

PRO/CON Debate:
Infectious Diseases Society of America
2016 HAP/VAP Guidelines

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Objectives

1. Describe major changes in the updated version of Infectious Diseases Society of America (IDSA) Guideline in regard to the classification and management of hospital-acquired and ventilator-associated pneumonia
2. Discuss the relative merits and weaknesses of the previous guideline's healthcare associated pneumonia (HCAP) designation compared to the new guideline's criteria for risk of multi-drug resistant organisms
3. Examine the role of biomarkers, such as procalcitonin, in the decision to start or stop antibiotics in the setting of hospital-acquired or ventilator-associated pneumonia
4. Review duration data in regard to management of patients with pneumonia due to infections from non-glucose-fermenting gram-negative bacilli



Resolved! The IDSA 2016 HAP/VAP
Guideline updates are therapeutically
sound, easy-to-implement, and
stewardship-forward.

Debate Format

- 3 topics for discussion
 1. Removal of 'health care associated pneumonia' (HCAP) from the IDSA guidelines
 2. Use of procalcitonin (PCT) in determining duration for PNA
 3. Duration of therapy in the treatment of PNA
- Each side will make an opening statement
- Rebuttals

Major changes between 2005 and 2016 guidelines

- Health care associated pneumonia removed from 2016 guidelines
- Judicious use of antibiotics
 - Recommendation that hospitals generate antibiograms to decide on empiric prescribing at an institutional level
 - Novel laboratory assays
 - Fewer blanket prescriptions for particular pathogens

Debate Point #1: Removal of HCAP from 2016 IDSA guidelines

TABLE 2. RISK FACTORS FOR MULTIDRUG-RESISTANT PATHOGENS CAUSING HOSPITAL-ACQUIRED PNEUMONIA, HEALTHCARE-ASSOCIATED PNEUMONIA, AND VENTILATOR-ASSOCIATED PNEUMONIA

- Antimicrobial therapy in preceding 90 d
 - Current hospitalization of 5 d or more
 - High frequency of antibiotic resistance in the community or in the specific hospital unit
 - Presence of risk factors for HCAP:
 - Hospitalization for 2 d or more in the preceding 90 d
 - Residence in a nursing home or extended care facility
 - Home infusion therapy (including antibiotics)
 - Chronic dialysis within 30 d
 - Home wound care
 - Family member with multidrug-resistant pathogen
 - Immunosuppressive disease and/or therapy
-

“The panel unanimously decided that HCAP should not be included in the HAP/VAP guidelines”

1. “Patients defined as having HCAP are not at high risk for MDR pathogens”
2. “Patient characteristics are important independent determinants of risk for MDR pathogens”

Risk Factors for Multidrug Resistant Pathogens

- Risk factors for MDR VAP
 - Prior intravenous use within 90-days
 - 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
- Risk factors for MDR HAP
 - Prior intravenous antibiotic use within 90-days
- Risk factors for MRSA VAP/HAP
 - Prior intravenous antibiotic use within 90-days
- Risk factors for MDR Pseudomonas VAP/HAP
 - Prior intravenous antibiotic use within 90-days

Debate Point #1: Removal of HCAP from 2016 IDSA guidelines

PRO

Trends in Antibiotic Use and Nosocomial Pathogens in Hospitalized Veterans With Pneumonia at 128 Medical Centers, 2006–2010

Barbara E. Jones,¹ Makoto M. Jones,^{2,3} Benedikt Huttner,⁹ Gregory Stoddard,⁶ Kevin Antoine Brown,⁵ Vanessa W. Stevens,⁴ Tom Greene,⁶ Brian Sauer,² Karl Madaras-Kelly,⁷ Michael Rubin,² Matthew Bidwell Goetz,⁸ and Matthew Samore²

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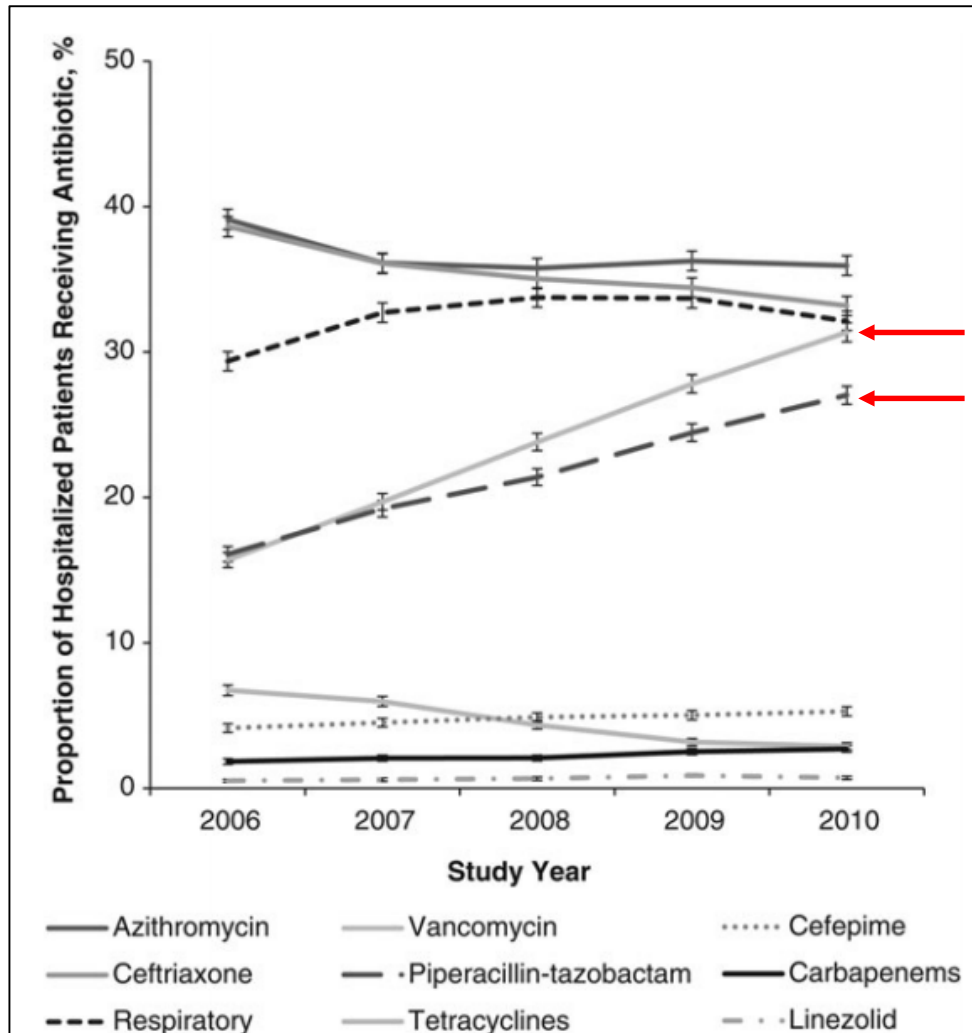
(See the Editorial Commentary by Mortensen on pages 1411–2.)

