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Geographic and Temporal Variation on the Frequency of Occurrence and Antimicrobial Susceptibility of Bacteria Isolated from Patients Hospitalised with Bacterial Pneumonia: Results from 20 Years of the SENTRY Program (1997–2016)

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Introduction

- The SENTRY Antimicrobial Surveillance Program (SENTRY) monitors the frequency of occurrence and antimicrobial susceptibility of organisms from various infection types worldwide
- Pneumonia is the second most common infection in hospitalised patients, and it is associated with significant morbidity and mortality
- The initial antimicrobial management of patients with pneumonia is mainly driven by the understanding of causative pathogens, and there are very limited data available on the frequency and antimicrobial susceptibility of organisms causing pneumonia
- In the SENTRY Program, bacterial isolates are consecutively collected (1 per infection episode) according to the infection type and sent to a central monitoring laboratory (JMI Laboratories, North Liberty, Iowa, USA) where they are tested for susceptibility by reference broth microdilution methods against many antimicrobial agents currently available for clinical use
- We evaluated the frequency and antimicrobial susceptibility patterns of pathogens collected during the 20 years of the SENTRY Program from patients hospitalised with bacterial pneumonia

Materials and Methods

Organism collection

- A total of 104,235 bacterial isolates were collected (1/patient) in 1997–2016 from 277 medical centres located in:
- Europe (n=30,985; 61 centres from 22 nations)
- North America (n=44,999; 113 centres)
- Asia-Pacific region (APAC; n=17,746; 86 centres from 13 nations)
- Latin America (n=10,505; 17 centres from 7 nations)
- Each participating centre was asked to collect consecutive bacterial isolates from lower respiratory tract specimens determined to be significant by local criteria as the reported probable cause of pneumonia
- Qualified sputum samples and isolates from invasive sampling (transtracheal aspiration, bronchoalveolar lavage, protected brush samples, etc.) were accepted
- Carbapenem-resistant *Enterobacteriaceae* (CRE) were defined as any isolate displaying MIC values of >2 mg/L for meropenem, imipenem (not applied for Proteus mirabilis or indole-positive Proteeae), and/or doripenem (CLSI, 2018)

Table 1. Overall frequency (1997–2016) of occurrence of organisms isolated from patients hospitalised with pneumonia stratified by geographic region

Overall frequency (rank order) by region			
Europe	North America	APAC	Latin America
21.8% (1)	20.6% (2)	20.6% (1)	27.4% (1)
19.3% (2)	30.2% (1)	15.5% (2)	19.8% (2)
11.0% (3)	9.0% (3)	14.8% (3)	12.1% (4)
9.6% (4)	5.1% (5)	5.8% (6)	4.6% (6)
6.8% (5)	3.2% (10)	13.9% (4)	13.5% (3)
6.4% (6)	6.2% (4)	6.0% (5)	5.1% (5)
3.9% (7)	4.7% (6)	3.5% (8)	2.1% (10)
3.4% (8)	4.2% (7)	3.4% (9)	2.3% (8)
3.3% (9)	3.8% (9)	2.7% (10)	2.5% (7)
2.9% (10)	4.0% (8)	4.2% (7)	2.6% (9)
	Europe 21.8% (1) 19.3% (2) 11.0% (3) 9.6% (4) 6.8% (5) 6.4% (6) 3.9% (7) 3.4% (8) 3.3% (9)	EuropeNorth America 21.8% (1) 20.6% (2) 19.3% (2) 30.2% (1) 11.0% (3) 9.0% (3) 9.6% (4) 5.1% (5) 6.8% (5) 3.2% (10) 6.4% (6) 6.2% (4) 3.9% (7) 4.7% (6) 3.4% (8) 4.2% (7) 3.3% (9) 3.8% (9)	EuropeNorth AmericaAPAC 21.8% (1) 20.6% (2) 20.6% (1) 19.3% (2) 30.2% (1) 15.5% (2) 11.0% (3) 9.0% (3) 14.8% (3) 9.6% (4) 5.1% (5) 5.8% (6) 6.8% (5) 3.2% (10) 13.9% (4) 6.4% (6) 6.2% (4) 6.0% (5) 3.9% (7) 4.7% (6) 3.5% (8) 3.4% (8) 4.2% (7) 3.4% (9) 3.3% (9) 3.8% (9) 2.7% (10)

