HEALTHCARE-ASSOCIATED PNEUMONIA:
EPIDEMIOLOGY, PATHOGENESIS & PREVENTION 2018

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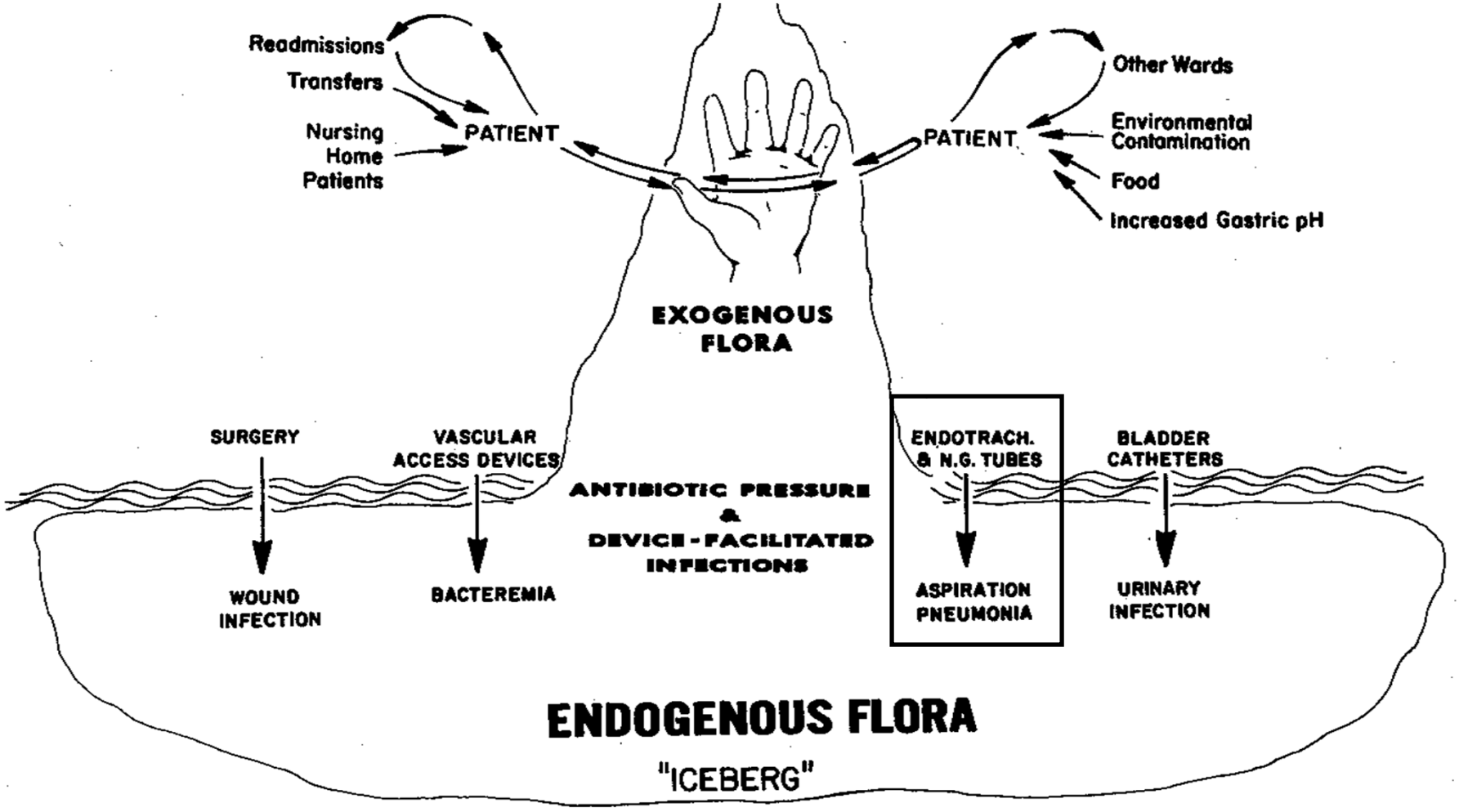
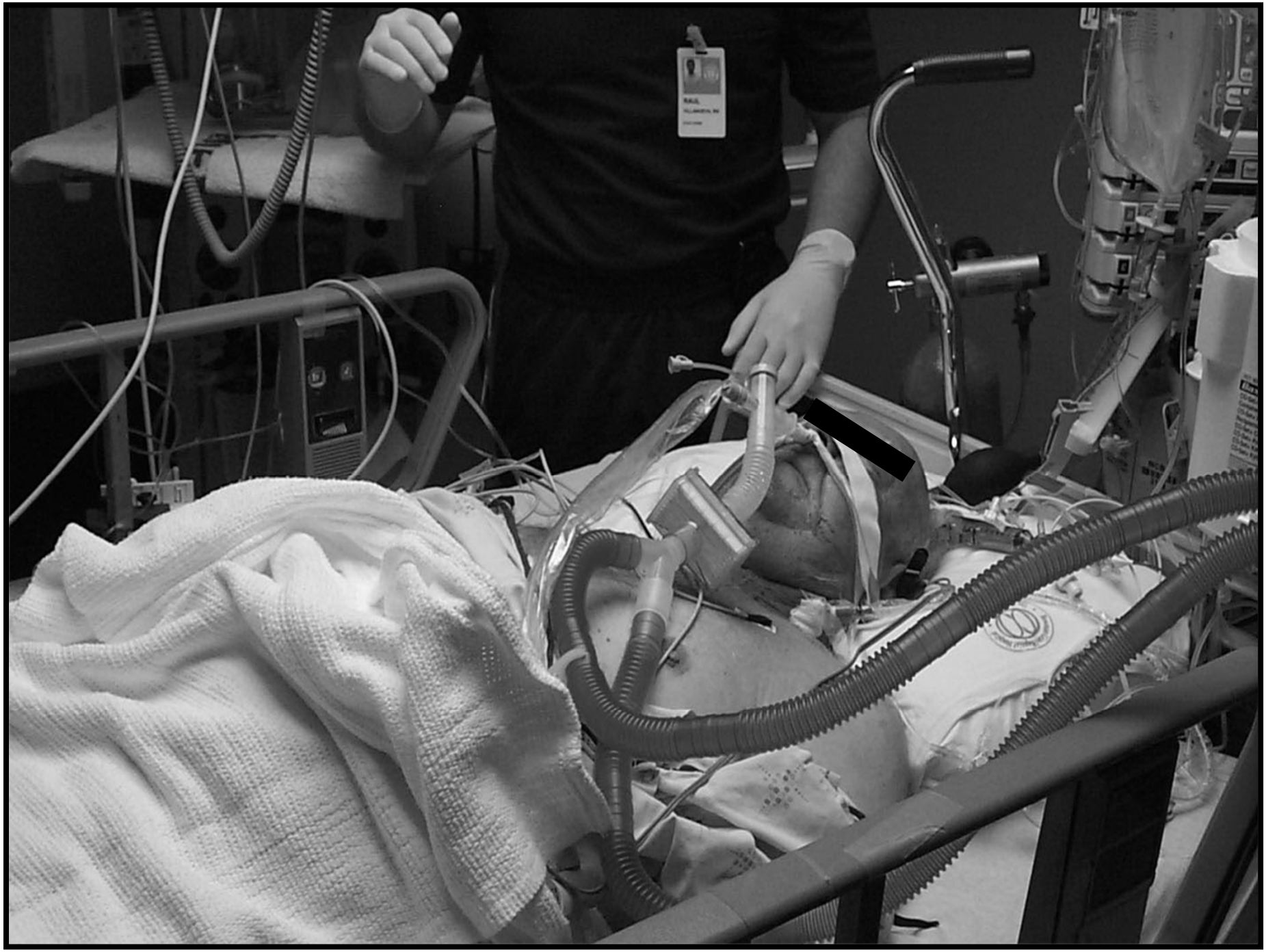
HAZARDS IN THE ICU



Weinstein RA. Am J Med 1991;91(suppl 3B):180S



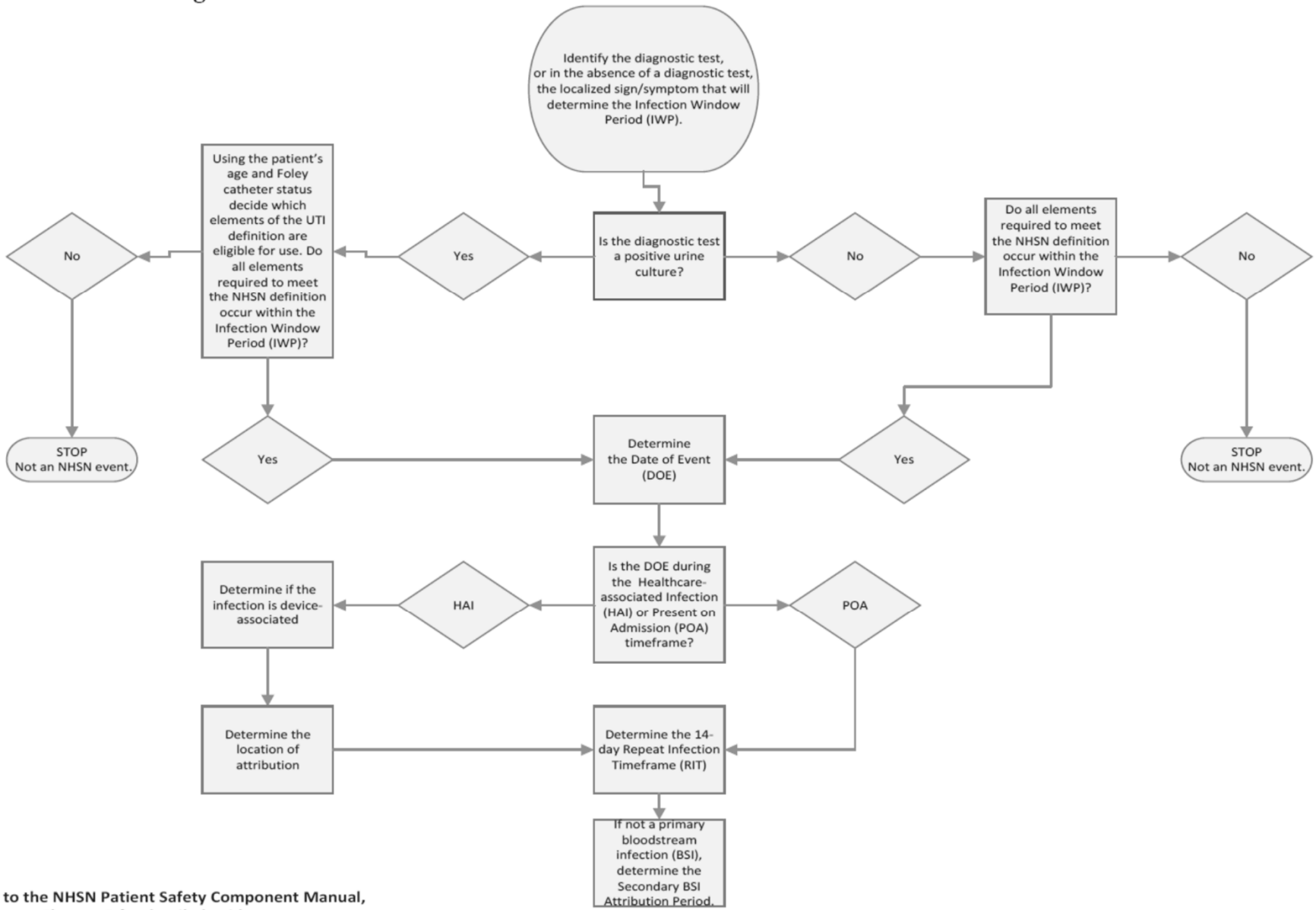
TOPICS: VAP & HAP

- Epidemiology
  - Impact of healthcare-associated infections
  - Definitions
  - NHSN surveillance definitions
  - Incidence and prevalence of HCAP, HAP, VAP
- Pathogenesis
  - Mechanisms of pneumonia
  - Microbiology
  - Risk factors
  - Diagnosis
- Prevention

GOALS OF LECTURE

- Understand the epidemiology of nosocomial pneumonia
  - Impact
  - Incidence
  - Risk factors for acquisition and mortality
- Understand the pathophysiology of VAP & HAP
  - Microbiology
  - Diagnosis
  - Treatment
- Understand methods of prevention

APPENDIX: Flow Diagram for NHSN Event Determination



Refer to the NHSN Patient Safety Component Manual, Chapter 2 for detailed guidance.

HEALTHCARE-ASSOCIATED PNEUMONIA

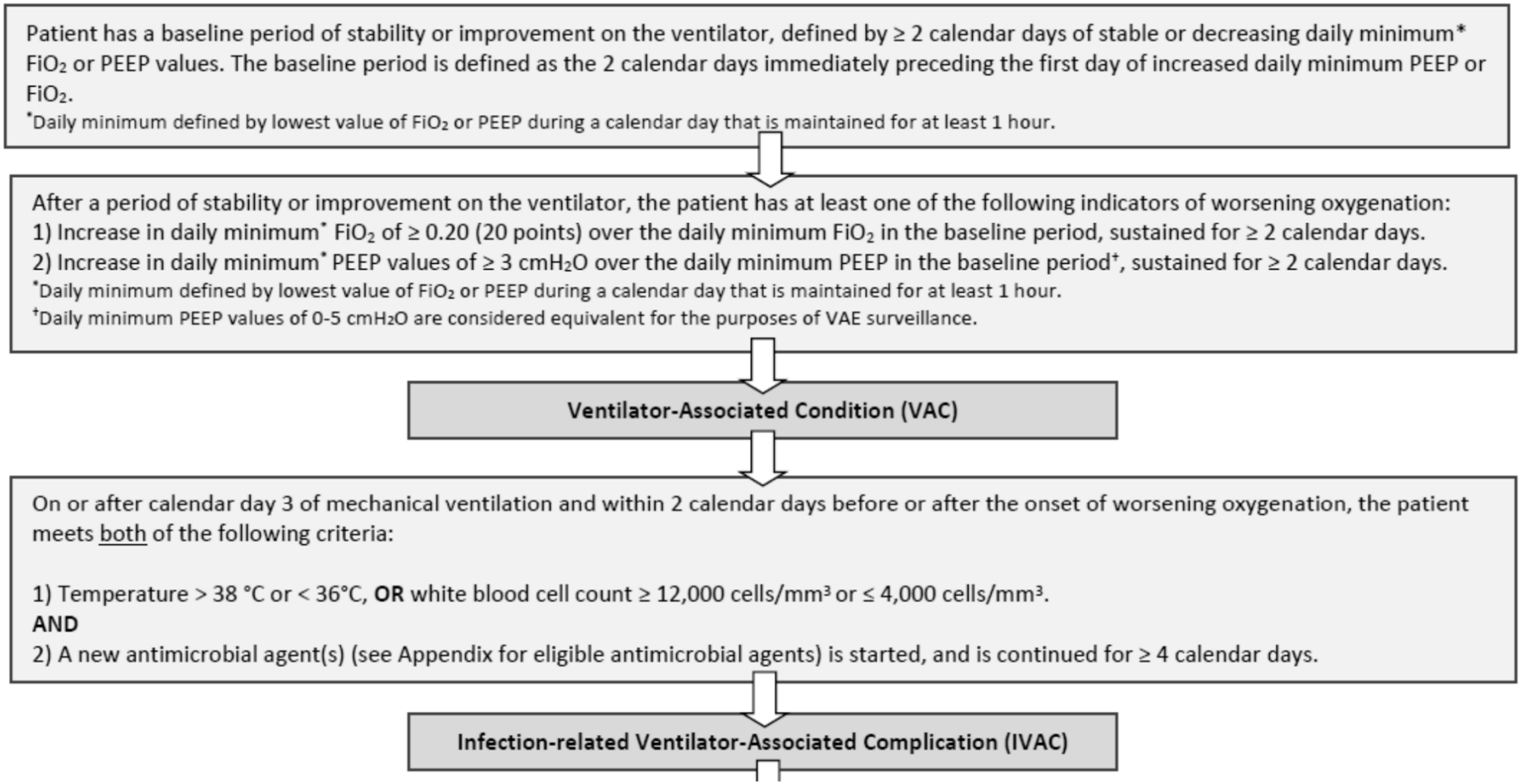
- VAE: VAEs are identified by using a combination of objective criteria: deterioration in respiratory status after a period of stability or improvement on the ventilator, evidence of infection or inflammation, and lab evidence of respiratory infection
- Pneumonia (PNEU): Pneumonia is identified using a combination of radiologic, clinical and laboratory criteria. For PNEU VAP the date of the event is the date when the first element used to meet PNEU infection criterion occurred for the first time within the 7-day infection window period.

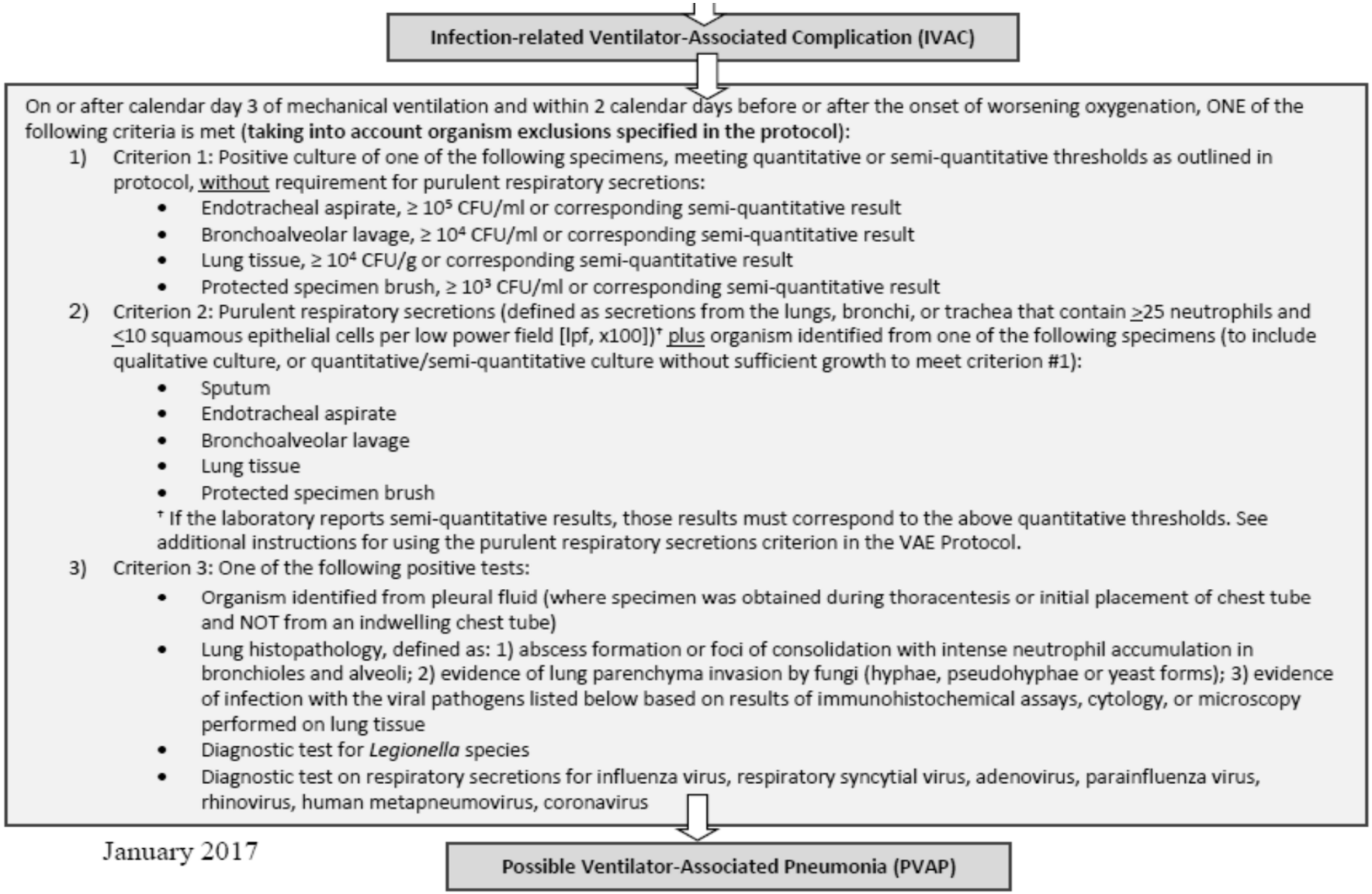
https://www.cdc.gov/nhsn/acute-care-hospital/vap/index.html, Jan 2017

PROBLEMS WITH VAP DEFINITION

- VAP definitions including the NHSN PNEU definitions (revised 2002), is that they require radiographic findings of pneumonia. Evidence suggests that CxR findings do not adequately identify VAP.
- Another major difficulty with the available VAP definitions is their reliance on specific clinical signs or symptoms, which are subjective and may be poorly or inconsistently documented in the medical record.
- The NHSN PNEU protocol includes multiple definition pathways and special criteria for selected patient populations (e.g., children, immunocompromised patients), increasing their complexity.
- The VAE definition algorithm is for use in surveillance; it is not a clinical definition algorithm and is not intended for use in the clinical management of patients.
- Remember these are surveillance definitions; they are NOT designed to be used to guide treatment decisions

Figure 1: Ventilator-Associated Events (VAE) Surveillance Algorithm





Candida species or yeast not otherwise specified, coagulase-negative *Staphylococcus* species, and *Enterococcus* species identified from blood cannot be deemed secondary to a PVAP, unless the organism was also identified from pleural fluid or lung tissue.

