Seirbhís Sláinte Níos Fearr á Forbairt | Building a Better Health Service

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Annual Epidemiological Report

November 2019

Antimicrobial Resistance in key pathogens causing invasive infections in Ireland, 2018

Key Facts

- There were 3,239 invasive infections caused by *E. coli*, 12.9% of which were third generation cephalosporin (3GC) resistant and 11.6% confirmed as extended-spectrum beta-lactamase (ESBL) producers. Four (0.1%) infections were due to carbapenemase-producers (all OXA-48 type)
- Of 1,188 *S. aureus* bloodstream infections (BSI), 12.4% were meticillin resistant (MRSA)
- There were 483 invasive infections caused by *K. pneumoniae*. Four (0.8%) infections were due to carbapenemase-producers (all OXA type)
- Of 419 *E. faecium* BSI, 40.2% were vancomycin resistant (VRE or VREfm)
- There were 455 invasive *S. pneumoniae* infections, with penicillin non-susceptible *S. pneumoniae* increasing to 20.7%
- Additional data on carbapenemase-producing Enterobacterales† (CPE):
    - There were 16 cases of invasive CPE, of which 15 were OXA-48
    - CPE was detected in 565 patients: 87% were associated with screening (i.e. from patients colonised with CPE) and 13% with clinical specimens. OXA-48 accounted for 70% of CPE

† includes all Enterobacterales species not just *E. coli* and *K. pneumoniae*

Suggested citation: HSE Health Protection Surveillance Centre. Antimicrobial Resistance in Ireland 2018: Dublin HSE HPSC; 2019

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Background to Antimicrobial Resistance Surveillance

Antimicrobial resistance (AMR) presents a major challenge, as infections caused by AMR pathogens result in higher morbidity and mortality, extended hospital stays and increased healthcare costs.

The European Antimicrobial Resistance Surveillance Network (EARS-Net) serves as a surveillance system to measure national levels of AMR by collecting routinely-generated antimicrobial susceptibility testing (AST) data on eight important bacterial pathogens. In 2018, the Irish case definition was aligned with the EARS-Net definition: data are collected on the first invasive isolate (blood or cerebrospinal fluid (CSF)) of each pathogen per patient per year, rather than per quarter, as previously utilised. EARS-Net does not distinguish clinically significant isolates from contaminants, nor does it routinely capture data on acquisition of infection (e.g., hospital versus community-acquired). In 2018, all laboratories participated in EARS-Net, with 100% coverage of the Irish population.

EARS-Net encourages the use of EUCAST guidelines and clinical breakpoints for AST in line with the EU case definitions. By the end of 2018, 35 of the 38 clinical microbiology laboratories in Ireland had switched to EUCAST, with just three laboratories still using CLSI guidelines. The figures presented in this report (Table 1) are based on data extracted from the EARS-Net database on **11th September 2019**.

Additional data on pneumococcal serotyping were provided by the Irish Meningitis and Sepsis Reference Laboratory (IMSRL) at the Children's University Hospital, Temple Street.

A voluntary enhanced surveillance programme for EARS-Net in Ireland was established in 2004, with participating laboratories invited to provide additional demographic and clinical data. In 2018, enhanced surveillance data were submitted on 1,770 individual records by 18 participating laboratories, representing 28% of all reports to EARS-Net. Table 2 displays demographic and other basic data for the major resistance profiles of pathogens reported to the EARS-Net enhanced surveillance.

Table 1. Summary of AMR by pathogen in Ireland, 2014-2018 (data correct as of 11/09/2019)

Pathogen	Year				
	2014	2015	2016	2017	2018
Number laboratories by year-end	**39**	**38**	**37**	**39**	**38**
%Coverage of population	*100*	*97*	*99*	*100*	*100*
E. coli					
Number of isolates	**2702**	**2647**	**2988**	**3124**	**3239**
%Ampicillin-R*	*68.9*	*66.3*	*68.0*	*69.5*	*67.6*
%Amoxicillin-clavulanic acid-R*	*37.1*	*39.6*	*38.3*	*49.9*	*49.8*
%Piperacillin/tazobactam-R*	*11.6*	*12.0*	*11.1*	*14.4*	*12.6*
%Cefoxitin-R*	*5.0*	*5.4*	*4.3*	*3.9*	*6.9*
%3GC-R*	*10.8*	*11.4*	*11.3*	*12.0*	*12.9*
%Cefotaxime/ceftriaxone-R*	*10.7*	*11.2*	*11.1*	*11.8*	*12.7*
%Ceftazidime-R*	*6.0*	*7.0*	*8.0*	*9.3*	*11.8*
%ESBL-producers*	*9.9*	*10.5*	*10.9*	*11.0*	*11.6*
%Ciprofloxacin-R*	*24.5*	*23.1*	*22.8*	*23.7*	*24.1*
%Gentamicin-R*	*9.9*	*10.3*	*9.4*	*10.1*	*10.5*
%Gentamicin/Amikacin/Tobramycin-R*	*12.4*	*12.2*	*11.3*	*12.1*	*11.8*
%Carbapenem†-R*	*0.1*	*0.1*	*0.1*	*0.2*	*0.1*
Number Carbapenemase-producers	***1***	***2***	***1***	***5***	***4***
%MDR*	*5.0*	*5.6*	*5.4*	*5.9*	*6.2*
S. aureus					
Number of isolates	**1076**	**1056**	**1142**	**1153**	**1188**
Number Meticillin-R (or MRSA)	**208**	**191**	**164**	**186**	**147**
%Meticillin-R (or MRSA)	*19.3*	*18.1*	*14.4*	*16.1*	*12.4*
K. pneumoniae					
Number of isolates	**356**	**387**	**453**	**479**	**483**
%Ampicillin-R*	*98.0*	*98.4*	*98.7*	*98.3*	*98.6*
%Amoxicillin-clavulanic acid-R*	*20.4*	*30.7*	*24.0*	*30.0*	*29.3*
%Piperacillin/tazobactam-R*	*16.6*	*20.4*	*16.2*	*19.2*	*17.4*
%Cefoxitin-R*	*5.2*	*5.8*	*5.4*	*4.7*	*8.0*
%3GC-R*	*11.5*	*14.5*	*13.5*	*14.6*	*14.5*
%Cefotaxime/ceftriaxone-R*	*10.5*	*13.3*	*13.0*	*12.8*	*14.2*
%Ceftazidime-R*	*9.9*	*10.4*	*13.3*	*12.7*	*12.6*
%ESBL-producers*	*10.8*	*12.8*	*11.8*	*12.6*	*14.5*
%Ciprofloxacin-R*	*13.5*	*16.8*	*11.5*	*15.9*	*18.6*
%Gentamicin-R*	*11.8*	*15.5*	*11.0*	*11.1*	*11.8*
%Gentamicin/Amikacin/Tobramycin-R*	*12.1*	*16.5*	*11.5*	*11.9*	*13.0*
%Carbapenem†-R*	*0.6*	*1.8*	*0.9*	*0.6*	*0.6*
Number Carbapenemase-producers	**2**	**6**	**4**	**4**	**4**
%MDR*	*7.3*	*7.5*	*5.8*	*6.1*	*8.3*
E. faecium					
Number of isolates	**390**	**406**	**423**	**442**	**419**
%Vancomycin-R (VREfm)	*44.9*	*45.9*	*44.3*	*38.2*	*40.2*
%Ampicillin-R*	*94.9*	*94.3*	*94.5*	*93.3*	*95.2*
%HLG-R*	*44.7*	*49.6*	*58.1*	*67.7*	*67.1*
%Linezolid-R*	*1.6*	*0.5*	*0.2*	*0.0*	*0.5*
%MDR*	*22.2*	*21.7*	*30.2*	*29.9*	*30.1*
E. faecalis					
Number of isolates	**307**	**292**	**290**	**340**	**332**
%Vancomycin-R (VREfa)	*2.3*	*1.4*	*0.7*	*0.6*	*0.6*
%Ampicillin-R*	*1.0*	*0.7*	*0.3*	*0.6*	*0.9*
%HLG-R*	*31.6*	*27.9*	*29.3*	*30.7*	*23.6*
%Linezolid-R*	*0.0*	*0.4*	*0.0*	*0.3*	*0.0*

* Not all isolates tested; † Carbapenems include imipenem, meropenem and ertapenem

Number of isolates presented in **bold**; proportions (%) presented in *italics*

R, Resistant; MRSA, Meticillin-Resistant *S. aureus* ; VREfm, Vancomycin-Resistant *E. faecium*

HLG, High-Level Gentamicin; 3GC, 3rd-Generation Cephalosporin (includes cefotaxime, ceftriaxone, ceftazidime)

ESBL, Extended-Spectrum Beta-Lactamase; MDR, Multi-Drug Resistant (see definition for each pathogen)

Continued overleaf…….

Table 1 (continued) Summary of AMR by pathogen in Ireland, 2014-2018 (data correct as of 11/09/2019)

Pathogen	Year				
	2014	2015	2016	2017	2018
Number laboratories by year-end	**39**	**38**	**37**	**39**	**39**
%Coverage of population	*100*	*97*	*99*	*100*	*100*
S. pneumoniae					
Number of isolates	**328**	**303**	**363**	**412**	**455**
of which notified to public health	324	300	356	400	453
Number serotyped	298	275	343	383	404
% serotyped	*90.9*	*90.8*	*94.5*	*93.0*	*88.8*
Number Penicllin-NS (or PNSP)	**56**	**53**	**60**	**65**	**94**
%Penicillin-NS*	*17.2*	*17.6*	*16.6*	*15.8*	*20.7*
of which: %HLR	*1.8*	*0.3*	*0.0*	*1.0*	*1.3*
%Int	*15.2*	*17.2*	*16.5*	*14.8*	*19.3*
%Erythromycin-R*	*13.9*	*13.9*	*13.0*	*12.9*	*13.6*
%Penicillin-NS/Erythromycin-R*	*10.0*	*9.8*	*9.0*	*8.6*	*9.1*
P. aeruginosa					
Number of isolates	**177**	**195**	**244**	**288**	**273**
%Piperacillin/tazobactam-R*	*14.1*	*11.3*	*12.7*	*14.0*	*8.1*
%Ceftazidime-R*	*7.5*	*7.2*	*10.2*	*9.6*	*8.4*
%Imipenem/meropenem-R*	*6.8*	*6.7*	*6.1*	*9.0*	*6.6*
%Ciprofloxacin-R*	*8.5*	*9.8*	*12.7*	*15.3*	*9.2*
%Gentamicin-R*	*5.1*	*3.6*	*10.7*	*9.1*	*5.5*
%Gentamicin/Amikacin/Tobramycin-R*	*5.6*	*4.1*	*10.7*	*9.0*	*5.5*
%MDR*	*5.7*	*4.1*	*8.6*	*8.5*	*3.1*
***Acinetobacter* spp.**					
Number of isolates	**89**	**86**	**68**	**66**	**62**
%Ciprofloxacin-R*	*5*	*5*	*1*	*8*	*2*
%Gentamicin-R*	*2*	*4*	*2*	*3*	*4*
%Gentamicin/Amikacin/Tobramycin-R*	*2*	*5*	*2*	*3*	*4*
%Imipenem/meropenem-R*	*1*	*6*	*0*	*6*	*2*
%MDR*	*1*	*1*	*0*	*2*	*0*
TOTAL EARS-NET PATHOGENS	**5425**	**5372**	**5971**	**6304**	**6451**

