9.4 Antimicrobial Resistance

a) Key Pathogens causing Bloodstream Infections

2016 Summary

- Estimated 99% coverage of the Irish population versus 97% in 2015
- There were 3,057 reports of invasive *E. coli* infection, an increase from 2,697 in 2015:
  - The proportion of invasive *E. coli* that were ESBL-producers (11.1%) was at its highest levels since surveillance began
  - One invasive *E. coli* isolate was a carbapenemase-producer, also known as carbapenem-resistant *Enterobacteriaceae* (CRE or CPE)
- There were 1,168 reports of *S. aureus* bloodstream infection (BSI), an increase from 1,082 in 2015:
  - Of those, 172 (14.7%) were meticillin-resistant *S. aureus* (MRSA). Compared with 2015, there was a 13.6% reduction in the number of MRSA BSI in 2016

    For acute hospitals, the rate of MRSA BSI was 0.043 cases per 1,000 bed days used (BDU), a decrease from 0.050 in 2015. An increase was observed in both the number (12.7% on 2015) and rate of meticillin-susceptible *S. aureus* (MSSA) BSI to 0.245 from 0.223 (2015)
  - The number, proportion and rate of MRSA BSI are at their lowest level since surveillance began; while the number and rate of MSSA BSI are at their highest level
- There were 431 reports of *E. faecium* BSI, an increase from 421 in 2015:
  - Vancomycin-resistant *E. faecium* (VREfm) accounted for 44.4%, one of the highest annual proportions reported to date
- There were 469 reports of invasive *K. pneumoniae* infection, an increase from 401 in 2015:
  - Resistance to all indicator antimicrobials decreased
  - In 2013, a multi-drug resistant *K. pneumoniae* (MDRKP) outbreak control team was established. The specific case definition for MDRKP is simultaneously an ESBL-producer and non-susceptible to both ciprofloxacin and gentamicin.

    The proportion of MDRKP causing invasive infections subsequently decreased to 7.1% (2016) from 12.3% (2013)
  - Four invasive *K. pneumoniae* isolates were carbapenemase-producers (CRE/CPE)
- There were 365 reports of invasive *S. pneumoniae* infection, an increase from 304 in 2015:
  - Of those, 60 (16.5%) were penicillin non-susceptible *S. pneumoniae* (PNSP), a decrease from 17.5% in 2015
  - The national rate of invasive pneumococcal infection increased compared with 2015 (7.7 per 100,000 population versus 6.6)
  - Serotype data were available for 341 (93.3%) of 365 invasive *S. pneumoniae* isolates. Results indicate good coverage (71.2%) for the 23-valent pneumococcal polysaccharide vaccine (PPV23) in its target population (adults ≥65 years)
- There were 250 reports of invasive *P. aeruginosa* infection, an increase from 201 in 2015, and resistance to all indicator antimicrobials, except for carbapenems, increased
- The data in this report was extracted from the EARS-Net database on **23rd October 2017**
- Enhanced surveillance data were provided on 2,593 records (cases or isolates under the EARS-Net definition) from 21 laboratories, representing 43% of all reported cases in 2016

Background

The European Antimicrobial Resistance Surveillance Network (EARS-Net), formerly known as the European Antimicrobial Resistance Surveillance System (EARSS), collects routinely-generated antimicrobial susceptibility testing (AST) data on seven important bacterial pathogens using the EARS-Net case definition. Participating laboratories in Ireland submit data on the "primary" or first isolate from blood or cerebrospinal fluid (CSF) per patient per quarter. EARS-Net does not distinguish clinically significant isolates from contaminants, nor does it distinguish between hospital-

Table 1. Summary of EARS-Net data by pathogen and year, 2010-2016

Pathogen	2010	2011	2012	2013	2014	2015	2016
Number laboratories by year-end	**40**	**41**	**41**	**41**	**39**	**38**	***37***
%Coverage of population	***100***	***100***	***100***	***100***	***100***	***97***	***99***
E. coli							
Number of isolates	**2170**	**2210**	**2450**	**2530**	**2771**	**2697**	***3057***
%Ampicillin-R*	*68.4*	*71.9*	*69.6*	*70.9*	*69.9*	*66.7*	***68.4***
%3GC-R*	*8.0*	*9.1*	*10.3*	*12.3*	*12.0*	*12.5*	***12.3***
%ESBL-producers*	*6.1*	*7.5*	*8.8*	*10.5*	*10.2*	*10.6*	***11.1***
%Ciprofloxacin-R*	*23.6*	*23.8*	*25.2*	*25.3*	*26.2*	*24.4*	***24.1***
%Gentamicin-R*	*9.4*	*8.7*	*9.7*	*9.8*	*11.2*	*11.0*	***10.2***
%Gentamicin/Amikacin/Tobramycin-R*	*11.9*	*12.4*	*12.8*	*12.9*	*14.5*	*13.4*	***13.2***
%Carbapenem[1]-R*	*0.0*	*0.0*	*0.1*	*0.1*	*0.1*	*0.2*	***0.2***
%MDR*	*11.8*	*13.2*	*13.6*	*14.6*	*15.0*	*14.5*	***14.3***
S. aureus							
Number of isolates	**1251**	**1095**	**1060**	**1094**	**1117**	**1082**	***1168***
Number Meticillin-R (or MRSA)	**305**	**263**	**242**	**222**	**217**	**199**	***172***
%Meticillin-R (or MRSA)	*24.4*	*24.0*	*22.8*	*20.3*	*19.4*	*18.4*	***14.7***
K. pneumoniae							
Number of isolates	**326**	**312**	**345**	**326**	**358**	**401**	***469***
%Ampicillin-R*	*99.1*	*100.0*	*98.5*	*99.1*	*100.0*	*99.3*	***99.4***
%3GC-R*	*10.2*	*8.0*	*11.9*	*21.2*	*13.1*	*17.5*	***16.8***
%ESBL-producers*	*5.1*	*5.6*	*8.8*	*18.4*	*11.0*	*13.3*	***12.9***
%Ciprofloxacin-R*	*10.5*	*13.2*	*11.9*	*20.9*	*17.3*	*21.6*	***16.6***
%Gentamicin-R*	*6.8*	*7.4*	*9.6*	*16.9*	*12.6*	*17.0*	***11.5***
%Gentamicin/Amikacin/Tobramycin-R*	*7.1*	*8.3*	*9.9*	*17.8*	*13.2*	*18.0*	***12.6***
%Carbapenem[1]-R*	*0.0*	*1.9*	*0.3*	*1.2*	*1.1*	*2.2*	***1.1***
%MDRKP[2]*	*2.2*	*4.6*	*5.3*	*12.3*	*8.2*	*9.8*	***7.1***
%MDR*	*8.0*	*9.0*	*10.2*	*19.7*	*13.7*	*19.8*	***14.7***
E. faecium							
Number of isolates	**392**	**364**	**392**	**409**	**405**	**421**	***431***
%Ampicillin-R*	*95.6*	*95.9*	*92.9*	*93.2*	*95.3*	*94.3*	***94.6***
%Vancomycin-R (VREfm)	*39.3*	*37.4*	*45.4*	*43.1*	*45.9*	*45.6*	***44.4***
%HLG-R*	*39.6*	*36.8*	*39.3*	*41.4*	*44.3*	*49.5*	***58.3***
%Linezolid-R*	*2.2*	*1.1*	*1.5*	*1.2*	*2.0*	*0.7*	***0.2***
%MDR*	*25.0*	*21.1*	*20.3*	*19.6*	*22.1*	*21.3*	***28.2***
S. pneumoniae							
Number of isolates	**314**	**327**	**321**	**311**	**331**	**304**	***365***
%Penicillin-NS*	*18.2*	*19.6*	*19.6*	*20.7*	*17.1*	*17.5*	***16.5***
of which: %HLR	*4.8*	*6.1*	*4.7*	*2.6*	*2.4*	*0.3*	***0.0***
%Int	*12.7*	*13.5*	*15.0*	*18.0*	*14.5*	*17.2*	***16.5***
%Erythromycin-R*	*15.7*	*18.9*	*16.9*	*17.9*	*13.8*	*15.2*	***13.2***
%Penicillin-NS/Erythromycin-R	*12.6*	*13.8*	*12.5*	*13.0*	*11.0*	*10.8*	***9.9***
E. faecalis							
Number of isolates	**298**	**265**	**298**	**336**	**315**	**294**	***296***
%Ampicillin-R*	*0.7*	*0.8*	*4.0*	*2.7*	*1.6*	*0.7*	***0.7***
%Vancomycin-R (VREfa)	*0.3*	*4.9*	*3.0*	*2.1*	*2.9*	*1.4*	***1.0***
%HLG-R*	*29.7*	*29.1*	*32.9*	*33.6*	*32.8*	*28.0*	***29.5***
%Linezolid-R*	*2.5*	*1.2*	*0.0*	*0.6*	*1.0*	*0.4*	***0.0***
P. aeruginosa							
Number of isolates	**222**	**184**	**219**	**207**	**182**	**201**	***250***
%Piperacillin/tazobactam-R*	*10.0*	*2.8*	*17.4*	*15.7*	*16.5*	*14.0*	***17.2***
%Ceftazidime-R*	*9.2*	*8.2*	*15.2*	*10.7*	*8.9*	*8.5*	***13.2***
%Imipenem/meropenem-R*	*8.3*	*12.0*	*19.4*	*13.1*	*11.6*	*16.4*	***13.2***
%Ciprofloxacin-R*	*13.2*	*12.6*	*20.6*	*15.0*	*13.7*	*13.5*	***16.4***
%Gentamicin-R*	*8.7*	*6.5*	*11.9*	*11.6*	*4.9*	*3.5*	***11.2***
%Gentamicin/Amikacin/Tobramycin-R*	*8.6*	*6.5*	*11.9*	*11.6*	*5.5*	*7.0*	***12.4***
%MDR*	*6.5*	*4.0*	*13.0*	*9.4*	*6.7*	*7.5*	***13.2***
***Acinetobacter* spp.**							
Number of isolates	*No data*	*No data*	*No data*	**91**	**93**	**87**	***69***
%Ciprofloxacin-R*				*3*	*8*	*7*	***1***
%Gentamicin-R*				*0*	*3*	*4*	***2***
%Gentamicin/Amikacin/Tobramycin-R*				*1*	*3*	*5*	***3***
%Imipenem/meropenem-R*				*4*	*4*	*6*	***0***
%MDR*				*0*	*2*	*3*	***0***