Susceptibility methods

- documents
- Figures 1 and 2)

- shown)

- (Figure 5)

Multidrug-resistant (MDR) Enterobacteriaceae and P. aeruginosa were defined as any isolate nonsusceptible (CLSI criteria) to ≥ 1 agent in ≥ 3 of the following antimicrobial classes: broad-spectrum cephalosporins, carbapenems, broad-spectrum penicillin combined with a β -lactamase inhibitor, fluoroquinolones, aminoglycosides, glycylcyclines (for *Enterobacteriaceae* only), and the polymyxins

 Organisms were tested for susceptibility by reference broth microdilution methods in a central laboratory

 Broth microdilution tests were conducted according to the current Clinical and Laboratory Standards Institute (CLSI) documents

 Susceptibility percentages and quality control results validation were based on the EUCAST (2018) and CLSI (M100; 2018)

Results

• Overall, Staphylococcus aureus (n=24,417) and Pseudomonas aeruginosa (n=22,575) were the most prevalent organisms in all regions, but with frequency of occurrence variations among regions (Table 1 and Figures 1 and 2)

• *P. aeruginosa* ranked first in Europe, APAC, and Latin America; S. aureus was most common in North America (Table 1 and

• *Klebsiella* spp. (KSP; n=11,337) ranked third in Europe (Figure 1), North America (Figure 2), and APAC, and fourth in Latin America, where *Acinetobacter* spp. ranked third (Table 1)

• Stenotrophomonas maltophilia ranked eighth in Europe (Table 1) and its frequency increased continuously from 2.7% in 1997 to 4.4% in 2016, whereas in North America it ranked seventh (Table 1) with a frequency that oscillated from a low of 2.9% in 2003-2004 to a high of 5.6% in 2013-2014 (data not shown)

 When comparing 1997–1998 data with 2015–2016 data, the proportion of gram-negative bacilli increased from 70.0%–74.7% to 80.9%–82.9% in Europe, APAC, and Latin America, but remained stable (65.5%–66.1%) in North America (data not

• MRSA rates decreased substantially in all 4 regions from 2005– 2006 to 2015–2016, especially in Europe (36.4% to 26.4%; Figure 3), North America (59.6% to 44.0%; Figure 4), and Latin America (50.7% to 34.8%; data not shown)

• *P. aeruginosa* susceptibility to meropenem decreased overall in the first 10 years of the program (see Figures 3 and 4 for Europe and North America), but increased in the last 10 years, in North America (from 72.9% to 77.3%), Latin America (from 63.4% to 75.2%) and APAC (from 68.3% to 80.3%), and in the last 6 years in Europe (from 61.1% to 66.2%)

• Among *Klebsiella* spp., susceptibility to ceftriaxone/meropenem decreased from 85.9%/99.3% to 58.6%/85.9% in Europe (Figure 3), from 91.8%/99.5% to 81.6%/93.5% in North America (Figure 4), from 67.1%/98.6% to 57.1%/83.6% in Latin America (data not shown), and from 80.7%/100.0% to 74.9%/93.9% in the APAC region (data not shown) during the study period

• The frequencies of MDR *Enterobacteriaceae* and CRE increased continuously from 1999 to 2016 in Europe and North America, whereas the frequency of MDR P. aeruginosa oscillated during the SENTRY surveillance period with frequencies in 2016 similar to those in 1999 in both regions

Figure 1. Frequency of occurrence for the main organisms isolated from patients hospitalised with pneumonia in Europe (SENTRY Program, 1997–2016)