* Not all isolates tested

Number of isolates presented in **bold**; proportions (%) presented in *italics*

R, Resistant; NS, Non-Susceptible [includes isolates with intermediate (Int) and high-level resistance (HLR)]

MDR, Multi-Drug Resistant (see definition for each pathogen)

Table 2. Age and gender breakdown of patients by pathogen with major resistance profiles in Ireland (data from laboratories participating in enhanced surveillance 2018 only). The proportion of isolates detected <48 hours and >5 days post-admission is also shown

Pathogen	Total for 2018	Percent female	Median age in years	Detected <48 hours after admission	Detected >5 days after admission
Escherichia coli	**838**	41%	68.6	76%	19%
Fluoroquinolone Resistant	**198 (24%)**	39%	73.8	75%	19%
Fluoroquinolone Susceptible	**640**	58%	66.9	76%	19%
Staphylococcus aureus	**413**	34%	63.9	65%	23%
Meticillin Resistant (MRSA)	**54 (13%)**	24%	72.4	59%	30%
Meticillin Susceptible (MSSA)	**359**	36%	62.6	66%	21%
Klebsiella pneumoniae	**137**	38%	64.8	55%	39%
Enterococci*	**196**	41%	67.1	37%	55%
Vancomycin Resistant (VRE)	**51 (26%)**	53%	61.2	8%	88%
Vancomycin Sensitive (VSE)	**145**	37%	69.2	48%	43%
Streptococcus pneumoniae	**120**	53%	62.8	93%	5%
Penicillin Non-Susceptible	**17 (14%)**	35%	72.7	94%	6%
Penicillin Susceptible	**103**	55%	61.2	93%	5%
Pseudomonas aeruginosa	**66**	36%	67.4	55%	38%

* Data for *E. faecium* and *E. faecalis* are combined

Epidemiology

Escherichia coli

E. coli is found in the normal gut flora of humans and animals. *E. coli* is the most frequent cause of urinary tract infections (UTI) and bloodstream infections (BSI) in humans, but is also associated with many other infections, including gastroenteritis, intra-abdominal infections and neonatal meningitis.

E. coli can develop resistance to the key antimicrobials used for treatment, potentially resulting in strains that are multi-drug resistant.

Resistance to third generation cephalosporins (3GC) in *E. coli* and other Enterobacterales (previously known as *Enterobacteriaceae*) is most often due to the production of extended-spectrum beta lactamases (ESBL), enzymes that confer resistance to most beta lactams, but not to carbapenems. ESBL-producers are also often resistant to other antimicrobial classes.

As the incidence of ESBLs increases, this results in reliance on last-resort antimicrobials, such as carbapenems for treatment of severe or invasive infections. This in turn facilitates the emergence and spread of carbapenem resistance, in particular due to carbapenemases, enzymes that confer resistance to almost all beta lactams, including carbapenems. The genes that encode carbapenemase production are found on plasmids, which are mobile genetic elements, facilitating spread between different species of Enterobacterales.

Antimicrobial resistance in *Escherichia coli*

In 2018, there were 3,239 reports of patients with invasive *E. coli* infections (3,235 from blood and four from CSF), a 4% increase from 2017 (n=3,124).

Table 1 displays the annual data since 2014 on the proportion of *E. coli* isolates resistant to the five indicator antimicrobials/antimicrobial classes: aminopenicillins (ampicillin or amoxicillin), 3GCs (cefotaxime, ceftriaxone or ceftazidime), fluoroquinolones (ciprofloxacin), aminoglycosides (gentamicin, tobramycin or amikacin) and carbapenems (meropenem or ertapenem):

- In 2018, 3GC resistance increased to 12.9%, the highest proportion since surveillance began. While there was no significant increase over the period 2014-2018, there has been an overall upward trend since 2011 (Figure 1)
- ESBL-producers accounted for 11.6% of isolates, the highest proportion since surveillance began. While there was no significant increase over the period 2014-2018, there has been an overall upward trend since 2011 (Figure 1)
- Resistance to fluoroquinolones and gentamicin, but not to aminoglycosides overall, increased slightly in 2018 compared with 2017 (Table 1)

- Aminopenicillin resistance was observed in 67.6% of isolates, although this has remained relatively stable. In 2018, Ireland had the highest proportion of aminopenicillin resistance in Europe (Figure 3). When resistance profiles to all indicator antimicrobials are examined, Ireland had the lowest proportion of fully susceptible isolates in Europe (Figure 4)
- Multi-drug resistance (MDR) in *E. coli* is of increasing concern:
    - Multi-drug resistant (MDR) *E. coli* is defined as combined resistance to 3GCs, fluoroquinolones and aminoglycosides
    - MDR *E. coli* accounted for 6.2% of isolates, a slight increase from 5.9% in 2017. While MDR increased over the period 2014-2018, the trend was not significant
    - In 2018, Ireland had one of the highest proportions of combined resistance in northern and western Europe (Figure 4)
    - No isolates were resistant to all five indicator antimicrobials, similar to 2017. Across Europe, only 40 such isolates displayed this resistance profile, an increase from 24 in 2017 and 11 in 2016
- Seven isolates (0.1%) were resistant to carbapenems:
    - Three of these were carbapenemase-producers, or CPE (all OXA-48-type)
    - A fourth isolate that was carbapenem-susceptible was found to be CPE (also OXA-48-type) (Table 3)
    - In the period 2012-2018, 33 *E. coli* invasive isolates were reported as carbapenem-resistant, with 13 confirmed to be CPE, of which two were also MDR
    - Carbapenem resistance among invasive *E. coli* isolates remains at low levels in Ireland and across Europe
- The majority of *E. coli* (78%) and MDR *E. coli* (79%) were detected within two days of admission to hospital (i.e., community-acquired)
- The majority of *E. coli* (76%) occurred in patients over 60 years (median age=74 years)

Enhanced surveillance findings:

- Healthcare-association was reported for 54% of fluoroquinolone-resistant *E. coli* (FQREC) BSI, versus 34% of fluoroquinolone-susceptible *E. coli* (FQSEC)
- The most common source of *E. coli* BSI was from urinary tract infection (48%), with 13% of FQREC and 3% FQSEC BSI reported as associated with a urinary catheter

Figure 1. **Trends for invasive *E. coli* infections in Ireland, 2011-2018: total numbers of *E. coli* with percentage third-generation cephalosporin resistant (3GC-R) and ESBL producer (ESBL+ve)**

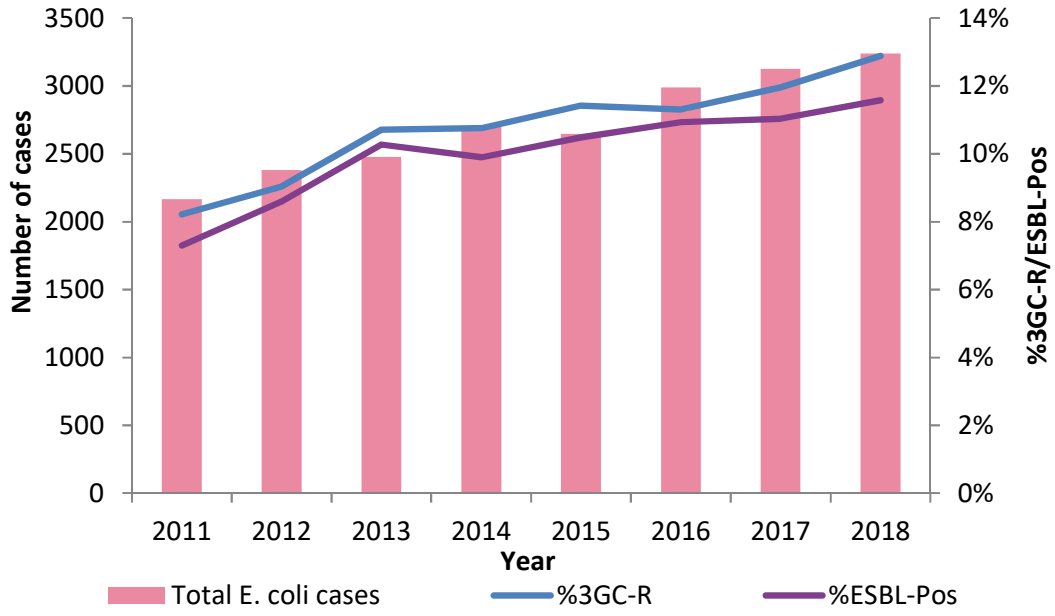
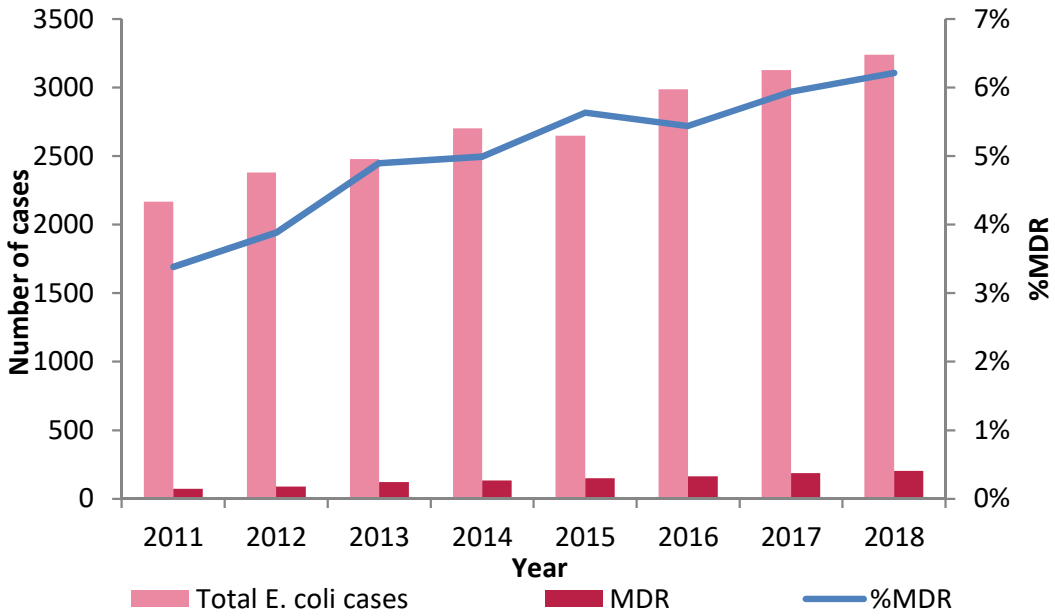


