

Epidemiology of Carbapenem Resistance Determinants Identified in Meropenem-Nonsusceptible *Enterobacterales* Collected as Part of a Global Surveillance Program, 2012 to 2017

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ABSTRACT To estimate the incidence of carbapenem-resistant Enterobacterales (CRE), a global collection of 81,781 surveillance isolates of Enterobacterales collected from patients in 39 countries in five geographic regions from 2012 to 2017 was studied. Overall, 3.3% of isolates were meropenem-nonsusceptible (MIC $\geq 2 \mu g/ml$), ranging from 1.4% (North America) to 5.3% (Latin America) of isolates by region. Klebsiella pneumoniae accounted for the largest number of meropenem-nonsusceptible isolates (76.7%). The majority of meropenem-nonsusceptible Enterobacterales carried KPC-type carbapenemases (47.4%), metallo- β -lactamases (MBLs; 20.6%) or OXA-48-like β -lactamases (19.0%). Forty-three carbapenemase sequence variants (8 KPC-type, 4 GES-type, 7 OXA-48-like, 5 NDM-type, 7 IMP-type, and 12 VIM-type) were detected, with KPC-2, KPC-3, OXA-48, NDM-1, IMP-4, and VIM-1 identified as the most common variants of each carbapenemase type. The resistance mechanisms responsible for meropenem-nonsusceptibility varied by region. A total of 67.3% of all carbapenemase-positive isolates identified carried at least one additional plasmidmediated or intrinsic chromosomally encoded extended-spectrum β -lactamase, AmpC β -lactamase, or carbapenemase. The overall percentage of meropenem-nonsusceptible Enterobacterales increased from 2.7% in 2012 to 2014 to 3.8% in 2015 to 2017. This increase could be attributed to the increasing proportion of carbapenemase-positive isolates that was observed, most notably among isolates carrying NDM-type MBLs in Asia/South Pacific, Europe, and Latin America; OXA-48-like carbapenemases in Europe, Middle East/Africa, and Asia/South Pacific; VIM-type MBLs in Europe; and KPC-type carbapenemases in Latin America. Ongoing CRE surveillance combined with a global antimicrobial stewardship strategy, sensitive clinical laboratory detection methods, and adherence to infection control practices will be needed to interrupt the spread of CRE.

Antimicrobial Agents

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KEYWORDS carbapenem-resistant *Enterobacterales*, surveillance, *Enterobacterales*, carbapenem resistant

Carbapenems are a class of broad-spectrum β -lactam antimicrobial agents often used to treat hospitalized patients who have failed initial therapy or those with severe infections caused by multidrug-resistant (MDR) pathogens. Carbapenems are highly active against *Enterobacterales* that possess Ambler class C cephalosporinases and/or class A β -lactamases, including extended-spectrum β -lactamases (ESBLs) (1). The appearance and global dissemination of successful clones of ESBL-producing *Enterobacterales* over the last 3 decades resulted in an increase in the use of carbapenems to treat infections caused by these organisms. Subsequently, carbapenem**Citation** Kazmierczak KM, Karlowsky JA, de Jonge BLM, Stone GG, Sahm DF. 2021. Epidemiology of carbapenem resistance determinants identified in meropenemnonsusceptible *Enterobacterales* collected as part of a global surveillance program, 2012 to 2017. Antimicrob Agents Chemother 65:e02000-20. https://doi.org/10.1128/AAC .02000-20.

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Biotix Therapeutics, Inc., Waltham, Massachusetts, USA **Received** 18 September 2020

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Accepted manuscript posted online 10 May 2021 Published 17 June 2021 resistant *Enterobacterales* (CRE) emerged, predominantly, but not exclusively, among *Klebsiella pneumoniae* (2–8).

Carbapenemases are β -lactamases capable of hydrolyzing carbapenems and most other β -lactams, resulting in carbapenem and multidrug resistance. Ambler class A (KPC and GES) and class D (OXA-48-like) carbapenemases possess a serine-based active site, while class B metallo- β -lactamases (MBLs; NDM, IMP, and VIM) have one or two zinc atoms in their active site (8, 9). Each carbapenemase type shows different substrate specificities, e.g., KPC hydrolyzes a broad spectrum of substrates, including penicillins, oxyimino-cephalosporins, older β -lactamase inhibitors (clavulanic acid, sulbactam, tazobactam), aztreonam, and carbapenems, while MBLs have a spectrum of hydrolysis similar to that of KPC but spare aztreonam, and OXA-48-like carbapenemases spare both cephalosporins and aztreonam but hydrolyze penicillins and weakly hydrolyze carbapenems (8, 9). CRE often cocarry multiple β -lactamases and determinants conferring resistance to antimicrobials from other drug classes, such as aminoglycosides and fluoroquinolones, resulting in an MDR phenotype (10).

Whereas carbapenemase production is the most frequent mechanism of carbapenem resistance identified in meropenem-nonsusceptible CRE, other mechanisms of resistance may be present in some clinical isolates, including hyperproduction of AmpC β -lactamases or ESBLs, combined with impaired outer membrane permeability due to porin mutations, upregulated efflux, and/or alterations in penicillin-binding proteins (8, 11–14). Resistance arising by non-carbapenemase-mediated mechanisms is indistinguishable phenotypically from carbapenemase-based resistance.

The primary objective of the current report was to describe the molecular epidemiology of β -lactamase resistance determinants identified in meropenem-nonsusceptible *Enterobacterales* collected as part of a global surveillance program from 2012 to 2017.

RESULTS

A total of 81,781 clinically significant Enterobacterales isolates that were considered probable causative agents of infection were collected from patients in 39 countries by medical laboratories participating in a global surveillance study from 2012 to 2017. Of these isolates, 2,666 (3.3%) tested as meropenem-nonsusceptible (MIC $\geq 2 \mu g/ml$). The 2,666 isolates were from various infection sources, including lower respiratory tract (n = 778), urinary tract (n = 631), skin and soft tissue (n = 581), intra-abdominal (n = 408), bloodstream (n = 266), and other sites of infection (n = 2) (see Fig. S1 in the supplemental material). The percentage of *Enterobacterales* isolates from each geographic region that tested as meropenem-nonsusceptible ranged from 1.4% (North America) to 5.3% (Latin America) (Fig. 1). The largest number of meropenemnonsusceptible isolates were comprised of K. pneumoniae (n = 2,046; 76.7%), followed by Enterobacter cloacae (n = 177; 6.6%) and Escherichia coli (n = 136; 5.1%), with the remaining \sim 12% of meropenem-nonsusceptible isolates composed of 101 isolates of Klebsiella spp., 79 isolates of Citrobacter spp., 70 isolates of Proteeae, 31 isolates of Serratia marcescens, 18 isolates of Enterobacter spp., and 8 isolates of Raoultella spp. (see Fig. S2).

The majority (47.4%, n = 1,263) of meropenem-nonsusceptible isolates collected globally carried KPC-type carbapenemases, whereas comparable percentages of isolates carried MBLs (20.6%, n = 548) or OXA-48-like β -lactamases (19.0%, n = 506), and few isolates carried GES-type carbapenemases (0.2%, n = 6) (Fig. 2A). MBL types were not equally common, with 61% of MBL-positive isolates carrying NDM-type, 30% carrying VIM-type, and 9% carrying IMP-type β -lactamases. No gene encoding a carbapenemase was detected in 15.5% (n = 413) of meropenem-nonsusceptible isolates; of these, 91.5% carried ESBL- and/or AmpC β -lactamase-coding genes detected by PCR or the intrinsic, chromosomally encoded β -lactamases common to *Citrobacter* spp., *Enterobacter* spp., *Providencia* spp., *Serratia* spp., and *K. oxytoca* and were assumed also to display reduced expression or loss of outer membrane porin proteins and/or



FIG 1 Distribution of meropenem-nonsusceptible *Enterobacterales* collected from 2012 to 2017. MEM-I, meropenem-intermediate, MIC of 2 µg/ml; MEM-R, meropenem-resistant, MIC of \geq 4µg/ml. Global, all surveyed regions; LA, Latin America (Argentina, Brazil, Chile, Colombia, Mexico, and Venezuela); EUR, Europe (Austria, Belgium, the Czech Republic, Denmark, France, Germany, Greece, Hungary, Italy, the Netherlands, Poland, Portugal, Romania, Russia, Spain, Sweden, Turkey, and the United Kingdom); AP, Asia/South Pacific (Australia, China, Hong Kong, Japan, Malaysia, the Philippines, South Korea, Taiwan, and Thailand); MEA, Middle East/Africa (Israel, Kenya, Kuwait, Nigeria, and South Africa); NA, North America (the United States). Isolates obtained from patients in North America were collected from 2012 to 2016 only.

upregulated efflux systems, which can lead to carbapenem resistance (Fig. 2A) (11–13). The remaining isolates were assumed to carry β -lactamases not included in the testing algorithm (e.g., SME, IMI/NMC-A [8]) and/or other resistance mechanisms, such as those described above; alternatively, these isolates may have carried β -lactamase genes that were not amplified with the primers used for detection.

The distribution of resistance mechanisms observed among meropenem-nonsusceptible isolates varied by region (Fig. 2B to F and Table 1). Among isolates collected in Europe, the percentages of different carbapenemase types were similar to those observed for the global collection of meropenem-nonsusceptible isolates, except that a larger proportion of isolates (30%) carried OXA-48-like β -lactamases, isolates carrying NDM-type and VIM-type MBLs were identified in comparable proportions (7 to 9%), and no isolates carrying IMP-type MBLs were identified (Fig. 2B). In Latin America and North America, KPC-positive isolates predominated, comprising 68 and 79% of the isolates collected, respectively. MBLs were found in 5 to 7% of meropenem-nonsusceptible isolates from these two regions and OXA-48-like β -lactamases were found, in low numbers, only among isolates from Latin America (Fig. 2C and F). In contrast, MBL-positive isolates comprised the majority of meropenem-nonsusceptible isolates collected in Asia/South Pacific and the Middle East/Africa regions (55 and 44%, respectively). In these two regions, approximately one-third of the meropenem-nonsusceptible isolates collected carried NDM-type MBLs. IMP-positive isolates were only found in Asia/South Pacific, except for two isolates that were detected in Latin America. Similar proportions of KPC-positive isolates (19 to 21%) were found in Asia/South Pacific and the Middle East/Africa region, whereas the proportion of isolates carrying OXA-48-like (29%) and VIM-type (8%) enzymes was greater among isolates collected in the Middle East/Africa region and approached that observed for Europe (Fig. 2D and E).

Forty-three carbapenemase sequence variants (8 KPC-type, 4 GES-type, 7 OXA-48-like, 5 NDM-type, 7 IMP-type, and 12 VIM-type variants) were identified among 2,253 meropenem-nonsusceptible isolates carrying one or more carbapenemases (Table 1; see also Fig. S3 in the supplemental material). KPC-2 (864 of 1,263 isolates, 68.4%), KPC-3 (388 of 1,263 isolates, 30.7%), OXA-48 (414 of 506 isolates, 81.8%), NDM-1 (283 of 336 isolates, 84.2%), IMP-4 (26 of 49 isolates, 53.1%), and VIM-1 (115 of 164 isolates, 70.1%) were the most commonly identified variants of these carbapenemase types. As shown in Table 1, KPC-2 made up the majority of KPC-type carbapenemases identified among isolates collected in Europe (350 of 624, 56.1%), Latin America (418 of 470,



FIG 2 Distribution of carbapenem resistance mechanisms identified in meropenem-nonsusceptible *Enterobacterales* isolates. (A) Meropenem-nonsusceptible isolates collected in all surveyed regions (n=2,666). (B) Isolates collected in Europe (n=1,441). (C) Isolates collected in Latin America (n=689). (D) Isolates collected in Asia/South Pacific (n=294). (E) Isolates collected in the Middle East/Africa (n=140). (F) Isolates collected in North America (n=102,2012 to 2016 only). No Cpase detected, no gene encoding a carbapenemase was detected by PCR. MBL + OXA-48-like (n=52) included NDM + OXA-48-like (Europe, n=26; Asia/South Pacific, n=17; Middle East/Africa, n=1) and VIM + OXA-48-like (Europe, n=6; Middle East/Africa, n=2). MBL + KPC (n=11) included VIM + KPC (Europe, n=7), NDM + KPC (Latin America, n=1; Asia/South Pacific, n=2). MBL + GES was composed of NDM + GES carbapenemase (Latin America, n=2). Two MBLs were composed of VIM + NDM (Europe, n=1).

88.9%), and Asia/South Pacific (60 of 62, 96.8%), whereas KPC-3 was more common among isolates collected in Middle East/Africa (15 of 26, 57.7%) and North America (53 of 81, 65.4%). OXA-48 was the major OXA-type found among isolates from Europe (398 of 432, 92.1%), but OXA-181 and OXA-232 were more prevalent in the Middle East/ Africa (30 of 41, 73.2%) and Asia/South Pacific (20 of 25, 80.0%). NDM-1 was the predominant NDM-type detected among isolates collected in all regions, but the numbers of isolates carrying NDM-5 and NDM-7 were notably increased in Middle East/Africa (9 of 51, 17.6%) and Asia/South Pacific (36 of 115, 31.3%). IMP-8 was the only IMP-type detected among meropenem-nonsusceptible *Enterobacterales* collected outside the Asia/South Pacific region. Similarly, few VIM-positive isolates were collected in regions other than Europe, and the majority of these carried VIM-1, although isolates carrying VIM-23 were notable in Latin America (8 of 11, 72.7%) (Table 1). KPC-type carbapenemases were carried most frequently by *K. pneumoniae* in all regions surveyed, ranging from 73.1% (19 of 26) of KPC-positive isolates collected in Middle East/Africa to 96.0% (599 of 624) of isolates from Europe; similarly, the majority of OXA-48-like β -lactamases

TABLE 1 Distribution of carbapenemase variants among	2,253 meropenem-nonsusceptible	e, carbapenemase-positive En	nterobacterales isolates
collected from 2012 to 2017			

