Tratamiento de la neumonía asociada a la ventilación mecánica: cómo aplicar las nuevas guías

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Disclosures

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Magnitude of the problem (I)

- VAP and HAP continue to be frequent complications of hospital care.
- Together, they account for 22% of all HAIs.
- About 10% of patients requiring MV develop VAP.
- VAP is responsible for half of ICU antibiotic prescriptions.

Magnitude of the problem (II)

- VAP

  - all cause-mortality: 20 – 50%

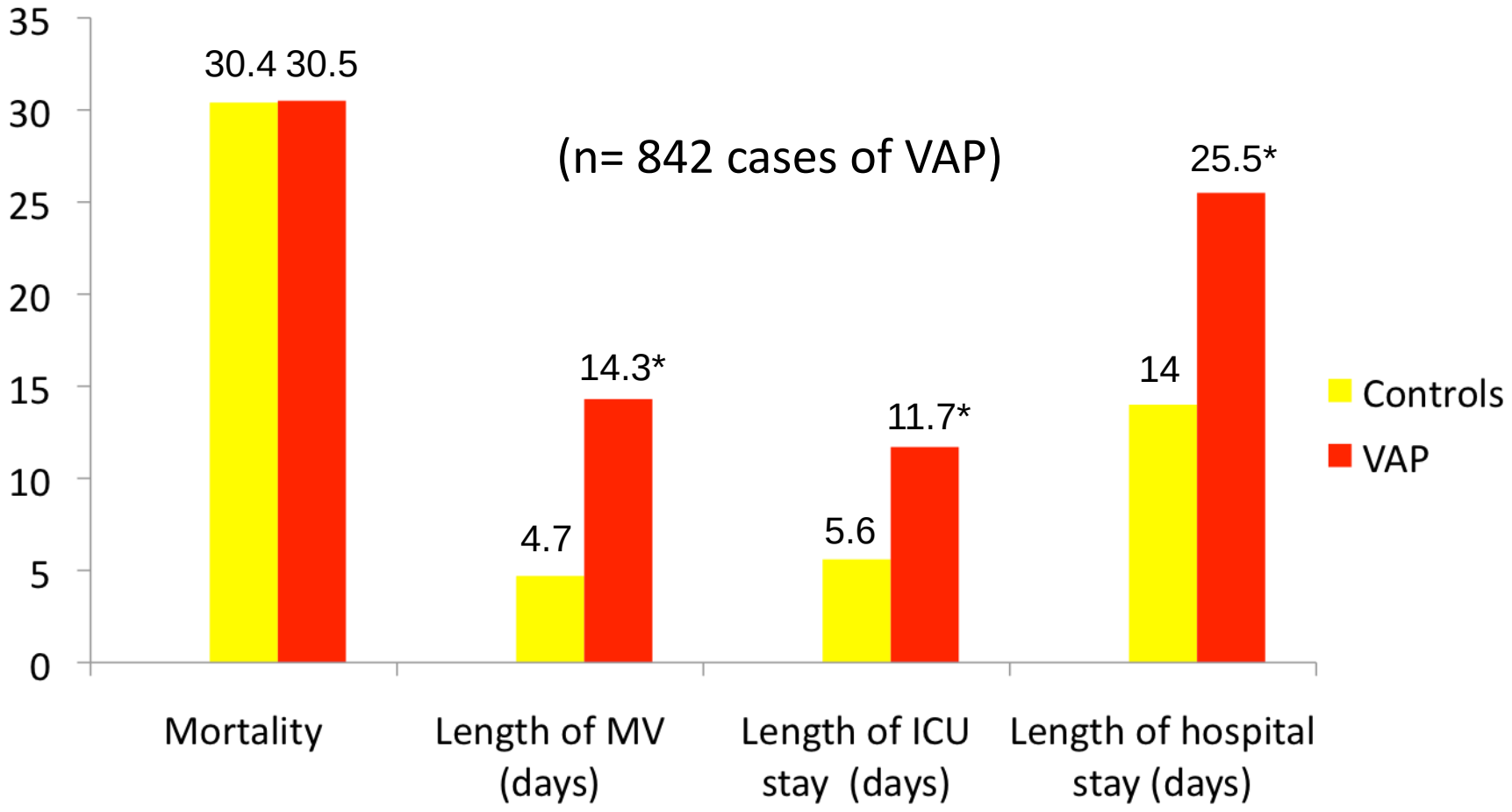
  - attributable mortality: 13%

- Prolonged length of MV: 7.4 – 11.5 days.

- Prolonged LOS: 8.7 – 13.1 days.

- The excess cost associated with VAP: $40,000 per patient.