* 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)]
MRSA, Meticillin-Resistant *S. aureus*; VREfm, Vancomycin-Resistant *E. faecium;* VREfa, Vancomycin-Resistant *E. faecalis*
HLG, High-Level Gentamicin; 3GC, 3rd-Generation Cephalosporin (includes cefotaxime, ceftriaxone, ceftazidime)
ESBL, Extended-Spectrum Beta-Lactamase; MDR, Multi-Drug Resistant
[1] Carbapenems include imipenem, meropenem and ertapenem; [2] MDRKP, MDR K. pneumoniae phenotype (ESBL-producer plus non-susceptibility to Ciprofloxacin and Gentamicin) OR carbapenemase-producer (e.g. KPC, OXA-48)

acquired, healthcare-associated and community-acquired infections. EARS-Net primarily serves as a surveillance system to measure national levels of antimicrobial resistance (AMR). In 2016, two of the 39 microbiology laboratories suspended their participation in EARS-Net, one in Q3 and one in Q4, resulting in an estimated 99% coverage of the Irish population. Overall, coverage has remained at over 95% since 2004.

EARS-Net encourages the use of EUCAST guidelines and clinical breakpoints for AST in line with the EU case definitions. By the end of 2016, 35 of the 39 Irish clinical microbiology laboratories had switched to EUCAST, with just four laboratories still using CLSI guidelines.

2016 Results

Escherichia coli

There were 3,057 reports (blood; 3,055 and CSF; 2) from 2,985 patients, an increase of 13% compared with 2,697 reports in 2015. **Table 1** displays the annual trends since 2008 in the proportion of *E. coli* isolates resistant to the five "indicator" antimicrobials/antimicrobial classes [ampicillin, third-generation cephalosporins (3GCs; cefotaxime, ceftriaxone or ceftazidime), fluoroquinolones (ciprofloxacin), aminoglycosides (gentamicin, amikacin or tobramycin) and carbapenems (meropenem or ertapenem)]:

- Of 3,055 isolates, 376 (12.3%) were resistant to 3GCs and of those, 324 were extended-spectrum beta-lactamase (ESBL)-positive and 51 ESBL-negative
- Of 3,056 isolates, 736 (24.1%) were resistant to ciprofloxacin
- Of 3,057 isolates, 311 (10.2%) were resistant to gentamicin [404 (13.2%) of 3,057 were aminoglycoside-resistant (i.e. resistant to gentamicin, tobramycin or amikacin)]
- Five (0.2%) of 3,047 isolates were resistant to carbapenems, one of which was confirmed to be a carbapenemase-producer (NDM)

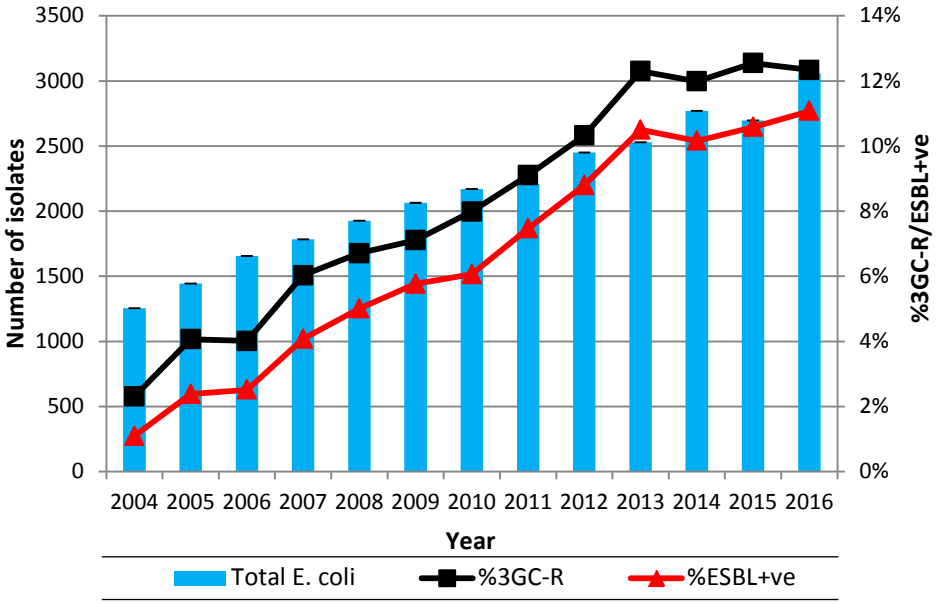


Figure 1. Trends for E. coli – total numbers of E. coli and percentage resistance to 3rd generation cephalosporins (3GC)/ESBL-positive

Table 2. Age and gender breakdown of patients by organism with major resistance profiles (data from laboratories participating in enhanced surveillance for 2016). The proportion of isolates detected <48 hours and >5 days post-admission is also shown

		Total for 2016	Percent female	Mean age in years	Detected <48 hours after admission	Detected >5 days after admission
Staphylococcus aureus	Meticillin Resistant (MRSA)	**95**	31%	68	64%	28%
	Meticillin Susceptible	**533**	39%	61.7	68%	21%
Streptococcus pneumoniae	Penicillin non-Susceptible	**18**	28%	71.3	89%	6%
	Penicillin Susceptible	**129**	51%	62.6	92%	6%
Enterococci	Vancomycin Resistant	**67**	39%	65.7	4%	84%
	Vancomycin Susceptible	**204**	40%	65.6	43%	49%
Escherichia coli	Fluoroquinolone Resistant	**307**	47%	73.4	72%	21%
	Fluoroquinolone Susceptible	**961**	56%	67.5	80%	17%
Klebsiella pneumoniae		**168**	38%	67	60%	33%
Pseudomonas aeruginosa		**111**	36%	68.2	59%	32%

The trend in resistance to 3GCs has stabilised at 12.0-12.5% since 2013 (**Figure 1**). Resistance to ciprofloxacin and aminoglycosides decreased in 2016 compared with 2015.

In 2016, Ireland had moderately high levels (10 to <25%) of resistance to 3GCs (**Figure 2**), ciprofloxacin and aminoglycosides (ranking 18th, 18th and 14th, respectively, out of 30 countries reporting to EARS-Net). The median proportions for resistance among EARS-Net countries were 14.3% for 3GCs, 26.5% for ciprofloxacin and 12.5% for aminoglycosides.

ESBLs are enzymes that confer resistance to most penicillins and cephalosporins (including 3GCs). ESBL-producing bacteria (including *E. coli* and *K. pneumoniae*) are also often resistant to other classes of antimicrobials and have emerged as important causes of healthcare-associated infection (HCAI). In 2016, ESBL producing invasive *E. coli* isolates were at the highest level since surveillance began (11.1%).

Of 3,055 isolates tested against all five "indicator" antimicrobials, 436 (14.3%) reported from 50 hospitals/institutions were identified as multi-drug resistant (MDR) *E. coli*, defined as resistance to three or more of the indicator antimicrobials OR any isolate with resistance to carbapenems, similar to 2015 (14.5%).

Staphylococcus aureus

There were 1,168 reports of *S. aureus* BSI from 1,143 patients, compared with 1,082 reports in 2015. Of those, 172 (14.7%) were MRSA, which represents the lowest annual proportion since surveillance began in 1999 (**Table 1** shows data from 2010 - 2016). In 2010, the proportion was 24.4%, the first year that MRSA accounted for <25% of *S. aureus* BSI in Ireland, thus changing from red to orange on the EARS-Net map and 2016 was the tenth successive year in which a decrease was observed (**Figure 3**). Overall, there was a 13.6% reduction in the number of reported MRSA BSI compared with 2015 (172 versus 199). In contrast, the total number of MSSA BSI increased by 12.7% compared with 2015 (996 versus 883).