A prospective evaluation of ventilator-associated conditions and infection-related ventilator-associated conditions

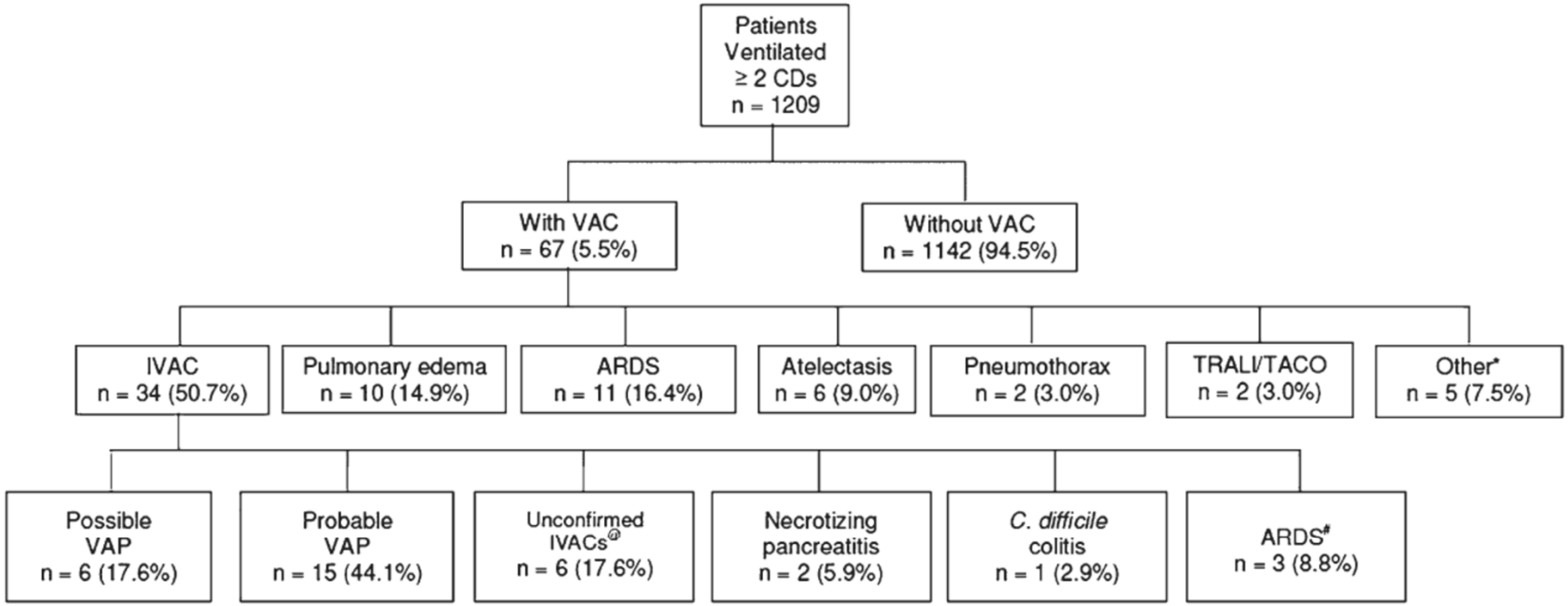


Figure 1 – *Analysis of patients with VACs and IVACs. Three VACs had more than one cause. *Other causes included untreated pneumonia, acute lung allograft rejection, malignant airway compression, and metastatic Hodgkin's lymphoma; #three cases met the technical criteria for an IVAC, but the reason for worsening oxygenation was thought to be ARDS; @patients meeting IVAC criteria without a clear source of infection were identified despite having clinical, radiographic, and microbiologic evaluations performed.* C. difficile = Clostridium difficile; *CD = calendar day; IVAC = infection-related ventilator-associated condition; TACO = transfusion-associated circulatory overload; TRALI = transfusion-related acute lung injury; VAC = ventilator-associated condition; VAP = ventilator-associated pneumonia.*

Boyer AF, et al. Chest 2015;147:68-81

Table 3: Threshold values for cultured specimens used in the PVAP definition

Specimen collection/technique	Values
Lung tissue	$\geq 10^4$ cfu/g tissue*
Bronchoscopically (B) obtained specimens	
Bronchoalveolar lavage (B-BAL)	$\geq 10^4$ cfu/ml*
Protected BAL (B-PBAL)	$\geq 10^4$ cfu/ml*
Protected specimen brushing (B-PSB)	$\geq 10^3$ cfu/ml*
Nonbronchoscopically (NB) obtained (blind) specimens	
NB-BAL	$\geq 10^4$ cfu/ml*
NB-PSB	$\geq 10^3$ cfu/ml*
Endotracheal aspirate (ETA)	$\geq 10^5$ cfu/ml*

cfu = colony forming units, g = gram, ml = milliliter
*Or corresponding semi-quantitative result.

Figure 1: Pneumonia Flow Diagram for Patients of Any Age

Facility ID#_____ **Event #**_____ **Event Date** __/__/____

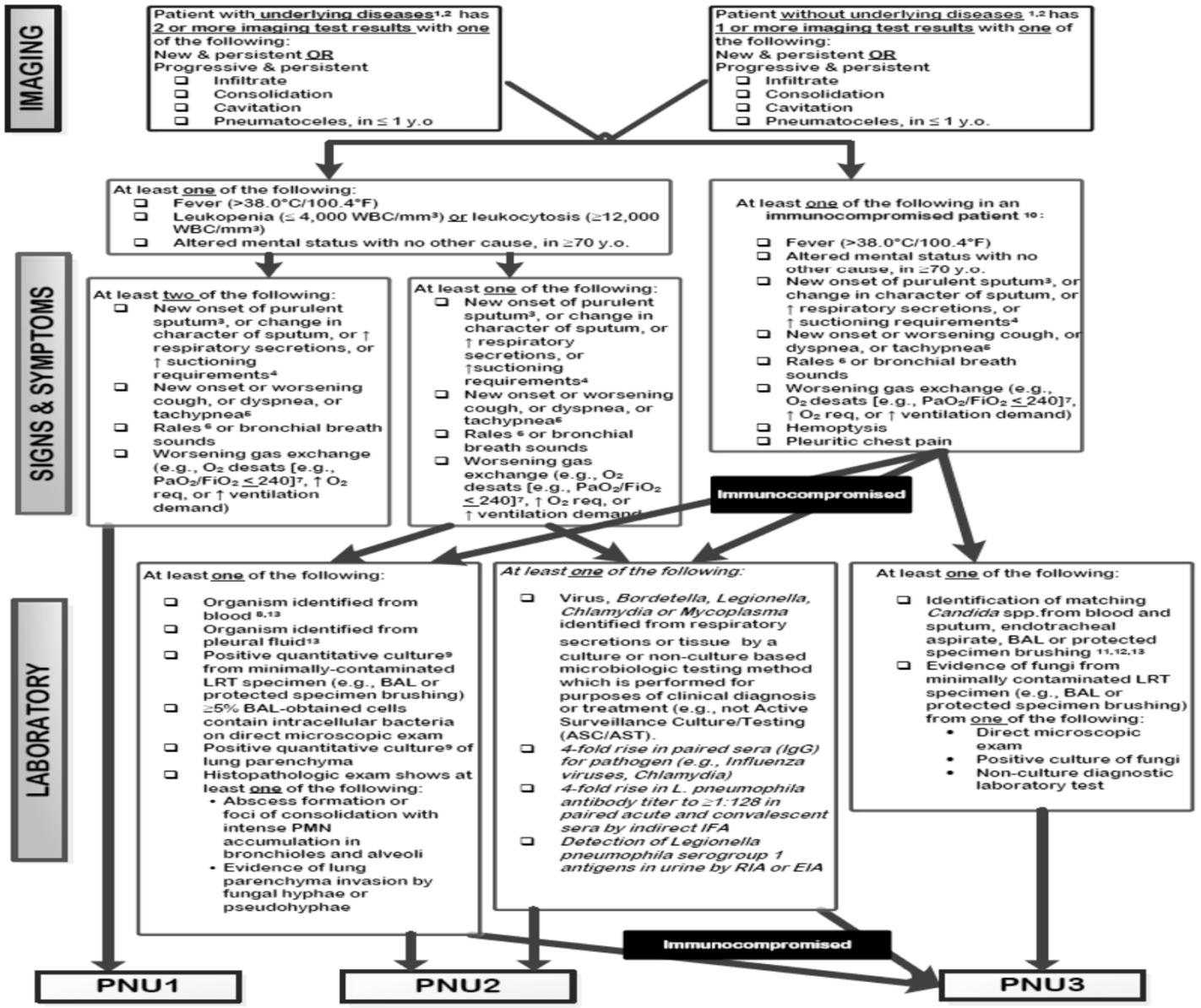


Figure 2: Pneumonia Flow Diagram, Alternative Criteria for Infants and Children

Facility ID#_____ **Event #**_____ **Event Date** __/__/____

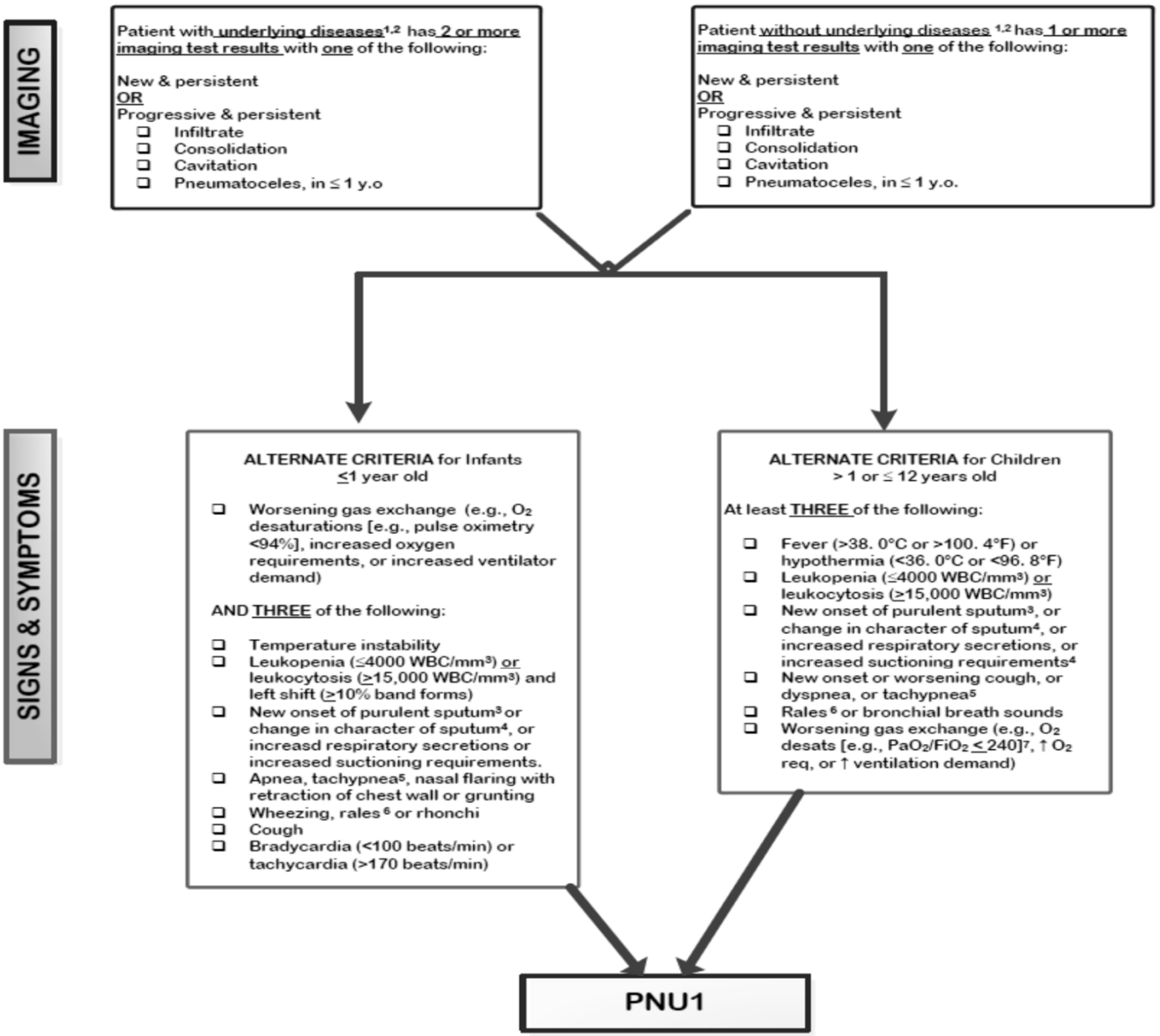


Table 1: Specific Site Algorithms for Clinically Defined Pneumonia (PNU1)

Imaging Test Evidence	**Signs/Symptoms/Laboratory**
Two or more serial chest imaging test results with at least ***one*** of the following[1,2]: New and persistent **or** Progressive and persistent • Infiltrate • Consolidation • Cavitation • Pneumatoceles, in infants ≤1 year old **Note:** In patients ***without*** underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), one definitive imaging test result is acceptable.[1]	For ANY PATIENT, at least ***one*** of the following: • Fever (>38.0°C or >100.4°F) • Leukopenia (≤4000 WBC/mm^3) or leukocytosis (≥12,000 WBC/mm^3) • For adults ≥70 years old, altered mental status with no other recognized cause And at least ***two*** of the following: • New onset of purulent sputum[3] or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough, or dyspnea, or tachypnea[5] • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations (e.g., PaO_2/FiO_2 ≤240)[7], increased oxygen requirements, or increased ventilator demand)
	ALTERNATE CRITERIA, for infants ≤1 year old: Worsening gas exchange (e.g., O_2 desaturations [e.g., pulse oximetry <94%], increased oxygen requirements, or increased ventilator demand) And at least ***three*** of the following: • Temperature instability • Leukopenia (≤4000 WBC/mm^3) or leukocytosis (≥15,000 WBC/mm^3) and left shift (≥10% band forms) • New onset of purulent sputum[3] or change in character of sputum[4], or increased respiratory secretions or increased suctioning requirements • Apnea, tachypnea[5], nasal flaring with retraction of chest wall or nasal flaring with grunting • Wheezing, rales[6], or rhonchi • Cough • Bradycardia (<100 beats/min) or tachycardia (>170 beats/min)
	ALTERNATE CRITERIA, for child >1 year old or ≤12 years old, at least ***three*** of the following: • Fever (>38. 0°C or >100. 4°F) or hypothermia (<36. 0°C or <96. 8°F) • Leukopenia (≤4000 WBC/mm^3) or leukocytosis (≥15,000 WBC/mm^3) • New onset of purulent sputum[3] or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough, or dyspnea, apnea, or tachypnea[5]. • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations [e.g., pulse oximetry <94%], increased oxygen requirements, or increased ventilator demand)

Table 2: Specific Site Algorithms for Pneumonia with Common Bacterial or Filamentous Fungal Pathogens and Specific Laboratory Findings (PNU2)

Imaging Test Evidence	**Signs/Symptoms**	**Laboratory**
Two or more serial chest imaging test results with at least ***one*** of the following[1,2]: New and persistent **or** Progressive and persistent • Infiltrate • Consolidation • Cavitation • Pneumatoceles, in infants ≤1 year old **Note**: In patients *without* underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), one definitive chest imaging test result is acceptable.[1]	At least ***one*** of the following: • Fever (>38.0°C or >100.4°F) • Leukopenia (≤4000 WBC/mm^3) or leukocytosis (≥12,000 WBC/mm^3) • For adults ≥70 years old, altered mental status with no other recognized cause And at least ***one*** of the following: • New onset of purulent sputum[3] or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough, or dyspnea or tachypnea[5] • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations [e.g., PaO_2/FiO_2 ≤240][7], increased oxygen requirements, or increased ventilator demand)	At least ***one*** of the following: • Organism identified from blood [8,13] • Organism identified from pleural fluid[9,13] • Positive quantitative culture[9] from minimally-contaminated LRT specimen (e.g., BAL or protected specimen brushing) • ≥5% BAL-obtained cells contain intracellular bacteria on direct microscopic exam (e.g., Gram's stain) • Positive quantitative culture[9] of lung tissue • Histopathologic exam shows at least ***one*** of the following evidences of pneumonia: o Abscess formation or foci of consolidation with intense PMN accumulation in bronchioles and alveoli o Evidence of lung parenchyma invasion by fungal hyphae or pseudohyphae

Table 3: Specific Site Algorithms for Viral, Legionella, and other Bacterial Pneumonias with Definitive Laboratory Findings (PNU2)

Imaging Test Evidence	**Signs/Symptoms**	**Laboratory**
Two or more serial chest imaging test results with at least ***one*** of the following[1,2]: New and persistent **or** Progressive and persistent • Infiltrate • Consolidation • Cavitation • Pneumatoceles, in infants ≤1 year old **Note:** In patients ***without*** underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), one definitive chest imaging test result is acceptable.[1]	At least ***one*** of the following: • Fever (>38.0°C or >100.4°F) • Leukopenia (≤4000 WBC/mm^3) or leukocytosis (≥12,000 WBC/mm^3) • For adults ≥70 years old, altered mental status with no other recognized cause And at least ***one*** of the following: • New onset of purulent sputum[3] or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough or dyspnea, or tachypnea[5] • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations [e.g., PaO_2/FiO_2 ≤240][7], increased oxygen requirements, or increased ventilator demand)	At least ***one*** of the following: • Virus, *Bordetella, Legionella, Chlamydia or Mycoplasma* identified from respiratory secretions or tissue by a culture or non-culture based microbiologic testing method which is performed for purposes of clinical diagnosis or treatment (e.g., not Active Surveillance Culture/Testing (ASC/AST). • Fourfold rise in paired sera (IgG) for pathogen (e.g., influenza viruses, *Chlamydia*) • Fourfold rise in *Legionella pneumophila* serogroup 1 antibody titer to ≥1:128 in paired acute and convalescent sera by indirect IFA. • Detection of *L. pneumophila* serogroup 1 antigens in urine by RIA or EIA

Table 4: Specific Site Algorithm for Pneumonia in Immunocompromised Patients (PNU3)

Imaging Test Evidence	**Signs/Symptoms**	**Laboratory**
Two or more serial chest imaging test results with at least ***one*** of the following[1,2]: New and persistent **or** Progressive and persistent • Infiltrate • Consolidation • Cavitation • Pneumatoceles, in infants ≤1 year old **Note:** In patients ***without*** underlying pulmonary or cardiac disease (e.g., respiratory distress syndrome, bronchopulmonary dysplasia, pulmonary edema, or chronic obstructive pulmonary disease), one definitive chest imaging test result is acceptable.[1]	Patient who is immunocompromised (see definition in footnote [10]) has at least ***one*** of the following: • Fever (>38.0°C or >100.4°F) • For adults ≥70 years old, altered mental status with no other recognized cause • New onset of purulent sputum[3], or change in character of sputum[4], or increased respiratory secretions, or increased suctioning requirements • New onset or worsening cough, or dyspnea, or tachypnea[5] • Rales[6] or bronchial breath sounds • Worsening gas exchange (e.g., O_2 desaturations [e.g., PaO_2/FiO_2 ≤240][7], increased oxygen requirements, or increased ventilator demand) • Hemoptysis • Pleuritic chest pain	At least ***one*** of the following: • Identification of matching *Candida* spp. from blood and sputum, endotracheal aspirate, BAL or protected specimen brushing.[11,12,13] • Evidence of fungi from minimally-contaminated LRT specimen (e.g., BAL or protected specimen brushing) from one of the following: – Direct microscopic exam – Positive culture of fungi – Non-culture diagnostic laboratory test Any of the following from: **LABORATORY CRITERIA DEFINED UNDER PNU2**