Figure 2. **Trends for invasive *E. coli* infections in Ireland, 2011-2018: total numbers of *E. coli* tested for multi-drug resistance (MDR)* with number and percentage that are MDR**



*Multi-drug resistance (MDR) defined as combined resistance to 3GCs, fluoroquinolones and aminoglycosides

Table 3. Data on carbapenem resistant compared with carbapenemase-producing *E. coli* in Ireland, 2011-2018

Year	Number CRE (*E. coli*)	Num CPE (CP-ECO)	Enzymes detected (numbers)
2011	0	0	
2012	2	0	
2013	2	0	
2014	2	1	NDM (1)
2015	6	2	NDM (1); OXA-48 (1)
2016	5	1	NDM (1)
2017	9	5	OXA-48 (5)*
2018	7	4	OXA-48 (4)*
Total	33	13	OXA-48 (10), NDM (3)

CRE, carbapenem-resistant Enterobacterales; CPE, carbapenemase-producing Enterobacterales

*includes one isolate where carbapenem-sensitive

Figure 3. Distribution of *E. coli* isolates from fully susceptible (blue) to resistance to 1-5 of the indicator antimicrobials in EU/EEA countries, 2018

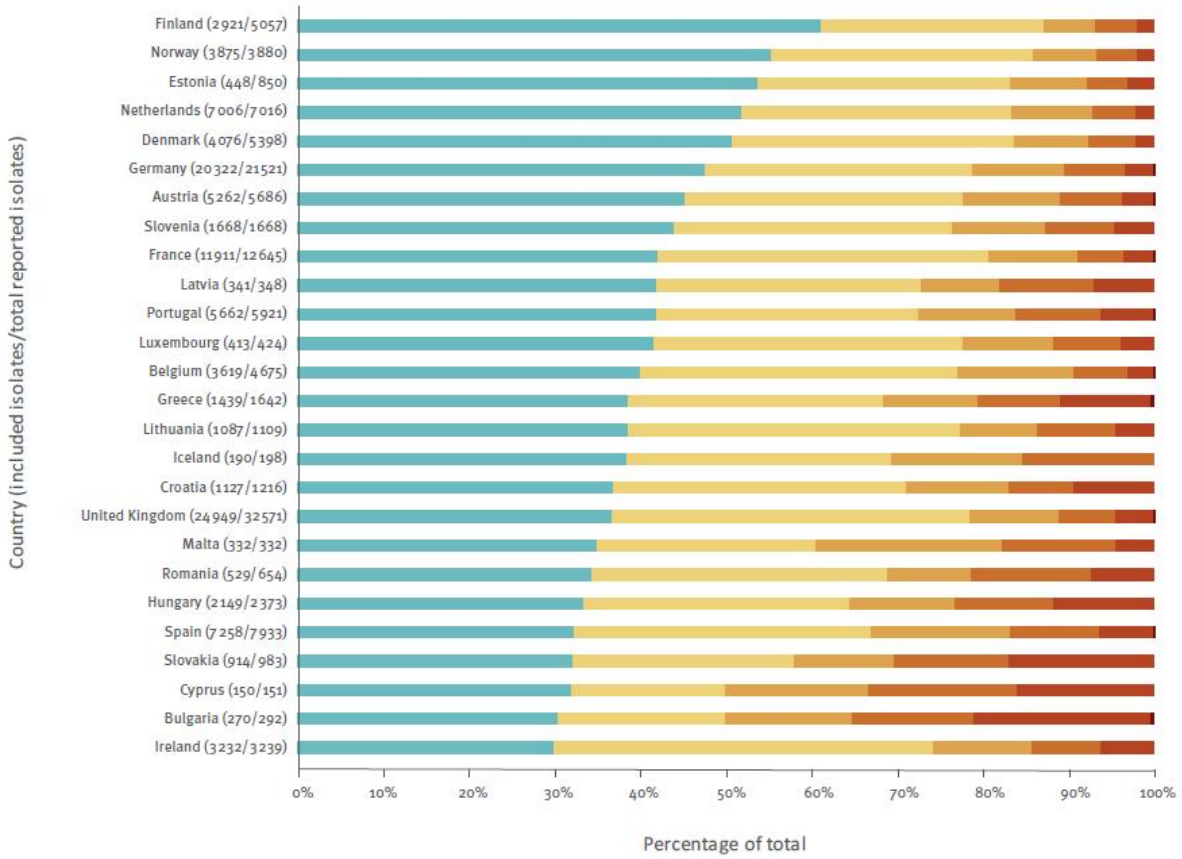
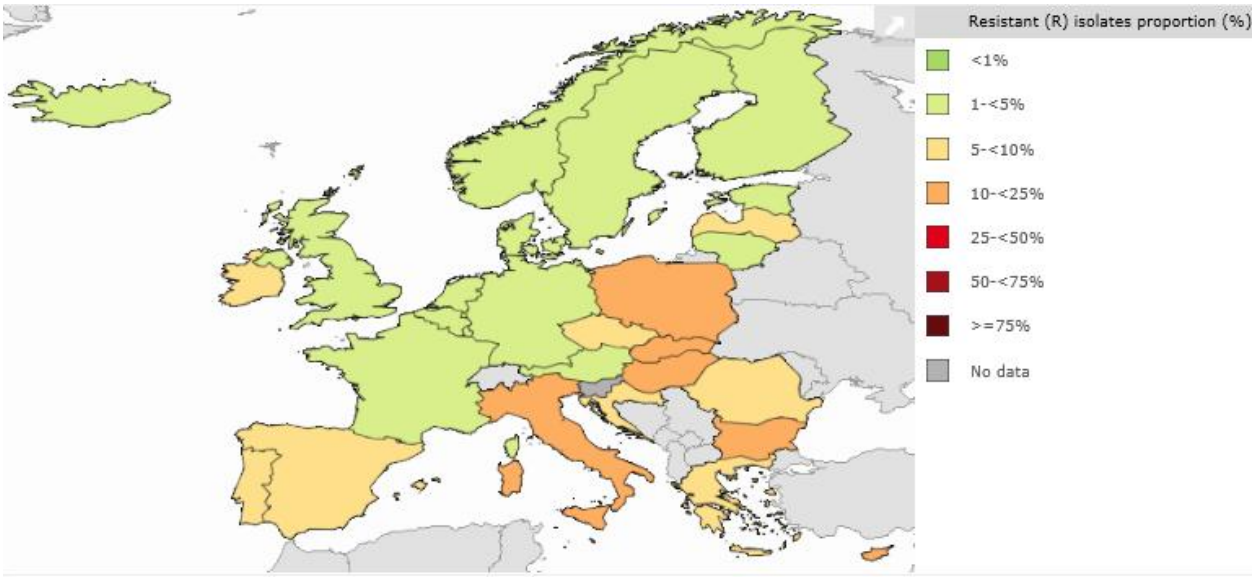


Figure kindly provided by Liselotte Diaz Högberg, European Centre for Disease Prevention and Control (ECDC)

Figure 4. Distribution of MDR *E. coli* (combined resistance to 3GCs, fluoroquinolones and aminoglycosides) in EU/EEA countries reported to EARS-Net in 2018



Map downloaded from the European Centre for Disease Prevention and Control (ECDC)'s Health Atlas of Infectious Diseases on 8th November 2019

Staphylococcus aureus

Staphylococcus aureus is commonly found on the skin and mucous membranes of healthy people. In addition to being one of the commonest causes of BSI, *S. aureus* is a frequent cause of skin, soft tissue and bone infections.

Flucloxacillin is the treatment of choice for *S. aureus* infections. Resistance to flucloxacillin, better known as meticillin resistance, is mediated by *mec*A, a gene that confers resistance to beta lactams.

Antimicrobial resistance in *S. aureus*

There were 1,188 reports of patients with *S. aureus* BSI, a 3% increase from 2017 (n=1,153).

Table 1 shows the annual data since 2014 on the proportion of *S. aureus* isolates resistant to meticillin:

- In 2018, 12.4% of cases were MRSA, a decrease from 16.1% in 2017 and the lowest annual proportion to date. The decrease over the past five years is statistically significant, with a downward trend since 2011 (Figure 5)
- Overall, there was a 21% decrease in the number of reported MRSA BSI compared with 2017 (147 versus 186 cases). In contrast, the total number of MSSA BSI increased by 8% (1,041 versus 967 cases)
- Calculating separate rates (numbers of cases per 1,000 patient days) for MRSA and MSSA, which are generally independent of each other, gives a better indication of the burden of these infections on acute care hospitals in Ireland. In 2018, the MRSA rate was 0.035 cases per 1,000 patient days, a decrease from 0.043 in 2017, while the MSSA rate increased from 0.228 to 0.245 (Figure 6)
- Despite decreasing trends in recent years, MRSA continues to be a problem in Irish hospitals. In 2018, Ireland had one of the highest proportions of MRSA in northern and western Europe (Figure 7)
- A slightly higher proportion of MRSA (40%) were temporally-associated with an admission episode at the reporting hospital (i.e. were isolated three days or more after admission) than MSSA (36%)
- The majority of *S. aureus* (54%) and MRSA (57%) isolates were reported by the nine tertiary hospitals, which comprised 44% of all patient bed days in 2018
- Almost two-thirds of *S. aureus* BSI (regardless of whether MRSA or MSSA) arose in males
- BSI due to MRSA were more likely to occur in older patients than MSSA: 75% of MRSA occurred in patients over 60 years (median age=73 years), compared with 61% of MSSA (median age=66 years)

Figure 5. **Trends for *S. aureus* bloodstream infections in Ireland, 2011-2018: total numbers of *S. aureus*/MRSA and percentage MRSA**

