

The Worldwide Panorama of *Acinetobacter baumannii* Group and *Stenotrophomonas maltophilia* in the Last 20 Years: Results from the SENTRY Antimicrobial Surveillance Program (1997–2016)

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Introduction

- Members of the *Acinetobacter baumannii* group (ACBg) and *Stenotrophomonas maltophilia* (SM) represent frequent causes of hospital-acquired infections worldwide, and these infections are generally associated with high morbidity and mortality rates, especially in patients receiving inappropriate empirical antimicrobial therapy
- These organisms can cause a wide range of infections, the most common being bacteremia and pneumonia, usually among intensive care unit patients
- Treatment of ACBg and *S. maltophilia* infections represents a significant clinical challenge because these pathogens exhibit notable inherent antibiotic resistance in addition to their ability to acquire and harbour diverse resistance determinants
- In the present study, we evaluated the resistance rates of ACBg and *S. maltophilia* isolated from medical centres enrolled in the SENTRY Antimicrobial Surveillance Program

Materials and Methods

- Between 1997 and 2016, a total of 15,491 ACBg and 6,821 *S. maltophilia* isolates were consecutively collected from >200 medical centres located in the Asia-Pacific (APAC), Latin American, European (including Turkey and Israel), and North American regions through the SENTRY Program
- The distribution of the isolates stratified by geographic region is shown in Table 1
- The participating centres were guided by a common protocol to collect single isolates from patients hospitalised with pneumonia (PIHP), bloodstream (BSI), skin and skin structure (SSSI), intra-abdominal (IAI), or urinary tract (UTI) infections
- Species identification confirmation and antimicrobial susceptibility testing (AST) were performed at the monitoring laboratory using conventional methods and/or matrix-assisted laser desorption ionization-time of flight mass spectrometry, and the broth microdilution method, respectively
 - AST results were interpreted by EUCAST criteria, except for minocycline and ampicillin-sulbactam for which CLSI breakpoints were applied
- An extensively drug-resistant (XDR) ACBg isolate was defined as any isolate **not** susceptible by EUCAST criteria to ≥ 1 drug of ≥ 3 of the following classes: aminoglycosides, carbapenems, fluoroquinolones, and polymyxins; and a pan drug-resistant (PDR) isolate was defined as any isolate resistant to all 4 classes listed for XDR
- Among ACBg isolates, susceptibility rates observed in the 1997–2000 and 2013–2016 periods were compared, except for colistin and ampicillin-sulbactam, which have been tested since 2005
- Among SM isolates, trimethoprim-sulfamethoxazole (TMS) susceptibility rates observed in the 2001–2004, 2005–2008, 2009–2012, and 2013–2016 periods were also compared