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L. Cui NCC 207 OXA-181 (7) NDM 5 (5) NDM 5 (7) OXA-123 (1) K. aerogenes KPC-2 (1) OXA-481 (4) NDM 1 (2) VIM-1 (2) K. asytoca KPC-2 (3) OXA-481 (4) NDM 1 (2) VIM-1 (3) K. asytoca KPC-2 (3) OXA-481 (4) NDM 1 (2) VIM-1 (3) K. preumoniae KPC-2 (3) OXA-481 (5) NDM 1 (2) VIM-1 (4) K. preumoniae KPC-2 (3) OXA-481 (3) NDM 1 (1) VIM-24 (1) K. preumoniae KPC-3 (257) OXA-162 (3) NDM 1 (1) VIM-42 (1) K. Pretageri OXA-484 (1) NDM 1 (1) VIM-42 (1) VIM-42 (1) V. K-2 (2) OXA-48 (3) NDM 1 (1) VIM-41 (1) VIM-42 (1) Asia/Pacific (255/13,046) C. freundiji KPC-2 (7) VIM-1 (3) VIM-1 (4) Latin America (525/13,046) C. freundiji KPC-2 (7) VIM-1 (3) VIM-1 (1) K. acrogenes KPC-2 (1) GES-2 (1) OXA-48 (3) NDM 1 (1) VIM-23 (2) K. acrogenes KPC-		E coli	kDC 2(2)		OVA 40 (0)		NDM 1 (5)	VIIVI-5I(1)
K. derogenes KPC-2 (1) OXA-232 (1) NDM-1 (2) K. aerogenes KPC-2 (1) OXA-48 (6) NDM-1 (2) VIM-44 (1) K. ayrloca KPC-2 (3) OXA-48 (6) NDM-1 (2) VIM-44 (1) K. preumoniae KPC-2 (3) OXA-48 (37) NDM-1 (8) VIM-12 (1) KPC-2 (2) OXA-48 (37) NDM-1 (8) VIM-12 (1) VIM-42 (1) KPC-2 (2) OXA-48 (2) NDM-1 (1) VIM-42 (1) VIM-42 (1) VM-2 (2) OXA-48 (2) NDM-1 (1) VIM-42 (1) VIM-42 (1) VM-2 (1) OXA-48 (2) NDM-1 (1) VIM-42 (1) VIM-42 (1) VM-2 (1) OXA-48 (2) NDM-1 (1) VIM-42 (1) VIM-42 (1) VM-2 (1) OXA-48 (2) NDM-1 (1) VIM-1 (1) VIM-1 (1) R ordinaria KPC-2 (2) OXA-48 (2) NDM-1 (1) VIM-1 (1) S. marcescens VC-2 (3) S NDM-1 (2) VIM-23 (2) K aerogenes KPC-2 (10) OXA-48 (2) NDM-1 (1) VIM-23 (2) K aerogenes		L. COII	KPC-3 (7)		OXA-48 (8)		NDM-5 (5)	v IIvi-1 (Z)
NDM-1 (2) NDM-1 (2) VIM-4 (1) K. avytoca KPC-2 (3) OXA-48 (4) NDM-1 (2) VIM-4 (1) K. avytoca KPC-2 (3) OXA-48 (4) NDM-1 (2) VIM-1 (3) K. pneumonice KPC-2 (33) GE5-6 (1) OXA-48 (3) NDM-1 (2) VIM-4 (2) KPC-3 (257) OXA-163 (3) NDM-16 (2) VIM-26 (1) VIM-26 (1) KPC-2 (2) OXA-48 (1) NDM-16 (2) VIM-26 (1) VIM-26 (1) KPC-2 (2) OXA-48 (3) NDM-1 (1) VIM-26 (1) VIM-26 (1) P. mirabilis - OXA-48 (3) NDM-1 (1) VIM-1 (1) P. mirabilis - OXA-48 (3) NDM-1 (1) VIM-1 (1) S. marcescens - OXA-48 (2) NDM-1 (1) VIM-1 (1) S. marcescens KPC-2 (7) OXA-48 (1) NDM-1 (2) VIM-1 (1) Latin America (525/13,046) C. feundii KPC-2 (2) NDM-1 (6) VIM-23 (2) E. colu KPC-2 (1) GES-2 (1) OXA-48 (1) NDM-1 (1) VIM-23 (2) <			Ki C 5 (7)		OXA-232 (1)			
K. aerogenes KPC-2 (1) OXA-16 (4) NDM-1 (2) VIM-1 (3) K. oxytoca KPC-3 (3) VIM-48 (6) NDM-1 (2) VIM-1 (3) K. preumonice KPC-3 (3) VIM-48 (6) NDM-1 (2) VIM-1 (2) K. preumonice KPC-3 (33) OXA-163 (2) NDM-1 (2) VIM-1 (2) K. PC-2 (2) OXA-163 (2) NDM-1 (2) VIM-1 (2) VIM-1 (2) K. PC-3 (2) OXA-163 (2) NDM-1 (2) VIM-2 (1) VIM-2 (2) OXA-48 (2) VIM-1 (1) VIM-2 (1) VIM-4 (1) OXA-48 (3) NDM-1 (1) VIM-1 (1) P. mirabilis OXA-48 (3) NDM-1 (1) VIM-1 (1) P. retigeri OXA-48 (3) NDM-1 (1) VIM-1 (1) R. planticola OXA-48 (3) NDM-1 (2) VIM-1 (1) S. marcescens OXA-48 (3) NDM-1 (2) VIM-1 (1) Latin America (525/13,046) C. feundii KPC-2 (7) NDM-1 (2) VIM-23 (2) E. cola cae KPC-2 (1) OXA-48 (4) NDM-1 (2) VIM-23 (2)					OXA-244 (1)			
K. oxyñoca KPC-2 (3) OXA-48 (6) NDM-1 (2) VIM-4 (1) K. pneumoniae KPC-3 (33) GE5-6 (1) OXA-48 (347) NDM-1 (8) VIM-4 (1) KPC-3 (2,2328) GE5-6 (1) OXA-48 (347) NDM-1 6 (2) VIM-2 (1) KPC-3 (2) OXA-163 (2) VIM-2 (1) VIM-2 (1) VIM-2 (1) KPC-3 (2) OXA-48 (2) VIM-2 (1) VIM-2 (1) VIM-2 (1) VA-48 (1) NDM-1 (1) VIM-1 (1) VIM-2 (1) VIM-2 (1) VA-48 (1) NDM-1 (1) VIM-1 (1) VIM-1 (1) VIM-2 (1) R ornithinolytica OXA-48 (2) VIM-1 (1) VIM-1 (1) R ornithinolytica OXA-48 (3) NDM-1 (2) VIM-1 (1) R ornithinolytica VIM-2 (1) VIM-2 (1) VIM-2 (1) R ornithinolytica KPC-2 (1) OXA-48 (2) VIM-2 (1) Latin America (525/13,046) C freundii KPC-2 (7) VIM-2 (1) VIM-2 (1) K corgica KPC-2 (10) GES-2 (1) OXA-48 (2) NDM-1 (1) VIM-2 (2) <		K. aerogenes	KPC-2 (1)		OXA-48 (4)		NDM-1 (2)	
KPC-3 (3) KPC-3 (2) NDM-16 (2) NDM-16 (2) VIM-42 (1) VIM-43 (3) VIM-1 (1) VIM-53 (2) VIM-23 (2) VIM-24 (1) VIM-24 (1) VIM-24 (1) VIM-24 (1) VIM-24 (1) VIM-24 (1)		K. oxytoca	KPC-2 (3)		OXA-48 (6)		NDM-1 (2)	VIM-1 (3)
K. pneumoniae KPC-2 (38) KPC-3 (257) GES-6 (1) (XPC-9 (2) (XPC-9 (2) (XPC-9 (2)) OXA-163 (2) (XPC-4) (2) (XPC-4) (2) NDM-16 (2) (XPC-4) (2) (XPC-4) (2) NDM-16 (2) (YIM-32 (1) (YIM-32 (1)) P. mirabilis CXA-48 (1) (XPC-4) (2) NDM-1 (1) (XPC-4) (2) NDM-1 (1) (YIM-42 (1)) VIM-12 (1) (YIM-42 (1)) P. mirabilis CXA-48 (1) (YIM-42 (1)) NDM-1 (1) VIM-12 (1) (YIM-42 (1)) VIM-12 (1) (YIM-42 (1)) P. mirabilis CXA-48 (3) (YIM-11 (1)) NDM-1 (1) VIM-11 (1) (YIM-11 (1)) P. mirabilis CXA-48 (3) (YIM-12 (1)) NDM-1 (1) VIM-12 (1) (YIM-11 (1)) S. marcescens CXA-48 (3) (YIM-12 (1)) NDM-1 (2) (YIM-23 (3)) VIM-12 (1) (YIM-23 (3)) Latin America (525/13,046) C. freundii (KPC-2 (2)) KPC-2 (2) (Z. coacae NDM-1 (2) (YIM-23 (2)) VIM-23 (3) (YIM-23 (3)) Latin America (525/13,046) C. freundii (KPC-2 (2)) KPC-2 (1) (Z. coacae KPC-2 (1) (KPC-3 (1)) OXA-232 (1) (XA-232 (1)) NDM-1 (6) (YIM-23 (2)) Latin America (525/13,046) C. freundii (X. cyricola KPC-2 (10) KPC-2 (1) (X- sergenes KPC-2 (10) NDM-1 (1) (X- sergenes KPC-2 (10) NDM-1 (1) (YIM-24 (1)) Asia/Pacific (231/14,138) C. freundii (X. cyricola KPC-2 (10) KPC-2 (1) (X- sergenes KPC-2 (10) NDM-1 (1) (X-			KPC-3 (3)					VIM-44 (1)
KPC-3 (257) OXA-163 (2) NDM-16 (2) VIM-32 (1) KPC-9 (2) OXA-181 (1) VIM-32 (1) VIM-32 (1) OXA-232 (6) OXA-481 (1) NDM-1 (1) VIM-42 (1) P. mirabilis OXA-48 (1) NDM-1 (1) VIM-12 (1) P. retugeri OXA-48 (2) NDM-1 (1) VIM-1 (1) P. struttii OXA-48 (3) NDM-1 (1) VIM-1 (1) R. pianticola OXA-48 (3) NDM-1 (1) VIM-1 (1) S. marcescens OXA-48 (3) NDM-1 (1) VIM-12 (1) Latin America (525/13,046) C. freundii KPC-2 (2) VIM-23 (1) VIM-23 (1) Latin America (525/13,046) C. freundii KPC-2 (2) VIM-23 (2) VIM-23 (2) K aerogenes KPC-2 (2) KPC-2 (2) NDM-1 (1) VIM-23 (2) K aerogenes KPC-2 (2) MDM-1 (2) VIM-23 (2) VIM-23 (2) K aerogenes KPC-2 (10) GES-2 (1) OXA-163 (4) NDM-1 (1) VIM-23 (2) K aerogenes KPC-2 (10) GES-2 (1) OXA-161 (4) NDM-1		K. pneumoniae	KPC-2 (338)	GES-6 (1)	OXA-48 (347)		NDM-1 (88)	VIM-1 (24)
KPC-9 (2) OXA-163 (2) VIII-26 (15) KPC-type (2) OXA-181 (1) VIII-42 (1) OXA-232 (6) OXA-232 (12) VIII-42 (1) DXA-232 (6) OXA-48 (1) NDM-1 (1) VIII-41 (1) P. mirabilis OXA-48 (3) NDM-1 (1) VIII-1 (1) P. stuartii OXA-48 (3) NDM-1 (1) VIII-1 (1) R aonithinolytica OXA-48 (3) NDM-1 (2) VIII-1 (1) S. marcescens OXA-48 (3) NDM-1 (2) VIII-23 (1) Latin America (525/13,046) C. freundii KPC-2 (7) VIII-23 (1) VIII-23 (1) E. colo KPC-2 (10) GES-2 (1) OXA-48 (2) VIII-23 (2) E. colo cace KPC-2 (2) NDM-1 (1) VIII-23 (2) K. aerogenes KPC-2 (10) GES-2 (1) NDM-1 (1) VIII-24 (1) K. varicola KPC-2 (10) GES-2 (1) NDM-1 (2) VIII-24 (1) K. varicola KPC-2 (10) GES-2 (1) NDM-1 (2) VIII-24 (1) K. varicola KPC-2 (10) GES-2 (1) NDM-1 (1) </td <td></td> <td></td> <td>KPC-3 (257)</td> <td></td> <td>OXA-162 (3)</td> <td></td> <td>NDM-16 (2)</td> <td>VIM-12 (1)</td>			KPC-3 (257)		OXA-162 (3)		NDM-16 (2)	VIM-12 (1)
KPC-type (2) OXA-181 (1) VIM-42 (1) OXA-232 (6) OXA-232 (12) OXA-232 (12) OXA-244 (12) OXA-48 (3) NDM-1 (1) VIM-1 (1) P. mirabilis OXA-48 (3) NDM-1 (1) VIM-1 (1) P. tertgeri OXA-48 (3) NDM-1 (1) VIM-1 (1) R. ornithinolytica OXA-48 (3) NDM-1 (1) VIM-1 (1) R. ornithinolytica OXA-48 (3) NDM-1 (2) VIM-1 (1) S. marcescens OXA-48 (3) NDM-1 (2) VIM-1 (1) Latin America (525/13,046) C. freundii KPC-2 (7) NDM-1 (6) VIM-23 (1) Latin America (525/13,046) C. freundii KPC-2 (7) NDM-1 (6) VIM-23 (1) Latin America (525/13,046) C. freundii KPC-2 (7) NDM-1 (1) VIM-23 (2) E. coli K. percogenes KPC-2 (2) NDM-1 (1) VIM-23 (2) K. aerogenes KPC-2 (10) GES-2 (1) OXA-163 (4) NDM-1 (1) K. percogenes KPC-2 (10) OXA-32 (1) NDM-1 (1) VIM-24 (1) K. variicol			KPC-9 (2)		OXA-163 (2)			VIM-26 (15)
OXA-224 (12) OXA-244 (12) OXA-244 (12) OXA-48 (1) NDM-1 (1) VIM-1 (5) P. rettgeri OXA-48 (3) NDM-1 (11) VIM-1 (14) P. stuartii OXA-48 (2) VIM-1 (11) VIM-1 (11) R. prinitrihinolytica OXA-48 (2) VIM-1 (11) VIM-1 (11) S. marcescens OXA-48 (3) NDM-1 (2) VIM-1 (1) Latin America (525/13,046) C. freundii KPC-2 (7) VIM-23 (1) VIM-23 (1) Latin America (525/13,046) C. freundii KPC-2 (2) NDM-1 (6) VIM-23 (1) E. coli KPC-2 (19) NDM-1 (6) VIM-12 (2) VIM-23 (2) E. coli KPC-2 (10) GES-2 (1) NDM-1 (6) VIM-23 (2) K. aerogenes KPC-2 (10) GES-2 (1) NDM-1 (1) VIM-23 (2) K. aerogenes KPC-2 (10) GES-2 (1) NDM-1 (1) VIM-23 (2) K. aerogenes KPC-2 (10) GES-2 (1) NDM-1 (1) VIM-24 (1) K. variicola KPC-2 (10) OXA-370 (1) NDA-1 (1) VIM-24 (1)			KPC-type (2)		OXA-181 (1)			VIM-42 (1)
P. mirabilis OXA-48 (1) NDM-1 (1) VIM-1 (5) P. rettgeri OXA-48 (3) NDM-1 (11) VIM-1 (1) P. stuarii OXA-48 (3) NDM-1 (11) VIM-1 (11) R. ornithinolytica OXA-48 (3) NDM-1 (12) VIM-1 (11) R. ornithinolytica OXA-48 (3) NDM-1 (2) VIM-1 (11) S. marcescens OXA-48 (3) NDM-1 (2) VIM-1 (11) Latin America (525/13,046) C. freundii KPC-2 (7) VIM-23 (2) Latin America (525/13,046) C. freundii KPC-2 (19) NDM-1 (6) VIM-23 (1) Latin America (525/13,046) C. freundii KPC-2 (19) NDM-1 (6) VIM-23 (2) Latin America (525/13,046) C. freundii KPC-2 (10) GES-2 (1) OXA-48 (3) NDM-1 (1) Latin America (525/13,046) C. freundii KPC-2 (2) NDM-1 (10) VIM-23 (2) Latin America (525/13,046) C. freundii KPC-2 (10) GES-2 (1) OXA-48 (4) NDM-1 (1) VIM-23 (2) Latin America (525/13,046) KPC-2 (10) GES-2 (1) OXA-163 (4) NDM-1 (1) VIM-23 (2) K coacae KPC-2					OXA-232 (6)			
P. mirabilis OXA-48 (1) NDM-1 (1) VIM-1 (1) P. rettgeri OXA-48 (2) VIM-1 (1) VIM-1 (1) P. stuartii OXA-48 (2) VIM-1 (1) VIM-1 (1) R. planticola OXA-48 (2) VIM-1 (1) VIM-1 (1) S. marcescens OXA-48 (3) NDM-1 (2) VIM-1 (1) Latin America (525/13,046) C. freundii KPC-2 (7) VIM-23 (1) L. Koseri KPC-2 (2) E. cobince KPC-2 (2) E. coli KPC-2 (14) GES-2 (1) OXA-232 (1) NDM-1 (6) VIM-23 (2) K. aerogenes KPC-2 (14) GES-2 (1) OXA-323 (1) NDM-1 (1) VIM-23 (2) K. aerogenes KPC-2 (14) GES-2 (1) OXA-323 (1) NDM-1 (1) VIM-24 (1) K. Caytora KPC-2 (10) GES-2 (1) OXA-330 (1) VIM-24 (1) VIM-24 (1) K. Variicola KPC-2 (10) KPC-3 (1) OXA-330 (1) NDM-1 (5) VIM-24 (1) MDM-1 (2) K. variicola KPC-2 (10) NDM-1 (5) NDM-1 (5) NDM-1 (5) Asia/Pacific (231/14,138) C. farmeri IMP-4 (7) ND					OXA-244 (12)			
P. retrigeri OXA-48 (3) NDM-1 (11) VIM-1 (11) P. stuartii OXA-48 (2) VIM-1 (11) VIM-1 (11) R. omithinolytica OXA-48 (3) NDM-1 (11) VIM-1 (11) S. marcescens OXA-48 (3) NDM-1 (2) VIM-1 (11) Latin America (525/13,046) C. freundii KPC-2 (7) VIM-23 (1) E. asburiae KPC-2 (2) NDM-1 (6) VIM-23 (1) E. colacae KPC-2 (2) NDM-1 (1) VIM-23 (2) K. aerogenes KPC-2 (10) GES-2 (1) OXA-48 (4) NDM-1 (1) K. pneumoniae KPC-2 (2) NDM-1 (1) VIM-23 (2) K. aerogenes KPC-2 (10) GES-2 (1) IMP-8 (2) NDM-1 (1) K. pneumoniae KPC-2 (10) GES-2 (1) IMP-8 (2) NDM-1 (1) K. variicola KPC-2 (10) GXA-320 (1) NDM-1 (24) VIM-24 (1) K. variicola KPC-2 (10) OXA-181 (1) NDM-1 (5) IMP-4 (7) NDM-1 (5) Asia/Pacific (231/14,138) C. farmeri IMP-4 (7) NDM-1 (5) IMP-4 (7) NDM-1 (5) S. marcescens KPC-2 (1)		P. mirabilis			OXA-48 (1)		NDM-1 (1)	VIM-1 (5)
Asia/Pacific (231/14,138) C. farmeri KPC-2 (1) VIM-1 (1) VIM-1 (1) Asia/Pacific (231/14,138) C. farmeri KPC-2 (1) VIM-1 (1) VIM-1 (1) Asia/Pacific (231/14,138) C. farmeri KPC-2 (1) VIM-1 (1) VIM-23 (2) Asia/Pacific (231/14,138) C. farmeri KPC-2 (1) VIM-23 (1) VIM-23 (2) Asia/Pacific (231/14,138) C. farmeri KPC-2 (1) VIM-23 (1) VIM-23 (2) K. variicola KPC-2 (1) OXA-48 (4) NDM-1 (6) VIM-1 (2) Asia/Pacific (231/14,138) C. farmeri KPC-2 (10) GES-2 (1) IMP-8 (2) NDM-1 (1) K. variicola KPC-2 (1) OXA-163 (4) NDM-1 (2) VIM-23 (2) K. variicola KPC-2 (10) OXA-163 (4) NDM-1 (1) VIM-23 (2) K. variicola KPC-2 (10) OXA-163 (4) NDM-1 (1) VIM-24 (1) K. variicola KPC-2 (1) NDM-1 (1) NDM-1 (2) VIM-24 (1) K. variicola KPC-2 (1) NDM-1 (1) NDM-1 (5) NDM-1 (6) K. variicola KPC-2 (1) NDM-1 (1) NDM-1 (2) NDM-1 (2)		P. rettgeri			OXA-48 (3)		NDM-1 (11)	VIIVI-1(1)
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Asia/Pacific (231/14,138) C, farmeri K PC-2 (1) VIM-1 (1) Asia/Pacific (231/14,138) C, farmeri K PC-2 (1) VIM-1 (1) Asia/Pacific (231/14,138) C, farmeri K PC-2 (1) VIM-1 (1) C, koseri KPC-2 (1) VIM-1 (2) VIM-1 (1) MDM-1 (2) VIM-1 (1) VIM-23 (3) VIM-23 (3) E, coli K PC-2 (19) VIM-23 (2) NDM-1 (6) VIM-23 (2) K, arengenes KPC-2 (10) GES-2 (1) OXA-163 (4) NDM-1 (1) VIM-23 (2) K, pneumoniae KPC-2 (10) GES-2 (1) OXA-370 (1) NDM-1 (2) VIM-24 (1) MPC-3 (49) OXA-370 (1) NDM-1 (5) VIM-24 (1) NDM-1 (5) MPC-2 (10) KPC-2 (10) OXA-181 (1) NDM-1 (5) VIM-24 (1) MP-8 (2) NDM-1 (1) NDM-1 (5) NDM-1 (5) VIM-24 (1) MPC-1 (1) K KPC-2 (10) OXA-181 (1) NDM-1 (5) NDM-1 (5) E, cloacae KPC-2 (1) MP-8 (2) NDM-1 (1) NDM-1 (1) NDM-1 (1) MP-8 (2) NDM-1 (1) NDM-1 (1) NDM-1 (1)		R. officiality incu P. planticola			OXA-48 (2)			VIIVI-I (I)
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Latin America (525/13,046) C. freundii E. cisouriae KPC-2 (7) KPC-2 (3) E. asburiae VIM-23 (1) KPC-2 (2) E. cloacae VIM-23 (1) KPC-2 (19) E. colacae KPC-2 (19) NDM-1 (6) VIM-1 (2) VIM-23 (3) E. colacae KPC-2 (19) NDM-1 (6) VIM-23 (2) K. aerogenes KPC-2 (10) GES-2 (1) OXA-232 (1) NDM-1 (1) VIM-23 (2) K. aerogenes KPC-2 (346) OXA-163 (4) NDM-1 (1) VIM-23 (2) VIM-24 (1) K. preumoniae KPC-2 (10) GES-2 (1) OXA-332 (1) NDM-1 (1) VIM-24 (1) KPC-3 (10) OXA-370 (1) OXA-370 (1) NDM-1 (5) NDM-1 (1) K. variicola KPC-2 (10) OXA-181 (1) NDM-1 (5) NDM-1 (5) Asia/Pacific (231/14,138) C. farmeri KPC-2 (10) NDM-1 (1) NDM-1 (5) Asia/Pacific (231/14,138) C. farmeri KPC-2 (1) NDM-1 (1) NDM-1 (1) C. koseri KPC-2 (1) IMP-8 (2) NDM-7 (4) NDM-1 (1) MP-4 (7) NDM-1 (1) NDM-7 (4) NDM-7 (4) NDM-7 (4) </td <td>5. marcescens</td> <td></td> <td></td> <td>0/07 40 (4)</td> <td></td> <td></td> <td>VIM-4 (1)</td>		5. marcescens			0/07 40 (4)			VIM-4 (1)
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Latin America (525/15,046) C. <i>Ireutiali</i> NPC-2 (7) VIM-23 (1) C. <i>koseri</i> KPC-2 (3) <i>E. colacae</i> KPC-2 (19) NDM-1 (6) VIM-23 (3) <i>E. coli</i> KPC-2 (14) GES-2 (1) OXA-232 (1) NDM-1 (6) VIM-23 (2) <i>K. aerogenes</i> KPC-2 (6) <i>K. oxytoca</i> KPC-2 (10) GES-2 (1) IMP-8 (2) NDM-1 (1) KPC-33 (2) <i>K. pneumoniae</i> KPC-2 (346) OXA-163 (4) NDM-1 (24) VIM-23 (2) <i>KPC</i> -3 (49) OXA-232 (1) VIM-24 (1) <i>KPC</i> -3 (01) OXA-370 (1) <i>KPC</i> -3 (01) OXA-370 (1) <i>KPC</i> -3 (01) OXA-370 (1) <i>KPC</i> -2 (10) <i>KPC</i> -2 (10) <i>KPC</i> -2 (10) <i>KPC</i> -2 (10) <i>KPC</i> -2 (10) <i>Asia/Pacific</i> (231/14,138) <i>C. farmeri</i> <i>R. ornithinolytica</i> KPC-2 (10) <i>IMP</i> -4 (2) NDM-1 (5) <i>IMP</i> -8 (2) NDM-1 (5) <i>IMP</i> -8 (2) NDM-1 (1) <i>S. marcescens</i> KPC-2 (10) <i>IMP</i> -4 (2) NDM-1 (1) <i>E. cloacae</i> KPC-2 (1) <i>IMP</i> -4 (1) NDM-1 (1) <i>IMP</i> -4 (1) NDM-1 (1) <i>IMP</i> -4 (3) NDM-7 (2) <i>IMP</i> -4 (3) NDM-7 (4) <i>IMP</i> -4	Latin America (525/12.046)	C fraundii						
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Asia/Pacific (231/14,138) C. farmeri C. freundii C. koseri E. cloacae KPC-2 (10) KPC-2 (10) KPC		R. ornitninolytica	KPC-3 (1)		UXA-181 (1)			
Asia/Pacific (231/14,138) C. farmeri C. freundii C. freundii C. koseri E. cloacae KPC-2 (1) KPC-		S. marcescens	KPC-2 (10)					
Asia/Pacific (231/14,138) C. farmeri NDM-1 (1) C. freundii IMP-4 (7) NDM-1 (5) IMP-8 (2) NDM-7 (4) NDM-1 (1) E. asburiae IMP-8 (1) NDM-1 (1) E. cloacae KPC-2 (1) IMP-14 (1) NDM-7 (2) E. cloacae KPC-2 (1) IMP-1 (1) NDM-7 (4) IMP-4 (3) NDM-7 (4) IMP-4 (3) NDM-7 (4)								
C. freundii IMP-4 (7) NDM-1 (5) IMP-8 (2) NDM-7 (4) C. koseri KPC-2 (1) IMP-8 (1) NDM-1 (1) E. asburiae IMP-4 (1) NDM-1 (1) IMP-14 (1) NDM-7 (2) E. cloacae KPC-2 (1) IMP-1 (1) NDM-7 (4) IMP-4 (3) NDM-7 (4) IMP-8 (1)	Asia/Pacific (231/14,138)	C. farmeri					NDM-1 (1)	
IMP-8 (2) NDM-7 (4) C. koseri KPC-2 (1) NDM-1 (1) E. asburiae IMP-8 (1) NDM-1 (1) E. cloacae KPC-2 (1) IMP-14 (1) NDM-7 (2) IMP-4 (3) NDM-7 (4) IMP-8 (1)		C. freundii				IMP-4 (7)	NDM-1 (5)	
C. koseri KPC-2 (1) NDM-1 (1) E. asburiae IMP-8 (1) NDM-1 (1) IMP-14 (1) NDM-7 (2) E. cloacae KPC-2 (1) IMP-1 (1) NDM-1 (17) IMP-4 (3) NDM-7 (4) IMP-9 (1)						IMP-8 (2)	NDM-7 (4)	
E. asburiae IMP-8 (1) NDM-1 (1) IMP-14 (1) NDM-7 (2) E. cloacae KPC-2 (1) IMP-1 (1) NDM-1 (17) IMP-4 (3) NDM-7 (4) IMP-9 (1)		C. koseri	KPC-2 (1)				NDM-1 (1)	
E. cloacae KPC-2 (1) IMP-1 (1) NDM-7 (2) IMP-1 (1) NDM-1 (17) IMP-4 (3) NDM-7 (4) IMP-9 (1)		E. asburiae						
E. Cloucue RPC-2 (1) IMP-1 (1) IMD-1 (17) IMP-4 (3) NDM-7 (4) IMD-8 (1)		E cloacao	KDC 2 (1)			IIVIP-14(1)	NDN 1 (17)	
וועוד־+ (כ) ועטעידע (+) ואסבע (1)		E. CIOUCUE	NPC-2(1)			IIVIP-1 (1)	NDM-7 (4)	
						IMP_Q (1)	NUIVI-7 (4)	