Impact of VAP on outcomes in a large US database

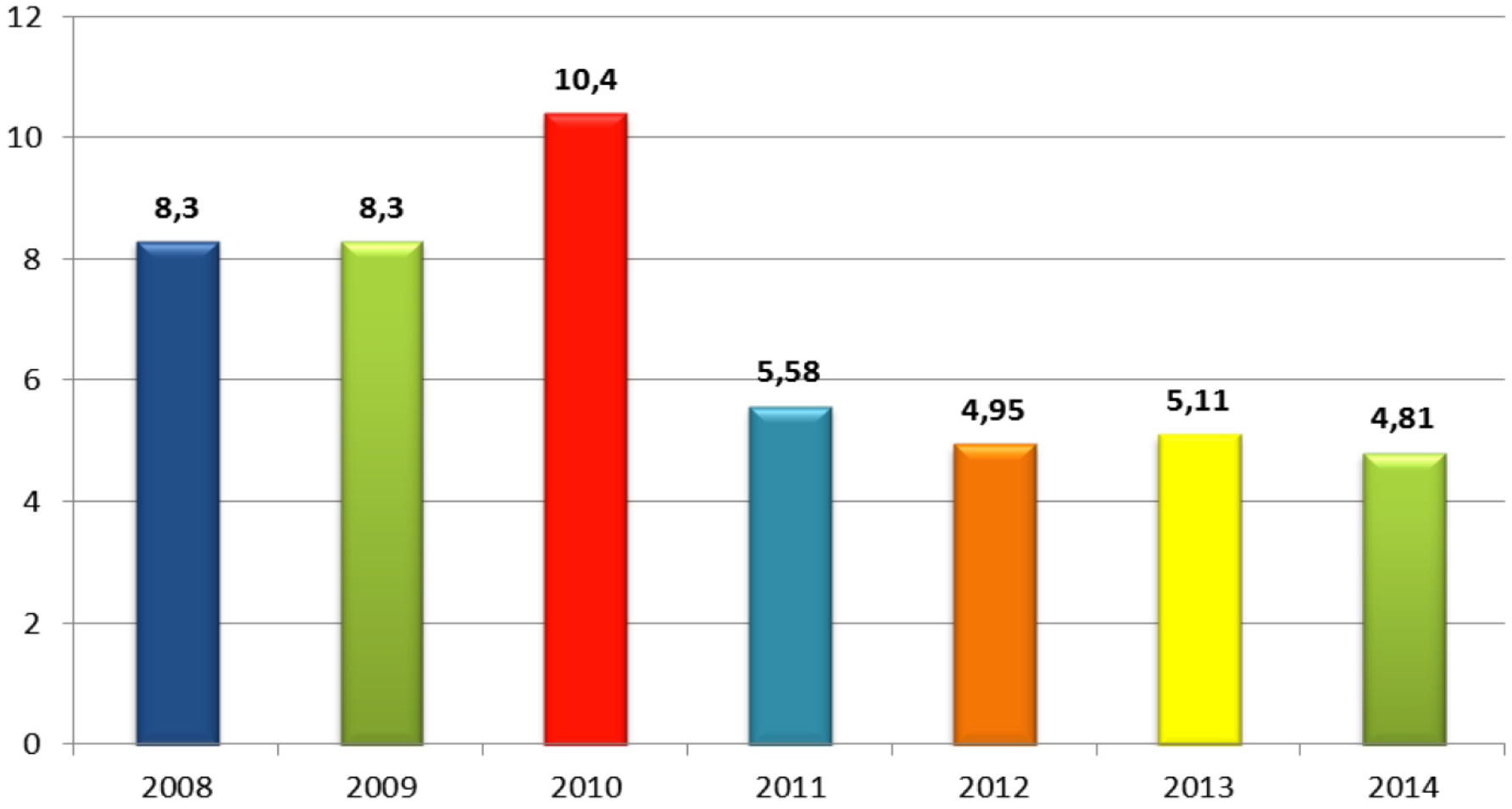


* p <0.0001

Rello J. Chest 2002

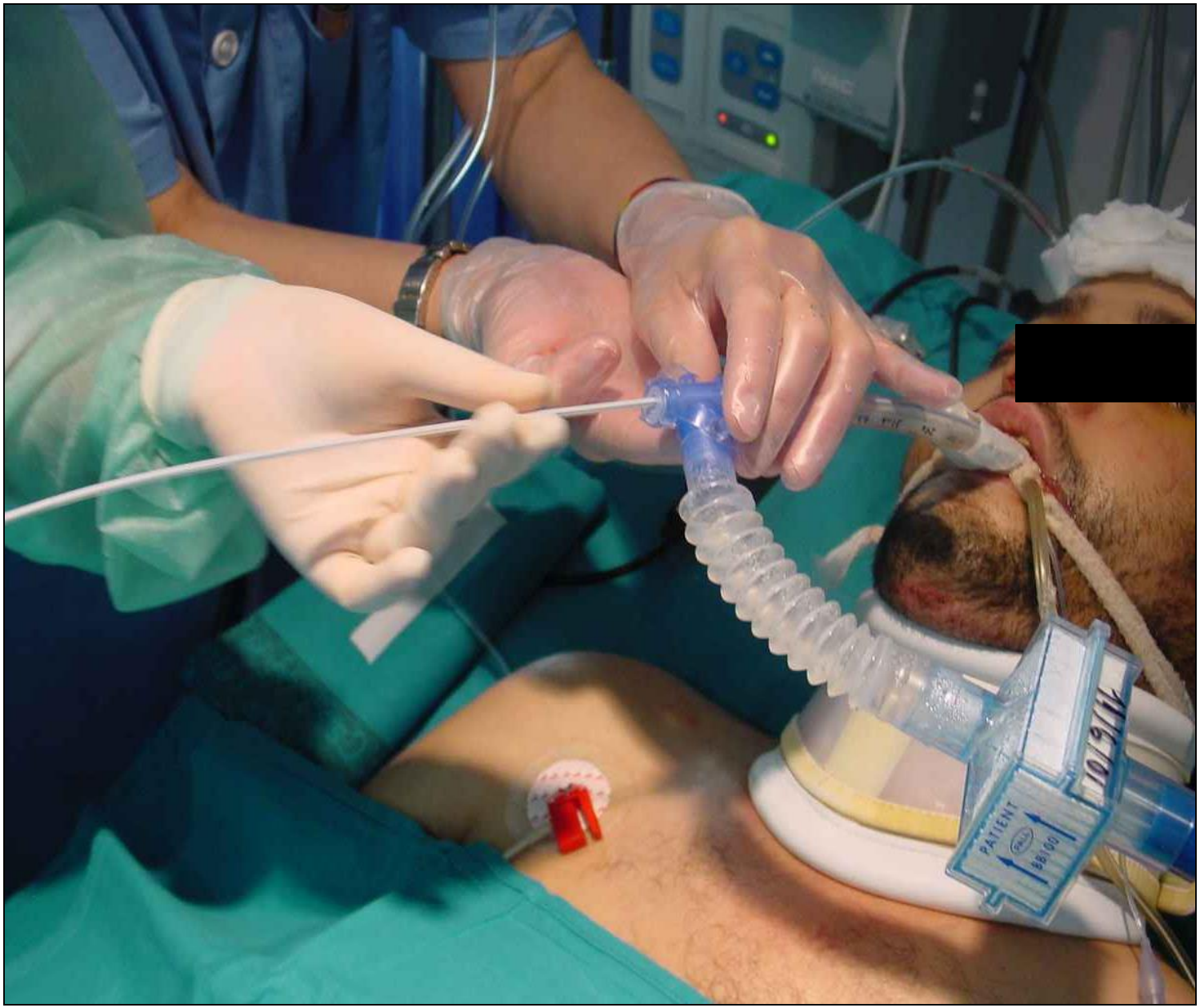
Incidence density of VAP

