Antimicrobial resistance in hospital acquired infections: Epidemiology mechanisms and management

9th August 2019

Overview

- Introduction
- Prevalence
- The spectrum of HAI syndromes
- Epidemiology of the HAI syndromes AMR and management principles
- Mechanism of resistance of the most common MDR bugs
- Prevention
- Summary

Introduction

- ICU is most frequently identifiable source of nosocomial infections
- Likelihood of occurrence of infection may increase by 6% for each day
- Urinary tract infections, pneumonia and bacteremia are currently the most common and pneumonia is by far the leading cause of death
- The empiric treatment of infections in the ICU demands an intimate knowledge of the epidemiology, the source, the type and the nature of infections as well as the antimicrobial resistance patterns of the invading organisms
- Some are unique to every ICU

Prevalence of HAI in ICU

- USA – 5-10%
- EU 18-20%
- Developing countries 51%
- Local data 30-35%

Agarwal *et al.* Journal of Infection (2006) 53, 98e105
JAMA. 2009;302(21):2323-2329. doi:10.1001/jama.2009.1754
Weiner *et al.* Infect Control Hosp Epidemiol 2016;37:1288–1301

Common infection syndromes in the ICU

- Those associated with supportive devices→ Device associated infections
  - CAUTI
  - Ventilator associated pneumonia
  - CRBSI/CLABSI
  - SSI

NHSN – CDC data

TABLE 2. Types of Healthcare-Associated Infections (HAIs) and Surgical Site Infections (SSIs) Reported to the National Healthcare Safety Network (NHSN), 2011–2014

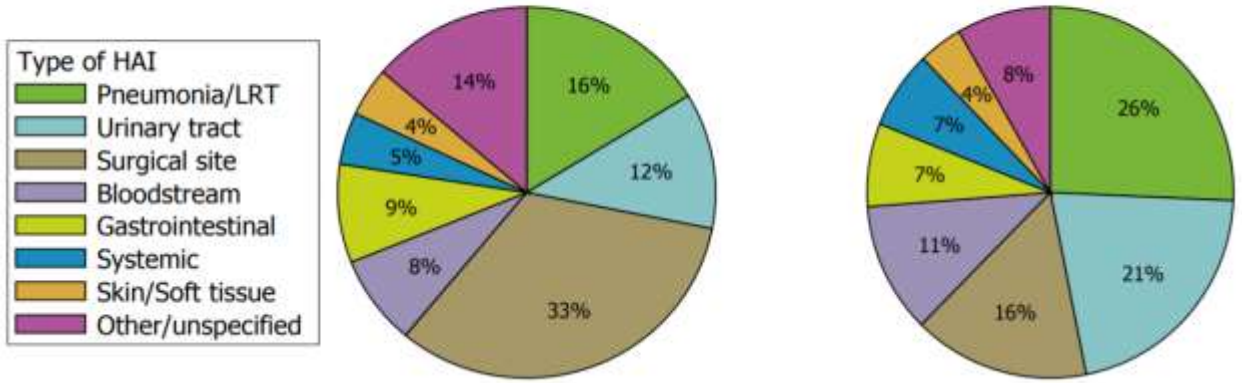
Type of HAI	No. (%) of events reported (n = 365,490)	No. (%) of pathogens reported (n = 408,151)
CLABSI	85,994 (23.5)	96,532 (23.7)
CAUTI	138,283 (37.8)	153,805 (37.7)
VAP[a,b]	8,133 (2.2)	8,805 (2.2)
SSI[b]	133,080 (36.4)	149,009 (36.5)
Type of Surgery	**No. (%) of SSIs**	**No. (%) of SSI pathogens**
Abdominal[c]	63,508 (47.7)	76,307 (51.2)
Breast[d]	886 (0.7)	946 (0.6)
Cardiac[e]	10,439 (7.8)	11,281 (7.6)
Kidney[f]	251 (0.2)	285 (0.2)
Neck[g]	146 (0.1)	212 (0.1)
Neurological[h]	1,945 (1.5)	2,168 (1.5)
Ob/Gyn[i]	22,231 (16.7)	20,725 (13.9)
Orthopedic[j]	31,539 (23.7)	34,341 (23.0)
Prostate[k]	53 (<0.1)	61 (<0.1)
Transplant[l]	644 (0.5)	815 (0.5)
Vascular[m]	1,438 (1.1)	1,868 (1.3)

NOTE. CAUTI, catheter-associated urinary tract infection; CLABSI, central line–associated bloodstream infection;

Weiner *et al.* Infect Control Hosp Epidemiol 2016;37:1288–1301

ECDC data

Figure 1. Distribution of HAI types by presence of HAI on admission, HAI present on admission (left) HAI onset during hospitalisation (right)



Indian data

- SSI was commonest (57.2%) followed by UTI (23.8%) and BSI (19.0%) respectively
- CLABSI (13.50%) was the most common followed by UTI (10.75%) and VAP (6.15%)
- Previous study from PGI – Pneumonia (23%) → Undifferentiated sepsis (10.5%)→ BSI (7%) → UTI (1.4%) → CRBSI
- Pneumonia (20%) → blood stream infection (12%) → VAT (3.53%) →CAUTI (1.6%)→ CDAD (1.35%) → CRBSI (0.81%)

Agarwal *et al.* Journal of Infection (2006) 53, 98e105
Indian Journal of Anaesthesia | Vol. 58| Issue 1 | Jan-Feb 2014

Hospital acquired and ventilator associated pneumonia

- HAP – 48 hours or more after admission and did not appear to be incubating at the time of admission
- VAP - >48 hours after endotracheal intubation

HAP/VAP rates

- Trend in Ventilator-Associated Pneumonia Rates Between 2005 and 2013

Table. Medicare Patient Safety Monitoring System Patient Characteristics and Observed VAP Rates

	No. (%)				
	2005-2006	2007, 2009	2010-2011	2012-2013	Total
Hospitals, No.	222	249	490	369	1330
MPSMS patients ≥65 y, No.	11 752	15 246	35 307	23 730	86 035
Condition					
AMI	1360 (11.6)	2223 (14.6)	7816 (22.1)	4693 (19.8)	16 092 (18.7)
Heart failure	2689 (22.9)	3268 (21.4)	9417 (26.7)	5999 (25.3)	21 373 (24.8)
Pneumonia	2889 (24.6)	4900 (32.1)	10 480 (29.7)	7353 (31.0)	25 622 (29.8)
Major surgery	4814 (41.0)	4855 (31.8)	7594 (21.5)	5685 (24.0)	22 948 (26.7)
Age, mean (SD), y	77.7 (7.8)	78.5 (8.3)	78.9 (8.4)	78.6 (8.5)	78.6 (8.4)
Sex					
Men	5293 (45.0)	6825 (44.8)	15 998 (45.3)	10 677 (45.0)	38 793 (45.1)
Women	6459 (55.0)	8421 (55.2)	19 309 (54.7)	13 053 (55.1)	47 242 (54.9)
Race[a]					
White	10 372 (88.3)	13 400 (87.9)	30 740 (87.1)	20 583 (86.7)	75 095 (87.3)
Black	785 (6.7)	1049 (6.9)	2869 (8.1)	1957 (8.3)	6660 (7.7)
Other	595 (5.1)	797 (5.2)	1698 (4.8)	1190 (5.0)	4280 (5.0)
Comorbidities					
Cancer	3072 (26.1)	3828 (25.1)	8529 (24.2)	5844 (24.6)	21 273 (24.7)
Diabetes	3856 (32.8)	5300 (34.8)	13 671 (38.7)	9186 (38.7)	32 013 (37.2)
Obesity	1416 (12.1)	2263 (14.8)	6712 (19.0)	5446 (23.0)	15 837 (18.4)
Cerebrovascular disease	2260 (19.2)	3155 (20.7)	7945 (22.5)	4956 (20.9)	18 316 (21.3)
Heart failure/pulmonary edema	5269 (44.8)	7083 (46.5)	18 921 (53.6)	12 075 (50.9)	43 348 (50.4)
Chronic obstructive pulmonary disease	4143 (35.3)	5315 (34.9)	13 003 (36.8)	8627 (36.4)	31 088 (36.1)
Smoking	1363 (11.6)	1995 (13.1)	4753 (13.5)	3652 (15.4)	11 763 (13.7)
Corticosteroids	863 (7.3)	1196 (7.8)	2879 (8.2)	1996 (8.4)	6934 (8.1)
Coronary artery disease	6159 (52.4)	8282 (54.3)	21 750 (61.6)	13 756 (58.0)	49 947 (58.1)
Renal disease	3277 (27.9)	4187 (27.5)	12 183 (34.5)	8593 (36.2)	28 240 (32.8)
Ventilated patients without a prior diagnosis of pneumonia (denominator)	295 (2.5)	308 (2.0)	743 (2.1)	510 (2.1)	1856 (2.2)
VAP cases (% of denominator)	32 (10.8)	23 (7.5)	77 (10.4)	52 (10.2)	180 (9.7)

Abbreviations: AMI, acute myocardial infarction; MPSMS, Medicare Patient Safety Monitoring System; VAP, ventilator-associated pneumonia.

[a] Race obtained from chart abstraction and provided here as a routine component of demographic data.

JAMA. 2016;316(22):2427-2429. doi:10.1001/jama.2016.16226

HAP/VAP rates from India and effect of preventive strategies

	January to April, 2010	January to December				January to July, 2015	Total
		2011	2012	2013	2014		
Patients	314	1421	1045	884	1176	619	5459
Patient days	3009	13,387	10,350	8731	10,903	5980	52,360
LOS (days), range (median)	3-57 (8)	3-69 (10)	3-65 (8)	3-60 (7)	3-76 (8)	3-93 (7)	3-76 (8)
Males/females	270/44	1224/197	899/146	740/144	962/217	526/93	40,621/838
VDs	2377	8114	7233	6114	8171	4269	36,278
Episodes of VAP	105	165	33	30	67	33	433
VAP rates/1000 VDs	44	20.3	4.5	4.9	8.1	7.7	11.9
Ventilator bundle compliance	10	74	78	82.4	78	84	67.7
Hand hygiene compliance	12	64	59.7	61	58	63	53

LOS: Length of stay, VAP: Ventilator-associated pneumonia, VDs: Ventilator days

Incidence of ventilator-associated pneumonia and impact of multidrug-resistant infections on patient's outcome: Experience at an Apex Trauma Centre in North India. Indian J Med Microbiol 2017;35:504-10

Risk factors for MDR VAP/HAP

Table 2. Risk Factors for Multidrug-Resistant Pathogens

Risk factors for MDR VAP
Prior intravenous antibiotic use within 90 d
Septic shock at time of VAP
ARDS preceding VAP
Five or more days of hospitalization prior to the occurrence of VAP
Acute renal replacement therapy prior to VAP onset
Risk factors for MDR HAP
Prior intravenous antibiotic use within 90 d
Risk factors for MRSA VAP/HAP
Prior intravenous antibiotic use within 90 d
Risk factors for MDR *Pseudomonas* VAP/HAP
Prior intravenous antibiotic use within 90 d

Abbreviations: ARDS, acute respiratory distress syndrome; HAP, hospital-acquired pneumonia; MDR, multidrug resistant; MRSA, methicillin-resistant *Staphylococcus aureus*; VAP, ventilator-associated pneumonia.

Clinical Infectious Diseases 2016;63(5):e61–111

VAP/HAP etiology

- Data from USA CDC NHSN 2011-2014
  - *Staph aureus 28.0%*
  - *Pseudomonas 21.8%*
  - *Klebsiella 9.8%*
  - *Escherichia coli 6.9%*
  - *Acinetobacter 6.8%*
  - *Enterobacter species 6.3%*

Clin Infect Dis. 2010 Aug;51 Suppl 1:S81-7

VAP/HAP aetiology

- *A. baumannii (54%)*
- *P. aeruginosa (21%)*
- *K. pneumoniae (13%)*
- *E. coli (3%)*
- *S. aureus (3%)*
- *Stenotrophomonas maltophilia (2%)*
- *Burkholderia cepacia (1%)*
- *Providencia (0.7%) and Candida* (0.7%)

Incidence of ventilator-associated pneumonia and impact of multidrug-resistant infections on patient's outcome: Experience at an Apex Trauma Centre in North India. Indian J Med Microbiol 2017;35:504-10

VAP/HAP etiology

VAP

Organism	Frequency (%)
Acinetobacter baumannii	20 (40.81)
Pseudomonas aeruginosa	8 (16.32)
Klebsiella pneumoniae	8 (16.32)
Polymicrobial	8 (16.32)
Enterobacter cloacae	2 (4.08)
MRSA	2 (4.08)
Burkholderia cephacia	1 (2.04)
Total	49 (100)

HAP

Organism	Frequency (%)
Acinetobacter baumannii	10 (62.5)
Pseudomonas aeruginosa	3 (18.75)
Klebsiella pneumoniae	1 (6.25)
Escherichia coli	1 (6.25)
Polymicrobial	1 (6.25)
Total	16 (100)

Table 5. Differences in Causative Pathogens of Hospital-Acquired Bacterial Pneumonia (HABP) and Ventilator-Associated pneumonia

	Percentage of cases			
	United States (n = 2585)		All regions (n = 7496)	
Pathogen	HABP	VABP	HABP	VABP
Staphylococcus aureus	36.5[a]	31.9[a]	26.6[a]	19.5[a]
Pseudomonas aeruginosa	19.0[a]	21.4[a]	22.4[a]	26.6[a]
Enterobacter species	8.6	8.8	7.5	7.0
Klebsiella species	8.0	6.6	10.5	10.2
Serratia species	5.5	6.5	4.1	4.1
Acinetobacter species	4.4	5.3	8.3[a]	14.3[a]
Top 6 species	80.4	80.5	79.4	81.7
Pathogens causing CABP[b]	3.3	6.6	2.6	4.1

[a] Significant difference in incidence rate between the United States and all regions.

[b] *Haemophilus influenzae*, *Streptococcus pneumoniae*, and *Moraxella catarrhalis*.

Data collected as a part of SENTRY antimicrobial surveillance program from patients in North America, Europe, and Latin America (1997-2008)

Clinical Infectious Diseases, Volume 51, Issue Supplement_1, 1 August 2010, Pages S81–S87, https://doi.org/10.1086/653053

Table 6. Variations in Drug Susceptibility Rates between Hospital-Acquired Bacterial Pneumonia (HABP) and VAP

Antimicrobial agent	Susceptibility, % (HABP/VABP)					
	Staphylococcus aureus	*Pseudomonas aeruginosa*	*Klebsiella* species	*Escherichia coli*	*Acinetobacter* species	*Enterobacter* species
Oxacillin	41/49[a]	…	…	…	…	…
Gentamicin	87/78	**72/66**	**82/71**	85/84	**25/18**	**87/81**
Levofloxacin	42/52[a]	60/58	**84/76**	72/74	**16/11**	88/89
Cefepime	41/49	**70/65**	**87/78**	91/87	**27/20**	93/91
Ceftazidime	41/49	**68/63**	**77/68**	**84/78**	12/10	62/64
Meropenem	41/49	**72/66**	>99/99	100/100	**58/46**	100/99
Piperacillin-tazobactam	41/49	**76/71**	**76/71**	86/82	**19/11**	71/70

NOTE. Data are from [14–18]. Boldface indicated ≥5% decrease in susceptibility for VABP isolates, compared with HABP isolates. More than a 10% lower susceptibility occurred with 3 drug-pathogen analyses.

[a] VABP *S. aureus* isolates were generally more susceptible to oxacillin and fluoroquinolones.