Persion (no. of CPE/		Carbapenem	ase type/varian	t (no. of isolates)			
no. of collected isolates) ^a	Organism	КРС	GES	OXA-48-like	IMP	NDM	VIM
					IMP-14 (2)		
					IMP-26 (1)		
	E. kobei	KPC-2 (1)					
	E. coli	KPC-2 (5)		OXA-181 (3)	IMP-59 (1)	NDM-1 (3)	
						NDM-5 (9)	
	K garaganas	kp(2)				NDM-7 (3)	
	K. derogenes	KPC-2 (3)			IIVIP-0 (1)		
	R. Oxytoca	KFC-2 (3)			IIVIF-4 (J)	NDM-7 (1)	
	K pneumoniae	KPC-2 (45)	GES-5 (1)	OXA-48 (5)	IMP-1 (2)	NDM-1 (45)	
	n. pricumoniae	KPC-12 (1)		OXA-181 (7)	IMP-4 (10)	NDM-4 (1)	
		KPC-17(1)		OXA-232 (10)	IMP-26 (5)	NDM-5 (1)	
					== (=)	NDM-7 (12)	
	P. mirabilis				IMP-26 (1)	NDM-1 (1)	
	P. rettgeri					NDM-1 (2)	
	P. stuartii						VIM-1 (1)
	S. marcescens	KPC-2 (1)			IMP-4 (1)		
					IMP-8 (1)		
					IMP-47 (1)		
Middle East/Africa (126/6,971)	C. freundii	KPC-2 (1)		OXA-181 (1)		NDM-1 (1)	
	E. asburiae			OXA-48 (1)		NDM-1 (1)	
	E. cloacae	KPC-2 (1)		OXA-48 (3)		NDM-1 (4)	VIM-4 (4)
		KPC-3 (1)		OXA-181 (1)			
	E. kobei			OXA-48 (2)			
	E. coli	KPC-2 (2)				NDM-1 (1)	
		KPC-3 (1)				NDM-5 (2)	
	K. aerogenes	KPC-2 (1)				NDM-1 (1)	
	K. oxytoca					NDM-1 (1)	VIM-1 (2)
	K. pneumoniae	KPC-2 (6)		OXA-48 (5)		NDM-1 (27)	VIIVI-I (I)
		KPC-3 (13)		OXA-181 (16)		NDM-5 (2)	
	D mirchilic			OXA-232 (12)		NDM-7 (5)	$VINA \in (A)$
	P. mildonis P. rettaeri					NDM-1 (5)	VIIVI-J (4)
	P stuartii					NDM-1 (1)	
	r. staarth						
North America (87/7,475)	C. farmeri	KPC-3 (1)					
	C. freundii	KPC-2 (3)					VIM-1 (1)
	E. asburiae	KPC-2 (2)					VIIVI-52 (1)
	E. cloacae	KPC-2 (1)					VIM-1 (1)
	E. coli	KPC-2 (2)					
		KPC-3 (3)					
		KPC-18 (2)					
	K. pneumoniae	KPC-2 (17)	GES-20 (1)			NDM-1 (2)	
		KPC-3 (49)					
		KPC-29 (1)					

^aMeropenem-nonsusceptible carbapenemase-positive isolates from Europe were collected in Austria, Belgium, the Czech Republic, Denmark, France, Germany, Greece, Hungary, Italy, the Netherlands, Poland, Portugal, Romania, Russia, Spain, Turkey, and the United Kingdom. Isolates from Latin America were collected in Argentina, Brazil, Chile, Colombia, Mexico, and Venezuela. Isolates from Asia/South Pacific were collected in Australia, China, Japan, Malaysia, the Philippines, South Korea, Taiwan, and Thailand. Isolates from Middle East/Africa were collected in Israel, Kenya, Kuwait, Nigeria, and South Africa. Isolates from North America were collected in the United States. Isolates carrying multiple carbapenemases were counted for each individual carbapenemase type.

were also found among *K. pneumoniae* (>80% of OXA-48-like positive isolates collected in Europe, Asia/South Pacific, and Middle East/Africa). Although a large proportion of the MBLs identified globally were also carried by *K. pneumoniae* (271 of 548, 49.5%), the incidence of other species or species groups was markedly enriched among MBL-positive isolates, including *E. cloacae* (n = 107, 19.5%), *Citrobacter freundii* (n = 40, 7.3%), *E. coli* (n = 34, 6.2%) and the Proteeae (n = 51, 9.3%) (Table 1).

A total of 67.3% (1,516 of 2,253) of all carbapenemase-positive isolates identified globally cocarried at least one additional plasmid-mediated or intrinsic chromosomally

encoded ESBL, AmpC β -lactamase or carbapenemase, including 49.2% (622 of 1,263) of KPC-positive isolates, 83.3% (5 of 6) of GES-positive isolates, 90.9% (460 of 506) of OXA-48-like-positive isolates, and 91.1% (499 of 548) of MBL-positive isolates (Table 2). Seventy-one isolates cocarrying two carbapenemases were collected in the Europe (n = 42), Asia/South Pacific (n = 20), Latin America (n = 6), and Middle East/Africa (n = 3) regions (Table 2 and Fig. 2B to E). These isolates were composed of 54 *K. pneumoniae*, six *C. freundii*, four *E. cloacae*, three *E. coli*, three *K. oxytoca*, and one *Providencia rettgeri* cocarrying NDM-type and OXA-48-like (n = 44), VIM-type and OXA-48-like (n = 8), VIM-type and KPC-type (n = 7), KPC-type and OXA-48-like (n = 4), KPC-type and NDM- or IMP-type (n = 2 of each), GES-type and NDM- or KPC-type (n = 2 and n = 1, respectively), and VIM-type and NDM-type (n = 1) carbapenemases. A total of 87.3% (62 of 71) of these isolates also harbored ESBLs or AmpC β -lactamases (Table 2).

The percentage of meropenem-nonsusceptible Enterobacterales collected over the course of this study increased from 2.7% of isolates collected globally in 2012 to 2014 to 3.8% of isolates collected in 2015 to 2017 (Fig. 3). At the regional level, the percentage of meropenem-nonsusceptibility increased among isolates collected in Europe (2.8% versus 4.3%), Asia/South Pacific (1.5% versus 2.6%), and Latin America (5.1% versus 5.4%) was stable among isolates collected in the Middle East/Africa (2.04% versus 1.97%) and decreased among isolates collected in North America (1.6% versus 1.0%). This overall increase could be attributed to the increasing proportion of carbapenemase-positive isolates that was observed, most notably among isolates carrying NDM-type MBLs in Asia/South Pacific, Europe, and Latin America; OXA-48-like carbapenemases in Europe, Middle East/Africa, and Asia/ South Pacific; KPC-type carbapenemases in Latin America; and VIM-type MBLs in Europe (Fig. 3). When countries that participated only or primarily during the 2012 to 2014 time period (China, Hong Kong, Malaysia, Kenya, and Nigeria) were removed from analysis, a larger increase in the percentage of meropenem-nonsusceptible Enterobacterales and increases in KPC-positive isolates and NDM-positive isolates were also revealed in the Asia/South Pacific and Middle East/Africa regions, respectively (see Fig. S4).