Despite the decrease in numbers and proportion of MRSA BSI in 2016, Ireland still had one of the higher proportions of MRSA in Europe (see http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/database.aspx for more detailed European data, including EARS-Net tables, charts and maps) (**Figure 4**). Ireland ranked 12th out of 30 countries reporting to EARS-Net (compared to 11th of 30 countries in 2015), with the median proportion of MRSA BSI at 13.8%. All countries with MRSA proportions higher than Ireland are located in Southern and Central/Eastern Europe.

The MRSA rate for all acute hospitals in 2016 was 0.043 cases per 1,000 BDU, a decrease from 0.050 in 2015, while the MSSA rate increased from 0.223 to 0.245 [rates are calculated from denominator data (BDU) obtained from the HSE's Business Information Unit for all acute public hospitals; and directly from private hospitals where available, where both numerator (*S. aureus* numbers) and denominator data have been provided].

Klebsiella pneumoniae

There were 469 reports of invasive *K. pneumoniae* infection (all from blood) from 453 patients, an increase of 17% from 2015 (n=401). **Table 1** displays annual trends since 2010 in the proportion of *K. pneumoniae* isolates resistant to the five "indicator" antimicrobials (as for *E. coli* above):

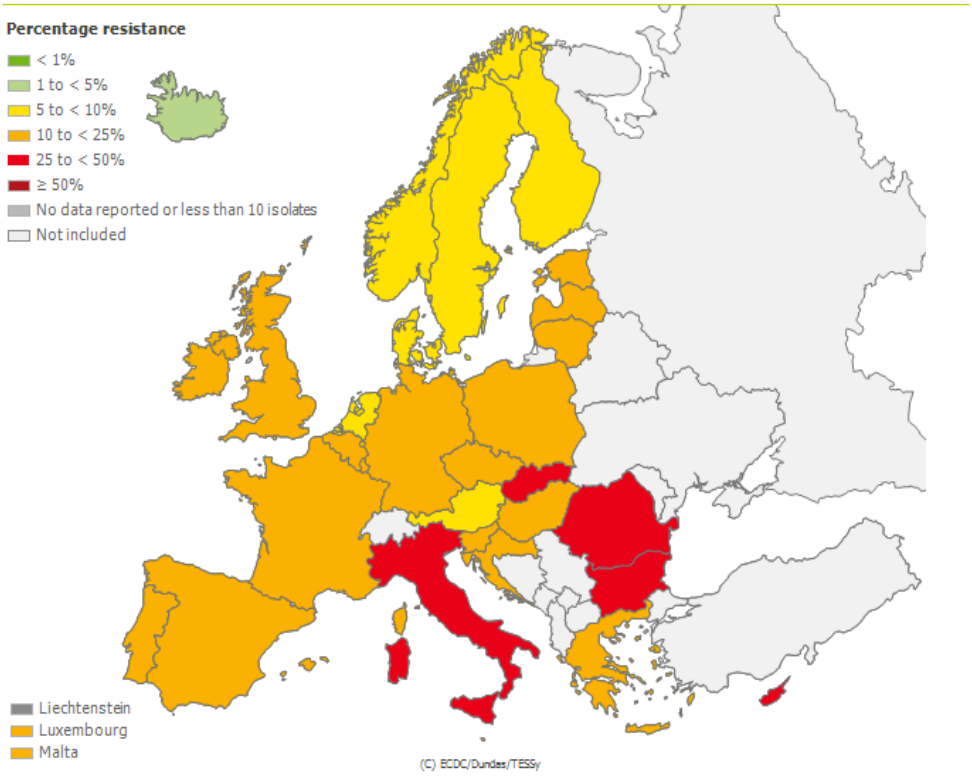


Figure 2. Distribution of 3rd-generation cephalosporin resistant E. coli in EARS-Net countries in 2016
Map downloaded from ECDC's TESSy database on 13/10/2017:
http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/database.aspx

- Of 469 isolates, 79 (16.8%) were resistant to 3GCs, of which 58 were ESBL-producers and 21 were ESBL-negative
- Of 469 isolates, 78 (16.6%) were resistant to ciprofloxacin
- Of 469 isolates, 54 (11.5%) were resistant to gentamicin [59 (12.6%) of 469 were aminoglycoside-resistant (i.e. resistant to gentamicin, tobramycin or amikacin)]
- Of 467 isolates, five (1.1%) were resistant to carbapenems, with four confirmed to be carbapenemase-producers reported from two hospitals (KPC; 3 and OXA-48; 1) and one confirmed not to be a carbapenemase-producer. This compares with seven in 2015 (OXA-48; 6 and KPC; 1), two in 2014 (OXA-48; 1 and KPC; 1), two in 2013 (both OXA-48) and four in 2011 (OXA-48; 3 and KPC; 1)

Three invasive *K. pneumoniae* isolates were reported as susceptible to ampicillin, which is suggestive of misidentification of species or misclassification, as *K. pneumoniae* are inherently resistant to ampicillin.

Resistance to 3GCs (**Figure 7**), ciprofloxacin and gentamicin/aminoglycosides all decreased in 2016 compared with 2015.

ESBLs were detected in 60 (12.9%) of 464 isolates tested. This represents a slight decrease from 13.3% in 2015.

Of 468 isolates, 69 (14.7%) reported by 25 hospitals/institutions that were tested against all five "indicator" antimicrobials were identified as MDR *Klebsiella pneumoniae*, a decrease from 19.8% in 2015.

In 2013, the Antimicrobial Resistance and Microbial Ecology (ARME) group at NUI Galway alerted HPSC to the presence of two predominant *K. pneumoniae* clones implicated in both patient infection and colonisation in a number of Irish hospitals. Both clones were simultaneously ESBL-positive and non-susceptible to ciprofloxacin and gentamicin. Some were also found to produce carbapenemases. Isolates meeting the definition are termed multi-drug resistant *K. pneumoniae* (MDRKP). From 2012 to 2013, the proportion of invasive *K. pneumoniae* that were MDRKP increased from 5.3% (18 of 342 isolates) to 12.3% (40 of 325 isolates), as displayed in Figure 8. An outbreak control team was established in October 2013 to evaluate this emerging threat and the proportion of MDRKP has subsequently decreased to 7.1% (33 of 464 isolates) in 2016.

In 2016, Ireland ranked 21st for 3GC, fluoroquinolone and aminoglycoside resistance in invasive *K. pneumoniae* among 30 countries reporting to EARS-Net. The median proportions among EARS-Net countries were 31.1%, 34.5% and 23.8%, respectively. With four reports of invasive carbapenem-resistant *K. pneumoniae* (0.9%), Ireland ranked joint 17th of 30 countries in 2016, with the median proportion among EARS-Net countries being 1.0% (**Figure 9**).

Enterococcus faecium

There were 431 reports of *E. faecium* BSI from 422 patients, an increase of 2.4% from 2015 (n=421). **Table 1** displays the annual trends since 2010 in the proportion of *E. faecium* isolates resistant to the three "indicator" antimicrobials (ampicillin, vancomycin and high-level gentamicin):

- Of 430 isolates, 191 (44.4%) were resistant to vancomycin *E. faecium* (VREfm), which is a slight decrease from 45.6% in 2015 (**Figure 5**)
- Of 410 isolates, 239 (58.3%) were resistant to high-level gentamicin, which is the highest proportion reported to date (**Figure 5**)
- Of 426 isolates, one (0.2%) was resistant to linezolid
- Of 404 isolates tested against the three "indicator" antimicrobials, 114 (28.2%) reported from 25 hospitals/institutions [with the majority (88; or 77%) coming from the nine tertiary hospitals] were resistant to all three and termed MDR *E. faecium*, which represents an increase from 21.3% in 2015

The proportion of VREfm first exceeded 40% in 2012 and appears to have levelled off at 43-45% since then.