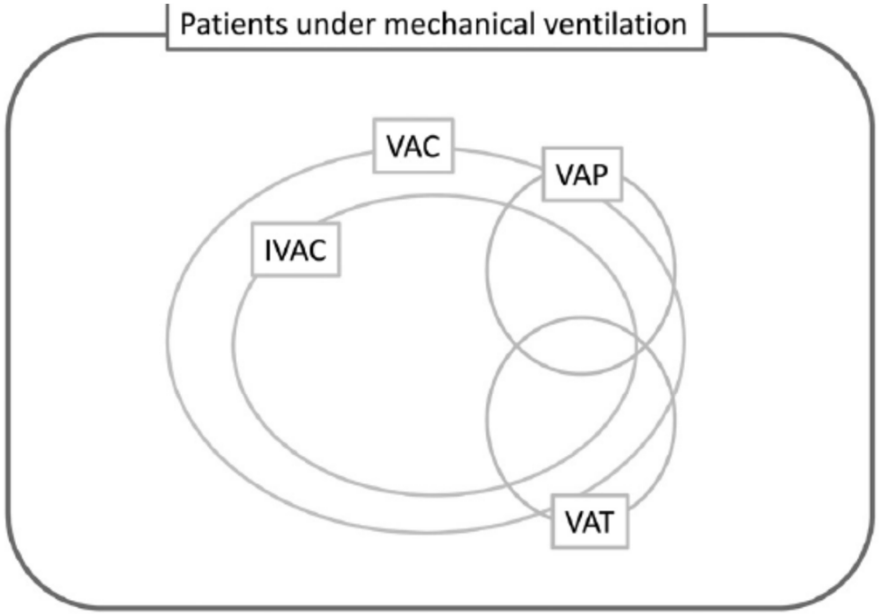


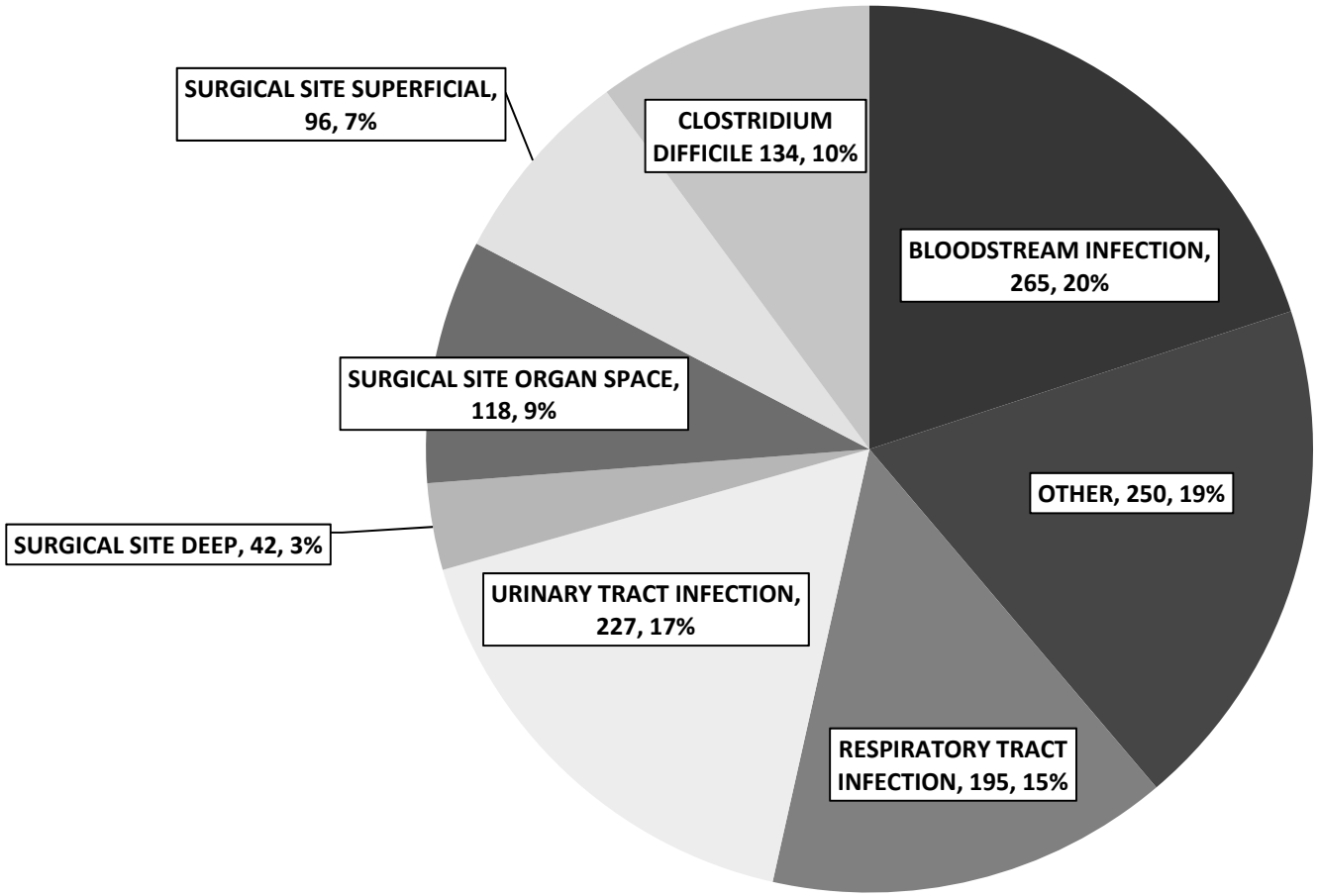
Figure 2. Ventilator-associated events, definitions, and nosology. *Ventilator-associated conditions (VACs)*: at least 2 calendar days of stable or decreasing daily minimum positive end-expiratory pressure (PEEP) or fraction of inspired oxygen (FiO_2) followed by rise in PEEP of at least 3 cm H_2O or rise in FiO_2 of at least 20 points sustained for at least 2 days. *Infection-related ventilator-associated complications (IVACs)*: VAC plus: temperature of less than 36°C or more than 38°C OR white blood cell (WBC) count of not more than 4 or at least 12×10^3 cells/mm^3 AND at least one new antibiotics continued for at least 4 days WITHIN 2 days of VAC onset EXCLUDING first 2 days on the ventilator. *Possible ventilator-associated pneumonia (VAP) (Centers for Disease Control and Prevention [CDC] definitions)*: IVAC plus: criterion 1: Positive culture meeting specific quantitative or semi-quantitative threshold; criterion 2: Purulent respiratory secretions AND identification of organisms NOT meeting the quantitative or semi-quantitative thresholds; criterion 3: Organisms identified from pleural fluid specimen, positive lung histopathology, and positive diagnostic test for Legionella species or selected respiratory viruses WITHIN 2 days of VAC onset EXCLUDING first 2 days on the ventilator. (The updated January 2017 definitions and comprehensive examples are detailed in the CDC National Healthcare Society Network website; https://www.cdc.gov/nhsn/pdfs/pscmanual/10-vae_final.pdf; accessed 23 October 2017.) *VAP*: radiographic criteria (new or progressive and persistent infiltrates or consolidation or cavitation); systemic criteria (temperature of less than 36°C or more than 38°C OR WBC count of not more than 4 or at least 12×10^3 cells/mm^3); pulmonary criteria (at least one of the following: (1) new onset or increase of purulent aspirates and (2) worsening gas exchange). *Ventilator-associated tracheobronchitis (VAT)*: criteria for VAP but without radiographic criteria.

Timsit J-F, F1000Research 2017

HAP & VAP: IMPACT

- Potential complications of mechanical ventilation
  - Pneumonia, acute respiratory distress syndrome (ARDS), pulmonary embolism, barotrauma, pulmonary edema, and death
- Incidence
  - >300,000 patients receive mechanical ventilation each year in the US
    - 10% TO 20% develop VAP
  - 2011, an estimated 157,000 healthcare-associated pneumonias in US
    - 39% were ventilator-associated (VAP)
- Mortality (VAP)
  - Patients 15-19 years, 24%; patients ≥85 years of age, 60%
  - Attributable mortality ~10%

Types of Infection, 2017



Bloodstream infections and infections categorized as 'other' accounted for a greater percentage of our 2017 infections compared to 2016, while Clostridium difficile and surgical site infections accounted for a smaller percentage of our 2017 infections compared to 2016

ESTIMATES OF HAIs OCCURRING IN ACUTE CARE HOSPITALS, US, 2011

Major Site of Infection	Estimated Number (%)
Pneumonia	157,500 (21.8%)
Gastrointestinal illness	123,000 (17.0%)
Urinary tract infections	93,000 (12.9%)
Primary bloodstream infections	71,900 (10.0%)
Surgical site infections from any inpatient surgery	157,000 (21.7%)
Other types of infection	118,500 (16.3%)
Estimated total number of infections in hospitals	721,800

Magill SS, et al. New Engl J Med 2014;370:1198

Table 4. **Estimated Numbers of Major Types of Health Care–Associated Infection in the United States in 2011.**

Type of Infection	Infections Identified in Survey	Surveyed Patients with Type of Infection	Estimated Infections in the United States*
	no.	*% (95% CI)*	*no. (95% CI)*
All health care–associated infections			
Pneumonia	110	24.3 (20.6–28.5)	157,500 (50,800–281,400)
Surgical-site infection	110†	24.3 (20.6–28.5)	157,500 (50,800–281,400)
Gastrointestinal infection	86	19.0 (15.6–22.8)	123,100 (38,400–225,100)
Urinary tract infection	65	14.4 (11.4–17.9)	93,300 (28,100–176,700)
Primary bloodstream infection	50	11.1 (8.4–14.2)	71,900 (20,700–140,200)
Eye, ear, nose, throat, or mouth infection	28‡	6.2 (4.2–8.7)	40,200 (10,400–85,900)
Lower respiratory tract infection	20	4.4 (2.8–6.6)	28,500 (6900–65,200)
Skin and soft-tissue infection	16	3.5 (2.1–5.6)	22,700 (5200–55,300)
Cardiovascular system infection	6	1.3 (0.5–2.7)	8,400 (1200–26,700)
Bone and joint infection	5	1.1 (0.4–2.4)	7,100 (1000–23,700)
Central nervous system infection	4	0.9 (0.3–2.1)	5,800 (700–20,700)
Reproductive tract infection	3	0.7 (0.2–1.8)	4,500 (500–17,800)
Systemic infection	1	0.2 (0.01–1.1)	1,300 (0–10,900)
Total			721,800 (214,700–1,411,000)
Infections in non-neonatal intensive care units			
Catheter-associated urinary tract infection	25	5.5 (3.7–7.9)	35,600 (9100–78,000)
Central-catheter–associated primary bloodstream infection	11	2.4 (1.3–4.2)	15,600 (3200–41,500)
Ventilator-associated pneumonia	35	7.7 (5.5–10.5)	49,900 (13,600–103,700)
Surgical-site infections attributed to Surgical Care Improvement Project procedures§	46	10.2 (7.6–13.2)	66,100 (18,700–130,300)
Hospital-onset infections caused by specific pathogens			
Clostridium difficile infection¶	56	12.4 (9.6–15.7)	80,400 (23,700–155,000)
MRSA bacteremia‖	7	1.5 (0.7–3.0)	9,700 (1700–29,600)

Magill SS, et al. New Engl J Med 2014;370:1198

PREVALENCE: ICU (EUROPE)

- Study design: Point prevalence rate
  - 17 countries, 1447 ICUs, 10,038 patients
- Frequency of infections: 4,501 (44.8%)
  - Community-acquired: 1,876 (13.7%)
  - Hospital-acquired: 975 (9.7%)
  - ICU-acquired: 2,064 (20.6%)
    - Pneumonia: 967 (46.9%)
    - Other lower respiratory tract: 368 (17.8%)
    - Urinary tract: 363 (17.6%)
    - Bloodstream: 247 (12.0%)

Vincent J-L, et al. JAMA 1995;274:639

PREVALENCE: ICU (WORLDWIDE)

- Study design: Point prevalence, 8 May 2007
  - **75 countries, 1265 ICUs, 13,796 adult patients**
- Frequency of infections: 7,087 (51%)
  - **Sites of infection**
    - **Respiratory tract:: 4,503 (63.5%)**
    - **Abdominal: 1,392 (19.6%)**
    - **Bloodstream: 1,071 (15.1%)**
    - **Renal/urinary tract: 1,011 (14.3%)**
- Antibiotic therapy: 71%
- Pathogens of infected patients: 47% GPC, 62% GNR, 19% fungi
- Infected patients had higher ICU (25.3% vs 10.7%) and hospital mortality (33.1% vs 14.8%)

Vincent J-L, et al. JAMA 2009;302:2333-2329

VENTILATOR-ASSOCIATED PNEU RATES, NHSN, 2012 (last year available)

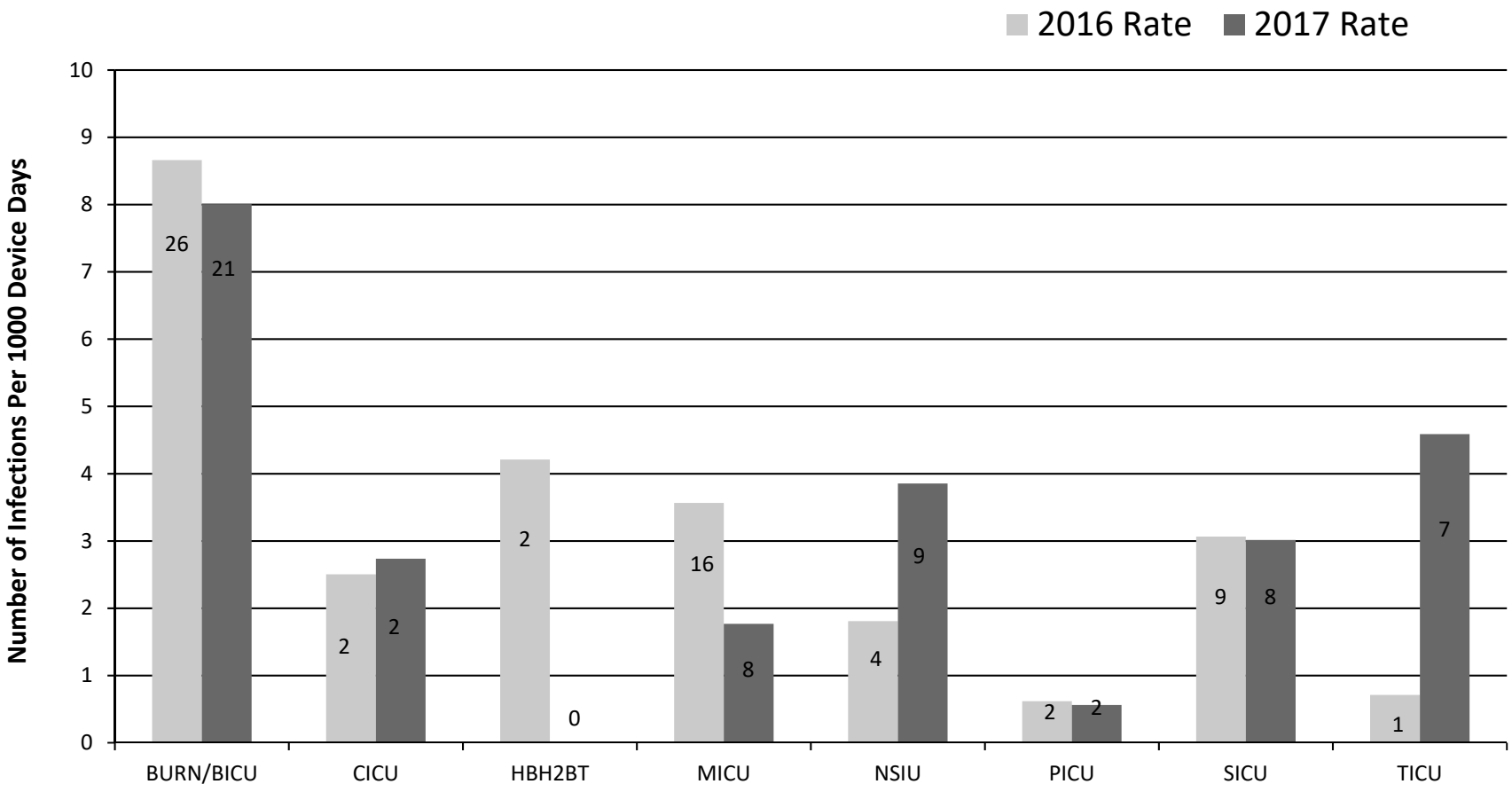
Table 6
Pooled means and key percentiles of the distribution of ventilator-associated PNEU rates and ventilator utilization ratios, by type of location, DA module, 2012

Ventilator-associated PNEU rate*					Percentile				
Type of location	No. of locations†	No. of VAP	Ventilator–days	Pooled mean	10%	25%	50% (median)	75%	90%
Acute Care Hospitals									
Critical Care Units									
Burn	36 (34)	86	19,503	4.4	0.0	0.0	1.1	6.7	10.9
Medical									
Major teaching	112 (111)	205	212,392	1.0	0.0	0.0	0.5	1.6	2.9
Medical									
All other	223 (197)	191	206,731	0.9	0.0	0.0	0.0	1.3	3.4
Medical cardiac	178 (170)	135	139,864	1.0	0.0	0.0	0.0	1.5	3.6
Medical/surgical									
Major teaching	152 (145)	372	234,972	1.6	0.0	0.0	0.9	2.2	3.9
Medical/surgical									
All other 15 beds	841 (660)	419	383,926	1.1	0.0	0.0	0.0	1.2	3.6
Medical/surgical									
All other >15 beds	405 (400)	666	711,280	0.9	0.0	0.0	0.4	1.3	2.8
Neurologic	23	62	20,859	3.0	0.0	0.0	0.2	2.5	7.0
Neurosurgical	76 (74)	210	98,026	2.1	0.0	0.0	1.5	2.9	3.8
Pediatric cardiothoracic	20	9	36,187	0.2	0.0	0.0	0.0	0.2	0.6
Pediatric medical	16 (9)	2	6,634	0.3					
Pediatric medical/surgical	142 (132)	113	147,441	0.8	0.0	0.0	0.0	0.9	2.4
Pediatric surgical	5 (4)	1	2,328	0.4					
Respiratory	7	4	6,037	0.7					
Surgical									
Major teaching	81 (80)	280	127,251	2.2	0.0	0.6	1.5	3.1	5.6

VENTILATOR-ASSOCIATED PNEU RATES, NHSN, 2012 (last year available)

Ventilator-associated PNEU rate*					Percentile				
Type of location	No. of locations†	No. of VAP	Ventilator–days	Pooled mean	10%	25%	50% (median)	75%	90%
Surgical									
All other	93 (88)	192	96,388	2.0	0.0	0.0	0.9	2.8	5.9
Surgical cardiothoracic	207 (203)	319	190,785	1.7	0.0	0.0	0.6	2.5	5.1
Trauma	75 (74)	508	141,314	3.6	0.0	0.8	2.6	6.0	9.4
Specialty Care Areas/Oncology									
Hematopoietic stem cell transplant	5	0	1,951	0.0					
Step-Down Units									
Adult step-down (post-critical care)	102 (82)	31	42,462	0.7	0.0	0.0	0.0	0.0	1.8
Pediatric step-down (post-critical care)	5 (4)	1	5,813	0.2					
Step-down NICU (level II)	7 (1)	0	119	0.0					
Inpatient Wards									
Medical	39 (22)	3	6,472	0.5	0.0	0.0	0.0	0.0	1.4
Medical/surgical	64 (35)	22	25,731	0.9	0.0	0.0	0.0	0.0	1.3
Pediatric medical	6 (5)	0	2,026	0.0					
Pediatric medical/surgical	11 (8)	0	3,146	0.0					
Pulmonary	9 (8)	7	7,241	1.0					
Surgical	8 (1)	0	107	0.0					
Telemetry	10 (5)	1	1,770	0.6					
Critical Access Hospitals									
Critical care units‡	67 (14)	3	2,964	1.0					
Non-critical care units§	9 (1)	4	2,660	1.5					
Long-Term Acute Care Hospitals‖									
Adult critical care	18 (17)	8	12,544	0.6					
Adult ward	195 (190)	103	316,632	0.3	0.0	0.0	0.0	0.3	1.4