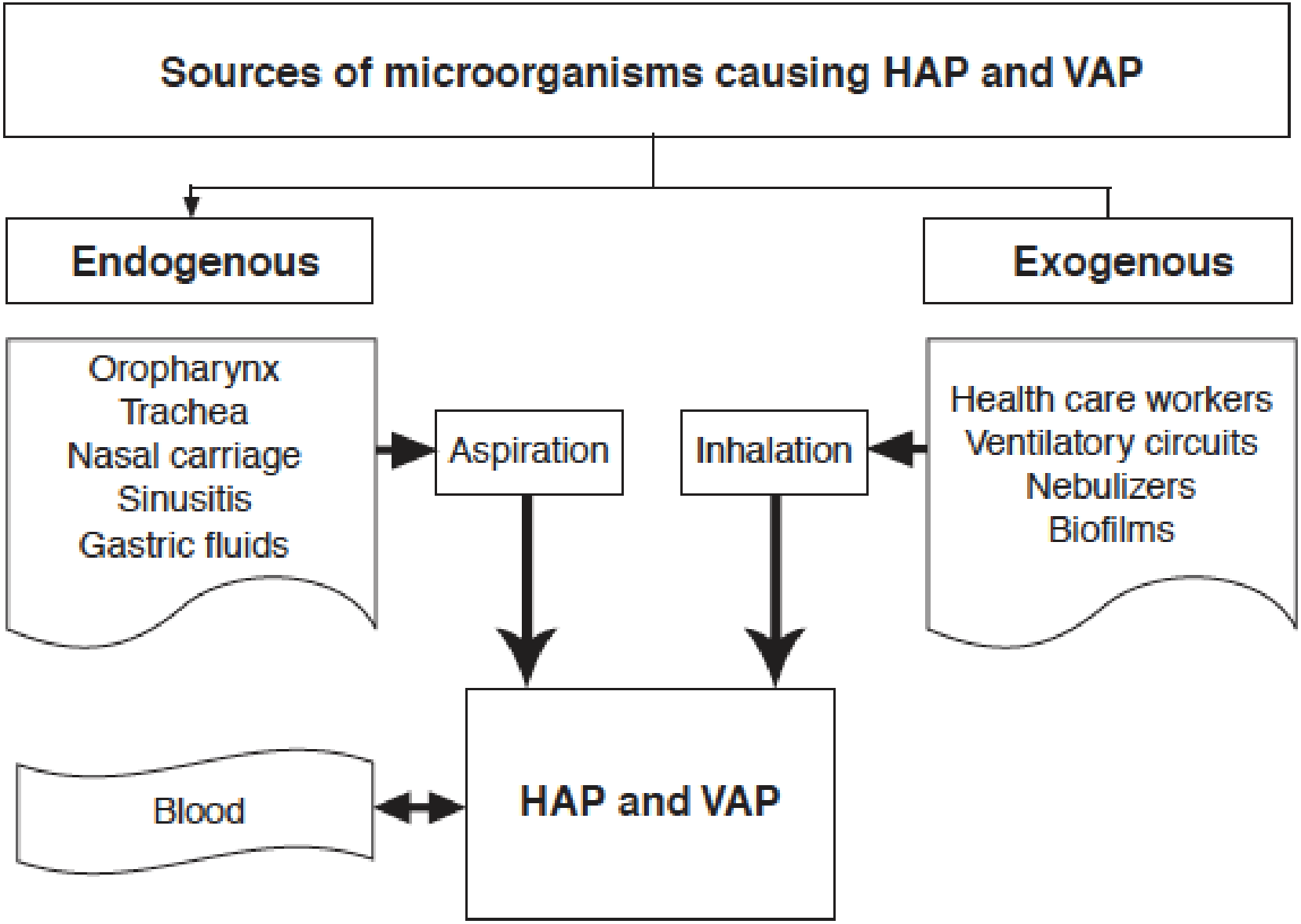
ICU: 34 Episodes: 157



Median: 4.8 episodes/1000 ventilator days

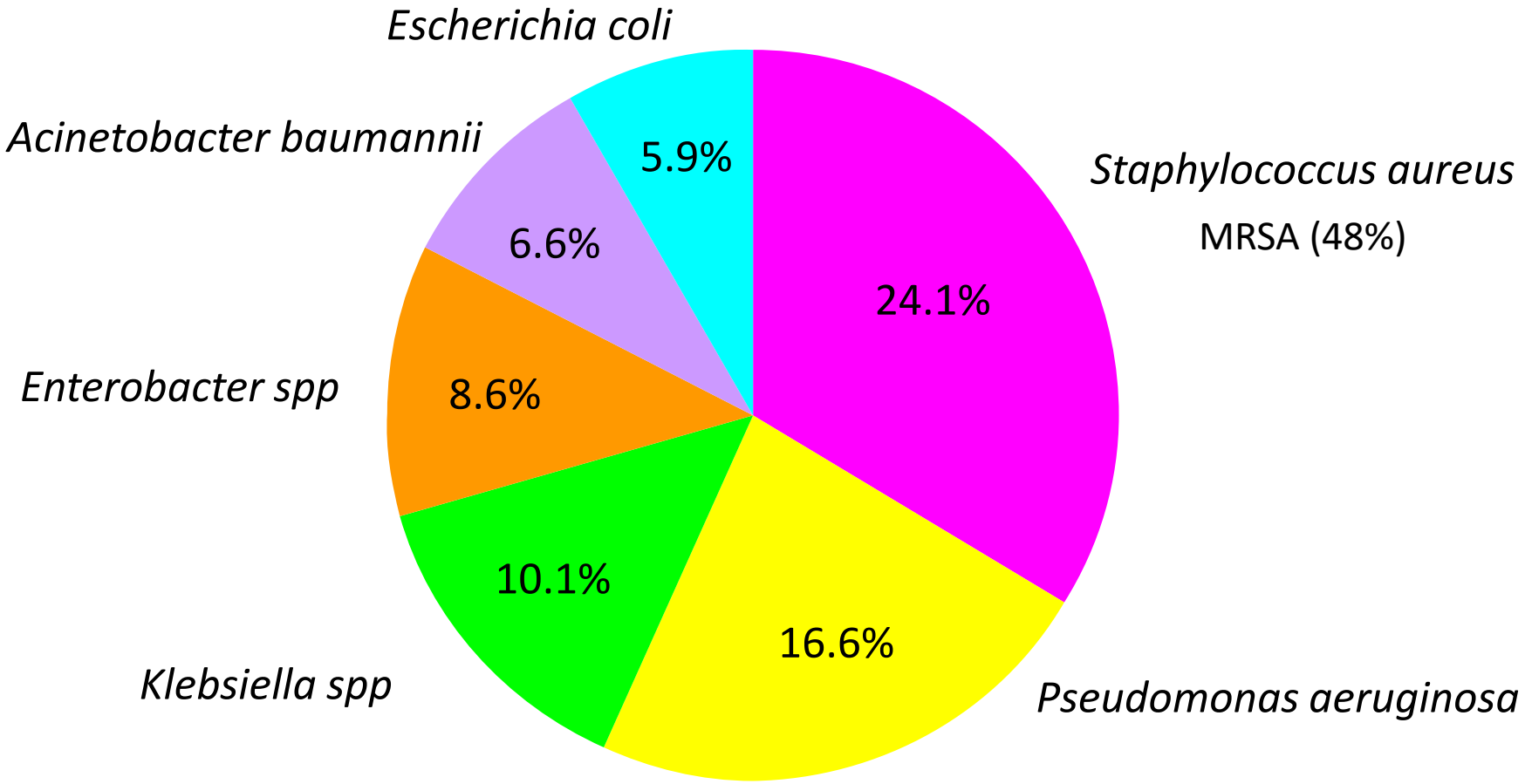
VINCat


PATIENT