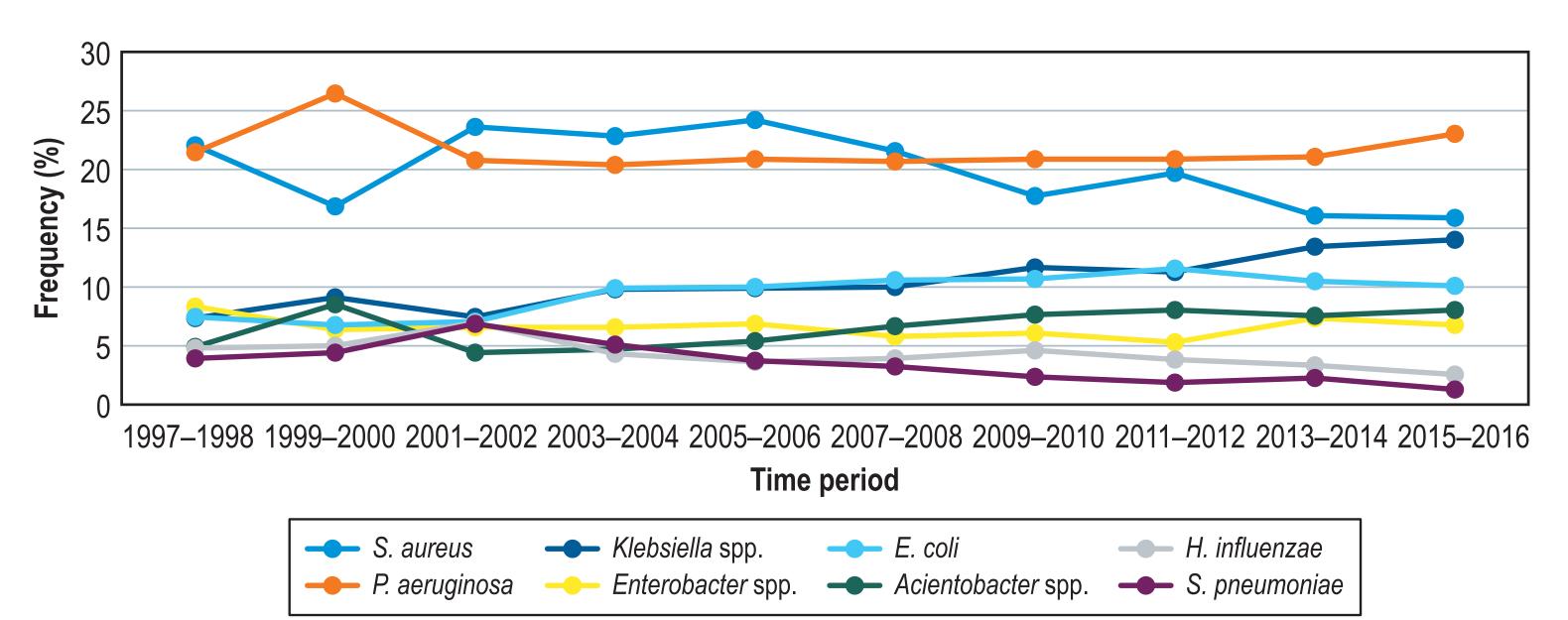


Figure 2. Frequency of occurrence for the main organisms isolated from patients hospitalised with pneumonia in North America (SENTRY Program, 1997–2016)

