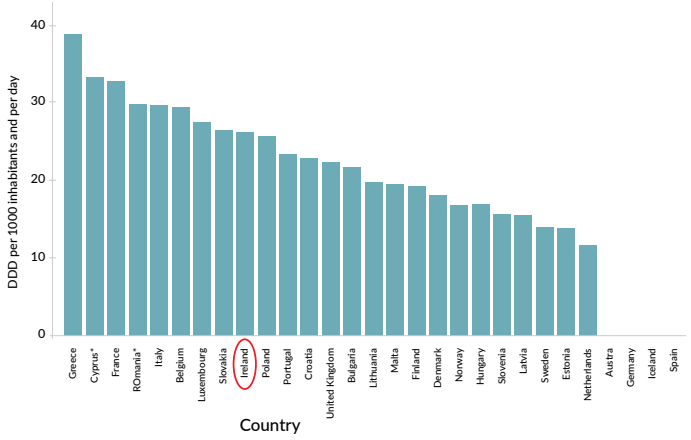


AMU in Humans

Ireland ranked 9th highest of 25 EU/ EEA Member States for antibacterial consumption in humans in 2016.

26.1 defined daily doses (DDD) per 1,000 inhabitants per day (DID).

Consumption of Antibacterials for systemic use (ATC group J01) in the community and hospital sector in Europe, reporting year 2016



Source: TESSy, The European Surveillance System on 2018-03-06

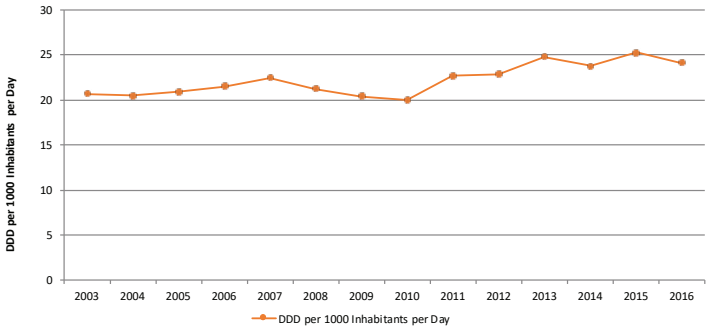
Community

Most human antimicrobial use in Ireland is in the community (90%). The overall trend has been increasing since 2004.

The most common antimicrobials used in the community in 2016:

- Penicillins (58%)
- Macrolides (18%)
- Tetracyclines (10%)

Annual Total Community AMU in Ireland: 2003-2016



Source: HPSC

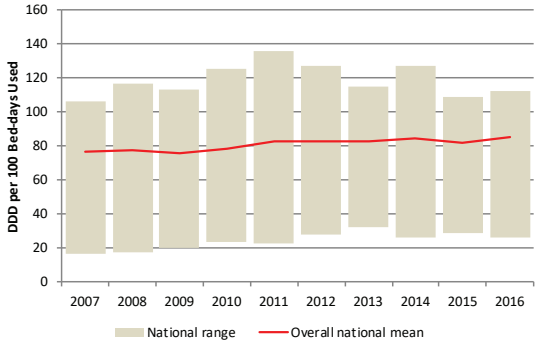
Hospitals

Acute hospitals in Ireland account for 10% of human antimicrobial use. The overall trend has been increasing over the last decade.

The most common antimicrobials used in hospitals in 2016:

- Penicillins (50%)
- Cephalosporins/ monobactams/ carbapenems (10%)
- Glycopeptides/ imidazoles/ nitrofurans (10%)

Annual Total Hospital AMU in Ireland: 2007 - 2016



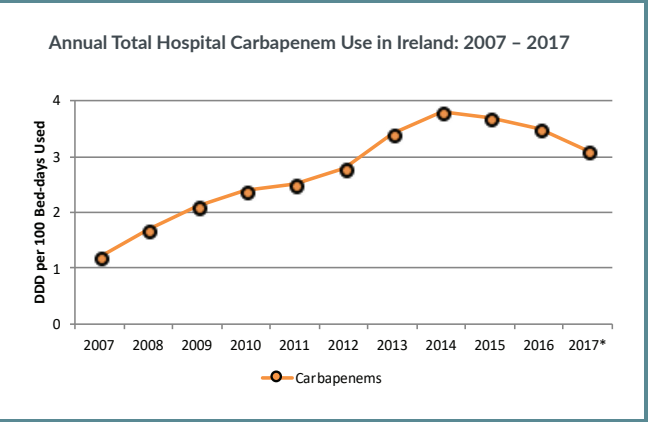
Source: HPSC

Carbapenem Use

Carbapenems are a class of critically important antimicrobials whose use should generally be reserved for treatment of severe or antimicrobial resistant Gram negative infection in humans.

Increased annual carbapenem use was observed nationally since 2007, peaking in 2014 (3.8 DBD), with reductions observed in subsequent years to 3.1 DBD in 2017.

The Health Service Executive (HSE) launched the national restricted antimicrobial policy in Quarter 3, 2016. This policy stipulated that access to carbapenems must be restricted in HSE-owned hospitals, under supervision of an infection specialist (e.g. consultant clinical microbiologist or infectious diseases (ID) physician).



Source: HPSC

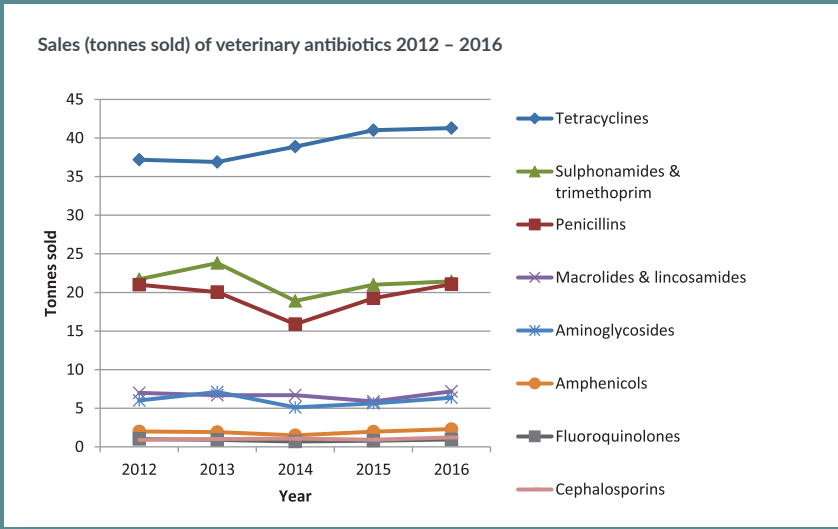
AMU in Animals

Ireland ranked 17th highest of 30 EU/ EEA member states for antimicrobial use in animals (mg/kg biomass) in 2016.

Based on sales data, most animal AMU in Ireland (66.6%) is formulated as premixes or oral remedies, presumed to be predominantly used as in-feed or in-water medication for the intensive pig and poultry sectors.

The antimicrobials most commonly sold for animal use in Ireland (by weight) are:

- Tetracyclines (39.9%)
- Sulphonamides & trimethoprim (20.7%)
- Penicillins (20.4%)



Source: HPRA

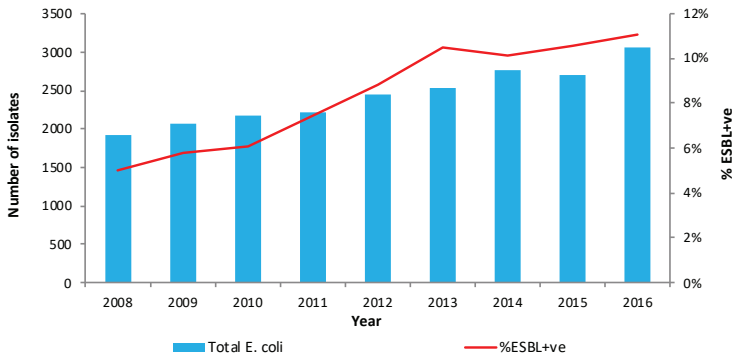
AMR in bacterial isolates from Humans

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

E. coli is by far the most common causative pathogen of bloodstream infection (BSI) in Ireland, with around 3,000 cases per year. When *E. coli* acquire the capacity to produce ESBLs, this enables them to resist the activity of most beta lactam antimicrobials (e.g. penicillins, cephalosporins, monobactams). This increases dependence on carbapenems for effective treatment of infection.

In 2016, of those *E. coli* causing blood stream infection, 11% were ESBL-producing *E. coli*. This is the highest level since surveillance began. Concerns about increased risk of ESBL-producing *E. coli* may in turn drive increased carbapenem use for empiric treatment of invasive infection.

Annual total *E.coli* BSI: 2008-2016 (%ESBL producing = red line)



Source: HPSC

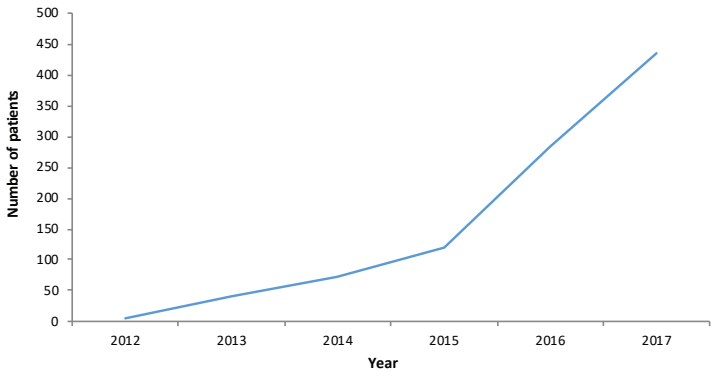
Carbapenemase-producing *Enterobacteriaceae* (CPE)

CPE are highly resistant Gram-negative bacilli against which carbapenems are generally not effective to treat infection.

CPE infection is more difficult and expensive to treat compared to infection with similar bacteria that are not carbapenemase producers. Infection with CPE is associated with increased patient morbidity and mortality. Compared with 2016, a 53% increase in patients with newly-confirmed CPE isolates was reported by the Irish national CPE Reference Laboratory to the end of 2017. Most of these patients were colonised rather than infected at the time of detection.

CPE was declared a National Public Health Emergency in Ireland on 25th October 2017.

Annual numbers of patients with CPE newly-confirmed: 2012-2017



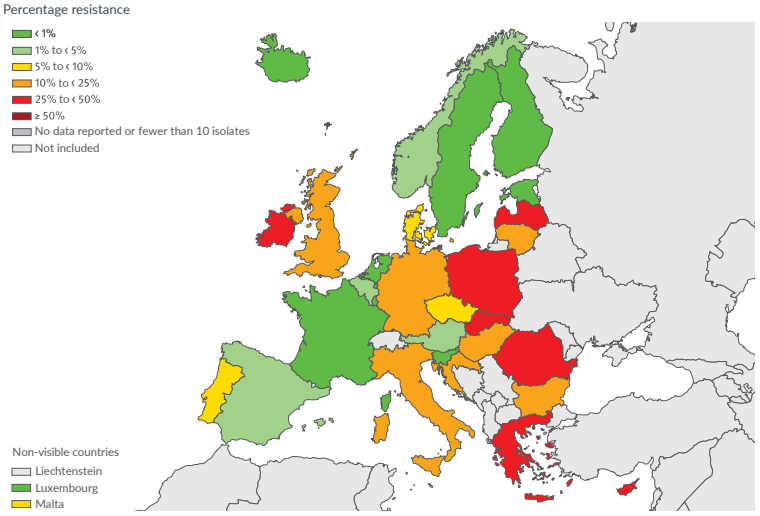
Source: NCPEARLS

Vancomycin resistant enterococci (VRE)

VRE cause invasive infection primarily in the very ill, elderly or immunocompromised patient. VRE bloodstream infection (BSI) is hard to treat compared with bloodstream infection with enterococci that are sensitive to vancomycin. Bloodstream infection with VRE is associated with worse outcomes for patients.

Of those *E. faecium* causing bloodstream infection in Ireland in 2016, 44% were VRE. From 2008 to 2015, this percentage was higher in Ireland than in any other country in Europe.

Percentage of vancomycin resistant *Enterococcus faecium* BSI in EU/EEA (2016)



Source: EARS-Net at ECDC; map accessed via www.ecdc.europa.eu 13/10/17

Zoonotic Bacteria

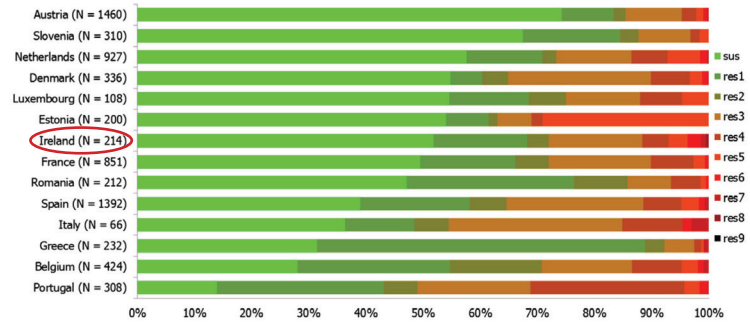
Salmonella

- In Ireland in 2016, one-quarter of human isolates were multi-drug resistant (MDR) (26.5% overall in EU)
- 24.6% were resistant to ciprofloxacin (11% overall in EU)
- Three ESBL-producing *Salmonella* isolates were detected (ESBL also detected in all those EU Member States, and one non-MS, that did testing)

Campylobacter

- In Ireland in 2016, only 17.9% of Campylobacter isolates from humans were identified to species level
- Antimicrobial susceptibility testing is not performed routinely
- In a recent Irish study (88 isolates: 79 *C. jejuni*, 9 *C. coli*), no macrolide resistance was detected.

Frequency distribution of *Salmonella* spp. Isolates from humans completely susceptible or resistant to one to nine antimicrobial classes in 2016 (14 EU Member States)



N: total number of isolates tested for susceptibility against the whole common set of antimicrobials for *Salmonella*; sus: susceptible to all antimicrobial classes of the common set for *Salmonella*; res1–res9: resistance to one up to nine antimicrobial classes of the common set for *Salmonella*.

Source: EUSR on AMR in zoonotic and indicator bacteria from humans, animals and food 2016 https://ecdc.europa.eu/sites/portal/files/documents/AMR-zoonotic-bacteria-humans-animals-food-2016_Rev3.pdf

AMR in bacterial Isolates from Animals

Zoonotic Bacteria

No CPE of animal origin were identified during 2014-2016.

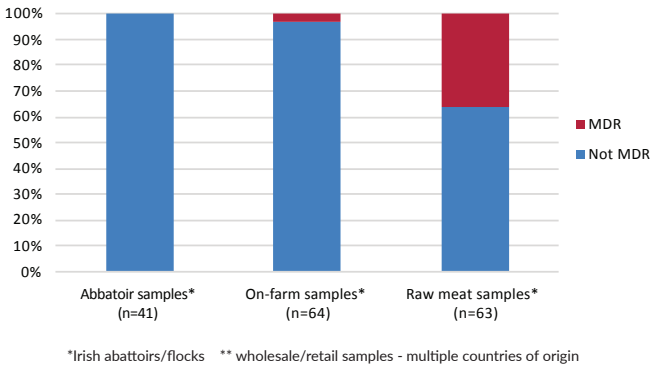
Salmonella

- Low levels of resistance were detected in *Salmonella* isolates from Irish poultry flocks.
- Multi-drug resistance (MDR) was higher in pig isolates than in poultry or cattle isolates.
- MDR and resistance to highest priority antimicrobials, was observed in *Salmonella* isolates from imported poultry meat.
- Resistance in *Salmonella* isolates from Irish pigs was higher than the EU average for some antimicrobials.

Campylobacter

- Resistance to important antimicrobials was absent (erythromycin) or below EU average (ciprofloxacin) in *C. jejuni* isolated from Irish poultry.

Occurrence of MDR in *Salmonella* isolates from poultry samples 2014-2016



Source: DAFM

Indicator (non-pathogenic) Bacteria

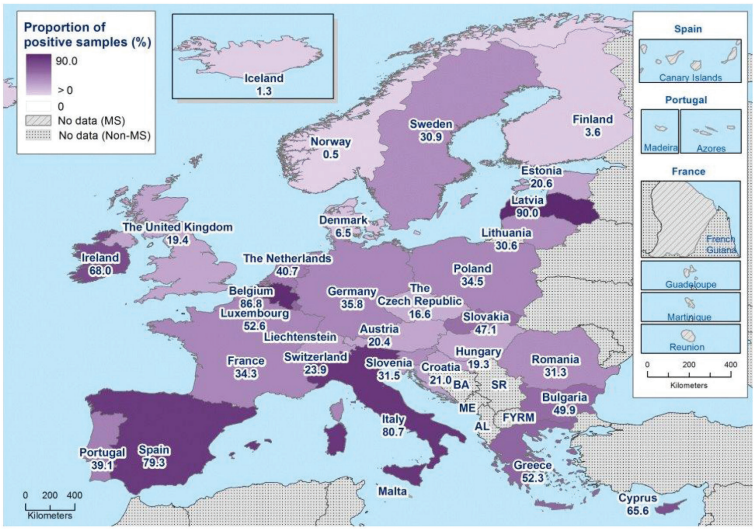
Indicator commensal *E. coli*

- More frequently resistant to antimicrobials commonly used in veterinary medicine.
- Proportion of MDR was higher in poultry compared to pig isolates.

ESBL-producing *E. coli*

- In 2016, the proportion of Irish poultry meat samples harbouring ESBL *E. coli* was above the EU average.

Presumptive ESBL *E. coli* from broilers, 2016 (specific monitoring)



Source: EFSA and ECDC, 2018. The European Union summary report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2016. EFSA Journal 2018;16(2):5182, 270 pp. https://doi.org/10.2903/j.efsa.2018.5182

For the first time, a report has been prepared using available data with the aim of providing an integrated picture of AMU and AMR in humans and food-producing animals in Ireland.

Available data on AMU for both humans and food-producing animals in Ireland is improving over time. AMR data on specific pathogens causing invasive infections in hospitalised patients is comprehensive, with national coverage. There is also good data on AMR in zoonotic and indicator bacteria from food-producing animals. Various initiatives are underway in both sectors to collect new data or to enhance use of existing AMU or AMR data.

However, there are gaps in the depth, breadth and the quality of AMU and AMR surveillance in Ireland:

- Human AMU data currently captures approximately 90% of acute hospital and 95% of community use. However, it is not currently possible to differentiate community AMU into that prescribed in primary care for patients residing in their own homes versus other settings, such as long-term care facilities.
- Food-animal AMU data is based on sales and this does not include a breakdown of usage by species, husbandry system or age group.
- Wholesale antimicrobial sales data (which is the current basis for obtaining data on both human AMU in the community and food-animal AMU) may not reliably equate to usage
- National surveillance of AMU does not currently include information on the appropriateness of the antimicrobials that are prescribed for use in either sector
- Neither is it possible to provide analysis of use to the level of the prescriber, which would assist in providing direct feedback to antimicrobial prescribers and critical information for developing educational programmes on antimicrobial stewardship
- Human AMR surveillance focuses on trends in invasive infections, such as bloodstream infection in hospitalised patients, while other much commoner infection types (e.g., urinary tract infections, wound infections) and infections in settings outside of hospitals are not currently subject to national surveillance
- To date, targeted surveillance for AMR in animals has been largely confined to pigs and poultry
- Currently there is no targeted surveillance for AMR in imported food products
- Currently there is no systematic surveillance for AMR in, or of antimicrobial discharges to, the environment.