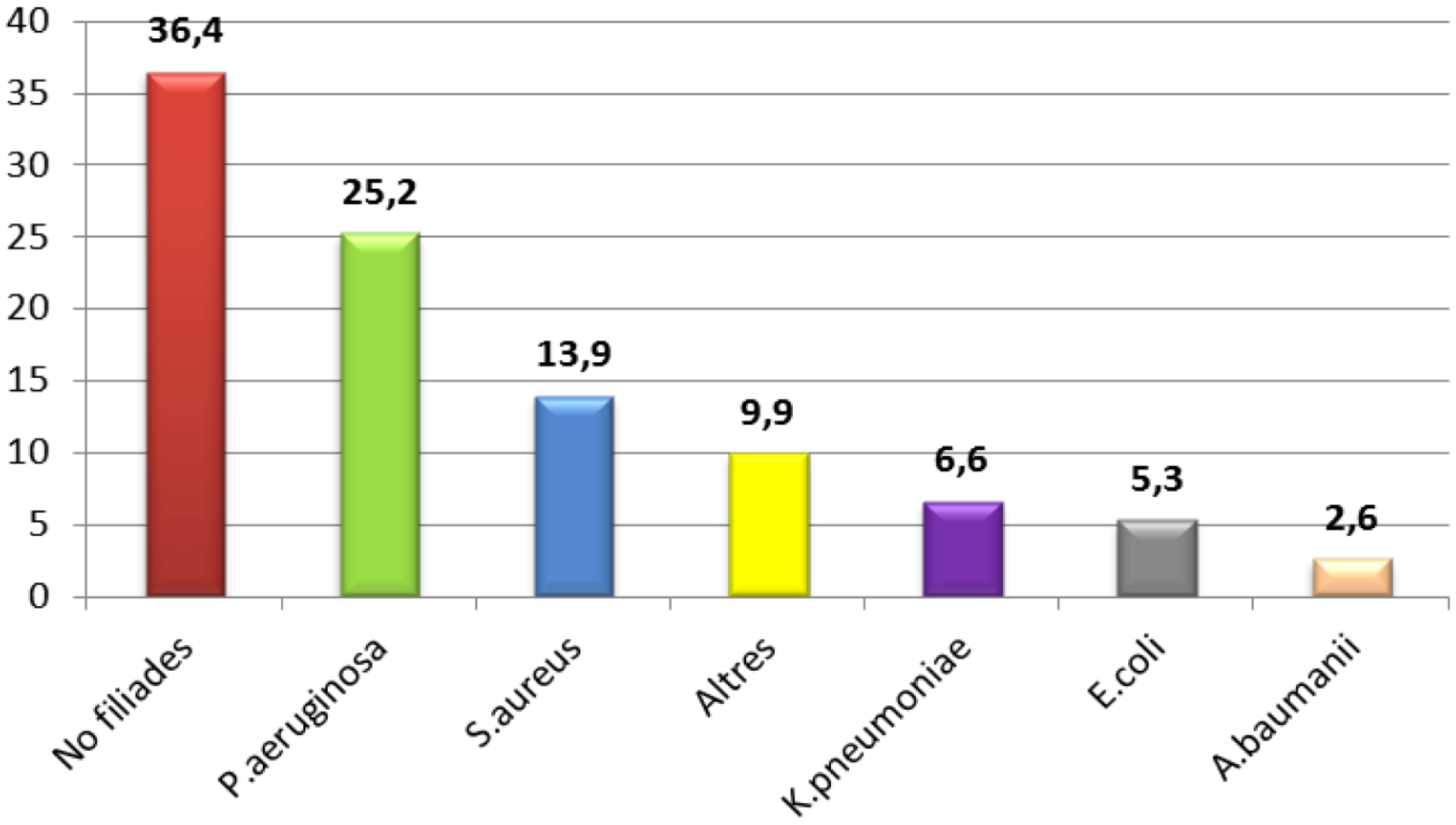
Rotstein C. Can J infect Dis Med Microbiol 2008

Distribution of pathogens associated with 8.474 cases of VAP reported to the CDC (2009-2010)