Background. In 2005, pneumonia practice guidelines recommended broad-spectrum antibiotics for patients with risk factors for nosocomial pathogens. The impact of these recommendations on the ability of providers to match treatment with nosocomial pathogens is unknown.

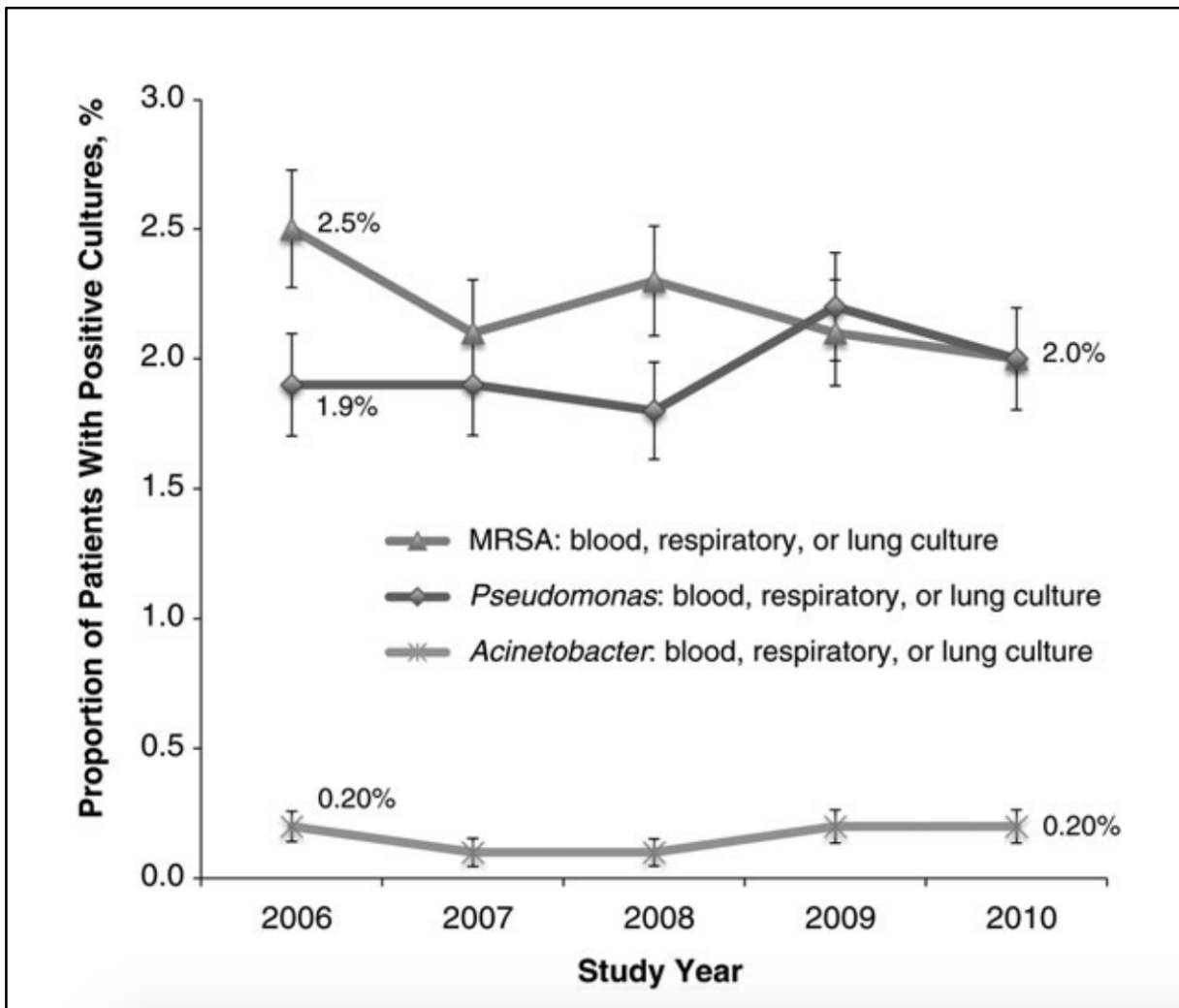
Methods. Among hospitalizations with a principal diagnosis of pneumonia at 128 Department of Veterans Affairs medical centers from 2006 through 2010, we measured annual trends in antibiotic selection; initial blood or respiratory cultures positive for methicillin-resistant *Staphylococcus aureus* (MRSA), *Pseudomonas aeruginosa*, and *Acinetobacter* species; and alignment between antibiotic coverage and culture results for MRSA and *P. aerugi-*

Jones et al

- Retrospective review of all pneumonia (CAP and/or HCAP) admissions across 128 VA hospitals nationwide
- Little patient level data, but:
 - Antibiotic prescribing matched with microbiology data
- Results:
 - 95,511 admissions for PNA over the 5 year study period
 - Average age 71, LOS 4 days, 12% initially admitted to ICU



Vancomycin
Pip/tazo



Epidemiology and Predictors of Multidrug-Resistant Community-Acquired and Health Care-Associated Pneumonia

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There are limited U.S. data describing the risk factors for multidrug-resistant organism (MDRO) isolation in community-acquired pneumonia (CAP) and health care-associated pneumonia (HCAP). However, concern for the presence of these pathogens drives the prescribing of empiric broad-spectrum antibiotics for CAP and HCAP. A retrospective study of all adults hospitalized with community-onset pneumonia (CAP and HCAP) at a large U.S. medical center from January 2010 to December 2011 was conducted. The objective was to ascertain the rate of pneumonia caused by MDROs and to evaluate whether HCAP is a risk factor for MDRO pneumonia. Univariate and propensity score-adjusted multivariate analyses were performed. A total of 521 patients (50.5% CAP and 49.5% HCAP) were included. The most common etiologies of pneumonia were primary viral and *Streptococcus pneumoniae*. MDROs were isolated in 20 (3.8%) patients overall, and MDROs occurred in 5.9% and 1.9% of HCAP and CAP patients, respectively. The presence of an MDRO was not associated with HCAP classification (odds ratio [OR] = 1.95; 95% confidence interval [95% CI], 0.66 to 5.80; $P = 0.23$) or with most of its individual components (hemodialysis, home infusion, home wound care, and ≥ 48 -h hospitalization in the last 90 days). Independent predictors of MDRO included the following: *Pseudomonas aeruginosa* colonization/infection in the previous year (OR = 7.43; 95% CI, 2.24 to 24.61; $P < 0.001$), antimicrobial use in the previous 90 days (OR = 2.90; 95% CI, 1.13 to 7.45; $P = 0.027$), admission from a nursing home (OR = 4.19; 95% CI, 1.55 to 11.31; $P = 0.005$), and duration of hospitalization in the previous 90 or 180 days ($P = 0.013$ and $P = 0.002$, respectively). MDROs were uncommon in HCAP and CAP. HCAP did not predict MDRO isolation. Local etiology of community onset pneumonia and specific MDRO risk factors should be integrated into therapeutic decisions to prevent empirical overprescribing of antibiotics for methicillin-resistant *Staphylococcus aureus* (MRSA) and *P. aeruginosa*.