DISCUSSION

This 2012-2017 global surveillance study provided a perspective on the incidence and carbapenemase carriage of meropenem-nonsusceptible Enterobacterales, which varied by geographic region, as reported by others (4–8, 15). Though it is difficult to compare results from independent studies that differ in study design and participation, others have reported broadly similar percentages of meropenem- or imipenem-resistant Enterobacterales (ranging between 1.2 and 1.9% of isolates collected in North America, 1.3 and 3.1% of isolates collected in the Asia/Pacific region, 3.2 and 3.7% of isolates collected in Europe, and 3.5 and 8.4% of isolates collected in Latin America) among isolates collected in 2014 to 2016 (16-18). Similar to other studies, the highest incidence of CRE was observed among K. pneumoniae (19-21). KPC-type, OXA-48-like, and MBL carbapenemases were each found among 14 to 15 Enterobacterales species, but KPC enzymes were predominantly carried by K. pneumoniae, and OXA-48-like enzymes were found mostly among K. pneumoniae and E. coli, in agreement with other reports (7, 22), whereas MBLs were proportionately more common among meropenem-nonsusceptible isolates of Enterobacter spp., Citrobacter spp., the Proteeae, and E. coli (20, 23). As observed by others, the majority of CRE isolates cocarried ESBLs and/or AmpC enzymes, and a number of isolates carried multiple carbapenemases (8). The production of multiple β -lactamases from different Ambler classes, likely encoded on multiple plasmids potentially harboring additional non- β -lactam resistance mechanisms, further adds to the challenges of effectively treating infections caused by these organisms (8, 24).

The overall geographical distribution of *Enterobacterales* isolates carrying different carbapenemase types reported in the present study agreed with published

	β -Lactamase types ^a		No. of		
Region	(no. of isolates)	Organism ^b	isolates	Molecular variant(s)	
Europe	GES carbapenemase + ESBL + AmpC + OSBL (1)	E. cloacae*	1	GES-6, CTX-M-15, TEM-OSBL	
	KPC \pm OSBL and/or spectrum	E. coli	1	KPC-2	
	undefined (346)		1	KPC-2, TEM-OSBL	
			6	KPC-3, TEM-OSBI	
		K. nneumoniae	3	KPC-2	
		n. pricamoniae	19	KPC-2 SHV-OSBI	
			1	KPC-2 TEM-OSBI	
			116	KPC-2 SHV-OSBL TEM-OSBL	
			3	KPC-3	
			30		
			20		
			162	KPC-3 SHV-OSBL TEM-OSBL	
			102	KPC-3 SHV-26 TEM-OSBI	
			1	KPC-3 SHV-26, TEM-OSBL	
	KPC + ESPI + OSPI (220)	E coli	1		
	KFC + ESBL = OSBL(239)	E. COII	1	KPC-2, CTX-IN-13, TEM-OSDL	
		Kovatocat	1	KPC 2	
		K. OXYLOCU	1		
			1		
			1	KPC-2, SHV-5, TEIVI-OSBL	
			1		
		K management	2		
		ĸ. pneumoniae		KPC-2, CTX-M-15, TEM-OSBL	
			26	KPC-2, CTX-M-15, SHV-OSBL, TEM-OSBL	
			1	KPC-2, CTX-M-27, SHV-OSBL, TEM-OSBL	
			1	KPC-2, SHV-5, TEM-OSBL	
			3/	KPC-2, SHV-12	
			81	KPC-2, SHV-12, TEM-OSBL	
			1	KPC-2, VEB-1, SHV-OSBL	
			21	KPC-2, VEB-1, SHV-OSBL, TEM-OSBL	
			1	KPC-2, VEB-1, SHV-12, TEM-OSBL	
			1	KPC-3, CTX-M-1, SHV-OSBL, TEM-OSBL	
			2	KPC-3, CTX-M-14, SHV-OSBL, TEM-OSBL	
			1	KPC-3, CTX-M-15	
			2	KPC-3, CTX-M-15, SHV-OSBL	
			47	KPC-3, CTX-M-15, SHV-OSBL, TEM-OSBL	
			1	KPC-3, CTX-M-15, SHV-28, TEM-OSBL	
			1	KPC-3, CTX-M-15, SHV-168, TEM-OSBL	
			2	KPC-3, SHV-12, TEM-OSBL	
			2	KPC-9, VEB-1, SHV-OSBL, TEM-OSBL	
			2	KPC-TYPE, CTX-M-15, SHV-OSBL, TEM-OSBL	
	KPC + AmpC \pm OSBL (25)	C. amalonaticus*	1	KPC-2, TEM-OSBL	
		C. freundii*	2	KPC-2, TEM-OSBL	
		E. cloacae*	1	KPC-2, TEM-OSBL	
			1	KPC-3	
		K. pneumoniae	1	KPC-2, ACT-TYPE, SHV-OSBL	
			8	KPC-2, CMY-4, SHV-OSBL	
			10	KPC-2, CMY-4, SHV-OSBL, TEM-OSBL	
			1	KPC-3, CMY-4, SHV-OSBL, TEM-OSBL	
	KPC + ESBL + AmpC \pm	C. freundii*	1	KPC-3, SHV-12	
OSE	OSBL (5)	E. cloacae*	1	KPC-2, CTX-M-15, TEM-OSBL	
		K. aerogenes*	1	KPC-2, VEB-1, TEM-OSBL	
		K. pneumoniae	2	KPC-2, CTX-M-15, MOX-2, SHV-OSBL, TEM-OSBL	
	KPC + GES carbapenemase + OSBL (1)	K. pneumoniae	1	KPC-2, GES-6, SHV-OSBL, TEM-OSBL	
	KPC + OXA-48-like + OSBL (1)	K. pneumoniae	1	KPC-2, OXA-163, SHV-OSBL, TEM-OSBL	
	OXA-48-like \pm OSBL (38)	E. coli	1	OXA-48, TEM-OSBL	

TABLE 2 Cocarriage of carbapenemases and other β -lactamases in 2,253 meropenem-nonsusceptible carbapenemase-positive *Enterobacterales* collected from 2012 to 2017

	eta -Lactamase types a		No. of	
Region	(no. of isolates)	Organism ^b	isolates	Molecular variant(s)
		K. pneumoniae	18	OXA-48, SHV-OSBL
			11	OXA-48, SHV-OSBL, TEM-OSBL
			2	OXA-232, SHV-OSBL
		P. mirabilis	1	OXA-48
		R. ornithinolytica	2	OXA-48
		R. planticola	3	OXA-48
	OXA-48-like + ESBL \pm	E. coli	6	OXA-48, CTX-M-15, TEM-OSBL
	OSBL (322)		1	OXA-48, CTX-M-24, TEM-OSBL
			1	OXA-244, CTX-M-15, TEM-OSBL
		K. oxytoca†	2	OXA-48
			3	OXA-48, TEM-OSBL
			1	OXA-48, CTX-M-14, CTX-M-27
		K. pneumoniae	2	OXA-48, CTX-M-3, SHV-OSBL
			6	OXA-48, CTX-M-3, SHV-OSBL, TEM-OSBL
			1	OXA-48, CTX-M-9-type, SHV-OSBL
			3	OXA-48, CTX-M-9-type, SHV-OSBL, TEM-OSBL
			1	OXA-48, CTX-M-14
			3	
			17	OXA-48, CTX-M-14, SHV-OSBL, TEM-OSBL
			2	OXA-48, CTX-M-14, CTX-M-15, SHV-OSBL, TEM-OSBL
			1	OXA-48, CTX-W-14, CTX-W-27, SHV-OSBL, TEM-OSBL
			Z 75	
			15	
			100	
			ו כ	
			2	OXA-48, $CTX-M-28$, $SHV-OSBL$, $TEW-OSBL$
			2	OXA-48, CTX-M-28, SHV-OSBL
			1	OXA 40, CTX-M-20, STW OSDE, TEM OSDE
			2	OXA-48, CTX-M-55, SHV-OSBI
			1	OXA-48 SHV-FSBI
			1	OXA-48 SHV-ESBL TEM-OSBL
			3	OXA-162. CTX-M-15. SHV-OSBL. TEM-OSBL
			1	OXA-163, CTX-M-3, SHV-OSBL, TEM-OSBL
			1	OXA-181, CTX-M-15, SHV-OSBL
			1	OXA-232, CTX-M-15, SHV-OSBL
			2	OXA-244, CTX-M-15, SHV-OSBL
			10	OXA-244, CTX-M-15, SHV-OSBL, TEM-OSBL
	OXA-48-like + AmpC \pm	C. amalonaticus*	1	OXA-48
	OSBL (17)	C. freundii*	1	OXA-48
			1	OXA-48, TEM-OSBL
		E. cloacae*	3	OXA-48
			1	OXA-162, ACC-4, DHA-1, TEM-OSBL
		E. coli	1	OXA-181, CMY-42
		K. aerogenes*	3	OXA-48
		K. pneumoniae	2	OXA-48, DHA-1, SHV-OSBL
		P. rettgeri*	1	OXA-48, TEM-OSBL
		S. marcescens*	3	OXA-48
	OXA-48-like + ESBL +	E. cloacae*	1	OXA-48, CTX-M-9-type, SHV-12
	AmpC \pm OSBL (22)		1	OXA-48, CTX-M-15, SHV-OSBL
			4	OXA-48, CTX-M-15, TEM-OSBL
			1	OXA-48, SHV-12, TEM-OSBL
		E. coli	6	OXA-181, CTX-M-15, CMY-42
		K. aerogenes*	1	OXA-48, CTX-M-15, TEM-OSBL
		K. pneumoniae	2	OXA-48, CTX-M-15, CMY-6, SHV-OSBL, TEM-OSBL
			3	OXA-48, CTX-M-15, DHA-1, SHV-OSBL, TEM-OSBL
		P. rettgeri*	2	OXA-48, PER-1, TEM-OSBL
		S. marcescens*	1	OXA-48, CTX-M-22, SHV-OSBL
	MBL \pm OSBL (25)	E. coli	2	NDM-1, TEM-OSBL
			2	NDM-5
			1	VIM-1
			1	VIM-1, SHV-OSBL

	β -Lactamase types ^a		No. of	
Region	(no. of isolates)	Organism ^b	isolates	Molecular variant(s)
		K. pneumoniae	5	NDM-1, SHV-OSBL
			1	VIM-1
			12	VIM-1, SHV-OSBL
			1	VIM-12, SHV-OSBL
	$MBL + ESBL \pm OSBL$ (74)	E. coli	1	NDM-5, CTX-M-15
		K. oxytoca†	1	VIM-1, CTX-M-3, SHV-12
			1	VIM-1, SHV-12
			1	VIM-44, SHV-12
		K. pneumoniae	25	NDM-1, CTX-M-15, SHV-OSBL
			21	NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL
			1	
			1	NDIVI-10, CTX-IVI-15, SHV-12, TEM-OSBL
			ן ר	VIN 1 CIVETS, STV-ESDL, TEN-OSDL
			2	VIM-1, SHV-3 VIM-1, SHV-12
			1	VIM-1 SHV-FSRI
			12	VIM-26 SHV-5
			1	VIM-26, SHV-FSBI
			1	VIM-42, SHV-12
		P. mirabilis	1	VIM-1, VEB-1, SHV-5, TEM-OSBI
	$MBL + AmpC \pm OSBL (56)$	C. freundii*	1	VIM-1
			1	VIM-1, TEM-OSBL
			1	VIM-1, FOX-7, TEM-OSBL
			1	VIM-4, TEM-OSBL
		E. asburiae*	1	VIM-1
		E. cloacae*	2	NDM-1
			11	VIM-1
			22	VIM-1, TEM-OSBL
			1	VIM-2
			1	VIM-4
		E. coli	1	NDM-1, CMY-6, TEM-OSBL
			1	NDM-5, CMY-42
		K. aerogenes*	2	NDM-1, CMY-4
		K. pneumoniae	2	NDM-1, CMY-6, SHV-OSBL
		P. mirabilis	4	VIM-1, CMY-16, TEM-OSBL
		P. rettgeri*	1	NDM-1, VIM-1
		R. ornithinolytica	1	VIM-1, CMY-13
		S. marcescens*	1	VIM-4
	MPL + ESPL + AmpC +	C formari*	ו ר	
	OSPL(72)	C. Turmen C. froundii*	2	
	03BE (73)	C. Ileunun	1	VIM-1, SHV-12 VIM-4 SHV-12
		E cloacae*	4	NDM-1 CTX-M-15
		L. cloucue	4	NDM-1 CTX-M-15 TEM-OSBI
			1	NDM-1 CTX-M-15 SHV-12 TEM-OSBI
			1	VIM-1, CTX-M-3, SHV-12, DHA-1, TEM-OSBL
			1	VIM-1, CTX-M-9-type
			1	VIM-1, CTX-M-9-type, SHV-12
			1	VIM-1, CTX-M-14, TEM-OSBL
			1	VIM-1, CTX-M-15, TEM-OSBL
			1	VIM-1, SHV-12
			3	VIM-1, SHV-12, TEM-OSBL
			1	VIM-4, CTX-M-9, SHV-12, TEM-OSBL
		E. coli	1	NDM-1, CTX-M-15, CTX-M-27, CMY-6, DHA-1, TEM-OSBL
			1	NDM-1, CTX-M-27, CMY-2
		K. oxytoca†	1	NDM-1, ACC-1, TEM-OSBL
			1	NDM-1, CMY-4
			1	VIM-1, ACC-1
		K. pneumoniae	1	NDM-1, CTX-M-15, CMY-4, SHV-OSBL, TEM-OSBL
			1	NDM-1, CTX-M-15, CMY-6, SHV-OSBL, TEM-OSBL
			4	NDM-1, CTX-M-15, CMY-6, DHA-type, SHV-OSBL, TEM-OSBL
			1	NDM-1, CTX-M-15, DHA-1, SHV-OSBL

	eta -Lactamase types a		No. of	
Region	(no. of isolates)	Organism ^b	isolates	Molecular variant(s)
			2	NDM-1, CTX-M-15, DHA-type, SHV-OSBL, TEM-OSBL
			1	NDM-1, CTX-M-15, SHV-5, CMY-6, TEM-OSBL
			1	NDM-1, CTX-M-15, SHV-5, CMY-6, DHA-type
		P. mirabilis	1	NDM-1, CTX-M-15, DHA-type, TEM-OSBL
		P. rettgeri*	10	NDM-1, CTX-M-15, TEM-OSBL
		P. stuartii*	1	VIM-1, SHV-5, TEM-OSBL
			1	VIM-1, VEB-1, TEM-OSBL
			12	VIM-1, VEB-1, SHV-5, TEM-OSBL
		S. marcescens*	2	NDM-1, CTX-M-15, TEM-OSBL
			1	VIM-1, SHV-12
	MBL + KPC (1)	K. pneumoniae	1	VIM-1, KPC-2
	MBL + KPC + ESBL \pm OSBL (2)	K. pneumoniae	2	VIM-26, KPC-2, SHV-12, TEM-OSBL
	MBL + KPC + AmpC + OSBL (2)	C. freundii*	1	VIM-1, KPC-3, SHV-OSBL
		K. pneumoniae	1	VIM-1, KPC-2, MOX-1, SHV-OSBL
	MBL + KPC + ESBL + AmpC + OSBL (2)	K. pneumoniae	2	VIM-1, KPC-2, SHV-12, CMY-13, TEM-OSBL
	MBI + OXA-48-like + OSBI (4)	K. pneumoniae	3	NDM-1, OXA-48, SHV-OSBI
		na priedinionide	1	NDM-1, OXA-232, SHV-OSBI
	MBI + OXA-48-like + FSBI +	K. pneumoniae	3	NDM-1, OXA-48, CTX-M-15
	OSBL (17)	na priedinionide	8	NDM-1 OXA-48 CTX-M-15 SHV-OSBI
	0002(17)		4	NDM-1 OXA-48 CTX-M-15 SHV-OSBL TEM-OSBL
			2	NDM-1 OXA-232 CTX-M-15 SHV-OSBL TEM-OSBL
	MBL + OXA-48-like +	C freundii*	5	VIM-31 OXA-48 TEM-OSBI
	AmpC + OSBI (8)	E cloacae*	1	NDM-1 OXA-48
		L. cloucuc	1	VIM-31 OXA-48
		E coli	1	
	MBL + OXA-48-like + FSBL +	K nneumoniae	1	NDM-1 OXA-48 CTX-M-15 CMV-6 SHV-OSBI
	AmpC + OSBI (3)	R. priedmonide	1	NDM-1 OXA-48, CTX-M-15, CMT 0, SHV-OSDL
	7 (inpe + 050E (5)		1	NDM-1, OXA-48, CTX-M-15, DHA-type, SHV-OSBL, TEM-OSBL
Latin America	KPC \pm OSBL and/or spectrum	E. coli	9	KPC-2
	undefined (211)		3	KPC-2, TEM-OSBL
			1	KPC-2, TEM-type
		K. pneumoniae	16	KPC-2
			68	KPC-2, SHV-OSBL
			3	KPC-2, TEM-OSBL
			84	KPC-2, SHV-OSBL, TEM-OSBL
			1	KPC-2, SHV-52
			1	KPC-2, SHV-120, TEM-OSBL
			8	KPC-3, SHV-OSBL
			15	KPC-3, SHV-OSBL, TEM-OSBL
			1	KPC-30, SHV-OSBL
		K. variicola	1	KPC-2
	KPC + ESBL \pm OSBL (207)	E. coli	1	KPC-2, CTX-M-15
		K. oxytoca†	2	KPC-2
			1	KPC-2, SHV-OSBL
			2	KPC-2, TEM-OSBL
			1	KPC-2, CTX-M-8, TEM-OSBL
			1	KPC-2, CTX-M-12
			1	KPC-2, CTX-M-15, TEM-OSBL
			1	KPC-2, SHV-2A
			1	KPC-2, SHV-12, TEM-OSBL
		K. pneumoniae	1	KPC-2, CTX-M-1, SHV-OSBL, TEM-OSBL
			1	KPC-2, CTX-M-1, CTX-M-2, SHV-OSBL, TEM-OSBL
			3	KPC-2, CTX-M-2, SHV-OSBL
			1	KPC-2, CTX-M-2, TEM-OSBL
			21	KPC-2, CTX-M-2, SHV-OSBL, TEM-OSBL
			1	KPC-2, CTX-M-2-type, SHV-OSBL, TEM-OSBL
			1	KPC-2, CTX-M-2, CTX-M-15, SHV-OSBL, TEM-OSBL
			1	KPC-2, CTX-M-9
			3	KPC-2, CTX-M-12
			2	KPC-2, CTX-M-12, SHV-OSBL

