HEALTHCARE-ASSOCIATED PNEUMONIA: DIAGNOSIS, TREATMENT & PREVENTION

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GOALS OF LECTURE

- Understand the methods to diagnose nosocomial pneumonia
- Review the treatment of nosocomial pneumonia
- Discuss the methods to prevent nosocomial pneumonia based on the SHEA Guideline

DIAGNOSIS

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

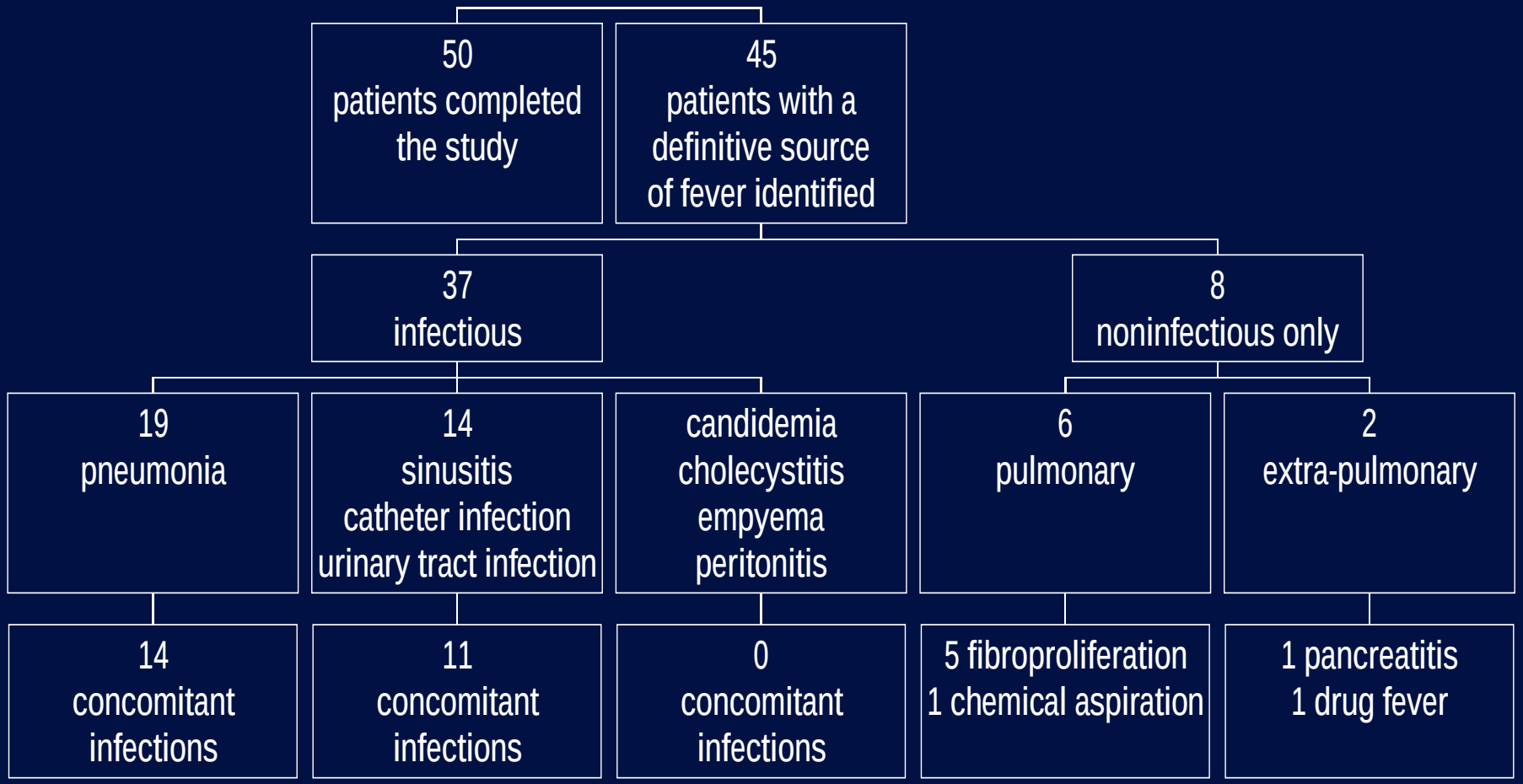
- Symptoms and signs: Fever, respiratory distress
- Chest radiography: Infiltrate, consolidation, cavity
- Laboratory: Leukocytosis, leukopenia
- Sputum: Purulence (WBC), culture
- Clinical diagnosis (ATS/IDSA)
  - New or progressive infiltrate
  - ≥2 of the following: Temperature >38 ^{o}C, leukocytosis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