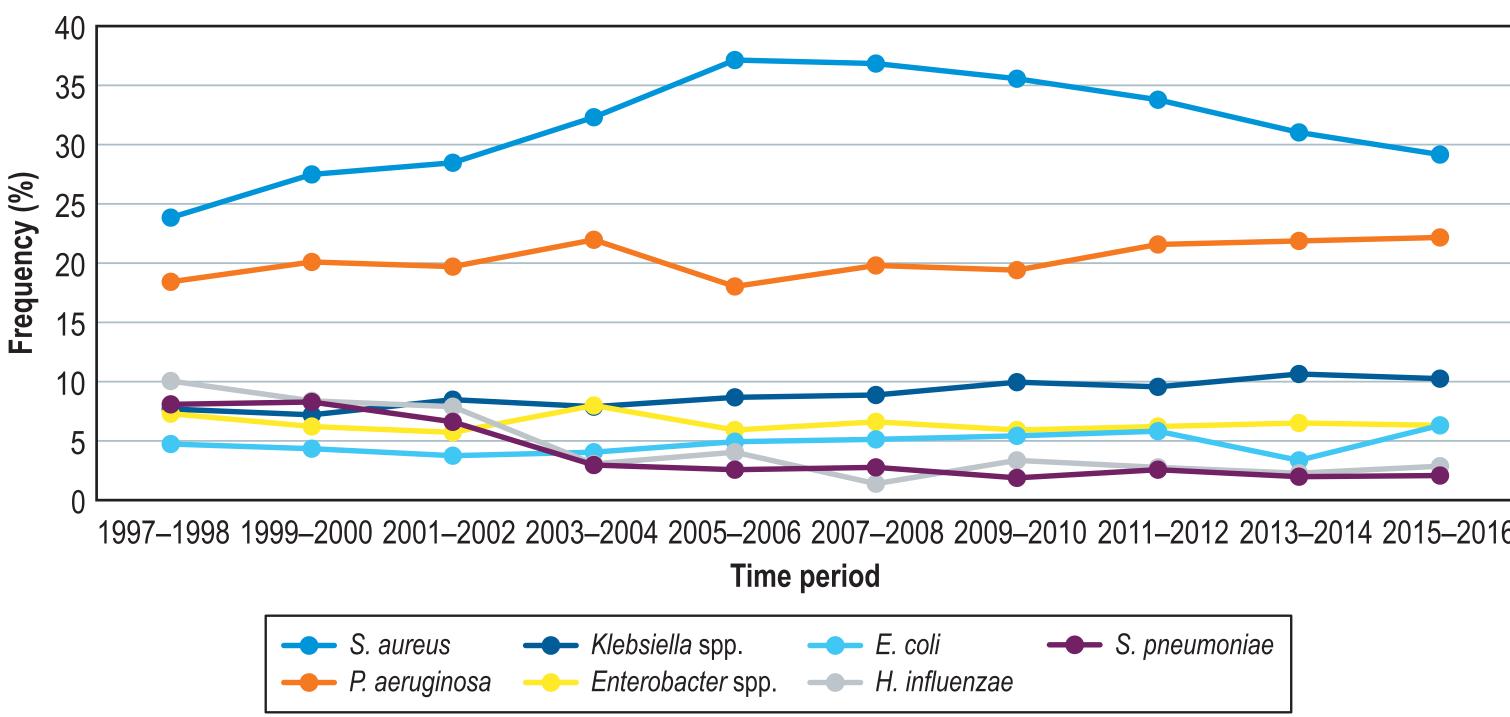