Region (no. of isolates) Organism? iolate Molecular variant(s) 3 KPC2, CTX,M-13, SHV-12 3 KPC2, CTX,M-14, SHV-05BL 3 KPC2, CTX,M-14, SHV-05BL 3 KPC2, CTX,M-15, SHV-05BL 20 KPC2, CTX,M-15, SHV-05BL 3 KPC2, CTX,M-15, SHV-05BL 21 KPC2, CTX,M-15, SHV-05BL 3 KPC2, CTX,M-15, SHV-05BL 23 KPC2, CTX,M-15, SHV-05BL 3 KPC2, CTX,M-15, SHV-05BL 24 KPC2, CTX,M-15, SHV-05BL 3 KPC2, CTX,M-15, SHV-05BL 25 KPC2, SHV-12, TKM-05BL 3 KPC2, SHV-12, TKM-05BL 26 KPC2, SHV-12, TKM-05BL 3 KPC2, SHV-12, TKM-05BL 27 KPC2, SHV-12, TKM-05BL 3 KPC2, SHV-12, TKM-05BL 28 KPC2, SHV-12, TKM-05BL 3 KPC2, SHV-12, TKM-05BL 29 KPC2, SHV-12, TKM-05BL 3 KPC3, SHV-12, TKM-05BL 20 KPC2, SHV-12, TKM-05BL 3 KPC2, SHV-12, TKM-05BL 20 KPC2, SHV-12, TKM-05BL 3 KPC2, TKM-15, SHV-05BL 21 KPC2, TKM-15, SHV-05BL		β -Lactamase types ^a		No. of	
Image: Second	Region	(no. of isolates)	Organism ^b	isolates	Molecular variant(s)
3 RPC-2 (TX-M-14) 4 RPC-2 (TX-M-14) 20 RPC-2 (TX-M-14) 20 RPC-2 (TX-M-15) 21 RPC-2 (TX-M-15) 25 RPC-2 (TX-M-15) 26 RPC-2 (TX-M-15) 27 RPC-2 (TX-M-15) 28 RPC-2 (TX-M-15) 29 RPC-2 (TX-M-15) 20 RPC-2 (TX-M-15) 21 RPC-2 (TX-M-15) 21 RPC-2 (TX-M-15) 22 RPC-2 (TX-M-15) 21 RPC-2 (TX-M-15) 22 RPC-2 (TX-M-15) 23 RPC-2 (TX-M-15) 24 RPC-2 (TX-M-15) 25 RPC-2 (TX-M-15) 26 RC-2 (TX-M-15) 27 RPC-2 (TX-M-15) 28				1	KPC-2, CTX-M-12, SHV-12
Image: Provide and the set of th				3	KPC-2, CTX-M-14
20 KPC-2 (TX M-15 SHV-OSBL TEM-OSBL 3 KPC-2 (TX M-15 SHV-OSBL 25 KPC-2 (TX M-15 SHV-OSBL 1 KPC-2 SHV-12 TEM-OSBL 2 KPC-2 SHV-12 TEM-OSBL 1 KPC-3 SHV-12 TEM-OSBL 1 KPC-3 SHV-12 TEM-OSBL 1 KPC-3 SHV-12 TEM-OSBL 1 KPC-3 SHV-12 TEM-OSBL 1 KPC-2 SHV-12 TEM-OSBL 1 KPC-2 SHV-12 TEM-OSBL 1 KPC-2 TCM-15 SHV-2 TEM-OSBL <td></td> <td></td> <td></td> <td>1</td> <td>KPC-2, CTX-M-14, TEM-OSBL</td>				1	KPC-2, CTX-M-14, TEM-OSBL
3 RPC2_CTX.M-15 SHV-OSBL 37 RPC2_CTX.M-15 SHV-OSBL 38 RPC2_CTX.M-15 SHV-OSBL 39 RPC2_CTX.M-15 SHV-OSBL 39 RPC2_SHV-12 TEMOSBL 4 RPC2_SHV-12 TEMOSBL 2 RPC2_SHV-12 TEMOSBL 2 RPC2_SHV-12 TEMOSBL 2 RPC2_SHV-12 TEMOSBL 2 RPC3_SHV-12 TEMOSBL 3 RPC3_SHV-12 TEMOSBL 4 RPC3_SHV-12 TEMOSBL 4 RPC3_SHV-12 TEMOSBL 4 RPC3_SHV-12 TEMOSBL 4 RPC3_SHV-12 TEMOSBL 5 RPC3_TTX.M-15, SHV-OSBL TEMOSBL 6 C. freundin* RPC3_TTX.M-15, SHV-OSBL 7 RPC3_TTX.M-				20	KPC-2, CTX-M-14, SHV-OSBL, TEM-OSBL
25 IRC-2, TCM-H15, SHV-OSBL TEM-OSBL 37 IRC-2, CTM-H15, SHV-OSBL TEM-OSBL 37 IRC-2, CTM-H3, SHV-OSBL, TEM-OSBL 37 IRC-2, CTM-H3, SHV-OSBL, TEM-OSBL 38 IRC-2, CTM-H3, SHV-OSBL, TEM-OSBL 39 IRC-2, STW-H2, SHV-OSBL, TEM-OSBL 30 IRC-2, STW-SB, TEM-OSBL 31 IRC-2, STW-SB, TEM-OSBL 32 IRC-2, STW-SB, TEM-OSBL 34 IRC-2, TEM-OSBL 34<				3	KPC-2 CTX-M-15
KPC + AmpC ± OSBL (32) R. ornthinolytical R. ornthinolytical RC = 2, TY + H = 5, SHV-JOSBL TEM-OSBL KPC + AmpC ± OSBL (32) RC = 2, SHV = 3, TEM-OSBL RC = 2, SHV = 3, TEM-OSBL RC = 2, SHV = 3, TEM-OSBL KPC + AmpC ± OSBL (32) RC = 1, SHV = 3,				25	KPC-2 CTX-M-15 SHV-OSBI
SP NC = C, TAW T, S, SHV-Spit, TEM-OSBL NC = C, TXW T, S, SHV-Spit, TEM-OSBL NC = C, TXW T, S, SHV-Spit, TEM-OSBL NC = C, TXW T, S, SHV-Spit, TEM-OSBL NC = C, TXW T, S, SHV-Spit, TEM-OSBL 2 NC = C, TXW T, S, SHV-Spit, TEM-OSBL 2 NC = C, TXW T, S, SHV-Spit, TEM-OSBL 2 NC = C, TXW T, S, SHV-Spit, TEM-OSBL 2 NC = C, TXW T, S, SHV-Spit, TEM-OSBL 2 NC = C, TXW T, S, SHV-Spit, TEM-OSBL 2 NC = C, TXW T, S, SHV-Spit, TEM-OSBL 2 NC = C, TXW T, S, SHV-Spit, TEM-OSBL 2 NC = C, TXW T, S, SHV-Spit, TEM-OSBL 3 NC = C, TXW T, S, SHV-SBL, TEM-OSBL 4 NC = S, TWH T, S, SHV-OSBL, TEM-OSBL 4 NC = S, TWH T, S, SHV-OSBL, TEM-OSBL 4 NC = S, TWH T, S, SHV-OSBL, TEM-OSBL 5 NC = T, TWH S, SHV-OSBL, TEM-OSBL 6 C, feundit NC = C, TWH S, SHV-OSBL, TEM-OSBL 6 NC = T, TWH S, SHV-OSBL, TEM-OSBL S, TWH T, SHV-OSBL, TEM-OSBL 7 NC = T, TWH S, SHV-OSBL, TEM-OSBL S, TWH T, TEM-OSBL 8 NC = T, TEM-OSBL S, TWH T, TEM-OSBL 9 NC = T, TWH S, SHV-OSBL, TEM-OSBL S, TWH T, TEM				25	
KPC + AmpC ± OSBL (32) R. ornithinalytica N C 2, 11 Am 15, 314 U 30B, 17EM-OSBL KPC + AmpC ± OSBL (32) R C 2, 11 Am 15, 314 U 30B, 17EM-OSBL KPC + AmpC ± OSBL (32) R C 2, 314 J, 314 U 30B, 17EM-OSBL RC 2, 314 J, 314 U 30B, 17EM-OSBL R C 2, 314 J, 314 U 30B, 17EM-OSBL RC 2, 314 J, 314 U 30B, 17EM-OSBL R C 2, 314 J, 314 U 30B, 17EM-OSBL RC 2, 314 J, 314 U 30B, 17EM-OSBL R C 2, 314 J, 314 U 30B, 17EM-OSBL RC 2, 314 J, 314 U 30B, 17EM-OSBL R C 2, 314 J, 314 U 30B, 17EM-OSBL RC 2, 314 J, 314 U 30B, 17EM-OSBL R C 2, 314 J, 314 U 30B, 17EM-OSBL RC 2, 314 J, 314 U 30B, 17EM-OSBL R C 2, 314 J, 314 U 30B, 17EM-OSBL RC 2, 314 J, 314 U 30B, 17EM-OSBL R C 2, 314 J, 314 U 30B, 17EM-OSBL RC 2, 314 J, 314 U 30B, 17EM-OSBL R C 2, 314 J, 314 U 30B, 17EM-OSBL RC 2, 714 J, 32 SH-S, 51EM-OSBL R C 2, 714 J, 314 U 30B, 17EM-OSBL RC 2, 714 J, 314 U 30B, 17EM-OSBL R C 2, 714 U 30B, 17EM-OSBL RC 2, 714 U 3, 714 U 30B, 17EM-OSBL R C 2, 714 U 30B, 17EM-OSBL RC 2, 714 U 3, 714 U 30B, 17EM-OSBL R C 2, 714 U 30B, 17EM-OSBL RC 2, 714 U 3, 714 U 30B, 17EM-OSBL R R C 2, 714 U 30B, 17EM-OSBL RC 2, 714 U 3, 714 U 30B, 17EM-OSBL R R C 2, 714 U 30B, 17EM-OSBL RC 2, 714 U 3, 714 U 30B, 1				37	KPC 2 CTV M 15 SUV ture TEM OSDL
Image: Second				1	KPC-2, CTX-M-15, SHV-Lype, TEM-OSBL
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				1	KPC-2, CTX-M-35, SHV-OSBL, TEM-OSBL
2 KPC 2, SHV-12 24 KPC 2, SHV-12, TEM-OSBL 1 KPC 2, SHV-12, TEM-OSBL 2 KPC 2, SHV-12, TEM-OSBL 4 KPC 3, CTK-M-12, SHV-12, TEM-OSBL 4 KPC 3, SHV-12, TEM-OSBL 4 KPC 3, SHV-12, TEM-OSBL 4 KPC 3, SHV-12, TEM-OSBL 5 KPC 2 4 KPC 3, SHV-12, TEM-OSBL 5 KPC 2 6 KPC 2, TEM-OSBL 6 KPC 2, TEM-OSBL 7 KPC 2, TEM-OSBL 8 KPC 2, TEM-OSBL 8 KPC 2, TEM-OSBL 9 KPC 4, TEM-OSBL 1 KPC 4, CT 4, TEM-OSBL 1 KPC 2, TEM-OSBL 1 KPC 2, TEM-OSBL 1 KPC 2, TEM-OSBL 1 KPC 2, TEM-OSBL 1<				1	KPC-2, CTX-M-67, SHV-OSBL
9 KPC 2, SHV-12 24 KPC 2, SHV-23, TEM-OSBL 1 KPC 2, SHV-23, TEM-OSBL 2 KPC 2, SHV-25BL 2 KPC 3, STV-42 4 KPC 3, STV-42, SHV-OSBL 4 KPC 3, STV-12, TEM-OSBL 4 KPC 2, TEM-OSBL 4 KPC 2, TEM-OSBL 4 KPC 2, TEM-OSBL 5 KPC 2, TEM-OSBL 6 KPC 2, TEM-OSBL 7 KPC 2, TEM-OSBL 8 KPC 2, TEM-OSBL 7 KPC 2, TEM-OSBL 8 KPC 2, TEM-OSBL 7 KPC 2, TEM-OSBL 8 KPC 2, TEM-OSBL 8 KPC 2, TEM-OSBL <td></td> <td></td> <td></td> <td>2</td> <td>KPC-2, SHV-5, TEM-OSBL</td>				2	KPC-2, SHV-5, TEM-OSBL
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				9	KPC-2, SHV-12
1 KPC2, SHV-23, TEM-OSBL 2 KPC2, SHV-25B, TEM-OSBL 2 KPC2, SHV-25B, TEM-OSBL 1 KPC3, CTX-M-2, SHV-OSBL, TEM-OSBL 1 KPC3, CTX-M-12, SHV-OSBL, TEM-OSBL 1 KPC3, CTX-M-12, SHV-OSBL, TEM-OSBL 1 KPC3, CTX-M-12, SHV-OSBL, TEM-OSBL 1 KPC3, STX-M-12, TEM-OSBL 1 KPC4, TEM-OSBL				24	KPC-2, SHV-12, TEM-OSBL
2 KPC2, SHV-ESBL KPC2, SHV-ESBL 1 KPC2, SHV-ESBL, TEM-OSBL 1 KPC3, CTX-M2, SHV-SBL, TEM-OSBL 1 KPC3, STX-M2, TEM-OSBL 1 KPC3, STX-M2, TEM-OSBL 1 KPC2, TEM-OSBL 2 KPC2, TEM-OSBL 3 KPC2, TEM-OSBL 4 KPC2, TEM-OSBL 5 marcescens* 1 KPC2, TCX-M2, TEM-OSBL 2 KPC2, TCX-M12, TEM-OSBL 2 KPC2, TCX-M14, TEM-OSBL <td></td> <td></td> <td></td> <td>1</td> <td>KPC-2, SHV-23, TEM-OSBL</td>				1	KPC-2, SHV-23, TEM-OSBL
2 KPC-2, STW-SBL KPC-3, STW-SBL 1 KPC-3, STW-SBL, TEM-OSBL 1 KPC-3, CTX-M-12, STW-OSBL 1 KPC-3, STW-SBL, TEM-OSBL 1 KPC-3, STW-12, TEM-OSBL 1 KPC-3, STW-12, TEM-OSBL 1 KPC-3, STW-12, TEM-OSBL 1 KPC-3, STW-15, STW-OSBL, TEM-OSBL 1 KPC-3, STW-5, TEM-OSBL 1 KPC-3, STW-5, TEM-OSBL 1 KPC-3, STW-5, TEM-OSBL 1 KPC-2, TEM-OSBL <				2	KPC-2, SHV-ESBL
1 KPC3, CTX-M2, SHW-05BL, TEM-OSBL 1 KPC3, CTX-M12, SHW-12, TEM-OSBL 1 KPC3, STX-M12, SHW-05BL, TEM-OSBL 1 KPC3, STX-M12, SHW-05BL, TEM-OSBL 1 KPC3, STX-M12, SHW-05BL, TEM-OSBL 1 KPC3, STX-M2, SHW-05BL, TEM-OSBL 1 KPC3, STX-M2, SHW-05BL, TEM-OSBL 1 KPC3, STX-M2, SHW-05BL, TEM-OSBL 1 KPC4, TEX-M5, STBW-05BL, TEM-OSBL 1 KPC4, TEX-M5, STBW-05BL, TEM-OSBL 1 KPC2, TEM-OSBL 2 KPC2, TEM-OSBL 3 KPC2 4 KPC2, TEM-OSBL 5 marcescens* 1 KPC2, TEM-OSBL 2 KPC2, CTX-M-12, TEM-OSBL 2 KPC2, CTX-M-12, TEM-OSBL 2 KPC2, CTX-M-12, TEM-OSBL 2<				2	KPC-2, SHV-ESBL, TEM-OSBL
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				1	KPC-3, CTX-M-2, SHV-OSBL, TEM-OSBL
9 KPC-3 (CTX-M-15 SHV-OSBL TEM-OSBL 1 1 KPC-3, SHV-12 4 KPC-3, SHV-12 4 KPC-3, SHV-12 4 KPC-3, SHV-12 5 KPC-4 6 c. freundii* 2 KPC-2 4 KPC-3, TEM-OSBL 5 KPC-2 6 c. koseri* 2 KPC-2, TEM-OSBL 6 c. koseri* 2 KPC-2, TEM-OSBL 6 KPC-2, TEM-OSBL 7 KPC-2 8 KPC-2 8 KPC-2 8 KPC-2 8 KPC-2 8 KPC-2 9 KPC-2 9 KPC-2 1				1	KPC-3, CTX-M-12, SHV-12, TEM-OSBL
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				9	KPC-3 CTX-M-15 SHV-OSBL TEM-OSBL
14 KPC-3, SHV-12, TEM-OSBL 15 KPC-17PE, CTXM-15, SHV-OSBL, TEM-OSBL 16 KPC-4, TEM-OSBL 17 KPC-2, SHV-5, TEM-OSBL 18 KPC-2, TEM-OSBL 19 KPC-2, TEM-OSBL 10 KPC-2, TEM-OSBL 11 KPC-2, TEM-OSBL 11 KPC-2, TEM-OSBL 11 KPC-2, TEM-OSBL 11 KPC-2, TEM-OSBL 12 KPC-2, TEM-OSBL 13 KPC-2, TEM-OSBL 14 KPC-2, TEM-OSBL 15 Kaerogenes* 16 KPC-2, CTX-M-2, TEM-OSBL 17 KPC-2, CTX-M-12, TEM-OSBL 18 KPC-2, CTX-M-12, TEM-OSBL 19 KPC-2, CTX-M-12, TEM-OSBL 10 KPC-2, CTX-M-12, TEM-OSBL 11 KPC-2, CTX-M-12, TEM-OSBL 11 KPC-2, CTX-M-13, TEM-OSBL 11 KPC-2, CTX-M-14, TEM-OSBL 12 KPC-2, CTX-M-14, TEM-OSBL				1	
Image: Second Stress R. ornithinolytica Image: R. ornithinolytica Image: R. ornithinolytica R. ornithinolytica Image: R. ornithinolytica Image: R. ornithinolytica Image: R. ornithinolytica KPC + AmpC ± OSBL (32) C. freundli Image: R. ornithinolytica Image: R. ornithinolytica C. koseri* Image: R. ornithinolytica Image: R. ornithinolytica Image: R. ornithinolytica KPC - 2 FEM-OSBL E. cloacae* S. RPC - 2 K. aerogenes* 3 KPC - 2 K. aerogenes* 3 KPC - 2 K. preumoniae KPC - 2 FEM-OSBL S. marcescens* 8 KPC - 2 GSBL (16) Image: Rec - 2 TEM-OSBL KPC + ESBL + AmpC ± C. freundli* KPC - 2 GSBL (16) Image: Rec - 2 KPC - 2 KPC - 2, CTX-M-12 TEM-OSBL E Goace* Image: Rec - 2 KPC - 2 TEM-OSBL K. aerogenes* Image: Rec - 2 KPC - 2 TEM-OSBL K. aerogenes* Image: Rec - 2 KPC - 2 TEM-OSBL				1/1	
R. ornithinolytica R. C-1 TFE, C, VAN-15, STV-OSBL, TEM-OSBL KPC + AmpC ± OSBL (32) C. freundil* RC-2, TEM-OSBL KPC + AmpC ± OSBL (32) C. kosert* Z KPC-2, TEM-OSBL C. kosert* Z KPC-2, TEM-OSBL KPC-2 KPC + TES, CN-OSBL KPC-2, TEM-OSBL KPC-2 KPC + ESBL + AmpC ± C. freundil* KPC-2, TEM-OSBL S. marcescens* KPC-2, TEM-OSBL KPC-2 KPC + ESBL + AmpC ± C. freundil* KPC-2, TEM-OSBL OSBL (16) KPC-2, TEM-OSBL KPC-2, TEM-OSBL KPC + ESBL + AmpC ± C. freundil* KPC-2, TEM-OSBL KPC + CSL + AmpC ± C. freundil* KPC-2, TEM-OSBL KPC + CSL + AmpC ± C. freundil* KPC-2, TEM-OSBL KPC + CSL + AmpC ± C. freundil* KPC-2, TEM-OSBL KPC + CSL + AmpC ± C. freundil* KPC-2, TEM-OSBL KPC + CSL + AmpC ± C. freundil* KPC-2, TEM-OSBL KPC + CSL + AmpC ± C. freundil* KPC-2, TEM-OSBL KPC + CSL + AmpC ± C. freundil* KPC-2, TEM-OSBL KPC + OXA + 48-like + OSBL + K pneumoniae KPC-2, CTX-M-15, TEM-OSBL <td></td> <td></td> <td></td> <td>14</td> <td></td>				14	
k PC + AmpC ± OSBL (32) K remulai k RPC-3, FKH-OSBL k PC - 4 K RPC-2, TEM-OSBL K RPC-2, TEM-OSBL L C koseri* K RPC-2, TEM-OSBL K RPC-2, TEM-OSBL E cloacae* K RPC-2, TEM-OSBL K RPC-2, TEM-OSBL K aerogenes* K RPC-2, TEM-OSBL K RPC-2, TEM-OSBL K preumoniae K RPC-2, TEM-OSBL K RPC-2, TEM-OSBL K preumoniae K RPC-2, TEM-OSBL K RPC-2, TEM-OSBL S marcescens* 8 KPC-2, TEM-OSBL K RPC-2, TEM-OSBL S marcescens* 1 KPC-2, TEM-OSBL K RPC-2, TEM-OSBL OSBL (16) 1 KPC-2, CTX-M-12, TEM-OSBL K RPC-2, CTX-M-13, TEM-OSBL K RPC-2, CTX-M-13, TEM-OSBL 1 KPC-2, CTX-M-13, TEM-OSBL K RPC-2, CTX-M-13, TEM-OSBL K aerogenes* 1 KPC-2, CTX-M-13, TEM-OSBL S marcescens* K RPC-2, CTX-M-13, TEM-OSBL K aerogenes* 2 KPC-2, CTX-M-13, TEM-OSBL S marcescens* K RPC-2, CTX-M-13, TEM-OSBL K aerogenes* 1 KPC-2, CTX-M-13, TEM-OSBL S marcescens* K RPC-2, CTX-M-13, TEM-OSBL K aerogenes* 2 K Aerogenes* 1 K RPC-2, CTX-M-13, TEM-OSBL <td></td> <td></td> <td>o</td> <td></td> <td>KPC-TYPE, CTX-M-15, SHV-OSBL, TEM-OSBL</td>			o		KPC-TYPE, CTX-M-15, SHV-OSBL, TEM-OSBL
KPC + AmpC ± OSBL [32) C. Ireundii* 2 KPC-2, TEM-OSBL C. koseri* 2 KPC-2, TEM-OSBL E. cloacae* 5 KPC-2, TEM-OSBL K. aerogenes* 6 KPC-2, TEM-OSBL K. aerogenes* 7 KPC-2, TEM-OSBL K. aerogenes* 8 KPC-2 S. marcescens* 8 KPC-2, TXM-3, TEM-OSBL VEC-2, CTX-M-12 KPC-2, CTX-M-12 KPC-2, CTX-M-12 OSBL (16) 1 KPC-2, CTX-M-12, STM-OSBL KPC-2, CTX-M-13, TEM-OSBL E. cloacae* 1 KPC-2, CTX-M-15, TEM-OSBL K. aerogenes* 2 KPC-2, CTX-M-15, TEM-OSBL S. marcescens* 1 KPC + OXA-48-like + OSBL (1) K. pneumoniae KPC-2, CTX-M-15, TEM-OSBL S. marcescens* 1 KPC-2, CTX-M-15, TEM-OSBL KPC + OXA-48-like + ESBL + K. pneumoniae 1 KPC-2, CTX-M-15, STM-OSBL SEL			R. ornithinolytica	1	KPC-3, SHV-5, TEM-OSBL
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$		$KPC + AmpC \pm OSBL (32)$	C. freundii*	2	KPC-2
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				1	KPC-2, TEM-OSBL
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			C. koseri*	2	KPC-2
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$				1	KPC-2, TEM-OSBL
$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			E. cloacae*	5	KPC-2
K. aerogenes* 3 KPC-2 K. pneumoniae 1 KPC-2 K. pneumoniae 1 KPC-2 S. marcescens* 8 KPC-2 1 KPC-2, TEM-OSBL KPC-3 OSBL (16) 1 KPC-2, CTX-M-12 1 KPC-2, CTX-M-12 KPC-2, CTX-M-13 1 KPC-2, CTX-M-15 KPC-2, CTX-M-15 1 KPC-2, CTX-M-15 KPC-2, CTX-M-15 2 KPC-2, CTX-M-15, TEM-OSBL KPC-2, CTX-M-15, TEM-OSBL 3 KPC-2, CTX-M-15, TEM-OSBL KPC-2, CTX-M-15, TEM-OSBL 4 KPC-2, CTX-M-15, TEM-OSBL KPC-2, CTX-M-15, TEM-OSBL 5 marcescens* 1 KPC-2, CTX-M-15, TEM-OSBL 5 Karoegenes* 2 KPC-2, CTX-M-15, TEM-OSBL 6 K pneumoniae 1 KPC-2, CTX-M-15, TEM-OSBL 7 K precuroniae 1 KPC-2, CTX-M-14, SHV-OS				8	KPC-2, TEM-OSBL
K. pneumoniae 1 KPC-2, FOX-5, SHV-OSBL, TEM-OSBL S. marcescens* 8 KPC-2 I KPC-2, TEM-OSBL VPC-2 TEM-OSBL OSBL (16) 1 KPC-2, TEM-OSBL I KPC-2, CTX-M-12, TEM-OSBL I KPC-2, CTX-M-12, TEM-OSBL I KPC-2, CTX-M-12, TEM-OSBL I KPC-2, CTX-M-12, TEM-OSBL I KPC-2, CTX-M-13 E. aburiae* 2 KPC-2, CTX-M-15 S KPC-2, CTX-M-15, TEM-OSBL S KPC-2, CTX-M-15, TEM-OSBL S KPC-2, CTX-M-15, TEM-OSBL S KPC-3, CTX-M-15, TEM-OSBL S KPC-4, CTX-M-15, TEM-OSBL S KPC-4, OXA-48-like + OSBL (1) K pneumoniae KPC-4, OXA-48-like + OSBL K pneumoniae KPC-4, OXA-48-like + OSBL K pneumoniae KPC-4, OXA-48-like + OSBL K pneumoniae K pneumoniae K PC-2, OXA-163, SHV-OSBL, TEM-OSBL KPC + OXA-48-like + ESBL ± K pneumoniae VXA-123, TEM-OSBL K preumoniae VXA-			K. aerogenes*	3	KPC-2
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$ \begin{array}{cccccccccccccccccccccccccccccccccccc$			5. marcescens	1	
NR C= CLSRC + Anipe 2 C. Ineuridari I NR C=2, CTX-M-12 OSBL (16) I KPC-2, CTX-M-12, TEM-OSBL I KPC-2, CTX-M-12, TEM-OSBL I KPC-2, CTX-M-12, TEM-OSBL I KPC-2, CTX-M-13, TEM-OSBL E. asburiae* 2 I KPC-2, CTX-M-13, TEM-OSBL KPC-2, CTX-M-15 KPC-2, CTX-M-15, TEM-OSBL S. marcescens* 1 KPC-2, CTX-M-15, TEM-OSBL S. marcescens* S. marcescens* 1 KPC-2, CTX-M-15, TEM-OSBL S. marcescens* KPC-2, CTX-M-15, TEM-OSBL S. marcescens* KPC-2, CTX-M-15, TEM-OSBL S. marcescens* S. marcescens* 1 KPC-2, CTX-M-15, TEM-OSBL KPC + OXA-48-like + OSBL (1) K. pneumoniae KPC-2, CTX-M-15, SHV-OSBL, TEM-OSBL OSBL (2) 1 OXA-323, TEM-OSBL TEM-OSBL OXA-48-like + ESBL ± K. pneumoniae 1 OXA-232, CTX-M-15, SHV-OSBL, TEM-OSBL OSBL (1) K. pneumoniae 1 OXA-232, CTX-M-15, SHV-OSBL, TEM-OSBL MBL ± OSBL (7) K. pneumoniae 3 NDM-1, SHV-OSBL, TEM-OSBL MBL ± OSBL (24)		KPC + ESRI + AmpC +	C froundii*	1	KPC_2 (TY-M-2 TEM-OSB)
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K. aerogenes* 2 KPC-2, CTX-M-14, TEM-OSBL 1 KPC-2, CTX-M-15, TEM-OSBL 5. marcescens* 1 KPC-2, CTX-M-15, TEM-OSBL KPC + OXA-48-like + OSBL (1) K. pneumoniae 1 KPC-2, CTX-M-15, CTX-M-59 KPC + OXA-48-like + ESBL + K. pneumoniae 1 KPC-2, OXA-163, SHV-OSBL, TEM-OSBL OSBL (2) 1 KPC-2, OXA-370, CTX-M-14, SHV-OSBL, TEM-OSBL OXA-48-like ± OSBL (4) E. coli 1 OXA-232, TEM-OSBL K. pneumoniae 1 OXA-232, TEM-OSBL R-ORIBINOSBL, TEM-OSBL OXA-48-like ± CSBL (4) E. coli 1 OXA-232, TEM-OSBL R. ornithinolytica 1 OXA-232, CTX-M-15, SHV-OSBL, TEM-OSBL OXA-48-like ± ESBL ± K. pneumoniae 1 OXA-232, CTX-M-15, SHV-OSBL OSBL (1) R. ornithinolytica 1 OXA-232, CTX-M-15, SHV-OSBL MBL ± OSBL (7) K. pneumoniae 3 NDM-1, SHV-OSBL MBL ± OSBL (24) E. coli 2 VIM-23, CTX-M-15 K. variicola 1 NDM-1 NDM-1 MBL ± ESBL ± OSBL (24) E. coli 2 VIM-23, CTX-M-15, SHV-OSBL K. pn				3	KPC-2, CTX-M-15, TEM-OSBL
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KPC + OXA-48-like + OSBL (1) K. pneumoniae 1 KPC-2, OXA-163, SHV-OSBL, TEM-OSBL KPC + OXA-48-like + ESBL + K. pneumoniae 1 KPC-2, OXA-163, CTX-M-2, SHV-OSBL, TEM-OSBL OSBL (2) 1 KPC-2, OXA-370, CTX-M-14, SHV-OSBL, TEM-OSBL EM-OSBL OXA-48-like ± OSBL (4) E. coli 1 OXA-232, TEM-OSBL K. pneumoniae 2 OXA-163, SHV-OSBL, TEM-OSBL RM-OSBL OXA-48-like + ESBL ± K. pneumoniae 1 OXA-232, TEM-OSBL NCA-48-like + ESBL ± K. pneumoniae 1 OXA-163, SHV-OSBL, TEM-OSBL OXA-48-like + ESBL ± K. pneumoniae 1 OXA-232, CTX-M-15, SHV-OSBL, TEM-OSBL NBL ± OSBL (7) K. pneumoniae 3 NDM-1, SHV-OSBL MBL ± SBL ± OSBL (24) E. coli 2 VIM-23, CTX-M-15 K. pneumoniae 1 NDM-1 NDM-1 MBL + ESBL ± OSBL (24) E. coli 2 VIM-23, CTX-M-15, SHV-OSBL K. pneumoniae 1 NDM-1 NDM-1 CTX-M-15, SHV-OSBL MBL + ESBL ± OSBL (24) E. coli 2 VIM-23, CTX-M-15, SHV-OSBL I NDM-1, CTX-M-16, SHV-OSBL 1 <td< td=""><td></td><td></td><td>S. marcescens*</td><td>1</td><td>KPC-2, CTX-M-15, CTX-M-59, TEM-OSBL</td></td<>			S. marcescens*	1	KPC-2, CTX-M-15, CTX-M-59, TEM-OSBL
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OXA-48-like + ESBL ± OSBL (1) MBL ± OSBL (7) MBL ± OSBL (7) MBL ± OSBL (7) K. pneumoniae K. variicola MBL + ESBL ± OSBL (24) K. variicola K. variicola K. variicola K. variicola K. variicola K. variicola MBL + ESBL ± OSBL (24) K. pneumoniae MBL + ESBL ± OSBL (24) MBL + ESBL ± OSBL (24) MBL + ESBL ± OSBL (24) MBL + ESBL ± OSBL (24) K. pneumoniae MDM-1, CTX-M-15, SHV-OSBL NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL			R ornithinolytica	1	OYA-181
OXA-40-like + ESBL ± K. pneumoniae 1 OXA-232, CTX-MI-13, SHV-OSBL, TEM-OSBL OSBL (1) MBL ± OSBL (7) K. pneumoniae 3 NDM-1, SHV-OSBL, TEM-OSBL K. variicola 1 NDM-1 MBL + ESBL ± OSBL (24) E. coli 2 VIM-23, CTX-M-15 K. oxytoca† 2 IMP-8, TEM-OSBL K. pneumoniae 1 NDM-1, CTX-M-15, SHV-OSBL K. pneumoniae 1 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 2 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL		OVA 49 like + ESPL +	K. onnumonjao	1	
MBL ± OSBL (7) K. pneumoniae 3 NDM-1, SHV-OSBL 3 NDM-1, SHV-OSBL, TEM-OSBL K. variicola 1 NDM-1 MBL + ESBL ± OSBL (24) E. coli 2 VIM-23, CTX-M-15 K. oxytoca† 2 IMP-8, TEM-OSBL K. pneumoniae 1 NDM-1, CTX-M-15, SHV-OSBL K. pneumoniae 1 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 2 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL			n. prieumoniue		07A-252, CTA-W-15, STV-050E, TEW-050E
MBL ± OSBL (7) K. pneumoniae 3 NDM-1, SHV-OSBL 3 NDM-1, SHV-OSBL, TEM-OSBL K. variicola 1 NDM-1 MBL + ESBL ± OSBL (24) E. coli 2 VIM-23, CTX-M-15 K. oxytoca† 2 IMP-8, TEM-OSBL K. pneumoniae 1 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 2 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL			<i>V</i>	2	
3 NDM-1, SHV-OSBL, TEM-OSBL MBL + ESBL ± OSBL (24) K. variicola 1 NDM-1 MBL + ESBL ± OSBL (24) E. coli 2 VIM-23, CTX-M-15 K. oxytoca† 2 IMP-8, TEM-OSBL K. pneumoniae 1 NDM-1, CTX-M-14, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 2 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL		$MBL \equiv OSBL\left(1 \right)$	ĸ. pneumoniae	3	
K. variicola 1 NDM-1 MBL + ESBL ± OSBL (24) E. coli 2 VIM-23, CTX-M-15 K. oxytoca† 2 IMP-8, TEM-OSBL K. pneumoniae 1 NDM-1, CTX-M-14, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 2 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL			<i>v</i> ,	5	
MBL + ESBL ± OSBL (24) E. coli 2 VIM-23, CTX-M-15 K. oxytoca† 2 IMP-8, TEM-OSBL K. pneumoniae 1 NDM-1, CTX-M-14, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 2 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL			K. variicola	1	NDM-1
K. oxytoca† 2 IMP-8, TEM-OSBL K. pneumoniae 1 NDM-1, CTX-M-14, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 2 NDM-1, CTX-M-15, TEM-OSBL 2 NDM-1, CTX-M-15, TEM-OSBL 1 NDM-1, CTX-M-15, TEM-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL		$MBL + ESBL \pm OSBL$ (24)	E. coli	2	VIM-23, CTX-M-15
K. pneumoniae 1 NDM-1, CTX-M-14, CTX-M-15, SHV-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL 2 NDM-1, CTX-M-15, TEM-OSBL 11 NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL 12 NDM-1, CTX-M-15, SHV-OSBL 13 NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL 14 NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL			K. oxytoca†	2	IMP-8, TEM-OSBL
1 NDM-1, CTX-M-15, SHV-OSBL 2 NDM-1, CTX-M-15, TEM-OSBL 11 NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL 1 NDM-1, CTX-M-15, SHV-OSBL			K. pneumoniae	1	NDM-1, CTX-M-14, CTX-M-15, SHV-OSBL
2 NDM-1, CTX-M-15, TEM-OSBL 11 NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL 1 NDM-1, CTX-M-15, SHV-ESBL, TEM-OSBL				1	NDM-1, CTX-M-15, SHV-OSBL
11 NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL 1 NDM-1, CTX-M-15, SHV-ESBL, TEM-OSBL				2	NDM-1, CTX-M-15, TEM-OSBL
1 NDM-1, CTX-M-15, SHV-ESBL, TEM-OSBL				11	NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL
				1	NDM-1, CTX-M-15, SHV-ESBL, TEM-OSBL