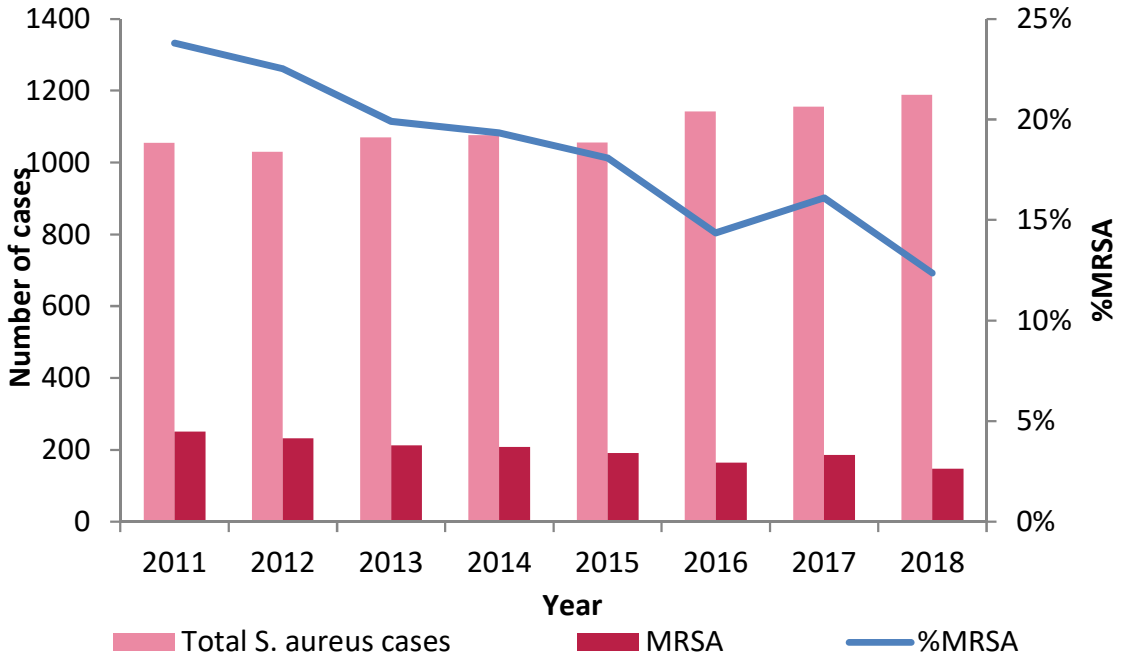
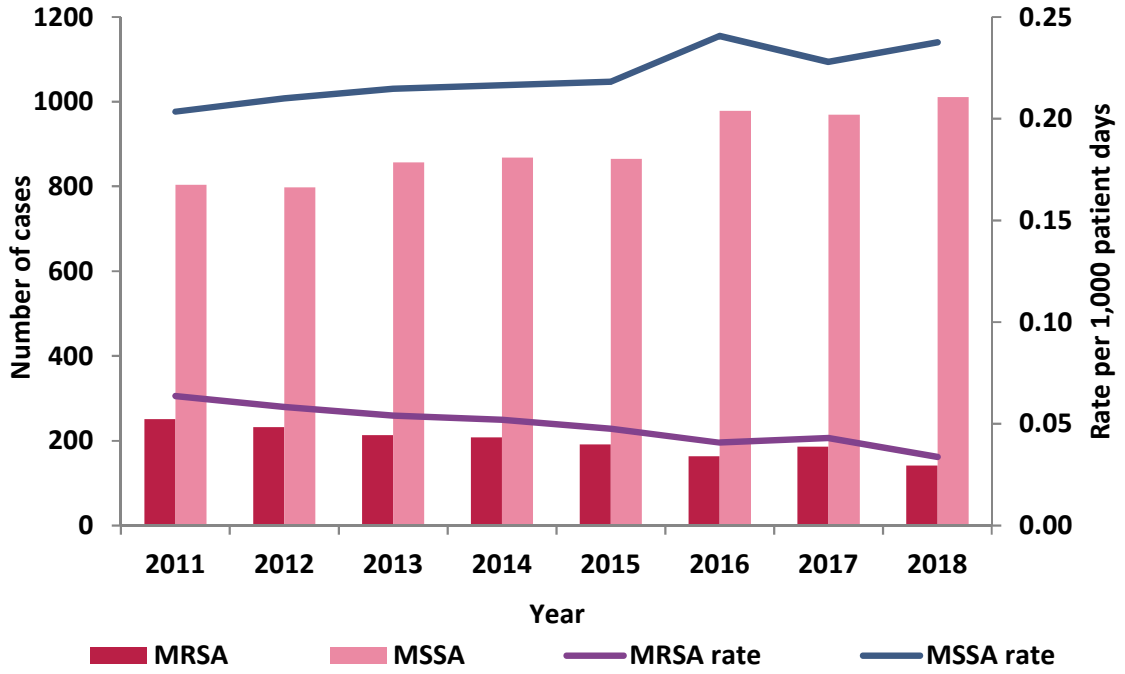


Figure 6. **Trends for *S. aureus* bloodstream infections in Ireland, 2011-2018: total numbers of *S. aureus*/MRSA and percentage MRSA**



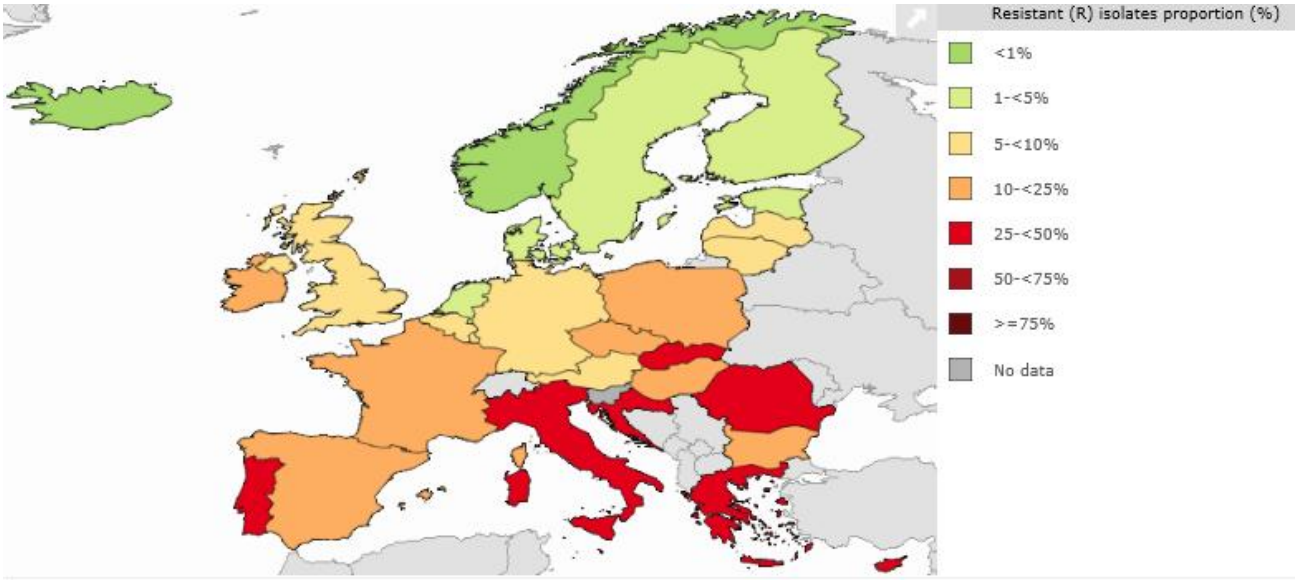
Enhanced surveillance findings:

- Healthcare-association was reported for 57% of MRSA and 50% of MSSA BSI
- Device-association was reported for 4% of MRSA and 16% of MSSA BSI
- Recent antimicrobial exposure was reported for 17% of patients with MRSA and 23% of patients with MSSA BSI
- The most common source for *S. aureus* BSI was skin and soft tissue infection of non-surgical wounds: MRSA; 13%, MSSA; 20%

Further data on *S. aureus* BSI in Ireland for the period 2011-2018, including breakdown by MRSA and MSSA, by acute hospital (both public and private) is available at the following link: http://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/europeanantimicrobialresistancesurveillancesystemearss/referenceandeducationalresourcematerial/saureusmrsa/latestsaureusmrsadata/

For more detailed European data on *S. aureus* and all other pathogens described in this report, including tables, charts and maps, see https://ecdc.europa.eu/en/antimicrobial-resistance/surveillance-and-disease-data/data-ecdc

Figure 7. Distribution of MRSA in EU/EEA countries reported to EARS-Net in 2018



Map downloaded from the European Centre for Disease Prevention and Control (ECDC)'s Health Atlas of Infectious Diseases on 8th November 2019

Klebsiella pneumoniae

Klebsiella pneumoniae resides in the normal human gut flora. Most *K. pneumoniae* infections are healthcare-associated, including pneumonia, wound infection, UTI and BSI.

Similar to *E. coli*, *K. pneumoniae* can develop resistance to key antimicrobials. Indeed, many ESBLs and carbapenemases were initially identified in *K. pneumoniae,* before spreading to *E. coli* and other Enterobacterales.

Antimicrobial resistance in *K. pneumoniae*

There were 483 reports of patients with invasive *K. pneumoniae* infection (482 from blood and one from CSF), similar to that reported in 2017(n=479).