Clinical Infectious Diseases, Volume 51, Issue Supplement_1, 1 August 2010, Pages S81–S87, https://doi.org/10.1086/653053

Drug susceptibility profile in VAP

Antimicrobial	Percentage susceptibility
Ampicillin	0
Ampicillin/sulbactam	2
Amikacin	13.6
Aztreonam	48
Ceftazidime	7
Ceftriaxone	7
Cefepime	13.6
Cefoperazone/sulbactam	11
Ceftriaxone/sulbactam	11
Cefepime/tazobactam	25
Ciprofloxacin	11
Chloramphenicol	14
Colistin	100*
Gentamicin	13.6
Levofloxacin	11
Meropenem	45
Netilmicin	23
Piperacillin	7
Piperacillin/tazobactam	8
Tigecycline	64 (not tested for *Pseudomonas*)

*Genera intrinsically resistant to colistin were not tested; all data shown in percentage

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Treatment: Principles

- Empiric treatment regimens based on local distribution of pathogens associated with VAP and their antimicrobial susceptibilities
- Every hospital to generate local antibiograms
- Agent active against MRSA for the empiric treatment of suspected VAP only in patients with any of the following: a risk factor for antimicrobial resistance, patients being treated in units where >10%–20% of S. aureus isolates are methicillin resistant, and patients in units where the prevalence of MRSA is not known
- For HAP and no risk of MRSA cover MSSA -piperacillin-tazobactam, cefepime, levofloxacin, imipenem, or meropenem
- Pseudomonas MDR is suspicion – Combination therapy Beta lactam + FQ or aminoglycosides

Clinical Infectious Diseases 2016;63(5):e61–111

Treatment: Principles

- VAP with MDR organisms susceptible to only polymyxin and AG – inhaled antibiotics
- Length of therapy 7 days
- De escalation of antibiotics based on culture sensitivity reports

Clinical Infectious Diseases 2016;63(5):e61–111

Table 1. Empiric Multidrug-Resistant Coverage for Suspected Hospital-acquired Pneumonia or Ventilator-acquired Pneumonia

Cover MRSA with vancomycin or linezolid if:

- Prior IV antibiotic use within 90 d, or
- At least 10–20% of isolates are methicillin resistant on the local antibiogram, or
- Local resistance patterns are unknown, or
- HAP with a high risk of mortality (need for ventilatory support due to HAP, septic shock), or
- VAP with MDR risk factors such as:
  - Prior IV antibiotic use within 90 d
  - Septic shock at the time of VAP
  - ARDS preceding VAP
  - Five or more days of hospitalization before occurrence of VAP
  - Acute renal replacement therapy before VAP onset

- Rx Vancomycin 15-20mg/kg every 8-12 hours
- Dose to obtain trough concentrations 15-20mcg/mL

Higher clinical success in patients with ventilator-associated pneumonia due to methicillin-resistant *Staphylococcus aureus* treated with linezolid compared with vancomycin: results from the IMPACT-HAP study

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Abstract

Introduction: Controversy exists regarding optimal treatment for ventilator-associated pneumonia (VAP) due to methicillin-resistant *Staphylococcus aureus* (MRSA). The primary objective of this study was to compare clinical success of linezolid versus vancomycin for the treatment of patients with MRSA VAP.

Methods: This was a multicenter, retrospective, observational study of patients with VAP (defined according to Centers for Disease Control and Prevention criteria) due to MRSA who were treated with linezolid or vancomycin. MRSA VAP was considered when MRSA was isolated from a tracheal aspirate or bronchoalveolar lavage. Clinical success was evaluated by assessing improvement or resolution of signs and symptoms of VAP by day 14. After matching on confounding factors, logistic regression models were used to determine if an association existed between treatment arm and clinical success.

Results: A total of 188 patients were evaluated (101 treated with linezolid and 87 with vancomycin). The mean ± standard deviation Acute Physiology and Chronic Health Evaluation (APACHE) II score was 21 ± 11 for linezolid- and 19 ± 9 for vancomycin-treated patients ($P = 0.041$). Clinical success occurred in 85% of linezolid-treated patients compared with 69% of vancomycin-treated patients ($P = 0.009$). After adjusting for confounding factors, linezolid-treated patients were 24% more likely to experience clinical success than vancomycin-treated patients ($P = 0.018$).

Conclusions: This study adds to the evidence indicating that patients with MRSA VAP who are treated with linezolid are more likely to respond favorably compared with patients treated with vancomycin.

Linezolid versus Vanco or Teico metanalysis

Eur J Clin Microbiol Infect Dis

Study or Subgroup	Linezolid Events	Total	Vancomycin Events	Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Deville2003	2	3	1	1	0.6%	0.83 [0.28, 2.51]
Jaksic2006	19	23	13	15	4.7%	0.95 [0.73, 1.25]
Kaplan2003	9	10	10	10	3.1%	0.90 [0.69, 1.18]
Kohno2007	11	34	6	19	2.3%	1.02 [0.45, 2.33]
Lin2008	19	26	18	33	4.7%	1.34 [0.91, 1.98]
Rubinstein2001	71	107	62	91	19.9%	0.97 [0.80, 1.18]
Stevens2002	20	39	16	32	5.2%	1.03 [0.65, 1.63]
Wunderink2003	114	168	111	171	32.6%	1.05 [0.90, 1.22]
Wunderink2008	20	30	10	20	3.6%	1.33 [0.80, 2.21]
Wunderink2012	95	165	81	174	23.4%	1.24 [1.01, 1.52]
Total (95% CI)		**605**		**566**	**100.0%**	**1.09 [0.99, 1.19]**
Total events	**380**		**328**			

Heterogeneity: Chi² = 7.76, df = 9 (P = 0.56); I² = 0%

Test for overall effect: Z = 1.83 (P = 0.07)

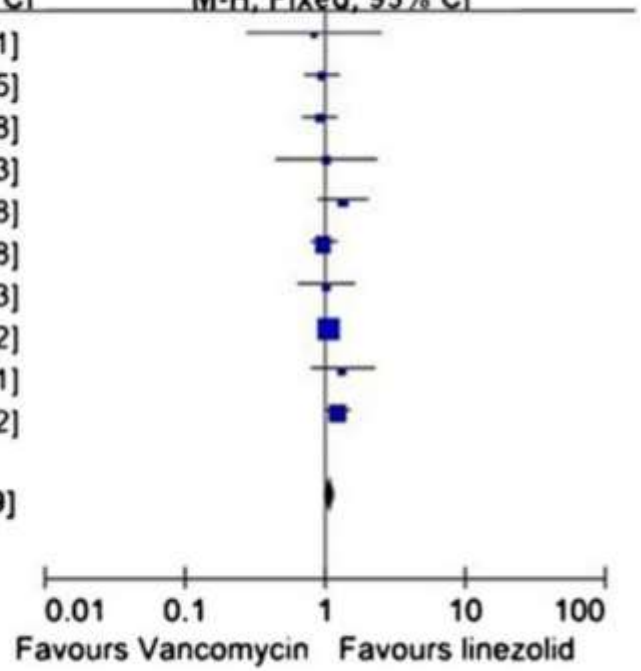


Fig. 3 Linezolid versus vancomycin: meta-analysis of treatment success for the clinically assessed patients

European Journal of Clinical Microbiology & Infectious Diseases September 2013, Volume 32, Issue 9, pp 1121–1128

Linezolid versus Vanco or Teico metanalysis

Study or Subgroup	Linezolid Events	Linezolid Total	Glycopeptides Events	Glycopeptides Total	Weight	Risk Ratio M-H, Fixed, 95% CI
Cepeda2004	10	12	15	22	5.1%	1.22 [0.83, 1.79]
Deville2003	2	3	1	1	1.0%	0.83 [0.28, 2.51]
Kohno2007	13	35	7	19	4.3%	1.01 [0.49, 2.09]
Lin2008	17	22	15	28	6.3%	1.44 [0.95, 2.18]
Rubinstein2001	36	53	28	39	15.5%	0.95 [0.72, 1.24]
Stevens2002	9	12	12	16	4.9%	1.00 [0.65, 1.54]
Wunderink2003	47	76	42	79	19.7%	1.16 [0.89, 1.53]
Wunderink2008	13	23	9	19	4.7%	1.19 [0.66, 2.16]
Wunderink2012	97	167	82	174	38.5%	1.23 [1.01, 1.51]
Total (95% CI)		**403**		**397**	**100.0%**	**1.16 [1.03, 1.31]**
Total events	244		211			

Heterogeneity: $Chi^2 = 4.63$, $df = 8$ ($P = 0.80$); $I^2 = 0\%$

Test for overall effect: $Z = 2.45$ ($P = 0.01$)

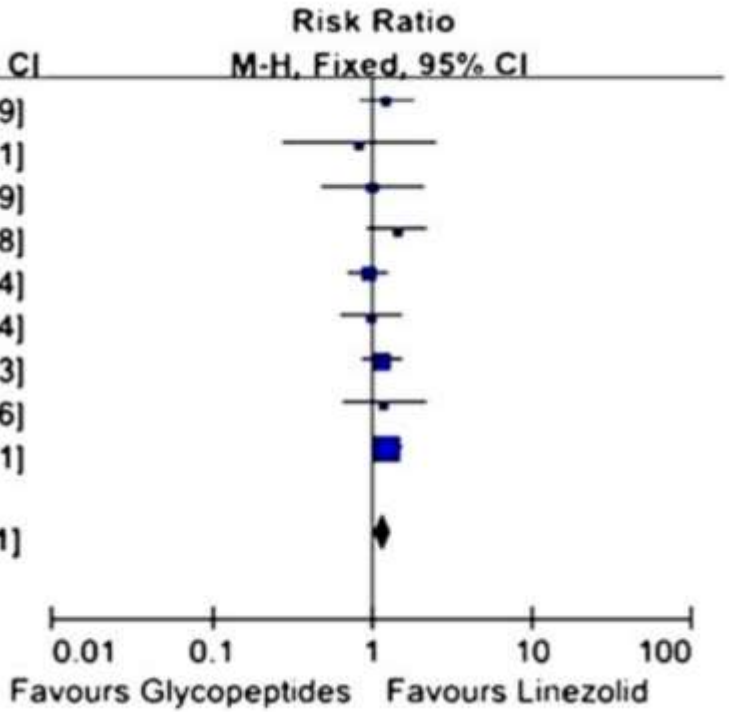


Fig. 5 Linezolid versus vancomycin: meta-analysis of microbiologic success for the clinically assessed patients

European Journal of Clinical Microbiology & Infectious Diseases September 2013, Volume 32, Issue 9, pp 1121–1128

Gram negative HAP/VAP

- ESBL organisms –
  - Carbapenems (except Doripenem)
  - Cephalosporins selectively depending on the prevalence of resistance to ceftazidime and cefepime
  - local cefepime resistance rates are high (ie, >10 percent)→Carbapenem
  - Ceftazidime avibactam non inferior to meropenem in REPROVE trial for MDR (ceftazidime resistant) gram negative HAP/VAP
- Carbapenem resistant (Carbapenemase producing)
  - Colistin/Polymyxin especially with Acinetobacter baumanii

Lancet Infect Dis 2018; 18: 285–95

Intravascular catheter-related bloodstream infection

- Lab confirmed blood stream infection
  - Recognized bacterial or fungal pathogen cultured from one or more blood cultures, and the pathogen is not related to an infection at another site
  - Common commensal organism (eg, coagulase-negative staphylococcus) in two or more blood cultures collected on different days or from different sites that is not related to an infection at another site and that occurs in the setting of one of the following signs or symptoms: fever (>38.0°C), chills, or hypotension
- CLABSI- BSI meeting at least one of the LCBI criteria above in a patient with a central line in place for >2 consecutive calendar days

Epidemiology

- US CDC data suggests decrease in incidence
  - 3.6 per 1000 central line days 2001
  - 1.5 per 1000 central line days 2009
  - 0.76 per 1000 central line days in 2013
- EU
  - CLABSI rate 1.8-2.4 per 1000 central line days 2016
  - ICU acquired BSI 3.7% patients staying > 2 days
  - BSIs was CLABSI in 43.6%, secondary to another infection 35.1% of cases, unknown origin in 21.4% of cases

European Centre for Disease Prevention and Control. Healthcare-associated infections acquired in intensive care units. In: ECDC. Annual epidemiological report for 2016. Stockholm: ECDC; 2018.
Sustaining Reductions in Central Line-Associated Bloodstream Infections in Michigan Intensive Care Units: A 10-Year AnalysisAm J Med Qual. 2016;31(3):197

Epidemiology

- Developing countries
  - Pooled incidence of CLABSI (422 ICUs 36 countries) in Latin America, Asia, Africa, and Europe from 2004 to 2009 6.8 per 1000 central line days
- Indian data
  - 5.1 per 1000 central line days
- PGI
  - 8.58 per 1000 central line days

Am J Infect Control. 2012;40(5):396
Infect Control Hosp Epidemiol. 2016 Feb;37(2):172-81

Epidemiology – causative organisms

Table 4. Number of isolates and percentages of the ten most frequently isolated microorganisms in ICU-acquired bloodstream infection (BSI) episodes by country, EU/EEA, 2016

Microorganism	Belgium (n=66)	Czech Republic (n=102)	Estonia (n=78)	France (n=3 058)	Germany (n=2 626)	Hungary (n=59)	Italy (n=979)	Lithuania (n=89)	Luxembourg (n=31)	Malta (n=14)	Poland (n=48)	Portugal (n=308)	Slovakia (n=19)	Spain (n=1 079)	United Kingdom (n=103)	Total (n=8 659)
Coagulase-negative staphylococci	28.3	29.3	15.7	18.8	25.3	31.6	17.3	38.1	13.3	0.0	22.2	22.2	0.0	29.3	19.8	20.5
Klebsiella spp.	10	15.2	25.7	12.1	8.4	10.5	17.7	8.3	16.7	14.3	5.6	5.6	27.7	15.6	17.6	14.1
Enterococcus spp.	13.3	5.4	24.3	11.9	20.2	7.0	11.6	4.8	3.3	14.3	11.1	11.1	19.1	13.8	11.0	12.4
Pseudomonas aeruginosa	6.7	7.6	8.6	11.8	4.4	19.3	10.4	2.4	6.7	14.3	27.8	27.8	8.5	9.0	3.3	11.1
Escherichia coli	18.3	7.6	7.1	11.0	9.4	7.0	9.0	8.3	10.0	14.3	0.0	0.0	10.6	7.2	11.0	9.7
Staphylococcus aureus	8.3	12.0	1.4	10.2	14.9	3.5	9.0	7.1	16.7	7.1	5.6	5.6	4.3	5.7	9.9	8.7
Enterobacter spp.	5.0	3.3	7.1	11.2	5.3	5.3	6.6	6.0	20.0	35.7	5.6	5.6	0.0	4.0	5.5	8.5
Candida spp.	8.3	10.9	8.6	8.8	8.5	3.5	5.8	2.4	10.0	0.0	0.0	0.0	0.0	8.4	17.6	8.0
Acinetobacter spp.	0.0	4.3	1.4	1.4	0.8	12.3	9.2	19	3.3	0.0	22.2	22.2	23.4	2.4	1.1	3.6
Serratia spp.	1.7	4.3	0.0	2.8	2.8	0.0	3.4	3.6	0.0	0.0	0.0	0.0	6.4	4.6	3.3	3.3

n = number of isolates
** Data from Germany refer only to primary bloodstream infections; data from both Italian networks*
Source: ECDC, HAI-Net patient-based and unit-based data 2016. United Kingdom: data from UK–Scotland only.
Coagulase-negative staphylococci: includes unspecified Staphylococcus *spp.*

Epidemiology – causative organisms

CDC NHSN 2011-2014

Coagulase-negative staphylococci – 16.4 percent

S. aureus – 13.2%

Enterococci – 15.2 %

Candida – 13.3 %

Klebsiella – 8.4%

E coli – 5.4 %

Enterobacter – 4.4 %

Pseudomonas – 4 %

Weiner *et al.* Infect Control Hosp Epidemiol 2016;37:1288–1301

Epidemiology – causative organisms

Pathogen	2013 (*n*=484), *n* (%)	2014 (*n*=621), *n* (%)	2015 (*n*=411), *n* (%)	2016 (*n*=501), *n* (%)
Gram-negative isolates				
Enterobacteriaceae				
Enterobacter species	11 (2)	13 (2)	0	5 (1)
Escherichia coli	24 (5)	25 (4)	28 (7)	26 (5)
Klebsiella species	51 (11)	50 (8)	101 (25)	106 (21)
Proteus species	4 (0.8)	9 (1)	5 (1)	5 (1)
Providencia species	10 (2)	13 (2)	0	3 (0.6)
Salmonella species	6 (1)	6 (1)	0	13 (2.5)
Serratia species	13 (3)	35 (6)	0	35 (7)
Non-*Enterobacteriaceae*				
Acinetobacter species	97 (20)	132 (21)	122 (30)	135 (27)
Aeromonas species	1 (0.2)	0	0	0
Burkholderia species	19 (4)	162 (26)	9 (2)	25 (5)
Stenotrophomonas species	34 (7)	34 (6)	28 (7)	13 (2.5)
Pseudomonas aeruginosa	87 (18)	30 (5)	40 (8)	38 (8)
Other Gram-negative bacteria[#]	19 (4)	19 (3)	0	5 (1)
Gram-positive isolates				
Enterococcus species	34 (7)	26 (4)	28 (7)	37 (7)
Staphylococcus species	74 (15)	67 (11)	50 (12)	54 (11)
Streptococcus species	0	0	0	1 (0.2)

[#]*Morganella* species, *Pantoea* species, *Achromobacter* species, *Chryseobacterium* species, *Elizabethkingia* species, *Ralstonia pickettii*, *Sphingomonas paucimobilis*

Khurana et al. Prevalence, etiology, and antibiotic resistance profiles of bacterial bloodstream infections in a tertiary care hospital in Northern India: A 4-year study. J Lab Physicians 2018;10:426-31.