Sievert DM. Infect Control Hosp Epidemiol 2013

Etiology of 157 episodes of VAP



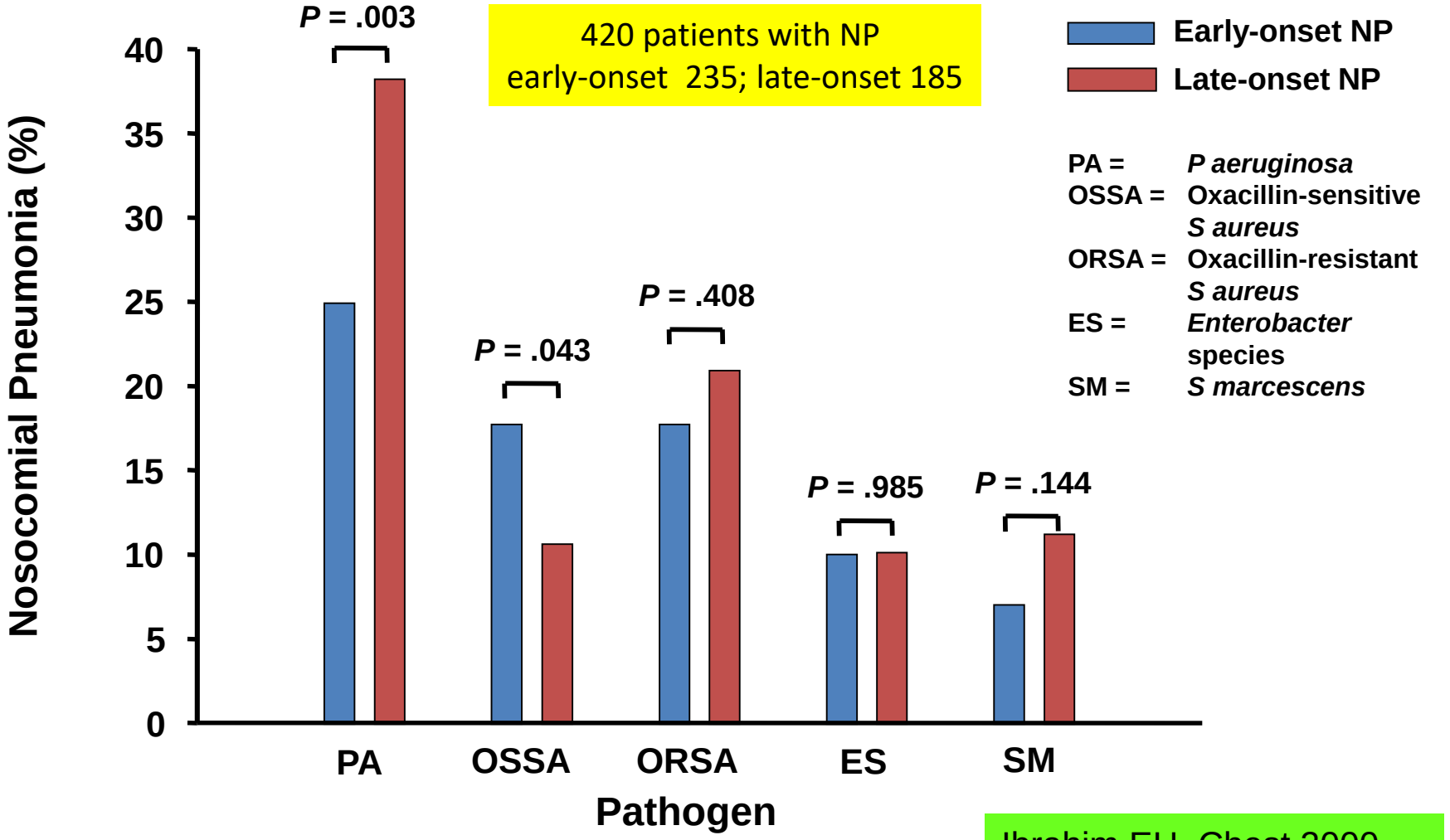
VINCat 2008 - 2014

Etiology of VAP according to the duration of intubation

Early-onset VAP (≤4 days)	Late-onset VAP (>4 days)
Community-acquired	Hospital-acquired
Streptococcus pneumoniae	*Pseudomonas aeruginosa*
Haemophilus influenzae	MRSA
Staphylococcus aureus	*Acinetobacter*
	Enterobacter
Antibiotic-sensitive	Antibiotic-resistant

Kollef M. Chest 2005

Pathogens associated with NP in the ICU



Ibrahim EH. Chest 2000

Factors associated with the development of VAP caused by MDR pathogens

Factors	Quality of evidence
• Use of antibiotics within 90 days prior to the occurrence of VAP • Severe sepsis on admission • Recent use of corticosteroids (≥14 days in the last 3 months)	Moderate quality
• ARDS preceding VAP • Receipt of renal replacement therapy prior to VAP onset • Greater than 5 days of hospitalization prior to the occurrence of VAP	Low quality

Clinical Infectious Diseases

IDSA GUIDELINE