Table 1 displays annual data since 2014 on the proportion of *K. pneumoniae* isolates resistant to the five indicator antimicrobials (as for *E. coli* above) *K. pneumoniae* are naturally resistant to aminopenicillins and any susceptible isolates that are reported represent either an error in identification or susceptibility testing:

- A similar proportion of 3GC resistance was reported in comparison to 2017 (14.5% versus14.6%), while 15.3% were ESBL producers, which is higher than in 2017 (but incomplete data was received for 13 isolates) (Figure 8)
- Resistance to fluoroquinolones (18.6%) and aminoglycosides (13.0%) increased compared with 2017
    - MDR *K. pneumoniae* is defined as combined resistance to 3GCs, fluoroquinolones and aminoglycosides and accounted for 8.3% of isolates, an increase from 2017 (6.1%)
    - Two isolates were resistant to all five indicator antimicrobials, compared with none in 2017 and four in 2016. Across Europe, 5.0% of isolates (n=1,799) displayed this resistance profile, an increase from 4.5% in 2016
- Six (1.2%) isolates were intermediate (n=3; 0.6%) or resistant (n=3; 0.6%) to carbapenems (Figure 8):
    - Four isolates were carbapenemase-producers, or CPE (all OXA-48-type)
    - In the period 2011-2018, 36 invasive *K. pneumoniae* isolates were reported as carbapenem- intermediate or -resistant, with 25 confirmed as CPE, of which 13 were resistant to all five indicator antimicrobials. In addition, another isolate that was carbapenem susceptible was found to be a CPE (Table 4)
    - As shown in Figure 9, carbapenem resistance among invasive isolates of *K. pneumoniae* in Ireland remains at a low level, unlike southern and eastern European countries, including Greece (63.9%) and Italy (29.5%)
- Ireland had one of the lowest rates of resistance in invasive *K. pneumoniae* isolates, including MDR *K. pneumoniae* (Figure 11)

- The majority of *K. pneumoniae* (54%) and MDR *K. pneumoniae* (60%) isolates were reported by the nine tertiary hospitals, which comprised 44% of all patient days in 2018
- The majority of MDR *K. pneumoniae* (59%) were associated with the reporting hospital (i.e. were isolated three days or more after admission)
- The majority of *K. pneumoniae* infections (70%) occurred in patients over 60 years (median age=69 years), with almost two-thirds (62%) of *K. pneumoniae* infections occurring in males

Enhanced surveillance findings:

- The majority of *K. pneumoniae* BSI were healthcare-associated (59%)
- The most common source of *K. pneumoniae* BSI was UTI (24%), with 5% of infections associated with a urinary catheter
- Recent antimicrobial exposure was noted in 12% of cases of *K. pneumoniae* BSI

Figure 8. Trends for invasive *K. pneumoniae* infections in Ireland, 2009-2018: total numbers of *K. pneumoniae* with percentage 3GC resistant (3GC-R), ESBL producer (ESBL+ve) and carbapenem resistant (CBP-R)

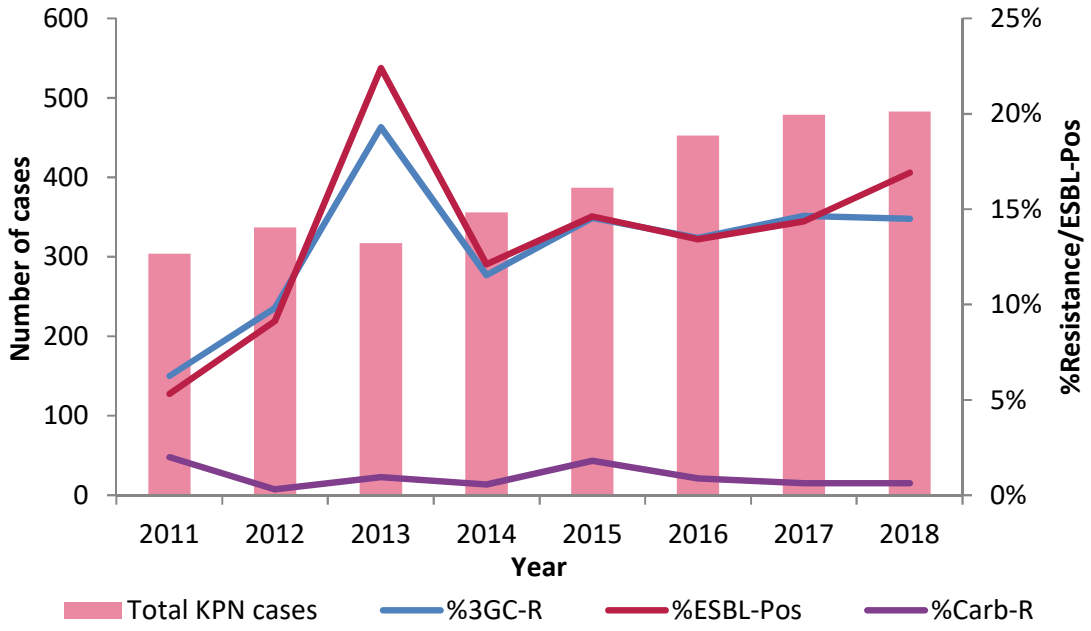


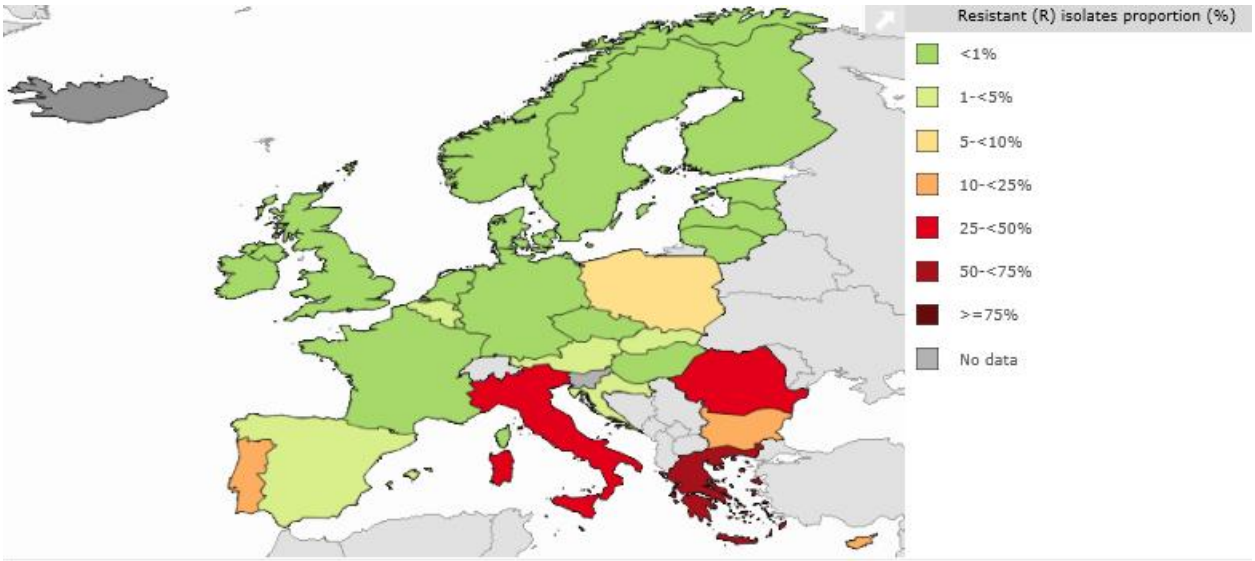
Table 4. Data on carbapenem resistant *K. pneumoniae* compared with carbapenemase-producing *K. pneumoniae* in Ireland, 2011-2018

Year	Number CRE (*K. pneumoniae*)	Num CPE (CP-KPN)	Enzymes detected (numbers)
2011	6	4	OXA-48 (3), KPC (1)
2012	1	0	
2013	4	2	OXA-48 (2)
2014	4	2	OXA-48 (1), KPC (1)
2015	7	6	OXA-48 (5), KPC (1)
2016	4	4	OXA-48 (3), KPC (1)
2017	4	4	OXA-48 (4)*
2018	6	4	OXA-48 (3), OXA-181/232 (1)
Total	36	26	OXA-48 (21), KPC (4), OXA-181-232 (1)

CRE, carbapenem-resistant Enterobacterales; CPE, carbapenemase-producing Enterobacterales

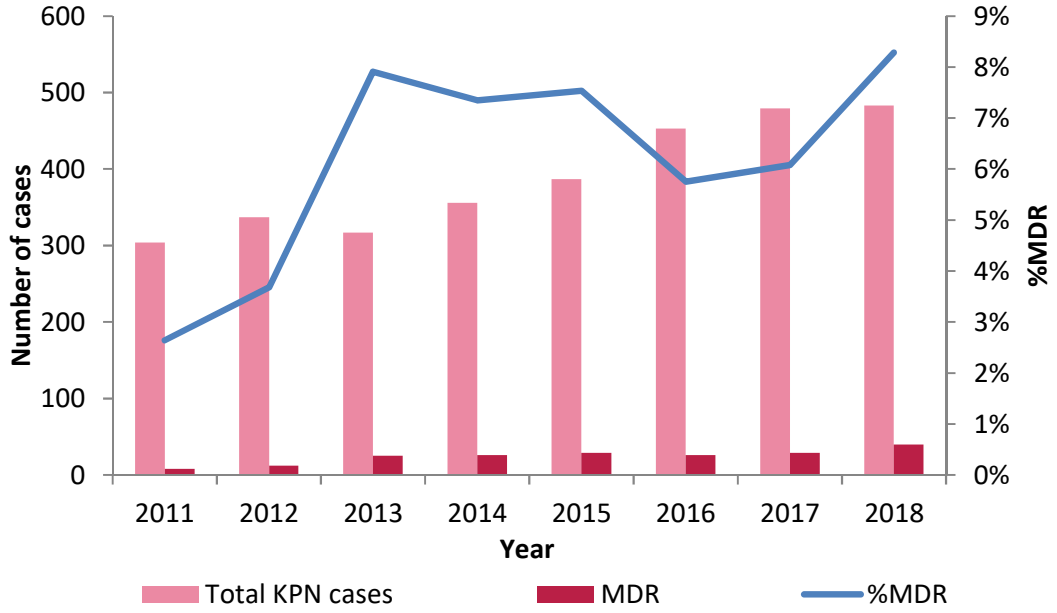
*includes one isolate where carbapenem-sensitive

Figure 9. Distribution of *K. pneumoniae* with carbapenem resistance in EU/EEA countries reported to EARS-Net in 2018