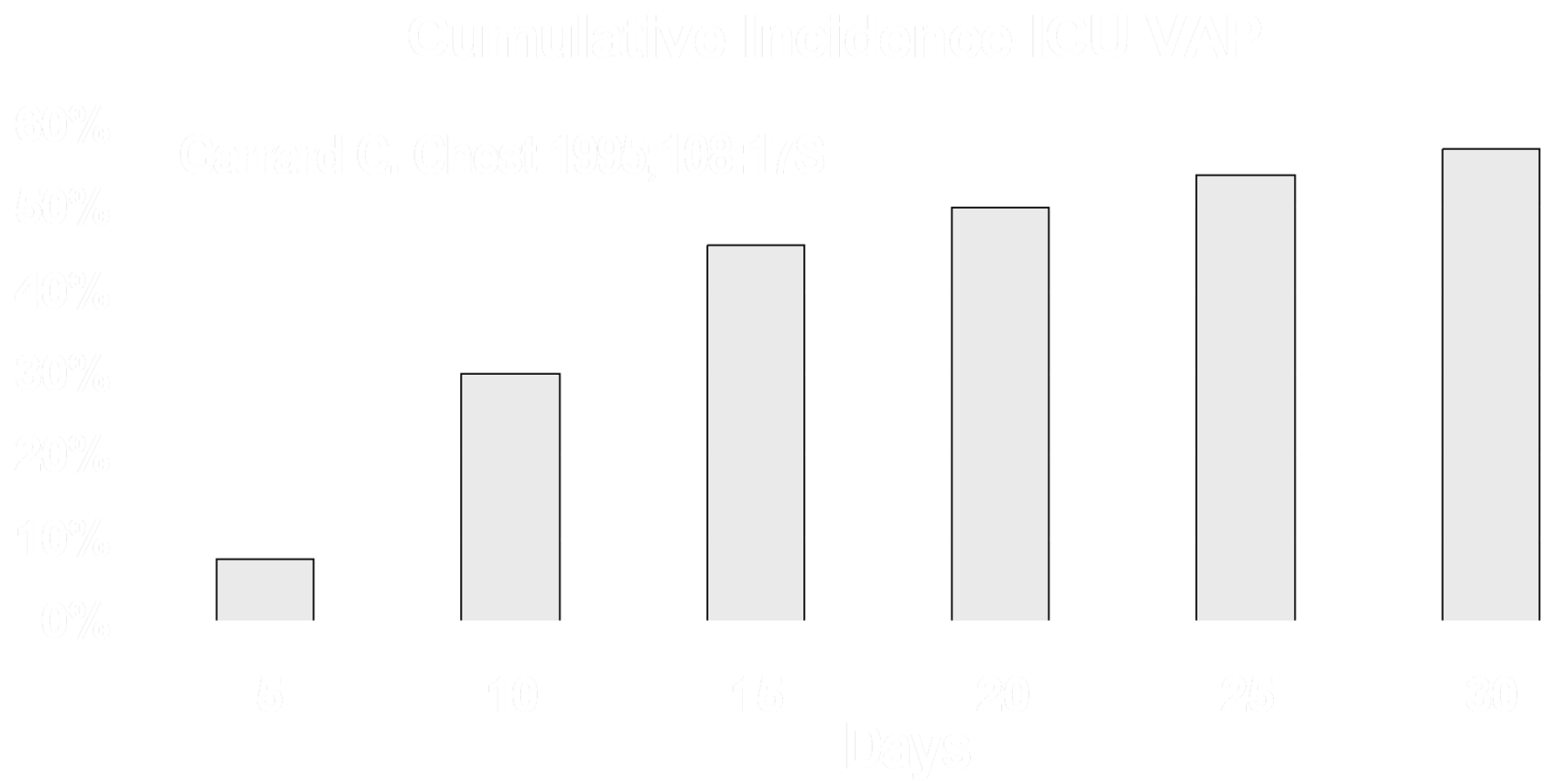
VAP/VAE Rates



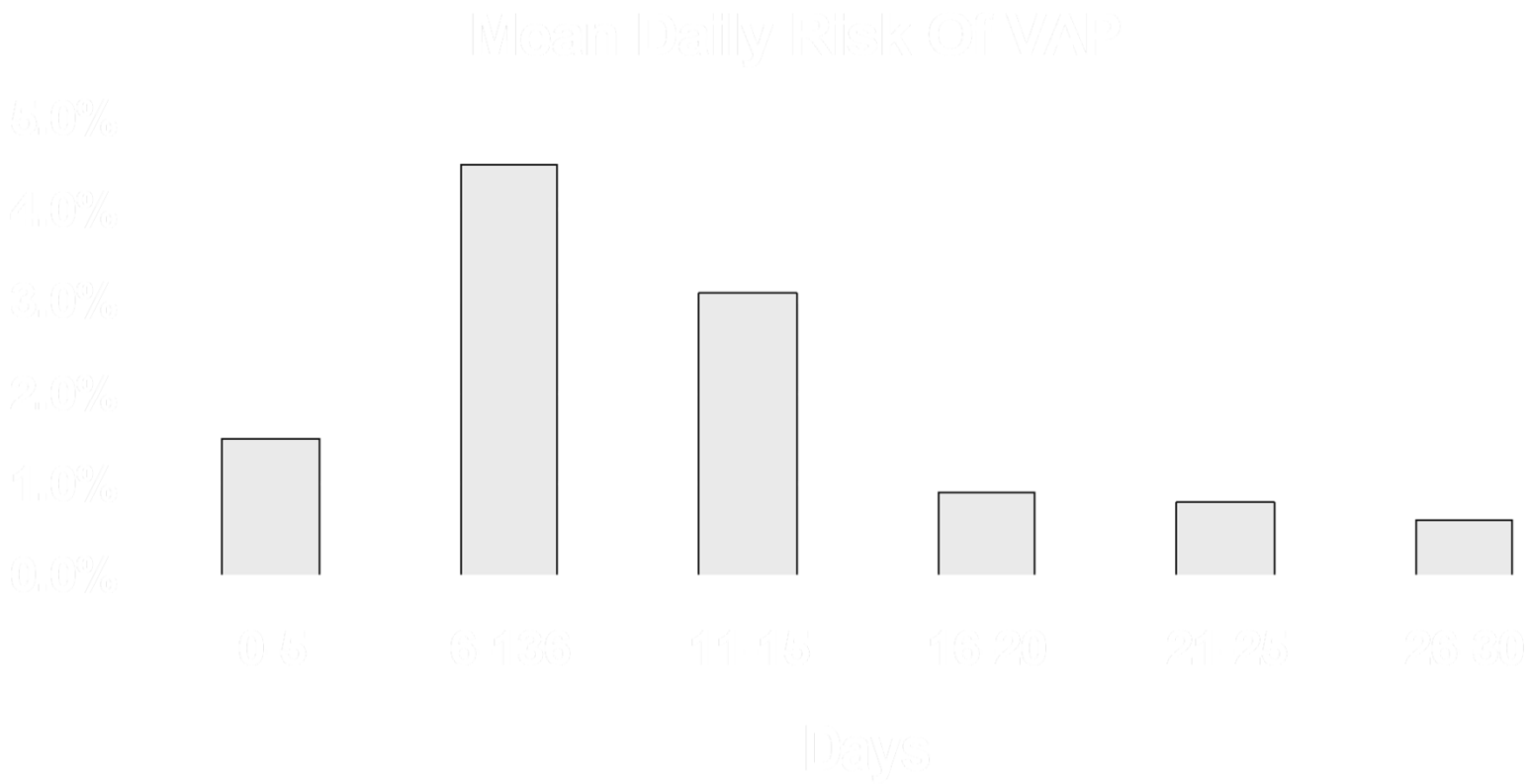
The number in each bar corresponds to the number of VAP/VAE infections for that unit

**Jan 1, 2013 – NHSN implemented new definition for patients ≥18 years; no relevant NHSN benchmarks*

VAP: TIME COURSE



VAP: TIME COURSE

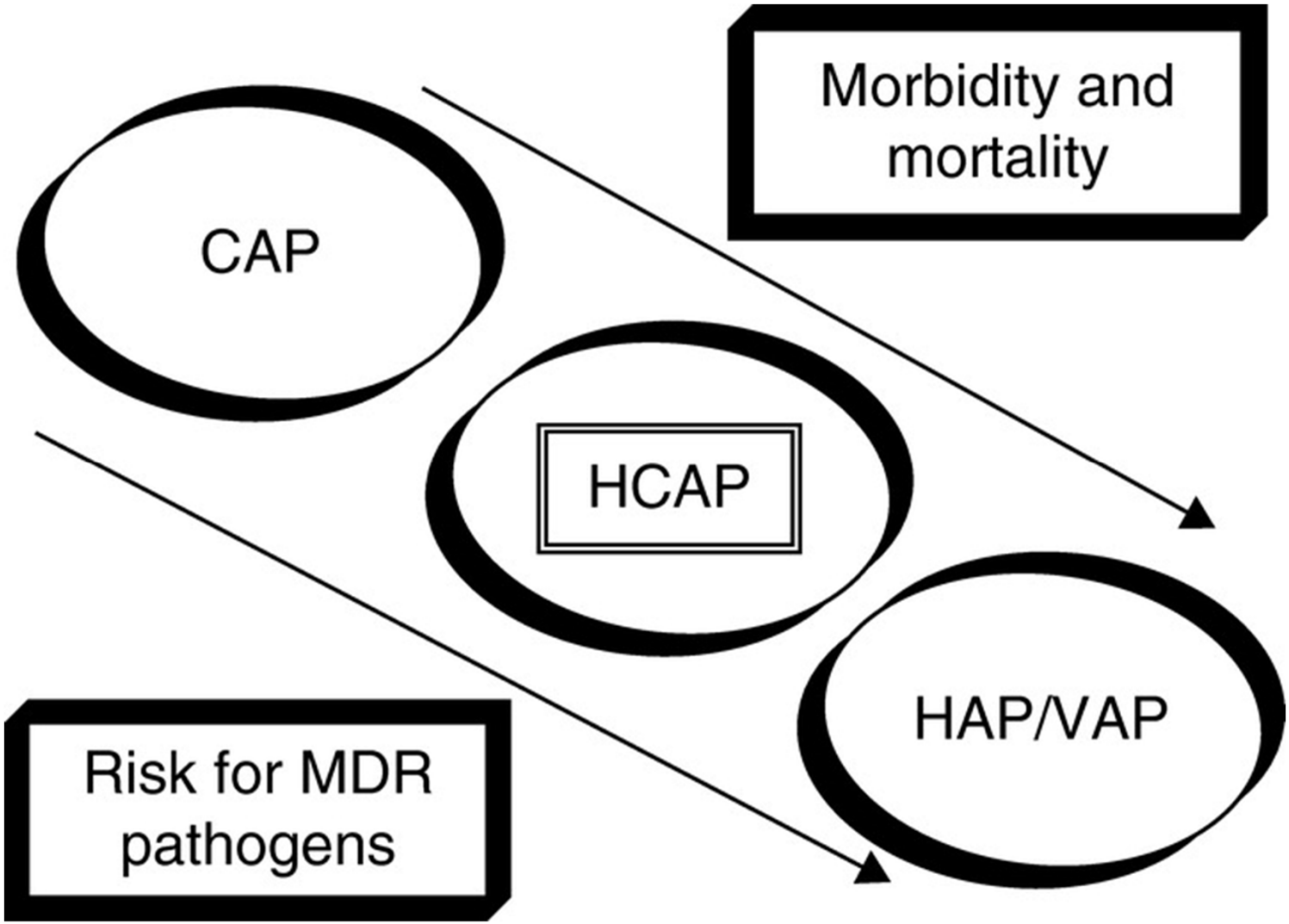


CAUSES OF LOWER RESPIRATORY TRACT INFECTIONS IN ADULTS

Organisms	Inhalation	Aspiration		Hemato-genous
		Community-acquired	Hostital-acquired	
Haemophilus influenzae				
Streptococcus pueumoniae				
Oropharyngeal streptococci and anaerobes				
Staphylococcus aureus				
Enterobacteriaceae				
Pseudomonas aeruginosa				
Legionellaceae				
Mycoplasma pneumoniae				
Chlamydia pneumoniae				
Viruses				
Histoplasma capsulatum				
Blastomyces dermatitidis				
Coccidioides immitis				
Mycobacteria				

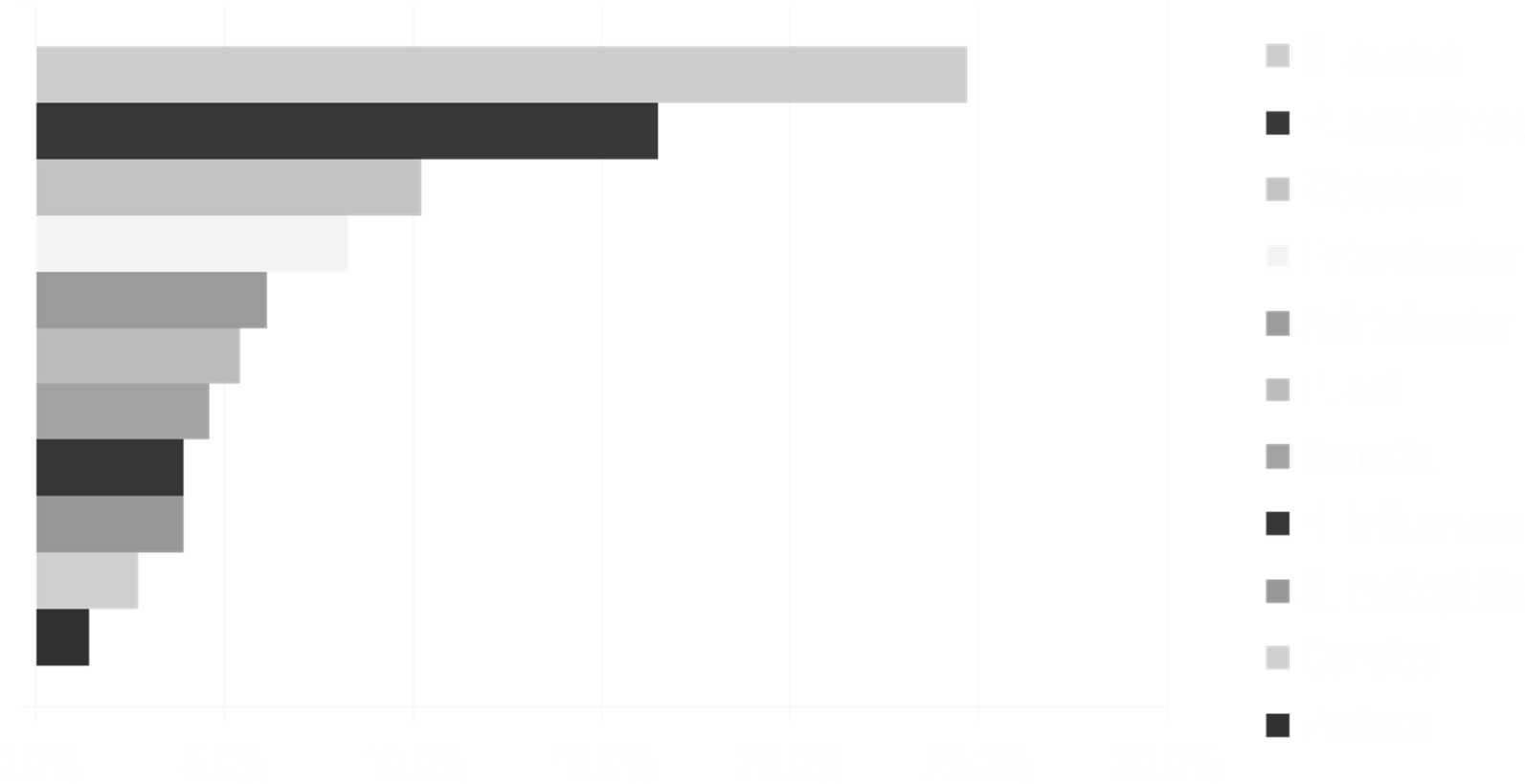
Common causes of infection

Less common cause of infection



Chroneou A, et al. Expert Opinion 2007;8:3117-31

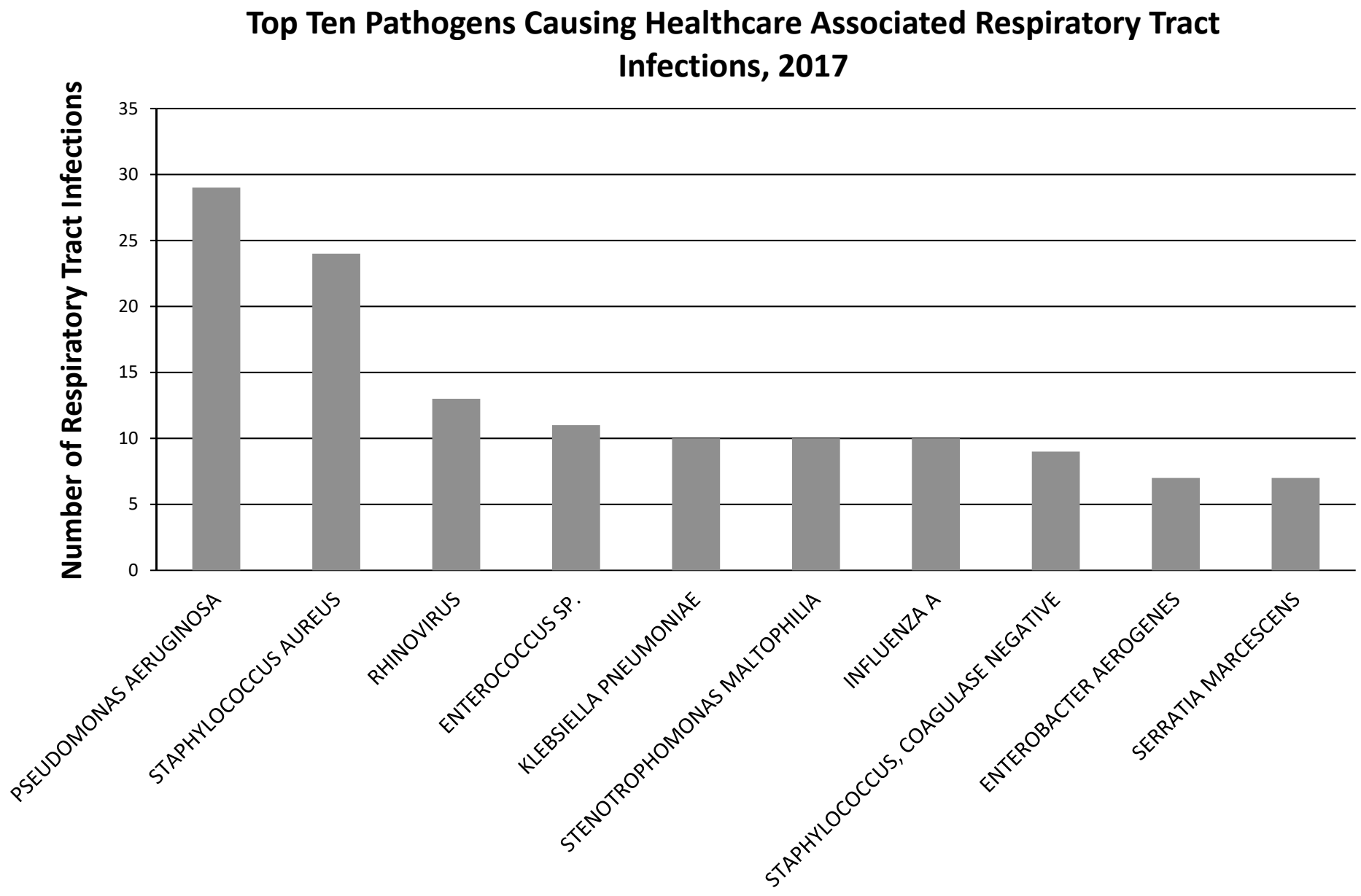
TOP PATHOGENS ASSOCIATED WITH VAP: NHSN, 2011-2014



McGill S NEJM 2014; 370: 1198

Table 3. Reported Causative Pathogens, According to Type of Infection.*

Pathogen	All Health Care–Associated Infections (N=504)†		Pneumonia (N=110)	Surgical-Site Infections (N=110)	GI Infections (N=86)	UTIs (N=65)	Bloodstream Infections (N=50)
	no. (%)	*rank*			*number (percent)*		
Clostridium difficile	61 (12.1)	1	0	0	61 (70.9)	0	0
Staphylococcus aureus	54 (10.7)	2	18 (16.4)	17 (15.5)	1 (1.2)	2 (3.1)	7 (14.0)
Klebsiella pneumoniae or *K. oxytoca*	50 (9.9)	3	13 (11.8)	15 (13.6)	1 (1.2)	15 (23.1)	4 (8.0)
Escherichia coli	47 (9.3)	4	3 (2.7)	14 (12.7)	1 (1.2)	18 (27.7)	5 (10.0)
Enterococcus species‡	44 (8.7)	5	2 (1.8)	16 (14.5)	5 (5.8)	11 (16.9)	6 (12.0)
Pseudomonas aeruginosa	36 (7.1)	6	14 (12.7)	7 (6.4)	1 (1.2)	7 (10.8)	2 (4.0)
Candida species§	32 (6.3)	7	4 (3.6)	3 (2.7)	3 (3.5)	3 (4.6)	11 (22.0)
Streptococcus species¶	25 (5.0)	8	7 (6.4)	8 (7.3)	2 (2.3)	2 (3.1)	2 (4.0)
Coagulase-negative staphylococcus species	24 (4.8)	9	0	7 (6.4)	0	1 (1.5)	9 (18.0)
Enterobacter species	16 (3.2)	10	3 (2.7)	5 (4.5)	0	2 (3.1)	2 (4.0)
Acinetobacter baumannii	8 (1.6)	11, tie	4 (3.6)	2 (1.8)	0	0	0
Proteus mirabilis	8 (1.6)	11, tie	1 (0.9)	5 (4.5)	0	1 (1.5)	0
Yeast, unspecified	8 (1.6)	11, tie	3 (2.7)	0	1 (1.2)	4 (6.2)	0
Stenotrophomonas maltophilia	8 (1.6)	11, tie	6 (5.5)	0	0	2 (3.1)	0
Citrobacter species	6 (1.2)	15, tie	2 (1.8)	1 (0.9)	0	1 (1.5)	0
Serratia species	6 (1.2)	15, tie	2 (1.8)	0	0	2 (3.1)	0
Bacteroides species	6 (1.2)	15, tie	0	5 (4.5)	1 (1.2)	0	0
Haemophilus species	6 (1.2)	15, tie	2 (1.8)	2 (1.8)	0	0	0
Viruses‖	3 (0.6)	19, tie	1 (0.9)	0	0	0	0
Peptostreptococcus species	3 (0.6)	19, tie	0	2 (1.8)	0	0	1 (2.0)
Klebsiella species other than *K. pneumoniae* and *K. oxytoca*	2 (0.4)	21, tie	1 (0.9)	0	0	0	1 (2.0)
Clostridium species other than *C. difficile*	2 (0.4)	21, tie	0	2 (1.8)	0	0	0
Prevotella species	2 (0.4)	21, tie	0	1 (0.9)	0	0	0
Morganella morganii	2 (0.4)	21, tie	0	1 (0.9)	0	1 (1.5)	0
Lactobacillus species	2 (0.4)	21, tie	0	0	1 (1.2)	0	1 (2.0)
Other organisms**	13 (2.6)	—	1 (0.9)	6 (5.5)	0	1 (1.5)	3 (6.0)


Top Ten Pathogens Causing Healthcare Associated Respiratory Tract Infections, 2017
Number of Respiratory Tract Infections
35
30
25
20
15
10
5
0
PSEUDOMONAS AERUGINOSA
STAPHYLOCOCCUS AUREUS
RHINOVIRUS
ENTEROCOCCUS SP.
KLEBSIELLA PNEUMONIAE
STENOTROPHOMONAS MALTOPHILIA
INFLUENZA A
STAPHYLOCOCCUS, COAGULASE NEGATIVE
ENTEROBACTER AEROGENES
SERRATIA MARCESCENS

PREVALENCE OF GNR VAP PATHOGENS FROM NOSOCOMIAL PNEUMONIA SURVEILLANCE STUDIES

		NHSN[27]	INFORM[28]		SENTRY		
Gram-negative groups	Year Location	2011–2012 USA	2011–2015 USA	2015 USA	2012[29] USA	2009–2012[26] USA	2009–2012[26] Europe and Mediterranean region
Non-fermenting bacteria	*Pseudomonas aeruginosa*	16.50%	39.56%[a]	22.70%	29.20%	20.90%[b]	20.90%[b]
	Acinetobacter spp.	6.10%	3.71%[a]	3.30%	2.70%	3.70%[b]	7.50%[b]
	Stenotrophomonas spp.	3.90%	NR	NR	4.70%	4.40%[b]	3.20%[b]
Enterobacteriaceae	*Citrobacter* spp.	0.70%	1.81%[a]	NR	NR	NR	NR
	Escherichia coli	5.40%	12.00%[a]	9.00%	5.50%	5.50%[b]	11.80%[b]
	Enterobacter spp.	8.30%	13.82%[a]	6.80%	7.70%	5.90%[b]	5.50%[b]
	Klebsiella spp.	10.20%	18.68%[a]	11.80%	10%	9.70%[b]	11.60%[b]
	Serratia spp.	4.60%	8.10%[a]	4.40%	5.90%	3.80%[b]	4.00%[b]

NR not reported

[a] Percent of Gram-negatives in VAP

[b] Percent of patients hospitalized with pneumonia

Rhodes NH, et al. Curr Infect Dis Rep 2018;20:3

RESISTANCE TRENDS IN CAUSATIVE PATHOGENS OF VAP

Pathogen	Incidence and resistance trends
MRSA	Rate in VAP: 12–42%[a]
	Rate of methicillin resistance is decreasing: 1.4–82%[b]
Pseudomonas aeruginosa	Rate in VAP: 21–61% especially for the second episode of VAP[a]
	MDR/XDR rates as high as 38–46% with 8–20% susceptible only to colistin [12–14]
	Meropenem with >10% increase in resistance in North America with susceptibility across all classes of antimicrobials at 60–71% [10]
Enterobacteriaceae	Rate in VAP: 5–19.1% with rising rates of resistance to all classes of antimicrobials[a] [9,10,13]
	Rates of ESBL of 40% in Asia [9]
Acinetobacter spp.	Rate in VAP: 4.8–36.5% (highest in Latin America and Asia) [9,10,13]
	MDR rate as high as 80% and XDR 50% with 30% susceptible only to colistin [9,10,13]
	Meropenem and doripenem with >10% increase in resistance [10], colistin-resistant cases reported [15]

Abbreviations: ESBL, extended spectrum β-lactamases; MDR/XDR, multidrug resistant/extremely drug resistant; MRSA, methicillin-resistant *Staphylococcus aureus*; SA, *Staphylococcus aureus*; VAP, ventilator-associated pneumonia.