DIAGNOSING NOSOCOMIAL PNEUMONIA (Meduri G, et al. Chest 1994;106:221)



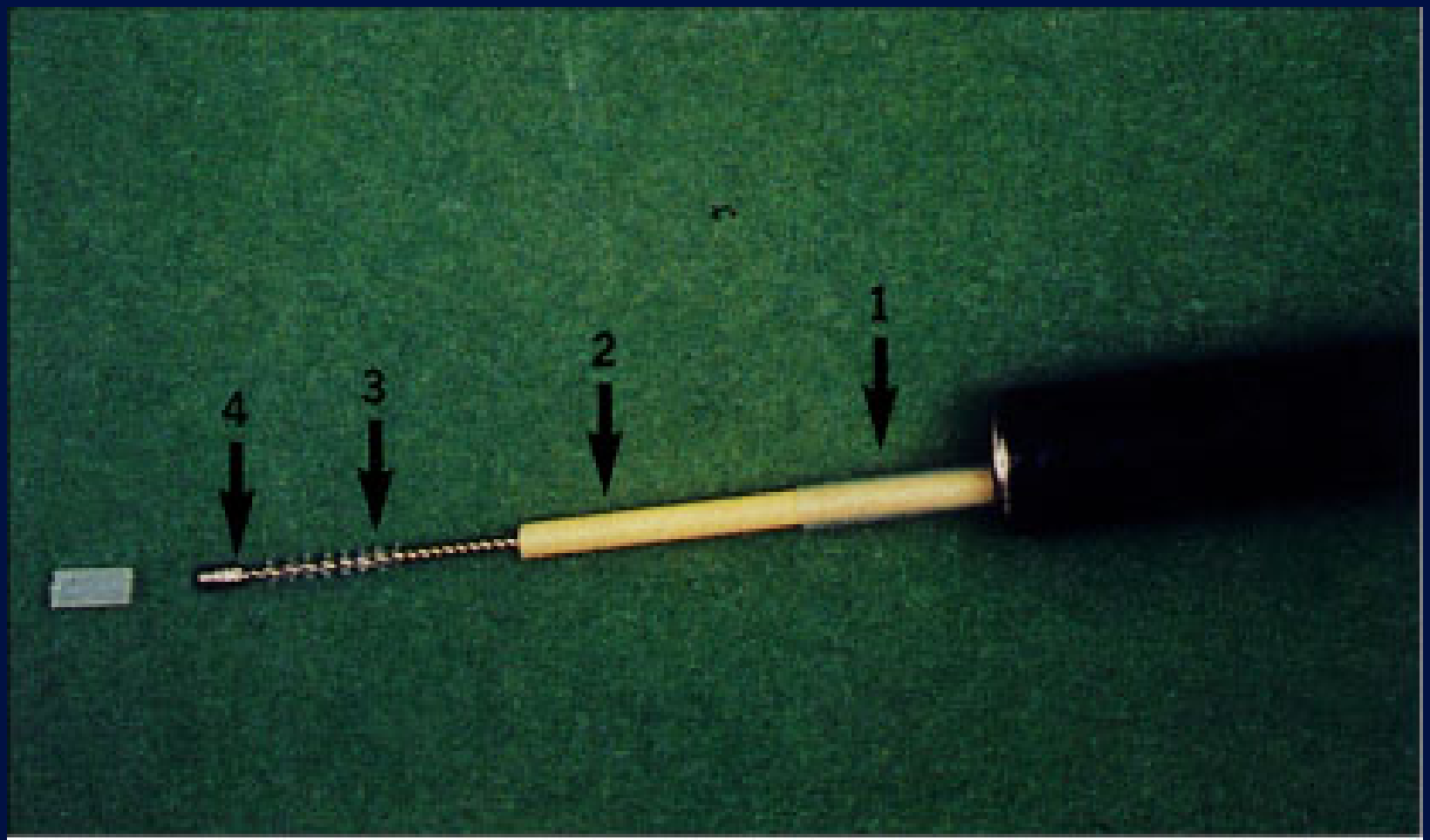
INDICATIONS FOR INVASIVE DIAGNOSIS

- 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)