It should be noted that this initial report is based largely on surveillance data for 2016 (cf Section 1.3), with the exceptions of CPE data for 2017 in humans and 2014/2015 data on AMR in pigs/poultry respectively. Importantly, attention is drawn to the fact that progress is already being made in tackling several of the surveillance gaps highlighted above. That progress will be reflected in the next and subsequent reports.

Addressing such surveillance gaps will improve Ireland's ability to respond to current and emerging AMR threats and will support antimicrobial stewardship efforts by providing better evidence for decision-making. The joint annual publication of a report on AMU and AMR will act as a continuing prompt over the coming years to progressively address these gaps in our knowledge and highlight our collective One Health efforts to tackle this major societal challenge in Ireland.

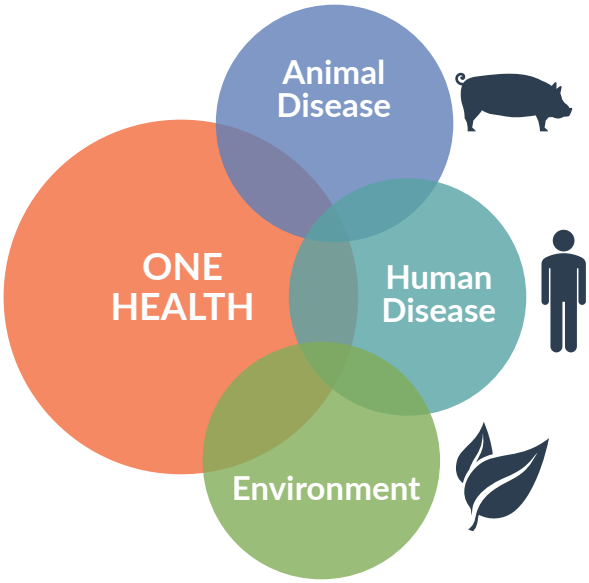
1. Introduction

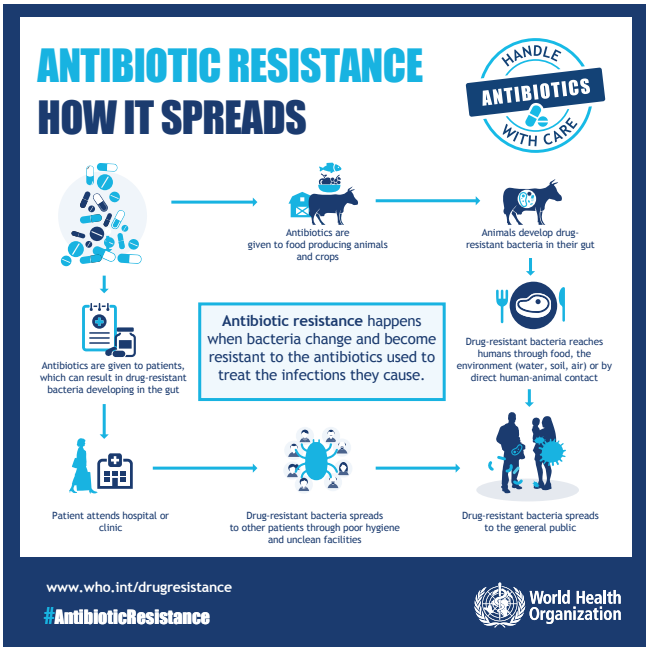
1.1 The Problem

Antimicrobials are medicines, mostly antibiotics, used to treat infections or disease in humans and animals. With increasing antimicrobial use (AMU), antimicrobial resistance (AMR) has emerged. AMR is internationally recognised as a major societal challenge. It has been identified as a national strategic risk facing Ireland. It is one of the most serious problems facing modern healthcare delivery. If prudent use of existing antimicrobials and evidence-based infection prevention and control measures were universally implemented and assured, and if effective novel antimicrobials can be developed and swiftly brought to market, an AMR crisis might be deferred.

A key area of concern is increasing AMR in a family of bacteria normally resident in the gut of humans and animals (*Enterobacteriaceae*). *Enterobacteriaceae* can be associated with some common and potentially serious infections such as cystitis and bloodstream infection. AMR in *Enterobacteriaceae* is severely limiting treatment options. No novel antimicrobial class effective against this family of bacteria has been brought to market in decades, although some enhancements of older antimicrobials have recently become available and may be valuable in some settings.

The 'One Health' concept recognises that the health of people is connected to the health of animals and the environment. Humans, animals, plants, food of animal origin and our environment all potentially constitute overlapping reservoirs of AMR. Given the serious health threat, a common understanding of AMR, and of the need for a One Health approach to tackle it, are of fundamental importance.





1.2 Aims & Target Audience

Monitoring AMU and AMR trends in humans and animals in Ireland, across Europe and worldwide is necessary to quantify the problem and to monitor the impact of interventions over time. Ireland's National Action Plan (iNAP) on Antimicrobial Resistance 2017-2020 was jointly launched by the Ministers for Health and for Agriculture Food and the Marine in October 2017. As part of iNAP, and in keeping with the One Health concept, Ireland has committed to develop and produce an annual One Health surveillance report on AMU and AMR.

This is Ireland's first such cross-sectoral report. It aims to promote increased awareness and understanding of the issues of AMU and AMR in both sectors, and the One Health collaborative approach to addressing these issues, by:

- Presenting AMU surveillance information in both sectors
- Presenting AMR surveillance information in both sectors
- Highlighting some relevant initiatives in both sectors
- Highlighting AMU and AMR surveillance gaps in both sectors
- Sharing the report with a wide target audience and seeking feedback to guide its future development

The intended target audience includes: undergraduate, postgraduate and qualified professionals working in the healthcare, veterinary, farming, food-production, environmental health and health protection sectors; the scientific, diagnostic, research and education community that underpins continuous development and excellence in these sectors; patients and their families; keepers of animals; other members of the general public; policy makers.

1.3 Scope of Report

This initial report focuses on the use of, and resistance to, antimicrobials (and of these, antibacterials) that are used to treat or prevent bacterial infections in humans and food-producing animals. Antivirals, antifungals or antiprotozoals are not included within its scope. Neither, on this occasion, are companion animals or environmental monitoring for AMR.

The report is based for the most part on surveillance data for 2016. The exceptions relate to (i) data from 2017 for carbapenemase producing *Enterobacteriaceae** (CPE) in humans and (ii) data from 2014 and 2015 from monitoring for AMR in poultry and pigs respectively (as mandatory monitoring in these species is done on alternate years as outlined below). In recognition of the increasing national incidence of CPE and declaration of CPE as a National Public Health Emergency in October 2017, CPE surveillance data to the end of 2017 is included.

**Enterobacteriaceae*: term changed in 2018 to *Enterobacterales* (Report predates terminology change. Hence, former term utilised) here)

1.4 One Health Surveillance Information

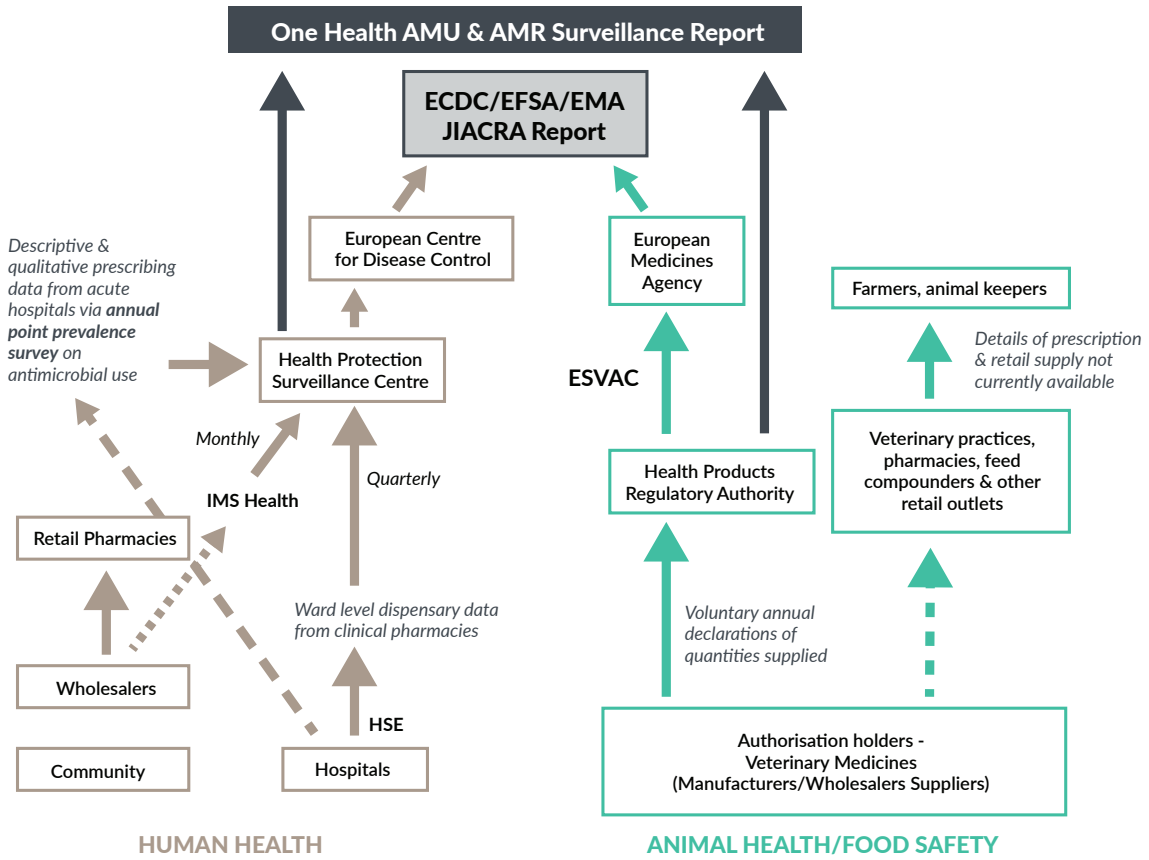
At EU level, data on AMU and AMR relating to humans and food-producing animals is jointly produced (JIACRA Report) by the European Centre for Disease Control (ECDC), the European Food Safety Authority (EFSA) and the European Medicines Agency (EMA).

In Ireland, data on AMU and AMR from both sectors is jointly collated at national level for the first time in this report. It is assembled via different channels. There is currently no central depository for this inter-sectoral data.

1.4.1 One Health AMU Data

- Data on human AMU is derived from pharmacy wholesale data (community) and hospital pharmacy dispensing data (acute hospital). This is detailed in Section 2.
- Data on animal AMU (both food-producing and companion animals) is based on voluntary declaration to the Health Products Regulatory Authority (HPRA) of wholesale quantities supplied by authorised manufacturers and distributors. This is detailed in Section 3.
- A One Health overview of the current situation in Ireland relating to the sources and flow of human and animal AMU data is presented in Figure 1.1.

Figure 1.1. Sources and Flow of Information on Antimicrobial Use

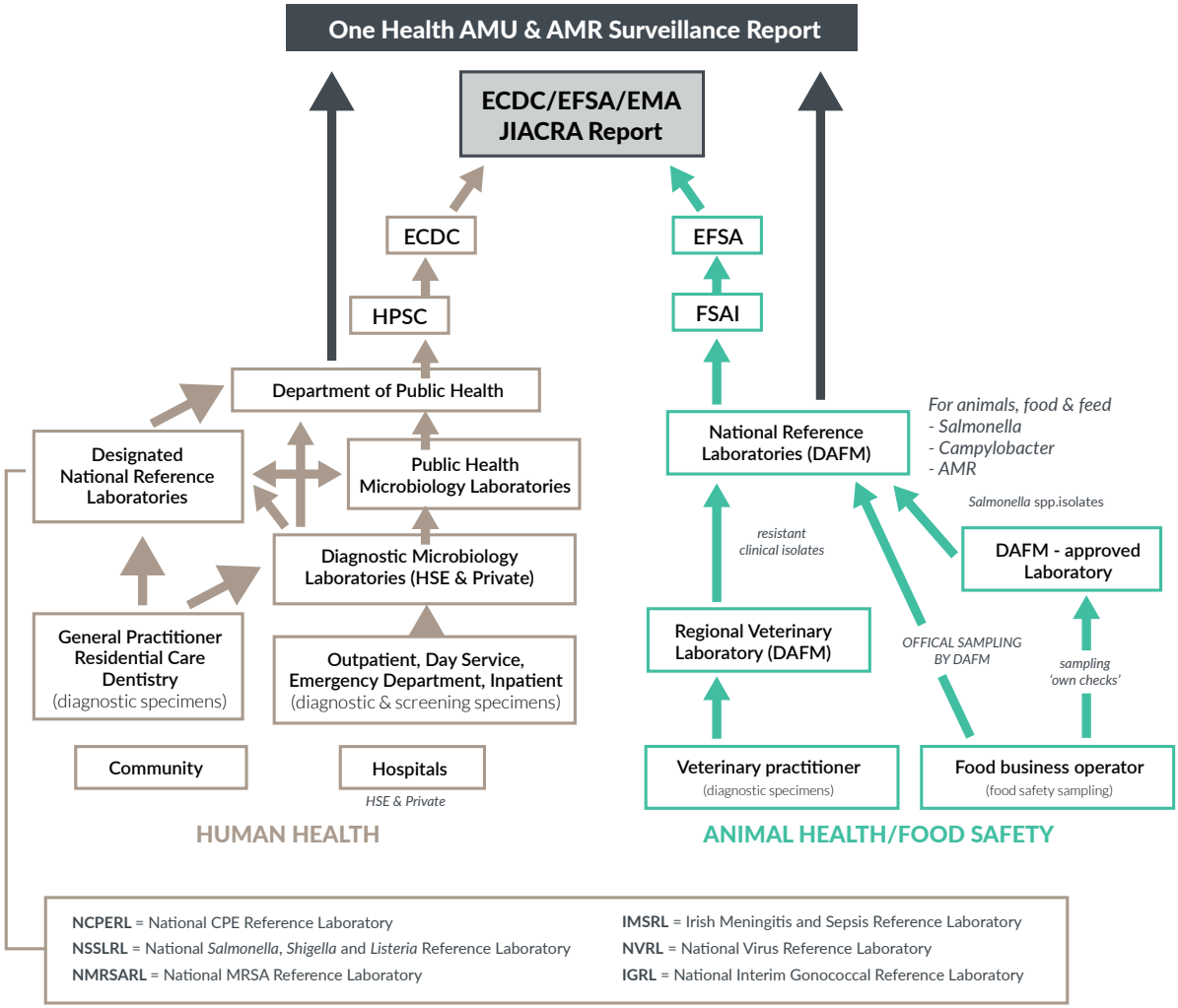


ESVAC = European Surveillance of Veterinary Antimicrobial Consumption
IMS Health = a pharmaceutical market research company

1.4.2 One Health AMR Data

- Data on AMR patterns in bacterial isolates from humans is obtained from diagnostic microbiology laboratories, public health microbiology laboratories and designated national reference laboratories. It is collated for inclusion in the Health Protection Surveillance Centre's (HPSC) annual epidemiological report. See Sections 4 & 5.
- Data on AMR in food-producing animals (primarily from the intensive pig and poultry sectors) is generated by the National Reference Laboratory (NRL) for AMR in animals, food and feed hosted by the Department of Agriculture, Food and the Marine (DAFM) at Backweston. The data is based on a mandatory, harmonised EU-wide monitoring programme [Appendix A]. See Sections 5 & 6.
- A One Health overview of the current situation in Ireland related to sources and flow of data on AMR in bacterial isolates from both sectors is summarised in Figure 1.2

Figure 1.2. Sources and Flow of Information on AMR in Bacterial Isolates



1.5 Human and Food-Animal Populations

The scale of Ireland's human and food-animal populations, which constitutes the country's One Health population base and the potential consumers of antimicrobials, is outlined below.

The main food-producing animal species in Ireland are cattle, sheep, pigs and broiler chickens. Broiler chickens are chickens bred and raised specifically for meat production.

Human Population

Over the two decade period 1996 - 2016, the human population of Ireland increased by 31.3%, from 3,626,087 to 4,761,865 [www.cso.ie].

The distribution of the population which could potentially have received antimicrobial treatment in 2016 is shown by Community Healthcare Organisation (CHO) in Figure 1.3.

Figure 1.3 Human Population by CHO 2016

Food-animal population

Ireland's food animal population is presented in Table 1.1. The populations of cattle, sheep and pigs increased by 3%, 3.4% and 3.6% respectively between 2015 and 2016.

Table 1.1. Livestock Survey Dec 2016 / Broiler Chickens Slaughtered 2017

Livestock Numbers (million)				
	CATTLE	SHEEP	PIGS	BROILER CHICKENS
2015	6.42	3.32	1.47	
2016	6.61	3.44	1.53	
% change	+3.0	+3.4	+3.6	
2017				87.49*

www.cso.ie/en/releasesandpublications/er/lsd/livestocksurveydecember2016

*Total no. broiler chickens slaughtered in Ireland in 2017 (source DAFM)

1.6 Critically Important Antimicrobials

The term critically important antimicrobial (CIA) refers to antimicrobials of last resort for treatment of human infection. Since 2005, the World Health Organisation (WHO) has produced a regularly updated list of all antimicrobials currently used for human medicine (mostly also used in veterinary medicine), grouped into three categories – critically important, highly important and important - based on their importance to human medicine. The list is intended to assist in managing AMR, ensuring that all antimicrobials, especially CIAs, are used prudently both in human and veterinary medicine. The most recently published list was in 2017 http://www.who.int/foodsafety/publications/cia2017.pdf. [Appendix B]

The most important, very important and important CIAs in human medicine in Ireland are shown below (Table 1.2). The three antimicrobial classes appointed as the most important CIAs are: **carbapenems** (meropenem, ertapenem), **polymyxins** (colistin) and **oxazolidinones** (linezolid, tedizolid).

Table 1.2. Categorisation of Critically Important Antimicrobials in Human Medicine in Ireland

Most important	Very important	Important
Carbapenems: meropenem, ertapenem	**4th generation cephalosporins:** cefepime	**3rd generation cephalosporins:** cefotaxime, ceftriaxone, ceftazidime
Polymyxins: colisitin	**5th generation cephalosporins:** ceftaroline	**Macrolides:** azithromycin, clarithromycin
Oxazolidinones: linezolid, tedizolid	**Monobactam:** aztreonam	**Glycopeptides:** vancomycin, teicoplanin
	Fluoroquinolones: ciprofloxacin, levofloxacin	**Phosphonic acid derivatives:** fosfomycin
	Glycylcycline: tigecycline	**Antimicrobials used to treat mycobacterial infections**
	Lipopeptide: daptomycin	
	Aminoglycoside: amikacin	

Source:HPSC

Colistin was largely abandoned as a treatment for bacterial infections in the 1970s owing to its toxicity and low renal clearance. It has been reintroduced in recent years as an antibiotic of 'last resort' against MDR pathogens. It is therefore alarming that resistance to colistin has become a significant concern, following the identification of a plasmid-mediated colistin resistance mechanism conferred by the *mcr-1* gene in late 2015. The global distribution of *mcr-1* over at least five continents is well documented. The current distribution of *mcr-1* points to a possible origin in Chinese livestock. https://www.nature.com/articles/s41467-018-03205-z Ireland did not detect the *mcr-1* gene in any human isolate tested during 2016. On the food-animal side a single *E.coli* isolate, from an imported raw chicken meat sample, was colistin resistant and harboured the *mcr-1* resistance gene.

2. Antimicrobial Use (AMU) in Humans

Key Points 2016

An overall increasing trend in antimicrobial use (both in the community and in acute hospitals) has been observed over the past decade, with community use accounting for 90% of use in 2016.

In 2016, community antimicrobial use was 24 defined daily doses (DDD) per 1,000 inhabitants per day (DID), a 4% reduction on 2015.