Guillamet CV, Kollef MH. Curr Opin Crit Care 2015;21:430-8

ETIOLOGIC AGENTS ASSOCIATED WITH HAP: NNIS vs INVASIVE DX

Pathogen	NNIS	INVASIVE DX
S. aureus (MRSA 55.7%)	19%	20.4%
S. Pneumoniae	NA	4.1%
Streptococcus spp.	3%	8.0%
Coagulase-negative staphylococcus	2%	1.4%
Enterobacteriaceae	26%	14.15
Pseudomonas aeroginosa	17%	24.4%
Acinetobacter spp.	4%	7.9%
Stenotrophomonas maltophilia	<1%	1.7%
Hemophilus spp.	7.1%	9.8%
Neisseria spp.	<1%	2.6%
Anaerobes	2%	0.9%
Fungi	7%	0.9%
Other (<1% each)		3.8%

Chastre J, Fagon J-Y. Am J Respir Crit Care Med 2002;165:867-903

MICROBIOLOGY

- Determinants of pathogens
  - Setting
  - Prior antibiotic use
  - Duration of hospitalization
    - Early (<5 days): *S. pneumoniae*, *H. influenzae*, MSSA
    - Late (≥5 days): *P. aeruginosa*, MRSA, Gram (-) bacilli
  - ICU stay
  - Colonization

COMMON PATHOGENS BY PRESENCE OR ABSENCE OF RISK FACTORS FOR MDROs

Table I. Common pathogenic organisms in ventilator-associated pneumonia according to presence or absence of risk factors for multidrug-resistant organisms[10]

Risk factors	Commonly isolated organisms
No risk factors	*Streptococcus pneumoniae* *Haemophilus influenzae* Antibacterial-sensitive enteric Gram-negative bacilli *Escherichia coli* *Klebsiella pneumoniae* *Enterobacter* spp. *Proteus* spp. *Serratia marcescens*
Late onset (>5 days) or one of the following risk factors: antimicrobial therapy in preceding 90 days, current hospitalization of ≥5 days, high frequency of antibacterial resistance in the community or in the specific hospital unit, presence of risk factors for HCAP (hospitalization for ≥2 days in the preceding 90 days, residence in a nursing home or extended care facility, home infusion therapy [including antibacterials], chronic dialysis within 30 days, home wound care, family member with multidrug-resistant pathogen), immunosuppressive disease and/or therapy	As above plus: *Pseudomonas aeruginosa* *K. pneumoniae* (ESBL) *Acinetobacter* spp. Methicillin-resistant *Staphylococcus aureus*

ESBL = extended-spectrum β-lactamase; **HCAP** = healthcare-associated pneumonia.

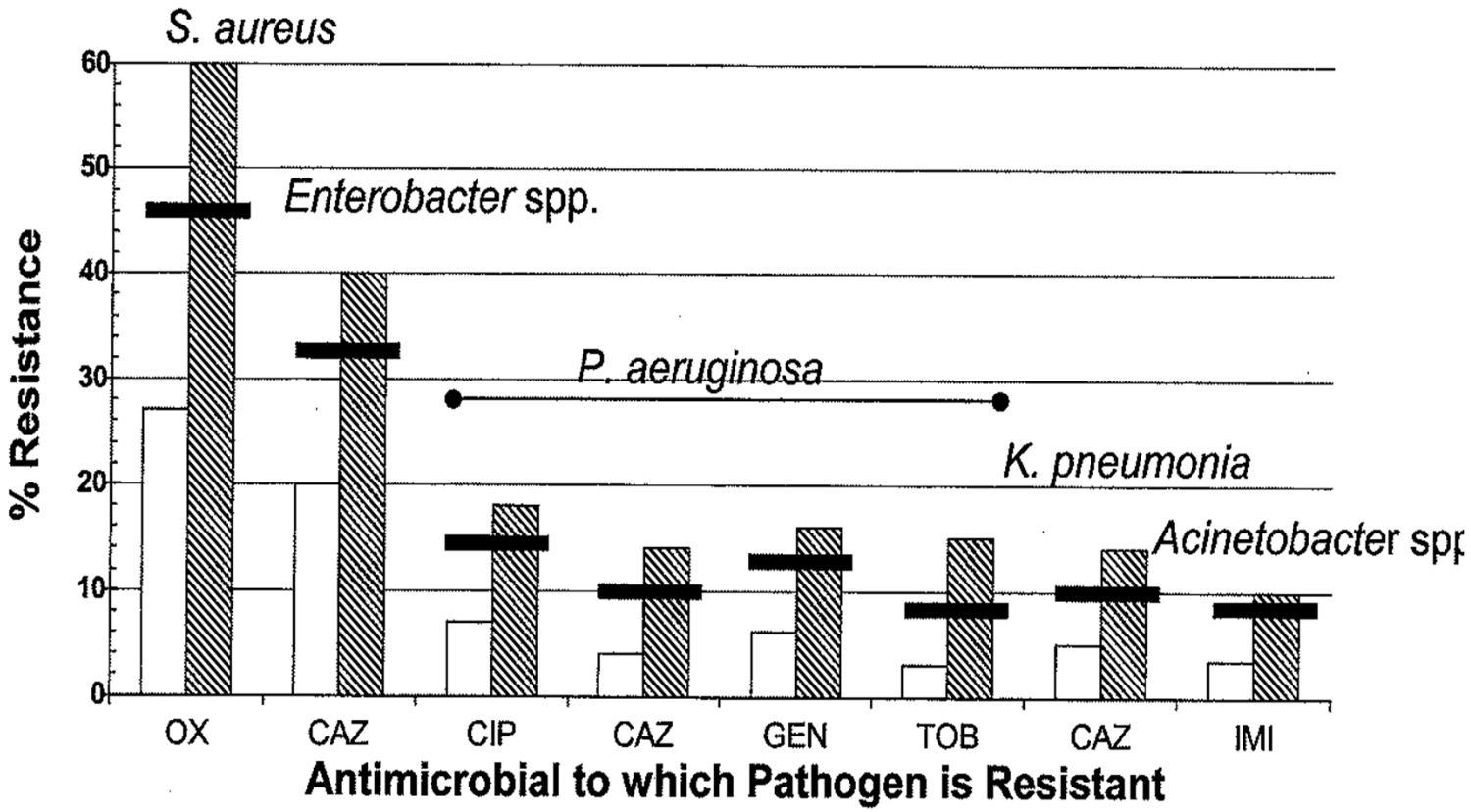
Vincent JL, et al. Drugs 2010;70:1927-1944

TABLE 3. Relative Frequency of Isolation of Selected Pathogens From Patients With Ventilator-Associated Pneumonia (VAP) and Nonventilated Patients With Hospital-Acquired Pneumonia (HAP), as a Function of Hospital Location of Care

	No. (%) of isolates			
	Patients with VAP[a]		Patients with HAP[b]	
Pathogen, by class	ICU	Non-ICU	ICU	Non-ICU
Gram-positive cocci				
Staphylococcus aureus				
Oxacillin-susceptible	35 (9.59)	2 (5.71)	13 (12.87)	23 (13.61)
Oxacillin-resistant	69 (18.90)	2 (5.71)	13 (12.87)	42 (24.85)[c]
Streptococcus pneumoniae	7 (1.92)	1 (2.86)	7 (6.93)	8 (4.73)
Gram-negative bacilli				
Enterobacter species	9 (2.47)	0 (0.00)	2 (1.98)	6 (3.55)
Escherichia coli	10 (2.74)	5 (14.29)[c]	3 (2.97)	5 (2.96)
Klebsiella pneumoniae	6 (1.64)	2 (5.71)	5 (4.95)	8 (4.73)
Serratia marcescens	8 (2.19)	2 (5.71)	3 (2.97)	2 (1.18)
Acinetobacter species	29 (7.95)	2 (5.71)	4 (3.96)	5 (2.96)
Stenotrophomonas maltophilia	25 (6.85)	2 (5.71)	2 (1.98)	1 (0.59)
Pseudomonas aeruginosa	60 (16.44)	10 (28.57)	11 (10.89)	14 (8.28)
Moraxella catarrhalis	6 (1.64)	0 (0.00)	2 (1.98)	5 (2.96)
Hemophilus species	18 (4.93)	0 (0.00)	4 (3.96)	2 (1.18)
Total, all pathogens	365	35	101	169

Weber DJ, et al. ICHE 2007;28:825-831

ICU (NNIS, 1989-99): Ventilator-Associated Pneumonia



Open bars ≤7 days hospitalization
Closed bars >7 days hospitalization

Fridkin SK. Crit Care Med 2001;29:N67

PATHOGENS AS A FUNCTION OF DURATION OF HOSPITALIZATION

TABLE 4. Frequency of Isolation of Selected Pathogens from Patients With Ventilator-Associated Pneumonia (VAP), as a Function of Duration of Hospitalization

Pathogen, by class	No. (%) of isolates		P
	Patients with early-onset VAP	Patients with late-onset VAP	
Gram-positive cocci			
Staphylococcus aureus			
Oxacillin-susceptible	12 (18.75)	24 (7.19)	.006
Oxacillin-resistant	8 (12.50)	63 (18.86)	.149
Streptococcus pneumoniae	4 (6.25)	4 (1.20)	.026
Gram-negative bacilli			
Enterobacter species	1 (1.56)	8 (2.40)	.561
Escherichia coli	2 (3.13)	13 (3.89)	.556
Klebsiella pneumoniae	1 (1.56)	7 (2.10)	.623
Serratia marcescens	2 (3.13)	8 (2.40)	.497
Acinetobacter species	0 (0.00)	31 (9.28)	.003
Stenotrophomonas maltophilia	1 (1.56)	26 (7.78)	.049
Pseudomonas aeruginosa	8 (12.50)	61 (18.26)	.176
Moraxella catarrhalis	2 (3.13)	4 (1.20)	.176
Hemophilus species	12 (18.75)	10 (2.99)	<.001
Total, all pathogens	64	334	

TABLE 5. Frequency of Isolation of Selected Pathogens From Nonventilated Patients With Hospital-Acquired Pneumonia (HAP), as a Function of Duration of Hospitalization

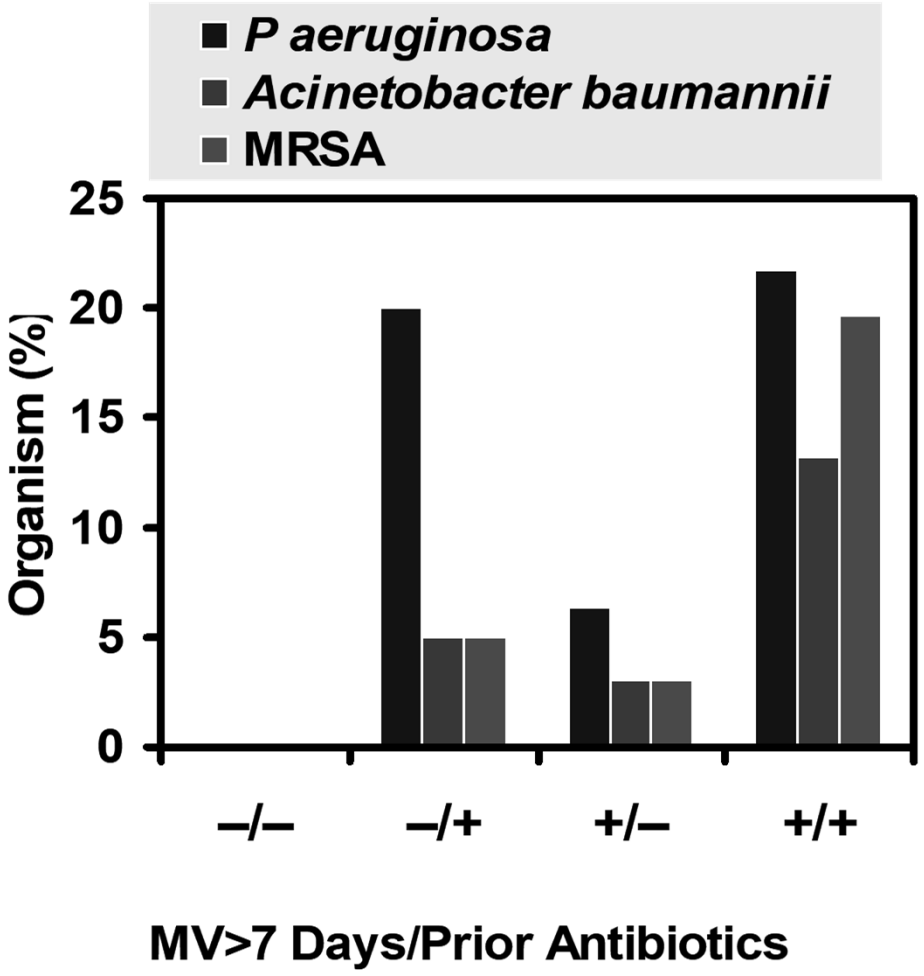
Pathogen	No. (%) of isolates		P
	Patients with early-onset HAP	Patients with late-onset HAP	
Gram-positive cocci			
Staphylococcus aureus			
Oxacillin-susceptible	13 (19.40)	22 (11.00)	.063
Oxacillin-resistant	8 (11.94)	47 (23.50)	.028
Streptococcus pneumoniae	8 (11.94)	7 (3.50)	.015
Gram-negative bacilli			
Enterobacter species	2 (2.99)	6 (3.00)	.639
Escherichia coli	1 (1.49)	7 (3.50)	.361
Klebsiella species	3 (4.48)	12 (6.00)	.454
Serratia marcescens	2 (2.99)	3 (1.50)	.369
Acinetobacter species	2 (2.99)	7 (3.50)	.598
Stenotrophomonas maltophilia	1 (1.49)	2 (1.00)	.581
Pseudomonas aeruginosa	2 (2.99)	23 (11.50)	.026
Moraxella catarrhalis	3 (4.48)	4 (2.00)	.244
Hemophilus species	4 (5.97)	4 (2.00)	.122
Total, all pathogens	67	200	

Weber DJ, et al. ICHE 2007;28:825-831

Antibiotic-Resistant VAP

Variable	*Odds Ratio*	P *Value*
Prior MV		
>7 days	***6***	***0.009***
Prior ABs	***13***	***<0.001***
Broad ABs	***4***	***0.025***

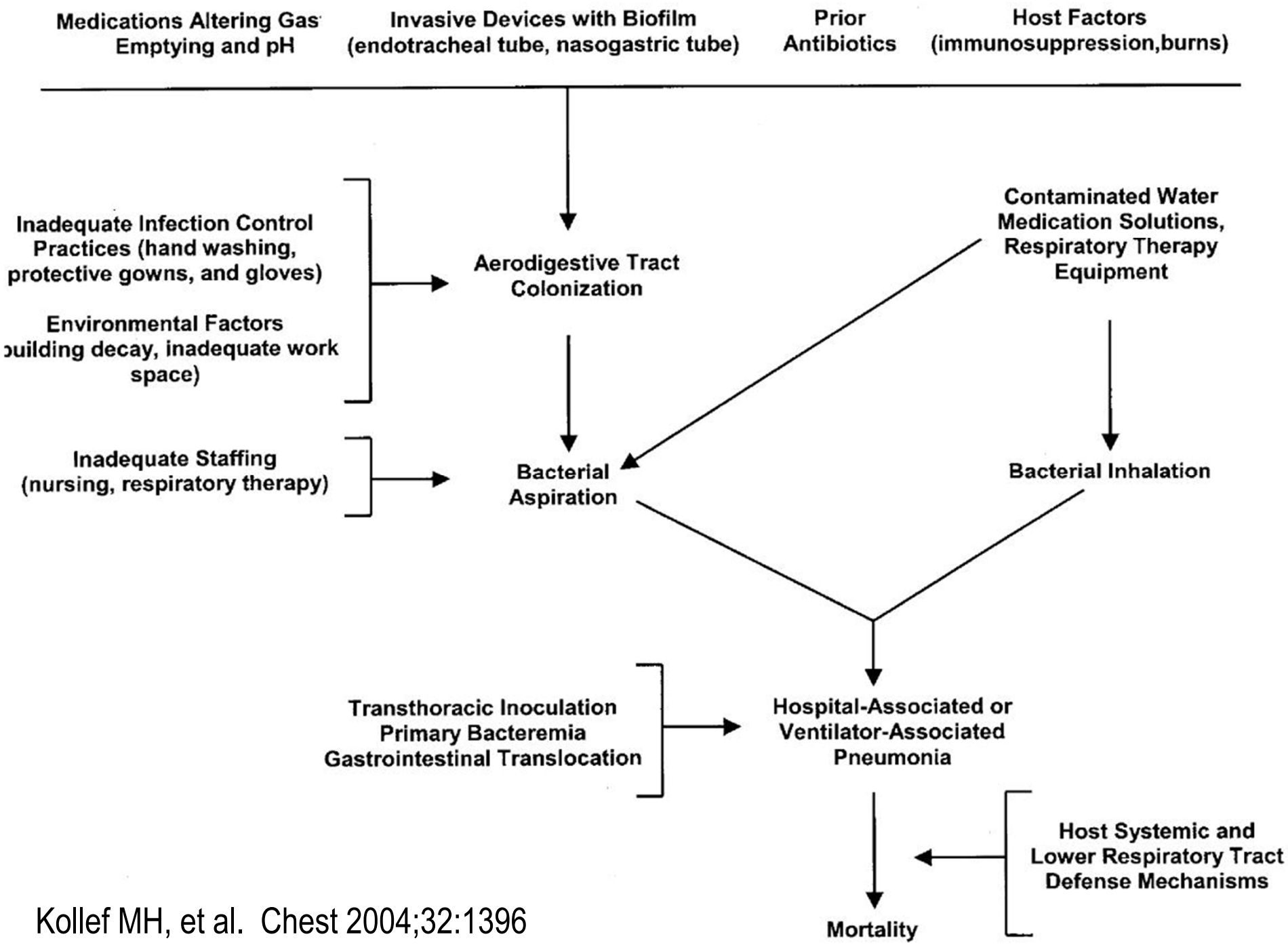
MV = Mechanical ventilation.
MRSA = Methicillin-resistant *S aureus.*



Trouillet JL, et al. *Am J Respir Crit Care Med*. 1998;157:531-539.