Gross et al, 2014

- Retrospective cohort at Nebraska Medical Center
 - All CAP and HCAP diagnoses (ICD9 + clinical definitions) in 2010 and 2011
- Patient level data was collected, patients were categorized as CAP or HCAP
- Primary outcome: isolation of an MDRO

N = 521	MDRO PNA	No MDRO PNA
HCAP (258)	15 (6%)	243 (94%)
CAP (263)	5 (2%)	258 (98%)

Multivariable analysis adjusted for comorbidities

Associated with MDRO

- Admission from NH
- Prior Pseudomonas colonization
- Prior antibiotic use within 90 days
- Days of prior hospitalization in prior 90 days
- Days of prior hospitalization in last 180 days

Not Associated with MDRO

- “HCAP”
- Hospitalization within 90 days
- Home IV infusion
- Outpatient hemodialysis
- Home wound care
- Prior MRSA colonization
- “Immunocompromised” state

Healthcare-Associated Pneumonia Does Not Accurately Identify Potentially Resistant Pathogens: A Systematic Review and Meta-Analysis

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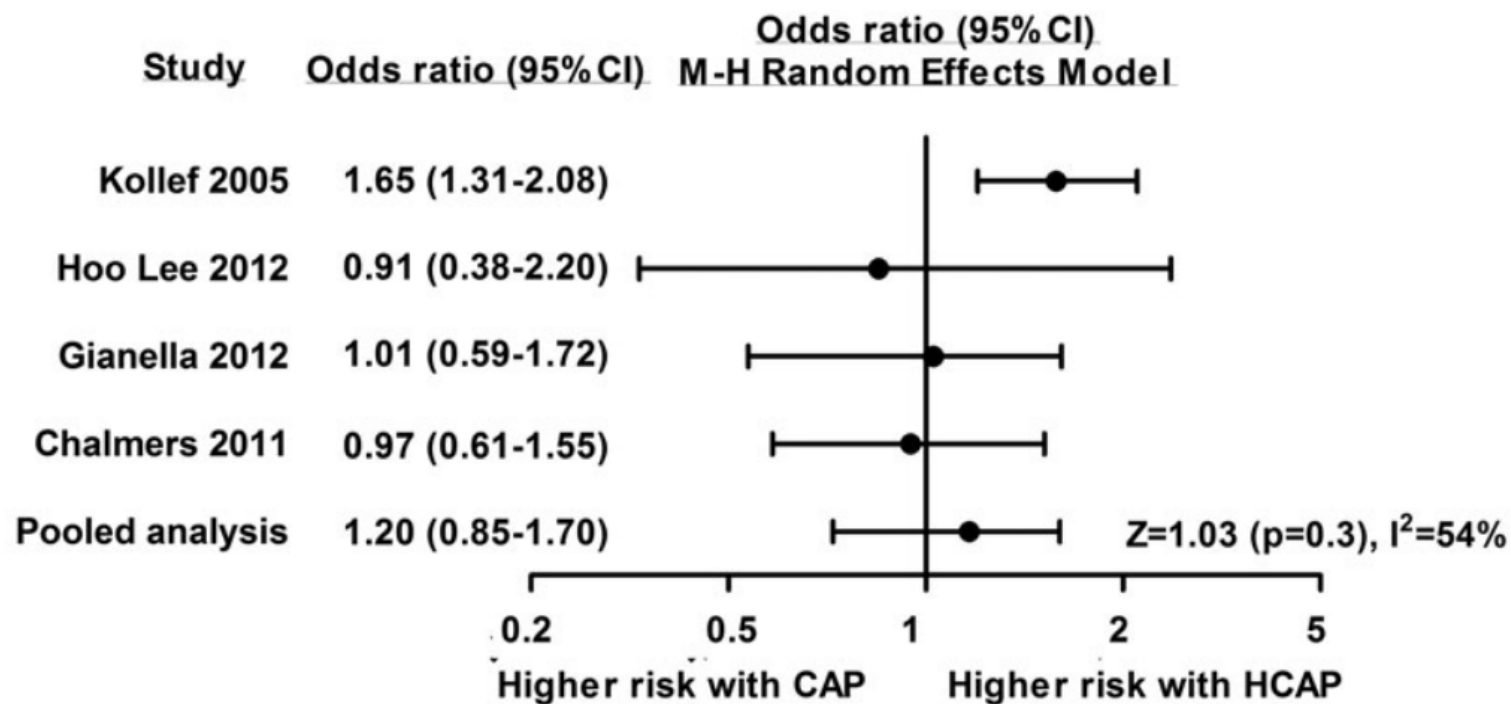
(See the editorial commentary by Restrepo and Aliberti on pages 340–1.)

Background. The 2005 American Thoracic Society/Infectious Diseases Society of America guidelines introduced a concept of healthcare-associated pneumonia (HCAP) to define patients at higher risk of antibiotic-resistant pathogens, thus requiring broad spectrum therapy. There has been no systematic evaluation of the ability of this definition to identify antibiotic-resistant pathogens.

Methods. We conducted a systematic review and meta-analysis of studies comparing the frequency of resistant pathogens (defined as methicillin-resistant *Staphylococcus aureus*, Enterobacteriaceae, and *Pseudomonas aeruginosa*) in populations with HCAP compared with populations with community-acquired pneumonia (CAP). Predictive accuracy was evaluated using the area under the receiver operator characteristic curve (AUC). The frequencies of

pathogens in each group were pooled using a random effects model.