	eta -Lactamase types a		No. of	
Region	(no. of isolates)	Organism ^b	isolates	Molecular variant(s)
			1	NDM-1, CTX-M-15, PER-1, SHV-OSBL, TEM-OSBL
			2	VIM-23, SHV-ESBL
			1	VIM-24, CTX-M-15, SHV-ESBL, TEM-OSBL
	MBL + AmpC \pm OSBL (9)	C. freundii*	1	VIM-23
		E. cloacae*	2	NDM-1
			3	VIM-23
		P. rettgeri*	3	NDM-1
	MBL + ESBL + AmpC \pm	E. cloacae*	4	NDM-1, CTX-M-15
	OSBL (8)		1	VIM-1, CTX-M-9
			1	VIM-1, CTX-M-9, TEM-OSBL
		P. rettgeri*	1	NDM-1, CTX-M-12
			1	NDM-1, CTX-M-12, TEM-OSBL
	MBL + GES carbapenemase +	E. coli	1	NDM-1, GES-2, CTX-M-55, TEM-OSBL
	ESBL + OSBL (2)	K. oxytoca†	1	NDM-1, GES-2, TEM-OSBL
	MBL + KPC + ESBL ± OSBL (1)	K. pneumoniae	1	NDM-1, KPC-2, CTX-M-15, SHV-OSBL, TEM-OSBL
Asia/Pacific	GES carbapenemase + ESBL (1)	K. pneumoniae	1	GES-5, SHV-12
	KPC \pm OSBL and/or spectrum	E. coli	2	KPC-2
	undefined (9)		2	KPC-2, TEM-OSBL
		K. pneumoniae	4	KPC-2, SHV-OSBL
			1	KPC-2, TEM-OSBL
	$KPC + ESBL \pm OSBL$ (36)	K. oxytoca†	1	KPC-2, SHV-12
		K. pneumoniae	2	KPC-2, CTX-M-3, SHV-OSBL, TEM-OSBL
			1	KPC-2, CTX-M-14, SHV-12, TEM-OSBL
			1	KPC-2, CTX-M-15, SHV-OSBL
			1	KPC-2, CTX-M-15, TEM-OSBL
			19	KPC-2, CTX-M-15, SHV-OSBL, TEM-OSBL
			1	KPC-2, CTX-M-24, SHV-OSBL
			1	KPC-2, CTX-M-55, SHV-OSBL, TEM-OSBL
			2	KPC-2, CTX-M-65, SHV-OSBL, TEM-OSBL
			2	KPC-2, CTX-M-65, SHV-12
			1	KPC-2, CTX-M-65, SHV-12, TEM-OSBL
			1	KPC-2, CTX-M-90, SHV-OSBL, TEM-OSBL
			1	KPC-2, SHV-12, TEIVI-USBL
			1	KPC-12, SHV-2A
	KDC + AmpC + OCPL (10)	E kohoi*	1	KPC-17, 3HV-12
	$KPC + AIIIpC \pm OSBL (10)$	E. KODEI" E. coli	1	
		L. COII K. garoganas*	3	KFC-2, CWT-2 KPC-2
		K. aerogenes	1	
		n. prieurioniue	1	KPC-2 CMV-2 SHV-OSBL TEM-OSBL
			1	KPC-2 DHA-1 SHV-OSBI
			1	KPC-2 DHA-1 SHV-OSBL TEM-OSBL
		S marcescens*	1	KPC-2
	KPC + FSBI + AmpC +	C. koseri*	1	KPC-2, CTX-M-3, TEM-OSBI
	OSBL (4)	E. cloacae*	1	KPC-2, SHV-12, DHA-1
	()	K. pneumoniae	1	KPC-2, CTX-M-27, DHA-1, SHV-OSBL
			1	KPC-2, CTX-M-55, DHA-1, SHV-OSBL, TEM-OSBL
	OXA-48-like \pm OSBL (1)	K. pneumoniae	1	OXA-48, SHV-OSBL
	OXA-48-like + ESBL \pm	K. pneumoniae	1	OXA-48, CTX-M-15, SHV-OSBL, TEM-OSBL
	OSBL (5)		4	OXA-181, CTX-M-15, SHV-OSBL, TEM-OSBL
	OXA-48-like + AmpC \pm OSBL (1)	E. coli	1	OXA-181, CMY-2, TEM-OSBL
	OXA-48-like + ESBL + AmpC \pm OSBL (1)	E. coli	1	OXA-181, CTX-M-15, CMY-2, TEM-OSBL
	MBL \pm OSBL (9)	E. coli	1	IMP-59, TEM-OSBL
		K. pneumoniae	1	IMP-1, SHV-OSBL
			1	IMP-4, TEM-OSBL