Ireland's rate of community antimicrobial use ranks mid-to-high compared with other European countries.

In 2016, the median rate of hospital antimicrobial use was 84.8 DDD per 100 bed days used (DBD), a 3.7% increase on 2015.

Ireland's rate of hospital antimicrobial use ranks mid-range compared with other European countries.

Source: HPSC Annual Epidemiological Report 2016
www.hpsc.ie/abouthpsc/annualreports/HSE%20HPSC%20Annual%20Report%20ready%202016.pdf

2.1 General

In Ireland, antimicrobials for human health are subject to prescription control. The supply of prescription-only medicines by mail order, including via the internet, is prohibited. (Medicinal Products (Prescription and Control of Supply) Regulations 2003 (S.I.No.540 of 2003), as amended).

The prospective surveillance of human AMU, particularly antibacterials, is important for healthcare professionals and policy makers to monitor local, regional and national rates, to break down use by antimicrobial class over time and to compare national trends with data from other European countries. Such data is useful to assess the impact of antimicrobial stewardship programmes and to identify targets for future intervention. Further qualitative information can be gleaned from repeated point prevalence surveys (PPS), the findings of which provide useful information for feedback to prescribers (e.g. on the reasons that antimicrobials are prescribed, the agents chosen, the routes of administration), along with quality prescribing indicators such as compliance with available guidance and documentation of the reasons for prescriptions.

2.2 Data Sources

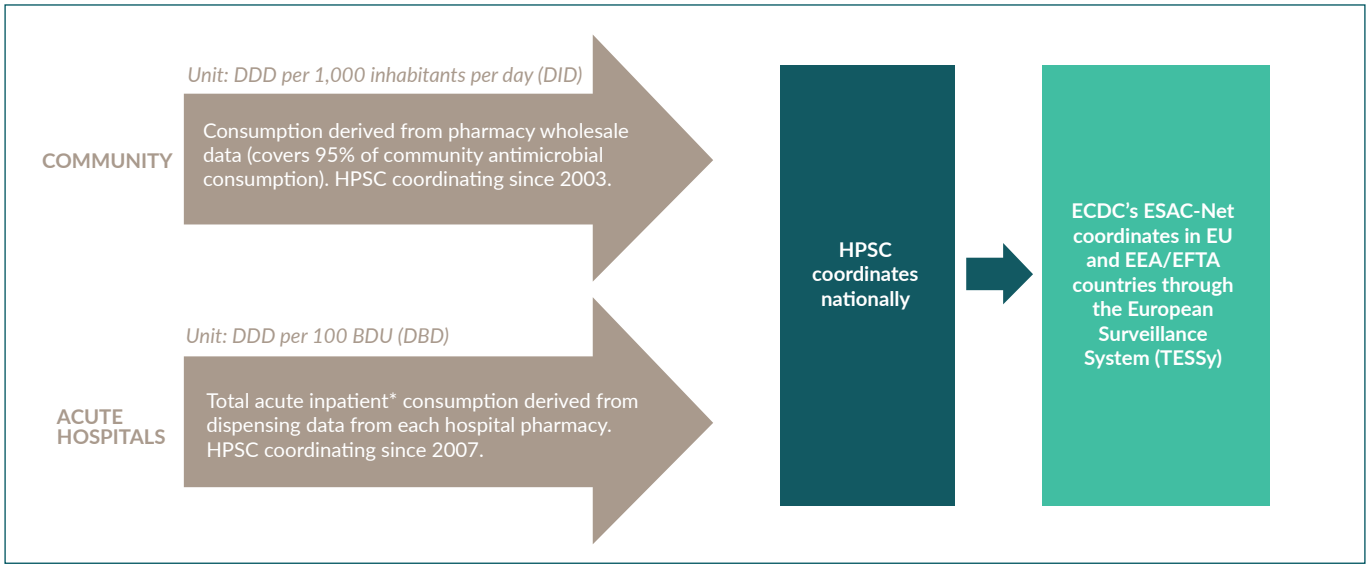
Ireland has an established national system for reporting of human systemic AMU in the community and in acute hospital settings, which is based in the Health Protection Surveillance Centre (HPSC). Ireland participates in the European Surveillance of Antimicrobial Consumption Network (ESAC-Net), coordinated by the European Centre for Disease Prevention and Control (ECDC). An overview is outlined (Figure 2.1).

There are some gaps in surveillance. With regard to hospital surveillance, data from private hospitals, the national outpatient parenteral antimicrobial therapy (OPAT) programme, antimicrobials dispensed to day cases, outpatients and external healthcare facilities are not included. On the community surveillance side, wholesale to retail pharmacy coverage is approximately 95%. Collectively, these gaps are estimated to account for 10% of antimicrobial use. Antimicrobial consumption is measured in defined daily doses (DDD), which is the assumed average maintenance dose per day for a drug used for its main indication in adults. Rates are calculated in DDD per 1,000 inhabitants per day (DID) for the community and DDD per 100 bed-days used (DBD) for hospitals.

COMMUNITY ANTIMICROBIAL USE DATA:
Antimicrobials for systemic use only (ATC Group J01) derived from sales data from the pharmacy wholesale market using IMS Health, a pharmaceutical market research company. The dataset contains regional, monthly wholesaler-to-retail pharmacy sales data from over 95% of the wholesalers and manufacturers in Ireland.
http://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/europeansurveillanceofantimicrobialconsumptionesac/PublicMicroB/SAPC/Reportml

HOSPITAL DATA:
Antimicrobial dispensing data from individual hospital pharmacy department dispensing records is converted into an internationally comparable unit of usage (DDD) by agent type. Quarterly data are extracted. Data are restricted to acute hospital inpatients. Dispensing to outpatients, day cases and external facilities are excluded. The data are based on the volume of antimicrobial drugs supplied to inpatient areas by hospital pharmacies. The data are not based on individual prescriptions and do not measure the appropriateness of antimicrobial therapy.
http://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/europeansurveillanceofantimicrobialconsumptionesac/surveillancereports/hospitalantibioticusereports/

Figure 2.1. Surveillance of Antimicrobial Use (AMU) in Ireland



*Data on antibiotics dispensed to outpatients, day cases and external facilities are excluded

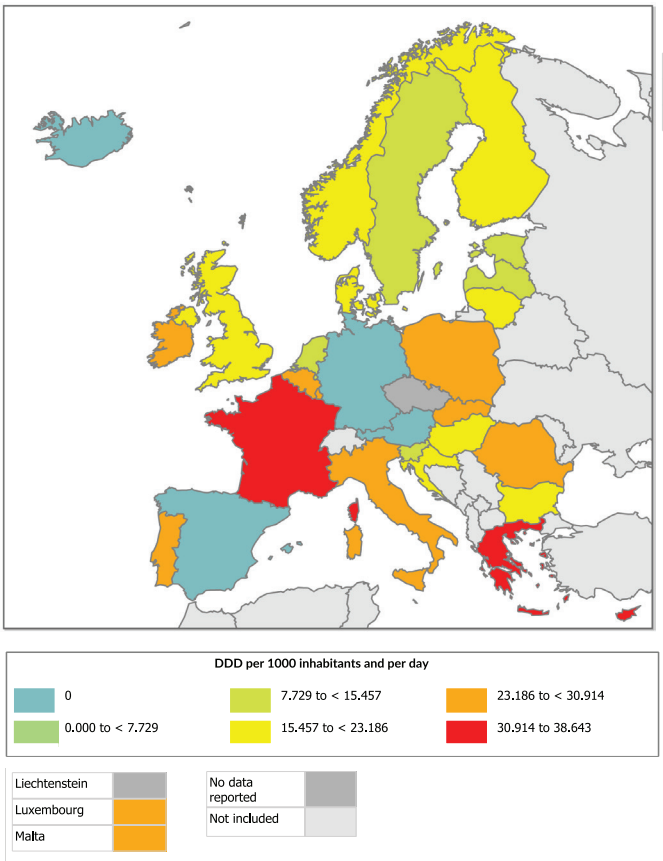
The antimicrobials under surveillance are antibacterials for systemic use (ATC group J01):
Beta-lactam penicillins (J01C); Other beta-lactams (J01D); Tetracyclines (J01A); Macrolides, lincosamides, streptogramins (J01F); Quinolones (J01M); Sulphonamides and trimethoprim (J01E); other J01 substances.

2.3 Overall Antimicrobial Use [Community and Hospitals]

In 2016, the overall use of antimicrobials for systemic use (ATC group J01) in the community and hospitals in Ireland was 26.1 DID. Ireland ranked 9th highest of 25 European countries for antimicrobial use in the human population (Figure 2.2).

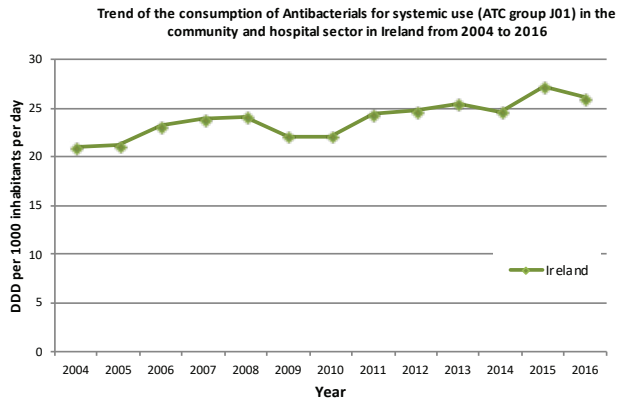
Overall antimicrobial use increased between 2004 and 2016 (Figure 2.3). Community antimicrobial prescribing accounts for the vast majority of use in humans in Ireland (90%).

Figure 2.2. Overall antimicrobial use (community and hospitals) Europe 2016



Source: Generated from ESAC-Net data submitted to TESSy, The European Surveillance System on 2018-04-26

Figure 2.3. Annual trends in overall antimicrobial use (community and hospitals) Ireland 2004 – 2016



Source: HPSC

Healthy Ireland Survey

Healthy Ireland is a national Framework for action to improve the health and wellbeing of the population of Ireland. Commissioned by the Department of Health, the Healthy Ireland Survey is an annual interviewer administered face-to-face survey of individuals aged over 15 years. It includes questions about antibiotic use and awareness.

From September 2016 to May 2017, data was collated from 7,487 individuals. Two in five participants had been prescribed an antibiotic in the previous year (Textbox 2.1).

Textbox 2.1

Health Ireland Survey (Hi)

Key Findings (Wave 3)

- 39% of participants were prescribed an antibiotic in the past 12 months
- 90% were aware that, if taken too frequently, antibiotics may not work in the future
- 71% were aware that resistance to antibiotics was a problem in hospitals

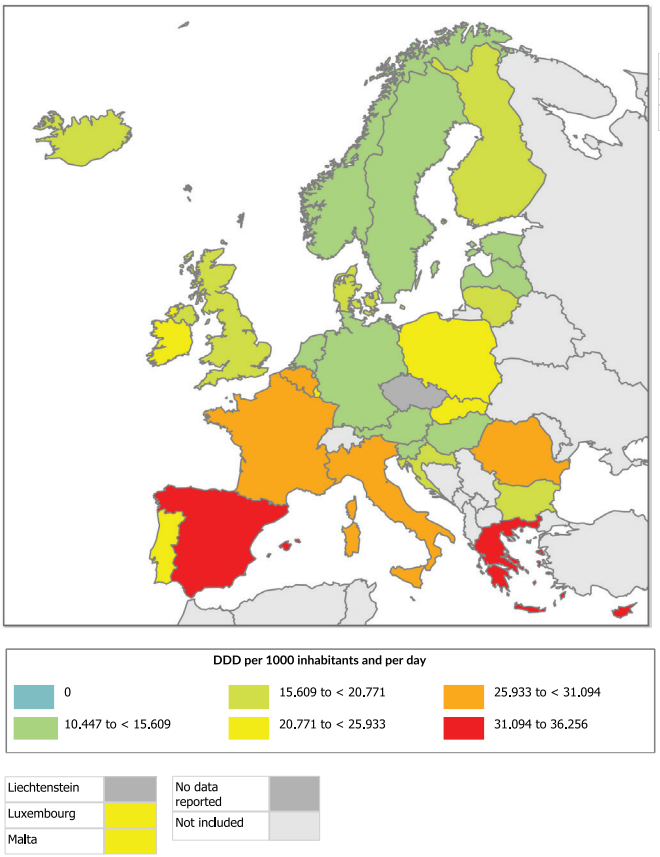
http://www.healthyireland.ie/wp-content/uploads/2017/10/Healthy-Ireland-Survey-Wave-3-Report-1.pdf

2.4 Community Antimicrobial Use

In 2016, community AMU for Ireland was 24.0 DID. Among European countries, the reported use of systemic antimicrobial agents (termed outpatient J01) ranged from 10.5 to 36.3 DID (2016 ESAC-Net report). Community AMU in Ireland was mid-to-high compared with other European countries (Figure 2.4).

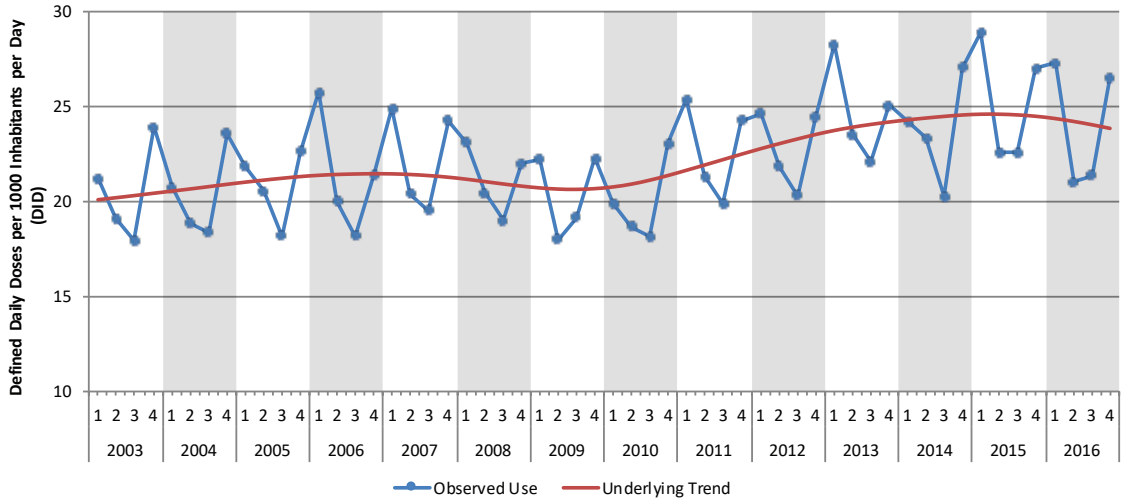
There has been an annual increasing trend in community antimicrobial use in Ireland since 2000 (Figure 2.5), with a marked seasonal fluctuation. The highest use is contemporaneous with periods of increased influenza activity. While antibacterials are ineffective against influenza, they may be empirically prescribed in the absence of confirmed viral infection or where there is concern about secondary bacterial infection.

Figure 2.4. Community antimicrobial use in Europe [2016] (Source: ECDC)



Source: ECDC

Figure 2.5. Quarterly and annual trends in community antimicrobial use in Ireland [2003 – 2016]



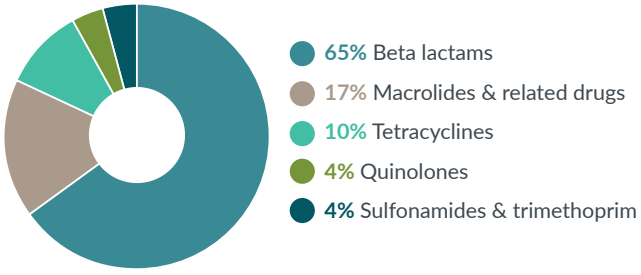
Source: HPSC

Commonest Antimicrobials

Beta lactams were the most commonly used antimicrobial class in Ireland in 2016, accounting for almost two-thirds of community use (Figure 2.6). When further divided by type, beta lactam-beta lactamase inhibitor combinations (e.g. co-amoxiclav) were most commonly used (6.8 DID), followed by broad spectrum penicillins (4.6 DID).

National guidelines for antimicrobial prescribing in the community were developed in Ireland from 2009, followed by the launch of the website www.antibioticprescribing.ie in 2012. It is noteworthy that beta lactam-beta lactamase inhibitor combinations are rarely recommended as first line therapy in the national guidelines.

Figure 2.6. Antimicrobial classes used in the community: Ireland [2016]



Source: HPSC

Long-term care facilities

Information on AMU in long-term care facilities is available from Ireland's participation in the HALT survey (Textbox 2.2).

Textbox 2.2

HALT Survey

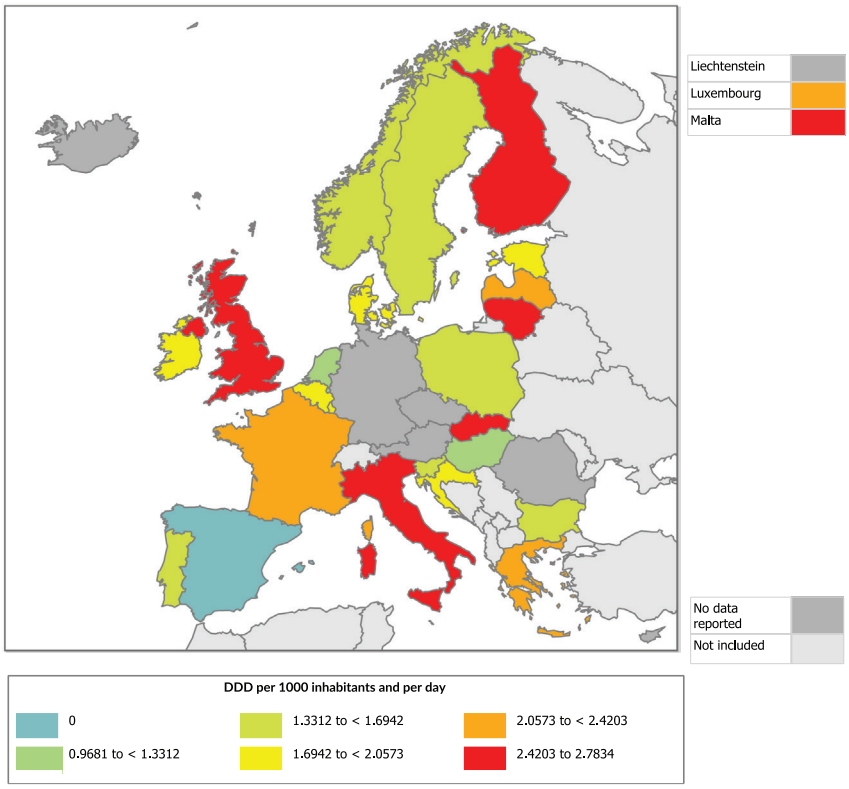
Ireland has participated in the European point prevalence surveys of healthcare-associated infections and antimicrobial use in long-term care facilities (LTCF), also known as the HALT survey, in 2010, 2013 and 2016

- In 2016, the median prevalence of antimicrobial use in 224 Irish long-term care facilities was 8.3%
- Most of those taking antimicrobials (83%) had commenced them while in the LTCF

2.5 Hospital Antimicrobial Use

In 2016, the median hospital AMU for Ireland was 84.8 DBD (data reported from 42 acute hospitals), a 3.7% increase on 2015 (81.8 DBD). Hospital antimicrobial use for Ireland in 2016 was mid-to-high compared with other European countries (Figure 2.7).