Epidemiology causative organisms

Organism	Frequency (%)
Acinetobacter baumannii	10 (31.24)
Pseudomonas aeruginosa	6 (18.75)
Klebsiella pneumoniae	3 (9.37)
Staphylococcus aureus	3 (9.37)
Polymicrobial	3 (9.37)
Candida	2 (6.25)
E coli	1 (3.13)
Serratia	1 (3.13)
Acinetobacter beriziniae	1 (3.13)
Delftia acidovorans	1 (3.13)
Enterococcus faecium	1 (3.13)
Total	32 (100)

Epidemiology AMR data

Table 3: Resistance among Gram-negative bacteria from bloodstream infections

Family	Genus	Year	Antibiotics tested (number of resistant strains [%])											
			Amikacin	Cefepime	Cefoperazone Sulbactam	Cefoxitin	Ceftazidime	Chloramphenicol	Ciprofloxacin	Imipenem	Netilmicin	Piperacillim -tazobactam	Tigecycline	Trimethoprim/ sulphamethoxazole
Enterobacteriaceae	*Enterobacter*	2013	0	3 (27)	3 (27)	8 (73)	9 (82)	7 (63)	4 (36)	4 (36)	7 (64)	8 (73)	3 (27)	11 (100)
		2014	2 (15)	7 (54)	2 (15)	12 (92)	7 (54)	7 (54)	3 (23)	0	2 (15)	0	7 (54)	6 (46)
		2015	0	0	0	0	0	0	0	0	0	0	0	0
		2016	2 (40)	1 (20)	3 (60)	NA	4 (80)	1 (20)	4 (75)	1 (20)	2 (40)	4 (80)	0	NA
	Escherichia	2013	9 (38)	23 (96)	15 (63)	18 (75)	24 (100)	15 (63)	23 (96)	20 (83)	16 (67)	22 (92)	5 (21)	24 (100)
		2014	10 (40)	24 (96)	14 (56)	15 (60)	24 (96)	8 (32)	25 (100)	8 (32)	10 (40)	15 (60)	1 (4)	19 (76)
		2015	11 (39)	27 (96)	18 (64)	NA	28 (100)	7 (25)	28 (100)	2 (7)	11 (39)	23 (82)	0	NA
		2016	14 (54)	23 (85)	15 (58)	NA	25 (96)	10 (38)	25 (96)	11 (42)	12 (46)	15 (58)	1 (4)	0
	Klebsiella	2013	44 (86)	49 (96)	44 (86)	50 (98)	49 (96)	34 (67)	36 (71)	26 (51)	22 (43)	36 (71)	18 (35)	51 (100)
		2014	29 (58)	40 (80)	32 (64)	37 (74)	39 (78)	14 (28)	34 (68)	30 (60)	28 (56)	33 (66)	7 (14)	33 (66)
		2015	64 (63)	99 (98)	70 (69)	NA	92 (91)	64 (63)	96 (95)	43 (43)	60 (59)	78 (77)	13 (13)	NA
		2016	101 (95)	99 (94)	98 (92)	NA	103 (97)	64 (60)	103 (97)	68 (64)	105 (99)	83 (78)	13 (12)	86 (81)
	Proteus	2013	3 (75)	4 (100)	3 (75)	4 (100)	4 (100)	0	4 (100)	4 (100)	1 (25)	4 (100)	0	NA
		2014	9 (100)	9 (100)	2 (22)	3 (33)	9 (100)	9 (100)	9 (100)	3 (33)	9 (100)	2 (22)	9 (100)	9 (100)
		2015	1 (20)	1 (20)	0	NA	0	4 (80)	1 (20)	0	1 (20)	4 (80)	0	NA
		2016	5 (100)	2 (40)	1 (20)	NA	5 (100)	2 (40)	5 (100)	2 (40)	5 (100)	1 (20)	3 (60)	NA
	Providencia	2013	7 (70)	6 (60)	7 (70)	9 (90)	8 (80)	5 (50)	8 (80)	5 (50)	4 (40)	9 (90)	5 (50)	10 (100)
		2014	12 (92)	12 (92)	11 (85)	7 (54)	12 (92)	9 (69)	12 (92)	12 (92)	12 (92)	1 (8)	1 (8)	5 (38)
		2015	0	0	0	0	0	0	0	0	0	0	0	0
		2016	0	0	0	NA	0	0	0	0	0	0	NA	NA
	Salmonella	2013	0	0	0	0	4 (67)	0	4 (67)	2 (33)	0	3 (50)	0	6 (100)
		2014	0	0	0	1 (17)	0	0	1 (17)	0	0	0	0	1 (17)
		2015	0	0	0	0	0	0	0	0	0	0	0	0
		2016	2 (15)	1 (8)	2 (15)	NA	0	1 (8)	2 (15)	0	0	0	0	0
	Serratia	2013	3 (23)	3 (23)	8 (62)	12 (92)	7 (54)	7 (46)	6 (45)	7 (54)	6 (46)	8 (62)	2 (15)	NA
		2014	26 (74)	0	5 (14)	10 (29)	28 (80)	9 (26)	12 (34)	12 (34)	25 (71)	1 (3)	8 (23)	0
		2015	0	0	0	0	0	0	0	0	0	0	0	0
		2016	28 (80)	2 (77)	14 (40)	NA	30 (86)	14 (40)	22 (63)	1 (3)	30 (86)	12 (34)	9 (26)	0

Khurana et al. Prevalence, etiology, and antibiotic resistance profiles of bacterial bloodstream infections in a tertiary care hospital in Northern India: A 4-year study. J Lab Physicians 2018;10:426-31.

Epidemiology AMR data

Table 3: Resistance among Gram-negative bacteria from bloodstream infections

Family	Genus	Year	Antibiotics tested (number of resistant strains [%])											
			Amikacin	Cefepime	Cefoperazone Sulbactam	Cefoxitin	Ceftazidime	Chloramphenicol	Ciprofloxacin	Imipenem	Netilmicin	Piperacillim -tazobactam	Tigecycline	Trimethoprim/ sulphamethoxazole
Non -*Enterobacteriaceae*	*Acinetobacter*	2013	77 (79)	93 (96)	64 (66)	0	93 (96)	59 (61)	57 (59)	37 (38)	54 (56)	46 (47)	29 (30)	97 (100)
		2014	112 (85)	11 (86)	112 (85)	132 (100)	121 (92)	15 (11)	124 (94)	107 (81)	104 (79)	109 (83)	4 (3)	NA
		2015	108 (89)	120 (98)	107 (88)	NA	119 (98)	120 (98)	121 (99)	117 (96)	65 (53)	120 (98)	23 (19)	121 (99)
		2016	124 (92)	126 (93)	123 (91)	NA	129 (96)	134 (99)	130 (96)	124 (92)	103 (76)	125 (93)	23 (17)	135 (100)
	Aeromonas	2013	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)	1 (100)
		2014	0	0	0	0	0	0	0	0	0	0	0	0
		2015	0	0	0	0	0	0	0	0	0	0	0	0
		2016	0	0	0	0	0	0	0	0	0	0	0	0
	Burkholderia	2013	NA	14 (74)	NA	4 (21)	14 (74)	10 (53)	9 (47)	6 (32)	6 (32)	4 (21)	9 (47)	19 (100)
		2014	NA	12 (7)	NA	145 (90)	4 (2)	NA	NA	53 (33)	NA	NA	7 (4)	NA
Non -*Enterobacteriaceae*		2015	NA	5 (56)	NA	NA	4 (44)	NA	NA	9 (100)	NA	NA	6 (67)	NA
		2016	NA	14 (56)	NA	NA	7 (28)	NA	NA	20 (80)	NA	NA	19 (76)	NA
	Pseudomonas	2013	23 (26)	42 (48)	17 (20)	76 (87)	56 (64)	61 (70)	59 (68)	40 (46)	47 (54)	57 (66)	31 (36)	87 (100)
		2014	9 (30)	10 (33)	10 (33)	29 (97)	11 (37)	17 (57)	10 (33)	9 (30)	9 (30)	NA	21 (70)	NA
		2015	21 (53)	25 (63)	24 (60)	NA	27 (68)	29 (73)	26 (65)	18 (45)	39 (98)	NA	8 (20)	40 (100)
		2016	23 (61)	21 (55)	15 (39)	NA	22 (58)	30 (79)	27 (71)	16 (42)	29 (76)	NA	19 (50)	38 (100)
	Stenotrophomonas	2013	NA	34 (100)	NA	34 (100)	NA	22 (65)	26 (76)	20 (59)	22 (65)	23 (68)	10 (29)	34 (100)
		2014	NA	33 (97)	NA	34 (100)	NA	NA	NA	32 (94)	NA	NA	NA	NA
		2015	NA	19 (68)	NA	NA	NA	NA	NA	28 (100)	NA	NA	NA	NA
		2016	NA	13 (100)	NA	NA	NA	NA	NA	13 (100)	NA	NA	NA	NA
	Other Gram-negative bacteria[a]	2013	14 (74)	16 (84)	9 (47)	14 (74)	16 (84)	16 (84)	13 (68)	10 (53)	11 (58)	15 (79)	8 (42)	19 (100)
		2014	6 (32)	19 (100)	16 (84)	19 (100)	19 (100)	18 (95)	3 (16)	6 (32)	6 (32)	0	0	19 (100)
		2015	0	0	0	0	0	0	0	0	0	0	0	0
		2016	4 (80)	5 (100)	4 (80)	NA	5 (100)	4 (80)	5 (100)	5 (100)	5 (100)	0	5 (100)	5 (100)
	P value		<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	<0.001	0.422
	df		3	3	3	3	3	3	3	3	3	3	3	3

Khurana et al. Prevalence, etiology, and antibiotic resistance profiles of bacterial bloodstream infections in a tertiary care hospital in Northern India: A 4-year study. J Lab Physicians 2018;10:426-31.

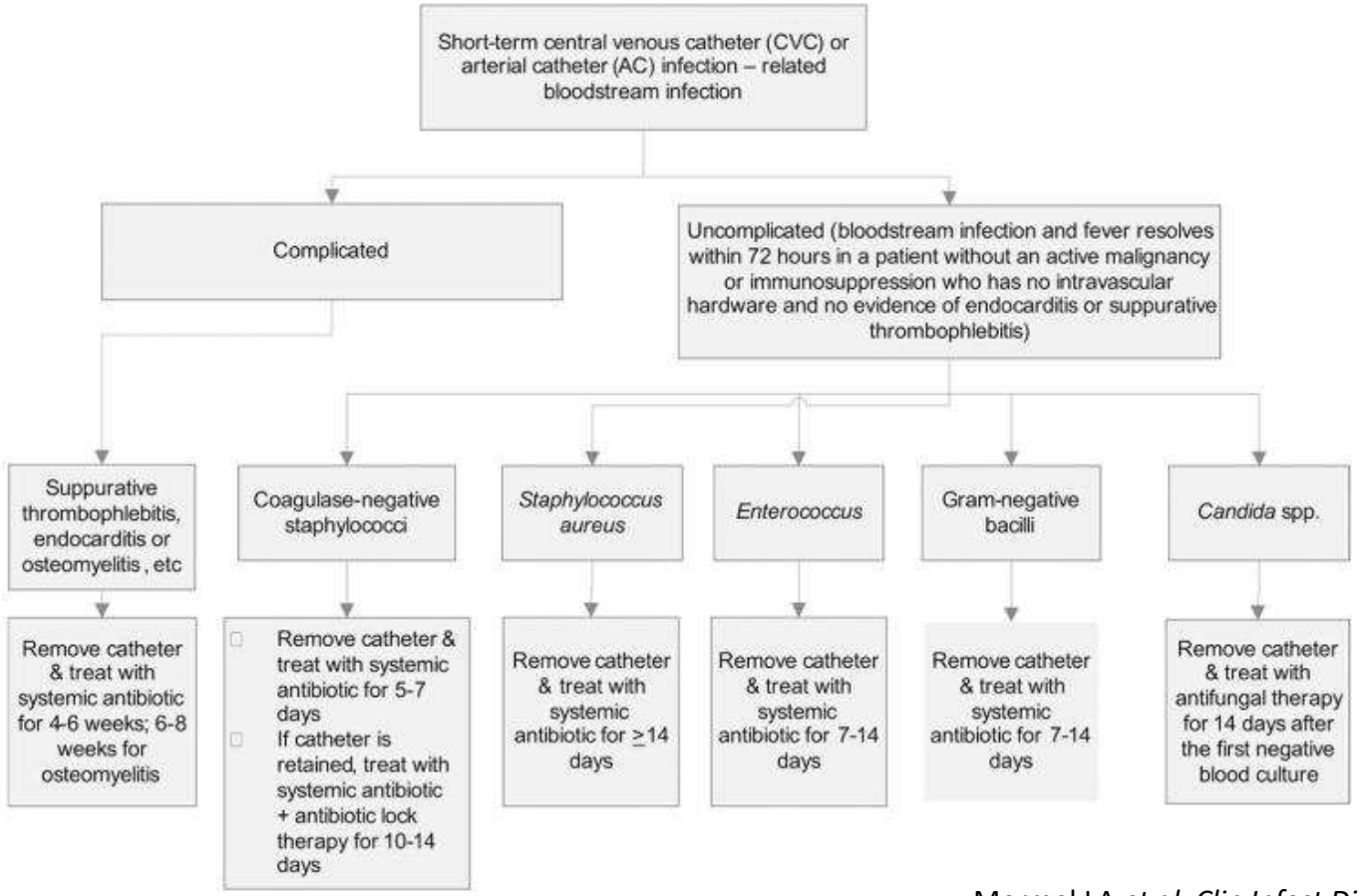
Risk factors for MDR gram negative bacteremia

- Hematopoietic stem cell transplant
- Liver failure
- Serum albumin <3 g/dL
- Solid organ transplant
- Diabetes
- Pulmonary disease
- Chronic hemodialysis
- HIV infection
- Treatment with glucocorticoids
- Receipt of prior antimicrobial therapy
- LOS prior to infection