Adjusted analysis

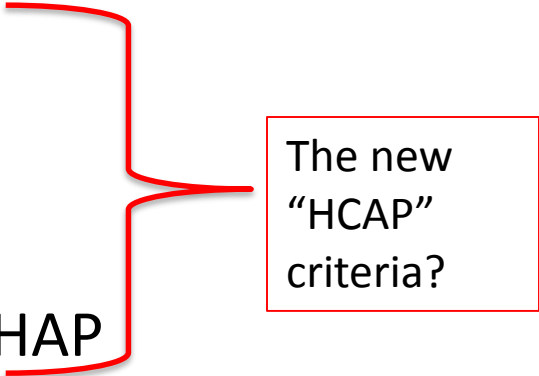


Debate Point #1: Removal of HCAP from 2016 IDSA guidelines

CON

Risk Factors for Multidrug Resistant Pathogens

- Risk factors for MDR VAP
 - Prior intravenous use within 90-days
 - 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
 - Risk factors for MDR HAP
 - Risk factors for MRSA VAP/HAP
 - Risk factors for MDR Pseudomonas VAP/HAP
- Prior intravenous use within 90-days



The new
“HCAP”
criteria?

AP is a 78 year-old woman with a PMH of HTN, CHF, GERD, and HTN was admitted from a nursing home with cough and fatigue. She has no known drug allergies. She is admitted to the ICU and you get paged.

- ✓ BP 110/65, HR 96, RR 36, T 37.9
- ✓ WBC 12.3
- ✓ CXR: Infiltrate in the left lower lobe.

Old IDSA PNA Guidelines:
This patient has HCAP.
Start broad spectrum antibiotics



New IDSA PNA Guidelines: There is no more HCAP. Page the team to determine if the pt has received IV antibiotics in the past 90-days.



INTERN

I'd like to start
piperacillin/tazobactam +
vancomycin for HCAP

ICU PHARMD

No (beat) HCAP is dead

INTERN

So what do I give?

ICU PHARMD

Has she received any IV
antibiotics in the last 90-days?

INTERN

She just got here and we have no
previous admission so, I dunno...



INTERN

I'd like to start
piperacillin/tazobactam +
vancomycin for HCAP

ICU PHARMD

No (beat) HCAP is dead

INTERN

So what do I give?

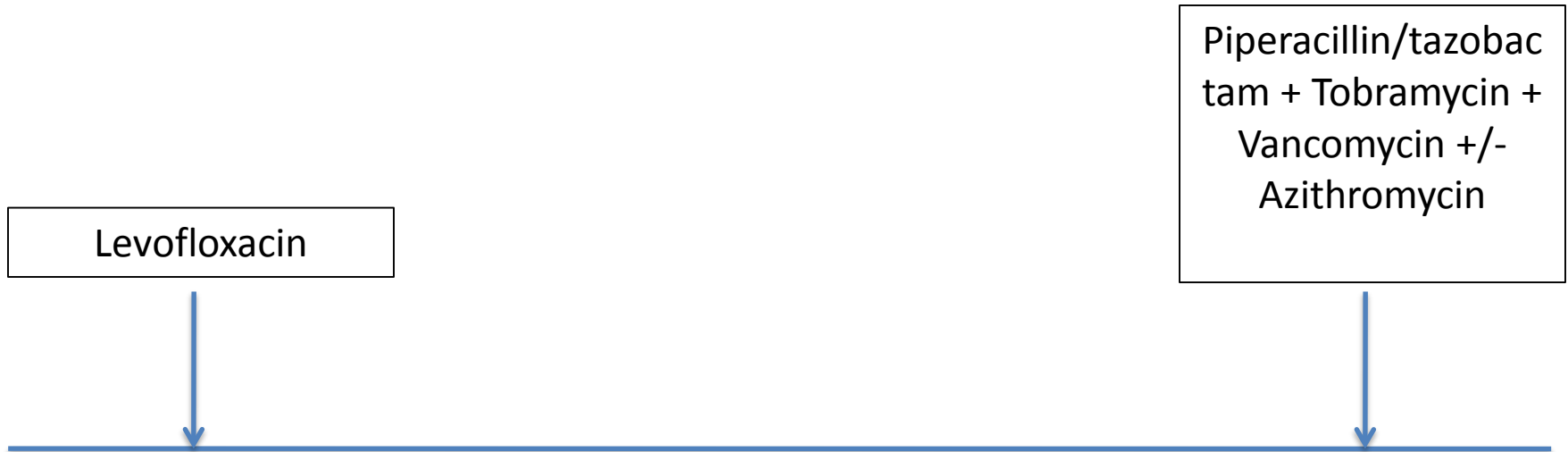
ICU PHARMD

Has she received any IV
antibiotics in the last 90-days?

INTERN

No, but she just finished a course
of oral levofloxacin for pyelo.

Management?



✓ If you choose levofloxacin alone, Does the fact that she comes from a nursing home give you some pause?

✓ If you chose P/T/V, how do you know if she has risk factors for “MDRO”?

Adapted from 2016 IDSA HAP Guideline Empiric Antibiotic Therapy for HAP

Not at High Risk of Mortality and no Factors Increasing the Likelihood of MRSA ^{b,c}	Not at High Risk of Mortality but With Factors Increasing the Likelihood of MRSA^{b,c}	High Risk of Mortality or Receipt of IV Antibiotics During the Prior 90-days^{a,c} (2 of the following)
Piperacillin-tazobactam OR	Piperacillin-tazobactam OR	Piperacillin-tazobactam OR
Cefepime OR	Cefepime or ceftazidime OR	Cefepime OR
Levofloxacin	Levofloxacin or cipro OR	Levofloxacin or cipro OR
	Levofloxacin or cipro OR	Levofloxacin or cipro OR
	Aztreonam	Aminoglycoside OR
	PLUS vancomycin or linezolid	Aztreonam
		PLUS vancomycin or linezolid

^a RF for mortality = need for ventilator support d/t PNA and septic shock

^b RF for MRSA = IV antibiotics during prior 90-days and MRSA rates unknown or > 20%

^c RF for gram-negative infection = IV antibiotics during prior 90-days

THE WALL STREET JOURNAL.

HEALTH | HEALTH & WELLNESS

The Bug Problem in Nursing Homes

Elderly residents are 'especially susceptible' to drug-resistant infections, researchers say.

By Lucette Lagnado

Updated May 15, 2017 11:41 a.m. ET

There's a bug problem in some nursing homes, and it's not what you think.

Residents of long-term care facilities are vulnerable to drug-resistant infections known as superbugs and can easily spread the deadly germs to others.