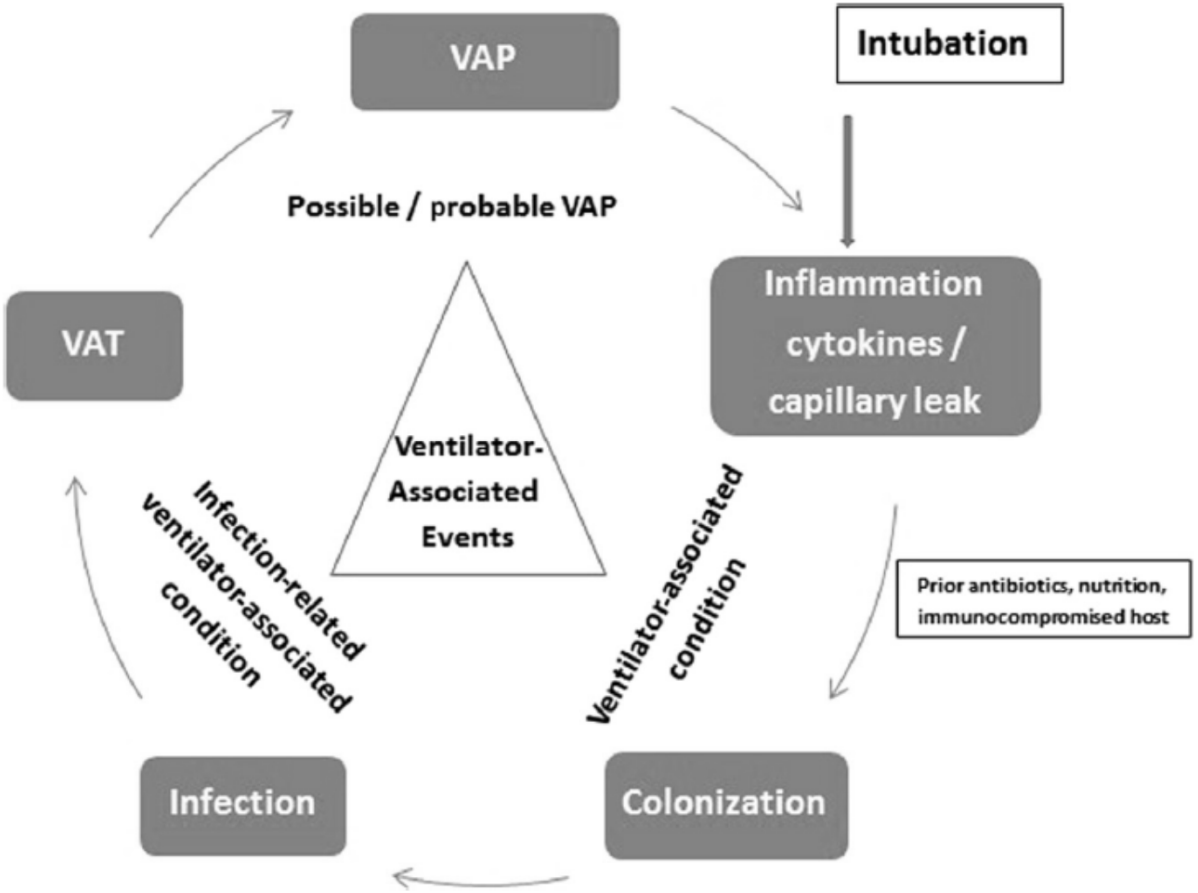
PATHOGENESIS

- Colonization, aspiration, pneumonia in the setting of impaired host defenses
- Inhalation
- Instillation
- Bacteremic spread
- Contiguous spread



Kollef MH, et al. Chest 2004;32:1396

RISKS OF VAP



Mehta A, Bhagat R. Clin Chest Med 2016;37:683-692

VAP: RISK FACTORS

Host-related risk factors	Intervention-related risk factors
Medical history and underlying illness	Peri-operative transfusion of blood products
Male gender	Duration of the mechanical ventilation
Extreme age	Reintubation
Prior central nervous system disorder	Supine head position in patients receiving enteral nutrition
Immunocompromised	Antibiotic therapy[a]
Acute underlying diseases	Enteral nutrition
Emergent surgery	Absence of subglottic secretion drainage[b]
Neurosurgery	Intra-hospital transports
Thoracic surgery	Continuous sedation, use of paralytic agents
Cardiac surgery	Nasogastric tubes
Burns	Tracheostomy
Re-intervention	Frequent ventilator circuit changes
Acute severity factors	Intracuff pressure of less than 20 cm H_2O
Organ system failure index of at least 3	
Acute renal failure	
Acute respiratory distress syndrome	
ECMO, intra-aortic support	
Ulcer disease	

Adapted from 2,35–38. [a]Antibiotic therapy protects from early-onset pneumonia due to susceptible bacteria but is a risk factor for late-onset pneumonia due to more resistant organisms. [b]Protective impact of subglottic secretion drainage is mainly demonstrated for cardiac surgery patients. ECMO, extra-corporeal membrane oxygenation.

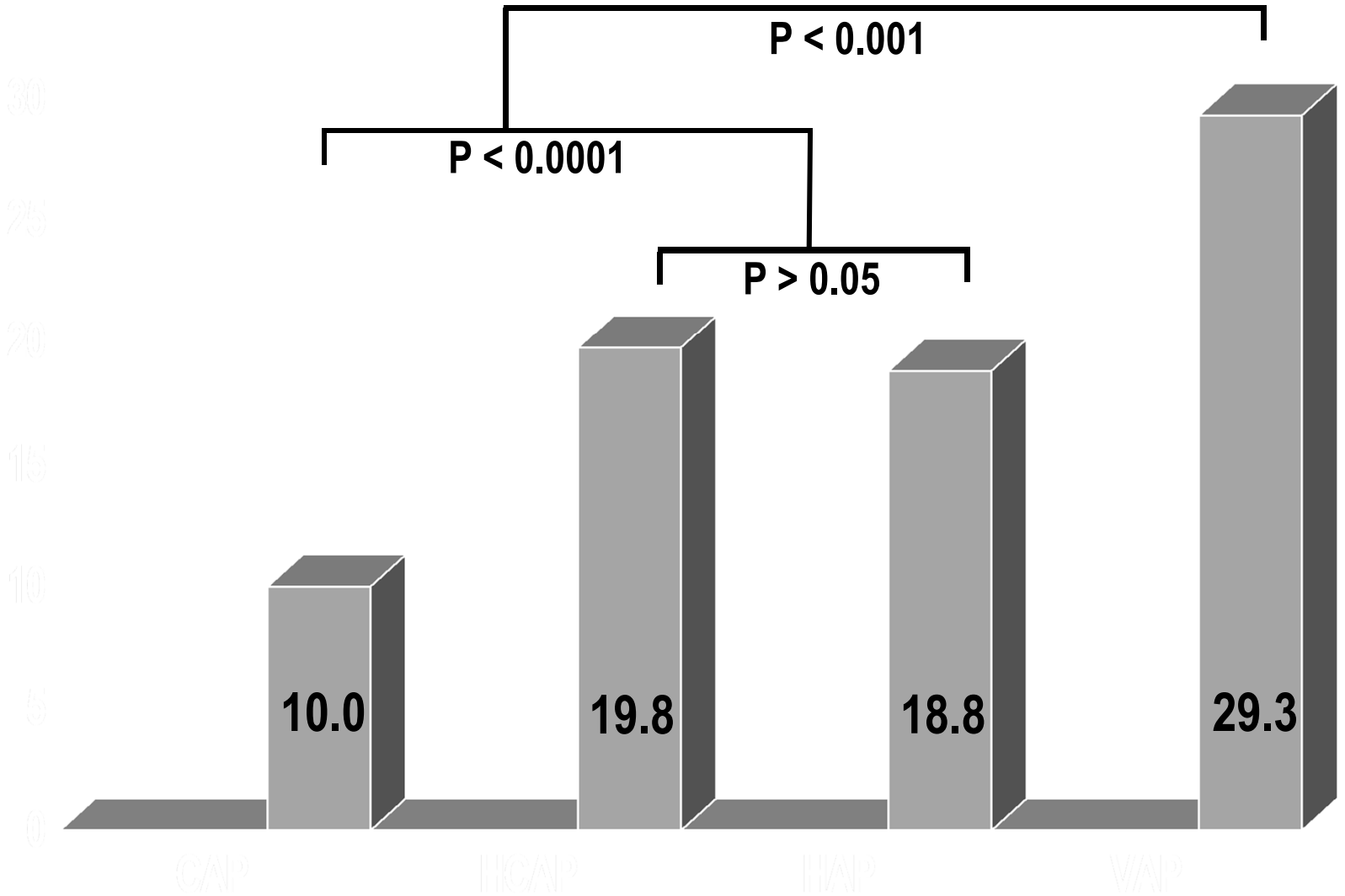
Timsit J-F, et al. F10000Research 2017, 6

RISK FACTORS FOR VAP: A RETROSPECTIVE COHORT STUDY

Variables	*VAP(+) n=178 (%)*	*VAP(–) n=974 (%)*	*P value*	*OR*	*95% CL*
Age	67.8±21.1	69.4±18.1	0.864		
Gender(Male)	102(57.3)	526(54.0)	0.416	1.14	0.82-1.60
APACHE II	21.5±5.4	19.2±4.9	<0.001		
Charlson co-morbidity index	3.9±1.6	2.7±3.0	<0.001		
Length of hospitalization (days)	26.7±16.3	18.1±12.7	<0.001		
Length of ventilation (days)	23.5±10.8	12.6±7.4	<0.001		
Previous history of hospitalization	63 (35.4)	191(19.6)	<0.001	2.25	1.57-3.22
Previous history of antibiotherapy	81 (45.5)	287(29.5)	<0.001	2.00	1.42-2.80
Steroid treatment	46 (25.8)	235(24.1)	0.624	1.10	0.75-1.60
Surgical procedure	44 (24.7)	286(29.4)	0.208	0.79	0.54-1.16
Reintubation	49 (27.5)	38 (3.9)	<0.001	9.36	5.75-15.24
Enteral nutrition	146 (82.0)	611(62.7)	<0.001	2.71	1.78-4.15
Underlying Diseases:					
Trauma	57 (32.0)	254(26.1)	0.100	1.34	0.93-1.91
COPD	40 (22.5)	63 (6.5)	<0.001	4.19	2.65-6.62
Cardiac disease	11 (9.6)	49 (5.0)	0.652	1.24	0.60-2.53
Cerebrovascular disease	72 (40.4)	295(30.3)	0.007	1.56	1.11-2.20
Diabetes mellitus	35 (19.7)	113(11.6)	0.003	1.86	1.20-2.89
Renal disease	27 (15.2)	126(12.9)	0.492	1.20	0.75-1.93
Organ failure	38 (18.5)	132(13.6)	0.007	1.73	1.13-2.64
Malignancy	21 (11.8)	98 (10.1)	0.571	1.20	0.70-2.02
Infectious disease	57 (32.0)	244(25.1)	0.052	1.41	0.98-2.02
Mortality	116 (65.2)	512(52.6)	0.002	1.69	1.19-2.39

Karatas M, et al. Pak J Med Sci 2016;32:817-22

%Hospital Mortality by Classification



Kollef MH, et al. Chest 2005;128:3854

METHODS OF DIAGNOSIS

- Clinical findings (symptoms, signs)
- Blood, pleural fluid analysis & cultures, tissue diagnosis
- Non-bronchoscopic
  - Endotracheal aspiration
  - Percutaneous needle aspiration
  - Blind bronchial sampling (“Blind” BAL)
- Bronchoscopic techniques
  - Protected specimen brush (PSB)
  - Bronchoalveolar lavage (BAL)

CLINICAL DIAGNOSIS

- Symptoms and signs: Fever, respiratory distress
- Chest radiography: Infiltrate, consolidation, cavity
- Laboratory: Leukocytosis, leukopenia
- Sputum: Purulence (WBC), culture
- Clinical diagnosis (ATS/IDSA)
  - New or progressive infiltrate
  - ≥2 of the following: Temperature >38 ^{o}C, leukocytosis or leukopenia, purulent secretions

DIFFERENTIAL DIAGNOSIS: FEVER AND PULMONARY INFILTRATES

- Pulmonary infection
- Pulmonary embolism
- Pulmonary drug reaction
- Pulmonary hemorrhage
- Chemical aspiration
- Sepsis with acute respiratory distress syndrome
- Drug reaction

DIAGNOSING VAP PNEUMONIA

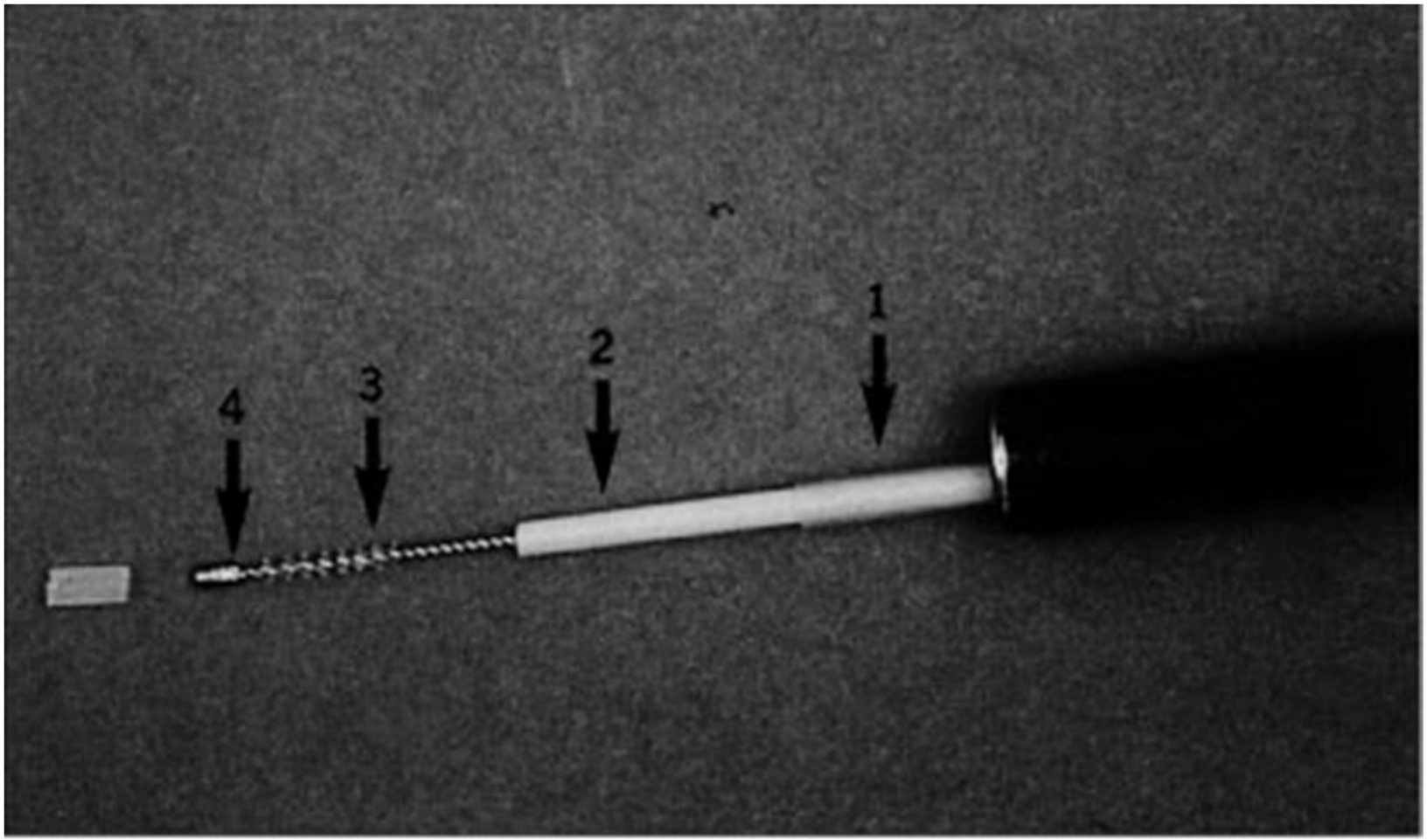
INDICATIONS FOR INVASIVE DIAGNOSIS

- Routine for all patients with possible nosocomial pneumonia?
- Targeted use of invasive diagnosis
  - Critically ill
  - Immunocompromised patient (esp. T-cell defect)
  - Deterioration on empiric therapy
  - Failure to respond to empiric therapy
  - Other therapeutic consideration (e.g., foreign-body)

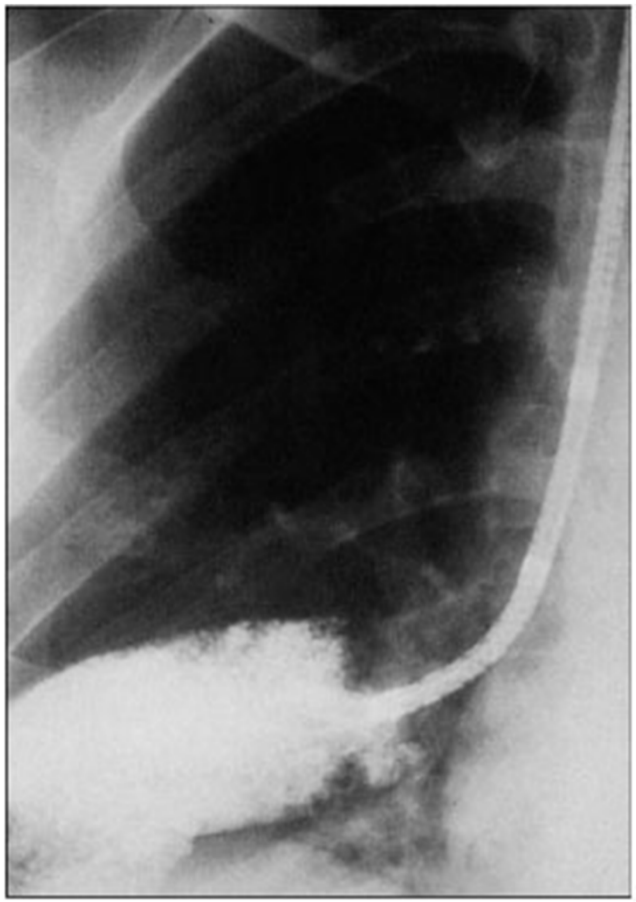
ASSESSMENT OF THE ADVANTAGES AND DISADVANTAGES OF THE DIFFERENT TECHNIQUES USED TO OBTAIN RESPIRATORY SECRETIONS FROM PATIENTS WHO HAVE SUSPECTED HAP

		Special equipment required (bedside + lab)	Skill required	Risk of technique	Sensitivity	Specificity
Noninvasive techniques						
	Expectorated sputum	0	0/+	0	+	+
	Endotracheal aspirate	+	+	0/+	++	+
	Blind distal airways sampling	++	++	+	++	++
Invasive procedures						
Perbronchoscopic	Protected specimen brush	+++	+++	++	+++	++++
	Bronchoalveolar lavage	+++	+++	++	++++	+++
	Protected bronchoalveolar lavage	++++	++++	++	++++	++++
Nonbronchoscopic	Percutaneous lung needle aspirate	+	+++	+++	++	++++
	Transtracheal aspiration	+++	++++	+++	+++	++
	Pleural fluid sampling	+	++	+	+	++++
Lung biopsy		++++	++++	+++	++++	++++

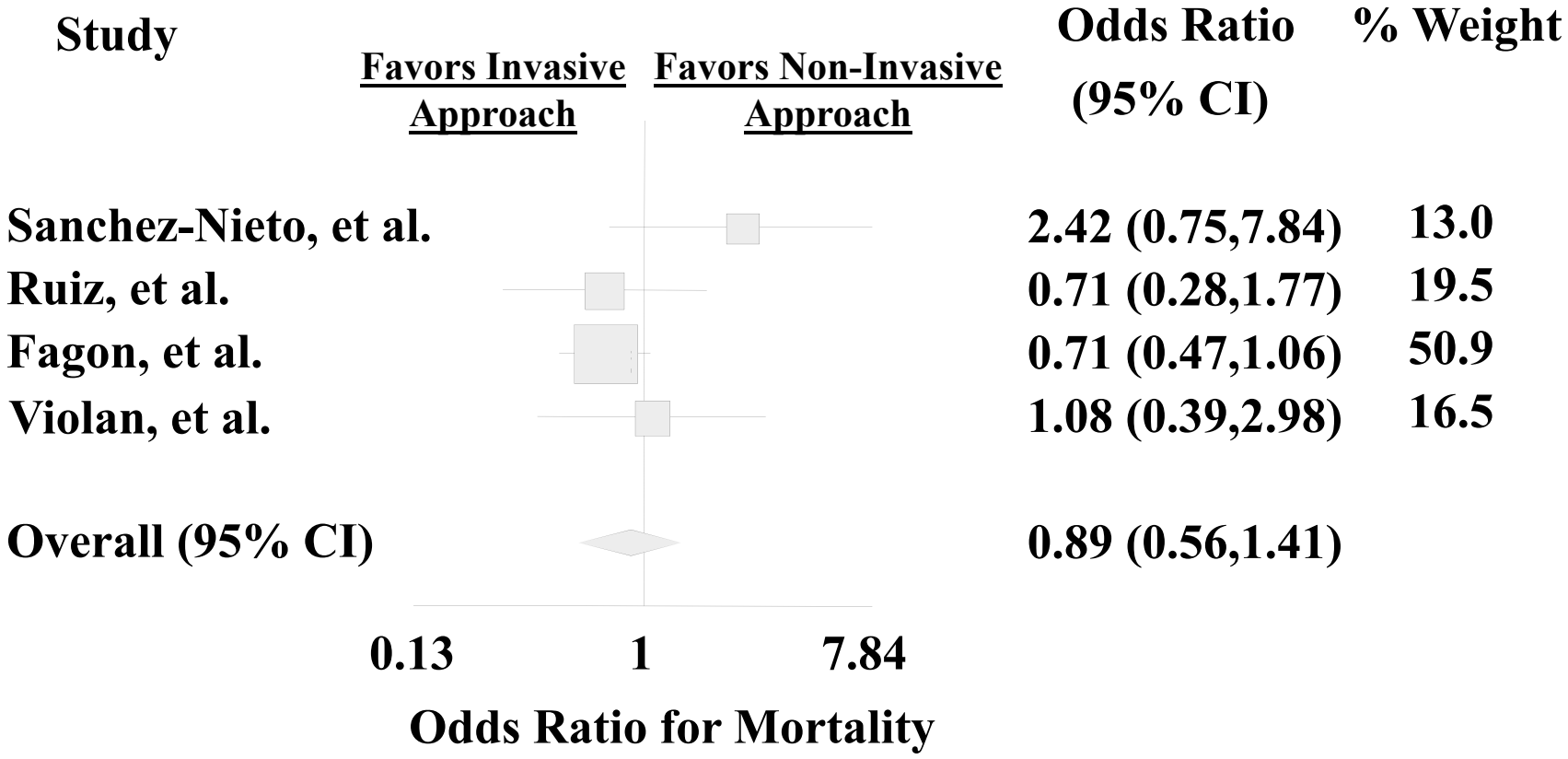
PROTECTED SPECIMEN BRUSH



BRONCHOALVEOLAR LAVAGE



Meta-analysis of Invasive Strategies for the Diagnosis of Ventilator-Associated Pneumonia & their Impact on Mortality*



*Random effects model; Test of heterogeneity p=0.247, for Odds ratio p=0.620

Shorr A, Kollef. MH Crit Care Med 2005;33:46.