Am J Med. 2002;112(3):204

Management principles

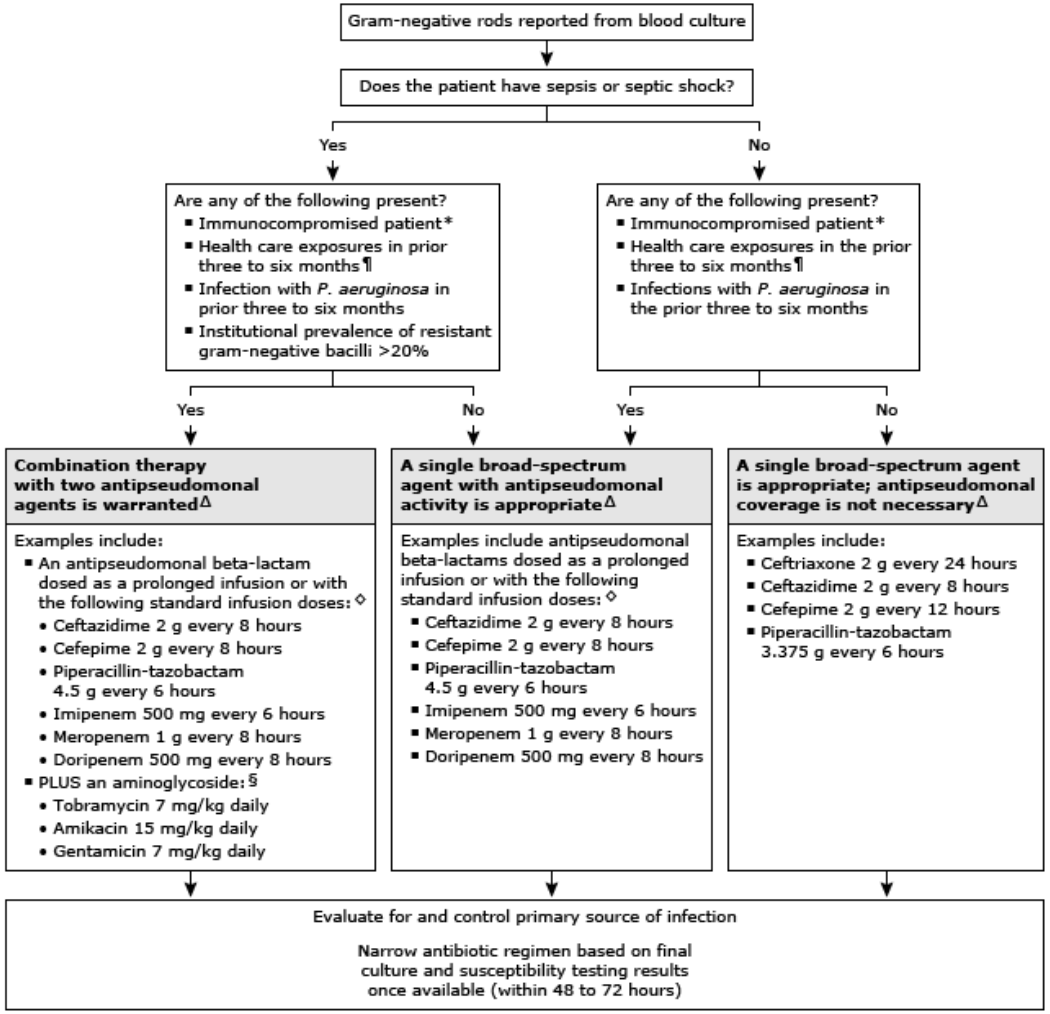
- Gram positive infections: Vancomycin is empirical therapy of choice



Mermel LA *et al. Clin Infect Dis*. 2009;49(1):1–45. doi:10.1086/599376

Management Principles

Algorithm for empiric antimicrobial selection for gram-negative bacillary bacteremia



Does combination antimicrobial therapy reduce mortality in Gram-negative bacteraemia? A meta-analysis

- 17 studies met the inclusion criteria, five prospective cohort studies, two prospective randomised trials, and ten retrospective cohort studies
- OR was 0·96 (95% CI 0·70–1·32), indicating no mortality benefit with combination
- Sub group analysis wrt year of study, study design and severity of illness – same results
- Pseudomonas aeruginosa bacteraemias showed a significant mortality benefit (OR 0·50, 95% CI 0·30–0·79)

Lancet Infect Dis 2004; 4: 519–27

Does combination antimicrobial therapy reduce mortality in Gram-negative bacteraemia? A meta-analysis

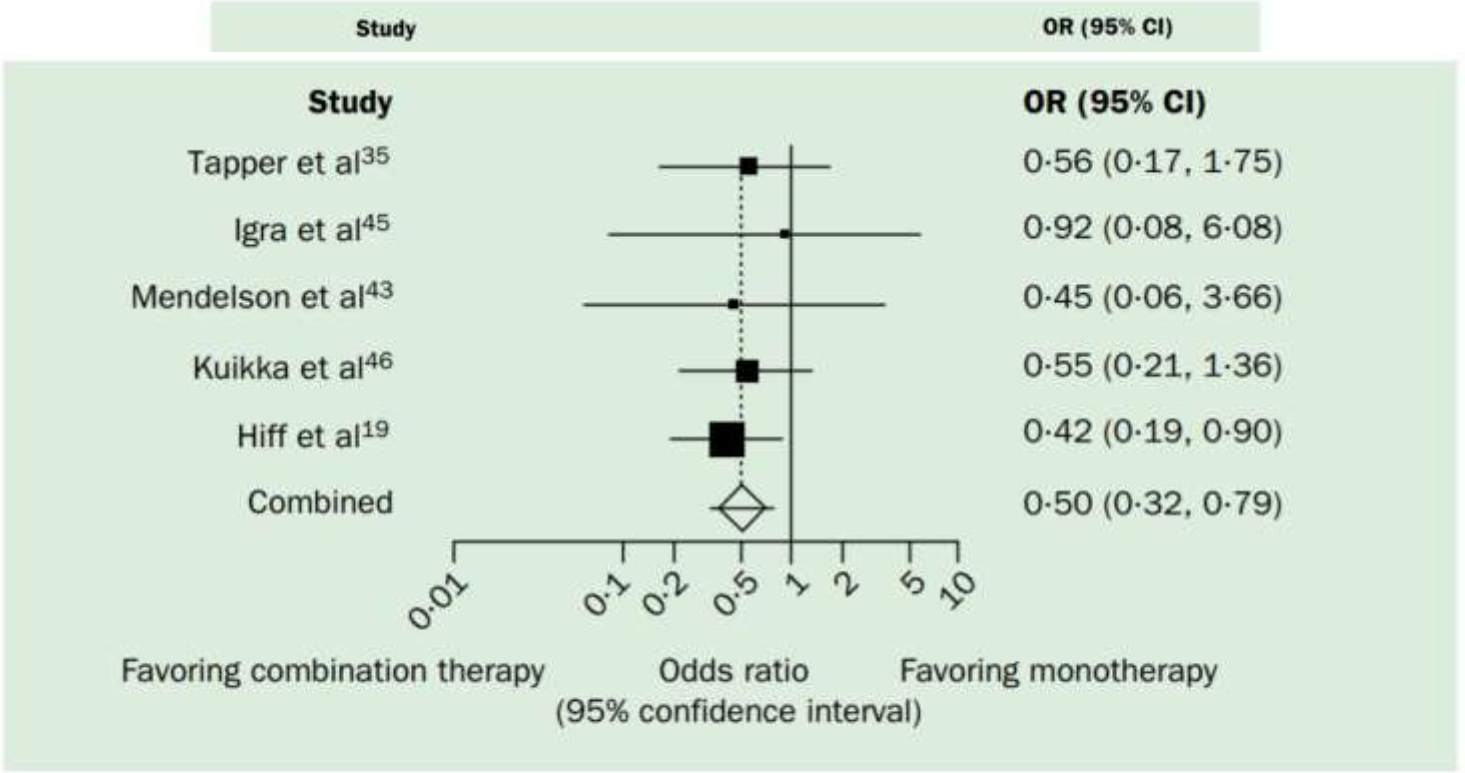


Figure 6. Analysis of studies comparing combination anti-infective therapy with monotherapy for reducing mortality of Pseudomonas *spp bacteraemia.The size of the squares is proportional to the reciprocal of the variance of the studies. The summary odds ratio is 0·50 (95% CI 0·32–0·79), indicating a mortality benefit with combination antimicrobial therapy.*

Figure 1. Analysis of studies comparing combination anti-infective therapy with monotherapy for reducing mortality of Gram-negative bacteraemia. The size of the squares is proportional to the reciprocal of the variance of the studies. The summary odds ratio is 0.96 (95% CI 0·70–1·32), indicating no mortality benefit with combination antimicrobial therapy.

Lancet Infect Dis 2004; 4: 519–27

Does combination antimicrobial therapy reduce mortality in Gram-negative bacteraemia? A meta-analysis

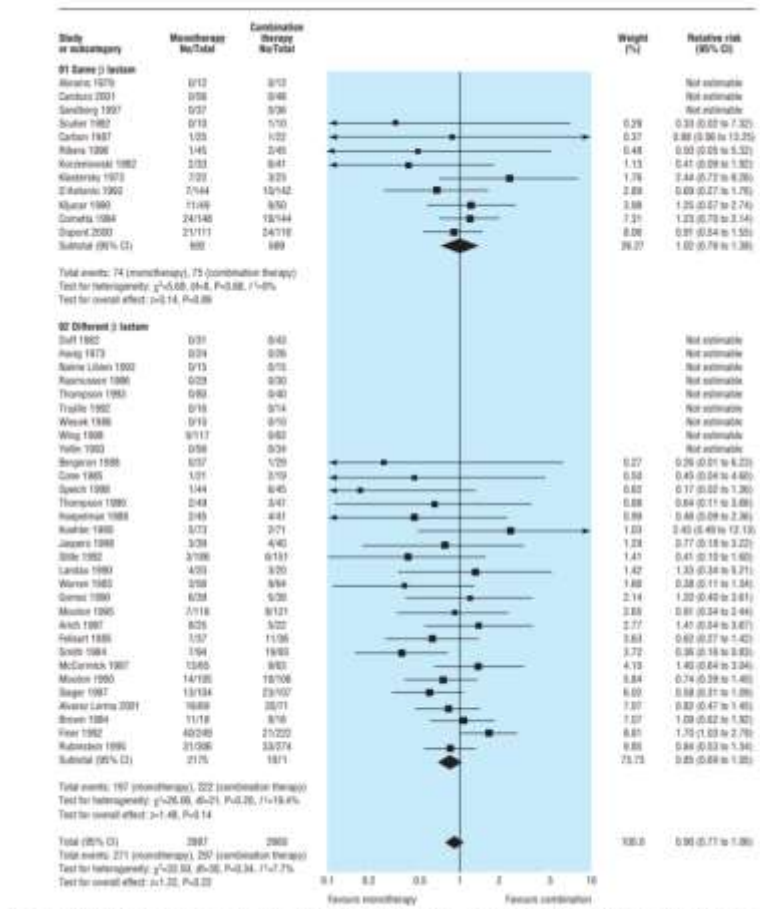
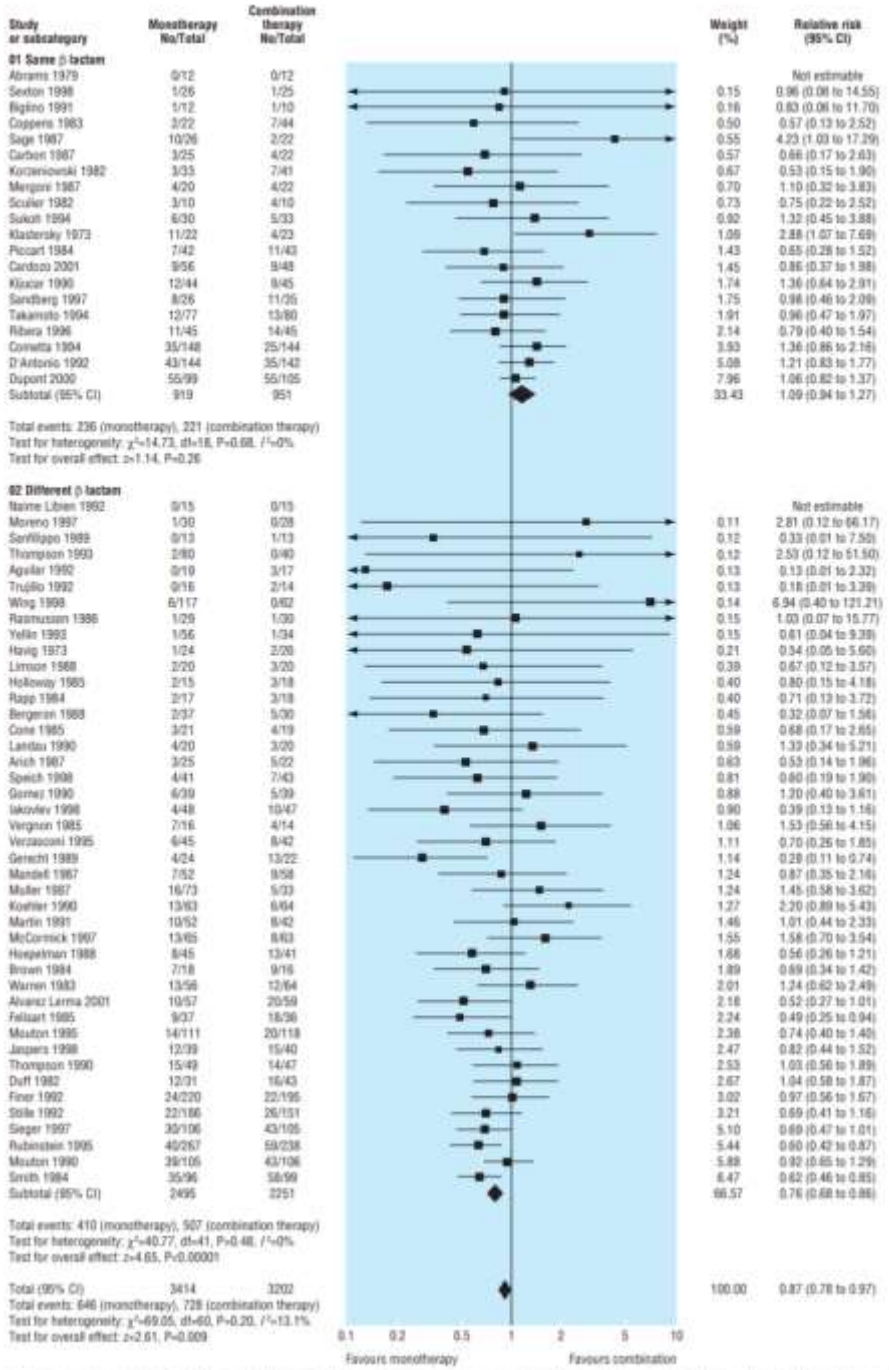


Fig 2 All cause fatality in comparison of β lactam monotherapy v β lactam-aminoglycoside combination therapy for treatment of sepsis. Log scale of relative risks (95% confidence intervals), random effect model. Studies ordered by weight

BMJ. 2004 Mar 20;328(7441):668. Epub 2004 Mar 2.



Clinical failure in comparison of β lactam monotherapy *v* β lactam-aminoglycoside combination therapy for treatment of sepsis. Log scale of relative risks (95%

BMJ. 2004 Mar 20;328(7441):668. Epub 2004 Mar 2.