Between 11% and 59% of nursing-home residents have been "colonized" with certain types of superbugs, putting them at more risk of developing a full-blown infection, according to researchers at Columbia...



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Major Article

Prevalence of multidrug-resistant gram-negative bacteria among nursing home residents: A systematic review and meta-analysis

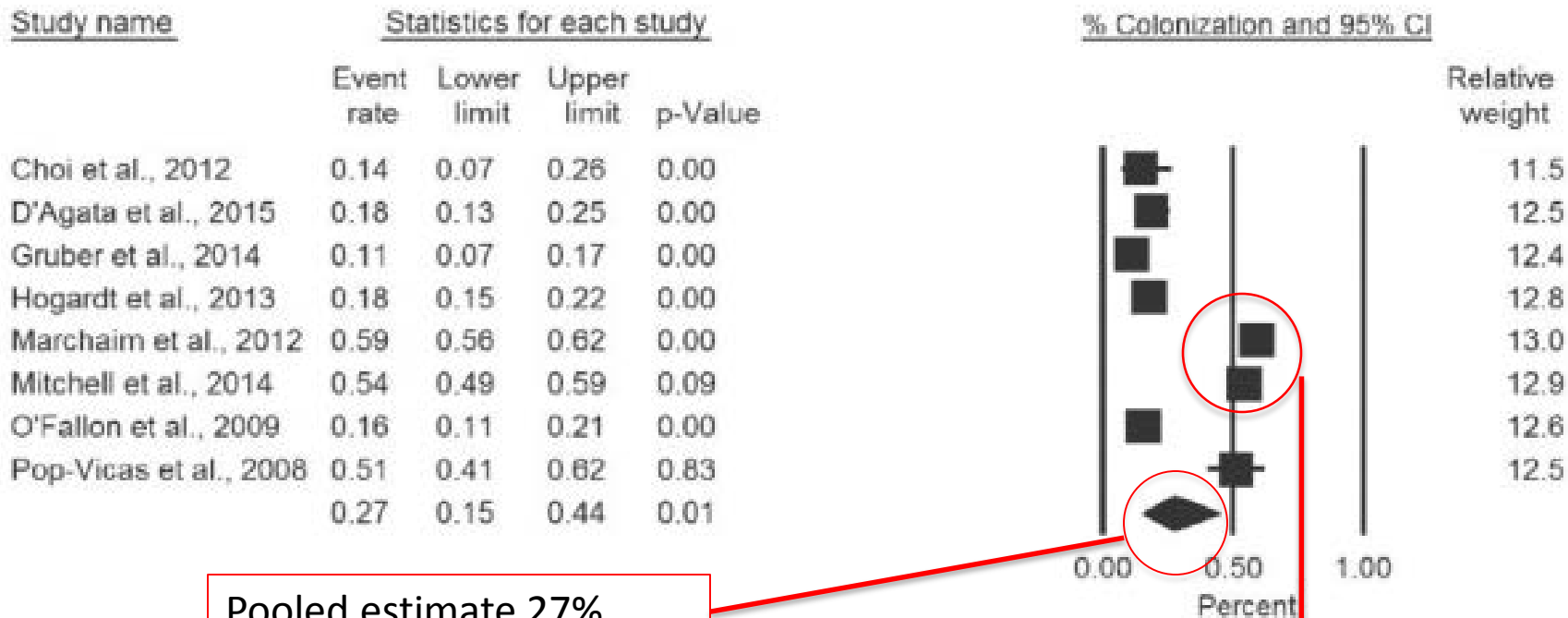


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- Meta-analysis of 8-studies (mostly in the US; 2005-2016) that describe colonization of MDR pathogens in ~2,700 nursing home residents
- No standard definition of MDR (resistant to ≥ 3 classes, ESBL)
- Site of colonization varied (sputum, urine, rectal swab)
- ~40% *E. coli*, ~25% *P. mirabilis*
- Pooled prevalence of MDR-GNB colonization 27% (95% CI, 15.2% - 44.1%)



Pooled estimate 27%

Highest rates from US studies

Random effects model. $p = 0.01$; Cochran's $Q = 405.7$. $I^2 = 98.3$

Gross, et al.

TABLE 3 Predictors of multidrug-resistant organisms^a

Risk factor	No. of patients (%)		Statistical measure ^b	
	Patients with MDRO pneumonia (n = 20)	Patients with pneumonia but no MDRO isolated (n = 501)	Univariate analysis	Multivariate analysis
Presence of HCAP	15 (75)	243 (49)	3.37 (1.35–8.41) 0.009	1.95 (0.66–5.80) 0.226
Hospitalization for 48 h in the last 90 days	9 (45)	158 (32)	1.78 (0.72–4.37) 0.211	1.23 (0.47–3.19) 0.678
Home infusion therapy home	0 (0)	4 (0.8)	0 (0) 0.999	0 (0) 0.999
Hemodialysis	1 (5)	27 (5.4)	0.92 (0.12–7.16) 0.940	0.627 (0.08–5.06) 0.661
Admission from a nursing home	13 (65)	114 (22.8)	6.31 (2.46–16.18) 0.027	4.19 (1.55–11.31) 0.005

Rebuttals

Debate Point #2: Use of Procalcitonin in de-escalation

XXIV. Should Discontinuation of Antibiotic Therapy Be Based Upon PCT Levels Plus Clinical Criteria or Clinical Criteria Alone in Patients With HAP/VAP?

Recommendation

1. For patients with HAP/VAP, we suggest using PCT levels plus clinical criteria to guide the discontinuation of antibiotic therapy, rather than clinical criteria alone (*weak recommendation, low-quality evidence*).

Remarks: It is not known if the benefits of using PCT levels to determine whether or not to discontinue antibiotic therapy exist in settings where standard antimicrobial therapy for VAP is already 7 days or less.