	β -Lactamase types ^a		No. of	
Region	(no. of isolates)	Organism ^b	isolates	Molecular variant(s)
			3	IMP-4, SHV-OSBL, TEM-OSBL
			1	NDM-1
			1	NDM-1, SHV-OSBL
		P. mirabilis	1	NDM-1
	MBL + ESBL \pm OSBL (60)	E. coli	1	NDM-1, CTX-M-3
			1	NDM-1, CTX-M-27
			1	NDM-1, CTX-M-27, SHV-31
			1	NDM-5, CTX-M-15
			2	NDM-5, CTX-M-15, TEM-OSBL
			1	NDM-7, CTX-M-15, TEM-OSBL
		K. oxytoca†	1	IMP-4
			1	IMP-4, TEM-OSBL
			1	IMP-4, SHV-12
			1	NDM-1, CTX-M-15, TEM-OSBL
			1	NDM-7, CTX-M-15, SHV-12, TEM-OSBL
		K. pneumoniae	1	IMP-1, CTX-M-3, SHV-OSBL
			2	IMP-4, CTX-M-15, SHV-OSBL
			4	IMP-4, CTX-M-15, SHV-OSBL, TEM-OSBL
			1	IMP-26, CTX-M-15, SHV-OSBL
			1	IMP-26, CTX-M-15, SHV-OSBL, TEM-OSBL
			1	IMP-26, CTX-M-16, SHV-28
			1	NDM-1, CTX-M-14, SHV-12
			2	
			2 1	NDIVI-1, CTX-IVI-TS, SHV-USBL
			1	
			14	
			1	NDIVI-1, CTX-IVI-13, CTX-IVI-27, TEIVI-O3BL
			1	
			1	
			1	NDM-5_CTX-M-15_SHV-OSBL
			1	NDM-7 CTX-M-15 SHV-OSBL
			5	NDM-7. CTX-M-15. SHV-OSBL, TEM-OSBL
			4	NDM-7, CTX-M-15, SHV-12, TEM-OSBL
	$MBL + AmpC \pm OSBL (32)$	C. freundii*	7	IMP-4. TEM-OSBL
			2	NDM-1
			1	NDM-7
			1	NDM-7, TEM-OSBL
			1	NDM-7, DHA-1
		E. asburiae*	1	IMP-14
			1	NDM-1
			2	NDM-7
		E. cloacae*	1	IMP-1
			3	IMP-4
			2	NDM-1
			2	NDM-1, DHA-1, TEM-OSBL
			1	NDM-7
		E. coli	1	NDM-5, CMY-42, TEM-OSBL
		K. pneumoniae	1	IMP-26, DHA-1, SHV-OSBL, TEM-OSBL
		P. mirabilis	1	IMP-26, DHA-1
		P. rettgeri*	2	NDM-1
		S. marcescens*	1	IMP-4, TEM-OSBL
			1	IMP-47, TEM-OSBL
	$MBL + ESBL + AmpC \pm$	C. tarmeri*	1	NDM-1, CTX-M-15, TEM-OSBL
	OSBL (42)	C. treundii*	2	IMP-8, SHV-12, TEM-OSBL
			1	NDM-1, CTX-M-3, SHV-12, TEM-OSBL
			1	
			1	NDIVI-1, SHV-31, DHA-15, TEM-OSBL
		C kees	1	NDW-7, CTX-M-15, TEM-USBL
		C. KOSERI*	1	
		E. asouriae^	1	IIVIT-O, STIV-12, IEIVI-USBL
		E. CIOUCUE"	1	IIVIT-0, CTA-IVI-22, TEIVI-U3DL

	eta -Lactamase types a		No. of	
Region	(no. of isolates)	Organism ^b	isolates	Molecular variant(s)
			2	IMP-14, CTX-M-15, TEM-OSBL
			1	IMP-26, SHV-12
			1	NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL
			1	NDM-1, CTX-M-15, SHV-12, SHV-31, TEM-OSBL
			1	NDM-1, CTX-M-15, SHV-31
			7	NDM-1, CTX-M-15, SHV-31, TEM-OSBL
			1	NDM-1, CTX-M-15, SHV-31, DHA-1, TEM-OSBI
			2	NDM-1 SHV-12
			1	NDM-7 CTX-M-15 TEM-OSBI
			2	NDM-7 SHV-12 TEM-OSBI
		E coli	2	NDM-5 CTX-M-15 CMV-2 TEM-OSBI
		L. COII	1	NDM-5 CTX-M-15 CMY-2 TEM-type
			1	NDM-7 CTX-M-14 CTX-M-15 CMY-2 TEM-OSBI
			1	NDM-7 CTY-M-15 DHA-1
		K aaroaanas*	1	
		n. delogenes	1	
		K proumonico	1	
		ĸ. prieumoniae	1	
			1	
		D / //**	1	NDM-7, CTX-M-15, DHA-1, SHV-OSBL, TEM-OSBL
		P. stuartii*	1	VIM-1, VEB-1, SHV-5, TEM-OSBL
		S. marcescens*	1	IMP-8, CTX-M-3
	$MBL + KPC + ESBL \pm OSBL (3)$	K. oxytoca†	2	IMP-4, KPC-2, SHV-12
		K. pneumoniae	1	NDM-7, KPC-2, CTX-M-15, SHV-OSBL, TEM-OSBL
	MBL + OXA-48-like + ESBL \pm	K. pneumoniae	1	NDM-1, OXA-48, CTX-M-15, SHV-OSBL
	OSBL (16)		1	NDM-1, OXA-48, SHV-ESBL
			3	NDM-1, OXA-181, CTX-M-15, SHV-OSBL, TEM-OSBL
			3	NDM-1, OXA-232, CTX-M-15, SHV-OSBL
			7	NDM-1, OXA-232, CTX-M-15, SHV-OSBL, TEM-OSBL
			1	NDM-4, OXA-48, CTX-M-14, CTX-M-15, SHV-OSBL, TEM-OSBL
	MBL + OXA-48-like + ESBL + AmpC + OSBL (1)	E. coli	1	NDM-5, OXA-181, CTX-M-15, CMY-2, TEM-OSBL
Middle East/Africa	KPC \pm OSBL and/or spectrum	E. coli	1	KPC-2
	undefined (18)		1	KPC-3
		K. pneumoniae	2	KPC-2
		· F	1	KPC-2, SHV-OSBL
			2	KPC-2, SHV-OSBL TEM-OSBL
			7	KPC-3, SHV-OSBI
			4	KPC-3 SHV-OSBL TEM-OSBL
	KPC + FSBI + OSBI (2)	K. pneumoniae	1	KPC-2, CTX-M-15, SHV-OSBL, TEM-OSBL
		na pricamornac	1	KPC-3 CTX-M-2 SHV-OSBL TEM-OSBL
	KPC + AmpC + OSBI (3)	E cloacae*	1	KPC-2 TEM-OSBI
		E. cioucuc E. coli	1	KPC-2 CMY-2 TEM-OSBI
		K aeroaenes*	1	KPC-2 TEM-OSBI
	KDC + ESPI + AmpC +	C froundii*	1	
		C. Ileanan E. cloacao*	1	
	03BE (3)	E. Cloucue K. proumonico	1	
		K. preumoniae	1	NPC-3, CTX-IN-15, SHV-12, DHA-25, TEIVI-OSBL
	OXA-48-like \pm OSBL (3)	ĸ. pneumoniae	2	OXA-181, SHV-OSBL
			1	OXA-181, SHV-OSBL, TEM-OSBL
	OXA-48-like + ESBL \pm	K. pneumoniae	1	OXA-48, CTX-M-14, SHV-OSBL
	OSBL (29)		1	OXA-48, CTX-M-15, SHV-OSBL
			3	OXA-48, CTX-M-15, SHV-OSBL, TEM-OSBL
			5	OXA-181, CTX-M-15, SHV-OSBL
			8	OXA-181, CTX-M-15, SHV-OSBL, TEM-OSBL
			1	OXA-232, CTX-M-15, SHV-OSBL
			10	OXA-232, CTX-M-15, SHV-OSBL, TEM-OSBL
	OXA-48-like + AmpC \pm	E. asburiae*	1	OXA-48
	OSBL (3)	E. kobei*	2	OXA-48
	OXA-48-like + ESBL +	C. freundii*	1	OXA-181, CTX-M-15
	AmpC \pm OSBL (3)	E. cloacae*	1	OXA-48, CTX-M-15, TEM-OSBL