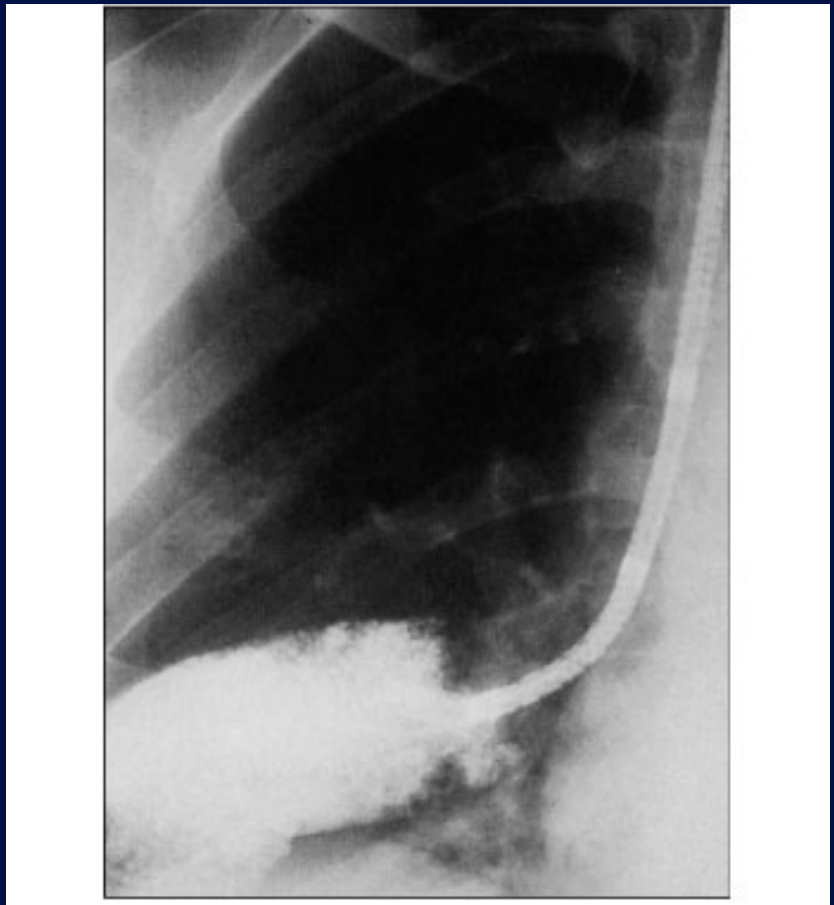
ASSESSMENT OF THE ADVANTAGES AND DISADVANTAGES OF THE DIFFERENT TECHNIQUES USED TO OBTAIN RESPIRATORY SECRETIONS FROM PATIENTS WHO HAVE SUSPECTED HAP