Procalcitonin (PCT)

- ✓ Some diagnostic markers are now standard of care (d-dimer, natriuretic peptide, troponin)
- ✓ Infection markers = low sensitivity (blood cx), low specificity (sputum cx due to contamination or ESR/CRP), or not practical (lung biopsy)
- ✓ PCT (procalcitonin) is a 116 amino acid polypeptide precursor peptide of calcitonin
- ✓ Released ubiquitously in response to endotoxin and inflammatory mediators during bacterial infection
- ✓ Part of the complex pro-inflammatory response of the innate immune system
- ✓ PCT is attenuated by $\text{INF-}\gamma$ (released in response to viral infections)
- ✓ Not influenced by corticosteroid

Debate Point #2: Use of Procalcitonin in de-escalation

PRO

Efficacy and safety of procalcitonin guidance in reducing the duration of antibiotic treatment in critically ill patients: a randomised, controlled, open-label trial



Evelien de Jong, Jos A van Oers, Albertus Beishuizen, Piet Vos, Wytze J Vermeijden, Lenneke E Haas, Bert G Loef, Tom Dormans, Gertrude C van Melsen, Yvette C Kluiters, Hans Kemperman, Maarten J van den Elsen, Jeroen A Schouten, Jörn O Streefkerk, Hans G Krabbe, Hans Kieft, Georg H Kluge, Veerle C van Dam, Joost van Pelt, Laura Bormans, Martine Bokelman Otten, Auke C Reidinga, Henrik Endeman, Jos W Twisk, Ewoudt M W van de Garde, Anne Marie G A de Smet, Jozef Kesecioglu, Armand R Girbes, Maarten W Nijsten, Dylan W de Lange

Summary

Background In critically ill patients, antibiotic therapy is of great importance but long duration of treatment is associated with the development of antimicrobial resistance. Procalcitonin is a marker used to guide antibacterial therapy and reduce its duration, but data about safety of this reduction are scarce. We assessed the efficacy and safety of procalcitonin-guided antibiotic treatment in patients in intensive care units (ICUs) in a health-care system with a comparatively low use of antibiotics.

Methods We did a prospective, multicentre, randomised, controlled, open-label intervention trial in 15 hospitals in the Netherlands. Critically ill patients aged at least 18 years, admitted to the ICU, and who received their first dose of antibiotics no longer than 24 h before inclusion in the study for an assumed or proven infection were eligible to participate. Patients who received antibiotics for presumed infection were randomly assigned (1:1), using a computer-generated list, and stratified (according to treatment centre, whether infection was acquired before or during ICU stay, and dependent on severity of infection [ie, sepsis, severe sepsis, or septic shock]) to receive either procalcitonin-guided or standard-of-care antibiotic discontinuation. Both patients and investigators were aware of group assignment. In the procalcitonin-guided group, a non-binding advice to discontinue antibiotics was provided if procalcitonin concentration had decreased by 80% or more of its peak value or to 0.5 µg/L or lower. In the standard-of-care group, patients were treated according to local antibiotic protocols. Primary endpoints were antibiotic daily defined doses and duration of antibiotic treatment. All analyses were done by intention to treat. Mortality analyses were completed for all patients (intention to treat) and for patients in whom antibiotics were stopped while being on the ICU (per-protocol analysis). Safety endpoints were reinstatement of antibiotics and recurrent inflammation measured by C-reactive protein concentrations and they were measured in the population adhering to the stopping rules (per-protocol analysis). The study is registered with ClinicalTrials.gov, number NCT01139489, and was completed in August, 2014.

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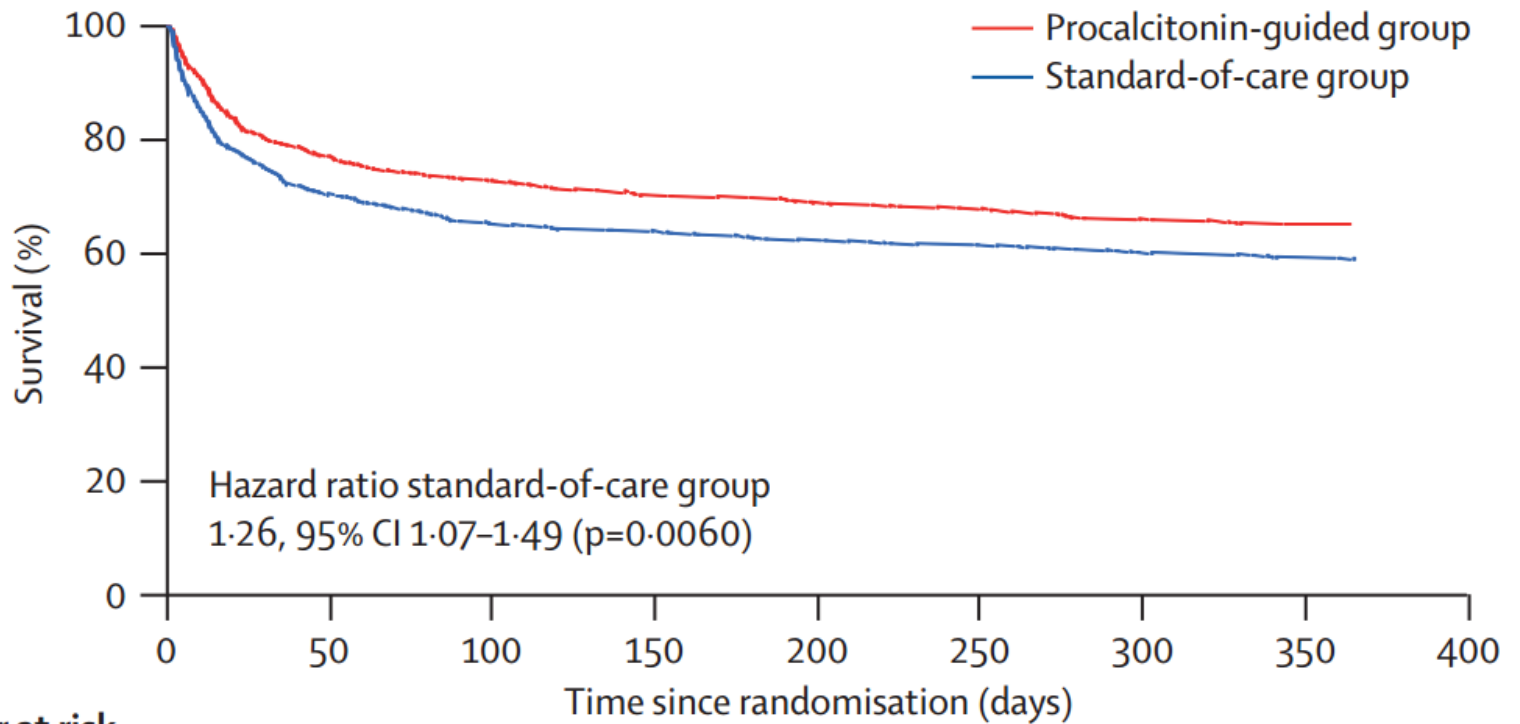
	Procalcitonin-guided group (n=761)	Standard-of-care group (n=785)	Between-group absolute difference in means (95% CI)	p value
Antibiotic consumption (days)				
Daily defined doses in first 28 days	7.5 (4.0 to 12.8)	9.3 (5.0 to 16.5)	2.69 (1.26 to 4.12)	<0.0001
Duration of treatment	5.0 (3.0 to 9.0)	7.0 (4.0 to 11.0)	1.22 (0.65 to 1.78)	<0.0001
Antibiotic-free days in first 28 days	7.0 (0.0 to 14.5)	5.0 (0 to 13.0)	1.31 (0.52 to 2.09)	0.0016
Mortality (%)				
28-day mortality	149 (19.6%)	196 (25.0%)	5.4% (1.2 to 9.5)	0.0122
1-year mortality	265 (34.8%)	321 (40.9%)	6.1% (1.2 to 10.9)	0.0158
Adverse events				
Reinfection	38 (5.0)	23 (2.9)	-2.1% (-4.1 to -0.1)	0.0492
Repeated course of antibiotics	175 (23.0)	173 (22.0)	-1.0% (-5.1 to 3.2)	0.67
Time (days) between stop and reinstatement of antibiotics	4.0 (2.0 to 8.0)	4.0 (2.0 to 8.0)	-0.22 (-1.31 to 0.88)	0.96
Costs				
Total cumulative costs of antibiotics	€150 082	€181 263	NA	NA
Median cumulative costs antibiotics per patient	€107 (51 to 229)	€129 (66 to 273)	€33.6 (2.5 to 64.8)	0.0006
Length of stay (days)				
On the intensive care unit	8.5 (5.0 to 17.0)	9.0 (4.0 to 17.0)	-0.21 (-0.92 to 1.60)	0.56
In hospital	22.0 (13.0 to 39.3)	22.0 (12.0 to 40.0)	0.39 (-2.69 to 3.46)	0.77