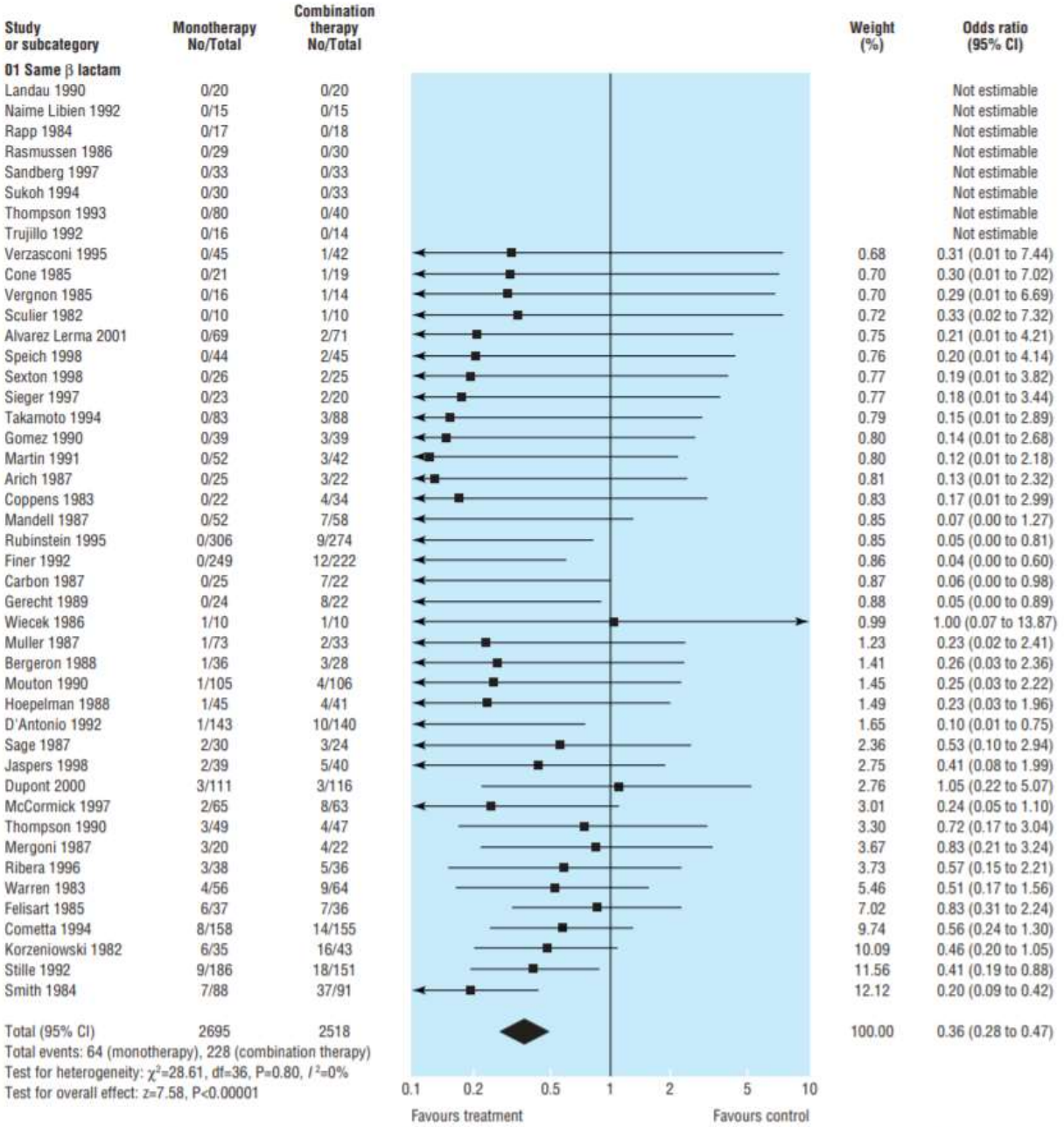


Fig 6 Adverse events: nephrotoxicity in comparison of β lactam monotherapy *v* β lactam-aminoglycoside combination therapy for treatment of sepsis. Log scale of relative risks (95% confidence intervals), random effect model. Studies ordered by weight

BMJ. 2004 Mar 20;328(7441):668. Epub 2004 Mar 2.

CAUTI

- Growth of ≥10^3 cfu/mL of uropathogenic bacteria with symptoms or signs compatible with UTI without other identifiable source in patient with indwelling urethral, indwelling suprapubic, or intermittent catheterization
- Asymptomatic bacteriuria – No symptoms with culture positive ≥10^5 cfu/mL
- Incidence – Bacteriuria 3-10% per day of catheterisation
- 10-25% develop symptoms and may be most common HAI
- 1.8% local data

CAUTI –risk

- Female sex
- Older age
- Diabetes
- Improper handling/ Inadequate care

Etiology

- *E. coli* — present in 24 percent of cases
- *Candida* spp (or yeast, not otherwise specified) — 24 percent

Table 1: Rate of h

	U
Percentage of the total health care associated infections (%)	1
No. of infection/1000 device days	9
Most common organism isolated (%)	P

UTI – Urinary tract infection, CLABSI – Central-line

Table 2: Organism isolated from various health care associated infections

Organism	Urine (%)	Blood (%)	Tracheal (%)
Acinetobacter species (51)	08 (9.5)	24 (26.9)	19 (41.3)
Pseudomonas aeruginosa (59)	30 (35.7)	13 (14.6)	16 (34.7)
Enterococcus species (25)	13 (15.4)	09 (10.1)	03 (6.5)
Klebsiella pneumonia (46)	13 (15.4)	26 (29.2)	7 (15.2)
Escherichia coli (12)	09 (10.7)	02 (2.2)	01 (2.1)
Candida species (14)	10 (11.9)	04 (4.4)	-
Staphylococcus aureus (11)	-	11 (12.3)	-
Morganella morganii (1)	01 (1.1)	-	-
Total	84	89	46

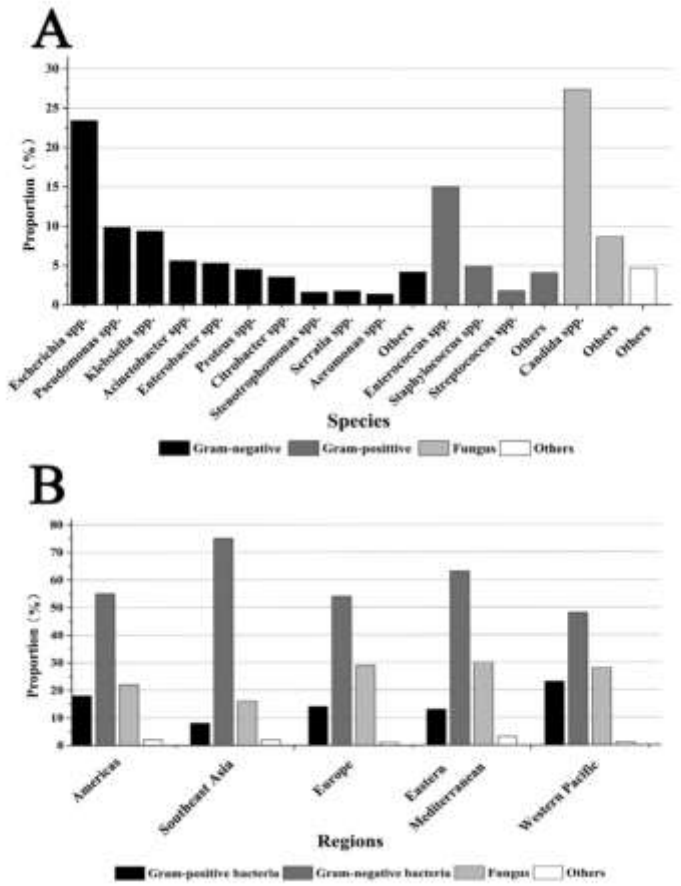
ssociated parameters

	VAP
	6.15
central line days	6.04/1000 ventilator days
neumoniae (29.2)	*Acinetobacter spp.* (41.3)

sociated pneumonias

Weiner *et al.* Infect Control Hosp Epidemiol 2016;37:1288–1301
Indian Journal of Anaesthesia | Vol. 58| Issue 1 | Jan-Feb 2014

Epidemiology of pathogens and antimicrobial resistance of catheter-associated urinary tract infections in intensive care units: A systematic review and meta-analysis



Epidemiology of pathogens and antimicrobial resistance of catheter-associated urinary tract infections in intensive care units: A systematic review and meta-analysis

- CAUTI incidence per 1,000 catheter days
  - 4.40 (95% CI, 2.76-6.04) in the America
  - 14.71 (95% CI, 3.98-25.45) in Southeast Asia
  - 9.50 (95% CI, 8.15-10.86) in Europe,
  - 9.96 (95% CI, 2.73-17.20) in the Eastern Mediterranean, and
  - 7.18 (95% CI, 4.95- 9.42) in the Western Pacific
  - Total weighted CAUTI 7.78 (95% CI, 7.04-8.53)

Epidemiology of pathogens and antimicrobial resistance of catheter-associated urinary tract infections in intensive care units: A systematic review and meta-analysis

Table 1
Antimicrobial resistance of gram-negative bacteria

Antimicrobial	*Escherichia* spp		*Klebsiella* spp		*Acinetobacter* spp		*Pseudomonas* spp		*Enterobacter* spp		*Proteus* spp	
	DRS (no.)	DRR (%)	DRS (no.)	DRR (%)	DRS (n)	DRR (%)	DRS (n)	DRR (%)	DRS (n)	DRR (%)	DRS (n)	DRR (%)
Amikacin	16	27.7	7	37.6	7	65.0	195	32.3	0	0.0	1	50.0
AMC	43	32.4	4	66.7	NA	NA	NA	NA	NA	NA	NA	NA
Ampicillin	255	87.3	52	90.3	28	95.9	17	88.3	NA	NA	NA	NA
SAM	143	55.1	27	62.8	16	69.6	NA	NA	NA	NA	NA	NA
Aztreonam	115	40.4	27	53.3	23	80.7	NA	NA	NA	NA	NA	NA
Cefalotin	5	62.5	1	100.0	NA	NA	NA	NA	NA	NA	NA	NA
Cefazolin	78	54.3	13	79.2	3	60.0	6	42.9	NA	NA	NA	NA
Cefepime	48	29.7	18	35.0	21	59.6	69	41.6	NA	NA	NA	NA
Cefoperazone	48	29.5	4	44.4	2	40.0	6	42.9	NA	NA	NA	NA
CSL	25	31.0	9	25.3	1	20.0	4	28.6	NA	NA	NA	NA
Cefuroxime	29	59.2	10	65.4	3	60.0	12	62.1	NA	NA	NA	NA
Cefotaxime	155	66.7	40	55.9	22	69.9	5	35.7	NA	NA	3	4.3
Cefotetan	7	8.6	4	10.8	22	95.7	NA	NA	NA	NA	NA	NA
Ceftazidime	861	51.6	545	68.3	28	78.7	15	51.7	12	33.9	1	50.0
Cac	28	71.8	10	71.4	NA	NA	NA	NA	NA	NA	NA	NA
CAT	7	17.9	5	35.7	NA	NA	NA	NA	NA	NA	NA	NA
Ceftriaxone	765	60.4	504	71.0	4	80.0	13	67.9	15	44.1	NA	NA
Ciprofloxacin	254	71.7	26	48.9	29	80.3	182	47.6	0	20.3	8	11.7
Colistin	NA	NA	NA	NA	0	0.0	0	0.0	NA	NA	NA	NA
Cotrimoxazole	119	67.4	32	51.7	24	85.5	12	85.7	0	0.0	NA	NA
Ertapenem	56	6.2	138	16.7	NA	NA	NA	NA	NA	NA	NA	NA
Fluoroquinolones	612	60.6	NA	NA	NA	NA	87	36.7	NA	NA	NA	NA
Gentamicin	188	59.6	25	40.0	28	84.0	6	31.3	0	0.0	NA	NA
Imipenem	87	5.8	199	13.0	210	55.1	341	36.0	0	0.0	1	50.0
Levofloxacin	22	81.5	5	55.6	2	40.0	5	32.1	NA	NA	NA	NA
Meropenem	82	6.0	195	13.3	190	43.9	271	37.8	NA	NA	NA	NA
Nalidixic acid	31	79.5	12	85.7	NA	NA	NA	NA	NA	NA	NA	NA
Nitrofurantoin	102	19.2	35	44.4	23	100.0	NA	NA	1	50.0	NA	NA
Norfloxacin	130	71.2	15	74.7	NA	NA	NA	NA	NA	NA	NA	NA
Ofloxacin	92	67.6	NA	NA	NA	NA	NA	NA	NA	NA	NA	NA
Piperacillin	17	77.3	3	50.0	NA	NA	276	42.1	NA	NA	NA	NA
TZP	14	20.3	12	46.0	5	56.7	280	41.2	NA	NA	NA	NA
Tetracycline	12	54.5	1	16.7	NA	NA	NA	NA	NA	NA	NA	NA
Tobramycin	51	31.7	4	44.4	NA	NA	3	21.4	NA	NA	NA	NA

AMC, amoxicillin/clavulanic acid; *Cac*, ceftazidime + clavulanic acid; *CAT*, ceftazidime + tazobactam; *CSL*, cefoperazone/sulbactam; *DRR*, drug resistance rate; *DRS*, drug-resistant strain; *NA*, not available; *SAM*, ampicillin/sulbactam; *TZP*, piperacillin/tazobactam.

Epidemiology of pathogens and antimicrobial resistance of catheter-associated urinary tract infections in intensive care units: A systematic review and meta-analysis

Table 2
Antimicrobial resistance of gram-positive bacteria isolated from CAUTIs

Antimicrobial	*Enterococcus* spp		*Staphylococcus* spp		*Streptococcus* spp	
	DRS (no.)	DRR (%)	DRS (no.)	DRR (%)	DRS (no.)	DRR (%)
Amikacin	2	33.3	0	0.0	NA	NA
Amoxicillin	NA	NA	2	100.0	NA	NA
Ampicillin	56	41.6	2	100.0	NA	NA
Azithromycin	12	54.5	NA	NA	NA	NA
Cefalexin	4	66.7	2	100.0	NA	NA
Cefepime	15	68.2	NA	NA	NA	NA
Cefuroxime	NA	NA	2	100.0	4	66.7
Ceftazidime	2	33.3	0	0.0	NA	NA
Ceftriaxone	18	81.8	NA	NA	NA	NA
Chloramphenicol	7	10.8	NA	NA	NA	NA
Ciprofloxacin	62	75.8	2	41.6	4	66.7
Cotrimoxazole	23	77.4	0	0.0	5	83.3
Erythromycin	55	83.9	NA	NA	NA	NA
Erytromycin	NA	NA	2	100.0	5	83.3
Gentamicin	41	60.2	2	100.0	4	66.7
Imipenem	0	0.0	0	0.0	NA	NA
Levofloxacin	48	73.8	NA	NA	NA	NA
Linezolid	0	0.0	NA	NA	NA	NA
Nitrofurantoin	40	57.9	NA	NA	NA	NA
Norfloxacin	15	68.2	2	100.0	NA	NA
Ofloxacin	16	72.7	NA	NA	NA	NA
Oxacillin	NA	NA	59	70.0	NA	NA
Penicillin	50	76.7	NA	NA	NA	NA
Quinuprin/Dupletin	1	2.3	NA	NA	NA	NA
Rifampicin	37	48.8	NA	NA	NA	NA
Streptomycin	31	39.2	NA	NA	NA	NA
Teicoplanin	1	2.9	NA	NA	NA	NA
Tetracycline	40	61.4	NA	NA	NA	NA
Vancomycin	12	3.4	NA	NA	NA	NA

CAUTIs, catheter-associated urinary tract infections; *DRR*, drug resistance rate; *DRS*, drug-resistant strain; *NA*, not available.

In comparison to CDC NHSN

- Antimicrobial-resistant rates in this study were higher
- *Escherichia* to fluoroquinolones (60.6% vs 34.8%)
- *Acinetobacter* to carbapenems (70.0% vs 64.0%)
- *Pseudomonas* to fluoroquinolones (36.7% vs 32.6%)
- *Enterococcus, Staphylococcus* resistant to ciprofloxacin and gentamicin
- Resistance of *Enterococcus* spp to vancomycin (3.4%) was lower than the values reported by the CDC's NHSN

Weiner *et al.* Infect Control Hosp Epidemiol 2016;37:1288–1301

CAUTI RICU

PGI RICU	Urine
	Frequency (%)
Escherichia coli	22 (47.8)
Enterococcus faecium	10 (21.7)
Klebsiella pneumoniae	7 (15.2)
Acinetobacter baumannii	3 (6.5)
Pseudomonas aeruginosa	1 (2.2)
Others	3 (6.5)
Total	46 (100)

Drugs	***E Coli***	***Klebsiella***	***Pseudomonas***	***Acinetobacter***
Carbapenem	20-25	44-48%	25-35%	70-95%
FQ	90%	60%	20-30%	60-95%
Cephalosporins	30-40%	40-60%	11-25%	70-95%

Management: Principles

- No data on routine catheter changes 2-4 weekly to prevent CAUTI
- No role of screening/treating asymptomatic bacteriuria
- Urine culture to be obtained prior to initiation of empirical therapy
- If an indwelling catheter has been in place for >2 weeks at the onset of CAUTI and is still indicated, the catheter should be replaced to hasten resolution of symptoms
- Seven days is the recommended duration for patients prompt resolution of symptoms and 10–14 days of treatment with a delayed response
- 3 days sufficient if catheter has been removed, age < 65 and no upper urinary tract symptoms

Clinical Infectious Diseases 2010; 50:625–663

HAI and AMR data from RICU 2002-03 & 2018-19

Organisms isolated 2006

Table 2 Organisms isolated in nosocomial infection

Microorganisms	Total	Pneumonia	Blood stream infection	Urinary tract infection	Others
Acinetobacter species	16 (34.8)	15	1	0	0
Pseudomonas aeruginosa	11 (23.9)	11	0	0	0
Escherichia coli	7 (15.2)	2	3	2	0
MRSA	4 (8.7)	3	1	0	0
Alcaligenes faecalis	2 (4.3)	2	0	0	0
Klebsiella pneumoniae	1 (2.2)	0	0	1	0
Candida species	2 (4.3)	0	2	0	0
Others	3 (4.5)	1	0	0	2
Total	46 (100)	34	7	3	2

Numbers in parentheses are percentages; MRSA: methicillin-resistant *Staphylococcus aureus*.