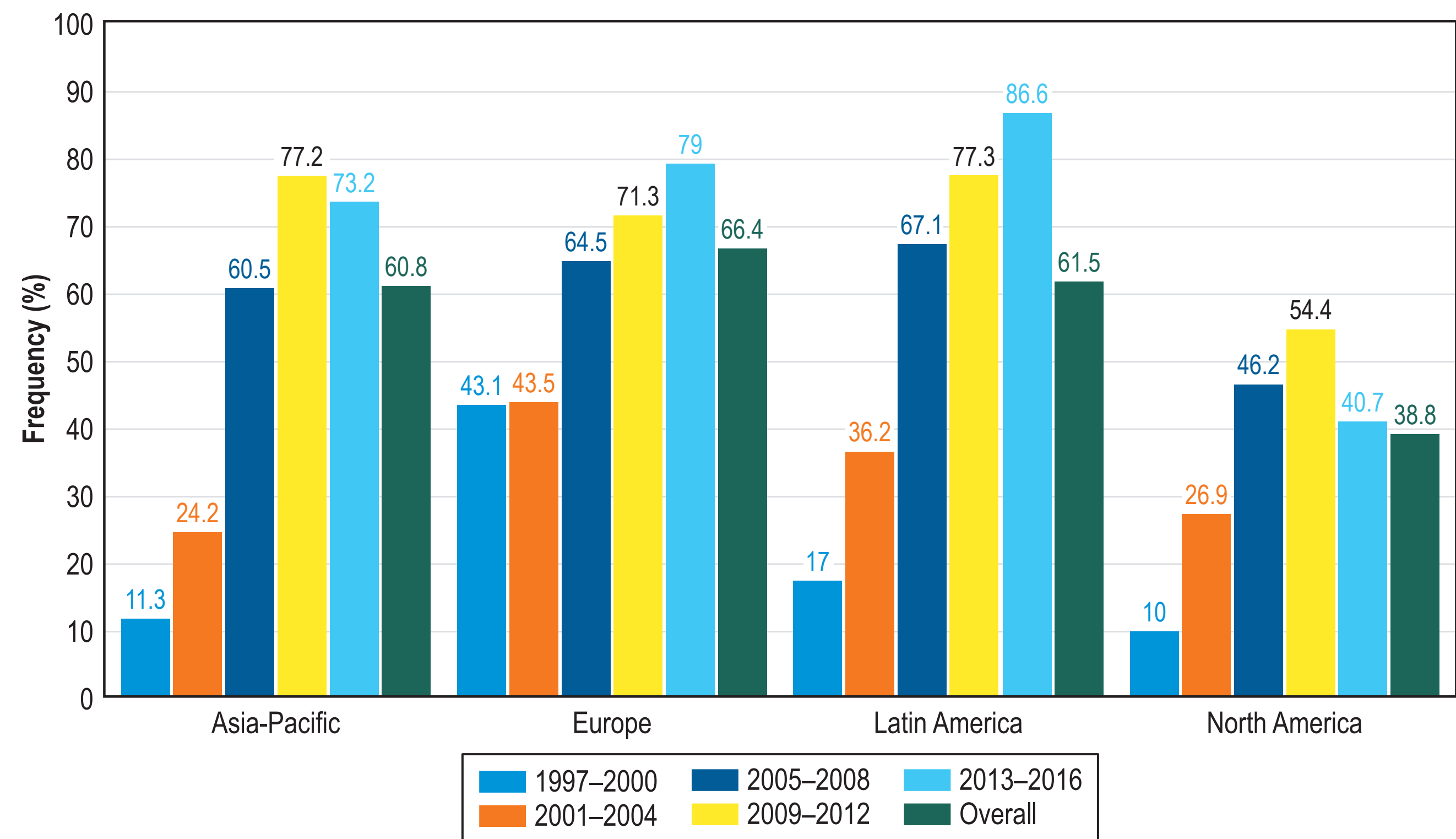
Results

- ACBg isolates were more frequently collected from patients hospitalised with pneumonia (n=6,988; 45.1% of isolates) and bloodstream infections (n=5,442; 35.1%)
- Colistin was the most active agent tested against ACBg isolates ($MIC_{50/90} \leq 0.5/2$ mg/L; 96.4% susceptible) followed by minocycline ($MIC_{50/90} \leq 1/ >8$ mg/L; 78.4% susceptible) in all geographic regions (Table 2)
- The overall susceptibility rates to colistin varied from 93.9% in Europe to 98.5% in the APAC region, whereas minocycline susceptibility rates varied from 70.1% in Europe to 91.1% in Latin America (Table 2)

Table 1. Distribution of organisms included in this investigation stratified by geographic region

Organism	No. of organisms				
	APAC	Europe	Latin America	North America	All regions combined
<i>A. baumannii</i> group	4,063	4,531	3,367	3,530	15,491
<i>S. maltophilia</i>	970	2,035	704	3,112	6,821

Figure 1. Frequency (%) of extensively drug-resistant (XDR) *A. baumannii* group isolates by geographic region and 4-year period