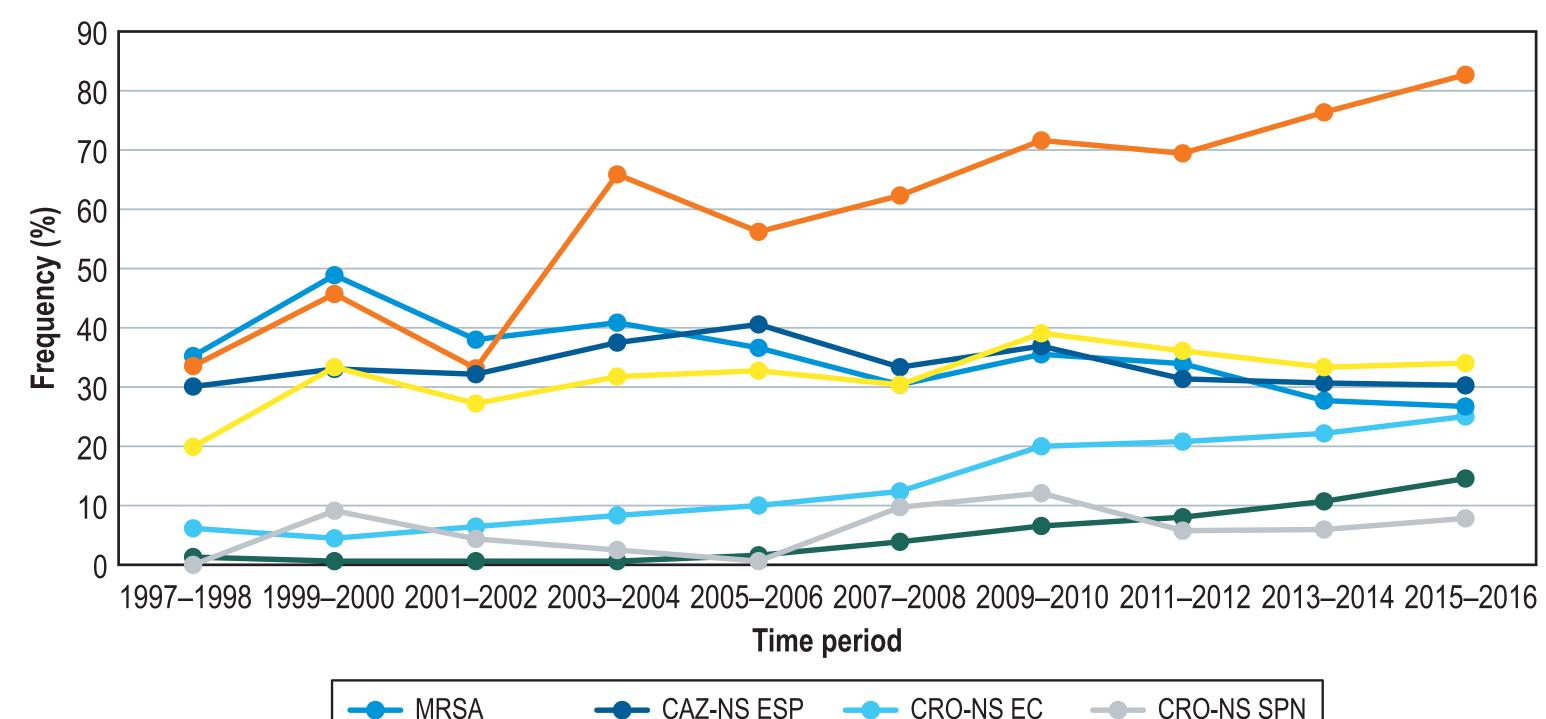