Sensitivity pattern of organisms isolated 2006

Table 3 Sensitivity pattern of organisms isolated

Organism	Antibiotic resistance (%)							
	Number	Cefotaxime	Amikacin	Ceftazidime	Ciprofloxacin	Piperacillin–tazobactam	Imipenem	Methicillin
Acinetobacter spp.	16	100	75	94	50	44	8 (12)	Not tested
Pseudomonas aeruginosa	11	100	27	82	28	9	16 (6)	Not tested
Escherichia coli	7	71	14	57	14	50 (4)	0 (3)	Not tested
MRSA	4	100	100	Not tested	100	Not tested	Not tested	100

Figure in parentheses denotes number tested, if not tested in all; MRSA: methicillin-resistant *Staphylococcus aureus*.

Organisms causing HAIs in RICU 2018-19

	Respiratory secretions	Blood culture	Pleural fluid	Skin and soft tissue infection
	Frequency (%)	Frequency (%)	Frequency (%)	Frequency (%)
Acinetobacter baumannii	**105 (43.4)**	31 (19.1)	**3 (20.0)**	10 (27.0)
Pseudomonas aeruginosa	56 (23.1)	16 (9.9)	1 (6.7)	2 (5.4)
Klebsiella pneumoniae	39 (16.1)	17 (10.5)	**3 (20.0)**	7 (18.9)
Staphylococcus aureus	19 (7.9)	20 (12.3)	**3 (20.0)**	12 (32.4)
Other *Staphylococcus spp. (CONS)*	-	**38 (23.5)**	1 (6.7)	
Escherichia coli	7 (2.9)	15 (9.3)	1 (6.7)	4 (10.8)
Other *Acinetobacter spp*	4 (1.7)	1 (0.6)	-	-
Serratia marcenses	4 (1.7)	1 (0.6)	-	-
Burkholderia cephacia	2 (0.8)	4 (2.5)	-	-
Candida	-	5 (3.1)	-	-
Enterococcus faecium	-	5 (3.1)	2 (13.3)	1 (2.7)
Enterobacter cloacae	2 (0.8)	-	1 (6.7)	-
Others	4 (1.7)	9 (5.6)	-	1 (2.7)
Total	242 (100)	162 (100)	15 (100)	37 (100)

	Urine	Genital tract	Intrabdominal drain
	Frequency (%)	Frequency (%)	Frequency (%)
Escherichia coli	22 (47.8)	**4 (50.0)**	2 (66.7)
Enterococcus faecium	10 (21.7)	2 (25.0)	1 (33.3)
Klebsiella pneumoniae	7 (15.2)	1 (12.5)	
Acinetobacter baumannii	3 (6.5)	1 (12.5)	
Pseudomonas aeruginosa	1 (2.2)		
Others	3 (6.5)		
Total	46 (100)	8 (100)	3 (100)

Sensitivity pattern of organism isolated 2018-19

- *ACB* (n = 153)
  - MDR 93.46%
  - XDR 3.9%
  - PDR 0.65%.
  - Pan sensitivite 1.96%

Antibiotics	Sensitive (%)	Intermediate (%)	Resistant No. (%)	Data not available (%)
Ceftazidime	1 (0.7)	1 (0.7)	139 (90.8)	12 (7.84)
Cefepime	1 (0.7)	1 (0.7)	144 (94.11)	7 (4.57)
Cefoperazone+ Sulbactum	17 (11.1)	24 (15.7)	108 (70.58)	4 (2.61)
Piperacillin+ Tazobactum	3 (2.0)	1 (0.7)	147 (96.07)	2 (1.30)
Amikacin	7 (4.6)	2 (1.3)	65 (42.48)	79 (51.63)
Gentamicin	4 (2.6)	1 (0.7)	50 (32.7)	98 (64.1)
Ciprofloxacin	3 (2.0)	1 (0.7)	146 (95.42)	3 (1.96)
Levofloxacin	3 (2.0)	5 (3.3)	110 (71.89)	35 (22.87)
Imipenem	3 (2.0)	1 (0.7)	145 (94.77)	4 (2.61)
Meropenem	3 (2.0)	1 (0.7)	104 (67.97)	45 (29.41)
Colistin	134 (87.58)	-	6 (3.9)	13 (8.49)
Minocycline	64 (41.8)	26 (17.0)	47 (30.7)	16 (10.5)
Tigecycline	56 (36.6)	12 (7.8)	18 (11.8)	67 (43.8)

Sensitivity pattern of organism isolated 2018-19

- *Pseudomonas* (n=76)
  - MDR 26.3%
  - XDR 1.31%
  - Pansensitive 72.3%

Antibiotics	Sensitive (%)	Intermediate (%)	Resistant No. (%)	Data not available (%)
Ceftazidime	53 (69.7)	4 (5.3)	17 (22.4)	2 (2.6)
Cefepime	32 (42.1)	6 (7.9)	14 (18.4)	24 (31.6)
Cefoperazone+ Sulbactum	34 (44.7)	4 (5.3)	9 (11.8)	29 (38.2)
Piperacillin+ Tazobactum	51 (67.1)	9 (11.8)	7 (9.2)	9 (11.8)
Amikacin	58 (76.3)	3 (3.9)	12 (15.8)	3 (3.9)
Gentamicin	39 (51.3)	1 (1.3)	8 (10.5)	28 (36.8)
Ciprofloxacin	50 (65.8)	1 (1.3)	20 (26.3)	5 (6.6)
Levofloxacin	44 (57.9)	4 (5.3)	17 (22.4)	11 (14.5)
Imipenem	51 (67.1)	-	20 (26.3)	5 (6.6)
Meropenem	25 (32.9)	2 (2.6)	14 (18.4)	35 (46.1)
Colistin	29 (38.2)	-	2 (2.6)	45 (59.2)
Tigecycline	3 (3.9)	1 (1.3)	18 (23.7)	54 (71.1)

Sensitivity pattern of organism isolated 2018-19

- *Klebsiella* (n= 74)
  - MDR 64.86%
  - PDR 5.41%
  - Pansensitive 29.73%

Antibiotics	Sensitive (%)	Intermediate (%)	Resistant No. (%)	Data not available (%)
Cefotaxime	5 (6.8)	1 (1.4)	28 (37.8)	40 (54.1)
Ceftazidime	6 (8.1)	3 (4.1)	29 (39.2)	36 (48.6)
Cefepime	16 (21.9)	3 (4.1)	43 (58.1)	12 (16.2)
Cefoperazone+ Sulbactum	20 (27.0)	-	46 (62.2)	8 (10.8)
Piperacillin+ Tazobactum	21 (28.4)	1 (1.4)	52 (70.3)	-
Amikacin	28 (37.8)	1 (1.4)	39 (52.7)	6 (8.1)
Gentamicin	6 (8.1)	5 (6.8)	6 (8.1)	57 (77)
Ciprofloxacin	16 (21.6)	9 (12.2)	44 (59.5)	5 (6.8)
Imipenem	27 (36.5)	9 (12.2)	36 (48.6)	2 (2.7)
Meropenem	15 (20.3)	-	33 (44.6)	26 (35.1)
Ertapenem	14 (18.9)	1 (1.4)	14 (18.9)	45 (60.8)
Colistin	43 (58.1)	1 (1.4)	4 (5.4)	26 (35.1)
Minocycline	8 (10.8)	3 (4.1)	17 (23.0)	46 (62.2)
Tigecycline	19 (25.7)	2 (2.7)	1 (1.4)	52 (70.3)

Sensitivity pattern of organism isolated 2018-19

- *E. coli* (n=55)
  - MDR 69.09%
  - PDR 2%
  - Pan-sensitive 29%

Antibiotics	Sensitive (%)	Intermediate (%)	Resistant No. (%)	Data not available (%)
Cefotaxime	1 (1.8)	-	22 (40.0)	32 (58.2)
Ceftazidime	1 (1.8)	1 (1.8)	16 (29.09)	37 (67.27)
Cefepime	6 (10.9)	-	24 (43.64)	25 (45.45)
Cefoperazone+ Sulbactum	18 (32.7)	9 (16.4)	19 (34.5)	9 (16.4)
Piperacillin+ Tazobactum	14 (25.5)	6 (10.9)	28 (50.90)	7 (12.72)
Amikacin	41 (74.54)	-	10 (18.2)	4 (7.27)
Gentamicin	11 (20.0)	-	13 (23.6)	31 (56.4)
Ciprofloxacin	2 (3.6)	-	49 (89.09)	4 (7.27)
Nalidixic acid	1 (1.9)	-	20 (37.0)	33 (61.1)
Imipenem	31 (56.4)	4 (7.3)	14 (25.5)	6(10.9)
Meropenem	18 (32.7)	-	11 (20.0)	26 (47.3)
Ertapenem	23 (41.8)	1 (1.8)	7 (12.7)	24 (43.6)
Cotrimoxazole	1 (1.8)	-	20 (36.4)	34 (61.8)
Colistin	27 (49.1)	-	2 (3.6)	26 (47.3)
Tigecycline	14 (25.5)	-	-	41 (74.5)
Nitrofurantoin	11 (20.0)	4 (7.3)	5 (9.1)	35 (63.6)

Sensitivity p[illegible]solated 2018-19

- *Staph aureus* (n=5[illegible]
  - MRSA 70%
  - MDR 81.48%

Antibiotics	Sensitive (%)
Oxacillin	16 (29.6)
Ciprofloxacin	3 (5.6)
Erythromycin	7 (13.0)
Clindamycin	13 (24.1)
Vancomycin	52 (96.3)
Teicoplanin	53 (98.1)
Linezolid	21 (38.9)

'obial agents'. Defini- microbials', 'resistant to all antimicrobials routinely teste

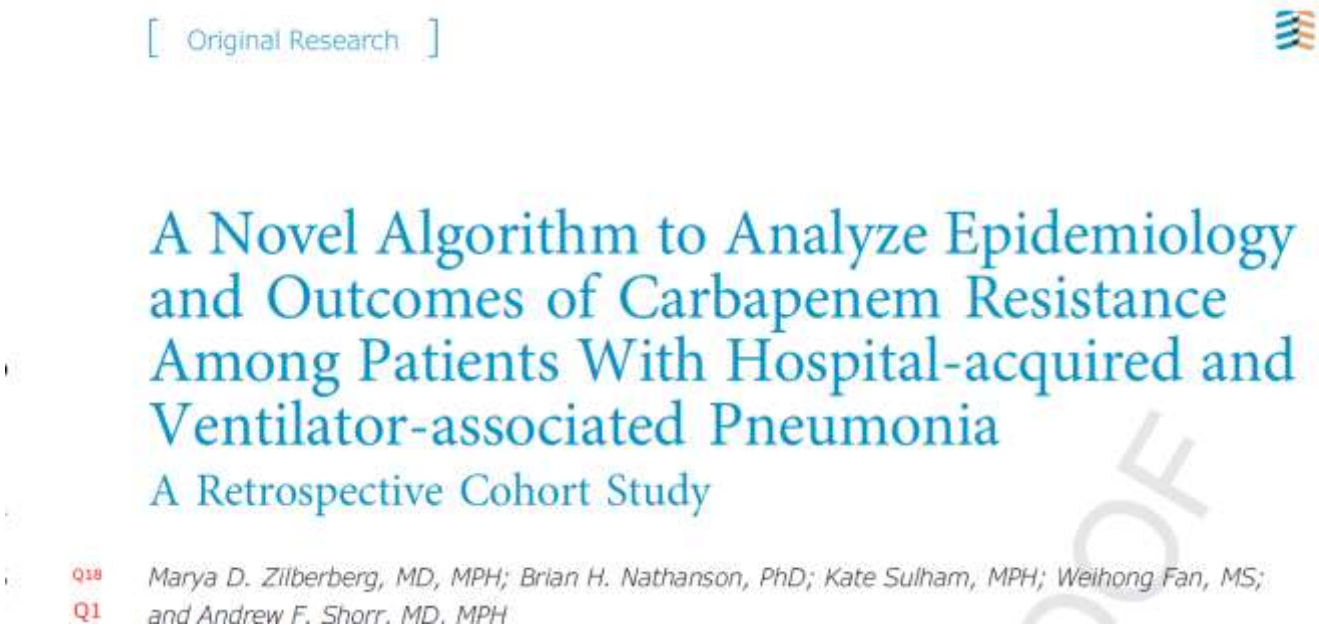
Antimicrobial category	Antimicrobial agent	Results of antimicrobial susceptibility testing (S or NS)
Aminoglycosides	Gentamicin	
Ansamycins	Rifampin/rifampicin	
Anti-MRSA cephalosporins	Ceftaroline	
Anti-staphylococcal β-lactams (or cephamycins)	Oxacillin (or cefoxitin)*	
Fluoroquinolones	Ciprofloxacin	
	Moxifloxacin	
Folate pathway inhibitors	Trimethoprim-sulphamethoxazole	
Fucidanes	Fusidic acid	
Glycopeptides	Vancomycin	
	Teicoplanin	
	Telavancin	
Glycylcyclines	Tigecycline	
Lincosamides	Clindamycin	
Lipopeptides	Daptomycin	
Macrolides	Erythromycin	
Oxazolidinones	Linezolid	
Phenicols	Chloramphenicol	
Phosphonic acids	Fosfomycin	
Streptogramins	Quinupristin-dalfopristin	
Tetracyclines	Tetracycline	
	Doxycycline	
	Minocycline	

Criteria for defining MDR, XDR and PDR in *S. aureus*
MDR (one or more of these have to apply): (i) an MRSA is always considered MDR by virtue of being an MRSA, (ii) non-susceptible to ≥1 agent in ≥3 antimicrobial categories.
XDR: non-susceptible to ≥1 agent in all but ≤2 categories.
PDR: non-susceptible to all antimicrobial agents listed.
*Oxacillin or cefoxitin represents all other β-lactams (and cephamycins) and resistance to either of these predicts non-susceptibility to all categories of β-lactam antimicrobials listed in this document, with the exception of the anti-MRSA cephalosporins (i.e. all categories of penicillins, cephalosporins, β-lactamase inhibitors and carbapenems currently approved up until 25 January 2011).
http://www.ecdc.europa.eu/en/activities/diseaseprogrammes/ARHAI/Pages/public_consultation_clinical_microbiology_infection_article.aspx.

Risks associated with HAIs

- Intervention
  - Intubation
  - Intubation with sub-glottic tube
  - Re-intubation
  - Invasive lines
- Patient related factors
  - CKD, RRT
  - Post Op
  - Prior hospital stay, prior antibiotic use
  - Immunosuppression
- Medication
  - Paralysis/sedation
  - Steroid use
- Multivariate analysis
  - Higher days of hospitalization prior to ICU
  - Endotracheal intubation
  - Use of invasive lines
  - Longer antibiotics use days
  - Longer LOS
  - Immunosuppressed state

MDR HAIs associated with increased mortality?