Data are median (IQR), n (%), or mean (95% CI). Between-group absolute differences were calculated using the mean values, percentage differences, and 95% CIs. NA=not applicable.

Table 2: Primary and secondary outcome measures

250

— Procalcitonin-guided group



Number at risk

Procalcitonin-guided group	761	554	525	503	496
Standard-of-care group	785	512	490	473	464

Time since randomisation (days)

Procalcitonin in critically ill patients: time to change guidelines and antibiotic use in practice



Getty Images/Swissland/Press Association Images

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[S1473-3099\(16\)00064-5](http://dx.doi.org/10.1016/S1473-3099(16)00064-5)

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Antibiotic overuse coupled with the emergence of multiresistant bacteria threatens public health. To address this issue, we must focus on implementation of antibiotic stewardship programmes to restrict use of antibiotics to only patients who would truly benefit from these drugs and to avoid long treatment courses. In addition to clinical parameters, monitoring of the blood marker procalcitonin allows individual tailoring of antibiotic therapy to the presence and resolution of systemic bacterial infection.^{1,2} Procalcitonin is upregulated by microbial toxins and pro-inflammatory mediators, and is downregulated as these substances subside during recovery from infection.³ Procalcitonin concentrations measured at hospital admission are strongly associated with detection of bacteraemia⁴ and severity of infection.⁵ Procalcitonin kinetics have prognostic implications with maintenance at specific

concentrations pointing towards treatment being unsuccessful.⁶

Randomised trials^{7,8} that enrolled more than 6000 patients assessed clinical effects of using procalcitonin stewardship protocols, mainly, for assessing the success of antibiotic treatment in respiratory infections. In the settings of primary care, emergency room, and hospital wards this approach resulted in large reductions in antibiotic consumption of 30–75%.⁸ Additionally, use of these protocols reduced the risk for treatment failure for patients with community-acquired pneumonia.⁹ Yet in the critical care setting, safety has been questioned by some, mainly for two reasons. First, the PRORATA trial¹⁰ investigating procalcitonin-guided antibiotic stewardship in critical care reported a 25% reduction in antibiotic exposure and non-inferiority for mortality

Debate Point #2: Use of Procalcitonin in de-escalation

CON

Practice Patterns and Outcomes Associated With Procalcitonin Use in Critically Ill Patients With Sepsis

David C. Chu,^{1,a} Anuj B. Mehta,^{1,a} and Allan J. Walkey^{1,2}

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- Real world experience of PCT in clinical setting
- Retrospective cohort using the Premier database (20% of hospitalized pts in the US) who were critically ill in an ICU
- Approximately 5% of pts in the S with sepsis had PCT measured
- Huge study! (20,750 patients in 107 hospitals)
 - 3,769 (18%) had PCT levels, 1,119 (~30%) had serial PCTs
- Primary endpoint = association b/w PCT and antibiotic days of therapy

Results

- Age 66 +/- 16 years, 50% women, 74% white
- ~35% PNA
- PCT orders associated with:
 - More antibiotic DOT (multivariable adjusted relative risk 1.17; 95% CI, 1.15 – 1.19)
 - Increased rates of *C. difficile* (multivariable adjusted relative risk 1.42; 95% CI, 1.09-1.19)
 - No difference in mortality (hazard ratio 1.05; 95% CI, 0.93 – 1.19)
 - Hospitals that never measured PCT and hospitals that had previously measured PCT, PCT remained a/w increased antibiotic DOT and C diff
- PCT testing during sepsis has been poorly implemented into real-world practice

Rebuttals

Debate Point #3: Treatment of
HAP/VAP should be 7 days

XXII. What Is the Optimal Duration of Antibiotic Therapy for HAP (Non-VAP)?

Recommendation

1. For patients with HAP, we recommend a 7-day course of antimicrobial therapy (*strong recommendation, very low-quality evidence*).

Remarks: There exist situations in which a shorter or longer duration of antibiotics may be indicated, depending upon the rate of improvement of clinical, radiologic, and laboratory parameters.

Debate Point #3: Treatment of
HAP/VAP should be 7 days

PRO

Comparison of 8 vs 15 Days of Antibiotic Therapy for Ventilator-Associated Pneumonia in Adults

A Randomized Trial

Jean Chastre, MD

Michel Wolff, MD

Jean-Yves Fagon, MD

Sylvie Chevret, MD

Franck Thomas, MD

Delphine Wermert, MD

Eva Clementi, MD

Jesus Gonzalez, MD

Dominique Jusserand, MD

Pierre Asfar, MD

Dominique Perrin, MD

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Context The optimal duration of antimicrobial treatment for ventilator-associated pneumonia (VAP) is unknown. Shortening the length of treatment may help to contain the emergence of multiresistant bacteria in the intensive care unit (ICU).

