



Objectives

Within the last decade, multi-drug resistance in gram-negative bacteria has increased across Europe. In Germany, a definition of multi-drug resistance has been introduced by the Commission for Hospital Hygiene and Infectious Disease Prevention in the context of recommendations on infection control and hygiene. This definition is applied to data from the German Antimicrobial Resistance Surveillance (ARS) System to study trends in German hospitals 2010 to 2013. ARS is a laboratory based sentinel system for continuous collection of data on antimicrobial resistance covering the whole spectrum of bacterial pathogens from hospital and ambulatory care.

Materials & Methods

Data on antimicrobial resistance of *Escherichia (E.) coli*, *Klebsiella (K.) pneumoniae*, *Pseudomonas (P.) aeruginosa* and *Acinetobacter (A.) baumannii* submitted by nine laboratories covering 214 hospitals (out of a total of 2000 hospitals in Germany) with continuous data submission for the period 2010 to 2013 were included.

Antimicrobial susceptibility testing is performed by automated systems. Isolates are classified as threefold (3MR) or fourfold resistant (4MR) based on SIR categorisation to indicator substances of four antibiotic classes as shown in figure 1. Irrespective of the phenotypical resistance, a strain with a confirmed carbapenemase is classified as 4MR.

Figure 1: Scheme of classification for multidrug-resistant Gram-negative bacteria
3MR - threefold resistance; 4MR - fourfold resistance; RI - resistant or intermediate; S - susceptible

Antibiotic class	Indicator	<i>Enterobacteriaceae</i>		<i>Pseudomonas aeruginosa</i>		<i>Acinetobacter baumannii</i>	
		3MR	4MR	3MR	4MR	3MR	4MR
Ureidopenicillins	piperacillin	RI	RI		RI	RI	RI
Third-generation cephalosporins	cefotaxime AND/OR ceftazidime	RI	RI	only one class	RI	RI	RI
Carbapenems	imipenem AND/OR meropenem	S	RI	S	RI	S	RI
Fluoroquinolones	ciprofloxacin	RI	RI		RI	RI	RI

adapted from: Hygienemaßnahmen bei Infektionen oder Besiedlung mit multiresistenten gramnegativen Stäbchen. Empfehlung der Kommission für Krankenhaushygiene und Infektionsprävention (KRINKO) beim Robert Koch-Institut (RKI). Bundesgesundheitsblatt Gesundheitsforschung Gesundheitsschutz 2012; 55:1311-54.

Results

Analysis is based on 207,895 non-duplicate clinical isolates of *E. coli*, 39,651 isolates of *K. pneumoniae*, 39,723 isolates of *P. aeruginosa* and 2,142 isolates of *A. baumannii* (2010-2011 only) from patients admitted to German hospitals during 2010 to 2013.

Results are displayed in table 1.

Table 1 Multi-drug resistance in *Escherichia coli*, *Klebsiella pneumoniae*, *Pseudomonas aeruginosa* and *Acinetobacter baumannii* in German hospitals 2010-2013:

Total number of isolates tested (N), percentages of threefold and fourfold resistance (3MR%, 4MR%) and 95%-confidence intervals (CI) by year.

Pathogen	Year	N	3MR%	CI 3MR	4MR%	CI 4MR
<i>E. coli</i>						
	2010	45,869	6.5	6.3-6.7	0.03	0.01-0.05
	2011	50,992	6.7	6.5-6.9	0.02	0.01-0.03
	2012	56,284	7.2	7.0-7.4	0.04	0.02-0.06
	2013	54,750	8.4	8.2-8.6	0.06	0.04-0.08
<i>K. pneumoniae</i>						
	2010	9,191	9.0	8.4-9.6	0.29	0.18-0.40
	2011	9,479	8.6	8.0-9.2	0.24	0.14-0.34
	2012	10,663	9.6	9.0-10.2	0.23	0.14-0.32
	2013	10,318	11.3	10.7-11.9	0.31	0.20-0.42
<i>P. aeruginosa</i>						
	2010	9,693	7.5	7.0-8.0	3.9	3.5-4.3
	2011	10,295	7.7	7.2-8.2	4.5	4.1-4.9
	2012	10,467	7.0	6.5-7.5	3.4	3.1-3.7
	2013	9,268	6.9	6.4-7.4	4.0	3.6-4.4
<i>A. baumannii</i>						
	2010	1,085	15.0	12.9-17.1	7.8	6.2-9.4
	2011	1,057	13.9	11.8-16.0	10.0	8.2-11.8

In *E. coli*, the proportion of 3MR rose from 6.5 percent of isolates tested in 2010 to 8.4 percent in 2013 with significant increases over the past three years whereas fourfold resistance was very rare in the permille range.

For *K. pneumoniae*, there was a comparable trend for 3MR on a higher level with a significant increase from 9.0 to 11.3 percent while the percentage of 4MR was stable between 0.2 and 0.3.

In *P. aeruginosa*, no trend over time could be seen with 3MR ranging from 6.9 to 7.7 percent as well as for 4MR ranging from 3.4 to 4.5 percent.

For *A. baumannii*, results are displayed only for the years 2010 and 2011 due to methodological reasons: From then on an increasing use of MALDI-TOF mass spectrometry for species identification resulted in a switch in the species distribution within *Acinetobacter spp.* (number of strains identified as *A. baumannii* decreased while number of strains identified as *A. baumannii complex* - including *A. pittii* and *A. nosocomialis* increased); thereby comparability of results over time is compromised.

In *A. baumannii*, proportions of multi-drug resistance are highest with 3MR at 15.0 percent in 2010 and 13.9 percent in 2011 and 4MR at 7.8 percent and 10.0 percent, respectively.

Conclusions

The definition of multi-drug resistance in gram-negative bacteria proposed by the German Commission of Hospital Hygiene and Infectious Disease Prevention is applicable to routine surveillance data, even retrospectively, as the required indicators are available in routine susceptibility testing. The almost unchanged percentage of 4MR in *K. pneumoniae* seems to contrast with the rising number of reported outbreaks with carbapenemase-producing strains – maybe a ten-percent coverage of the surveillance system is not sufficient to reflect changes in resistance mainly occurring in outbreaks.

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