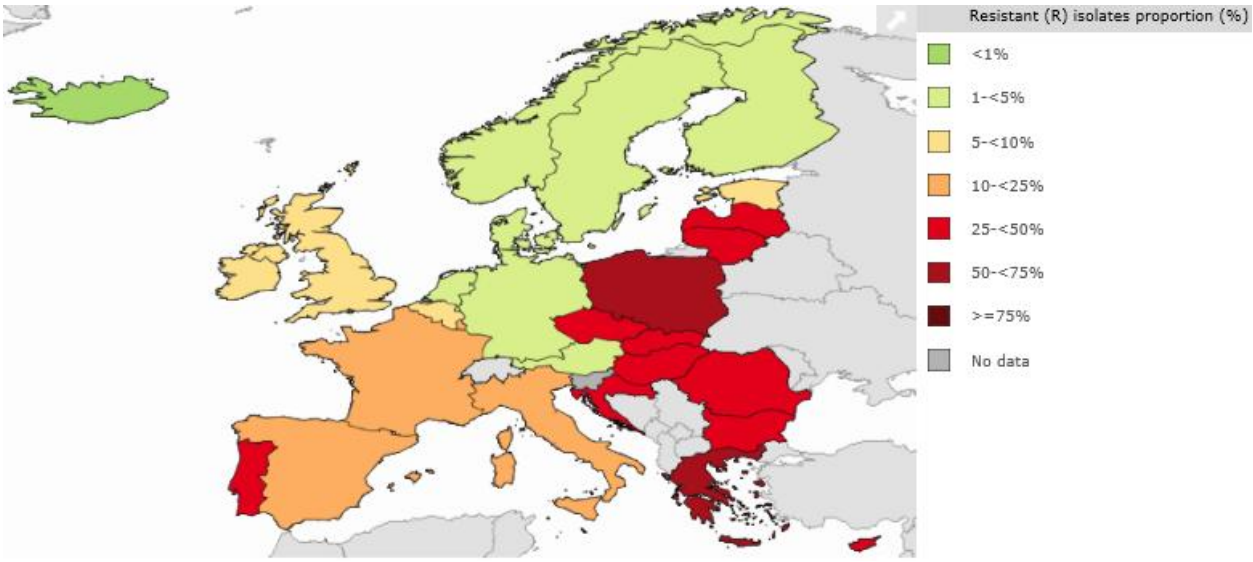
Map downloaded from the European Centre for Disease Prevention and Control (ECDC)'s Health Atlas of Infectious Diseases on 8th November 2019

Figure 10. Trends for invasive *K. pneumoniae* infections in Ireland, 2009-2018: total numbers of *K. pneumoniae* tested for MDR*, with number and percentage MDR



*Multi-drug resistance defined as resistance to combined resistance to 3GCs, fluoroquinolones and aminoglycosides

Figure 11. Distribution of MDR *K. pneumoniae* (defined as combined resistance to 3GCs, fluoroquinolones and aminoglycosides) in EU/EEA countries reported to EARS-Net in 2018



Map downloaded from the European Centre for Disease Prevention and Control (ECDC)'s Health Atlas of Infectious Diseases on 8th November 2019

Enterococci

Enterococci reside in the normal human gut flora. They can cause infections, including BSI, in severely ill and immunocompromised patients. The majority of infections are due to *Enterococcus faecium* and *Enterococcus faecalis*.

The enterococci are naturally resistant to many antimicrobials, including to low levels of aminoglycosides (e.g. gentamicin). Resistance to vancomycin and high-level gentamicin can emerge by the bacteria acquiring specific resistance genes.

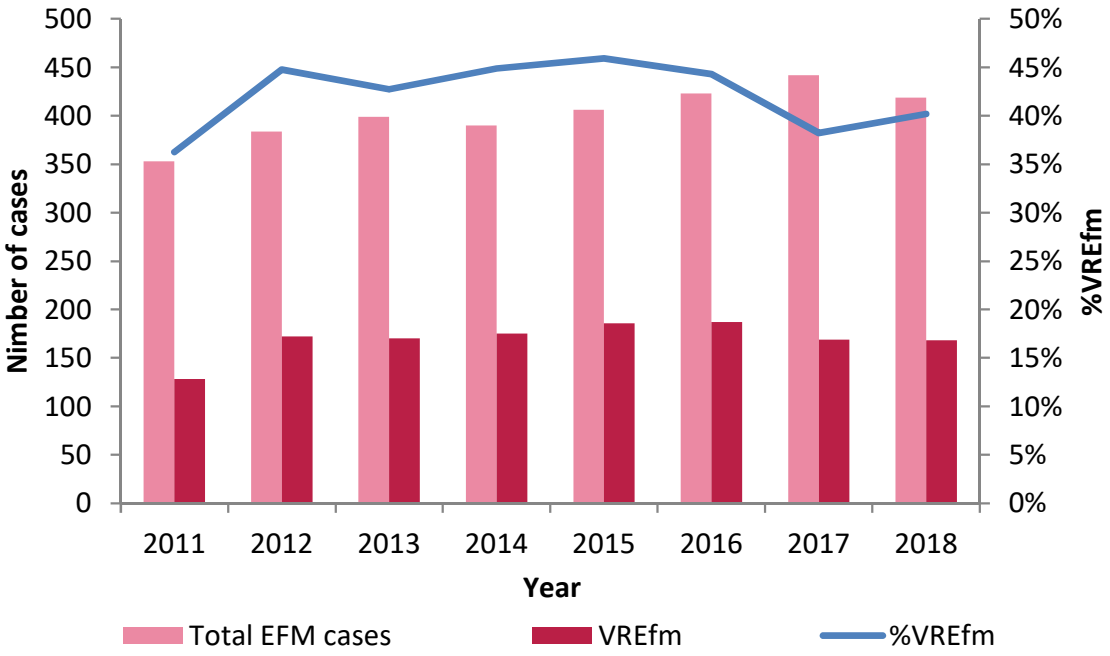
Antimicrobial resistance in *E. faecium*

In 2018, there were 419 reports of patients with *E. faecium* BSI, a decrease of 5% from 2017 (n=442).

Table 1 displays the annual trends since 2014 in the proportion of *E. faecium* isolates resistant to the three indicator antimicrobials: ampicillin, vancomycin and high-level gentamicin:

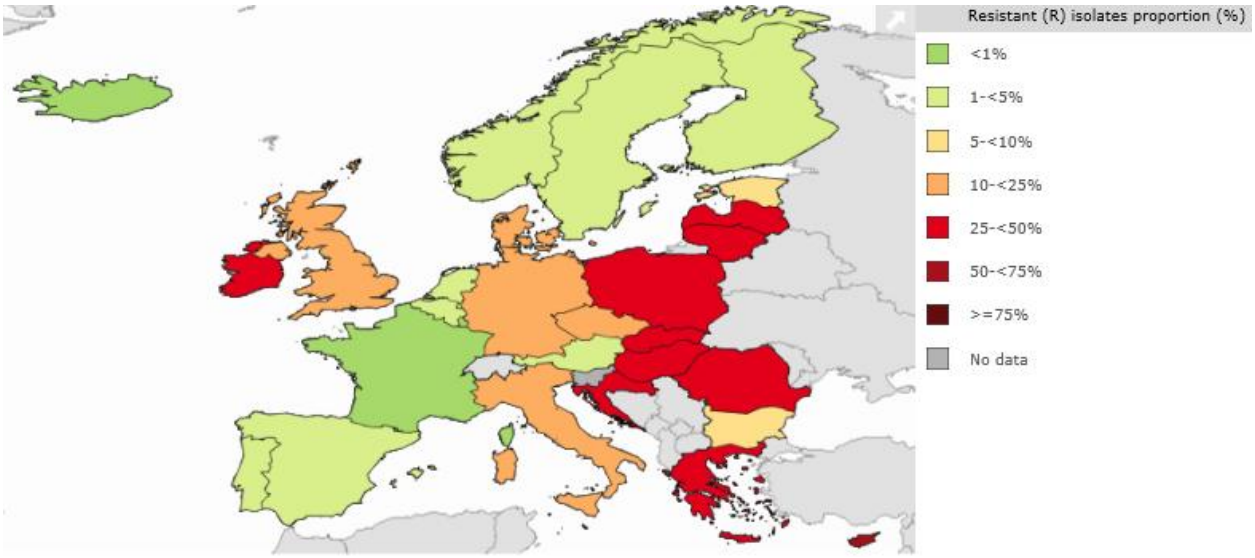
- Vancomycin resistance was observed in 40.2% of isolates (VREfm), which represents an increase from 38.2% in 2017 (Figure 12)

Figure 12. Trends for *E. faecium* BSI in Ireland, 2011-2018: total numbers of *E. faecium* and percentage vancomycin-resistant *E. faecium* (VREfm)



- Resistance to all three indicator antimicrobials (MDR *E. faecium*) was reported for 30.1% of isolates, which is similar to that in 2017 (29.9%)
- In 2018, Ireland ranked third after Cyprus (59.1%) and Romania (40.3%) and was among ten countries in Europe reporting proportions of VREfm over 25% (Figure 13). Fourteen countries have reported increasing trends, compared with three reporting decreasing trends
- Two isolates (0.5%) were reported as resistant to linezolid
- The majority of *E. faecium* (61%) and VREfm (68%) BSI were reported by the nine tertiary hospitals (which comprised 44% of all patient days in 2018)
- The majority of *E. faecium* (77%) and VREfm (86%) BSI were associated with the hospital of admission (i.e. were isolated three days or more after admission)
- The majority of *E. faecium* (71%) BSI occurred in patients over 60 years (median age=70 years), with just over half (53%) occurring in males

Figure 13. Distribution of VREfm in EU/EEA countries reported to EARS-Net in 2018



Map downloaded from the European Centre for Disease Prevention and Control (ECDC)'s Health Atlas of Infectious Diseases on 8th November 2019

Antimicrobial resistance in *E. faecalis*

There were 332 reports of patients with *E. faecalis* BSI, a decrease of 2% from 2017 (n=340).

Table 1 displays annual trends since 2014 in the proportions of *E. faecalis* isolates with resistance to the three indicator antimicrobials (as for *E. faecium* above):

- Two isolates (0.6%) were resistant to vancomycin (VREfa). VREfa remains at low levels in Ireland
- No isolates were resistant to linezolid
- The majority of *E. faecalis* (55%) were detected within two days of admission to hospital.
- The majority of *E. faecalis* (76%) occurred in patients over 60 years (median age=73 years) with approximately two-thirds of *E. faecalis* infections occurring in males

Enhanced surveillance findings (data for *E. faecium* and *E. faecalis* combined):

- Healthcare-association was reported for 92% of the vancomycin-resistant enterococcal (VRE) and 60% of the vancomycin-susceptible enterococcal (VSE) BSIs
- Device-association was reported for 6% of VRE and 8% of VSE BSI

Streptococcus pneumoniae

Streptococcus pneumoniae resides in the normal upper respiratory tract flora. It is the main cause of community-acquired pneumonia and otitis media and is also associated with invasive infections, including BSI and meningitis.

The treatment of choice for pneumococcal infection is penicillin. Resistance to penicillin can arise due to alterations in the penicillin-binding proteins (PBPs), the target sites for penicillin in the bacterial cell wall, resulting in lowered affinity of these PBPs for penicillin. The level of resistance to penicillin can be intermediate or high-level, depending on the exact alteration to the PBP. It is important to determine the exact level of resistance (or non-susceptibility), as this will influence the treatment options that are available, depending on the site of infection.