Figure 3. Frequency of occurrence of the key resistance phenotypes in Europe (SENTRY Program, 1997–2016)



Abbreviations: MRSA, methicillin-resistant S. aureus; MER-NS ACB, meropenem-nonsusceptible Acinetobacter spp.; CAZ-NS ESP, ceftazidimenonsusceptible *Enterobacter* spp.; MER-NS PSA, meropenem-nonsusceptible *P. aeruginosa*; CRO-NS EC, ceftriaxone-nonsusceptible *E. coli*; MER-NS KSP, meropenem-nonsusceptible *Klebsiella* spp.; and CRO-NS SPN, ceftriaxone-nonsusceptible *S. pneumoniae*.

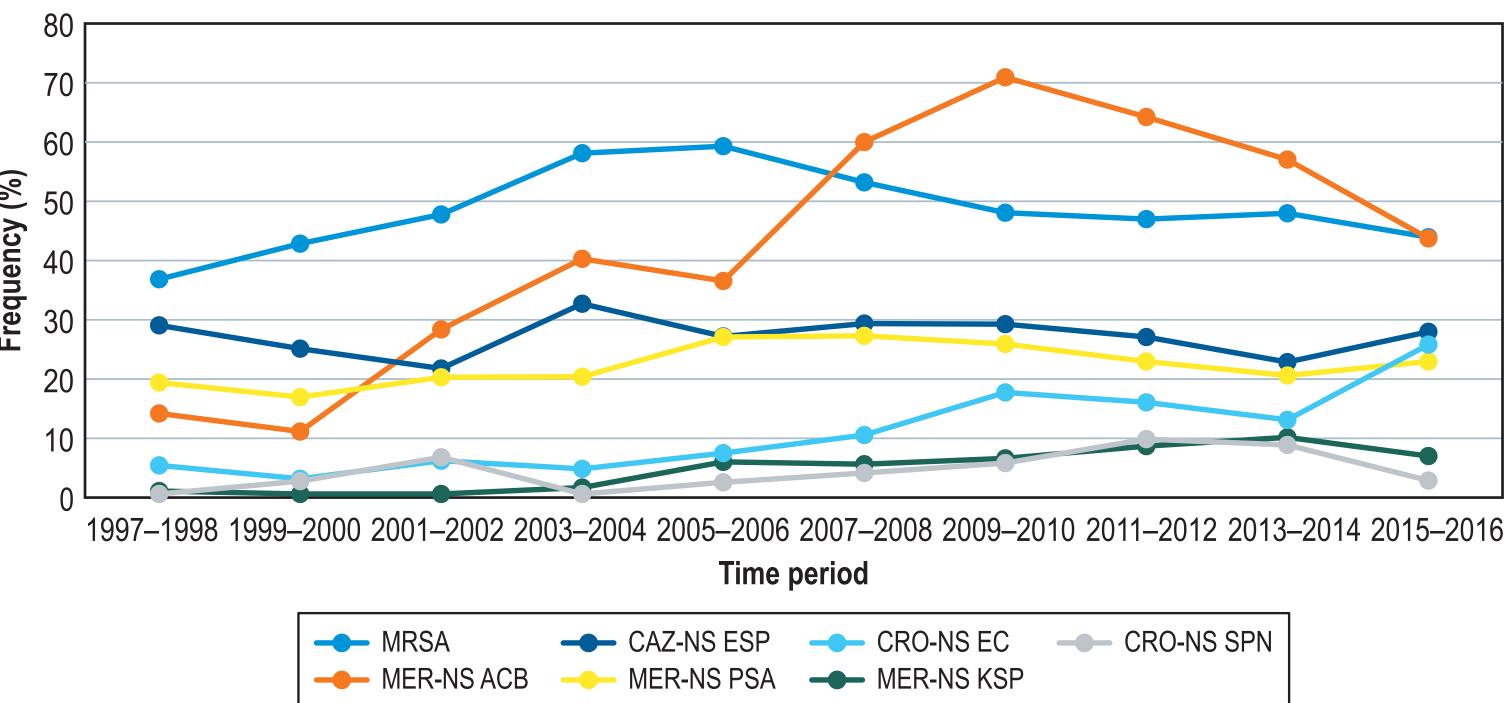
---- MER-NS ACB

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---- CRO-NS EC ---- CRO-NS SPN MER-NS PSA — MER-NS KSP