Figure 2.7. Hospital antimicrobial use in Europe [2016]

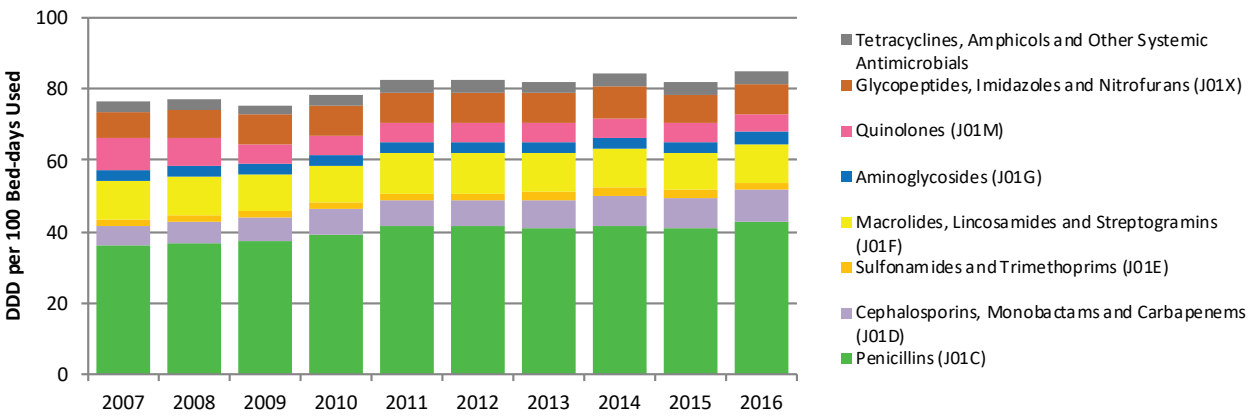


Source: ECDC

Commonest Antimicrobials

There has been an upward trend in annual national median hospital AMU in Ireland since 2007. Breakdown by the main antimicrobial classes is shown (Figure 2.8). Beta lactams combined (penicillins, cephalosporins, monobactams and carbapenems) accounted for 61% of hospital AMU in 2016.

Figure 2.8. Annual hospital antimicrobial use in Ireland, by main antimicrobial subgroups: 2007 – 2016

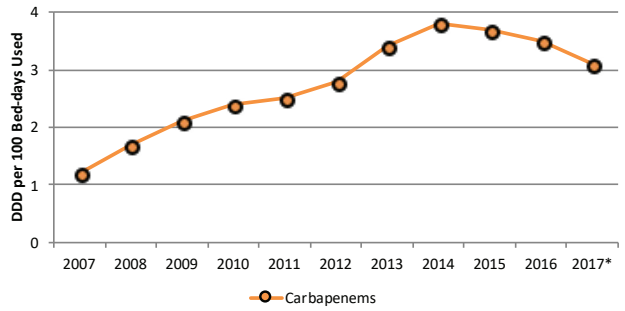


Source HPSC

As one of the critically important antimicrobial (CIA) classes, carbapenems are reserve agents which should be used for treatment of infections due to antimicrobial resistant organisms and infection in critically ill patients where the infecting organism or its antimicrobial susceptibility pattern has not been established. Increased annual carbapenem use was observed nationally from 2007, peaking in 2014 (3.8 DBD), with reductions observed in subsequent years to 3.1 DBD in 2017 (Figure 2.9).

Figure 2.9. Annual national carbapenem use in acute Irish hospitals: 2007 – 2017*

*results provisional for 2017 data to end Q4



Source HPSC
http://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/europeansurveillanceofantimicrobialconsumptionesac/PublicMicroB/SACHC/Report1.html

Surveillance of hospital AMU does not indicate whether or not the level of antimicrobial use is appropriate for a given patient population. For example, higher levels of AMU among tertiary hospitals may be appropriate, depending on the patient case-mix. Furthermore, DDD calculations are based on adult dosing and may therefore underestimate antimicrobial use in paediatric settings.

National Annual Antimicrobial Point Prevalence Survey
Since 2009, Irish hospitals have been invited to participate in the national annual antimicrobial point prevalence survey. Twenty-one hospitals participated in the first survey in 2009, increasing to 41 by autumn 2016 (2016 results, Textbox 2.3).

Textbox 2.3

National Annual Antimicrobial Point Prevalence Survey 2016

- The median prevalence of antimicrobial use was 37.8% (i.e. on any given day, just under 38% of patients in our hospitals are on an antibiotic to treat an infection or to prevent them from getting an infection). This level is higher than the average prevalence among European hospitals in general.
- Overall, 74.9% of antimicrobials prescriptions were compliant with local antimicrobial guidelines or microbiology/ID physician advice specific to combined antimicrobial choice, duration, dose and formulation.

2.6 Conclusion

The community accounts for about 90%, and hospitals for about 10%, of human antimicrobial use in Ireland.

Between 2004-2015, Ireland's overall human AMU trend was generally upwards. A slight dip occurred in 2016. Both hospital and community AMU were in the mid-to-high range compared with other European countries in 2016. Reductions in hospital use of carbapenems (critically important antimicrobials) have been observed since 2014.

There are some gaps in existing surveillance of AMU in Ireland:

- With regard to hospital AMU, data from private hospitals, antimicrobials dispensed to day cases, outpatients and external healthcare facilities are not included.
- AMU by the national outpatient parenteral antimicrobial therapy (OPAT) programme is not included.
- For community AMU, wholesale to retail pharmacy coverage is approximately 95% and wholesale data may not equate to AMU data
- Collectively, these gaps are estimated to account for 10% of antimicrobial use.

Several programmes and interventions have been established to support more rational antimicrobial prescribing in hospitals and in the community. A number of such initiatives are outlined (Textbox 2.4)

Textbox 2.4

Examples of programmes/interventions supporting more rational antimicrobial prescribing

1. GP Out of Hours Quality Improvement project, which has resulted in dramatic improvements in prescribing

2. Promotion of primary care guidelines, with emphasis on choosing 'preferred' agents https://www.hse.ie/eng/services/list/2/gp/antibiotic-prescribing/ (which is probably responsible for the decrease in overall community use since 2015, and there are also prescribing quality indicators from HSE's Primary Care Reimbursement Service (PCRS) that have shown a marked improvement over the same time period)

3. Start Smart, Then Focus. An Antibiotic Care Bundle for Hospitals (from the Royal College of Physicians of Ireland (RCPI) and the Royal College of Surgeons of Ireland (RCSI)) https://www.hse.ie/eng/services/publications/clinical-strategy-and-programmes/start-smart-stay-focused.pdf

4. Start Smart collaborative (supported antimicrobial quality improvement projects in ten acute hospitals)

5. HSE policy on making carbapenems one of the restricted antimicrobials in hospitals, and associated national key performance indicators (KPIs)

6. National gentamicin prescribing guidelines, and associated improvement collaborative

7. Support for antimicrobial stewardship in nursing homes, through the National Community Infection Prevention and Control Nurse Network and the joint HPSC & RCSI Annual Safe Patient Care Course

3. Antimicrobial Use (AMU) in Animals

Key Points 2016

Ireland ranked 17th highest of 30 EU/EEA member states for antimicrobial use in animals (when measured in milligrams of active compound per estimated kilogram of animal biomass) in 2016.

A 6.7% increase in the overall sales of veterinary antimicrobials in Ireland was recorded for the year 2016.

Most animal AMU in Ireland (66.6%) is formulated as premixes or oral remedies, presumed to be predominantly used as in-feed or in-water medication for the intensive pig and poultry sectors.

The antimicrobials most commonly used in animals in Ireland (by weight) are:
- Tetracyclines (39.9%)
- Sulphonamides & Trimethoprim (20.7%)
- Penicillins (20.4%)

This Section is primarily based on 'Report on consumption of veterinary antibiotics in Ireland during 2016'. HPRA Health Products Regulatory Authority. Available at: http://www.hpra.ie/docs/default-source/default-document-library/report-on-consumption-of-veterinary-antibiotics-in-ireland-during-2016367b0a2697826eee9b55ff00008c97d0.pdf?sfvrsn=0

3.1 General

The '*National Farmed Animal Health Strategy 2017-2022*' recognises the important role played by veterinary medicines in terms of disease prevention, in limiting the impact of disease outbreaks when they do occur, and in protecting the welfare of animals. However it highlights the risk to public health if such products are not used appropriately and prudently in animals farmed for food production, and specifically focuses on the threat posed by AMR.

Many of the antimicrobials used in the treatment of animals are the same drugs as those used in human medicine, albeit that approximately 88% of veterinary drugs used in Ireland comprise older drug classes including penicillins, tetracyclines, potentiated sulphonamides and aminoglycosides. Antimicrobials have been used widely in the treatment of animals since the 1950s and are universally accepted as being indispensable for treating animals.

The use of antimicrobials in animals is a potentially important risk factor for the selection and dissemination of resistant microorganisms and determinants (i.e. bacterial genes) from animals to humans. This risk arises via the consumption of produce (milk, eggs, honey, meat) from treated animals, but also from contact with treated animals themselves (be they companion animals or food-producing animals) as well as their environment. Although the relative contribution of resistance development within animal production systems is not quantified and is subject to debate, there is no doubt that antimicrobial resistant organisms are transmitted between animals and humans and it is now unquestioned that actions need to be taken within the agriculture sector to reduce the rate of resistance development overall. There is a need to safeguard the effectiveness of antimicrobials as a precious resource in both human healthcare and veterinary medicine through responsible use by all under the 'One Health' banner.

3.2 Data Sources

The Health Products Regulatory Authority (HPRA) is the competent authority for gathering information nationally on the consumption of veterinary antimicrobial drugs, in accordance with a programme known as European Surveillance of Veterinary Antimicrobial Consumption (ESVAC) which is coordinated by the European Medicines Agency (EMA). Reports on veterinary consumption of antimicrobial drugs for recent years can be accessed on the HPRA website www.hpra.ie.

Companies marketing veterinary antimicrobials in Ireland were requested to submit annual returns for quantities of individual presentations of product supplied in the State during 2016. The data to be provided were described in a format prescribed by the ESVAC protocol (www.ema.europa.eu). Data were collated on a total of 51 individual antimicrobial substances contained in over 900 product presentations which have been authorised for use in Ireland (including both medicines authorised nationally by the HPRA as well as those authorised centrally by the EU Commission). The data are based on self-declarations by applicant companies and have not been subject to independent verification or audit. It should be noted that certain other veterinary antimicrobials (such as those authorised under special licence by the Department of Agriculture, Food and the Marine) and human antimicrobials (which might be prescribed or used by veterinary practitioners where there is not a suitable veterinary alternative authorised) were not included in this analysis. However, the contribution from these sources to the overall figure is likely to be very small.

The data were collated by the HPRA and reviewed for discrepancies before being entered into the ESVAC database for validation. The database includes data from other countries within the European Union, as well as some neighbouring countries. The methodology for collection is a harmonised approach that is followed in each of the European Member States.

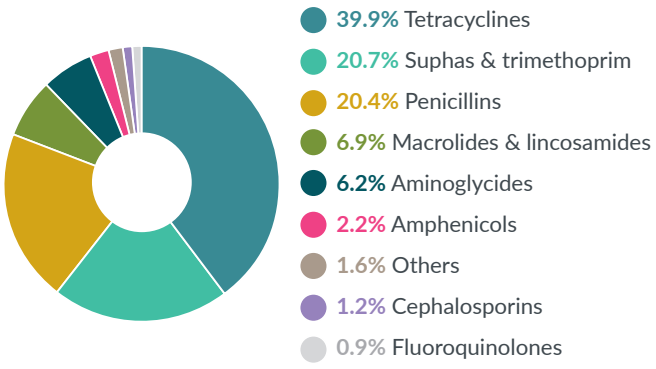
The analysis of the data in respect of individual substances of the same antimicrobial classes have been grouped together and classified under the appropriate class headings. In this report the headings are as follows: penicillins, amphenicols, tetracyclines, fluoroquinolones, aminoglycosides, macrolides, lincosamides, sulphonamides & trimethoprim (TMP), cephalosporins and other classes.

The HPRA advise that this consumption data should be interpreted with caution as annual consumption (sales) figures vary within certain limits and such variation is regarded as normal. In addition they note that the data are based on the voluntary declarations by marketing authorisation holders of the supply of their products.

3.3 Overall Antimicrobial consumption in animals

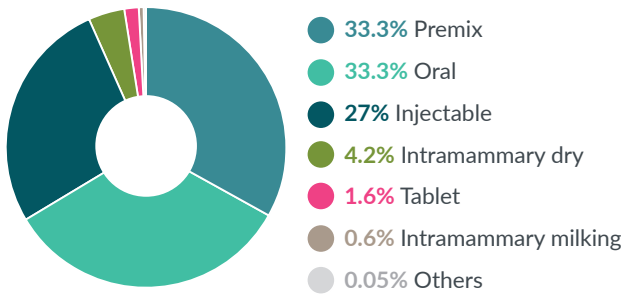
The total tonnage of veterinary antibiotics sold in Ireland was 103.4 tonnes in 2016. These results are broken down by antibiotic classes supplied into the market in Figure 3.1 and by pharmaceutical form in Figure 3.2 below:

Figure 3.1. Distribution of sales (based on tonnes sold) of veterinary antibiotics supplied in 2016 in Ireland



Source: HPRA

Figure 3.2. Pharmaceutical form breakdown of veterinary antibiotics sold in 2016 in Ireland



Source: HPRA

3.4 Discussion

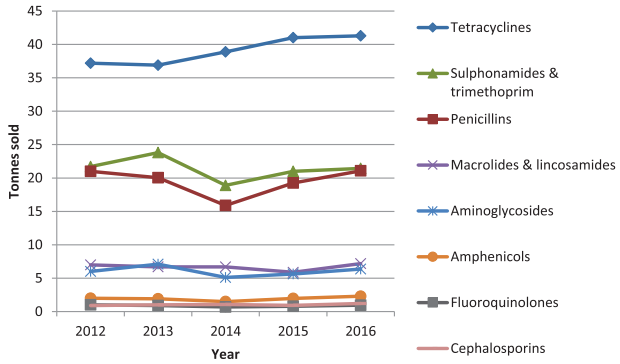
The data collected indicates that sales of veterinary antibiotics increased by approximately 6.5 tonnes in 2016 (Table 3.1). From the table below it can be seen that the overall tonnage fluctuates from year to year.

Table 3.1. Sales (tonnes sold) of veterinary antibiotics for the years 2012 - 2016

	2012	2013	2014	2015	2016
Tonnes sold	97.4	99.1	89.4	96.9	103.4

An investigation of sales on a class basis, highlights that tetracyclines comprise a substantial portion of overall tonnage, representing 39.9% of the total (Fig 3.3). The sales of sulphonamides & trimethoprim, penicillins and aminoglycosides remained consistent with the general trend observed in the previous years. The overall proportion of sales based on tonnes sold remained relatively unchanged (Fig 3.3).

Figure 3.3. Sales (tonnes sold) of veterinary antibiotics for the years 2012 – 2016



Source: HPRA

In particular, the sales of the critically important antibiotics, 3rd & 4th generation cephalosporins, fluoroquinolones and macrolides remained broadly in line with the ranges observed previously (Table 3.2).

Table 3.2. Sales (tonnes sold) of 3rd & 4th generation cephalosporins, fluoroquinolones and macrolides & lincosamides for the years 2012 – 2016

	2012	2013	2014	2015	2016
3rd & 4th gen. cephalosporins	0.21	0.17	0.24	0.22	0.25
Fluoroquinolones	1.00	0.89	0.69	0.79	0.94
Macrolides & lincosamides	7	6.7	6.7	5.9	7.2

Source: HPRA

The proportion of pharmaceutical forms (i.e. presentations of product) supplied to the market was similar compared with previous years (Fig 3.2). Premixes and oral remedies (oral pastes, powders, solutions and boluses) each accounted for 33.3% of sales. The next major group consisted of injectable products accounting for 27.0% of sales.

The range of veterinary antibiotic products in Ireland continues to expand with an additional 21 products authorised in 2016. This was offset by a small number of products being withdrawn. However, it should be noted that not all authorised products are marketed. These authorisations may support the marketing of the products in international markets or may be held by the companies concerned for strategic or commercial purposes.

3.5 Conclusion

A 6.7% increase in the overall sales of veterinary antibiotics was recorded for the year 2016. It is not known if this marks a true indication of increased use, or may be explained by other factors. As noted previously by HPRA, fluctuations in annual sales within a range of plus or minus 5% may occur, due to a variety of factors such as seasonal disease prevalence, changes in the size of the national herd or product held in the supply chain between years.

Currently, the available information on AMU in food-producing animals is based on sales and, as such, does not provide a breakdown of use by species and age-group of animals treated or the specific indication for treatment (at farm/herd level). Therefore, a number of initiatives have been taken to try and address this knowledge gap and encourage reduced and more prudent use of antimicrobials in Irish farming systems - either as funded research (Textbox 3.1) or as part of industry-led disease control programmes (Textbox 3.2).

Textbox 3.1

Research projects aimed at better understanding drivers of antimicrobial usage (AMU) in pig production

DAFM and Teagasc support and contribute to a number of collaborative research projects with Irish Universities (notably UCD and CIT) and international partners – which collectively aim to better understand the key drivers of AMU in the pig industry

WELPIG
Exploring the link between poor welfare, production diseases, antimicrobial usage and resistance on Irish pig farms (2014-2017; TEAGASC-funded)
https://www.teagasc.ie/animals/pigs/research/research-current-projects/welpig/

Key objectives:
- To determine risk factors (housing, management, nutritional, biosecurity etc.) for antimicrobial (AM) usage on Irish pig farms
- To determine information on social drivers for AM prescribing by veterinarians and AM administration by pig farm personnel
- To quantify the range and extent of AM usage in the production cycle in both high and low usage herds and to determine the relationship with pig welfare

PATHSURVPIG
Investigation of respiratory disease on Irish pig farms, associated risk factors, and the relationship with performance, welfare and antimicrobial use (2014-2018, DAFM funded)
https://www.teagasc.ie/animals/pigs/research/research-current-projects/pathsurvpig/

Key objectives:
- To identify infectious diseases of primary importance to the Irish pig industry, their effects on growing-finishing efficiency and to assess associated risk factors
- To identify the prevalence and aetiology of pleurisy and bronchopneumonia in Irish slaughter pigs and the effects on carcass quality and farm profitability
- To develop cost efficient diagnostic tools for the management of respiratory disease in Irish pigs
- To undertake cost-benefit analysis of disease and welfare problems on Irish pig farms and current treatment and preventive measures

AMURAP
Antimicrobial Use and Resistance in Animal Production (2016-2020, DAFM funded)
https://www.agriculture.gov.ie/research/fundedprojects/agriculture/animalproduction/antimicrobialuseandresistanceinanimalproduction/

Key objectives:
- To better understand the current use of antibiotics in Irish pig farms, and factors involved, to help farmers reduce their use with no economic loss
- To determine the actual effect of specific antimicrobial use practices on the occurrence of resistance in zoonotic and commensal bacteria

Textbox 3.2

CellCheck

An industry-led initiative to prevent and control bovine mastitis and improve milk quality will encourage reduced and more prudent usage of antimicrobials in Irish dairy production

Subclinical mastitis can be a significant problem in dairy production resulting in poor milk quality due to elevated somatic cell (leucocyte) counts in milk. Occasional cases of clinical mastitis also occur in milking cows. Streptococcal and staphylococcal species are the pathogens most frequently associated with bovine mastitis. However affected cows are almost invariably predisposed to infection by underlying environmental or husbandry factors such as inadequate hygienic standards or milking practices.