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]

Kalil AC, et al. Clin Infect Dis 2016;63:e61-111

IDSA EVIDENCE BASED RECOMMENDATIONS

	Strong Recommendation	Weak (Conditional) Recommendation
Patients	Most individuals in this situation would want the recommended course of action, and only a small proportion would not.	The majority of individuals in this situation would want the suggested course of action, but many would not.
Clinicians	Most individuals should receive the intervention. Adherence to this recommendation according to the guideline could be used as a quality criterion or performance indicator. Formal decision aids are not likely to be needed to help individuals make decisions consistent with their values and preferences.	Recognize that different choices will be appropriate for individual patients and that you must help each patient arrive at a management decision consistent with his or her values and preferences. Decision aids may be useful in helping individuals to make decisions consistent with their values and preferences.
Policy makers	The recommendation can be adopted as policy in most situations.	Policymaking will require substantial debate and involvement of various stakeholders.

IDSA VAP MANAGEMENT RECOMMENDATIONS, 2016

- Should patients with suspected VAP be treated on the basis of invasive sampling (e.g., bronchoscopy) or by another method
  - We suggest noninvasive sampling with semiquantitative cultures to diagnose VAP, rather than invasive sampling with quantitative cultures and rather than noninvasive sampling with quantitative cultures (weak, very-low quality)
- If Invasive Quantitative Cultures Are Performed, Should Patients With Suspected VAP Whose Culture Results Are Below the Diagnostic Threshold for VAP (PSB With <103 Colony-Forming Units [CFU]/mL, BAL With <104 CFU/mL) Have Their Antibiotics Withheld Rather Than Continued?
  - For patients with suspected VAP whose invasive quantitative culture results are below the diagnostic threshold for VAP, we suggest that antibiotics be withheld rather than continued (weak, very-low quality)

IDSA VAP MANAGEMENT RECOMMENDATIONS, 2016

- In Patients With Suspected HAP (Non-VAP), Should Treatment Be Guided by the Results of Microbiologic Studies Performed on Respiratory Samples, or Should Treatment Be Empiric?
  - We suggest that patients with suspected HAP (non-VAP) be treated according to the results of microbiologic studies performed on respiratory samples obtained noninvasively, rather than being treated empirically (weak, very low-quality)
- In Patients With Suspected HAP/VAP, Should Procalcitonin (PCT) Plus Clinical Criteria or Clinical Criteria Alone Be Used to Decide Whether or Not to Initiate Antibiotic Therapy?
  - For patients with suspected HAP/VAP, we recommend using clinical criteria alone, rather than using serum PCT plus clinical criteria, to decide whether or not to initiate antibiotic therapy (strong, moderate-quality)
  - Same for sTREM-1 (strong, moderate-quality) and CRP (weak, low-quality)

IDSA VAP MANAGEMENT RECOMMENDATIONS, 2016

- In Patients With Suspected HAP/VAP, Should the Modified Clinical Pulmonary Infection Score (CPIS) Plus Clinical Criteria, or Clinical Criteria Alone, Be Used to Decide Whether or Not to Initiate Antibiotic Therapy?
  - For patients with suspected HAP/VAP, we suggest using clinical criteria alone, rather than using CPIS plus clinical criteria, to decide whether or not to initiate antibiotic therapy (weak, low-quality)
- Should Patients With Ventilator-Associated Tracheobronchitis (VAT) Receive Antibiotic Therapy?
  - In patients with VAT, we suggest not providing antibiotic therapy (weak, low quality)
  - Note: Tracheobronchitis is NO longer reported to NHSN
- Should Selection of an Empiric Antibiotic Regimen for VAP Be Guided by Local Antibiotic-Resistance Data?
  - We recommend that empiric treatment regimens be informed by the local distribution of pathogens associated with VAP and their antimicrobial susceptibilities.

IDSA VAP MANAGEMENT RECOMMENDATIONS, 2016

- What Antibiotics Are Recommended for Empiric Treatment of Clinically Suspected VAP?
  - We suggest including an 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 (Table 2), 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 know (weak, low-quality)
  - If empiric coverage for MRSA is indicated, we recommend either vancomycin or linezolid (strong, moderate-quality)
  - We suggest prescribing 2 antipseudomonal antibiotics from different classes for the empiric treatment of suspected VAP only in patients with any of the following: a risk factor for antimicrobial resistance (Table 2), patients in units where >10% of gram-negative isolates are resistant to an agent being considered for monotherapy, and patients in an ICU where local antimicrobial susceptibility rates are not available (weak, low-quality)
  - We suggest prescribing one antibiotic active against P. aeruginosa for the empiric treatment of suspected VAP in patients without risk factors for antimicrobial resistance who are being treated in ICUs where ≤10% of gram-negative isolates are resistant to the agent being considered for monotherapy (weak, low-quality)
  - If possible avoid aminoglycosides (weak, low-quality) and colistin (weak, very low-quality)

IDSA VAP MANAGEMENT RECOMMENDATIONS, 2016

- What Antibiotics Are Recommended for Empiric Treatment of Clinically Suspected HAP (Non-VAP)?
  - For patients being treated empirically for HAP, we recommend prescribing an antibiotic with activity against *S. aureus* (strong, very low-quality)
  - For patients with HAP who require empiric coverage for MRSA, we recommend vancomycin or linezolid rather than an alternative antibiotic (strong, low-quality)
  - For patients with HAP who are being treated empirically and have no risk factors for MRSA infection and are not at high risk of mortality, we suggest prescribing an antibiotic with activity against MSSA (weak, very low-quality)
  - For patients with HAP who are being treated empirically, we recommend prescribing antibiotics with activity against *P. aeruginosa* and other gram-negative bacilli (weak, very low-quality)
  - For patients with HAP who are being treated empirically and have factors increasing the likelihood for Pseudomonas or other gram-negative infection (ie, prior intravenous antibiotic use within 90 days; also see Remarks) or a high risk for mortality, we suggest prescribing antibiotics from 2 different classes with activity against *P. aeruginosa* (weak, very low-quality)

IDSA VAP MANAGEMENT RECOMMENDATIONS, 2016

- See Guideline For Recommendations on the following:
  - Role of inhaled antibiotics
  - Treatment of VAP/HAP due to MRSA
  - Treatment of VAP/HAP due to *P. aeruginosa*
  - Treatment of VAP/HAP due to ESBL GNRs
  - Treatment of VAP/HAP due to CRE
  - Treatment of VAP/HAP due to *Acinetobacter*
- Duration of therapy
  - For patients with VAP (strong, moderate-quality) and HAP (strong, moderate-quality), we recommend a 7-day course of antimicrobial therapy
- De-escalation vs fixed duration of therapy
  - For patients with HAP/VAP, we suggest that antibiotic therapy be de-escalated rather than fixed (weak, very low-quality)

RISK FACTORS FOR MULTI-DRUG 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.

Kalil AC, et al. Clin Infect Dis 2016;63:e61-111

IDSA TREATMENT RECOMMENDATIONS

Table 3. Suggested Empiric Treatment Options for Clinically Suspected Ventilator-Associated Pneumonia in Units Where Empiric Methicillin-Resistant *Staphylococcus aureus* Coverage and Double Antipseudomonal/Gram-Negative Coverage Are Appropriate

A. Gram-Positive Antibiotics With MRSA Activity	B. Gram-Negative Antibiotics With Antipseudomonal Activity: β-Lactam–Based Agents	C. Gram-Negative Antibiotics With Antipseudomonal Activity: Non-β-Lactam–Based Agents
Glycopeptides[a] Vancomycin 15 mg/kg IV q8–12h (consider a loading dose of 25–30 mg/kg × 1 for severe illness)	Antipseudomonal penicillins[b] Piperacillin-tazobactam 4.5 g IV q6h[b]	Fluoroquinolones Ciprofloxacin 400 mg IV q8h Levofloxacin 750 mg IV q24h
OR	OR	OR
Oxazolidinones Linezolid 600 mg IV q12h	Cephalosporins[b] Cefepime 2 g IV q8h Ceftazidime 2 g IV q8h	Aminoglycosides[a,c] Amikacin 15–20 mg/kg IV q24h Gentamicin 5–7 mg/kg IV q24h Tobramycin 5–7 mg/kg IV q24h
	OR	OR
	Carbapenems[b] Imipenem 500 mg IV q6h[d] Meropenem 1 g IV q8h	Polymyxins[a,e] Colistin 5 mg/kg IV × 1 (loading dose) followed by 2.5 mg × (1.5 × CrCl + 30) IV q12h (maintenance dose) [135] Polymyxin B 2.5–3.0 mg/kg/d divided in 2 daily IV doses
	OR	
	Monobactams[f] Aztreonam 2 g IV q8h	

Choose one gram-positive option from column A, one gram-negative option from column B, and one gram-negative option from column C. Note that the initial doses suggested in this table may need to be modified for patients with hepatic or renal dysfunction.

Table 4. Recommended Initial Empiric Antibiotic Therapy for Hospital-Acquired Pneumonia (Non-Ventilator-Associated Pneumonia)

Not at High Risk of Mortality[a] and no Factors Increasing the Likelihood of MRSA[b,c]	Not at High Risk of Mortality[a] but With Factors Increasing the Likelihood of MRSA[b,c]	High Risk of Mortality or Receipt of Intravenous Antibiotics During the Prior 90 d[a,c]
One of the following:	One of the following:	Two of the following, avoid 2 β-lactams:
Piperacillin-tazobactam[d] 4.5 g IV q6h	Piperacillin-tazobactam[d] 4.5 g IV q6h	Piperacillin-tazobactam[d] 4.5 g IV q6h
OR	OR	OR
Cefepime[d] 2 g IV q8h	Cefepime[d] or ceftazidime[d] 2 g IV q8h	Cefepime[d] or ceftazidime[d] 2 g IV q8h
OR	OR	OR
Levofloxacin 750 mg IV daily	Levofloxacin 750 mg IV daily	Levofloxacin 750 mg IV daily
	Ciprofloxacin 400 mg IV q8h	Ciprofloxacin 400 mg IV q8h
	OR	OR
Imipenem[d] 500 mg IV q6h	Imipenem[d] 500 mg IV q6h	Imipenem[d] 500 mg IV q6h
Meropenem[d] 1 g IV q8h	Meropenem[d] 1 g IV q8h	Meropenem[d] 1 g IV q8h
	OR	OR
	Aztreonam 2 g IV q8h	Amikacin 15–20 mg/kg IV daily
		Gentamicin 5–7 mg/kg IV daily
		Tobramycin 5–7 mg/kg IV daily
		OR
		Aztreonam[e] 2 g IV q8h
	Plus: Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg × 1 for severe illness)	Plus: Vancomycin 15 mg/kg IV q8–12h with goal to target 15–20 mg/mL trough level (consider a loading dose of 25–30 mg/kg IV × 1 for severe illness)
	OR	OR
	Linezolid 600 mg IV q12h	Linezolid 600 mg IV q12h
		If MRSA coverage is not going to be used, include coverage for MSSA. Options include: Piperacillin-tazobactam, cefepime, levofloxacin, imipenem, meropenem. Oxacillin, nafcillin, and cefazolin are preferred for the treatment of proven MSSA, but would ordinarily not be used in an empiric regimen for HAP.
If patient has severe penicillin allergy and aztreonam is going to be used instead of any β-lactam–based antibiotic, include coverage for MSSA.		

	CEFTOLOZANE/ TAZOBACTAM	CEFTAZIDIME/ AVIBACTAM	MEROPENEM/ VABORBACTAM
TRADE NAME	Zerbaxa	Avycaz	Vabomere
INDICATIONS	cIAI, cUTI	cIAI, cUTI, HAP, VAP	cUTI
Improved coverage against *Enterobacteriaceae*	Class A (TEM, SHV, CTX-M)	Class A (TEM, SHV, CTX-M, KPC) Class C (Amp C) Class D (OXA)	Class A (TEM, SHV, CTX-M, KPC) Class C (Amp C)
Spectrum *Pseudomonas* Gram positive cocci Anaerobes	 Yes No (some Strep) +/-	 Yes No (some Strep) +/-	 Yes (same as meropenem) Yes (same as meropenem) Yes (same as meropenem)
Dose	IV, 1.5g Q 8 hr (adults)*	IV, 2.5g Q 8 hr (adults)*	IV, 4g Q 8 hr (adults)*
Comments on Coverage	Improved activity against *P. aeruginosa*; no expanded cover for *Acinetobacter* or *Stenotrophomonas*	Improved activity against ESBLs including KPCs; no expanded cover for *Acinetobacter* or *Stenotrophomonas*	Expanded coverage for CRE; no expanded coverage for *Acineto-bacter*, *P. aeruginosa,* or *Stenotrophomonas*

* Requires dosage adjustment for decreased renal function

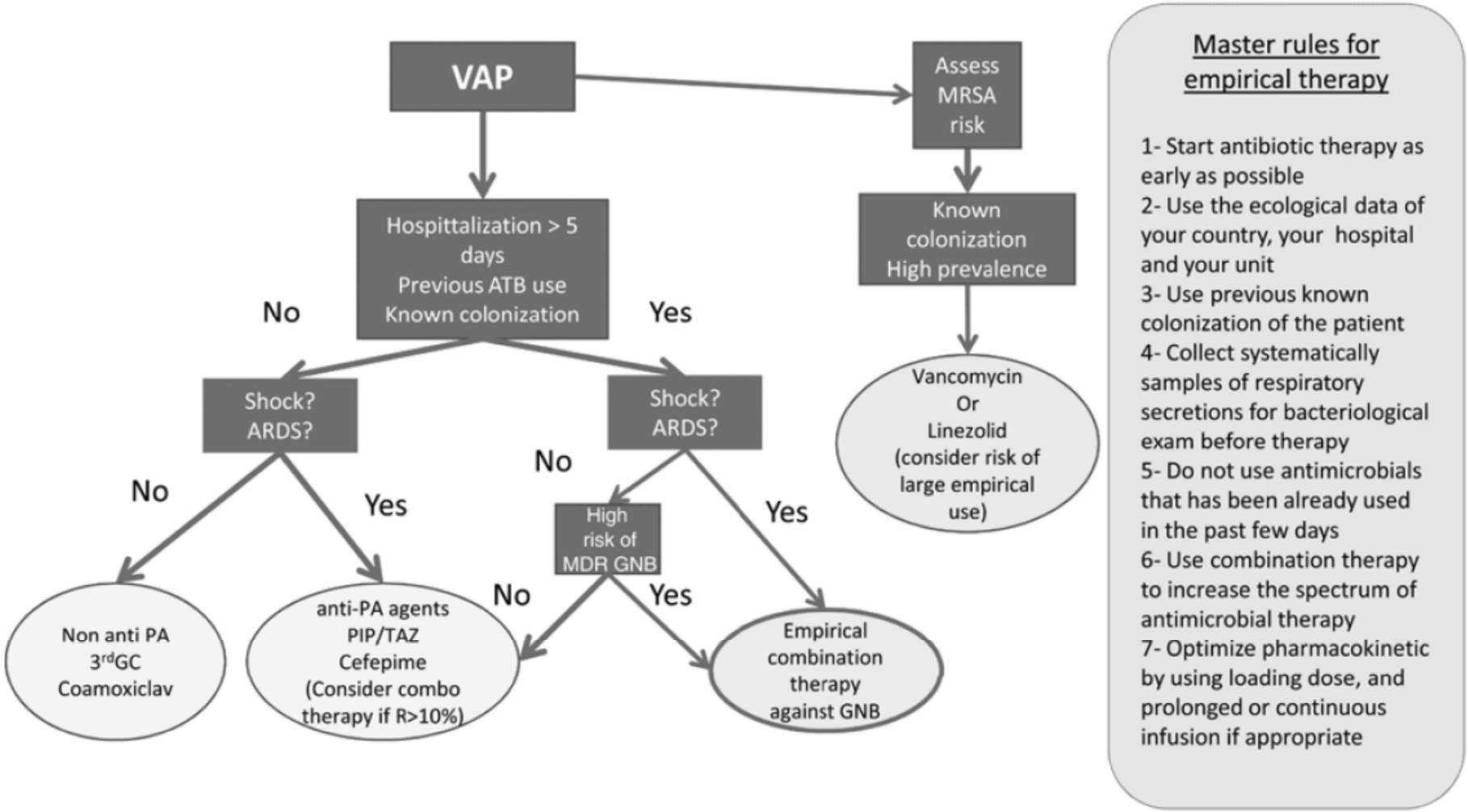


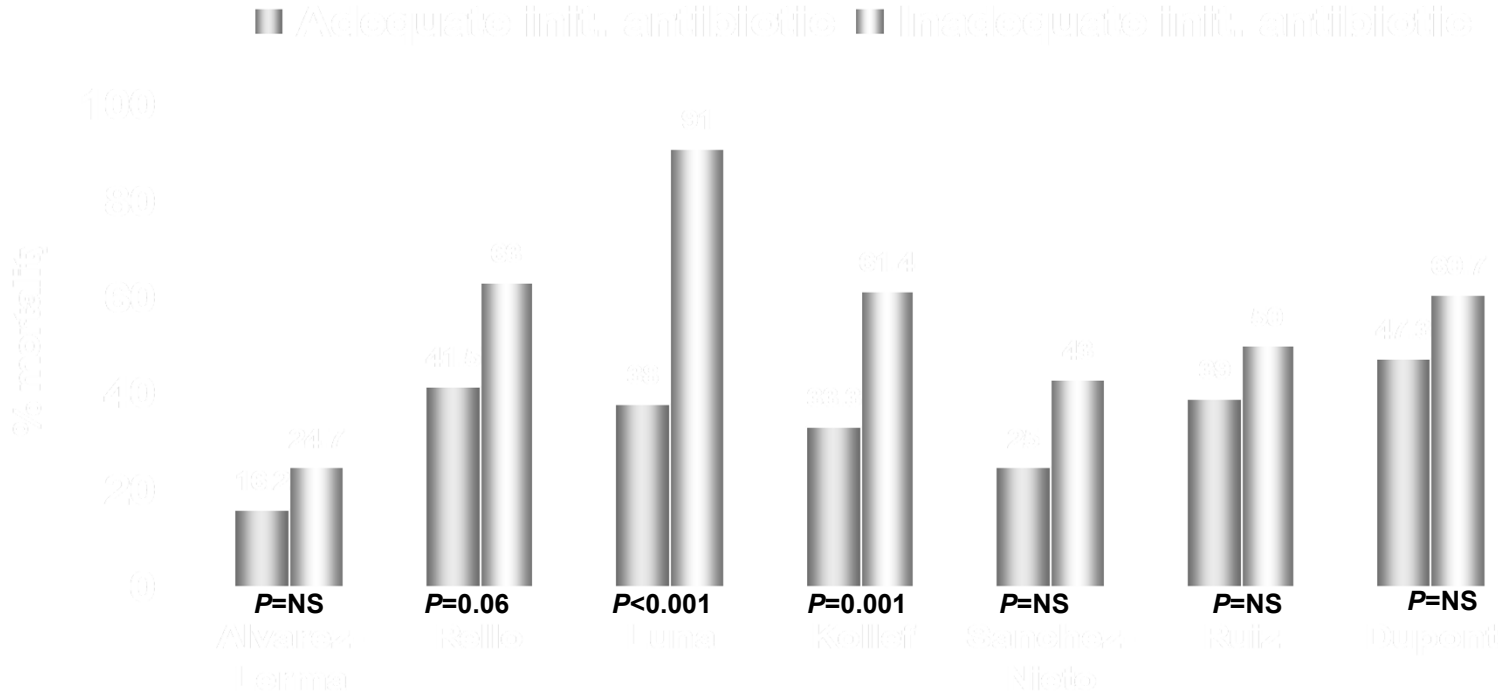
Figure 3. Proposed strategy for empirical therapy. *In areas with a risk of multidrug-resistant and carbapenemase-producing bacteria, the empirical choice should be decided on the basis of local ecology. 3rd GC, third-generation cephalosporin; ARDS, acute respiratory distress syndrome; ATB, antibiotics; GNB, Gram-negative bacteria; MDR, multidrug-resistant; MRSA, methicillin-resistant *Staphylococcus aureus*; PA, *Pseudomonas aeruginosa*; PIP/TAZ, piperacillin-tazobactam; R, Resistant; VAP, ventilator-associated pneumonia.