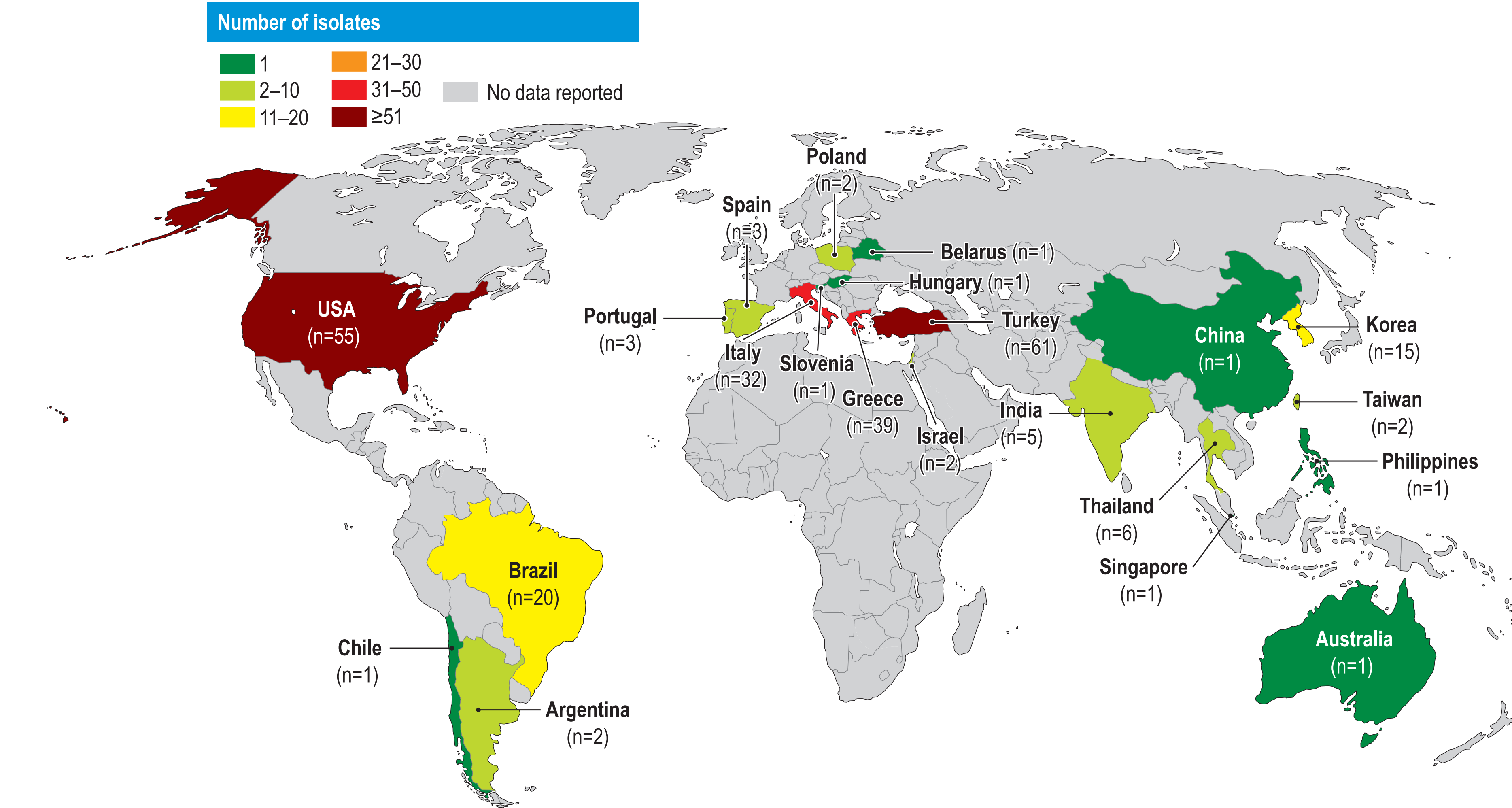
- Meropenem ($MIC_{50} >8$ mg/L) and ampicillin-sulbactam ($MIC_{50} >16$ mg/L) showed limited activity against ACBg, with meropenem susceptibility rates varying from 35.6% in Europe to 59.7% in North America, and susceptibility rates to ampicillin-sulbactam (CLSI) varying from 21.6% in Latin America to 54.8% in North America (Table 2)
- Important decreases in susceptibility rates among ACBg isolates were observed for all antimicrobial agents in all regions over time, except for ampicillin-sulbactam and minocycline in North America (Table 3)
- The highest frequency of XDR ACBg isolates overall was observed for Europe (66.4%) followed by Latin America (61.5%), APAC (60.8%), and North America (38.8%; Figure 1)
- The frequency of XDR ACBg isolates increased during the study period (1997–2016) in Europe and Latin America, and from 1997–2000 to 2009–2012 in North America and the APAC region, where the frequency of XDR ACBg isolates decreased from 2009–2012 to 2013–2016 (Figure 1)
- A total of 255 of 15,491 (1.6%) ACBg isolates exhibited resistance to carbapenems and polymyxins
 - These ACBg isolates were collected from 22 countries; countries with the highest number of isolates were Turkey (61 isolates; 5.2% of isolates from Turkey), United States (55 isolates; 1.6%), Greece (39 isolates; 10.8%), Italy (32 isolates; 7.5%), Brazil (20 isolates; 1.3%), and South Korea (15 isolates; 3.9%; Figure 2)

Table 2. Overall (1997–2016) susceptibility rates for *A. baumannii* group and *S. maltophilia* against select antimicrobial agents