Antimicrobials, usually in an intra-mammary injectable format, are frequently relied upon both to treat clinical mastitis in lactating cows and to control or prevent subclinical mastitis in non-lactating cows. However, the choice of antimicrobial is not routinely supported by laboratory data, as culture and sensitivity testing is generally only undertaken where there have been persistent herd problems and treatment failures. Notwithstanding this, the available data (assembled by DAFM Regional Veterinary Laboratories) suggests that the majority of mastitis-causing bacteria isolated from mastitic milk samples remain susceptible to older antimicrobial compounds such that there is little or no bacteriological indication for using newer compounds considered more critical for human healthcare.

Animal Health Ireland (AHI) is a not-for-profit organisation, tasked with pursuing effective control strategies for economically important diseases of livestock which are not subject to international regulation. AHI co-ordinates and facilitates the national mastitis control programme, "CellCheck", which is developed and delivered in partnership with industry bodies representing farmers, processors, service providers and government and is focused on establishing best practice in the prevention and control of mastitis.

CellCheck has been working in partnership with the DAFM Regional Veterinary Laboratory (RVL) in Limerick to harmonize methods and standards of commercial services available for mastitic milk samples. The RVL has developed a proficiency test (PT) scheme, which all commercial laboratories offering milk culture are welcome to participate in. Phase 1 of the PT scheme focused on bacterial identification, and provides participating laboratories with an opportunity to evaluate their methods and results on a quarterly basis, and score their performance. Phase 2 of the PT scheme will look at standards of sensitivity testing services on offer. Participating laboratories also contribute results from commercial samples received into a central, anonymized database, which means that there is a more comprehensive understanding of the pathogens causing mastitis in Irish herds, and any related antimicrobial resistance patterns. Any commercial laboratory that successfully participates in the DAFM PT scheme is recognised as a 'CellCheck Partner Lab', delivering mastitic milk sample services to an agreed standard and undergoing continual evaluation in this area.

Ultimately it is expected that more reliable information will guide treatment choices and encourage reduced and more prudent usage of antimicrobials in the prevention and control of bovine mastitis.

4. Antimicrobial Resistance (AMR) in Bacterial Isolates from Humans

Key Points 2016

Carbapenemase producing *Enterobacteriaceae**(CPE) (2017)

CPE was declared a national public health emergency on 25th October 2017 in response to rising national numbers of patients with newly-detected CPE colonisation or infection [282 in 2016; 433 in 2017]

There were 14 notifications of invasive CPE infection in 2017

The predominant carbapenemase type in Ireland is OXA-48

Key pathogens causing bloodstream infections (BSI) (2016)

Annual increases in AMR were observed for *Enterobacteriaceae* (*Escherichia coli*, *Klebsiella pneumoniae*) and *enterococci* (*Enterococcus faecium*, *Enterococcus faecalis*)

In 2016, of those *E. coli* causing bloodstream infection, 11% were extended spectrum beta lactamase (ESBL)-positive *E.coli*

In 2016, of those *E. faecium* causing blood stream infection, 44% were vancomycin resistant

In 2016, both the number and proportion of BSI caused by *Staphylococcus aureus* that were methicillin resistant (MRSA) fell to lowest recorded levels. Of *S. aureus* causing bloodstream infection, 14.7% were methicillin resistant

Neisseria gonorrhoeae infection (2016)

Increase in gonococcal isolates with high level azithromycin resistance (HL-AziR) detected since 2015

*Note: Terminology change in 2018 for *Enterobacteriaceae* = *Enterobacterales*

4.1 General

In Ireland, national AMR surveillance has concentrated on key pathogens causing bloodstream infections (BSI) that are included in the list of Notifiable Diseases (Infectious Disease Regulations) and captured through participation in the European Antimicrobial Resistance Network (EARS-Net). There has been over 95% population coverage since 2004. Additionally, through a network of microbiology laboratories with specialist research interests and designated national reference laboratory (NRL) functions for certain additional pathogens on the list of Notifiable Diseases, AMR trends are also available for other microorganisms: carbapenemase producing *Enterobacteriaceae* (CPE), zoonoses such as salmonellosis and sexually transmitted infections due to *Neisseria gonorrhoeae*.

An overview of terminology related to AMR in *Enterobacteriaceae* is displayed (Figure 4.1). Explanations are given for key enzymes which, when produced by *Enterobacteriaceae*, enable them to become resistant to certain antimicrobials. These enzymes are extended spectrum beta lactamases (ESBLs) and carbapenemases.

4.2 Carbapenemase producing Enterobacteriaceae (CPE)

Carbapenemase Producing *Enterobacteriaceae* CPE* was first reported in Ireland in 2009. Since then, CPE has caused outbreaks in acute hospitals and long-term care facilities. In 2017, fifteen outbreaks were reported (an increase from five in 2016).

Transmission in healthcare facilities can result in closure of beds, wards and units as an outbreak control measure, thereby removing essential capacity to provide services, to admit patients from Emergency Departments and to address waiting lists effectively. Due to the rapid and worrying increase in incidence, the Minister for Health declared CPE a national public health emergency on 25th October 2017. The sequence of national actions which culminated in the activation of this national CPE public health emergency is outlined below (Textbox 4.1).

*The term Carbapenem Resistant *Enterobacteriaceae* CRE is often used as synonymous with CPE. However, the categories CPE and CRE differ in significant technical respects.

Figure 4.1. Terminology related to *Enterobacteriaceae* and resistance to beta lactam antimicrobials

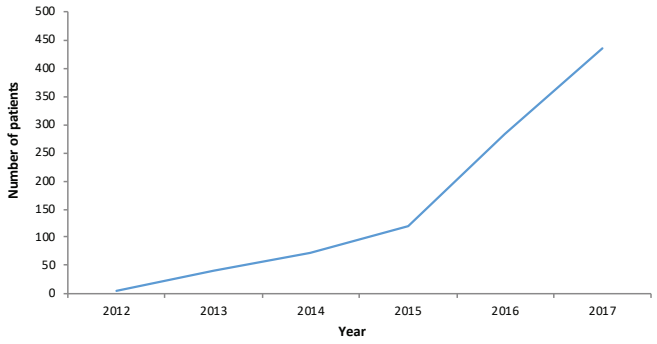
Textbox 4.1

National Actions in response to the emergence of CRE/CPE in Ireland

- March 2011: CRE made notifiable. Category '*unusual cluster or changing pattern of illness*'
- June 2011: Voluntary national CRE enhanced surveillance scheme established
- September 2011: invasive CRE infection (blood, cerebrospinal fluid or normally sterile site) became notifiable
- October 2012: Designation of national CPE reference laboratory (NCPERL) at University Hospital Galway
- January 2017: Transition from voluntary to mandatory national CPE enhanced surveillance scheme, requiring all Irish microbiology laboratories to report quarterly data to HPSC, including those serving public and private hospitals
- August 2017: Acute public hospitals required to return monthly indicators related to CPE to the Health Service Executive (HSE)
- October 2017: National CPE public health emergency activated by Minister for Health. National Public Health Emergency Team (NPHET) formed by Department of Health to oversee response. CPE Expert Group subsequently established to provide expert advice to NPHET

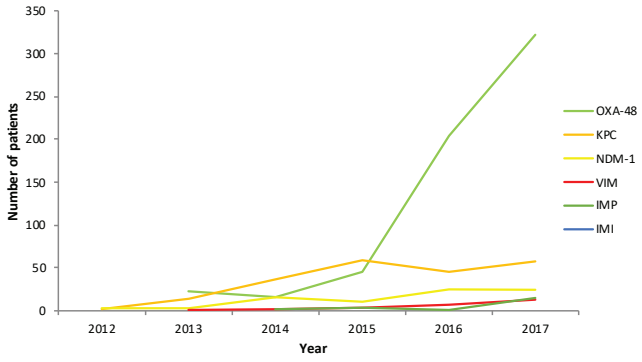
Irish microbiology laboratories are requested to submit all newly-detected isolates from both diagnostic and screening specimens that are suspected to contain CPE, or locally-identified as CPE, to the National CPE Reference Laboratory (NCPERL) for confirmation or further characterisation. In 2017, 433 patients with newly-detected CPE were identified (2016 = 282). Figure 4.2 displays annual patients with newly confirmed CPE by NCPERL and Figure 4.3 displays an annual breakdown of carbapenemases by type, demonstrating the predominance of OXA-48 in Ireland since 2016.

Figure 4.2. Annual numbers of patients with CPE newly-confirmed: 2012 – 2017



Source: NCPERLS (CPE Monthly Update Report Feb 2018: HPSC, NCPERLS & BIU)

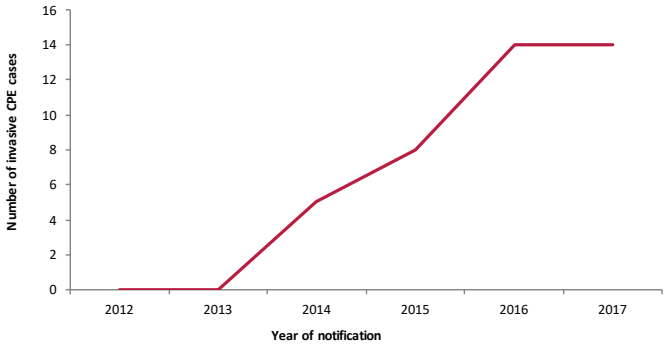
Figure 4.3. Annual numbers of patients with CPE newly-confirmed by carbapenemase type: 2012 – 2017



Source: NCPERLS (CPE Monthly Update Report Feb 2018: HPSC, NCPERLS & BIU)

CPE infection is deemed to be invasive when the organism is grown from a body site which would normally be expected not to contain bacteria (e.g. blood, cerebrospinal fluid or other sterile site). Invasive infection was made notifiable in Ireland in September 2011. A sharp increase in invasive CPE notifications occurred between 2013 and 2016. A total of 14 cases of invasive CPE infection were notified in 2017, similar to 2016 (Figure 4.4).

Figure 4.4. Annual notifications of Invasive CPE infections (2012–2017)



Source: CIDR (From CPE Monthly Update Report Issued June 2018: HPSC, NCPERLS & BIU)

The spread of CPE in Ireland is potentially in a containment phase. However, the window for containment is finite. Urgent prevention and control measures are required for both acute and community healthcare settings to address the threat to public health and sustainability of health delivery service systems.

4.3 AMR Trends in Key Pathogens causing Bloodstream Infections (BSI)

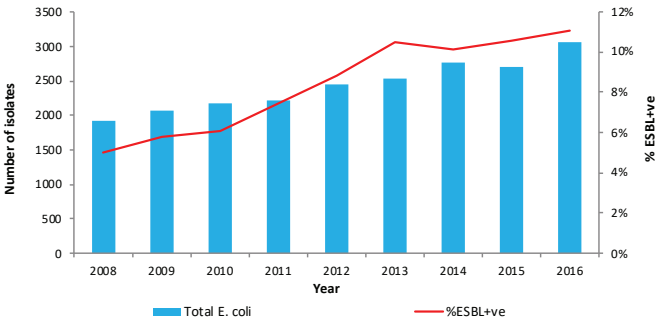
EARS-Net aims to provide comparable and validated data on the prevalence and spread of AMR in selected bacteria causing invasive human infection across the EU/EEA. The bacteria under surveillance include Gram-positive organisms (*Streptococcus pneumoniae*, *Staphylococcus aureus*, *Enterococcus faecalis* and *Enterococcus faecium*) and Gram-negative organisms (*E. coli* and *Klebsiella pneumoniae* which are both important members of the *Enterobacteriaceae* family, *Pseudomonas aeruginosa* and *Acinetobacter* spp). In Ireland, EARS-Net participant laboratories submit data on the first invasive isolate per patient per quarter to HPSC. Overall, population coverage for EARS-Net has remained over 95% since 2004.

4.3.1 *Escherichia coli (E. coli)*

E. coli are part of the normal intestinal flora in humans. They can, however, invade other body sites leading to serious infections such as BSI, pneumonia, urinary tract infection (UTI) and meningitis. They are a common cause of community and healthcare acquired BSI which generally occurs secondary to other infections such as UTI or wound infections.

E. coli is one of two members of the *Enterobacteriaceae* family included in EARS-Net surveillance. It is the commonest microorganism causing BSI in Ireland, with 3,057 *E. coli* BSI reported in 2016. Of those *E. coli* causing BSI, the proportion that are ESBL-producing *E. coli* has been increasing annually; it was 11% in 2016, the highest level since surveillance began (Figure 4.5).

Figure 4.5. Annual total number of E. coli BSI in Ireland, with % ESBL producing: 2004 – 2016

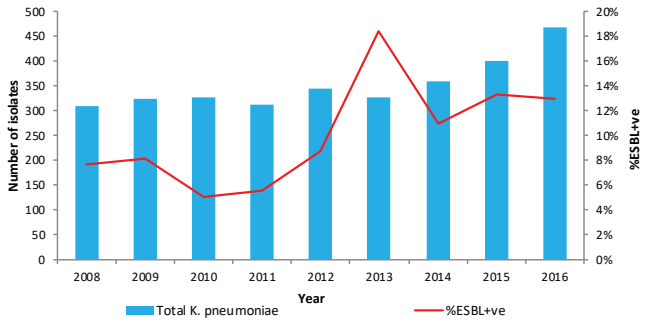


Source: HPSC

4.3.2 *Klebsiella pneumoniae (K. pneumoniae)*

K. pneumoniae is the second member of the *Enterobacteriaceae* family included in EARS-Net surveillance. It causes fewer BSI annually in Ireland than *E. coli* (n=469 in 2016). In 2016, of those *K. pneumonia* causing BSI, the proportion that were ESBL-producing was 12.9% (Figure 4.6).

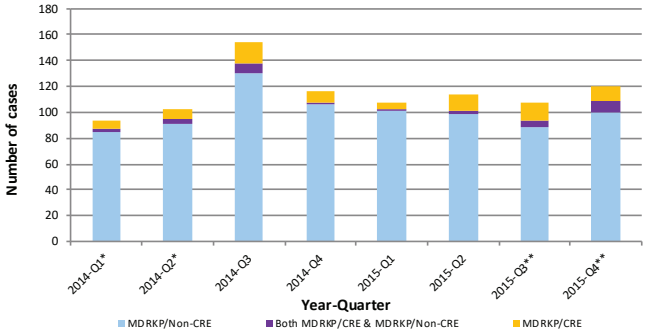
Figure 4.6. Annual total numbers of *K. pneumoniae* BSI in Ireland, with % ESBL producing: 2004 – 2016



Source: HPSC

Multi-drug resistance (MDR) is a term used to describe bacteria that are resistant to three or more different antimicrobial classes. In 2013, a national increase in *K. pneumoniae* isolates reported to EARS-Net that were MDR (MDRKP) was observed. A national MDRKP outbreak control team was established to further evaluate this emerging threat. Microbiology laboratories were required to report detection of MDRKP from all specimens, not limited to invasive isolates (e.g. BSI) to HPSC from January 2014. In the first three years of surveillance (2014-2016), it became apparent that MDRKP was already widely distributed throughout the Irish healthcare system, with 1,449 cases reported by 53 acute hospitals (Figure 4.7). In 2016, the number of MDRKP cases that were carbapenem resistant (n=119) almost doubled compared with 2015 (n=61).

Figure 4.7. Quarterly total numbers of multi-drug resistant *K. pneumoniae* (MDRKP) in Ireland: 2014 – 2016



Source: HPSC Annual Epidemiological Report 2016

http://www.hpsc.ie/abouthpsc/annualreports/HSE%20HPSC%20Annual%20Report%20ready%202016.pdf (Annual Epidemiological Report 2016 HPSC – Enhanced Surveillance MDRKP p165)

4.3.3 *Pseudomonas aeruginosa (P. aeruginosa)* & *Acinetobacter baumanii (A. baumanii)*

P. aeruginosa and *A. baumanii* are Gram-negative microorganisms that exist widely in the environment. They are primarily environmental organisms that may be associated with infection in compromised and critically ill patients (opportunistic pathogens). While *P. aeruginosa* and *A. baumanii* are not members of the *Enterobacteriaceae* family, they remain important pathogens because of their propensity to also develop AMR. They have been implicated in outbreaks in healthcare settings.

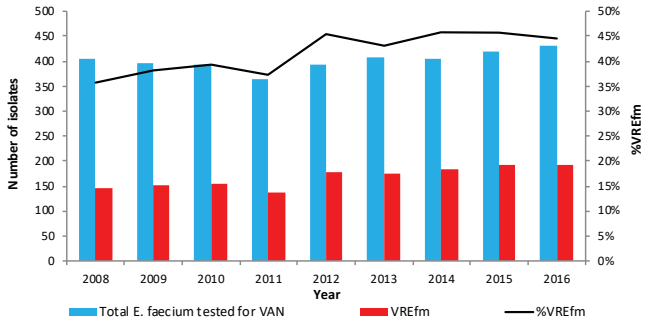
In 2016, there were 250 invasive *P. aeruginosa* infections notified, with 13.2% (n=33) identified as MDR, the highest proportion since surveillance began in 2006. There were 69 invasive *Acinetobacter* spp infections notified in 2016, none of which was categorised as MDR.

4.3.4 *Enterococcus faecium (E. faecium)*

Enterococci are Gram-positive bacteria found in the bowel of humans and animals. In most cases enterococci live harmlessly in the bowel (colonisation or carriage). Occasionally, they can escape the bowel and cause infection elsewhere in the body – UTI, wound infection or BSI. Those who are hospitalised, critically ill or immunocompromised and those with indwelling devices are most at risk of infection.

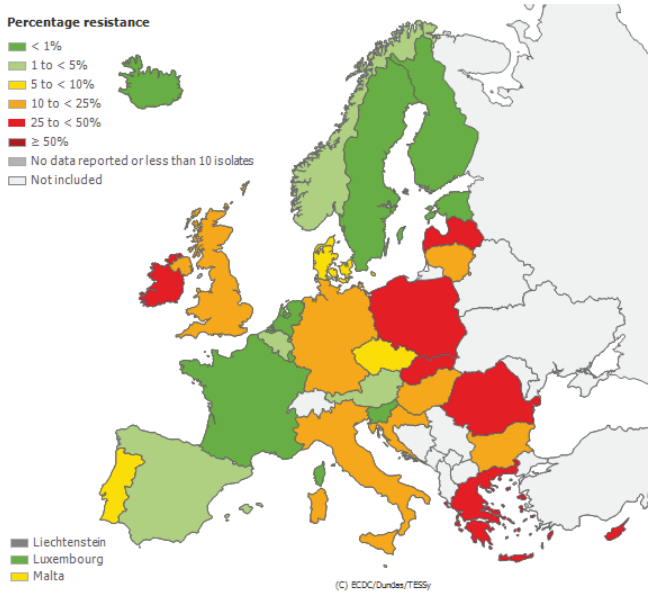
Enterococcus faecium and *Enterococcus faecalis* are the most common species causing infection in humans. *E. faecium* in particular, are inherently resistant to several commonly used antimicrobial classes, leaving few treatment options available for infection. When enterococci develop resistance to vancomycin they are termed vancomycin resistant enterococci (VRE). Enterococci may be transmitted from person-to-person through direct contact or contact with surfaces or items contaminated by enterococci. In Ireland, there were 431 *E. faecium* BSI reported in 2016. Of those, 44.4% were VRE (Figure 4.8). From 2008 to 2015, Ireland had the highest proportion of vancomycin resistant *E. faecium* (VREfm) among EU Member States. Ireland's profile remained among the highest in 2016 (Figure 4.9).