[Original Research]

CHEST

A Novel Algorithm to Analyze Epidemiology and Outcomes of Carbapenem Resistance Among Patients With Hospital-acquired and Ventilator-associated Pneumonia

A Retrospective Cohort Study

Q18 Marya D. Zilberberg, MD, MPH; Brian H. Nathanson, PhD; Kate Sulham, MPH; Weihong Fan, MS;
Q1 and Andrew F. Shorr, MD, MPH

- Among 8,969 patients with HAP/VAP, 1,059 isolates (11.8%) were carbapenem resistant
- carbapenem resistance had higher comorbidity burden
- *Pseudomonas aeruginosa* was the most common
- No significant mortality difference among those with CR vs those with CS
- Increased LOS and excess cost – statistically significant

Pneumonia caused by extensive drugresistant *Acinetobacter baumannii* among hospitalized patients: risk factors and mortality

Table 3 Comparison of clinical data for pneumonia-related characteristics in HAP patients with XDRAB and non-XDRAB

	XDRAB (*N* = 21) *N* (%)	Non-XDRAB (*N* = 42) *N* (%)	*P*-value
Age, y[a]	77.5 ± 11.6	68.6 ± 18.4	0.023
Gender (M/F), n	17/4	23/19	0.079
APACHE II score[a]	21.9 ± 6.8	18.0 ± 4.9	0.011
Related to hospitalization[a]	18 (85.7)	30 (71.4)	0.347
Days of mechanical ventilation before XDRAB (days)	10.5 ± 11.6	5.2 ± 5.8	0.059
Hospital days before XDRAB (days)	18.3 ± 11.3	12.6 ± 11.2	0.064
Length of stay in the ICU (days)	30.1 ± 20.0	21.4 ± 21.7	0.127
Length of stay in the hospital (days)	45.5 ± 28.8	38.5 ± 24.2	0.199
Associated disease, n (%)			
COPD	13 (61.9)	9 (21.4)	0.001
Diabetes mellitus	2 (9.5)	10 (40.4)	0.307
Malignancy	2 (9.5)	9 (21.4)	0.411
Cardiac disease	13 (61.9)	6 (14.2)	0.000
Renal disease	5 (23.8)	2 (4.7)	0.065
Neurological disease	8 (38.0)	22 (52.3)	0.422
Device, n (%)			
Urinary catheter	21 (100.0)	36 (85.7)	0.172
Nasogastric tube	21 (100.0)	36 (85.7)	0.172
Mechanical ventilation	16 (76.1)	31 (73.8)	1.000
Drug usage, n (%)			
Glucocorticoids	10 (47.6)	18 (42.8)	0.720
PPIs	14 (66.7)	32 (76.1)	0.422

Mortality 42.8% vs 35.7%(*P* 0.58)

Li et al. BMC Infectious Diseases (2017) 17:371

Multi-drug resistant organism infections in a medical ICU: Association to clinical features and impact upon outcome

- Retrospective case–control study
- MDR HAI vs Non MDR HAI
- 127 patients – 177 controls
- *MRSA>Pseudomonas>Kp>ACB*
- Risks a/w MDR:
  - Infection and cardiac disease as a cause of admission
  - LOS in ward/ICU days on the ventilator
  - Days with a central venous catheter, tracheostomy
  - Prior hospitalization, prior antibiotic use
  - Use of vasopressors
  - Past history of surgery
  - White blood cell count >10,000/mm^3 on admission

Med Intensiva. 2018 May;42(4):225-234

Multi-drug resistant organism infections in a medical ICU: Association to clinical features and impact upon outcome

- Appropriate empiric antibiotic therapy in 82.6% in MDR grp
- No statistically significant difference in 28-day ICU mortality rate was observed between MDR positive and MDR negative patients (20% vs 12.4%, *p*=0.07).

Med Intensiva. 2018 May;42(4):225-234

MDR HAIs associated with increased mortality?

Table 1. Antibiotic resistance rates of *Klebsiella pneumoniae*.

Antibiotic	n (Sensitive)	n (Resistance)	Total	% (Resistance)
Tigecycline	140	59	199	29.6
Colistin	114	85	199	42.7
Trimethoprim-sulfamethoxazole	119	88	207	42.5
Gentamicin	93	115	208	55.3
Amikacin	93	114	207	55.1
Meropenem	91	117	208	56.3
Imipenem	86	122	208	58.7
Levofloxacin	56	152	208	73.1
Ciprofloxacin	57	151	208	72.6
Piperacillin-tazobactam	35	173	208	83.2
Cefoperazone-sulbactam	33	168	201	83.6
Cefepime	18	189	207	91.3
Ceftazidime	19	189	208	90.9

Risk Factors Affecting Patterns of Antibiotic Resistance and Treatment Efficacy in Extreme Drug Resistance in Intensive Care Unit-Acquired *Klebsiella Pneumoniae* Infections: A 5-Year Analysis
Med Sci Monit. 2019; 25: 174–183.

Risk Factors Affecting Patterns of Antibiotic Resistance and Treatment Efficacy in Extreme Drug Resistance in Intensive Care Unit

- 208 KP-HAI patients
- 64.9% pneumonia, 21.2% CLABSI, 4.8% BSI, 3.8% UTI and 6.3% other infections (skin soft tissue and surgical site infections)
- Least resistance Tigecycline (29.6%) > Colistin (42.7%) > Septran (42.5%) > Carbapenem (56.3%)
- Risks of MDR/XDR – Prior use of Carbapenems, CLABSI, secondary BSI COPD, Hospitalised for pneumonia
- Survival analysis and analysis based on antibiotic combinations used

Risk Factors Affecting Patterns of Antibiotic Resistance and Treatment Efficacy in Extreme Drug Resistance in Intensive Care Unit-Acquired *Klebsiella Pneumoniae* Infections: A 5-Year Analysis
Med Sci Monit. 2019; 25: 174–183.

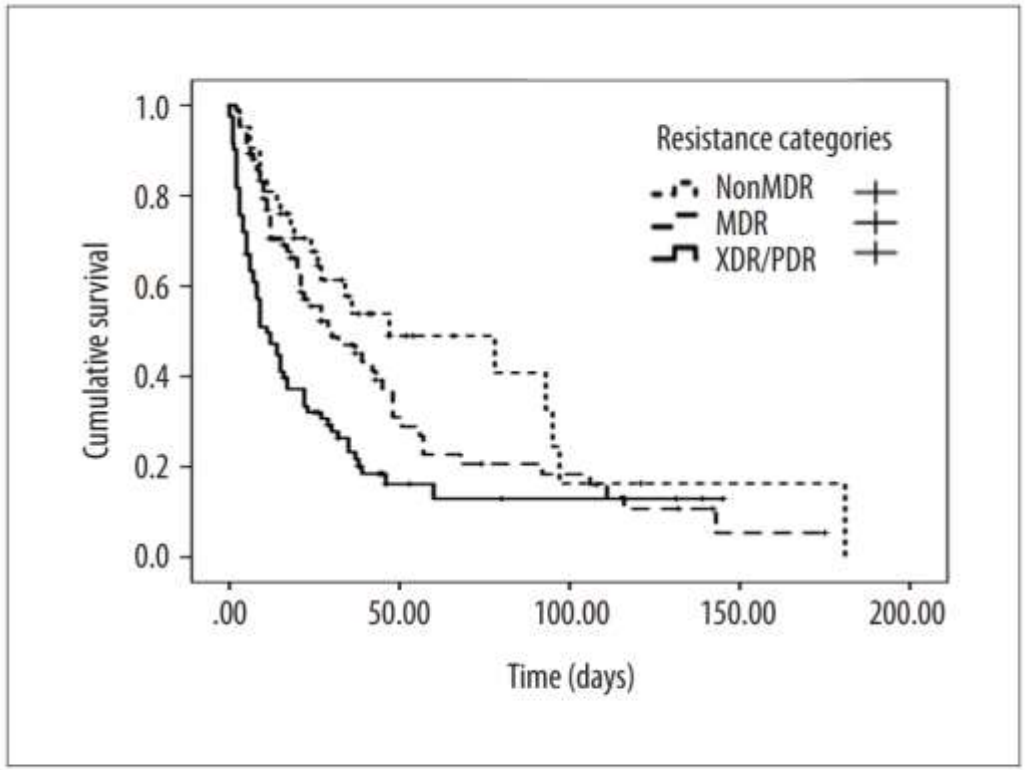


Figure 1. The relation between antibiotic resistance categories and cumulative survival.

Survival time of non-MDR, MDR, and XDR-PDR groups were 69.5±12.3, 48.4±6.4, and 31.5±5.7 days, respectively

- Combination of double antibiotics was the most-prescribed treatment (55.0%)

Table 3. Effect of Antibiotic combinations on patient survival (Cox regression with enter method).

		HR	95.0% CI for HR	
		p	Lower	Upper
XDR-PDR	**<0.001**	1.485	1.244	1.773
TGC-CP-CS	**0.027**	1.401	1.039	1.890
TGC-CP	**0.049**	1.259	1.001	1.583
TGC-CS	0.326	1.149	0.871	1.516
TGC-TMPS	**0.018**	0.709	0.532	0.943
CP-CS	0.720	0.938	0.659	1.334

Model Chi-square=33.83, p≤0.001. Variables included to Cox analyze: non-MDR – non-multiple drug resistance; MDR– multiple drug resistance; XDR-PDR – extensive drug resistance/pan-drug resistance; TGC-CP-CS – Tigecycline, Carbapenem, and Colistin; TGC-CP – Tigecycline and Carbapenem; TGC-CS – Tigecycline and Colistin; TGC-TMPS – Tigecycline and Trimethoprim-sulfamethoxazole); CP-CS – Carbapenem and Colistin).

Table 4. One-to-one effect of antibiotic groups on patient survival (Cox regression with enter method).

		HR	95.0% CI for HR	
		p	Lower	Upper
XDR-PDR	**<0.001**	1.481	1.238	1.772
Combinations with TMPS	**0.005**	0.460	0.267	0.794
Combinations with TGC	0.196	1.267	0.885	1.814
Combinations with CP/ single	0.370	1.171	0.829	1.655
Combinations with CS	0.432	1.148	0.814	1.618

Model Chi-square=29.78, p≤0.001. XDR-PDR – extensive drug resistance/pan-drug resistance; TMPS – Trimethoprim-sulfamethoxazole; TGC – Tigecycline; CP – Meropenem); CS – Colistin.

Resistance mechanisms

MRSA

- Methicillin resistance requires the presence of the *mec* gene; strains lacking a *mec* gene are not methicillin resistant
- mecA gene codes for an altered PBP namely PBP2a
- PBP2a has a low affinity for β-lactam antibiotics including methicillin
- ***Staphylococcal* chromosomal casette** — The SCC*mec* cassette is a mobile genetic element that contains the *mec* gene and is found in *Staphylococcal* species

Spread of MRSA

- Spread of existing resistant clones
- Acquisition of SCCmec by a methicillin-sensitive *S. aureus* (MSSA)
- Enzymatic degradation -β-lactamases (penicillin)
- MsrA efflux pump – macrolide resistance
- SCCmec has resulted in *Coagulase negative staph* acquiring methicillin resistance

Types of MRSA

CA-MRSA	HA-MRSA	LA-MRSA
Skin and soft tissue infections, pneumonia	Post-op wound infections, osteomyelitis, pneumonia	Wound infections, pneumonia
PVL + several other exotoxins Virulent	absent	absent
Less drug resistant	MDR	Drug resistance is more than CA-MRSA
High rate of infection	High rate of colonisation	-

MDR Gram Negative bacteria

- Commonly associated with HAI in India

- *Acinetobacter baumannii, Klebsiella pneumoniae, Pseudomonas aeruginosa*, *Escherichia coli* are the common organisms

- Carbapenem resistance and colistin resistance are the major problems

Resistance mechanisms

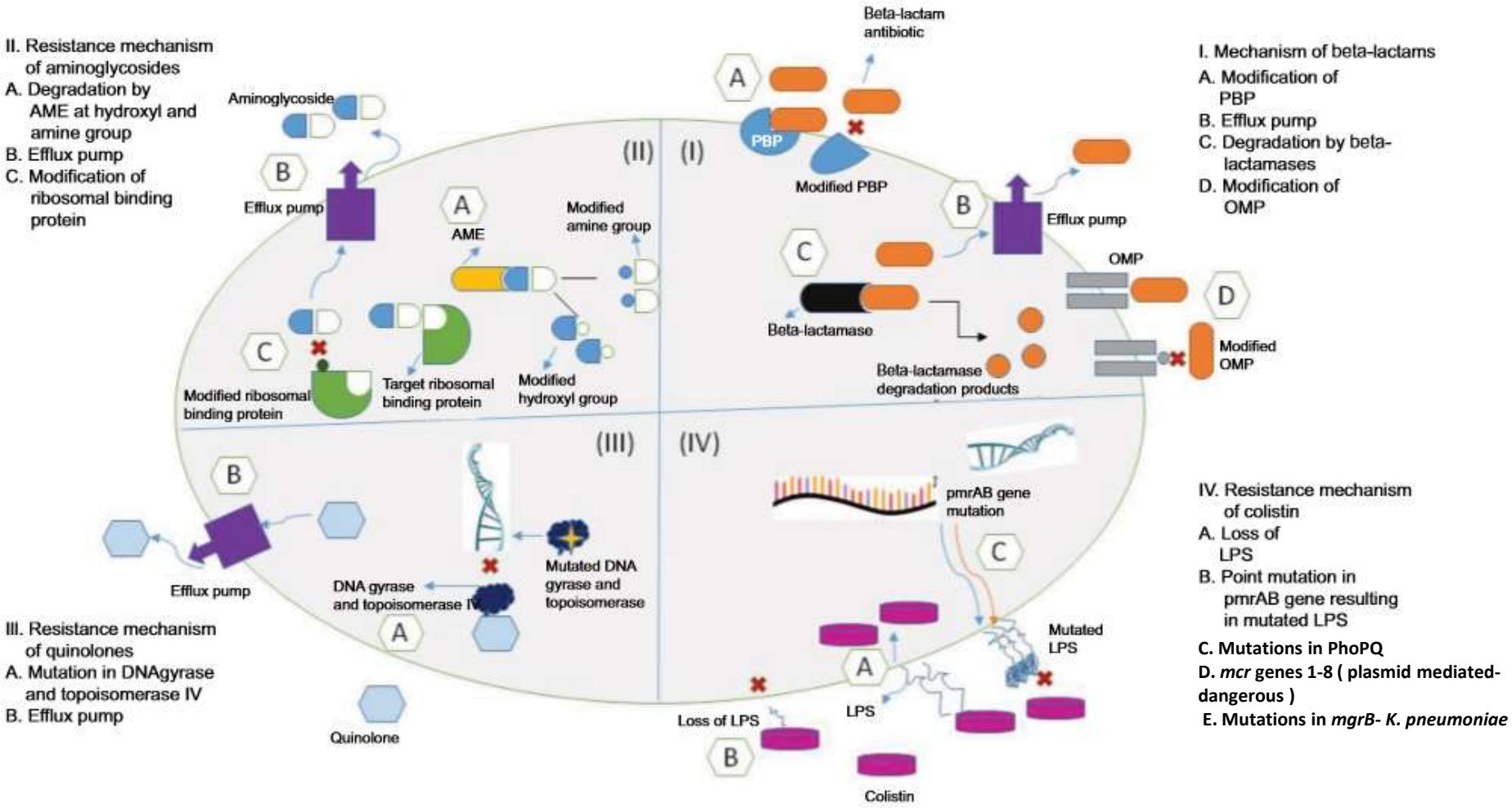


Figure 1 Different mechanisms of resistance in MDR-GNB (I) beta-lactams; (II) aminoglycosides; (III) quinolones; (IV) colistin.
Abbreviations: AME, aminoglycoside modifying enzyme; LPS, lipopolysaccharide; OMP, outer membrane porin; PBP, penicillin-binding protein.