Organism / antimicrobial agent (no. of isolates tested)	% susceptible (EUCAST)*				
	Asia-Pacific	Europe	Latin America	North America	All
<i>A. baumannii</i> group (15,491)					
Amikacin	38.0	29.9	22.7	67.5	39.0
Tobramycin	38.9	46.0	44.6	65.9	48.3
Meropenem	40.5	35.6	41.0	59.7	43.5
Levofloxacin	30.7	18.1	14.6	46.1	27.0
Colistin	98.5	93.9	98.1	95.5	96.4
Minocycline	75.5	70.1	91.1	81.6	78.4
Ampicillin-sulbactam	27.3	25.2	21.6	54.8	31.6
<i>S. maltophilia</i> (6,821)					
Trimethoprim-sulfamethoxazole	93.0	96.3	94.7	96.9	96.0
Levofloxacin	80.3	83.7	87.8	78.7	81.4
Minocycline	98.2	99.2	99.7	99.6	99.3

* Susceptibility rates calculated according to the EUCAST criteria, except for CLSI criteria applied to ampicillin-sulbactam and minocycline when testing ACBg; and levofloxacin and minocycline when testing *S. maltophilia*.

Figure 2. Distribution of 255 *A. baumannii* group isolates exhibiting resistance to carbapenems and polymyxins referred to the SENTRY Program (1997–2016) according to the country of isolation



- Only 9.4% of these 255 isolates were susceptible to amikacin, 8.2% were susceptible to gentamicin, and 24.7% were susceptible to tobramycin based on EUCAST criteria (data not shown)
- A total of 159 ACBg isolates (1.0%) were resistant (EUCAST criteria) to fluoroquinolones, carbapenems, aminoglycosides, TMS, and the polymyxins; these isolates were considered pan drug-resistant as defined earlier, although 43.5% of these isolates were still susceptible to minocycline per CLSI criteria
- S. maltophilia* isolates were also more frequently isolated from PIHP (3,830; 56.2%) and BSI (2,268; 33.3%) in all geographic regions
- The most active compounds tested against *S. maltophilia* were minocycline ($MIC_{50/90}$ 0.5/2 mg/L; 99.3% susceptible [CLSI]), TMS ($MIC_{50/90} \leq 0.5/1$ mg/L; 96.1% susceptible [EUCAST]), tigecycline ($MIC_{50/90}$ 0.5/2 mg/L [data not shown]), and levofloxacin ($MIC_{50/90}$ 1/4 mg/L; 81.4% susceptible; Table 2)
- Among *S. maltophilia* isolates, the highest TMS susceptibility rates were observed for isolates collected from North America (96.9%), followed by isolates from Europe (96.3%), Latin America (94.7%), and APAC (93.0%; Table 2)
- Overall TMS susceptibility rates decreased from 97.2% in 2001–2004 to 95.6% in 2013–2016
 - Susceptibility rates varied in 2013–2016 according to the geographic region, with higher rates in Europe (96.5%) and North America (95.8%) and lowest rates in Latin America (91.5%) and APAC (92.5%; Figure 3)
- A total of 80 of 6,821 (1.2%) *S. maltophilia* isolates exhibited resistance to TMS ($MIC >4$ mg/L [EUCAST]) and levofloxacin ($MIC >4$ mg/L [CLSI]); these isolates were more commonly isolated from the United States (34 isolates; 1.2% of US isolates), Brazil (6 isolates; 2.2%), China (6 isolates; 1.8%), and Chile (5 isolates; 4.9%); see Figure 4