Figure 4.8. Annual total numbers of *E. faecium* BSI, with % resistant to vancomycin (VREfm): 2004 – 2016



Source: HPSC Annual Epidemiological Report 2016

Figure 4.9. Distribution of vancomycin-resistant *E. faecium* (VREfm) in EARS-Net countries in 2016



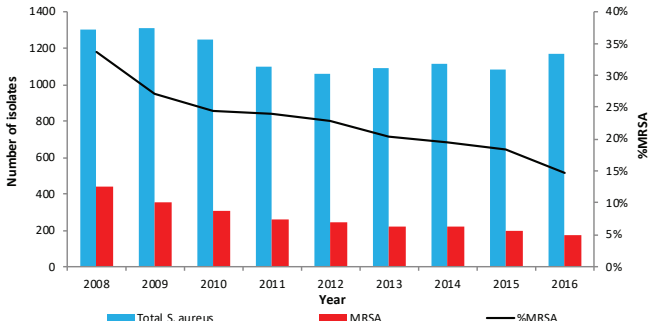
Source: EARS-Net at ECDC; map accessed via www.ecdc.europa.eu 13/10/17

4.3.5 *Staphylococcus aureus (S. aureus)*

S. aureus commonly colonises the skin and nose. Meticillin-resistant *Staphylococcus aureus* (MRSA) is *S. aureus* that has become resistant to most of the beta lactam antimicrobials commonly used to treat infection. *S. aureus* can cause severe infection such as BSI, infective endocarditis, pneumonia and skin and soft tissue infections. *S. aureus* infection can be fatal. Much work has been carried out by the National MRSA Reference Laboratory (NMRSARL) which has enhanced the understanding of the virulence features, clinical effects and epidemiology. National guidelines were updated in 2013.

There were 1,168 *S. aureus* BSI reported in Ireland in 2016. Of those, 172 (14.7%) were MRSA. The numbers and proportion of bloodstream infections due to MRSA have been decreasing since 2006 (Figure 4.10). Despite this, Ireland ranked 12th highest of 30 countries reporting to EARS-Net in 2016.

Figure 4.10. Annual total numbers of *S. aureus*/MRSA BSI, with % MRSA: 2004 – 2016



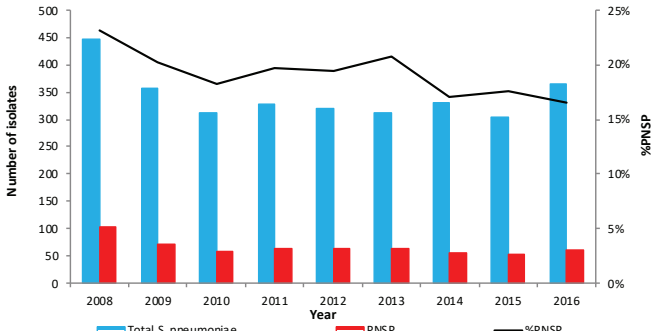
Source: HPSC Annual Epidemiological Report 2016

4.3.6 *Streptococcus pneumoniae (S. pneumoniae)*

S. pneumoniae (pneumococcus) is the most common bacterial cause of community-acquired pneumonia and a common cause of BSI and meningitis in children and adults. In recent years, many pneumococci have become resistant to some of the antimicrobials used to treat pneumococcal infections.

In 2016, 365 invasive *S. pneumoniae* infections were reported. Penicillin non-susceptible *S. pneumoniae* (PNSP) accounted for 16.5% (n=60) of all isolates tested against penicillin (n=364). There has been a downward trend in PNSP causing invasive infections in Ireland since 2013 (Figure 4.11). However, in 2016, Ireland ranked 8th highest of 29 European countries for PNSP. Erythromycin resistance was reported in 13.2% of isolates tested (n=47), with 9.9% of isolates reported as simultaneously PNSP and erythromycin resistant.

Figure 4.11. Annual total numbers of *S. pneumoniae* and PNSP BSI in Ireland, with % PNSP: 2008 – 2016

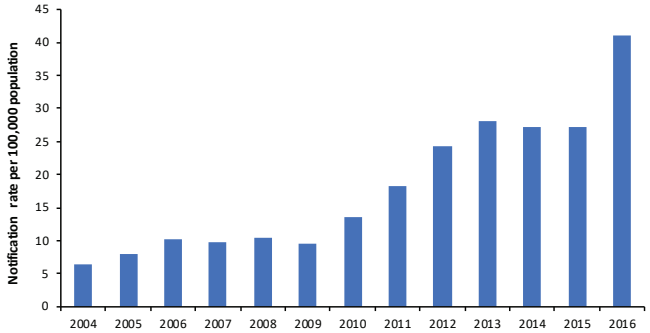


Source: HPSC

4.4 AMR Trends in *Neisseria gonorrhoeae* (*N. gonorrhoeae*)

Gonorrhoea, caused by *Neisseria gonorrhoeae*, is a notifiable disease in Ireland. It is the second most commonly reported sexually transmitted infection (STI) after chlamydia. Prior to 2013, limited surveillance data was available. Case-based notification began in 2013. The national burden of *N. gonorrhoeae* infection has been increasing annually, with 1,957 cases reported in 2016, a 51% increase on 2015 (Figure 4.12).

Figure 4.12. Annual total notification rates for *N. gonorrhoeae* in Ireland: 2004 – 2016

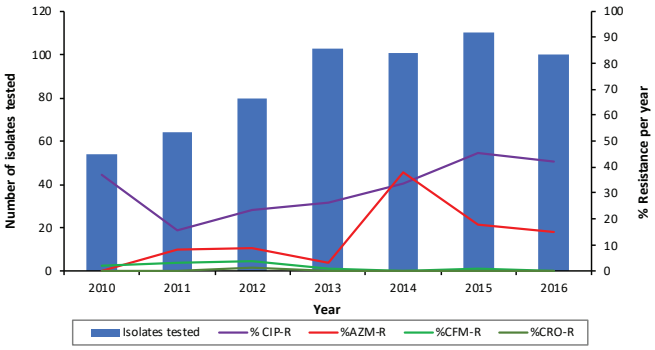


Source: HPSC

As *N. gonorrhoeae* is a fastidious organism with special requirements for microbiological culture and antimicrobial susceptibility testing, molecular-based testing methods (e.g., polymerase chain reaction) have become the mainstay of diagnosis. Therefore an isolate for antimicrobial susceptibility testing is frequently not available. In Ireland, referral of isolates to the national Interim Gonococcal Reference Laboratory for susceptibility testing is advised. The Laboratory has participated in the European Gonococcal Antimicrobial Surveillance Programme (Euro-GASP) since 2010.

N. gonorrhoeae can develop reduced susceptibility and resistance to the recommended empiric treatment options. In Ireland, 10 cases of high-level azithromycin resistance (HL-AziR) (MIC>256 mg/L) were reported from 2011 to 2016, with reduced susceptibility to extended spectrum cephalosporins; cefixime and ceftriaxone also described. These are regarded as last-resort treatment options. Current treatment guidelines recommend dual therapy, comprising ceftriaxone and azithromycin, in an effort to delay the development of resistance to ceftriaxone. However, if azithromycin becomes ineffective against *N. gonorrhoea*, there will be no further barriers to the development of ceftriaxone resistance. Annual trends in reduced/intermediate gonococcal susceptibility and resistance for key antimicrobials since 2010 are displayed in Figure 4.13. In 2016, gonococcal susceptibility results were submitted to Euro-GASP for 5% of *Neisseria gonorrhoea* isolates.

Figure 4.13. Annual trends in *N. gonorrhoeae* isolates with reduced/ intermediate susceptibility or resistance to key antimicrobials: 2010 – 2016



CIP-R, ciprofloxacin resistant; AZM-R, azithromycin resistant; CFM-R, cefixime resistant; CRO-R, ceftriaxone resistant

Source:HPSC

In response to concerns regarding increasing AMR, national guidelines for the prevention and control of *N. gonorrhoeae* were published in 2017. These cover prevention, surveillance, clinical management, laboratory diagnosis and public health response.
http://www.hpsc.ie/az/hivstis/sexuallytransmittedinfections/gonorrhoea/amrgonorrhoea/AMR Gonorrhoea guidelines documetn FINAL 2017.pdf

5. AMR in Zoonotic Bacterial Isolates from Humans and Animals

Key Points 2016

Salmonella isolates from humans

One-quarter of human isolates were MDR; 24.6% were resistant to ciprofloxacin and three ESBL-producing isolates were detected

Salmonella isolates from animals

Low levels of AMR were detected in *Salmonella* isolates from Irish poultry flocks

MDR and resistance to critically Important antimicrobials (CIAs) was observed in *Salmonella* isolates from imported poultry meat

Resistance in *Salmonella* isolates from Irish pigs was higher than the EU average for some antimicrobials

Campylobacter isolates from humans

In 2016, only 17.9% of *Campylobacter* isolates were identified to species level

No macrolide resistance was detected in a recent study (88 isolates)

Campylobacter isolates from animals (poultry)

Resistance to important antimicrobials was absent (erythromycin) or below EU average (ciprofloxacin) for *C. jejuni* isolated from Irish poultry.

5.1 General

Zoonoses are infections that are transmissible between animals and humans. Infections caused by *Campylobacter* and *Salmonella* can be acquired directly from animals, via environmental exposure or through the ingestion of contaminated foodstuffs. *Campylobacter* infection was the most commonly reported zoonosis in the EU in 2016. The increasing EU trend since 2008 stabilised during 2012–2016. The decreasing EU trend for human salmonellosis cases since 2008 ended during 2012–2016.

AMR in zoonotic bacteria obtained from food-producing animals is of particular concern as this can compromise the effective treatment of infections in humans. For several years, ECDC and the European Food Safety Authority (EFSA) have been producing an annual AMR report, under the EU Action Plan against AMR - One Health approach that addresses AMR in both humans and animals. High levels of MDR in *Salmonella* and *Campylobacter* bacteria have been observed in recent years.

Data Sources

The National *Salmonella*, *Shigella* and *Listeria* Reference Laboratory (NSSLRL) based in Galway has been providing reference services on *Salmonella* isolates from humans since 2000. There is currently no national reference laboratory in Ireland for the routine typing of *Campylobacter* isolates. It should be noted that most *Campylobacter* diagnosis in human clinical laboratories now uses molecular methods, with no organism cultured and therefore no isolate for identification to species level or for susceptibility testing. With few clinical laboratories identifying isolates to species level, information on *Campylobacter* species in the human population is limited. Data on resistance patterns in *Salmonella* and *Campylobacter* isolates from animals was obtained from the National Reference Laboratory for AMR (in animals, feed and food) hosted by DAFM at its Backweston Laboratory Complex.

5.2 Salmonella

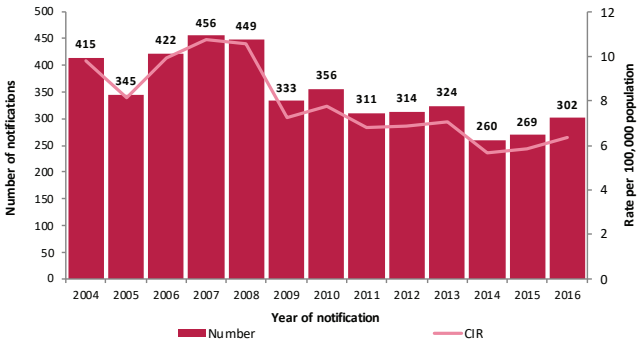
Salmonella live in the intestinal tract of domestic and wild animals including chicken, cattle, pigs and reptiles. *Salmonella* can be transmitted through direct contact with infected animals or humans, by contact with faecally contaminated environments, or by ingestion of faecally contaminated food or beverages. Foreign travel is a well-recognised risk factor for salmonellosis in Ireland. Human infection typically presents as an acute gasteroenteritis.

NOTE: In general, in this report, different salmonella serovars are referred to by the abbreviated form of S. (representing *Salmonella* and the serovar name for example Typhimurium (S. Typhimurium). The formal name, for example *Salmonella enterica* subspecies *enterica* serovar Typhimurium is not spelled out in each case). The term "monophasic S. Typhimurium" is used here as it is widely accepted to refer to isolates that have the antigenic formula of S. Typhiumurium except that they do not express both phases of the flagellar antigen that defines the serovar Typhimurium.

5.2.1 AMR Patterns in *Salmonella* Isolates from Humans

In 2016, 302 cases were notified corresponding to a crude notification rate of 6.3/100,000 (Figure 5.1). Overall, 46% of cases were travel-associated (for the 90% of notifications where country of infection was reported). Disease acquired in Ireland was more commonly caused by *S.* Typhimurium and monophasic Typhimurium strains (40%) than by *S.* Enteritidis strains (20%), with other strains making up the remaining 40% of cases. By contrast, disease acquired in Europe was most commonly associated with *S.* Enteritidis (56%), followed by other strains (28%), with *S.* Typhimurium and monophasic Typhimurium strains accounting for only 16% of cases. For cases associated with acquisition in the rest of the world, non-Enteritidis, non-Typhimurium cases predominated (65%), *S.* Enteritidis accounting for 24% and *S.* Typhimurium and monophasic Typhimurium strains for 11% of cases.

Figure 5.1. Salmonellosis notifications and Crude Incidence Rate (CIR) by year of notification



Source: HPSC Annual Epidemiological Report 2016]

In 2016, a total of 309 human clinical *Salmonella* isolates were typed (including 7 *S.* Typhi and 6 *S.* Paratyphi). *S.* Typhimurium (14.2%), its monophasic variant 4,[5],12 : i :- (13.3%) and *S.* Enteritidis (26.9%) predominated, constituting 54.4% of human isolates.

More than half of the human isolates (54%) were susceptible to all antimicrobial agents tested. One-quarter (25.9%) were MDR (resistant to three or more different classes of antibiotics). Of those that were MDR, 8.4% had the profile of resistance to ampicillin, streptomycin, sulphonamide and tetracycline (ASSuT or ASuT) and were mainly monophasic *S.* Typhimurium.

Three ESBL-producing isolates were detected. These included an *S.* Agona isolate with mixed ESBL producing and non-ESBL producing populations, a monophasic *S.* Typhimurium (4,[5],12:i:-) and an *S.* Unnamed which did not express any O antigens. None of these isolates were associated with a record of recent foreign travel. In contrast, of the two AmpC producing *Salmonella*, an *S.* Anatum isolate and *S.* Infantis isolate were received from patients with travel to Spain and the Philippines respectively.

Seventy-six isolates of *Salmonella* resistant to ciprofloxacin were detected (24.6%). High level resistance to ciprofloxacin (>2mg/l) is rare among *Salmonella* but a ciprofloxacin-resistant *S.* Kentucky clonal group has arisen and spread from North Africa in the last decade. Six such isolates were typed in the NSSLRL in 2016, one of which had a history of foreign travel to Spain, another to Pakistan and another to the Philippines.

The NSSLRL added two new antibiotics, azithromycin and tigecycline, to its testing panel at the end of 2013, based on advice from ECDC, to detect emerging resistances. Resistance to azithromycin was detected in isolates from six patients, including one with foreign travel to Thailand and another to Malaysia. No isolates exhibited tigecycline resistance.

5.2.2 AMR Patterns in *Salmonella* Isolates from Food-Producing Animals

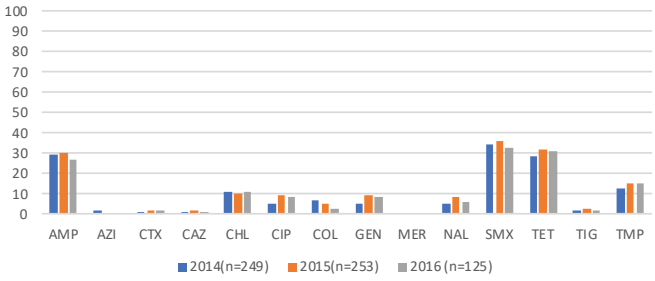
A multi-annual national *Salmonella* control plan in Ireland is aimed at reducing the incidence of *Salmonella* infection in pigs and poultry. It involves sampling and testing across the food-chain (feed and other inputs; environmental and animal sampling in production units and processing plants; retail product). This programme generates a broad range of *Salmonella* isolates as detailed below.

Antimicrobial susceptibility testing was carried out on *Salmonella* isolates that were derived from samples collected by DAFM ("official samples") and samples tested by commercial laboratories (on behalf of food business operators) as part of the national *Salmonella* control programme in poultry and pigs as well as veterinary clinical isolates submitted mainly by the DAFM Regional Veterinary Laboratories.

In the three-year period (2014 - 2016), 627 isolates obtained mainly from the major food producing animal species (pigs, poultry and cattle) or the associated production environment and 34 isolates from animal by-products or feeds were analysed. The majority of these isolates were derived from raw meat samples and abattoir sampling of pigs and poultry. In addition, isolates were obtained from samples collected on poultry farms as part of the *Salmonella* National Control Plan and from clinical submissions. Remaining isolates came from animal by-products that had been subject to heat treatment, animal feeding-stuffs, environmental samples and other food products.

The overall pattern of resistance of *Salmonella* isolates to the prescribed panel of antimicrobials against which they have to be tested is illustrated for the period 2014 to 2016 (Figure 5.2).

Figure 5.2. Occurrence of resistance to selected antimicrobials in *Salmonella* isolates from animals in each of the three years 2014 - 2016



Source: DAFM

Table 5.1. Percentage of isolates of the 12 most prevalent *Salmonella* serovars 2014 – 2016 that are resistant to different antimicrobials

Antimicrobial	Abbreviation	Typhimurium (n=118)	Monophasic Salmonella Typhimurium (n=82)	Bredeney (n=48)	Kentucky (n=44)	Enteritidis (n=40)	Dublin (n=32)	Brandenburg (n=29)	Derby (n=25)	Infantis (n=21)	Kimuenza (n=17)	Schwarzengrund (n=17)	London (n=15)
Ampicillin	AMP	57	91	2	7	8	3	0	16	10	0	6	0
Azithromycin	AZI	0	1	0	0	0	0	0	4	0	0	0	0
Cefotaxime	CTX	0	0	0	0	3	0	0	0	0	0	0	0
Ceftazidime	CAZ	0	0	0	0	3	0	0	0	0	0	0	0
Chloramphenicol	CHL	36	23	2	0	0	0	0	4	10	0	6	0
Ciprofloxacin	CIP	3	0	2	2	18	3	0	4	38	0	6	0
Colistin	COL	1	0	0	0	5	91	0	0	0	0	0	0
Gentamicin	GEN	9	34	2	0	3	0	0	0	0	0	6	0
Meropenem	MER	0	0	0	0	0	0	0	0	0	0	0	0
Nalidixic Acid	NAL	3	0	2	2	18	3	0	4	38	0	6	0
Sulfamethoxazole	SMX	64	98	2	7	3	3	0	48	48	0	6	7
Tetracycline	TET	52	93	0	2	3	3	14	52	43	0	0	13
Tigecyline	TIG	9	0	0	0	3	0	0	0	0	0	0	0
Trimethoprim	TMP	26	29	0	2	0	0	0	28	10	0	0	13

Source: DAFM

Antimicrobial not used in animals, but from an antimicrobial class which is used

Antimicrobial used in animals and humans

Antimicrobial from class used only in humans

The antimicrobials included in the testing of *Salmonella* and *E. coli* are as follows: ampicillin (AMP), azithromycin (AZI), cefotaxime (CTX), ceftazidime (CAZ), chloramphenicol (CHL), ciprofloxacin (CIP), colistin (COL), gentamicin (GEN), meropenem (MER), nalidixic acid (NAL), sulphamethoxazole (SMX), tetracycline (TET), tigecycline (TIG), trimethoprim (TMP).

The resistance patterns in the 12 most frequently isolated *Salmonella* serovars for the period 2014 to 2016 were compared (Table 5.1). S. Typhimurium and its monophasic variants comprised the majority of the animal- derived isolates and were the most resistant to antimicrobials. The number of S. Enteritidis isolates tested in 2015 was unusually high (33) due to an outbreak in broiler flocks.