Between 2008 and 2015, Ireland had the highest proportion of VREfm in Europe. In 2016, Ireland ranked second

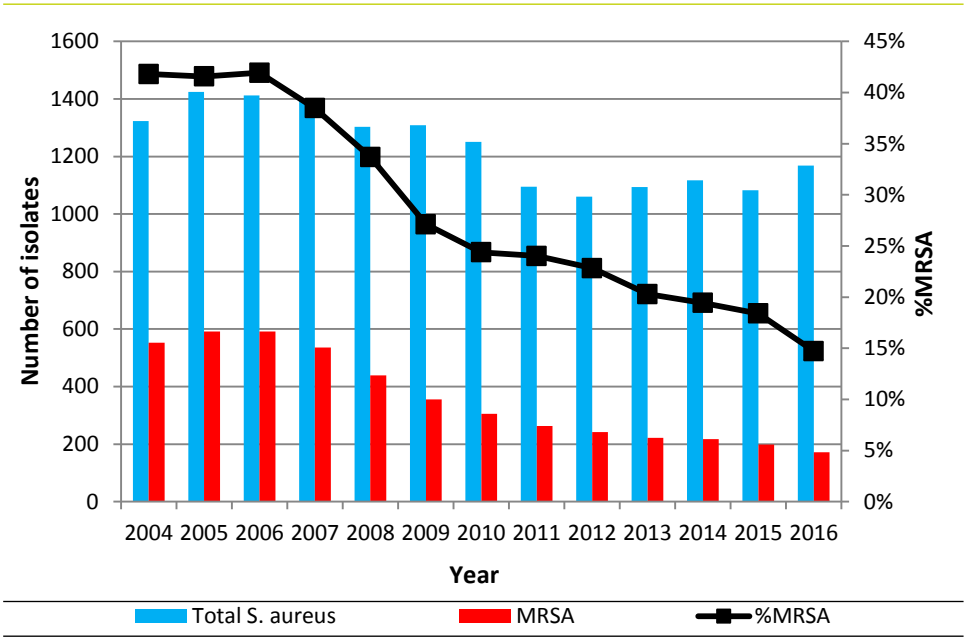


Figure 3. Trends for S. aureus – total numbers of S. aureus/MRSA and percentage MRSA

after Cyprus (46.3%; note: overall numbers were low). In addition, five other countries reported proportions over 25%: Romania, Latvia, Greece, Slovakia and Poland (**Figure 6**). The median proportion of VREfm in EARS-Net countries was 8.1%, a decrease from 9.9% in 2015.

Streptococcus pneumoniae

There were 365 reports of invasive *S. pneumoniae* infection (360 from blood and five from CSF) from 364 patients, a 20% increase on 2015 (n=304). **Table 1** displays annual trends since 2010 in the proportions of *S. pneumoniae* isolates non-susceptible/resistant to penicillin and erythromycin.

Penicillin non-susceptible *S. pneumoniae* (PNSP) accounted for 16.5% (n=60) of all isolates tested against penicillin (n=364) (**Figure 10)**, a reduction from 17.5% (2015). Of the PNSP isolates, all were intermediately-resistant (Int; MIC = 0.1 – 1mg/L) for laboratories following the Clinical Laboratory Standards Institute (CLSI) guidelines (for non-meningitis syndrome via oral administration) and (MIC = 0.1 – 2 mg/L) for those following European Committee on Antimicrobial Susceptibility Testing (EUCAST) non-meningitis guidelines. Penicillin susceptibility was not determined for one isolate. Forty-seven (13.2% of 355) isolates were resistant to erythromycin.

Ireland remained among European countries with the highest proportions of PNSP ranking 8th of 29 countries in 2016 (median proportion, 10.5%). Moderately high levels of erythromycin resistance were seen, with Ireland ranking 14th of 29 countries (median proportion, 13.8%). This is similar

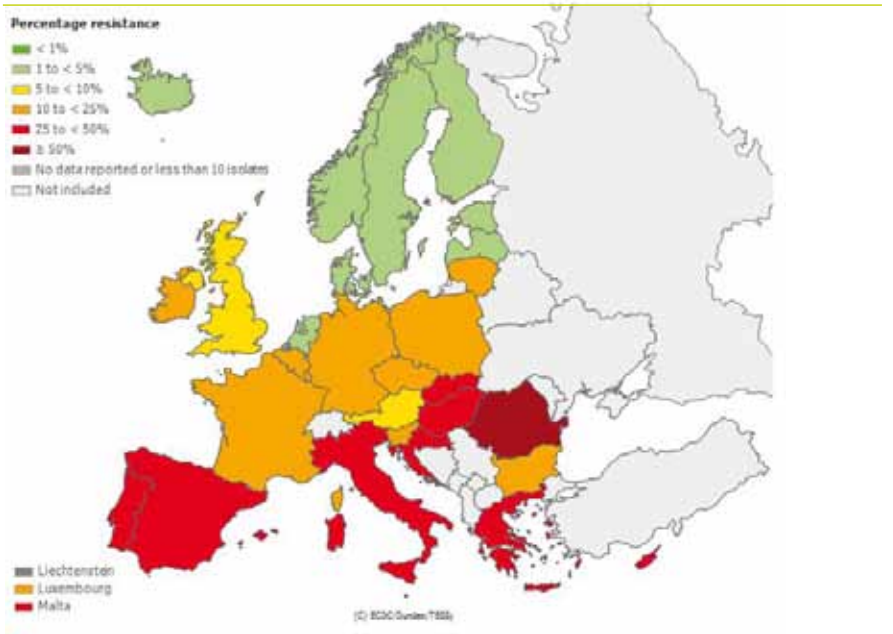


Figure 4. Distribution of MRSA in EARS-Net countries in 2016
Map obtained from ECDC on 13/10/2017:
http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/database.aspx

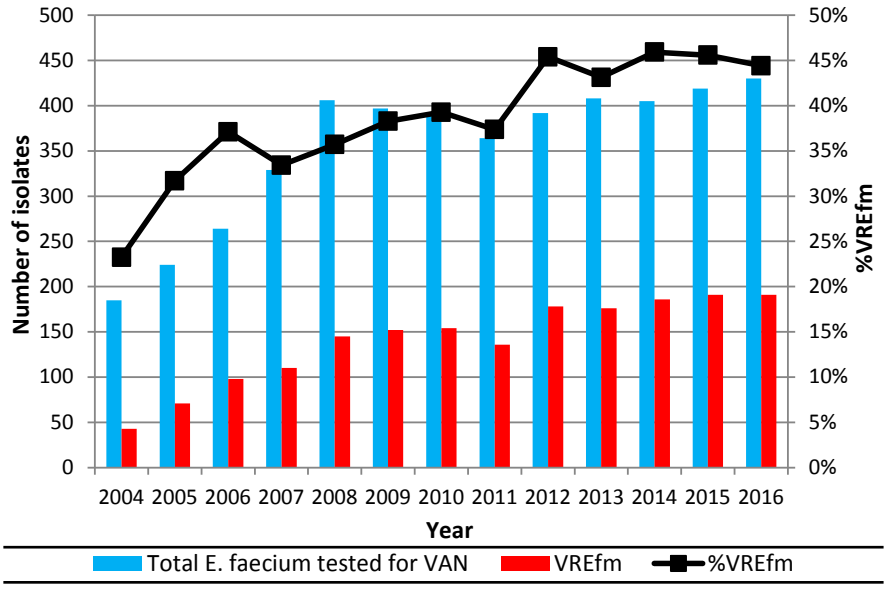


Figure 5. Trends for E. faecium – total numbers of E. faecium and percentage resistance to vancomycin (VREfm)

to the situation observed in much of Southern and Central/ Eastern Europe.

Of 354 isolates tested against both penicillin and erythromycin in 2016, 35 (9.9%) were simultaneously PNSP (all intermediately resistant) and erythromycin-resistant, which is a decrease from 2015 (10.8%).

In 2007, a national pilot project was established as a collaborative initiative between RCSI/Beaumont Hospital, Children's University Hospital, Temple St and HPSC, with the aim of providing baseline serotyping data on invasive *S. pneumoniae* isolates. This project pre-dates the introduction of the 7-valent pneumococcal conjugate vaccine (PCV7) into the childhood immunisation schedule in September 2008. PCV13 replaced PCV7 from September 2010.

In 2016, serotype data were available for 341 pneumococcal isolates reported by 30 of the 31 laboratories reporting pneumococcal isolates to EARS-Net, representing 93.4% of all pneumococcal isolates reported:

- Of 184 isolates from patients aged ≥65 years, 131 (71.2%) belonged to serotypes included in the PPV23 vaccine
- Twenty isolates were referred for typing from patients aged <2 years (the target population for the PCV13 vaccine) and three of these were serotypes included in the vaccine

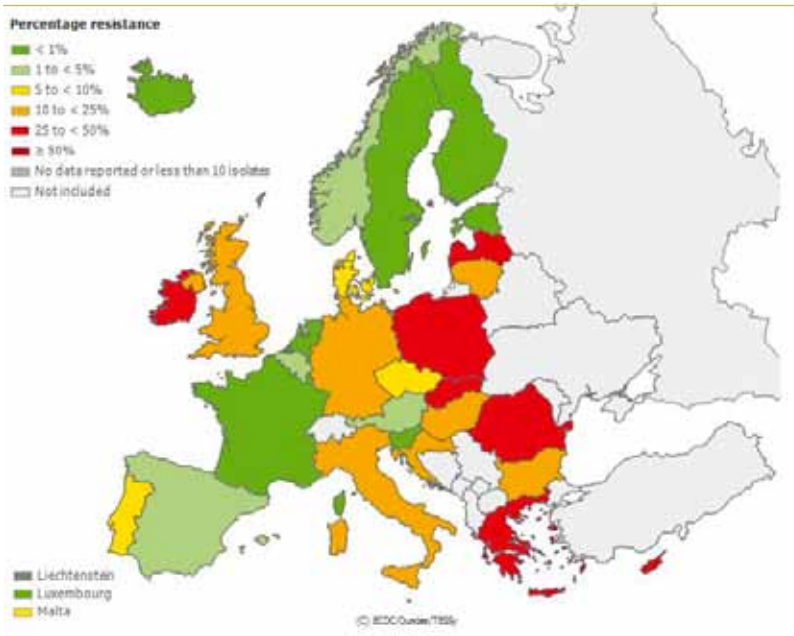


Figure 6. Distribution of vancomycin-resistant E. faecium (VREfm) in EARS-Net countries in 2016. Map downloaded from ECDC's TESSy database on 13/10/2017: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/database.aspx