Antimicrobial resistance in *S. pneumoniae*

There were 455 reports of patients with invasive *S. pneumoniae* infection (451 from blood and four from CSF), an increase of 10% from 2017(n=412).

Table 1 displays annual trends since 2014 in the proportions of *S. pneumoniae* isolates non-susceptible/resistant to penicillin and erythromycin:

- Penicillin non-susceptible *S. pneumoniae* (PNSP) accounted for 20.7% (19.3% intermediately-resistant and 1.3% high-level resistant, or HLR) of all isolates tested against penicillin in 2018, which represents an increase from 15.8% in 2017 (Figure 14)
- Erythromycin resistance was reported for 13.6% of isolates, an increase from 12.9% in 2017
- PNSP and erythromycin co-resistance was reported for 9.1% of isolates, an increase from 2017 (8.6%)
- The proportion of PNSP in Ireland has fluctuated over the period 2014 to 2018 (Figure 14). Ireland has moderately-high proportions of PNSP compared to other EU/EEA countries. However, data may not be comparable across all countries due to the potential for different interpretive criteria to be applied, depending on the guidelines used and the site of infection
- The proportion of isolates with high-level resistance to penicillin decreased from 6% in 2011 to just over 1% in 2018
- Serotyping results were available for 89% of invasive pneumococcal isolates:
    - Of all invasive *S. pneumoniae* cases, 10 serotypes comprised almost 75% of all isolates: 8 (20%), 19A† (12%), 12F (9%), 22F (7%), 3† and 9N (6% each), 23B and 35B (4% each), and 15A and 33F (4% each); 24 serotypes comprised the remaining 25%

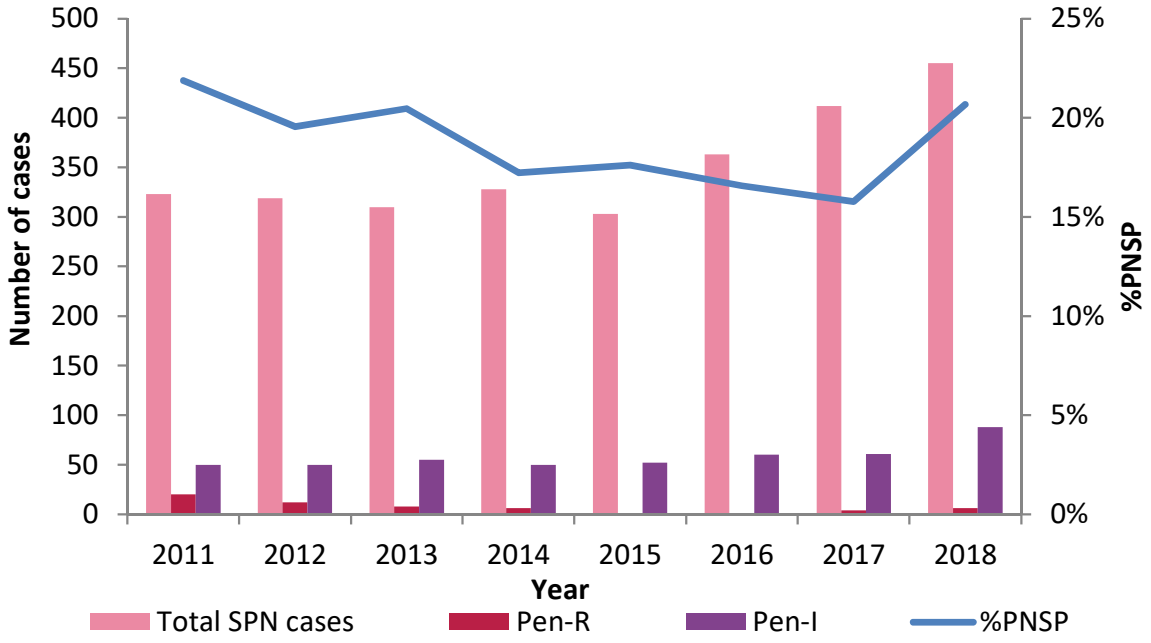
- Among PNSP isolates, four serotypes predominated: 19A (30%), 35B (15%), 23B (14%) and 15A (10%), with 14 serotypes making up the remainder. Of the six PNSP isolates with HLR to penicillin, four belonged to serotype 19A
- Following the introduction of pneumococcal conjugate vaccines (PCV) into the childhood immunisation schedule (PCV-7 in 2008, replaced by PCV-13 in 2010), there has been a shift in the predominant serotypes causing invasive pneumococcal disease (IPD):
  - In 2008 non-PCV-13 serotypes comprised almost 30% of all serotypes causing invasive IPD and this increased to 77% in 2018
  - In 2008, non-PCV-13 serotypes comprised just over 10% of all serotypes causing PNSP invasive infections and this increased to almost 60% in 2018. Of approximately 40% of PCV-13 serotypes, the majority (74%) were 19A

†Serotypes 3 and 19A are included in PCV13; However, the vaccine may not always result in a strong immune response against these serotypes

For more details on the effects of vaccination on IPD, see the separate annual epidemiological report:

http://www.hpsc.ie/abouthpsc/annualreports/

Figure 14. Trends for invasive *S. pneumoniae* infections in Ireland, 2009-2018: total numbers of *S. pneumoniae* and penicillin-resistant (Pen-R) and penicillin-intermediate (Pen-I) *S. pneumoniae* (PNSP) and percentage penicillin non-susceptible *S. pneumoniae* (%PNSP)



- The majority of *S. pneumoniae* (96%) and PNSP (87%) were isolated within two days of hospital admission
- The majority of *S. pneumoniae* (64%) occurred in patients over 60 years (median age=68 years) with males and females equally likely to get a *S. pneumoniae* infection

Enhanced surveillance findings:

- The majority of both PNSP and penicillin-susceptible *S. pneumoniae* BSI were community-acquired
- Respiratory tract infection remained the most common source of pneumococcal BSI

Pseudomonas aeruginosa and Acinetobacter spp.

Pseudomonas aeruginosa and *Acinetobacter* spp. are widely found in the environment and thrive in moist conditions, including on medical equipment such as catheters and ventilators. They are opportunistic pathogens in immunocompromised patients and cause infections, such as pneumonia, UTI and BSI.

P. aeruginosa and *Acinetobacter* spp. are inherently resistant to many antimicrobials. Hence, if resistance develops to those agents to which they remain susceptible, this can seriously compromise treatment options.

Antimicrobial resistance in *Pseudomonas aeruginosa*

In 2018, there were 273 reports of patients with invasive *P. aeruginosa* infection (272 from blood and one from CSF), a decrease of 5% from 2017 (n=288).

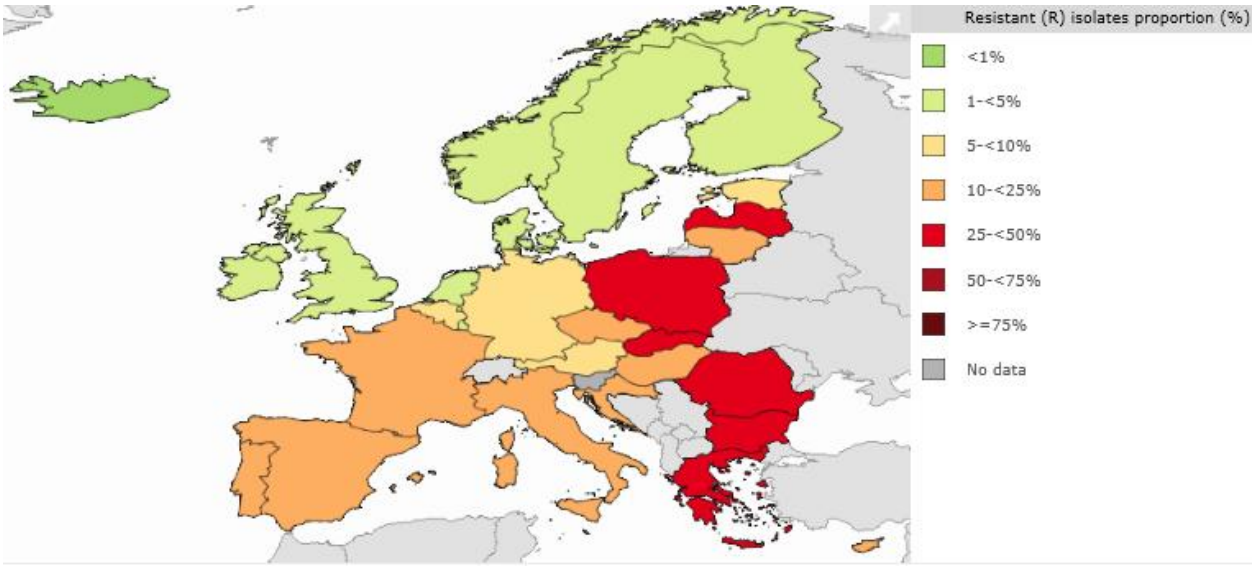
Table 1 displays annual trends since 2014 in the proportion of *P. aeruginosa* isolates resistant to the five indicator antimicrobials/antimicrobial classes: piperacillin-tazobactam, ceftazidime, carbapenems (meropenem or imipenem), fluoroquinolones (ciprofloxacin) and aminoglycosides (gentamicin, amikacin or tobramycin):

- Of isolates tested against all five indicator antimicrobials, 3.1% were identified as MDR *P. aeruginosa*, defined as resistance to three or more of the indicator antimicrobials. This represents a decrease from 2017 (8.5%)
- AMR of *P. aeruginosa* isolates in Ireland for each of the five indicator antimicrobials, as well as for MDR (Figure 15), are at moderately-low levels in comparison with other European countries
- The majority of *P. aeruginosa* (51%) isolates were reported by the nine tertiary hospitals (which comprised 44% of all patient days in 2018)
- The majority of *P. aeruginosa* (79%) occurred in patients over 60 years (median age=72 years), with approximately two-thirds of *P. aeruginosa* infections occurring in males

Enhanced surveillance findings:

- The majority of *P. aeruginosa* BSI were healthcare-associated (65%)
- The most common source of *P. aeruginosa* BSI was UTI (18%), with 8% of infections associated with a urinary catheter
- Recent antimicrobial exposure was noted in 9% of cases of *P. aeruginosa* BSI

Figure 15. Distribution of MDR *Pseudomonas aeruginosa* in EU/EEA countries reported to EARS-Net in 2018



Map downloaded from the European Centre for Disease Prevention and Control (ECDC)'s Health Atlas of Infectious Diseases on 8th November 2019