Management of Adults With Hospital-acquired and Ventilator-associated Pneumonia: 2016 Clinical Practice Guidelines by the Infectious Diseases Society of America and the American Thoracic Society

Andre C. Kalil,[1,a] Mark L. Metersky,[2,a] Michael Klompas,[3,4] John Muscedere,[5] Daniel A. Sweeney,[6] Lucy B. Palmer,[7] Lena M. Napolitano,[8] Naomi P. O'Grady,[9] John G. Bartlett,[10] Jordi Carratalà,[11] Ali A. El Solh,[12] Santiago Ewig,[13] Paul D. Fey,[14] Thomas M. File Jr,[15] Marcos I. Restrepo,[16] Jason A. Roberts,[17,18] Grant W. Waterer,[19] Peggy Cruse,[20] Shandra L. Knight,[20] and Jan L. Brozek[21]

Clin Infect Dis 2016; 63: e61-111

- Empiric antibiotic treatment
- MRSA
- *Pseudomonas aeruginosa*
- Carbapenem-resistant pathogens
- Duration of antibiotics

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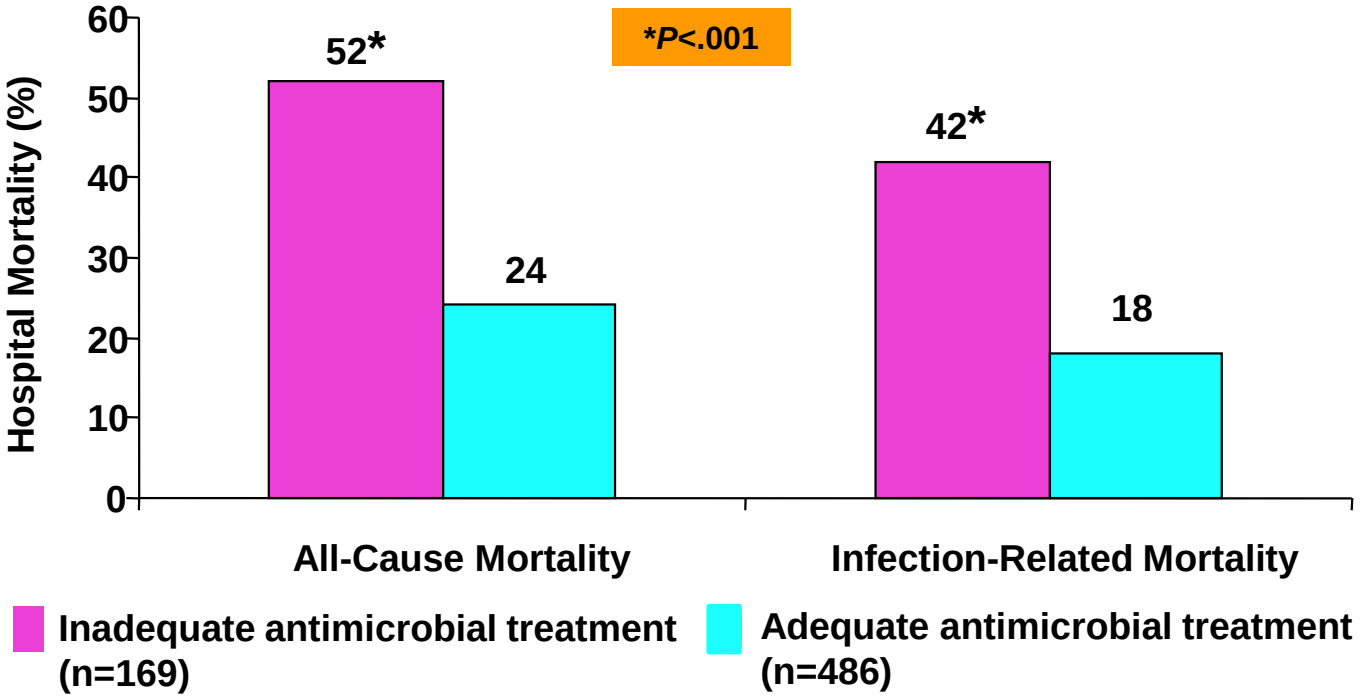
Importance of initial, appropriate antibiotic therapy



Should selection of an empiric antibiotic regimen for VAP be guided by local antibiotic therapy?