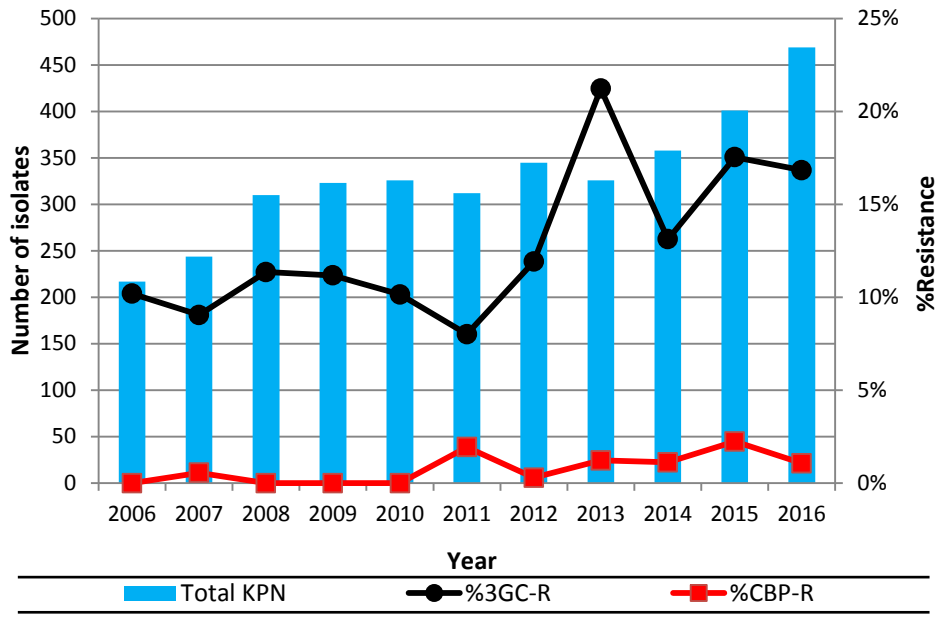


Figure 7. Trends for K. pneumoniae – total numbers of K. pneumoniae and percentage resistance to 3rd generation cephalosporins (3GCs) and carbapenems (CBP)

The most common serotypes identified were: 8 and 12F (n=39), 3 (n=30), 19A (n=27), 22F (n=25), 33F (n=23), 9N (n=19), 15F (n=14) and 24F (n=11) representing 66.6% of all isolates typed.

Of the 60 PNSP isolates, 56 (93%) were serotyped:
- Of 18 isolates from patients age ≥65 years, 16 (89%) belonged to serotypes included in the pneumococcal polysaccharide vaccine (PPV23) vaccine
- Of five isolates from children <2 years, one belonged to a serotype included in the PCV13 vaccine

The most common serotypes identified were: 19A (n=17), 15A (n=10) and 5B (n=5) representing 57% of all PNSP isolates typed.

Ongoing surveillance of the predominant serotypes is required, as strains with non-vaccine serotypes have been reported to increase in prevalence following the introduction of conjugate vaccines in other countries. Hence the need for a fully-resourced Irish pneumococcal reference laboratory. The separate chapter on invasive pneumococcal disease (IPD) in Ireland in 2016 contains additional information on pneumococcal serotyping.

In 2016, the rate of IPD in Ireland was estimated at 7.7 cases per 100,000 population, a decrease compared with 6.6 in 2015 [note that both rates were calculated using 2016 Census data; with the rates adjusted to account for the reduced population coverage by EARS-Net in each year].

Enterococcus faecalis
There were 296 reports of *E. faecalis* BSI from 289 patients, compared with 294 reports in 2015. **Table 1** displays annual trends since 2010 in the proportions of *E. faecalis* isolates resistant to the three "indicator" antimicrobials (as for *E. faecium*):
- Of 295 isolates, three (1.0%) were resistant to vancomycin (VREfa), with Ireland ranking 9th amongst European countries for resistance. The proportion of VREfa in Ireland has decreased from the highest reported proportion of 4.9% in 2011. In 2016, the median proportion in Europe was 0.1%
- Of 271 isolates, 80 (29.5%) were resistant to high-level gentamicin
- Of 292 isolates, none were resistant to linezolid

Two isolates were reported resistant to ampicillin, which is suggestive of misidentification of species or misclassification, as resistance to ampicillin is rare in *E. faecalis*.

Pseudomonas aeruginosa
There were 250 reports of invasive *P. aeruginosa* infection (blood; 245 and CSF; 5) from 243 patients, a 24.3% increase on 2015 (n=201). **Table 1** displays annual trends since 2010 in the proportion of the 250 *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)]:
- 43 (17.2%) were resistant to piperacillin-tazobactam
- 33 (13.2%) were resistant to ceftazidime
- 33 (13.2%) were resistant to imipenem or meropenem
- 42 (16.8%) were resistant to ciprofloxacin
- 28 (11.2%) were resistant to gentamicin [31 (12.4%) of 250 were aminoglycoside-resistant (i.e. resistant to gentamicin, tobramycin or amikacin)]

In 2016, resistance to all but one of the indicator antimicrobials (imipenem/meropenem) increased compared with 2015.

Thirty-three (13.2%) of 250 isolates reported from 18 hospitals that were tested against all five "indicator"

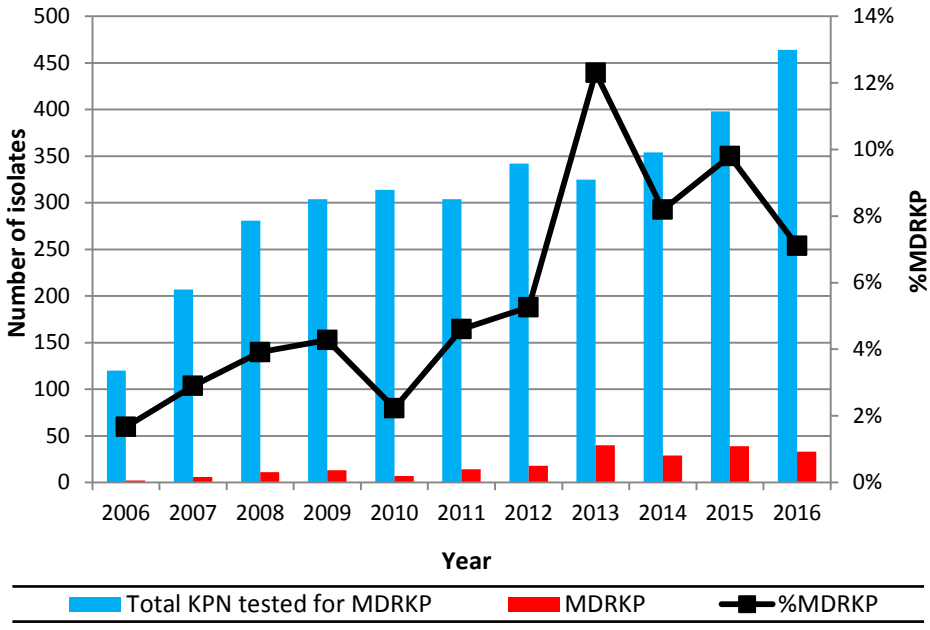


Figure 8. Trends for K. pneumoniae isolates with the MDRKP phenotype (simultaneously ESBL-producers and non-susceptible to both ciprofloxacin and gentamicin and/or a carbapenemase-producer) –– numbers and percentage with MDRKP phenotype

antimicrobials were identified as MDR *Pseudomonas aeruginosa*, defined as resistance to three or more of the indicator antimicrobials. This is the highest proportion of MDR *Pseudomonas aeruginosa* since surveillance began in 2006.

Antimicrobial resistance levels amongst *P. aeruginosa* isolates in Ireland are at moderately low levels in comparison with other European countries, with Ireland ranking between 16th and 24th of 30 countries for all five indicator antimicrobials.