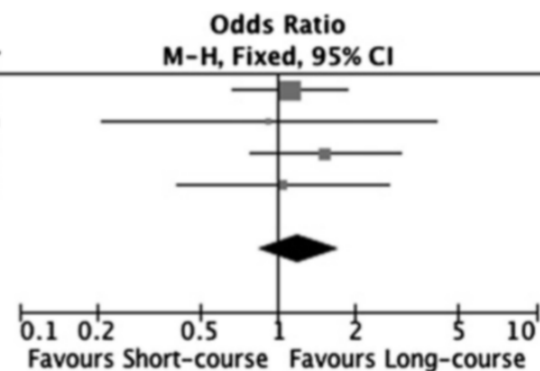
Objective To determine whether 8 days is as effective as 15 days of antibiotic treatment of patients with microbiologically proven VAP.

Design, Setting, and Participants Prospective, randomized, double-blind (until day 8) clinical trial conducted in 51 French ICUs. A total of 401 patients diagnosed as having developed VAP by quantitative culture results of bronchoscopic specimens and who had received initial appropriate empirical antimicrobial therapy were enrolled between May 1999 and June 2002.

Intervention A total of 197 patients were randomly assigned to receive 8 days and 204 to receive 15 days of therapy with an antibiotic regimen selected by the treating physician.

Main Outcome Measures Primary outcome measures—death from any cause, microbiologically documented pulmonary infection recurrence, and antibiotic-free days—were assessed 28 days after VAP onset and analyzed on an intent-to-treat basis.

Study or Subgroup	Short-course		Long-course		Weight	Odds Ratio		Year
	Events	Total	Events	Total		M-H, Fixed, 95% CI		
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: $\text{Chi}^2 = 0.77$, $\text{df} = 3$ ($P = 0.86$); $I^2 = 0\%$								
Test for overall effect: $Z = 0.99$ ($P = 0.32$)								



IDSA:

- “We also found no differences between short-course antibiotic regimens (ie, 7–8 days) and long-course regimens (ie, 10–15 days) in terms of mortality, clinical cure, and recurrent pneumonia.”
- “Of note, the specific subpopulation with VAP due to non-glucose-fermenting gram-negative bacilli was analyzed, and no differences were observed for:
 - Pneumonia recurrence (OR, 1.42; 95% CI, .66–3.04; P = .37)
 - Mortality (OR, 0.94; 95% CI, .56–1.59; P = .83)”

Debate Point #3: Treatment of HAP/VAP should be 7 days

CON

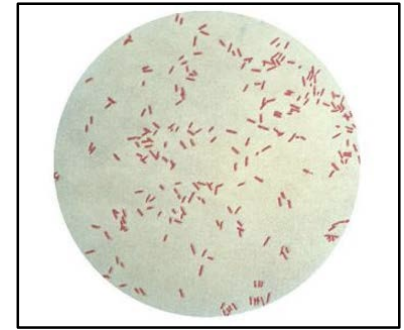
LENGTH OF THERAPY

XXI. Should Patients With VAP Receive 7 Days or 8–15 Days of Antibiotic Therapy?

Recommendation

1. For patients with VAP, we recommend a 7-day course of antimicrobial therapy rather than a longer duration (*strong recommendation, moderate-quality evidence*).

Remarks: There exist situations in which a shorter or longer duration of antibiotics may be indicated, depending upon the rate of improvement of clinical, radiologic, and laboratory parameters.



Article	Study Design	Results
Castre J, et al. Comparison of 8 vs 15 days of antibiotic therapy for ventilator-associated pneumonia in adults. JAMA 2003	RCT: 8 days vs. 15 days Adult ICU pts with VAP 51 ICUs in France Primary outcome = death from any cause or recurrence	n = 401 pts total May 1999 to June 2002 <i>Pseudomonas</i> (~19%), <i>E coli</i> (8-10%), MSSA (~12%), MRSA (~7%) ➤ Death @ 28-days after VAP onset: ~19% (8-day group) vs 17% (15-day group) ➤ Recurrence (NF-GNR): in the 8-day group was ~40% (8-day group) vs. ~25% (15-day group)
Pugh R, et al. Short-course versus prolonged-course antibiotic therapy for hospital-acquired pneumonia in critically ill adults. Cochrane Database Syst Rev 2015	Meta-analysis to assess short vs. prolonged courses for HAP/HAP Critically ill adults Included RCTs comparing duration	n = 6 studies; 1088 patients VAP pts; short course (7-8 days) had more AB-free days, decreased recurrence of VAP d/t MDROs. For NF-GNB group, recurrence greater after short course therapy in two studies OR 2.18 (95% CI 1.14 – 4/16), but no difference in mortality

Rebuttals

Closing Arguments

Assessment Question #1

According to IDSA's 2016 HAP/VAP Guidelines, which of the following is a risk factor for multi-drug resistant pathogens in patients with pneumonia?

- A. Nursing home residence
- B. Prior intravenous antibiotic use within 90 days
- C. Chronic dialysis within 30-days
- D. Family member with drug-resistant pathogen

Assessment Question #2

According to IDSA's 2016 HAP/VAP Guidelines, which of the following is a risk factor for multi-drug resistant pathogens in patients with ventilator acquired pneumonia?

- A. Prior intravenous antibiotic use within 90 days
- B. Septic shock at time of VAP
- C. Five or more days of hospitalization prior to the occurrence of VAP
- D. All of the above

Assessment Question #3

Which of the following regimens is appropriate empiric therapy for a ventilator associated pneumonia?

- A. Levofloxacin
- B. Piperacillin/tazobactam and azithromycin
- C. Ceftazidime and vancomycin
- D. Cefepime, tobramycin, and linezolid

Assessment Question #4

Which of the following is TRUE in regard to use of procalcitonin (PCT) levels in the diagnosis and management of HAP/VAP?

- A. IDSA recommends that PCT is used to help diagnose bacterial pneumonia
- B. PCT use without an institutional protocol may lead to increased utilization of antibiotics
- C. PCT has similar sensitivity and specificity as c-reactive protein in the diagnosis of bacterial pneumonia
- D. All of the above are true

Assessment Question #5

According to IDSA's 2016 HAP/VAP Guidelines, HAP due to which of the following organisms warrants a 7-day duration of treatment?

- A. *Streptococcus pneumoniae*
- B. *Pseudomonas aeruginosa*
- C. Carbapenem-resistant *Klebsiella pneumoniae*
- D. All of the above

- Why has government been instituted at all? Because the passions of man will not conform to the dictates of reason and justice without constraint.

-- Alexander Hamilton

- Why has ~~government~~ (IDSA guidelines) been instituted at all? Because the passions of ~~man~~ (prescribers) will not conform to the dictates of reason and justice without constraint.

-- Alexander Hamilton