	eta -Lactamase types a		No. of	
Region	(no. of isolates)	Organism ^b	isolates	Molecular variant(s)
			1	OXA-181, CTX-M-15, TEM-OSBL
	MBL \pm OSBL (8)	K. pneumoniae	2	NDM-1, SHV-OSBL
			1	NDM-1, SHV-OSBL, TEM-OSBL
			1	NDM-5, SHV-OSBL
		P. mirabilis	4	VIM-5
	MBI + FSBI + OSBI (33)	K. oxvtoca†	1	NDM-1, CTX-M-15, TEM-OSBI
			2	VIM-1
		K nneumoniae	1	NDM-1 CTX-M-15
		n. prieumoniae	1	
			15	
			1	
			1	
			1	NDM-1, CTX-M-15, SHV-55, TEM-OSBL
			1	
			1	NDM-5, CTX-M-15, SHV-OSBL, TEM-OSBL
			1	NDM-7, CTX-M-15, SHV-OSBL
			4	NDM-7, CTX-M-15, SHV-OSBL, TEM-OSBL
			1	VIM-1, CTX-M-15, SHV-OSBL, TEM-OSBL
	MBL + AmpC \pm OSBL (7)	E. coli	1	NDM-5, CMY-42
			1	NDM-5, CMY-42, TEM-OSBL
		P. rettgeri*	3	NDM-1
			1	NDM-1, TEM-OSBL
			1	NDM-1, DHA-type
	MBL + ESBL + AmpC \pm	C. freundii*	1	NDM-1, CTX-M-9-type
	OSBL (11)	E. asburiae*	1	NDM-1, VEB-1, TEM-OSBL
		E. cloacae*	2	NDM-1, CTX-M-15
			2	NDM-1, CTX-M-15, TEM-OSBL
			1	VIM-4. CTX-M-9
			1	VIM-4, CTX-M-100, TEM-OSBI
		E coli	1	NDM-1 CTX-M-15 CMY-6
		K aeroaenes*	1	
		P stuartii*	1	NDM-1 PER-12 DHA-type
	MPL + OVA 49 like + OSPL (1)	K proumonico	1	
	MPL + OXA 49 like + O3DL(1)	F. cloacao*	1	VIM = 0 VA = 0 VA = 0
	MDL + OAA-40-IIRE +	E. Cloucue	I	VIIVI-4, OXR-48, CIVIT-4
		Г. ala a a a a*	1	VINA A OVA 40 CUV 12 CMV A TEM OCDI
	MBL + OXA-48-IIKe + ESBL +	E. cloacae*	I	VIM-4, OXA-48, SHV-12, CMY-4, TEM-OSBL
	AmpC + OSBL(1)			
North Amorica	GES carbananamasa ±	K nneumoniae	1	GES-20 SHV-OSBI
North America		n. pheumoniae	1	GE3-20, 5110-05DE
	$VDC \pm OSPL and/or construm$	E coli	1	KDC 2 TEM OCRI
	$KPC \pm OSBL and/or spectrum$	E. COII	1	KPC-2, TEIM-USBL
	undefined (57)		1	KPC-3
			2	KPC-3, TEM-OSBL
			2	KPC-18, TEM-OSBL
		K. pneumoniae	1	KPC-2
			2	KPC-2, SHV-OSBL
			8	KPC-2, SHV-OSBL, TEM-OSBL
			2	KPC-3
			6	KPC-3, SHV-OSBL
			1	KPC-3, TEM-OSBL
			30	KPC-3, SHV-OSBL, TEM-OSBL
			1	KPC-29, SHV-OSBL, TEM-OSBL
	KPC + ESBL \pm OSBL (16)	K. pneumoniae	1	KPC-2, CTX-M-15, SHV-OSBL
			1	KPC-2, CTX-M-15, SHV-28, TEM-OSBL
			1	KPC-2, CTX-M-124, SHV-OSBL
			1	KPC-2, SHV-12
			2	KPC-2, SHV-12, TEM-OSBL
			1	KPC-3, CTX-M-15, SHV-OSBL, TFM-OSBI
			1	KPC-3, SHV-12
			8	KPC-3, SHV-12, TEM-OSBI
	KPC + AmpC + OSRI (3)	C farmeri*	1	KPC-3
		C freundii*	1	KPC-2
		c. neunun	•	

	eta -Lactamase types a		No. of	
Region	(no. of isolates)	Organism ^b	isolates	Molecular variant(s)
			1	KPC-2, TEM-OSBL
	KPC + ESBL + AmpC \pm	C. freundii*	1	KPC-2, VEB-1B, TEM-OSBL
	OSBL (5)	E. asburiae*	2	KPC-2, SHV-30, TEM-OSBL
		E. cloacae*	1	KPC-2, SHV-5, TEM-OSBL
		E. coli	1	KPC-2, CTX-M-15, CMY-2, TEM-OSBL
	$MBL + ESBL \pm OSBL$ (2)	K. pneumoniae	2	NDM-1, CTX-M-15, SHV-OSBL, TEM-OSBL
	MBL + AmpC \pm OSBL (3)	C. freundii*	1	VIM-1
			1	VIM-32
		E. cloacae*	1	VIM-1

^{*a*}OSBL, original-spectrum β -lactamase: TEM-type and SHV-type β -lactamases that do not contain amino acid substitutions associated with ESBL activity (e.g., TEM-1, SHV-1, SHV-11); Spectrum undefined: TEM-type and SHV-type β -lactamases whose spectrum of activity has not be determined biochemically; ESBL, extended-spectrum β -lactamase; MBL, metallo- β -lactamase.

^{b*}, presumed to also carry the intrinsic chromosomally encoded AmpC β-lactamase common to this species; †, presumed to also carry the intrinsic chromosomally encoded ESBL common to this species.

reports. KPC was the predominant carbapenemase type detected globally, and the largest numbers of KPC-positive isolates were collected in the United States, Argentina, Brazil, Colombia, Greece, Italy, Israel, China, and the Philippines (data not shown), consistent with reports of their endemicity in all but one of these countries (6, 7, 25-28). The largest numbers of meropenem-nonsusceptible OXA-48-likepositive Enterobacterales isolates were observed in Turkey, Russia, Romania, Spain, Belgium, the United Kingdom, Kuwait, and South Africa (data not shown). Isolates carrying OXA-48 are reported to be endemic in Turkey and countries in the Middle East and North Africa, whereas isolates carrying OXA-48-like β -lactamases (e.g., OXA-181 and OXA-232) are prevalent in the Indian subcontinent, though both OXA-48-positive and OXA-48-like-positive isolates have disseminated widely to countries in Europe, Asia, the Pacific, and southern Africa, including those noted in our study (6, 22, 29, 30). Isolates carrying OXA-48-like enzymes were rarely identified in Latin America and the variants found as part of this study were consistent with those reported by others (27). No OXA-48-like-positive isolates were collected in the United States during the surveyed time period, likely reflecting both their low incidence and good susceptibility to meropenem, the sentinel carbapenem used in this study (31-33). NDM-positive Enterobacterales were found in all regions in this study, consistent with reports of their worldwide dissemination (6, 7, 23), but composed the greatest percentage of meropenem-nonsusceptible isolates in the Asia/South Pacific and Middle East/Africa regions. In other studies, NDM was the most commonly identified carbapenemase reported in a surveillance study conducted in the Asia/South Pacific region from 2008 to 2014 (34) and was observed in the greatest number of African countries in literature searches of carbapenem-resistant organisms (35, 36); NDM was also the most common carbapenemase identified in isolates collected from African patients in a small surveillance study conducted in 2014 to 2015 (37). IMP-positive Enterobacterales were most common in the Asia/South Pacific region and also identified in a small percentage of isolates collected in Latin America, consistent with published reports (7, 8, 20, 27). VIM-positive isolates were found in highest proportions in Europe, Middle East/Africa, and Latin America, primarily in countries where they have been reported by others (7, 26, 27, 35).

The present study demonstrated that the overall percentage of meropenem-nonsusceptible *Enterobacterales* has increased over time on the global and most regional levels. These increases are likely partly attributable to increasing proportions of carbapenemase-positive *Enterobacterales* isolates, most notably those carrying OXA-48-like and NDM-type enzymes. Others have also noted the growing incidence and dissemination of isolates carrying these carbapenemase types. Increasing CRE rates were reported for the SENTRY global surveillance study and were attributed in part to an



FIG 3 Comparison of the distribution of carbapenem resistance mechanisms identified in meropenem-nonsusceptible *Enterobacterales* isolates collected from 2012 to 2014 and from 2015 to 2017. Region (no. of isolates collected in 2012 to 2014/no. of isolates collected in 2015 to 2017): Global, all surveyed regions (38,190/43,591); LA, Latin America (5,317/7,729); EUR, Europe (18,301/21,850); AP, Asia/South Pacific (7,087/7,051); MEA, Middle East/Africa (3,281/3,690); NA, North America (4,204/3,271 [2015 to 2016 only]). No Cpase detected, no gene encoding a carbapenemase was detected by PCR. Isolates carrying multiple carbapenemases were counted for each individual carbapenemase type.

increase in isolates carrying genes encoding NDM and OXA-48 variants identified in 2014 to 2016 compared to an earlier time period (21). In Europe, the incidence of CPE and a worsening epidemiological situation were documented in a series of expert reports, which also reported an increase in and rapid spread of OXA-48-positive and NDM-positive Enterobacterales in 2015 relative to prior years (3, 19, 26, 38, 39); similarly, increases in the incidence of NDM-positive isolates and/or OXA-48-positive isolates have been reported on the country level (40-43). In Asia, increasing trends in NDMpositive E. coli and E. cloacae and KPC-positive K. pneumoniae were reported in China in 2013 to 2016, whereas increasing trends in both KPC-positive and OXA-48positive K. pneumoniae were observed in Taiwan in 2012 to 2015 (28, 44). Increases in carbapenem-resistant K. pneumoniae also have been documented in Malaysia, Singapore, Philippines, Thailand, and Vietnam in recent years, and NDM-positive isolates are commonly identified in these countries (45). In Latin America, NDM has been reported in several species and as part of outbreaks, notably in Mexico, which was the source of \sim 55% of the NDM-positive isolates identified in that region as part of this study (27, 46, 47).

The strength of the present study is that it is a global, multiyear study employing standardized antimicrobial susceptibility and molecular testing methods that were used consistently throughout its course. However, it also has limitations. The study was not designed to determine the prevalence of resistance mechanisms, since investigators were requested to collect a predefined number of isolates of select species comprising major clinically relevant pathogens and pathogens that pose unique treatment challenges. Furthermore, the relatively limited number of medical centers participating in each country may not provide a representation of the full range and diversity of CRE existing in each region. Changes in study participation by individual medical centers and countries over the 6 years surveyed also must be taken into consideration when evaluating regional trends. Only meropenem-nonsusceptible isolates were screened for carbapenemase carriage, likely resulting in an underestimate of the number of isolates carrying OXA-48-like β -lactamases and potentially biasing the results toward resistance mechanisms more specific to meropenem than carbapenems in general (32, 48). Finally, sequence typing was not performed because of the volume of isolates examined.

In the absence of appropriate control measures, CRE can disseminate readily among patients in health care environments. Timely detection of CRE is critical to facilitate optimal implementation of infection prevention and control measures and to inform clinicians who must choose treatment regimens (49–51). Current treatment options for CRE infections include combinations of polymyxins, tigecycline, fosfomycin, and aminoglycosides; β -lactam/non- β -lactam inhibitor combinations utilizing diazabicyclooctanones (ceftazidime-avibactam and imipenem-relebactam) or boronic acid derivatives (meropenem-vaborbactam); and a siderophore cephalosporin (cefiderocol). β -lactam/non- β -lactam inhibitor combinations MBL-positive *Enterobacterales* (aztreonam-avibactam and cefepime-taniborbactam) and derivatives of older drug classes are also in development (1, 52–54). However, ongoing CRE surveillance combined with a global antimicrobial stewardship strategy, sensitive clinical laboratory detection methods, and adherence to infection control practices will be needed to interrupt the progressive spread of CRE.

MATERIALS AND METHODS

Bacterial isolate collection. Nonduplicate isolates of *Enterobacterales* were collected from patients with urinary tract infections (n = 22,872), skin and soft tissue infections (n = 19,838), lower respiratory tract infections (n = 18,405), intra-abdominal infections (n = 14,964), bloodstream infections (n = 5,559; isolates collected only in 2014 to 2017), and other infections (n = 143) by 232 medical laboratories located in 39 countries in Asia/South Pacific (n = 14,138), Europe (n = 40,151), Latin America (n = 13,046), the Middle East/Africa (n = 6,971), and North America (n = 7,475). Medical centers were requested to contribute a target number of isolates of specified bacterial species regardless of antibiotic susceptibility. Each isolate was deemed to be a clinically significant pathogen by diagnostic algorithms in use in each participating laboratory and was considered the probable causative agent of infection. Participating countries by year are listed in Table S1 in the supplemental material. Nine countries (Austria, China, Hong Kong, Kenya, Malaysia, Nigeria, Poland, Sweden, and the United States) participated in fewer than 6 years of the study.

Antimicrobial susceptibility testing and screening for β -lactamase genes. All isolates were shipped to a central reference laboratory (IHMA, Schaumburg, IL), where species identification of all isolates was confirmed by matrix-assisted laser desorption ionization–time of flight mass spectrometry (Bruker Daltonics, Bremen, Germany). Antimicrobial susceptibility testing was performed at IHMA by broth microdilution following Clinical and Laboratory Standards Institute (CLSI) guidelines (55, 56). *Enterobacterales* isolates testing as nonsusceptible to meropenem (MIC $\geq 2 \mu g/ml$) were screened for the presence of β -lactamase genes encoding carbapenemases (KPC, OXA-48-like, GES, NDM, IMP, VIM, SPM, and GIM) and other β -lactamases (TEM, SHV, CTX-M-1 group, CTX-M-2 group, CTX-M-8 group, CTX-M-9 group, CTX-M-25 group, VEB, PER, ACC, ACT, CMY, DHA, FOX, MIR, and MOX) using a combination of microarray and multiplex PCR assays, followed by amplification and sequencing of the full-length genes and comparison to publicly available databases (57).

SUPPLEMENTAL MATERIAL

Supplemental material is available online only. **SUPPLEMENTAL FILE 1**, PDF file, 0.3 MB.

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and a former employee of Pfizer. All authors provided analysis input and have read and approved the final manuscript.

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