Acinetobacter spp.
There were 69 reports of invasive infection caused by *Acinetobacter spp.* (blood; 67 and CSF; 2) from 68 patients, a reduction on 87 reports in 2015. **Table 1** displays annual trends since 2013 in the proportion of *Acinetobacter spp.* isolates resistant to the three "indicator" antimicrobials/ antimicrobial classes [carbapenems (meropenem or imipenem), fluoroquinolones (ciprofloxacin) and gentamicin]:

- Of 65 isolates, none were resistant to imipenem or meropenem
- Of 68 isolates, one was resistant to ciprofloxacin
- Of 63 isolates, one was resistant to gentamicin [two of 65 were aminoglycoside-resistant (i.e. resistant to gentamicin, tobramycin or amikacin)]

Of 63 isolates, none were identified as MDR *Acinetobacter spp.*, i.e. resistant to all three "indicator" antimicrobials.

Enhanced Surveillance
The voluntary EARS-Net enhanced surveillance programme was established in 2004. Laboratories participating in EARS-Net are invited to provide additional demographic and clinical data on invasive pathogens causing BSI.

In 2016, enhanced surveillance data on 2,593 individual records (cases or isolates under the EARS-Net definition) were submitted from 21 participating laboratories, representing 43% of all reports to EARS-Net. **Table 2** displays demographic and other basic data for the major resistance profiles of pathogens reported to EARS-Net enhanced surveillance.

- *S. aureus* BSI
  - 54% of MRSA and 45% of MSSA BSIs were healthcare-associated
  - 24% of MRSA BSIs were device-associated with
    - 5% CVC/CVC-PICC-associated, 8% PVC-associated
  - 20% of MSSA BSIs were device-associated with
    - 10% CVC/CVC-PICC-associated, 5% PVC-associated

- Enterococcal BSI
  - 91% of VRE and 61% of vancomycin-susceptible enterococcus (VSE) BSIs were healthcare-associated
  - 30% of VRE BSIs were device-associated with
    - 24% CVC/CVC-PICC-associated
  - 18% of VSE BSIs were device-associated with
    - 11% CVC/CVC-PICC-associated

- *E. coli* BSI
  - 39% of fluoroquinolone-resistant *E. coli* (FQREC) and 27% of fluoroquinolone-susceptible *E. coli (FQSEC)* BSIs were healthcare-associated
  - The most common source of *E. coli* bloodstream infection was urinary tract infection, with 48% FQREC BSI and 44% FQSEC urinary catheter-associated

Conclusion
For the tenth consecutive year, the proportion of *S. aureus* BSI attributable to MRSA further declined to 14.7%, the lowest reported level since Ireland joined EARS-Net in 1999. The decline may be partly attributable to improvements in infection prevention and control interventions, such as improved healthcare worker awareness of the importance of hand hygiene, standard and contact precautions,

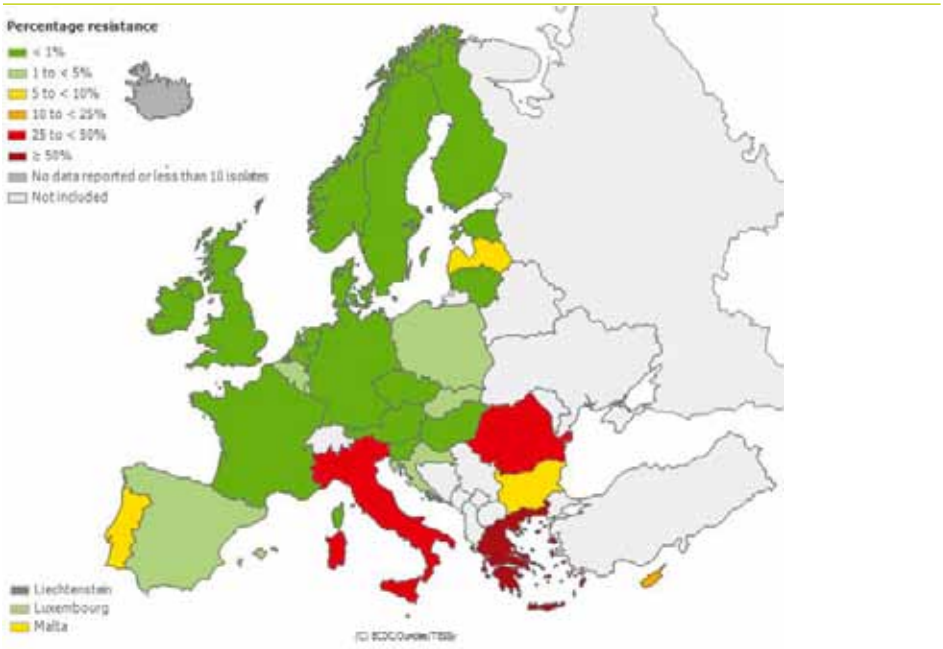


Figure 9. Distribution of carbapenem-resistant K. pneumoniae in EARS-Net countries in 2016
Map downloaded from ECDC's TESSy database on 13/10/2017:
http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/database.aspx

screening of patients for MRSA carriage and the availability of decolonisation regimens to eradicate MRSA carriage. The development of and strengthening of hospital invasive device insertion and maintenance protocols (e.g., care bundles), antimicrobial stewardship programmes and restricted prescribing of certain broad spectrum antimicrobials, particularly in response to other healthcare associated infections, such as *Clostridium difficile* infection, may also have positively contributed to the decreasing proportion of MRSA BSI.

Unfortunately, antimicrobial resistance in other important BSI causative pathogens increased further and remains a cause for concern.

In 2016, Ireland had the second highest proportion of VREfm BSI (44.4%) in Europe after Cyprus (46.3%; but note low numbers). Five other countries also reported proportions over 25% and therefore appeared red on the map.

Following the establishment of the national multi-drug resistant *K. pneumoniae* (MDRKP) outbreak control team (OCT) in 2013 to look at the emerging problem of MDRKP, initial recommendations were made to try to control the spread of MDRKP strains in healthcare settings. Due to the wide-reaching nature of this outbreak and the growing threat posed by antimicrobial resistance, the OCT proposed that a national task force should be established with greater powers to influence and implement changes in policy and infrastructure needed. In 2016, there were five reported cases of invasive carbapenemase-producing *K. pneumoniae* (CRE) infection in Ireland.

Infections caused by antimicrobial-resistant bacteria result in excess patient mortality, morbidity and costs to the healthcare system. Rising levels of AMR threaten many aspects of healthcare that we currently take for granted. It is critical that comprehensive infection prevention and control and antimicrobial stewardship programmes continue to be developed and maintained at all levels and settings within the Irish health service. To this end, it is vital that recommendations and guidelines produced by the HSE RCPI Clinical Advisory Group on HCAI and AMR are implemented. HPSC thanks all the microbiology laboratories for their continued participation and enthusiasm for the EARS-Net project.

See http://www.hpsc.ie for further details of EARS-Net, antimicrobial resistance and enhanced BSI surveillance in Ireland

European data are available at: http://ecdc.europa.eu/en/healthtopics/antimicrobial_resistance/database/Pages/database.aspx

b) Enhanced surveillance of Carbapenemase-Producing Carbapenem Resistant Enterobacteriaceae (CRE/CPE)

2016 Summary

Number of cases of colonisation or infection with enhanced data = 107. This represented an increase compared with 98 (2015) and 63 (2014). In contrast, the National Carbapenemase Producing *Enterobacteriaceae* Reference Laboratory Service (CPEaRLS) at Galway University Hospital confirmed carbapenemase production in 362 *Enterobacteriaceae* isolates in 2016 compared to 139 (2015)

The clinical significance of the CRE isolate was reported for 100 patients, representing colonisation in the majority (n=78; 78%). CRE infection was reported for 22 patients

Background

Carbapenem-resistant *Enterobacteriaceae* (CRE) are multi-drug resistant Gram-negative bacteria and includes

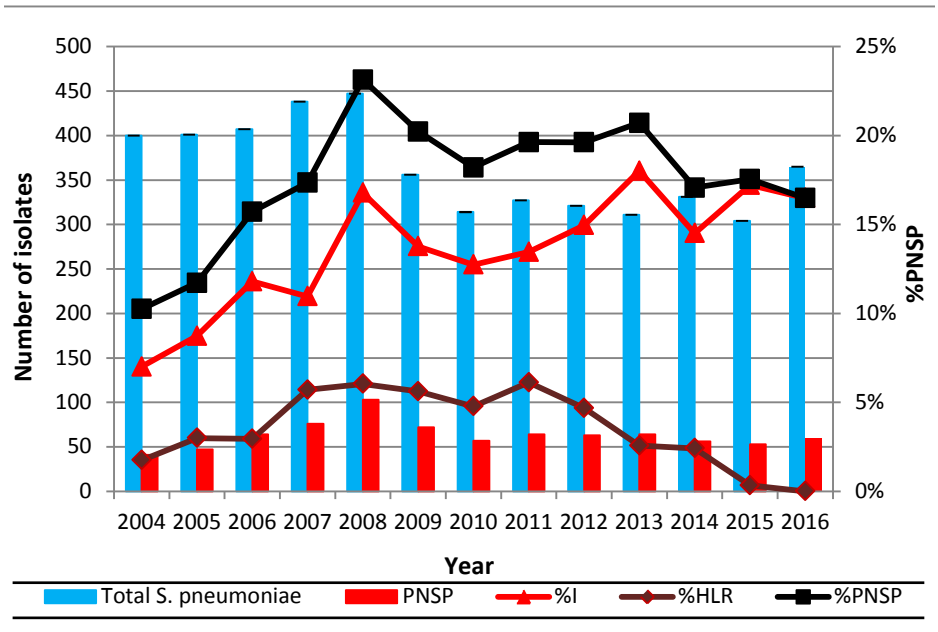


Figure 10. Trends for S. pneumoniae – total numbers of S. pneumoniae/PNSP and percentage PNSP HLR, High-level resistant; I, Intermediately resistant

carbapenemase enzyme producers and those bacteria that are resistant to carbapenems (e.g. imipenem, meropenem) as a result of a combination of resistance mechanisms (such as broad-spectrum β-lactamases and bacterial cell porin loss). These bacteria can be easily spread between patients in healthcare settings and have the ability to cause infections for which effective antimicrobial therapy may be lacking.