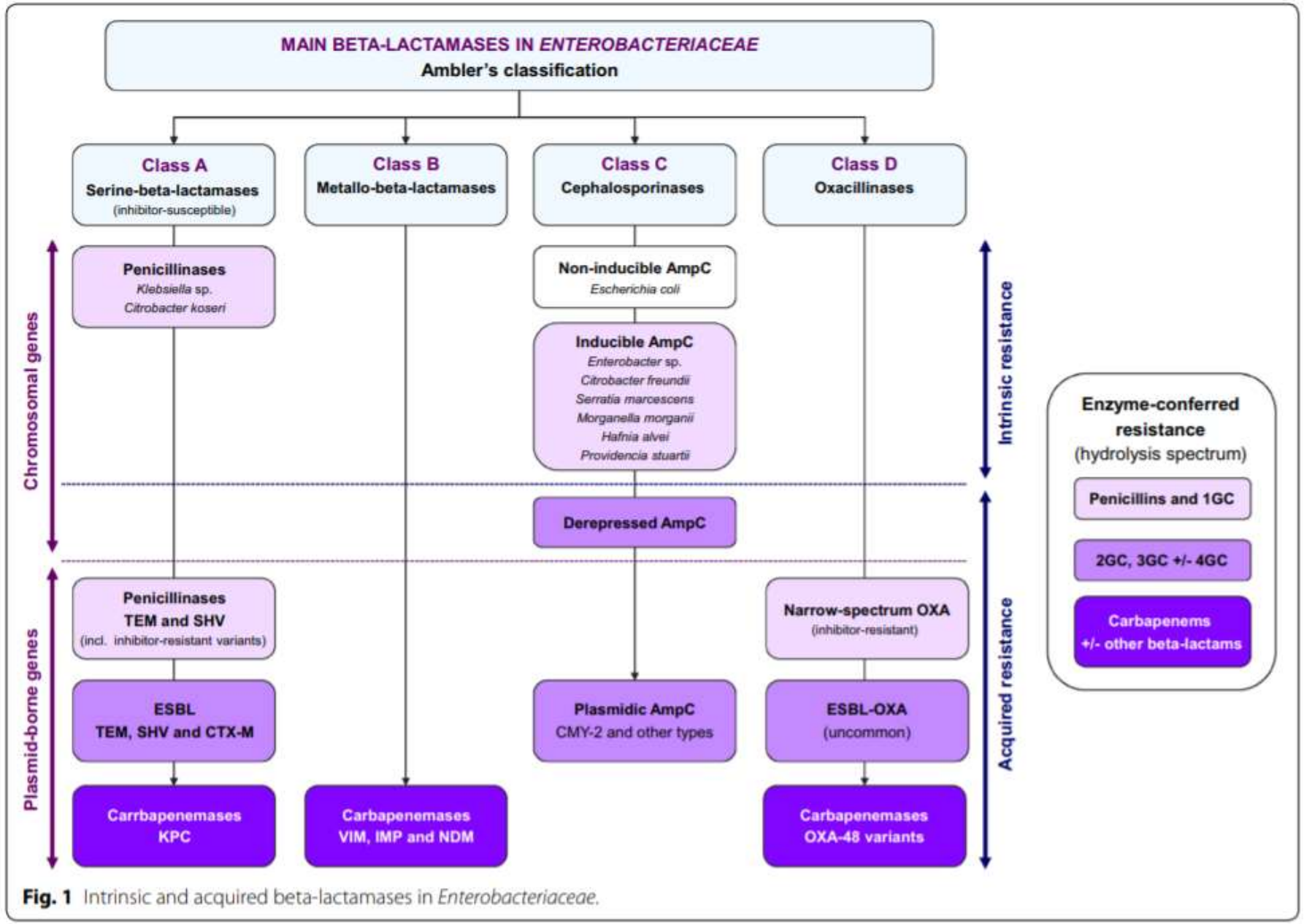


Fig. 1 Intrinsic and acquired beta-lactamases in *Enterobacteriaceae*.

Carbapenemases

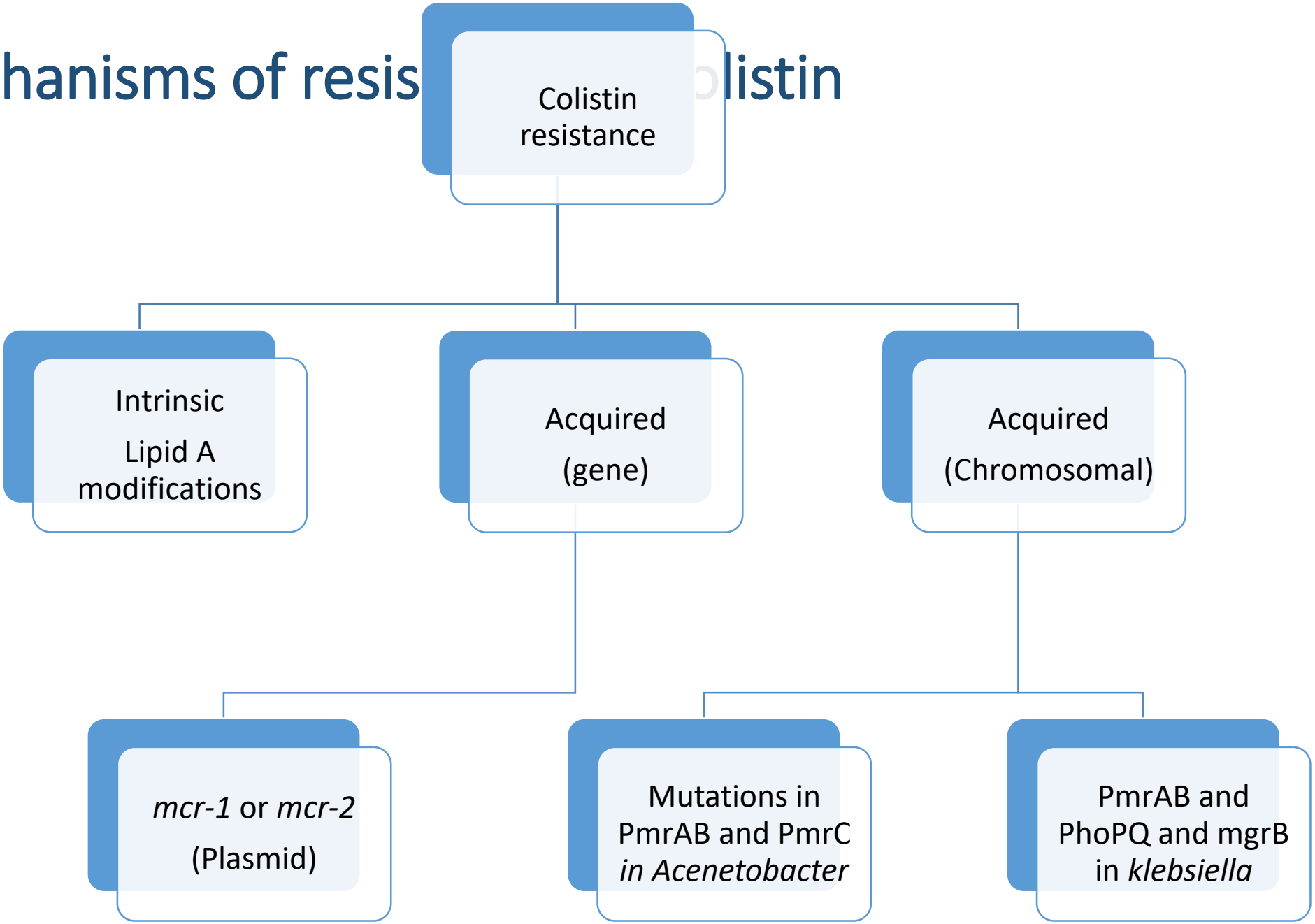
- The carbapenem-hydrolyzing beta-lactamase is an important emerging mechanism of antimicrobial resistance among nosocomial gram-negative pathogens
- Based on amino acid homology Class A,B,C,D
- Transmission of these genes occur frequently in hospital settings both chromosomally mediated and plasmid mediated
- Many genes NDM 1 (Class B) and KPC (class A) are found in bacteria in hospital environment in North India and have associated with outbreaks
- Currently phenotyping testing is only routinely available

Carbapenemases

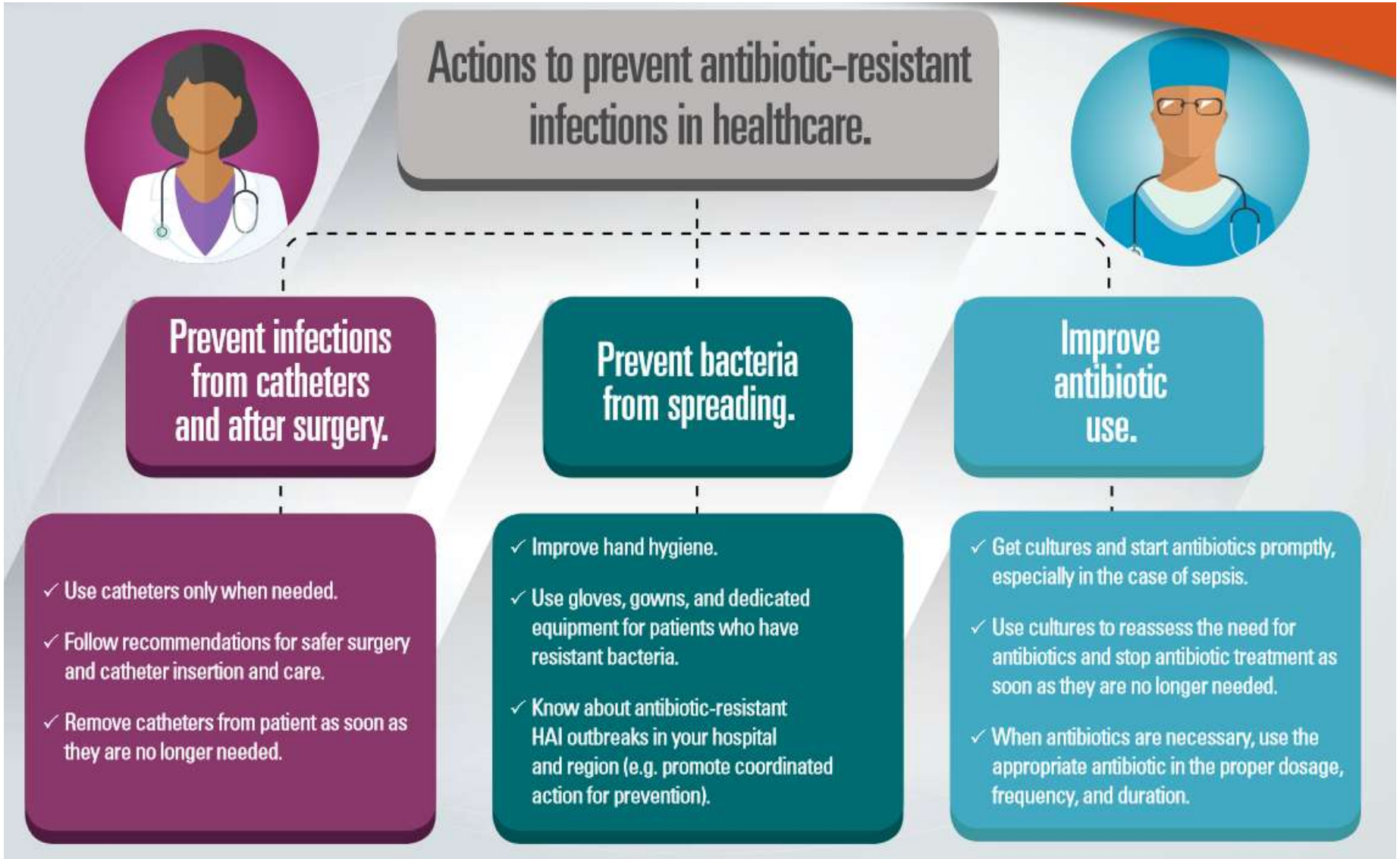
- Genotypic testing may be warranted in future as new beta lactam beta lactamase inhibitors enter pipeline

- Metalobeta lactamase – Aztreonam
- KPC (Class A) – Ceftazidime avibactam (KPC is not common in India, we have NDM)

Mechanisms of resis listin



Prevention of AMR in HAI


Actions to prevent antibiotic-resistant infections in healthcare.
Prevent infections from catheters and after surgery.
✓ Use catheters only when needed.
✓ Follow recommendations for safer surgery and catheter insertion and care.
✓ Remove catheters from patient as soon as they are no longer needed.
Prevent bacteria from spreading.
✓ Improve hand hygiene.
✓ Use gloves, gowns, and dedicated equipment for patients who have resistant bacteria.
✓ Know about antibiotic-resistant HAI outbreaks in your hospital and region (e.g. promote coordinated action for prevention).
Improve antibiotic use.
✓ Get cultures and start antibiotics promptly, especially in the case of sepsis.
✓ Use cultures to reassess the need for antibiotics and stop antibiotic treatment as soon as they are no longer needed.
✓ When antibiotics are necessary, use the appropriate antibiotic in the proper dosage, frequency, and duration.

Intravascular catheter care

General recommendations for prevention of infections associated with any intravascular catheter in adult and pediatric patients

Health care worker education and training
Educate health care workers regarding indication for intravascular catheter use, proper procedures for the insertion and maintenance, and infection control measures to prevent intravascular catheter-associated infections.
Hand hygiene
Observe proper hand hygiene either by washing hands with conventional antiseptic-containing soap and water or with waterless alcohol-based gels or foams. Use of gloves does not obviate the need for hand hygiene.
Aseptic technique during catheter insertion and care
Maintain aseptic technique for the insertion and care of intravascular catheters. Use maximal barrier precautions when inserting arterial or central venous catheters.
Catheter site care
Disinfect clean skin with an appropriate antiseptic before catheter insertion and at the time of dressing changes. A 2% chlorhexidine-based preparation is preferred, but there is no recommendation for its use in infants less than two months of age.
Use sterile gauze or sterile transparent semipermeable dressing to cover the catheter site.
Do not use topical antibiotic ointment or creams on insertion sites (except for dialysis catheters).
Replacement of intravascular catheters
Remove any intravascular catheter that is no longer essential.
Replacement of administration sets
Replace administration sets, including secondary sets and add-on devices, no more frequently than at 72-hour intervals, unless clinically indicated. Replace tubing used to administer blood, blood products, or lipid emulsions within 24 hours of initiating the infusion. Replace tubing used to administer propofol infusions every 6 to 12 hours, depending on its use, per the manufacturer's recommendation.
Parenteral fluids
Complete the infusion of lipid containing solutions within 24 hours of hanging the solution.
Complete the infusion of lipid emulsions alone within 12 hours of hanging the solution.
Complete infusions of blood or other blood products within four hours of hanging the blood.
Intravenous injection ports
Clean injection ports with 70% alcohol or an iodophor before accessing the system.

VAP bundle

Use non-invasive positive pressure ventilation in selected populations
Manage patients without sedation whenever possible
Interrupt sedation daily
Assess readiness to extubate daily
Perform spontaneous breathing trials with sedatives turned off
Facilitate early mobility
Utilize endotracheal tubes with subglottic secretion drainage ports for patients expected to require greater than 48 or 72 hours of mechanical ventilation
Change the ventilator circuit only if visibly soiled or malfunctioning
Elevate the head of the bed to 30 to 45°
Oral decontamination with CHG

Principles of optimal antimicrobial use

- Initiation of appropriate empirical therapy
- Tailoring therapy once culture reports available
- Shortest effective duration of exposure
- Conversion to oral antibiotics as soon as possible
- Pharmacokinetic monitoring

Stewardship programme

- Antimicrobial stewardship -systematic measurement and coordinated interventions designed to promote optimal use of antimicrobial agents, by advocating selection of appropriate antimicrobial drug regimens (including dosing, duration of therapy, and route of administration)
- Antibiotic oversight
  - Prospective audit and feedback vs Preauthorisation
- Establishing facility specific antibiotic protocols
- Point of care interventions
  - PK monitoring
  - Dose adjustments
  - Allergy assessments
- Establish and renew antibiograms

Stewardship programme

Metrics for evaluation of stewardship program interventions to improve antibiotic use and clinical outcomes

Process measures	Outcome measures
▪ Excess days of therapy (ie, unnecessary days of therapy avoided based on accepted targets and benchmarks)* ▪ Duration of therapy ▪ Proportion of patients compliant with facility-based guideline or treatment algorithm* ▪ Proportion of patients with revision of antibiotics based on microbiology data ▪ Proportion of patients converted to oral therapy	▪ Hospital length of stay ▪ 30-day mortality ▪ Unplanned hospital readmission within 30 days ▪ Proportion of patients diagnosed with hospital-acquired *Clostridioides* (formerly *Clostridium*) *difficile* infection or other adverse event(s) related to antibiotic treatment* ▪ Proportion of patients with clinical failure (eg, need to broaden therapy, recurrence of infection)

* These metrics are applicable for antibiotic stewardship program interventions to reduce antibiotic treatment of asymptomatic bacteriuria, which, in most cases, should not be treated; therefore, the other metrics do not apply.

Summary

- 4 HAI syndromes with pneumonia and blood stream infections majority
- MDR gram negative bugs *Acinetobacter* > *Pseudomonas* commonest pathogens
- Initial empirical antimicrobial of choice should remain colistin/polymyxin
- Vancomycin/Linezolid in certain subgroups
- Preventive measures to tackle AMR go beyond the boundaries of ICU and include surveillance, stewardship and awareness