- We recommend that all hospitals regularly generate and disseminate a local antibiogram, ideally one that is specific to their ICU population.

- We recommend that empiric treatment regimens be informed by the local distribution of pathogens associated with VAP and their antimicrobial susceptibilities.

What antibiotics are recommended for empiric treatment of clinically suspected VAP?

- Coverage for *S. aureus*, *P. aeruginosa* and other GNB.
- Vancomycin or linezolid for pts with risk factors for resistance, pts being treated in units where >10-20% of *S. aureus* isolates are MRSA or when its prevalence is not known.
- Two antipseudomonal antibiotics from different classes for pts with risk factors for resistance (prior ATB use, 90 d), pts in units where >10% of isolates are resistant or when its prevalence is not know.
- Avoid: aminoglycosides and colistin if alternative agents with adequate activity against GNB are available.

A. Gram positive ATBs with MRSA activity	B. Beta-lactam based agents (anti-Pseudomonal activity)	C. Non beta-lactam based agents (anti-Pseudomonal activity)
Glycopeptides Vancomycin 15 mg/kg iv q 12h (consider a loading dose of 25-30 mg/kgx 1 for severe illness) OR Oxazolidinones Linezolid 600 mg/ iv q 12h	Cephalosporins Cefepime 2 g iv q 8-12 h Ceftazidime 2 g iv q 8 h OR Carbapenems Imipenem 500 mg iv q 6 h Meropenem 1-2 g iv q 8h OR Anti-Pseudomonal Penicllins Piperacillin-tazobactam 4.5 g iv q 6h OR Monobactams Aztreonam 2 g iv q 8 h	Fluoroquinolones Ciprofloxacin 400 mg iv q 8 h Levofloxacin 750 mg iv q 24 h OR Aminoglycosides Amikacin 15-20 mg/kg iv q24h Gentamicin 5-7 mg/kg iv q24h Tobramycin 5-7 mg/kg iv q24h OR Polymixins Colistin 5 mg/kg iv x 1 (loading dose) followed by 2.5 mg x (1.5 x Cr Cl + 30) iv q12h (mainenance dose)

- Empiric antibiotic treatment
- MRSA
- *Pseudomonas aeruginosa*
- Carbapenem-resistant pathogens
- Duration of antibiotics

What antibiotics should be used for the treatment for MRSA VAP/HAP?

- MRSA VAP/HAP must be treated with either vancomycin or linezolid rather than other antibiotics or antibiotic combinations

Remarks: The choice between linezolid and vancomycin should be governed by patient-specific risk factors such as blood cell counts, concurrent prescriptions for serotonin reuptake inhibitors, renal function, and cost.

Treatment of HAP with linezolid vs vancomycin: A systematic review and meta-analysis

9 randomized trials with a total of 4026 patients

	RD		
Mortality:	0.01%	(CI 95% -2.1% to 2.1%;	P= 0.992)
Clinical response:	0.9%	(CI 95% -1.2% to 3.1%;	P= 0.409)
MRSA eradication:	6.4%	(CI 95% -4.1% to 16.9%;	P= 0.230)

GI effects were more frequent with linezolid, but no differences were found with renal failure, thrombocytopenia and drug discontinuation due to adverse events

Kalil AC. BMJ Open 2013

- Empiric antibiotic treatment
- MRSA
- *Pseudomonas aeruginosa*
- Carbapenem-resistant pathogens
- Duration of antibiotics

Which antibiotic should be used to treat patients with VAP/HAP due to *Pseudomonas aeruginosa*?

- Choice of ATB must be based upon the results of antimicrobial susceptibility testing.
- Aminoglycoside monotherapy should be avoided.

Should monotherapy or combination therapy be used to treat patients with VAP/HAP due to *Pseudomonas aeruginosa*?

- For pts who are not in septic shock or at high risk for death, monotherapy rather combination therapy must be used.
- For pts with septic shock or at high risk of death, combination therapy rather than monotherapy must be used.

- Empiric antibiotic treatment
- MRSA
- *Pseudomonas aeruginosa*
- Carbapenem-resistant pathogens
- Duration of antibiotics

Which antibiotic should be used to treat patients with VAP/HAP due to carbapenem-resistant pathogens?

- In patients with VAP/HAP caused by a carbapenem-resistant pathogen that is sensitive only to polymyxins, intravenous polymyxins with adjunctive inhaled colistin must be used.

Remarks: Colistin for inhalation should be administered promptly after being mixed with sterile water. This recommendation was made by the FDA after a report that a cystic fibrosis patient died after being treated with a premixed colistin formulation.

- Empiric antibiotic treatment
- MRSA
- *Pseudomonas aeruginosa*
- Carbapenem-resistant pathogens
- Duration of antibiotics

Should patients with VAP receive 7 days or 8-15 days of antibiotic therapy?