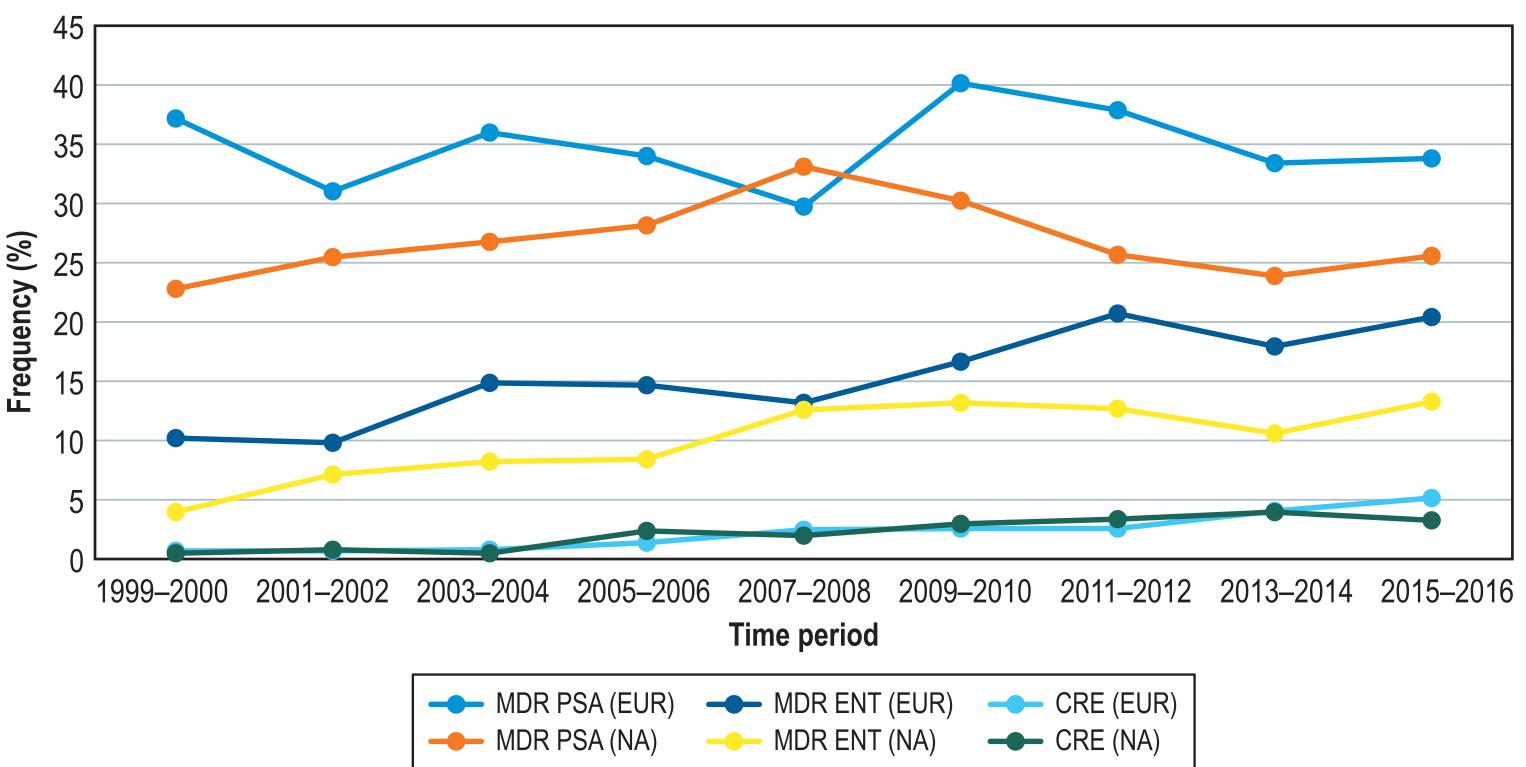
- Rank order and antimicrobial susceptibility of bacteria isolated from patients hospitalised with pneumonia varied widely by geographic region and over the 2 decades of SENTRY
- P. aeruginosa and S. aureus were the most common pathogens isolated from patients with pneumonia in all geographic regions, and represented 36.1% (APAC) to 50.8% (North America) of all organisms cultured

Figure 4. Frequency of occurrence of the key resistance phenotypes in North America (SENTRY Program, 1997–2016)



IRSA, methicillin-resistant S. aureus; MER-NS ACB, meropenem-nonsusceptible Acinetobacter spp.; CAZ-NS ESP, ceftazidime-Enterobacter spp.; MER-NS PSA, meropenem-nonsusceptible P. aeruginosa; CRO-NS EC, ceftriaxone-nonsusceptible E. coli; MER-NS KSP, meropenem-nonsusceptible Klebsiella spp.; and CRO-NS SPN, ceftriaxone-nonsusceptible S. pneumoniae.

Figure 5. Frequency of multidrug-resistant *P. aeruginosa*, MDR Enterobacteriaceae (MDR ENT), and carbapenem-resistant Enterobacteriaceae (CRE) in Europe (EUR) and North America (NA) over time (SENTRY Program, 1999–2016)



Abbreviations: MDR, multidrug-resistant; PSA, P. aeruginosa; ENT, Enterobacteriaceae; EUR, Europe; NA, North America; CRE, carbapenemresistant Enterobacteriaceae



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Conclusions

• The occurrence of some key resistance phenotypes increased, whereas others decreased over the 20 years

 Resistance to third-generation cephalosporins and carbapenems increased continuously among Enterobacteriaceae in all geographic regions during the SENTRY Program (1997–2016)

Acknowledgements

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