Fluoroquinolones and Cephalosporins

Low levels of resistance overall were observed to the fluoroquinolones and 3rd and 4th generation cephalosporins, which are the treatments of choice in human *Salmonella* infections. Forty-five animal-derived *Salmonella* isolates (7% of the total) were resistant to ciprofloxacin; thirty of these derived from poultry meat, some of which was imported product. *S.* Infantis and *S.* Enteritidis comprised most of the ciprofloxacin resistant isolates. Plasmid mediated fluoroquinolone resistance, which is easily transferable between bacteria, was identified in four of the isolates. Eight ESBL-producing animal-derived *Salmonella* isolates were detected. These isolates were resistant to cefotaxime (a 3rd generation cephalosporin), resistance to which indicates ESBL activity. Seven were co-resistant to ciprofloxacin and other antimicrobials; all seven were derived from raw poultry meat imported from South America, Asia or Eastern Europe. The isolates possessed different resistance genes, which reflected their different geographic origins. Resistant *S.* Heidelberg from South America comprised the majority of these resistant isolates; similar isolates from this source have been observed by the NRL since 2011. In addition, a single ESBL producing isolate (*S.* Rissen) was obtained from a pork sample.

Other antimicrobials of medical importance

Azithromycin and tigecycline, although not used to treat animals, were included to screen for resistance in Gram-negative bacteria from animals.

- Resistance to azithromycin was only observed in three isolates of three different serovars in 2014, two of which were obtained from turkey meat and one from a pig carcase swab
- Tigecycline resistance (combined with tetracycline resistance) was observed in two isolates obtained from poultry (*S.* Enteritidis and *S.* Heidelberg) and 12 obtained from pigs (mainly S. Typhimurium) over the three-year period (2014 - 2016).

All but one of 37 colistin-resistant *Salmonella* isolates were either *S.* Dublin or *S.* Enteritidis, serovars that are considered to be inherently resistant to colistin, but susceptible to other antimicrobials. No known transmissible resistance genes such as mcr were identified in any of the resistant strains.

All isolates were susceptible to meropenem, which is used to screen for carbapenamase production.

Antimicrobials commonly used in veterinary medicine

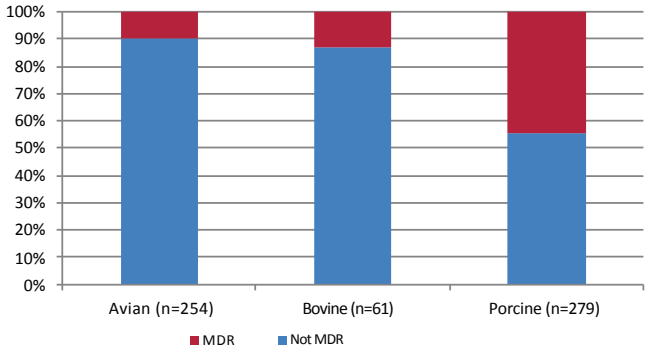
Resistance in *Salmonella* isolates from animal sources was highest to those antimicrobial classes that are commonly used in veterinary medicine (such as early generation beta-lactams, sulphonamides, and tetracyclines). Resistance to these antimicrobials in *Salmonella* isolates from Irish pigs was high relative to other EU countries. This reflects the high proportion of *S.* Typhimurium and its monophasic variants, some subtypes of which (such as DT104) are associated with MDR.

MDR

MDR *Salmonella* was more frequently evident in isolates from pigs (45% of isolates) than in those from either poultry (10%) or cattle (13%). Only a third of porcine isolates, but more than three quarters of the isolates from birds, were fully susceptible to the antimicrobials assessed (Figure 5.3).

The frequency of MDR (and of resistance to chloramphenicol and gentamicin) in *S.* Typhimurium isolates from Irish pigs was above the EU average, whereas the levels of resistance to antimicrobials (particularly the levels of MDR and of resistance to ciprofloxacin) in *Salmonella* isolates from Irish broilers were well below the EU average. This was attributed to the absence of MDR clones such as *S.* Kentucky ST198 and MDR *S.* Infantis in Irish flocks and the extremely low prevalence of *S.* Typhimurium and *S.* Enteritidis, relative to other countries.

Figure 5.3. Occurrence of MDR in *Salmonella* isolates from main food producing animal species 2014-2016

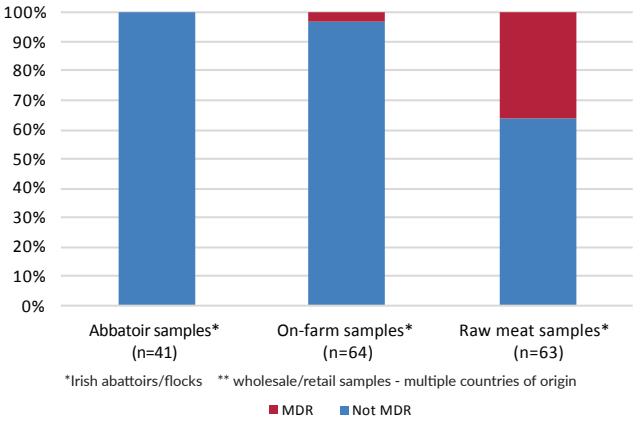


Source: DAFM

The level of MDR was markedly higher in *Salmonella* isolates from raw poultry meat (from broiler chickens, hens and turkeys; wholesale and retail product) from multiple countries of origin than in *Salmonella* isolates obtained from sampling at Irish farms and abattoirs (Figure 5.4). Eight of these isolates from raw poultry meat were resistant to five or more antimicrobials. They originated from Brazil (S. Heidelberg; n = 3), Austria (*S.* Infantis; n = 1), Thailand (1,4,12:-:1,2; n = 1), Ukraine (*S.* Schwarzengrund; n = 1) and the Netherlands (*S.* Bredeney; n =1). The origin of the eighth isolate (*S.* Saintpaul) was not traceable.

Although MDR *Salmonella* was more frequently detected in imported poultry meat than in domestically produced broilers, the true prevalence of MDR bacteria in this category of sample is not currently known as the isolates reported on here were acquired through passive surveillance rather than structured surveillance at retail level.

Figure 5.4. Occurrence of MDR in *Salmonella* isolates from poultry samples 2014-2016



Source: DAFM

5.3 Campylobacter

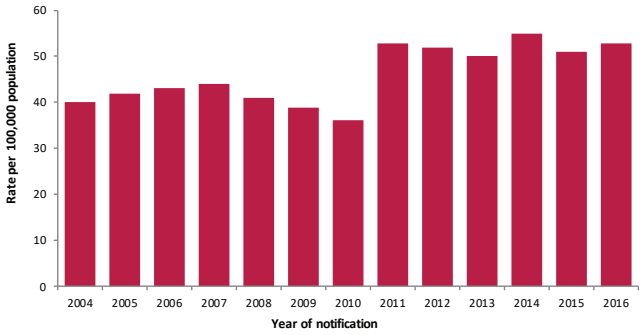
Like *Salmonella* infection, campylobacteriosis typically presents as an acute gastroenteritis. *Campylobacter* is the most commonly reported cause of gastrointestinal bacterial infection in humans in Ireland and Europe [EU Summary Report ECDC/EFSA]. The species most commonly associated with human infections is *C. jejuni*.

5.3.1 AMR Patterns in *Campylobacter* Isolates from Humans

There were 2,513 notifications of campylobacter infection in 2016 in Ireland, representing a crude incidence rate (CIR) of 52.8/100,000 population (Figure 5.5). In recent years there has been a move away from traditional culture-based methods towards molecular detection of campylobacter DNA in faecal specimens by Irish microbiology laboratories.

There is currently no national reference laboratory for *Campylobacter* in Ireland. Therefore culture, speciation, antimicrobial susceptibility testing and typing of *Campylobacter* species is not routine practice. In 2016, just 17.9% (n=451) of isolates were identified to species level. Of those, 93% (n=420) were *C. jejuni* and 6% (n=27) were *C. coli*.

Figure 5.5. Annual Campylobacter Infection CIR/100,000 population in Ireland: 2004 – 2016



Source: HPSC Annual Epidemiological Report 2016

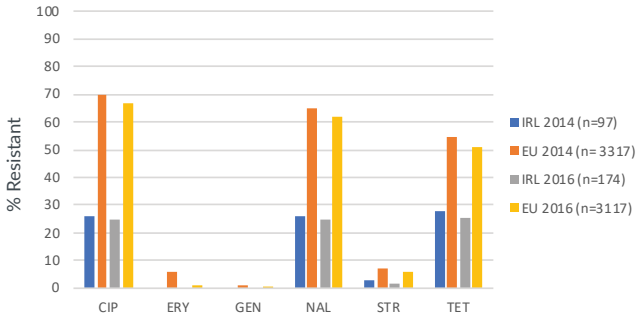
In a recent study (Conference Abstract ECCMID 2018: Madrid, Spain) undertaken by the regional Public Health Laboratory (PHL) HSE-Dublin, stored *Campylobacter* spp isolates cultured from stools of symptomatic sporadic cases submitted to the laboratory over a 10-year period (2006-2016) were included and whole genome sequencing (WGS) performed. To date, 88 *Campylobacter* isolates (79 *C. jejuni* and 9 *C. coli*) were included. Non species specific results indicate resistance gene cmeB (marker of the gene complex encoding multidrug efflux pump) was found in 95% while the blaOXA-61 β-lactamase, tet(O) (tetracycline) and quinolone (Thr86Ile gyrA mutation) resistance genes, were detected in 72%, 24% and 43%, respectively. Macrolide resistance (23S rRNA A2059G or ermB gene) was not detected which correlated with phenotypic findings. The evidence supported that macrolides remain as the empiric treatment of choice. It was recommended that periodic campylobacter culture with WGS surveillance be introduced nationally to augment the primary diagnostic testing by PCR.

5.3.2 AMR Patterns in *Campylobacter* Isolates from Food-Producing Animals

Human infection is frequently attributed to the handling of raw poultry-meat or the consumption of undercooked poultry-meat, as poultry-meat is frequently contaminated with these bacteria (46.7% of fresh broiler meat samples collected from across the EU in 2015 were positive for *Campylobacter* species). An industry-led initiative in Ireland is attempting to tackle this problem, to reduce the prevalence of infection in poultry flocks and the levels of contamination in poultry-meat.

Antimicrobial susceptibility testing was undertaken on 271 *Campylobacter jejuni* isolates obtained from intestinal contents of broilers (n=97 in 2014; n=174 in 2016) and the results were compared with those from across the EU (Figure 5.6).

Figure 5.6. Occurrence of resistance to selected antimicrobials in *Campylobacter jejuni* isolates from chicken intestinal contents - Ireland and EU [2014 and 2016]



Source: DAFM

The same pattern was evident in *Campylobacter* isolates from Irish broilers in both years – with highest levels of resistance exhibited to ciprofloxacin, nalidixic acid and tetracycline. The same pattern was evident across Europe but a greater percentage of isolates obtained from elsewhere in Europe were resistant to those three antimicrobials than in Ireland.

The resistance levels to ciprofloxacin in Europe in 2014 ranged from 3.9% to 100% in individual countries, with a distinct North- South gradient; resistance levels were lowest in Northern European countries and highest around the Mediterranean. Resistance in Irish isolates was relatively low. Ireland's level of MDR was the 5th lowest in Europe in both 2014 and 2016, the Scandinavian countries having the lowest resistance levels. No resistance was detected in Irish isolates to either erythromycin or gentamicin.

6. AMR in Indicator Bacterial Isolates in Animals

Key Points 2016

Indicator commensal ***E. coli***

Most frequently resistant to antimicrobials commonly used in veterinary medicine

MDR higher in poultry compared to pig isolates

ESBL E. coli

The proportion of Irish poultry meat samples carrying ESBL-producing *E. coli* was above the EU average

6.1 General

E. coli are normally present in the gut flora of healthy animals. Most *E. coli* do not usually cause gastrointestinal disease in the host animal (commensal flora). AMR in bacteria that are normally resident in the gut is of interest because AMR can be transferred between bacteria via transmissible genetic elements (e.g. plasmids). Surveillance of AMR in *E. coli* may be indicative of the effect of selective pressure being exerted by the use of antimicrobials in the host animals. Therefore they are referred to as 'indicator' *E. coli*.

ESBLs and AmpC are two categories of enzymes produced by some bacteria, which can hydrolyse 3rd and 4th generation cephalosporins, making the bacteria resistant to these drugs. The two enzyme categories are effective against a different range of antimicrobials, which means the resistant bacteria can be distinguished and categorised according to their resistance patterns. In *E. coli*, the genes encoding ESBL production are carried on transferrable genetic elements such as plasmids, which can be easily exchanged between bacteria. AmpC encoding genes are ordinarily present on the genome of *E. coli* and can be up- regulated to produce resistance or can also be transmitted on mobile genetic elements. Infections with ESBL-/AmpC-producing bacteria are particularly significant from a human healthcare perspective because they tend to be associated with higher levels of mortality, MDR and the necessity for treatment with reserve antimicrobials.

Carbapenems are antimicrobials licensed exclusively for use in humans. The screening of animal samples for carbapenemase-producing *E. coli* was introduced across the EU in 2015, in order to detect any evidence of emergence of this type of resistance in bacterial isolates from animals.

6.2 Data Sources

Data on resistance patterns in *E. coli* isolates from animals was obtained from the National Reference Laboratory for AMR (in animals, feed and food) hosted by DAFM at Backweston.

Monitoring and reporting of AMR in indicator commensal bacteria commenced in 2014. *E. coli* isolates obtained from intestinal contents of healthy animals at slaughter were screened for resistance against a prescribed panel of antimicrobials (as detailed in Appendix A), with sampling of broiler chickens and pigs in alternate years (Table 6.1). Specific screening for ESBL-/ AmpC-producing *E. coli* in food-producing animals commenced Europe-wide in 2015, using a method recommended by EFSA and the European Reference Laboratory. Samples were cultured using selective media containing Cefotaxime at 1mg/L, which inhibited the growth of susceptible bacteria, allowing any ESBL-/ AmpC-producing *E. coli*, even if present in low numbers, to be detected. These resistant bacteria then underwent susceptibility testing and were assigned to the ESBL or AmpC categories on the basis of their resistance patterns. In 2015 and 2016, all of the samples screened for ESBL- and AmpC-producing *E. coli* were also screened for carbapenemase-producing *E. coli*.

Table 6.1 Number of isolates of indicator *E. coli* or samples screened

		Source & number of *E. coli* isolates screened
Antimicrobial-resistant *E. coli*	2014	Broiler chickens (intestinal contents; n = 167)
	2015	Pigs (intestinal contents; n = 147)
	2016	Broiler chickens (intestinal contents; n = 170)
		Source & number of samples screened
ESBL-/AmpC-producing *E. coli* (& Carbapenemase-producing *E. coli*)	2015	Pigs (intestinal contents, n = 145; pork, n =237) & Beef (n = 276)
	2016	Broiler chickens (intestinal contents, n = 300; chicken-meat n = 300)

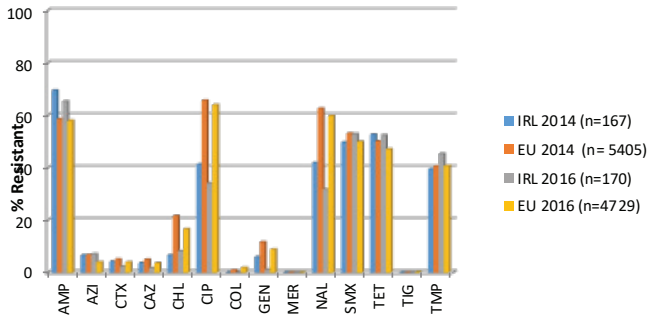
6.3 AMR in Indicator *E. coli* (2014 – 2016)

None of the *E. coli* isolates obtained from animals over the three year period 2014-2016 were resistant to colistin, meropenem or tigecycline.

6.3.1 Poultry (broiler chickens)

Percentages of AMR isolates were highest for ampicillin, sulphamethoxazole and tetracycline in both 2014 and 2016 (Figure 6.1). The percentage of Irish *E. coli* isolates resistant to ampicillin was slightly higher than the EU average whereas the percentage resistant to chloramphenicol and gentamicin was lower. With regard to those antimicrobials of highest priority in human medicine there was little evidence of resistance, except for fluoroquinolones, where the percentage of Irish isolates resistant to ciprofloxacin was significantly lower than the EU average.

Figure 6.1. AMR patterns in indicator *E. coli* from broilers: Ireland and EU [2014 and 2016]



Source: DAFM

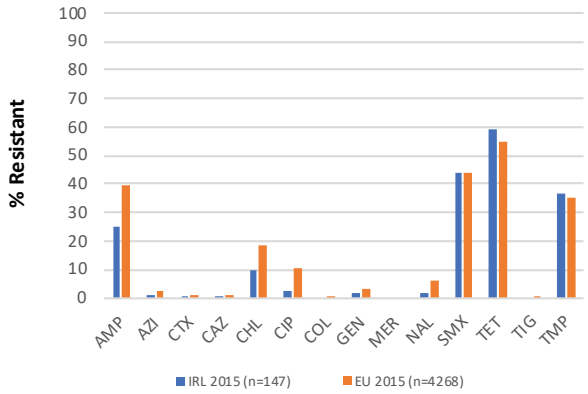
Fewer than 5% of isolates were resistant to 3rd generation cephalosporins each year; 4 of the 11 resistant isolates were also resistant to ciprofloxacin. In 2014 and 2016 respectively, 6.6% and 7.1% of isolates were resistant to azithromycin, comparable to the EU average.

Fewer than 20% of indicator *E. coli* isolates from poultry were fully susceptible to all antimicrobials (16% in 2014 and 18% in 2016), while more than 40% were MDR (48% in 2014 and 45% in 2016). The level of ciprofloxacin resistance in MDR isolates decreased from 60% in 2014 to 53% in 2016.

6.3.2 Pigs

Although the same pattern of resistance was evident in isolates from pigs as in those from broilers, with the highest levels of resistance to ampicillin, sulphamethoxazole, tetracycline and trimethoprim, the percentage of resistant isolates was lower for pigs than for poultry. Resistance to ampicillin, chloramphenicol and ciprofloxacin was lower in Irish isolates than the EU average while resistance to tetracycline was slightly higher (Figure 6.2).

Figure 6.2. AMR patterns for indicator *E. coli* from pigs: Ireland and EU (2015)



Source: DAFM

Two isolates were resistant to azithromycin. One isolate was resisant to cefotaxime and ceftazidime and susceptible to fluoroquinolones.

The proportion of MDR in indicator *E. coli* from pigs was about half that seen in poultry isolates. Ciprofloxacin resistance was found in three of 34 MDR isolates.

6.3.3 Inter-species comparison

In both animal species, resistance patterns observed in Ireland were similar to the EU. Although the percentage of isolates that were resistant and MDR were greater in *E. coli* from broilers than from pigs, Ireland fared worse when compared to other EU Member States for pigs (11th highest level of MDR) than for poultry (16th highest level of MDR).

6.4 Specific Screening for ESBL/ Amp C-producing *E. coli*

6.4.1 Poultry (broiler chickens)

68% and 19% of samples of intestinal contents collected from broilers at slaughter yielded ESBL- and AmpC-producing *E. coli*, respectively (Table 6.2). Chicken meat sampled at retail outlets also yielded very high percentages of ESBL- and AmpC-producing *E. coli* (49% and 17%, respectively). A greater proportion of chicken meat samples labelled as Irish in origin yielded these types of isolate (73% of 218 samples) when compared with chicken meat imported from other European countries (48% of 82 samples). The frequency of isolation of ESBL- and AmpC-producing *E. coli* from both intestinal contents and meat obtained from Irish broilers was amongst the highest in Europe. A subset of 55 ESBL-producing *E. coli* underwent genotyping using PCR and Sanger sequencing as well as whole genome sequencing. These isolates harboured ESBL resistance genes that are widely disseminated in poultry production Europe wide.