Detection of confirmed carbapenemase-producing CRE, hereafter known as CRE, became notifiable in Ireland in March 2011 under the category of 'unusual cluster or changing pattern of illness'. Upon amendment to the Infectious Diseases Regulations in September 2011, invasive CRE infection (blood, CSF or normally sterile site) became notifiable in its own category. A voluntary CRE enhanced surveillance scheme was established in June 2011 and reporting of isolates from any site, whether colonisation or infection is encouraged.

Enhanced surveillance data

Data was received on 107 confirmed CRE cases from 14 laboratories. Five CRE outbreaks from three acute hospitals and one nursing home were reported in 2016 (OXA-48; 3, OXA-48 and VIM CRE combined; 1 and NDM; 1). **Figure 1** displays annual trends in CRE cases and types reported to enhanced surveillance since 2011. Of 104 patients, 68 were male (65%). The median age was 75 years (range: 8 months – 99 years).

Patient location

At the time of CRE detection, 73 patients (77%) were hospitalised, 18 (19%) were in long-term care facilities (vs. three in 2015) and four (4%) were in the community. Of the 73 hospitalised patients, 47 (64%) had been admitted from home, 14 (19%) were transfers from another acute hospital, seven had been admitted from long-term care/ nursing homes (10%) and the source of admission was not provided for the remaining four patients (5%). Of the 14 patients who had been transferred from another acute hospital, one was repatriated from a hospital abroad (Guatemala).

Time to CRE colonisation/infection (interval between admission to first detection of CRE) could be calculated for 65 patients (89%), with a median interval of 10 days (range: 0 – 181).

Presence of other multi-drug resistant organisms (MDROs)

At the time of CRE detection, 50 patients (47%) were already known to be colonised or infected with at least one other MDROs, including MRSA; 22, VRE; 25, ESBL-producing *Enterobacteriaceae*; 11, *C. difficile* infection; 2 and MDR *K. pneumoniae;* 1 (note: 10 patients were colonised with two other MDROs and one with three others), and 35 of those were inpatients.

Travel history

Foreign travel in the past 12 months was reported for seven patients (7%) to six countries (Cyprus, Guatemala, India, Moldova, Morocco, Spain and UK) and 45 (42%) reported no foreign travel. The travel history was unknown for the remaining 55 (51%).

Risk factors

Risk factor data were reported on 96 patients; 53 (50%) had more than one risk factor. Hospitalisation in the past 12 months (75; 70%); history of admission to intensive care in the last 12 months (22; 21%) and history of surgery in the past six months (18; 17%). Risk factor data was unknown or not provided for 11 patients and five had no identifiable risk factors (5%).

Reported underlying co-morbidities included: diabetes mellitus (18); chronic lung disease (17); immunocompromise (11); renal disease (11); urological abnormality (10) and liver disease (2).

Prior antimicrobial exposure

Antimicrobial exposure history prior to isolation of CRE was provided for 55 patients (53%), 46 of whom were hospitalised and 22 of whom received more than one antimicrobial class:

- β-lactam/β-lactamase inhibitor combination agents - 41 (75%)
- Carbapenems - 16 (29%)
- Cephalosporins - 10 (18%)
- Fluoroquinolones - 10 (18%)
- Aminoglycosides - 9 (16%)
- Co-trimoxazole - 4 (7%)
- Colistin - 2 (4%)

Clinical significance and source of infection

The clinical significance of the CRE isolate was reported for 100 patients, representing colonisation in the majority (n=78). CRE infection was reported for 22 patients; urinary tract infection (n=7), respiratory tract infection (n=5), skin/ soft tissue infection (n=3), two cases of intra-abdominal infection (n=2) and BSI (n=1).

Specimen type

The majority of CRE (n=69; 66%) were isolated from screening swabs (rectal or stoma) or faeces. Blood accounted for six (6%), one from gall bladder, 17 from urine (16%), five from sputum (5%) and seven from various other wound swabs and tips. Specimen type was unknown for two isolates.

Outcome

Outcome was reported for 54 of the 73 hospitalised patients (74%):

- Discharged = 35 (65%)
- Still inpatient at the time the surveillance form was returned (n=11; 20%, six of whom had already had CRE infection. However, it is not known if the remaining five CRE colonised patients subsequently went on to develop CRE infection later in the hospital admission)
- Death (n=8; 15%). For one death, CRE detection represented infection. However, the potential contribution of CRE infection to patient death was not collected. Date of death was provided for all patients, with a median interval from detection of CRE to death of 13.5 days (range = 2 – 99)
- Outcome was also reported for fifteen non-hospitalised patients, five of whom survived, all of whom were residents in a long-term care facility: two of these were reported to have had CRE infection and these patients died 10 and 39 days post-diagnosis, respectively. The interval to death for

the remaining three patients was greater than 200 days.

Enterobacteriaceae species
Klebsiella pneumoniae accounted for the majority (n=44; 41%) of CRE isolates (compared with 33% of isolates in 2015). In addition, there were nine *K. oxytoca*, 16 *Escherichia coli*, 22 *Citrobacter* spp., 11 *Enterobacter* spp., two *Serratia marcescens* and one *Raoultella* spp.

Carbapenemase types reported
The carbapenemases were: OXA-48 (44; 41%), KPC (37; 35%), NDM (18; 17%), VIM (5) and IMP (1), with two not specified.

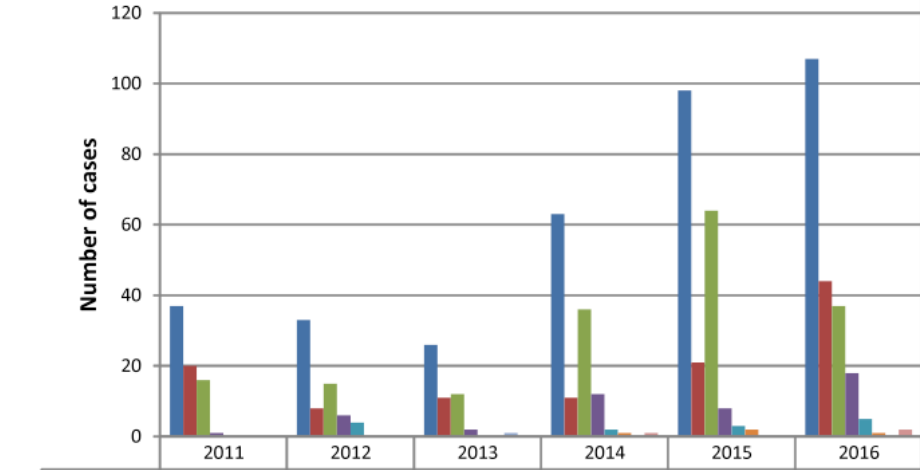
Susceptibility of isolates
Susceptibility testing data was provided on 104 of 107 isolates (97%):

- Carbapenems
  - Meropenem: reported on 94 isolates, with 73 resistant (77%); minimum inhibitory concentrations (MIC) ranged from 0.064 to >256 mg/L
  - Ertapenem: reported on all 96 isolates, with 87 resistant (91%); MIC ranged from 0.094 to >256 mg/L
- Aminoglycosides: reported on 104 isolates, with 62 (60%) resistant to one or more of the aminoglycosides listed below
  - Gentamicin: 103 isolates; 55 resistant (53%)
  - Tobramycin: 60 isolates; 33 resistant (55%)
  - Amikacin: 93 isolates; 11 resistant (12%)
- Fluoroquinolones: 93 isolates; 66 resistant (71%)
- Tigecycline: 70 isolates; 24 resistant (34%)
- Colistin: 58 isolates; one resistant

Conclusion
In 2016, 107 cases reflected a 9% increase on 98 cases in 2015. However, reference laboratory data indicated there were at least three-times (314%) more confirmed cases. In response to the emergence of CRE and suboptimal participation in voluntary enhanced surveillance, it was decided to replace voluntary with mandatory reporting by microbiology laboratories from January 2017.