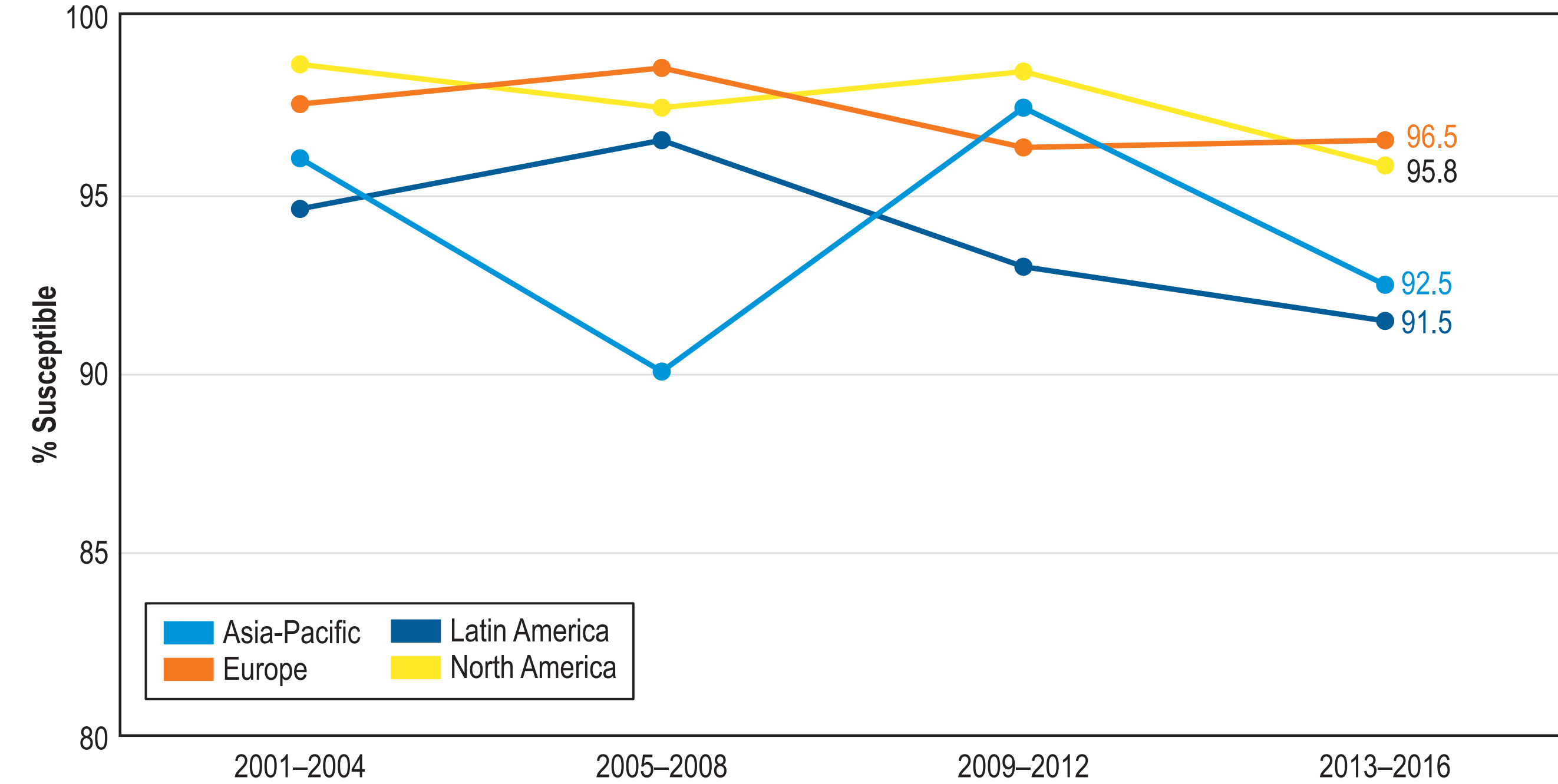
Table 3. Susceptibility rates of *A. baumannii* group isolates for selected drugs by geographic region and 4-year periods

Geographic region	ACBg susceptibility rates (EUCAST)* stratified by antimicrobial agent and time period									
	Meropenem		Levofloxacin		Amikacin		Ampicillin-sulbactam		Colistin	
	1997–2000	2013–2016	1997–2000	2013–2016	1997–2000	2013–2016	2005–2008	2013–2016	2005–2008	2013–2016
Asia-Pacific	87.6	22.0	63.9	20.4	74.6	29.2	35.8	21.2	99.2	95.5
Europe	55.7	22.2	24.4	13.7	31.7	22.7	31.5	19.2	99.2	89.6
Latin America	81.3	13.7	23.1	12.4	22.7	17.6	29.3	16.4	99.2	96.6
North America	88.8	55.0	64.4	49.3	83.7	70.0	54.6	59.0	98.4	93.6
All regions	77.0	31.5	41.6	25.8	50.5	37.9	36.2	31.6	99.1	92.6

ACBg, *Acinetobacter baumannii* group.

* Percent susceptible per EUCAST criteria, except for CLSI criteria applied to ampicillin-sulbactam and minocycline.

Figure 3. Trimethoprim-sulfamethoxazole susceptibility rates of *S. maltophilia* isolates by geographic region and 4-year periods



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Conclusions

- Over the last 20 years, we have witnessed important susceptibility rate reductions to numerous antimicrobial agents (including carbapenems and, more recently, colistin) in all geographic regions among ACBg isolates
- In general, TMS resistance among *S. maltophilia* isolates remained low and relatively stable during the 20 years of SENTRY Program

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