A single *E. coli* isolate, cultured during the ESBL/ AmpC screening was colistin resistant and harboured the *mcr-1* resistance gene, as well as genes encoding resistance to cefotaxime, sulphamethoxazole and tetracycline. It originated from a raw chicken meat sample that had been imported.

Colistin is a drug of last resort in human infections. Even though licensed for use in veterinary medicine, it has been very sparingly used in food-producing animals in Ireland. Although mcr-mediated colistin resistance has been reported in *Salmonella* and *E. coli* from humans and animals globally since 2015, the colistin resistant *E. coli* isolate described here is the first report from Ireland of transferrable colistin resistance in an animal-derived sample.

6.4.2 Pigs

10% of samples of intestinal content collected from slaughter pigs yielded ESBL-producing *E. coli* and 19% yielded AmpC-producing *E. coli*. A much lower percentage of the pork samples that were tested yielded either ESBL- or AmpC-producing *E. coli*, reflecting the efficacy of hygienic measures taken to avoid faecal contamination of carcases during processing.

6.4.3 Beef

No ESBL- or AmpC- producing *E. coli* were isolated from Irish beef samples screened and very few samples of beef collected in other EU countries yielded either type of isolate.

Table 6.2. % samples of different types that yielded ESBL- and/or AmpC-producing *E. Coli*

Year	Matrix	Origin	% samples positive ESBL	% samples positive Amp-C	% samples positive ESBL + Amp C
2015	**Pig Intestinal contents**	IRL	10.3	19.3	0.7
		EU	31.9	9.7	1.5
	Pork	IRL	0.8	0.8	0
		EU	7	2.3	0.4
	Beef	IRL	0	0	0
		EU	5	1.8	0.3
2016	**Chicken Intestinal contents**	IRL	68	18.7	0
		EU	37.2	27.6	3.2
	Chicken meat	IRL	49	16	0.3
		EU	32.5	24.1	2.1

Source: DAFM

6.4.4 Inter-species comparison

The prevalence of resistant isolates in Irish pig intestinal contents and meat compared favourably, in general, with levels seen in other countries in 2015. However, the relatively high number of AmpC- producing *E. coli* recovered was unusual compared to results from the rest of Europe. This pattern, where the yield of AmpC-producing *E. coli* from pigs exceeded that of ESBL-producing *E. coli*, may reflect the pattern of antimicrobial use in Irish pigs.

Of most concern is the very high prevalence of ESBL-producing *E. coli* in Irish broilers. Ninety-nine per cent of ESBL *E. coli* were MDR and 31% were co- resistant to fluroquinolones. This suggests that the use of antimicrobials other than cephalosporins might select for ESBL bacteria in the chicken gut flora in the absence of cephalosporin use. These findings emphasise the importance of reduced and more prudent use of antimicrobials of all classes by the poultry sector.

AMR patterns in clinical isolates from food-producing animals are also monitored with a particular emphasis on characterising isolates which exhibit evidence of ESBL activity or other significant AMR pattern (Textbox 6.1).

6.5 Specific Screening for Carbapenamase-producing *E. coli*

In 2015 and 2016, all of the samples screened for ESBL- and AmpC-producing *E. coli* were also screened for carbapenamase-producing *E. coli* and all were negative.

Textbox 6.1

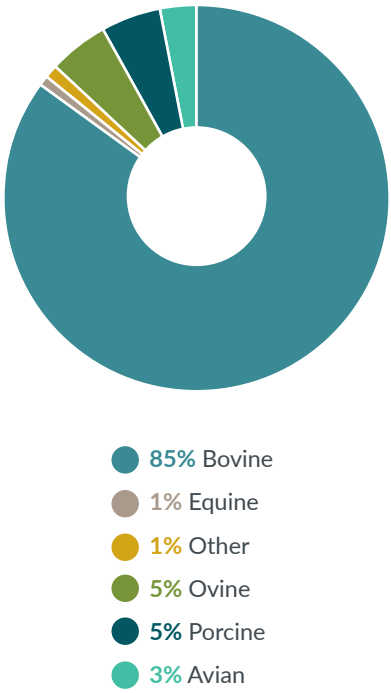
Antimicrobial Resistance Patterns in Clinical Bacterial Isolates from animals

Regional Veterinary Laboratories (RVLs) operated by the Department of Agriculture, food and the Marine (DAFM) provide a laboratory diagnostic service to the farming community on referral by private veterinary practitioners – accepting carcases of fallen animals for post mortem examination and clinical specimens collected from animals on farm.

Any bacterial isolates obtained from these submissions which are significant from a veterinary or zoonotic perspective are subject to antimicrobial susceptibility testing (AST), which is performed in accordance with internationally recognised (OIE) methodologies. These bacteria include common causes of animal diseases such as mastitis (e.g. *Staphylococcus aureus*, *Streptococcus uberis*), pneumonia (e.g. *Pasteurella multocida*, *Mannheimia haemolytica*,) or enteric disease in farm animals (e.g. *Salmonella* Typhimurium, *Salmonella* Dublin and enterobacteria). There is a particular focus on isolates showing evidence of extended spectrum *beta-lactamase* (ESBL) activity.

In 2016, as in previous years, the vast majority of bacteria on which antimicrobial susceptibility testing was performed came from samples of bovine origin (see pie chart below) reflecting the caseload of RVLs. Only one of these isolates in 2016, from a bovine milk sample, was identified as resistant to a combination of amoxicillin and clavulanate but this isolate was not resistant to cefpodoxime (a marker of ESBL activity). Further information on AMR in clinical isolates from food-producing animals is available in All-island Disease Surveillance Reports https://www.agriculture.gov.ie/rvlreport/

Sources of isolates for antimicrobial susceptibility testing originating from domestic animal species tested by DAFM Regional Veterinary Laboratories in 2016 (n=1,763)



7. Looking Ahead

'Much of the human health data required in Ireland is already generated through the HSE's Departments of Public Health and the HPSC, the public health microbiology laboratories and existing sector specific research projects and computer systems. Comprehensive community surveillance data systems need to be developed.

However, the analysis, interpretation and use of this data for action remains ad hoc and a key element of iNAP is the development and implementation of an integrated national surveillance system which ensures that actions taken in response to threats posed by antimicrobial resistance are timely, coordinated and proportionate. Surveillance data in the animal health sector requires further development and co-ordination both within the animal health sector and with the human health sector so as to provide further evidence to inform future actions in relation to best practice for antimicrobial usage and to address AMR'

iNAP *p59*

iNAP
PROTECTING ANTIBIOTICS FOR THE FUTURE
ANTAIBHEATHAIGH A CHOSAINT DON TODHCHAÍ

Ireland has committed to develop and produce an annual One Health surveillance report on AMU and AMR. This first such report makes use of available data collected in human health and animal health surveillance / monitoring systems with different aims and primary purposes for each sector. It represents a first step towards integrated surveillance in Ireland using a One Health approach. It should pave the way for more timely future reports incorporating additional surveillance information on AMU in human healthcare (including the community), more data on AMU in food producing-animals, the inclusion of data for companion animals and information on environmental monitoring for AMR. A dedicated and resourced team, with supporting resources, would be important to ensuring the sustainability of an annual One Health AMU and AMR report for Ireland.

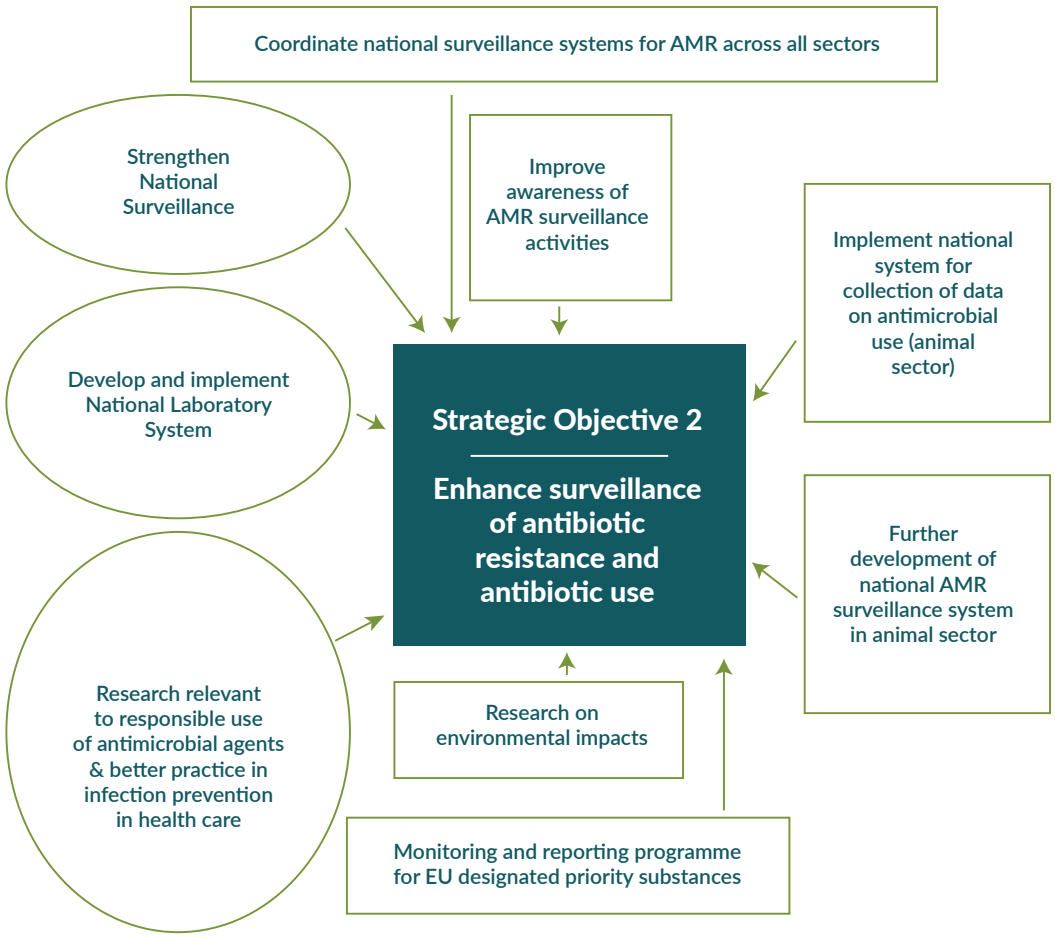
*i*NAP, Ireland's National Action Plan on Antimicrobial Resistance (2017 - 2020), presented strategic interventions and activities with reference to the five strategic objectives published by the WHO to tackle AMR:

1. Improving awareness and knowledge of AMR
2. Enhancing surveillance of antibiotic resistance and antibiotic use
3. Reducing infection and disease spread
4. Optimising the use of antibiotics in human and animal health
5. Promoting research and sustainable investment in new medicines, diagnostic tools, vaccines and other interventions

*i*NAP identified surveillance challenges and gaps for both sectors. Under 'Strategic Objective 2: Enhance surveillance of antibiotic resistance and antibiotic use' it has laid out strategic interventions (Box 7.1) – listing activities, designating responsibilities and incorporating timelines. This surveillance report should serve as a springboard to advance the cause of further development, coordination and integration.

Textbox 7.1

Ireland's National Action Plan on AMR (iNAP) Strategic Objective 2: Strategic Interventions



Improved surveillance systems, with the timely production of essential information, can promote prudent antimicrobial use in hospitals, in the community and in agriculture. Several Eurobarometer surveys on AMR carried out since 2010 show that the level of awareness of the relationship between the use of antimicrobials and the development and spread of AMR is still low.

More must be done to raise awareness and to provide education about AMR. Education on AMR has a pivotal role to play for all stakeholders – health care workers, laboratory staff, veterinary professionals, farmers and the general public. However, education and awareness-raising do not automatically translate into behaviour change. Identifying and exploiting drivers and incentives to achieve the desired change on a sustainable basis is essential to realising the goal of reduced antimicrobial use and antimicrobial resistance.

This joint surveillance report, and its successors in turn, will be a useful source of data to progress understanding of the need for, and to promote, responsible antimicrobial use throughout the One Health domain.

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Appendix A: EU-wide monitoring of AMR in food-producing animals

Official monitoring of AMR in bacterial isolates from food-producing animals has been carried out in the EU since 2007 (Commission Decision 2007/407/EC) and is aimed at establishing AMR levels, detecting trends and new and emerging resistance patterns. A new programme of monitoring and reporting of resistance in zoonotic and commensal bacteria came into force in November 2013, with the publication of decision 2013/652/EU. This extended the monitoring programme from that implemented since 2007, with increased emphasis on resistance in indicator commensal bacteria.

In Ireland, the testing component prescribed in this legislation, is carried out by the Department of Agriculture, Food and the Marine Laboratory Services, which is designated as the National Reference Laboratory (NRL) for Antimicrobial Resistance in animals, feed and food, under Regulation 882/2004.

Sampling and bacterial susceptibility testing are carried out as recommended by EFSA and the European Reference Laboratory (EURL); it is harmonised across Member States. It is targeted at the intensive (pig and poultry) sectors and focuses on one or other sector in alternate years. In 2014 and 2016 the programme focused on poultry (meat- producing broiler chickens) and in 2015 on pigs.

The bacterial isolates that are screened for AMR in this programme are: *Campylobacter* spp. from chickens, *Salmonella* spp. from chickens and pigs and indicator *E. coli* from chickens, pigs and cattle. The susceptibility of isolates to standardised panels of antimicrobials is assessed using a methodology prescribed by the EU Reference Laboratory. Some of these antimicrobial compounds, although not licensed for use in animals, are included to screen for patterns of resistance which would be of particular concern from a public health perspective or because these compounds are closely related to antimicrobials that may be used in veterinary medicine.

The surveillance programme has been increasingly targeted at resistance to critically important antimicrobials (CIAs), in particular carbapenems and 3rd & 4th generation cephalosporins, because of their critical importance in treatment of infections in humans.

Bacterial isolates are designated as resistant or susceptible to a particular antimicrobial using interpretative criteria (epidemiological cut-offs) set by the European Committee on Antimicrobial Susceptibility Testing (EUCAST).

The results of the official testing carried out by the NRL are collated and transmitted to EFSA annually, where they are included in the EU summary report on AMR in zoonotic and indicator bacteria from humans, animals and food.

Antimicrobials used in Susceptibility Testing of *Salmonella* and *E. coli* of Animal Origin

Antimicrobial Class Initial screening plate**	Class used in animals	Antimicrobial	Abbreviation	Antimicrobial used in animals	ECOFF * (mg/L)	
					Salmonella	*E. coli*
Penicillin	√	Ampicillin	AMP	√	>8	>8
Macrolide	√	Azithromycin	AZI		>16	>16
3rd/ 4th Generation Cephalosporins	√	Cefotaxime	CTX		>0.5	>0.25
		√	Ceftazidime	CAZ	>2	>0.5
Amphenicol	√	Chloramphenicol	CHL		>16	>16
Quinolones	√	Ciprofloxacin	CIP		>0.06	>0.06
		Nalidixic Acid	NAL		>16	>16
Polymixin	√	Colistin	COL	√	>2	>2
Aminoglycoside	√	Gentamicin	GEN	√	>2	>2
ESBL confirmatory plate**						
Cephalosporin,	√	Cefoxitin	FOX		>8	>8
		Cefepime	CEF		NA***	>0.125
		Cefotaxime	CTX		>0.5	>0.25
		Cefotaxime + Clavulanic acid	CTX + CLAV		NA****	NA****
		Ceftazidime	CAZ		>2	>0.5
		Ceftazidime/ Clavulanic acid	CAZ + Clav		NA****	NA****
Carbapenem		Meropenem	MER		>0.125	>0.125
		Etrapenem	ETR		>0.06	>0.06
		Imipenem	IMI		>1	>0.5
Penicllin	√	Temocillin	TEM		>32	>32

* Epidemiological cut- off
** Second plate used if CTX/ CAZ/ MER resistant
*** Not available
****Not applicable

Appendix B: WHO List of Critically Important Antibiotics for Human Medicine (5th Rev) Oct 2016 http://www.who.int/foodsafety/publications/cia2017.pdf

WHO Critically Important Antimicrobials for Human Medicine 5th revision

Advisory Group on Integrated Surveillance of Antimicrobial Resistance (AGISAR)
October 2016

Summary of classification and prioritization of antimicrobials categorized as Critically Important, Highly Important and Important

Medically Important Antimicrobials

	Antimicrobial class	Criterion (Yes=●)				
	CRITICALLY IMPORTANT ANTIMICROBIALS	**C1**	**C2**	**P1**	**P2**	**P3**
Critically Important	*HIGHEST PRIORITY*					
Highest Priority	*Cephalosporins (3rd, 4th and 5th generation)*	●	●	●	●	●
	Glycopeptides	●	●	●	●	●
	Macrolides and ketolides	●	●	●	●	●
	Polymyxins	●	●	●	●	●
	Quinolones	●	●	●	●	●
	HIGH PRIORITY					
	Aminoglycosides	●	●		●	●
	Ansamycins	●	●	●	●	
	Carbapenems and other penems	●	●	●	●	
	Glycylcyclines	●	●	●		
	Lipopeptides	●	●	●		
	Monobactams	●	●	●		
	Oxazolidinones	●	●	●		
	Penicillins (natural, aminopenicillins, and antipseudomonal)	●	●		●	●
	Phosphonic acid derivatives	●	●	●	●	
	Drugs used solely to treat tuberculosis or other mycobacterial diseases	●	●	●	●	
Highly Important	**HIGHLY IMPORTANT ANTIMICROBIALS**	**C1**	**C2**	**P1**	**P2**	**P3**
	Amidinopenicillins		●	NA		
	Amphenicols		●			
	Cephalosporins (1st and 2nd generation) and cephamycins		●			
	Lincosamides		●			
	Penicillins (anti-staphylococcal)		●			
	Pseudomonic acids		●			
	Riminofenazines	●				
	Steroid antibacterials		●			
	Streptogramins		●			
	Sulfonamides, dihydrofolate reductase inhibitors and combinations		●			
	Sulfones	●				
	Tetracyclines	●				
Important	**IMPORTANT ANTIMICROBIALS**	**C1**	**C2**	**P1**	**P2**	**P3**
	Aminocyclitols			NA		
	Cyclic polypeptides					
	Nitrofurantoins					
	Nitroimidazoles					
	Pleuromutilins					

C1 Criterion 1

The antimicrobial class is the sole, or one of limited available therapies, to treat serious bacterial infections in people.

C2 Criterion 2

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.

P1 Prioritization criterion 1

High absolute number of people, or high proportion of use in patients with serious infections in health care settings affected by bacterial diseases for which the antimicrobial class is the sole or one of few alternatives to treat serious infections in humans.

P2 Prioritization criterion 2

High frequency of use of the antimicrobial class for any indication in human medicine, or else high proportion of use in patients with serious infections in health care settings, since use may favour selection of resistance in both settings.

P3 Prioritization criterion 3

The antimicrobial class is used to treat infections in people for which there is evidence of transmission of resistant bacteria or resistance genes from non-human sources.

WHO CIA list 5th rev. : http://who.int/foodsafety/publications/antimicrobials-fifth/en/
AGISAR: http://who.int/foodsafety/areas_work/antimicrobial-resistance/agisar/en

WHO/NMH/FOS/FZD/17.1

World Health Organization

Rialtas na hÉireann
Government of Ireland

Prepared by the Department of Health & the Department of Agriculture

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