Acknowledgements:
Sincere thanks to colleagues working in microbiology laboratories and infection prevention and control teams across Ireland for submitting enhanced surveillance data on patients with CRE.

Sincere thanks also to colleagues in the CPEaRLS, Galway University Hospital for data on confirmed carbapenemase-producing *Enterobacteriaceae* in 2016 (Source: CPEaRLS annual report 2016).



	2011	2012	2013	2014	2015	2016
TOTAL	37	33	26	63	98	107
OXA	20	8	11	11	21	44
KPC	16	15	12	36	64	37
NDM	1	6	2	12	8	18
VIM		4		2	3	5
IMP				1	2	1
IMI			1			
Other/Unk				1		2

Figure 1. Annual trends in CRE cases and carbapenemase types reported to voluntary enhanced surveillance (2011 – 2016)

Please note that the reduction in reported cases between 2012 and 2013 reflects under-reporting rather than a true decline in CRE. Almost twice as many isolates were confirmed by the CPEaRLS, Galway University Hospital in 2013 (n=50), approximately one-third as many isolates in 2014 (n=87) and 2015 (n=143) and over three-times as many isolates in 2016 (n=362) than were reported to the voluntary CRE enhanced surveillance scheme

c) Enhanced Surveillance of Multi-Drug Resistant K. pneumoniae (MDRKP)

2016 Summary

- Comparing 2016 with 2015, there was a 19% increase in the total numbers of MDRKP reported
- The MDRKP/CRE phenotype increased by approximately two-fold (195%): with 119 cases reported, compared with 61 cases in 2015

Background

A national increase in multi-drug-resistant *Klebsiella pneumoniae* (MDRKP) was first identified by the Antimicrobial Resistance and Microbial Ecology (ARME) Group at NUI Galway in the autumn of 2013. Following this, an increase in BSI caused by MDRKP was also confirmed through the Irish EARS-Net data reported to the HPSC. An outbreak control team (OCT) was established at HPSC in October 2013 to review existing surveillance data and request additional data from hospital laboratories. Following this, prospective mandatory national surveillance for MDRKP commenced in January 2014.

Case definition

The first isolate per patient per quarter of *K. pneumoniae* derived from any specimen type (both clinical and screening) that are (1) ESBL-producers and non-susceptible to both ciprofloxacin and gentamicin OR non-susceptible to 3rd generation cephalosporins (3GC) and ciprofloxacin and gentamicin, where investigation for ESBLs is not routinely carried out **[MDRKP/Non-CRE]** AND/OR (2) carbapenemase-producers **[MDRKP/CRE]**.

Results (2014 – 2016)

For the three years of surveillance, 1,449 MDRKP cases were reported by 53 (88%) of 60 acute hospitals in Ireland (Table 1). Seven acute hospitals; specialty (n=5), general (n=1) and private (n=1) did not report any cases.

MDRKP/Non-CRE accounted for 1,215 (84%) and MDRKP/CRE for 234 (16%). Of the MDRKP/CRE cases, 23% also fulfilled the MDRKP/Non-CRE criteria, but were categorised as MDRKP/CRE for the purposes of this report

Clinical specimens accounted for the majority of MDRKP isolates (n=1,171; 81%). However, an upward trend is evident in the proportion detected from screening specimens (rectal swabs/faeces); 25% in 2016 versus 16% in both 2014 and 2015

While two-thirds of cases were associated with patients admitted to or attending an acute hospital, one-third of cases were detected in patients attending general practice or residents of long-term care facilities (LTCF)

Of 804 MDRKP cases from hospital inpatients:

- Information on antimicrobial therapy for MDRKP infection was provided for 484 (58%), of whom 282 (58%) had required antimicrobial therapy for MDRKP infection prior to case notification
- Information on patient isolation was provided for 553 (66%), of whom 465 (84%) were isolated within 24 hours of the laboratory reporting MDRKP detection. Therefore, 16% were not isolated and the isolation status of 34% was either not provided or unavailable

Trends (2016 versus 2015)

In 2016, there were 534 cases of MDRKP (415 MDRKP/Non-CRE and 119 MDRKP/CRE) from 480 patients, with some previously known patients with MDRKP reported again in a different quarter. This reflects **an increase of 19%** from 449 cases (388 MDRKP/Non-CRE and 61 MDRKP/CRE) from 385 patients in 2015. Excluding repeat notifications from the same patient, defined as **one isolate per patient over the 12-month period**, there was **an increase of 25%** from 385 cases in 2015 to 480 cases in 2016 (Table 1).

In 2016, the number of MDRKP/CRE cases **increased by almost two-fold (or 195%),** with 119 cases (representing 22% of all MDRKP cases) reported (Table 1) compared with 61 cases in 2015 (14% of all MDRKP cases).

By the end of 2016, it was evident that MDRKP was widely distributed across the Irish healthcare system, with rapid and concerning increases in the proportion that were also carbapenem resistant. In light of these findings, it was decided to step down mandatory national enhanced MDRKP surveillance at the end of Q4 2016 and to replace it with mandatory national enhanced surveillance for carbapenemase-producing carbapenem resistant *Enterobacteriaceae* (CRE/CPE) effective Q1 2017.

Table 1. Annual summary of MDRKP cases: 2014 to 2016

	TIME PERIOD								
	2014		2015		2016		TOTAL		
	Jan-Dec		Jan-Dec		Jan-Dec		Jan 2014-Dec 2016		COMMENT ON TOTAL DATA
	n	%	n	%	n	%	n	%	
MDRKP (based on case definition of 1st isolate per patient per quarter, see Table 1 above)	466		449		534		1449		of which 976 cases (67%) associated with 53 (of 60) acute hospitals (including outpatients)
Patients with MDRKP (based on one isolate per patient per year)	411		385		480		1276		of which 876 cases (69%) associated with 53 (of 60) acute hospitals (including outpatients)
of which: MDRKP/Non-CRE	363	88%	332	86%	379	79%	1074	84%	
MDRKP/CRE	48	12%	53	14%	101	21%	202	16%	71 KPC, 88 OXA-48, 42 NDM, 1 NDM/OXA-48

Further information on MDRKP in Ireland is available on the HPSC website at:
http://www.hpsc.ie/a-z/microbiologyantimicrobialresistance/europeanantimicrobialresistancesurveillancesystemearss/referenceandeducationalresourcematerial/klebsiellapneumoniae/dataonmultidrugresistantkpneumoniae/MDRKP%20Update_Jan2014-Dec2016%20data_Final.pdf

Acknowledgements:
Sincere thanks to colleagues working in microbiology laboratories and infection prevention and control teams across Ireland for submitting enhanced surveillance data on patients with MDRKP.

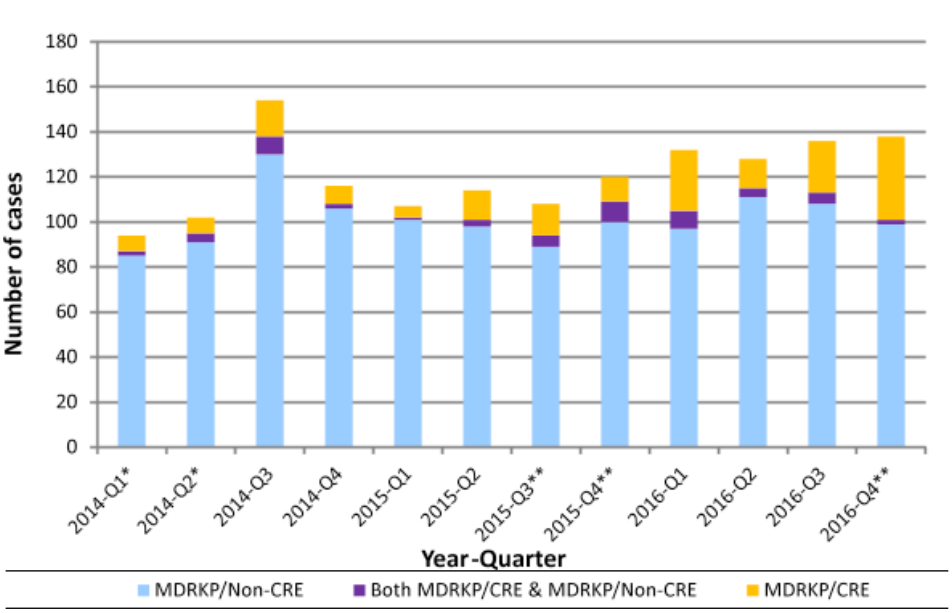


Figure 1. Quarterly MDRKP cases (CRE and Non-CRE): Q1 2014 – Q4 2016
*No data from one tertiary hospital for Q1-2 2014; ** No data from one general hospital for Q3-4 2015 and Q4 2016