- For patients with VAP, a 7-day course of antimicrobial therapy rather than a longer duration should be used.

Remarks: There exist clinical situations in which a longer duration of antibiotics may be indicated, for example in patients with the delayed clinical improvement.

Short- vs long-duration antibiotic regimens for VAP: A systematic review and mata-analysis

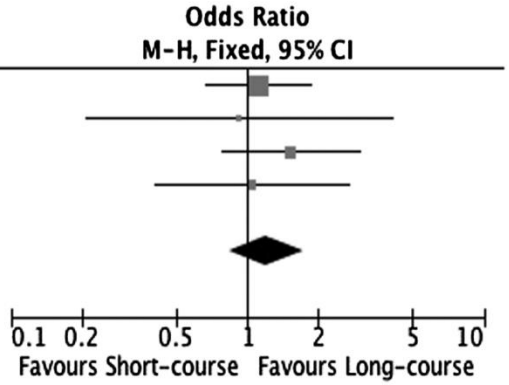
4 RCTs comparing short (7-8 days) with long (10-15 days) regimens

Mortality

Study or Subgroup	Short-course Events	Total	Long-course Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Chastre et al	37	197	35	204	51.6%	1.12 [0.67, 1.86]	2003
Fekih Hassen et al	5	14	6	16	6.7%	0.93 [0.21, 4.11]	2009
Kollef et al	26	115	18	112	26.1%	1.53 [0.78, 2.97]	2012
Capellier et al	10	116	9	109	15.7%	1.05 [0.41, 2.69]	2012
Total (95% CI)		442		441	100.0%	1.20 [0.84, 1.72]	
Total events	78		68				

Heterogeneity: $Chi^2 = 0.77$, df = 3 (P = 0.86); $I^2 = 0\%$

Test for overall effect: Z = 0.99 (P = 0.32)

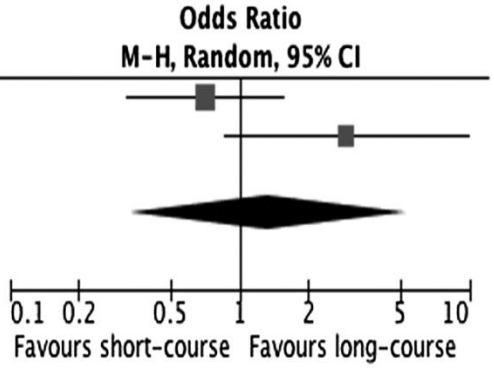


Mortality in pts with non-fermentative-GN bacteria

Study or Subgroup	Short-course Events	Total	Long-course Events	Total	Weight	Odds Ratio M-H, Random, 95% CI	Year
Chastre et al	15	64	19	63	55.7%	0.71 [0.32, 1.56]	2003
Kollef et al	12	47	4	38	44.3%	2.91 [0.86, 9.93]	2012
Total (95% CI)		111		101	100.0%	1.33 [0.33, 5.26]	
Total events	27		23				

Heterogeneity: $Tau^2 = 0.73$; $Chi^2 = 3.62$, df = 1 (P = 0.06); $I^2 = 72\%$

Test for overall effect: Z = 0.40 (P = 0.69)



Dimopoulos G. Chest 2013

Antibiotic-free days

Study or Subgroup	Short-course Mean	SD	Total	Long-course Mean	SD	Total	Weight	Mean Difference IV, Random, 95% CI
Chastre et al	13.1	7.4	197	8.7	5.2	204	50.1%	4.40 [3.14, 5.66]
Fekih Hassen et al	4.14	1.9	14	1.75	1.6	16	49.9%	2.39 [1.12, 3.66]
Total (95% CI)			211			220	100.0%	**3.40 [1.43, 5.37]**

Heterogeneity: $Tau^2 = 1.61$; $Chi^2 = 4.88$, df = 1 (P = 0.03); $I^2 = 79\%$

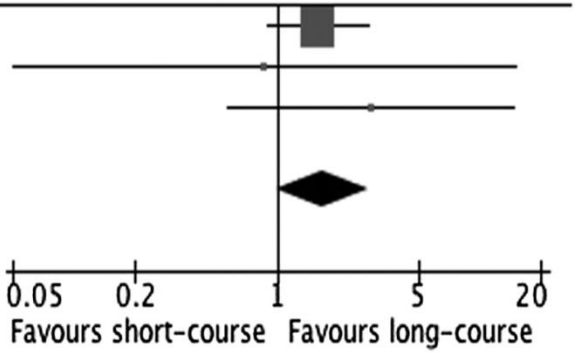
Test for overall effect: Z = 3.38 (P = 0.0007)

Relapses

Study or Subgroup	Short-course Events	Total	Long-course Events	Total	Weight	Odds Ratio M-H, Fixed, 95% CI	Year
Chastre et al	33	197	23	204	86.4%	1.58 [0.89, 2.81]	2003
Fekih Hassen et al	1	16	1	14	4.6%	0.87 [0.05, 15.28]	2009
Capellier et al	6	116	2	109	9.0%	2.92 [0.58, 14.78]	2012
Total (95% CI)		329		327	100.0%	**1.67 [0.99, 2.83]**	
Total events	40		26				

Heterogeneity: $Chi^2 = 0.69$, df = 2 (P = 0.71); $I^2 = 0\%$

Test for overall effect: Z = 1.91 (P = 0.06)



Dimopoulos G. Chest 2013

Muchas gracias por su atención!

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