Timsit J-F, F1000Research 2017

EMPIRIC THERAPY: GENERAL RULES

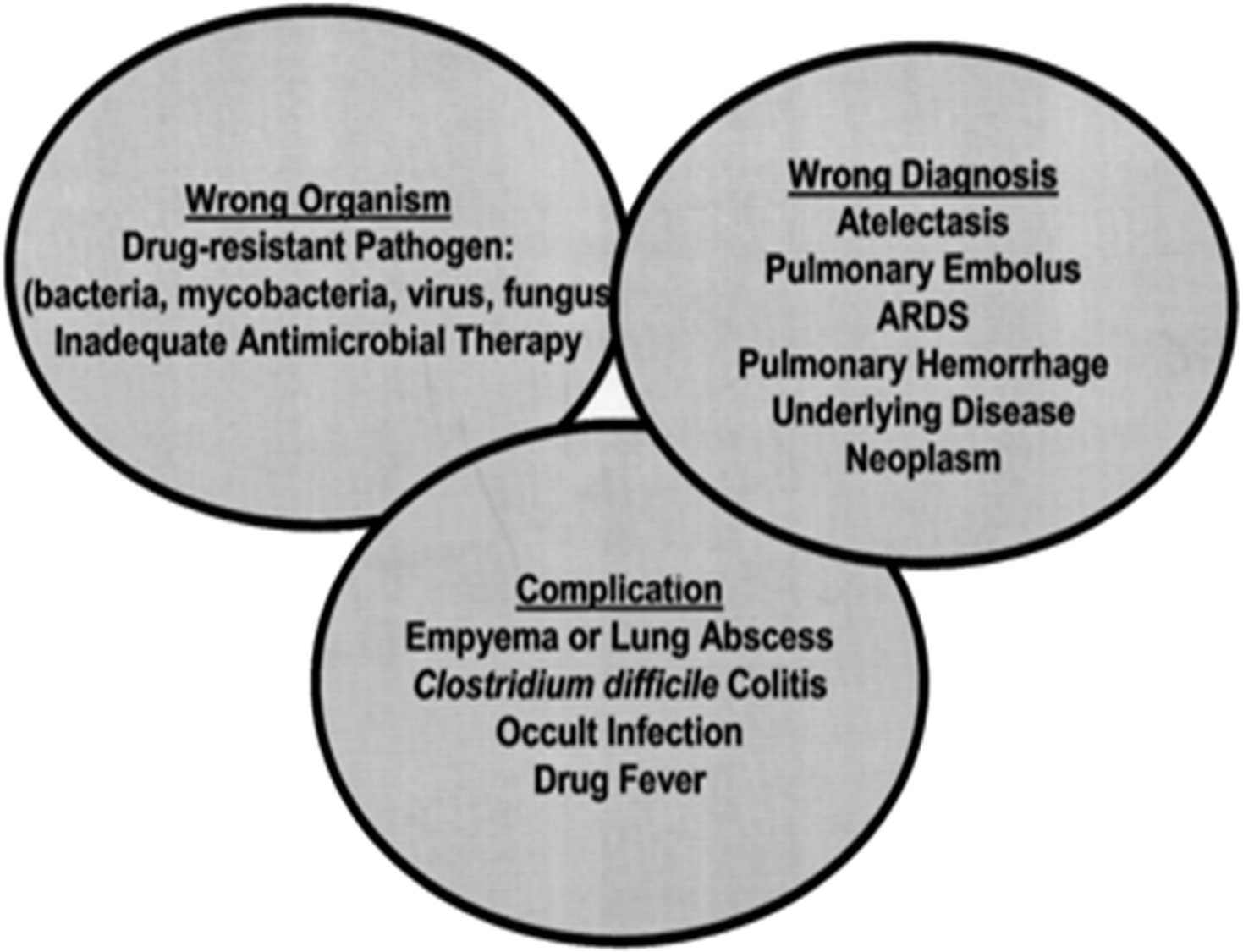
- Know the flora and susceptibilities of the pathogens causing nosocomial pneumonia at your own institution
- Obtain history of antibiotic-allergies from all patients (adjust regimen appropriately)
- Choose empiric therapy to minimize drug interactions
- Dose adjust (when appropriate) in patients with renal and/or hepatic failure
- Consider specific contraindications or precautions (e.g., pregnancy)
- All other things being equal use the least expensive therapy
- Follow IDSA Guideline
- Provide appropriate non-antibiotic care

HAP: The Importance of Initial Empiric Antibiotic Selection



Alvarez-Lerma F. *Intensive Care Med* 1996 May;22(5):387-394.
Rello J, Gallego M, Mariscal D, et al. *Am J Respir Crit Care Med* 1997 Jul;156(1):196-200.
Luna CM, Vujacich P, Niederman MS, et al. *Chest* 1997;111(3):676-685.
Kollef MH and Ward S. *Chest* 1998 Feb;113(2):412-20.
Sanchez-Nieto JM, Torres A, Garcia-Cordoba F, et al. *Am J Respir Crit Care Med*. 1998;157:371-376.
Ruiz M, Torres A, Eqig, S, et al. *Am J Respir Crit Care Med.* 2000;162:119-125.
Dupont H, Mentec H, Sollet, JP, et al. *Intensive Care Med*. 2001;27(2):355-362

Assessment of Nonresponders



ATS/IDSA. Am J Respir Crit Care Med 2005;171:388-416

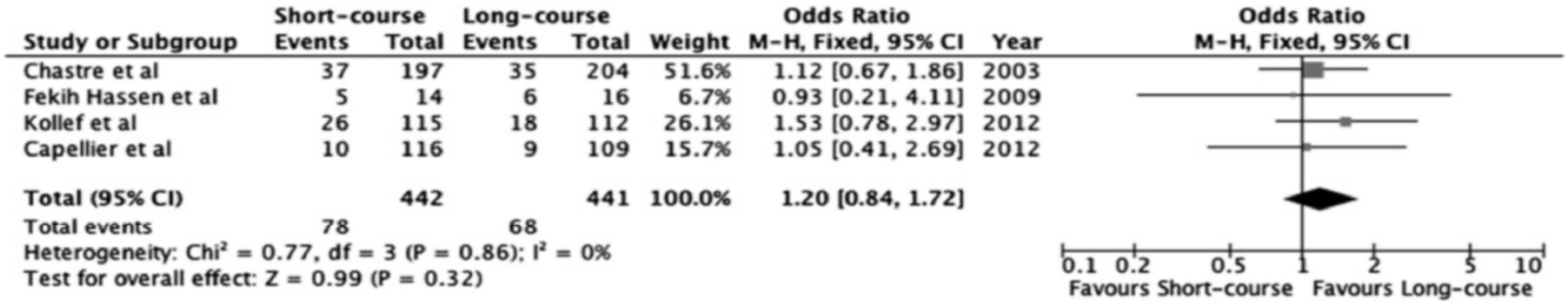
DURATION OF THERAPY: STUDY DESIGN

- Authors: Chastre J, et al. JAMA 2003;290:2988
- Study goal: Compare 8 vs 15 days of therapy for VAP
- Design: Prospective, randomized, double-blind (until day 8), clinical trial
  - VAP diagnosed by quantitative cultures obtained by bronchoscopy
- Location: 51 French ICUs (N=401 patients)
- Outcomes: Assessed 28 days after VAP onset (ITT analysis)
  - Primary measures = death from any cause
  - Microbiologically documented pulmonary infection recurrence
  - Antibiotic free days

DURATION OF THERAPY: RESULTS

- Primary outcomes (8 vs 15 days)
  - Similar mortality, 18.8% vs 17.2%
  - Similar rate of recurrent infection, 28.9% vs 26.0%
    - MRSA, 33.3% vs 42.9%
    - *Nonfermenting GNR, 40.6% vs 25.4%* ($p<0.05$)
  - *More antibiotic free days, 13.1% vs 8.7%* ($p<0.001$)
- Secondary outcomes (8 vs 15 days)
  - Similar mechanical ventilation-free days, 8.7 vs 9.1
  - Similar number of organ failure-free days, 7.5 vs 8.0
  - Similar length of ICU stay, 30.0 vs 27.5
  - Similar frequency death at day 60, 25.4% vs 27.9%
  - *Multi-resistant pathogen (recurrent infection),* 42% v 62% ($p=0.04$)

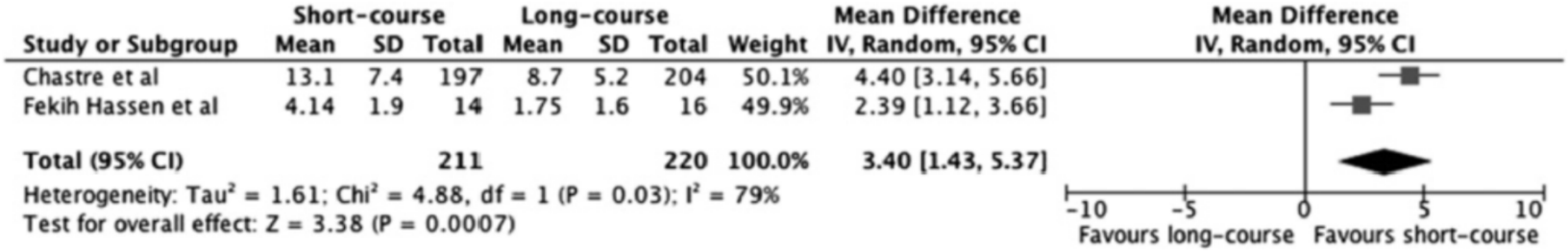
SHORT VS LONG DURATION ANTIBIOTIC THERAPY FOR VAP: A META-ANALYSIS



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)

FIGURE 2. ORs of mortality. Vertical line is the "no difference" point in mortality between the two arms. Horizontal lines are 95% CI. ■ = OR; the size of each square denotes the proportion of information provided by each trial. ◆ = pooled OR for all trials. df = degrees of freedom; M-H = Mantel-Haenszel.



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)

FIGURE 4. Weighted mean difference of antibiotic-free days. Vertical line is the "no difference" point in antibiotic-free days between the two arms. Horizontal lines are 95% CI. See Figure 2 legend for explanation of symbols and expansion of abbreviations.

Dinopoulis G, et al. Chest 2013;144:1759-67

THERAPY: SUMMARY

- Negative lower respiratory tract cultures can be used to stop antibiotic therapy if obtained in the absence of an antibiotic change in past 72 hours
- Early, appropriate, broad spectrum therapy, antibiotic therapy should be prescribed with adequate doses to optimize antimicrobial efficacy
- An empiric therapy regimen should include agents that are from a different antibiotic class than the patient is currently receiving
- Mortality reduced by initial use of appropriate antibiotics
- De-escalation of antibiotic should be considered once data are available on the results of the patient's cultures and clinical response
- A shorter duration of therapy (7-8 days) is recommended for patients with uncomplicated HAP, VAP, or HCAP who have had a good clinical response

RECOMMENDATIONS TO DECREASE RISK OF VAP, US

Recommendation	CDC, 2003	IDSA, 2005	APIC, 2005	SHEA, 2014
Hand hygiene	Yes	Yes	Yes	----
Microbiologic monitoring	Yes	Yes	Yes	Yes
Device removal	----	----	Yes	Yes
Avoid intubation	Yes	Yes	Yes	----
Reduction of antibiotics	----	----	Yes	----
Avoid reintubation	Yes	Yes	----	----
Promote NIV if possible	Yes	Yes	Yes	Yes
Orogastric tube	Yes	Yes	----	----
Cuff pressure (mmHg)	----	20	----	----
Bed elevation	Yes	Yes	Yes	Yes
Subglottic aspiration	No	Yes	Yes	Yes
Oral decontamination	No	No	No	No
Selective gut decontamination	No	No	No	No

Adapted from Passaro L, et al. Antimicrobial Resistance Infect Control 2016;5:43

INFECTION CONTROL AND HOSPITAL EPIDEMIOLOGY AUGUST 2014, VOL. 35, NO. 8

SHEA/IDSA PRACTICE RECOMMENDATION

Strategies to Prevent Ventilator-Associated Pneumonia in Acute Care Hospitals: 2014 Update

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GRADING THE QUALITY OF EVIDENCE

Grade	Definition
I. High	Highly confident that the true effect lies close to that of the estimated size and direction of the effect. Evidence is rated as high quality when there is a wide range of studies with no major limitations, there is little variation between studies, and the summary estimate has a narrow confidence interval.
II. Moderate	The true effect is likely to be close to the estimated size and direction of the effect, but there is a possibility that it is substantially different. Evidence is rated as moderate quality when there are only a few studies and some have limitations but not major flaws, there is some variation between studies, or the confidence interval of the summary estimate is wide.
III. Low	The true effect may be substantially different from the estimated size and direction of the effect. Evidence is rated as low quality when supporting studies have major flaws, there is important variation between studies, the confidence interval of the summary estimate is very wide, or there are no rigorous studies, only expert consensus.

NOTE. Based on Grades of Recommendation, Assessment, Development, and Evaluation (GRADE)[239] and the Canadian Task Force on Preventive Health Care.[240]

PREVENTION OF VAP: BASIC PRACTICES

- Avoid intubation if possible
  - Use noninvasive positive pressure ventilation (NIPPV)
- Minimize sedation
  - Manage ventilated patients without sedatives whenever possible {II}
  - Interrupt sedation once a day (spontaneous awakening trial) for patients with contraindications {I}
  - Assess readiness to extubate once a day (spontaneous breathing trial) in patients without contraindications {I}
- Maintain and improve physical conditioning {II}
- Minimize pooling of secretions above the ET tube
  - Provide ET tubes with subglottic secretion drainage ports for patients likely to require greater than 48-72 hours of intubation {II}

PREVENTION OF VAP: BASIC PRACTICES

- Elevate the head of the bed to 30^{o}-45^{o} {II}
- Maintain ventilator circuits
  - Change the ventilator circuit only if visibly soiled or malfunctioning {I}
  - Followed CDC guidelines for sterilization and disinfection of respiratory care equipment {II}

PREVENTION OF VAP: SPECIAL APPROACHES

- Interventions that decrease duration of mechanical ventilation, length of stay, and/or mortality but for which insufficient data on possible risks are available
  - Selective decontamination of the oropharynx to decrease microbial burden of the aerodigestive tract {I}
- Interventions that may lower VAP rates but for which there are insufficient data at present to determine their impact on duration of mechanical ventilation, length of stay, and mortality
  - Oral care with CHG {II}
  - Prophylactic probiotics {II}
  - Ultrathin polyurethane endotracheal tubes {III}
  - Automated control of endotracheal tube cuff pressure (III}
  - Mechanical tooth brushing {III}

CHG VS PLACEBO FOR ORAL CARE TO REDUCE VAP

- Meta analysis included RCTs evaluating the effects of oral CHG in critically ill patients receiving VAP for ≥48 hours; included 38 RCTs (6016 participants)
- High quality evidence from 18 RCTs (2451 participants, 86% adults) shows that CHX mouthrinse or gel, as part of OHC, reduces the risk of VAP compared to placebo or usual care from 25% to about 19% (RR 0.74, 95% confidence intervals (CI) 0.61 to 0.89, P = 0.002, I2 = 31%).

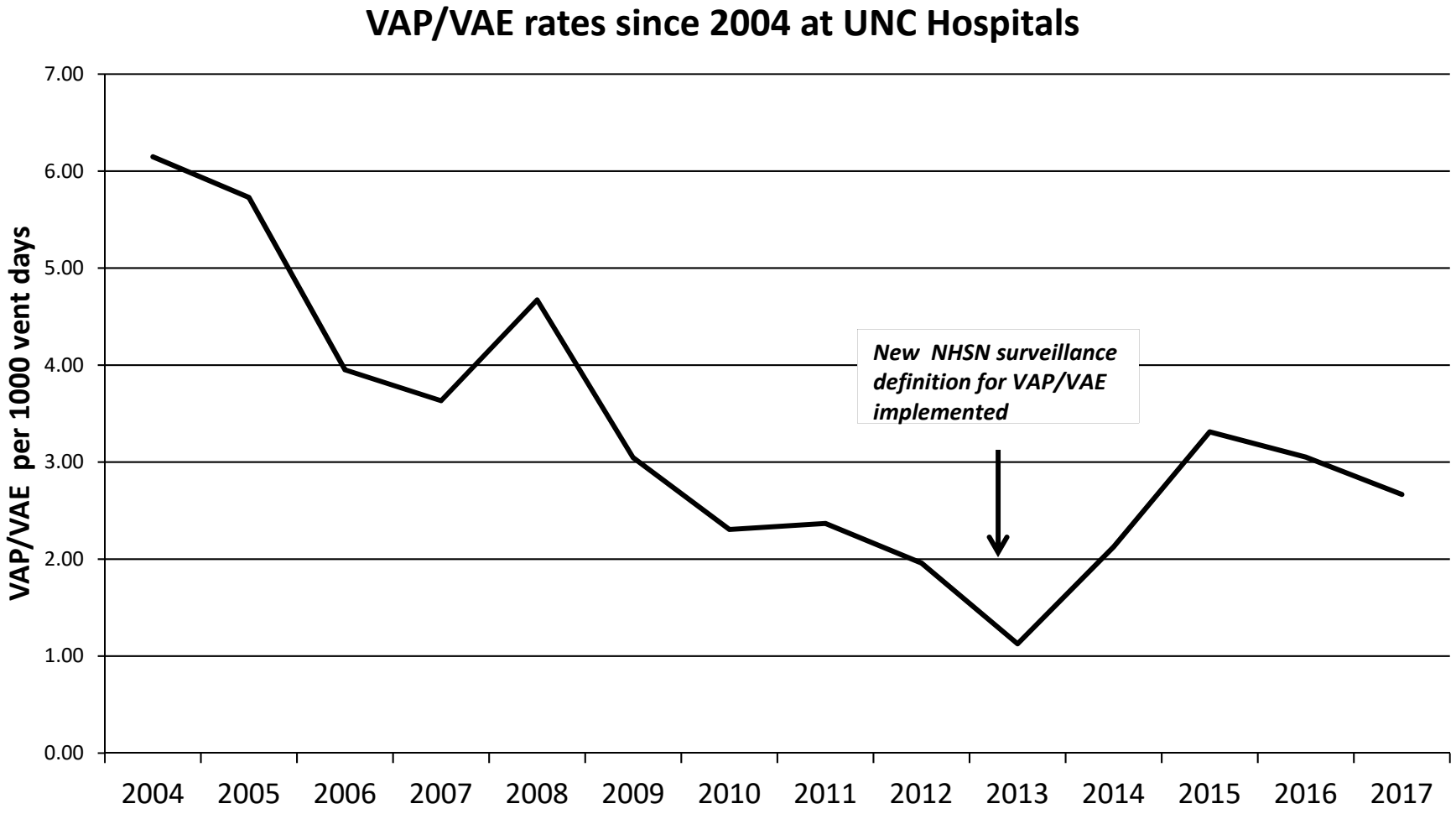
Hua F, et al. Cochrane Database Syst Rev 2016; Oct 25

PREVENTION OF VAP: APPROACHES NOT RECOMMENDED

- Generally not recommended for VAP prevention: interventions that may lower VAP rates but good-quality evidence suggests no impact on duration of mechanical ventilation, length of stay, or mortality
  - Silver-coated endotracheal tubes {II}
  - Kinetic beds and oscillation therapy {II}
  - Prone positioning {II}
- Definitively not recommended for VAP prevention
  - Stress ulcer prophylaxis {II}
  - Early tracheotomy {I}
  - Monitoring residual gastric volumes {II}
  - Early parenteral nutrition {II}

TABLE 2. Summary of Recommendations for Preventing Ventilator-Associated Pneumonia (VAP) in Adult Patients

Recommendation	Rationale	Intervention	Quality of evidence
Basic practices	Good evidence that the intervention decreases the average duration of mechanical ventilation, length of stay, mortality, and/or costs; benefits likely outweigh risks	Use noninvasive positive pressure ventilation in selected populations[57,58]	High
		Manage patients without sedation whenever possible[46,61]	Moderate
		Interrupt sedation daily[62]	High
		Assess readiness to extubate daily[47,66-68]	High
		Perform spontaneous breathing trials with sedatives turned off[48]	High
		Facilitate early mobility[49,70-75,78]	Moderate
		Utilize endotracheal tubes with subglottic secretion drainage ports for patients expected to require greater than 48 or 72 hours of mechanical ventilation[50]	Moderate
		Change the ventilator circuit only if visibly soiled or malfunctioning[88-91]	High
		Elevate the head of the bed to 30°–45°[84-86]	Low[a]
Special approaches	Good evidence that the intervention improves outcomes but insufficient data available on possible risks	Selective oral or digestive decontamination[93-96]	High[b]
	May lower VAP rates but insufficient data to determine impact on duration of mechanical ventilation, length of stay, or mortality	Regular oral care with chlorhexidine[98,101-104]	Moderate
		Prophylactic probiotics[111-114]	Moderate
		Ultrathin polyurethane endotracheal tube cuffs[120,121]	Low
		Automated control of endotracheal tube cuff pressure[122,123]	Low
		Saline instillation before tracheal suctioning[124]	Low
		Mechanical tooth brushing[125,126]	Low
Generally not recommended	Lowers VAP rates but ample data suggest no impact on duration of mechanical ventilation, length of stay, or mortality	Silver-coated endotracheal tubes[127]	Moderate
		Kinetic beds[128]	Moderate
		Prone positioning[87,129-134,c]	Moderate
	No impact on VAP rates, average duration of mechanical ventilation, length of stay, or mortality[c]	Stress ulcer prophylaxis[135,136]	Moderate
		Early tracheotomy[137]	High
		Monitoring residual gastric volumes[138]	Moderate
		Early parenteral nutrition[139]	Moderate
No recommendation	No impact on VAP rates or other patient outcomes, unclear impact on costs	Closed/in-line endotracheal suctioning[141-143]	Moderate



*The new VAP/VAE definition implemented Jan 2013 is more specific than the previous definition, so it is harder to meet criteria; this definition change likely led to a decrease in the number of VAPs in 2013, and an increase in the number of tracheobronchitis infections. *Beginning July 1, 2014, if an infection did not meet the NHSN VAE definition, IPs investigated whether it met the NHSN previously used VAP definition. Therefore, there is an increase in the number of VAP/VAE infections reported since 2014. Of note, in 2017, there were 12 infections classified as VAE and 47 infections that met the VAP definition.*

CONCLUSIONS I

- Nosocomial pneumonia remains an important cause of patient morbidity and mortality in the US
- Nosocomial pneumonia results in a more prolonged hospital stay and increased cost
- Local epidemiology of pathogens and antibiograms are critical to empiric and directed chemotherapy
- Determining the etiologic agent(s) of nosocomial pneumonia is problematic even with new invasive diagnostic techniques

CONCLUSIONS II

- Use of empiric, broad-spectrum regimens remain critical to favorable patient outcomes
- Single-drug regimens may be appropriate for some low-risk patients, but two-drug regimens with broad spectrum (including *P. aeruginosa*) are necessary for high-risk patients
- Prevention is superior to treatment

THANK YOU!!