		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		++++	++++	+++	++++	++++

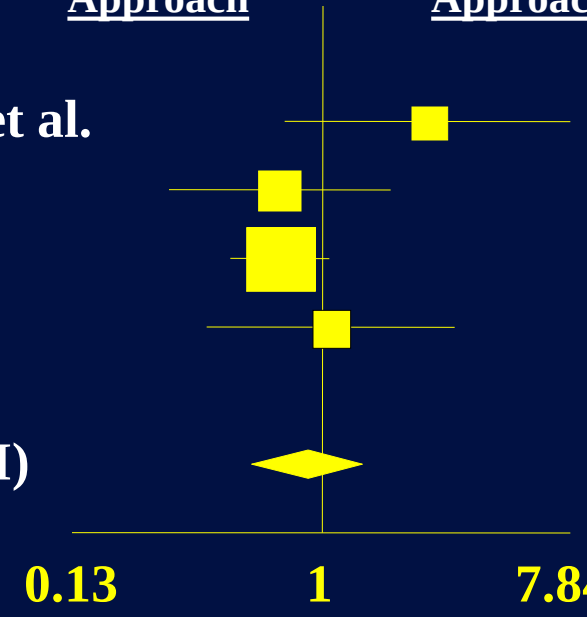
PROTECTED SPECIMEN BRUSH



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

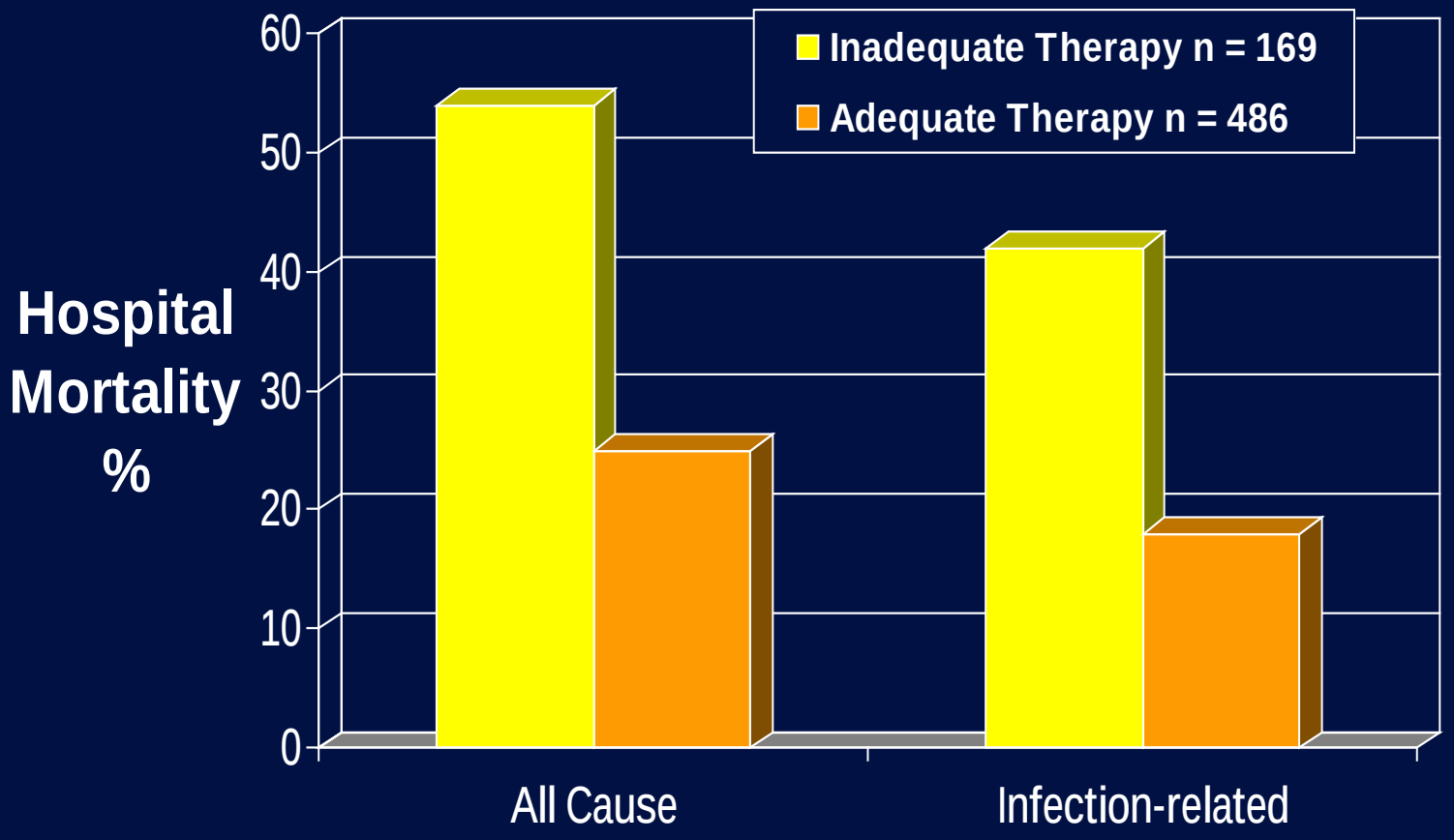
Shorr A, Kollef. MH Crit Care Med 2005;33:46.