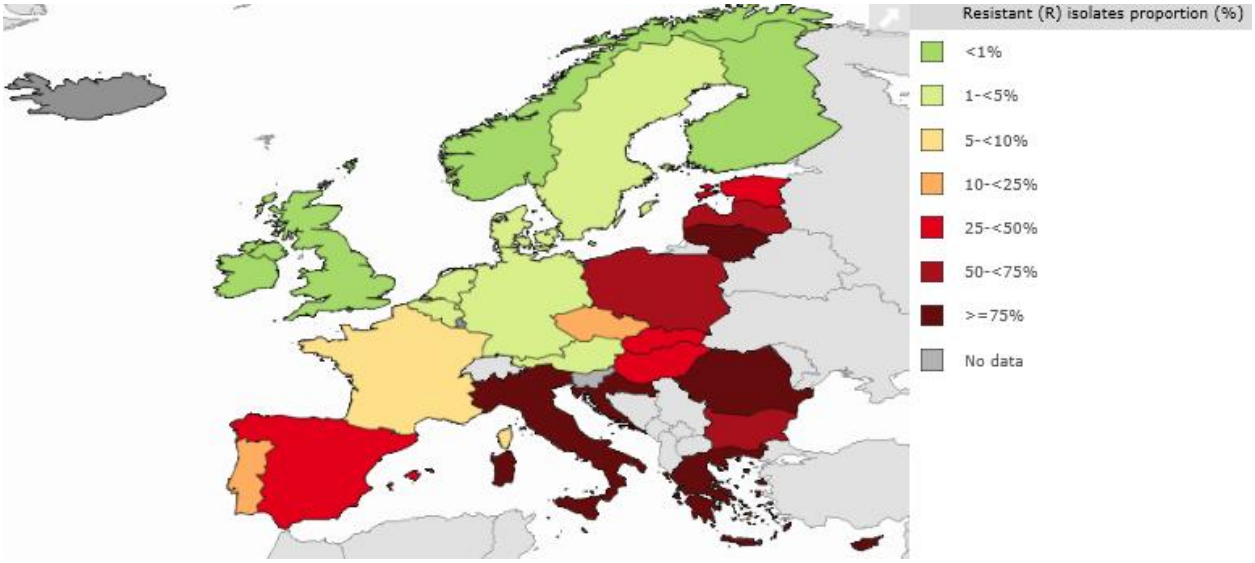
Antimicrobial resistance in *Acinetobacter* spp.

In 2018, there were 62 reports of BSI due to *Acinetobacter* spp., compared with 66 in 2017.

Table 1 displays annual data since 2014 in the proportion of *Acinetobacter* spp. isolates with resistance to the three indicator antimicrobials/antimicrobial classes: carbapenems (meropenem or imipenem), fluoroquinolones (ciprofloxacin) and gentamicin:

- No MDR *Acinetobacter* spp., i.e. resistant to all three indicator antimicrobials, were identified
- AMR among *Acinetobacter* spp. in Ireland remains at low levels (Figure 16)
- The majority of *Acinetobacter spp.* (56%) isolates were reported by the nine tertiary hospitals (which comprised 44% of all patient days in 2018)
- The majority of *Acinetobacter spp.* (68%) were isolated within two days of hospital admission
- Only 39% of *Acinetobacter* spp. occurred in patients over 60 years (median age=53 years), which is the lowest proportion among this age group for all eight EARS-Net pathogens under surveillance, while 29% of infections occurred in paediatric patients, the highest proportion among this age group for all the pathogens. The majority (58%) of *Acinetobacter* spp. infections occurred in males

Figure 16. Distribution of MDR *Acinetobacter* spp. in EU/EEA countries reported to EARS-Net in 2018



Map downloaded from the European Centre for Disease Prevention and Control (ECDC)'s Health Atlas of Infectious Diseases on 8th November 2019

Further information on EARS-Net available on HPSC website

Further information on EARS-Net and antimicrobial resistance in Ireland can be found at:

https://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/europeanantimicrobialresistancesurveillancesystemearss/

European data can be found at:

https://ecdc.europa.eu/en/about-us/partnerships-and-networks/disease-and-laboratory-networks/ears-net

Invasive Carbapenemase-producing Enterobacterales (CPE) infection

Background

Invasive carbapenem-producing Enterobacterales (CPE) infection, previously known as carbapenem-resistant *Enterobacteriaceae* (CRE), became notifiable in Ireland from January 2012.

For surveillance purposes, the case definition is based on laboratory criteria only: any person with reference laboratory confirmation of CPE from a normally sterile site should be reported to public health as an invasive CPE case.

Data were extracted from the Computerised Infectious Diseases Reporting (CIDR) system on 1st October 2019.

Epidemiology

In 2018, there were 16 notifications of invasive CPE infection, all from blood (BSI):

- Ten cases were associated with six tertiary hospitals, five cases with three general hospitals and one from a paediatric hospital
- The predominant carbapenemase was OXA-48 (n=15), with one case due to VIM
- Four Enterobacterales species accounted for all invasive CPE infections: *Enterobacter cloacae* (n=7) and *E. coli*, *K. pneumoniae* and *Klebsiella oxytoca* (n=3 each)
- The median patient age was 69 years (range = 6-93), with a male predominance (n=12; 75%)

Table 5. Distribution of carbapenemases causing invasive CPE infection in Ireland, 2012-2018

Carbapenemase type	2012	2013	2014	2015	2016	2017	2018	2012-2018
OXA	0	0	2	6	6	13	15	**42**
KPC	0	0	2	2	3	0	0	**7**
NDM	0	0	0	0	3	0	0	**3**
VIM	0	0	1	0	1	0	1	**3**
IMP	0	0	0	0	1	1	0	**2**
Total	**0**	**0**	**5**	**8**	**14**	**14**	**16**	**57**

There were no invasive CPE infections notified prior to 2014. Since 2014, 57 invasive cases of CPE were notified, with OXA-48 accounting for almost 75% of these (Figure 17).

Further information on CPE available on HPSC website

Further information on CPE in Ireland can be found at:

https://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/strategyforthecontrolofantimicrobialresistanceinirelandsari/carbapenemresistantenterobacteriaceaecre/

Further information on EARS-Net and antimicrobial resistance in Ireland can be found at:

Data from the enhanced surveillance of Carbapenemase-producing Enterobacterales, 2018 can be found at:

https://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/strategyforthecontrolofantimicrobialresistanceinirelandsari/carbapenemresistantenterobacteriaceaecre/surveillanceofcpeinireland/cpeannualreports/

Public health implications

AMR remains an important threat in Ireland. In October 2017, Ireland's national action plan on AMR (iNAP) was published, outlining the strategy to prevent AMR from 2017 to 2020.

Over the past five years, the numbers of invasive infections reported to EARS-Net have steadily increased by almost 20% with the biggest increases seen in *P. aeruginosa* (54%), *S. pneumoniae* (39%), *K. pneumoniae* (36%) and *E. coli* (20%).

As the commonest pathogen detected in BSI, with the majority of cases community-acquired, it is concerning that Ireland was the EU country with the lowest proportion of fully susceptible *E. coli* BSI in 2018. While there has been encouraging progress in addressing community antimicrobial use in Ireland in recent years, much work remains to be done.

Infections due to ESBL-producing *E. coli* and *K. pneumoniae*, as well as with resistance to many of the other commonly used antimicrobials (combined resistance or MDR) have become more common. Recent increases in resistance to carbapenems, regarded as reserve antimicrobials for treatment of AMR infections and infections in seriously ill patients have also been observed. Increasing incidence of carbapenemase-producing *Enterobacterales* (CPE) in Ireland prompted declaration of a national public health emergency in October 2017. Across Europe, resistance levels have generally been higher in *K. pneumoniae* than in *E. coli* but this is not the case for Ireland, where resistance levels have been similar or lower in *K. pneumoniae*.

The inclusion of invasive CPE infection on the list of notifiable infectious diseases in Ireland is important, because relying on data about carbapenemase production in *E. coli* (n=4) and *K. pneumoniae* (n=4) BSI from EARS-Net surveillance in 2018 underestimated the actual burden of invasive CPE infection (n=16)

Meticillin resistance in *S. aureus* BSI decreased significantly over five years from 19% in 2014 to 12% in 2018. However, Ireland still has one of the higher rates of meticillin resistance in northern Europe and the rate of BSI due to MSSA has not been decreasing.

Ireland has long had one of the highest proportions of vancomycin-resistance in *E. faecium* (VREfm) in Europe and was one of only two countries in 2018 where the numbers of *E. faecium* exceeded those of *E. faecalis*. While the proportion of VREfm in Ireland has decreased in recent years, VREfm has been increasing in many European countries with no obvious geographical pattern. The reasons for the predominance of *E. faecium* and especially VREfm in Ireland are not well-understood.

With the recent increase in invasive *S. pneumoniae* infections, serotyping data from IMSRL has provided invaluable data on the different serotypes in circulation. Ongoing surveillance of the predominant serotypes is required, as strains with non-vaccine serotypes are known to increase in prevalence following the introduction of conjugate vaccines and this has been demonstrated in Ireland. Such surveillance data will inform subsequent vaccine development in order to target emerging serotypes not covered by current vaccines. The

separate chapter on invasive pneumococcal disease (IPD) in Ireland in 2018 contains additional information on pneumococcal serotyping.

Despite the overall increase in the number of invasive *S. pneumoniae* infections, the decrease in the proportion of isolates with high-level resistance to penicillin is encouraging. Some of this may be related to conjugate pneumococcal vaccines selectively targeting serotypes that are typically associated with resistance, but is also likely to be driven by decreasing community antimicrobial use (for which there is a temporal association).

It is important that AMR surveillance in Ireland continues to evolve, to detect other new and emerging pathogens and resistance mechanisms. For example, *Candida auris* is a relatively new pathogen, first identified in 2009, that is often MDR. To date, it has not been reported in Ireland. In recent years, it has emerged in a number of countries as a cause of hospital outbreaks. Strains of *E. coli* with resistance to colistin were reported from China in 2015. Colistin is a critically important antimicrobial, used to treat MDR infections, such as those due to CPE. The gene responsible for this resistance is called *mcr*1 and is carried on a plasmid that can be transferred easily to other strains of *E. coli* and to other bacterial species. Linezolid resistance in enterococci can be due to the presence of another gene (*optr*A), with the potential to spread to other strains.

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- Staff of the Irish Meningitis and Sepsis Reference Laboratory
- Staff of the National Carbapenemase Producing Enterobacteriaceae Reference Laboratory Service (NCPERLS)
- Staff of the National MRSA Reference Laboratory
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