TREATMENT

EMPIRIC THERAPY: GENERAL RULES

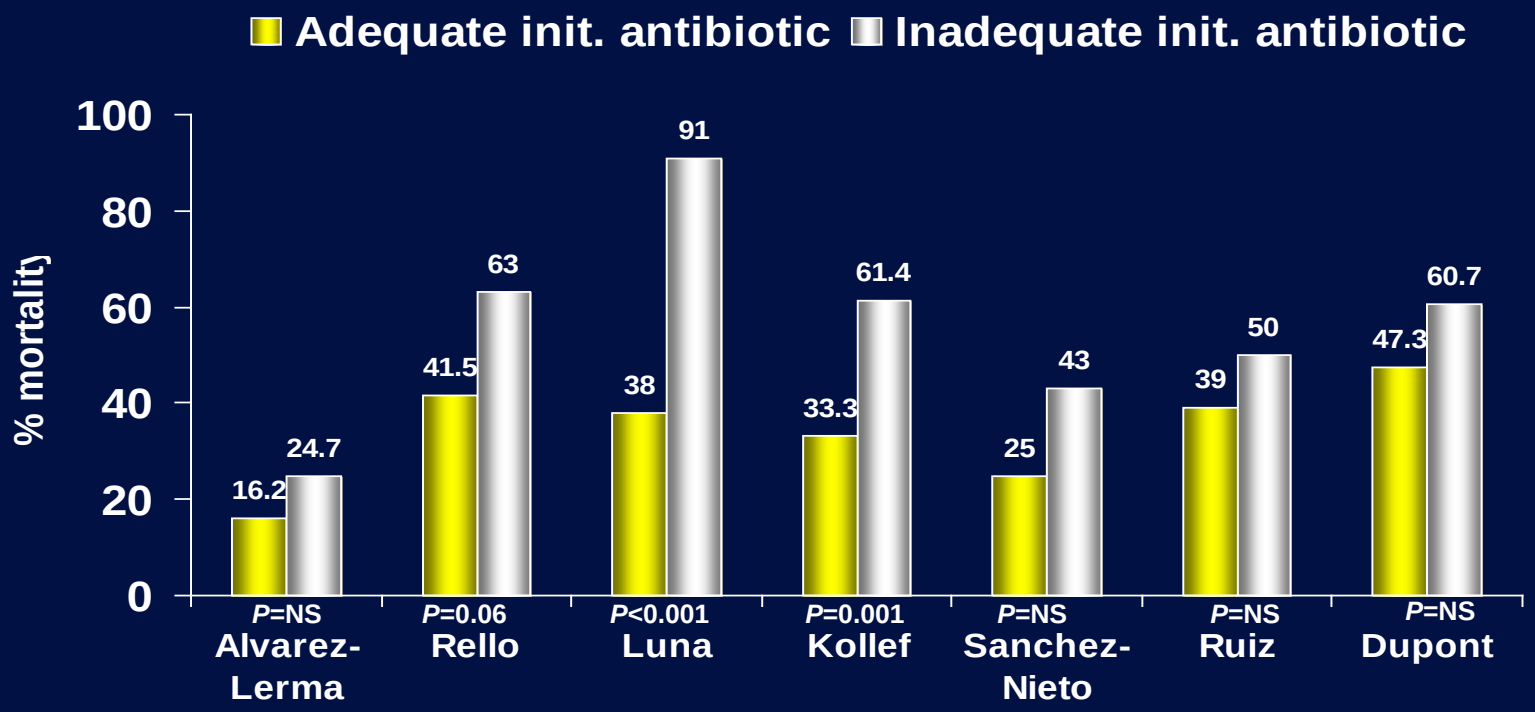
- Know the flora and susceptibilities of the pathogens causing nosocomial pneumonia at your own institution
- Obtain history of antibiotic-allergies from all patients (adjust regimen appropriately)
- Choose empiric therapy to minimize drug interactions
- Dose adjust (when appropriate) in patients with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

IMPACT OF ANTIMICROBIALS

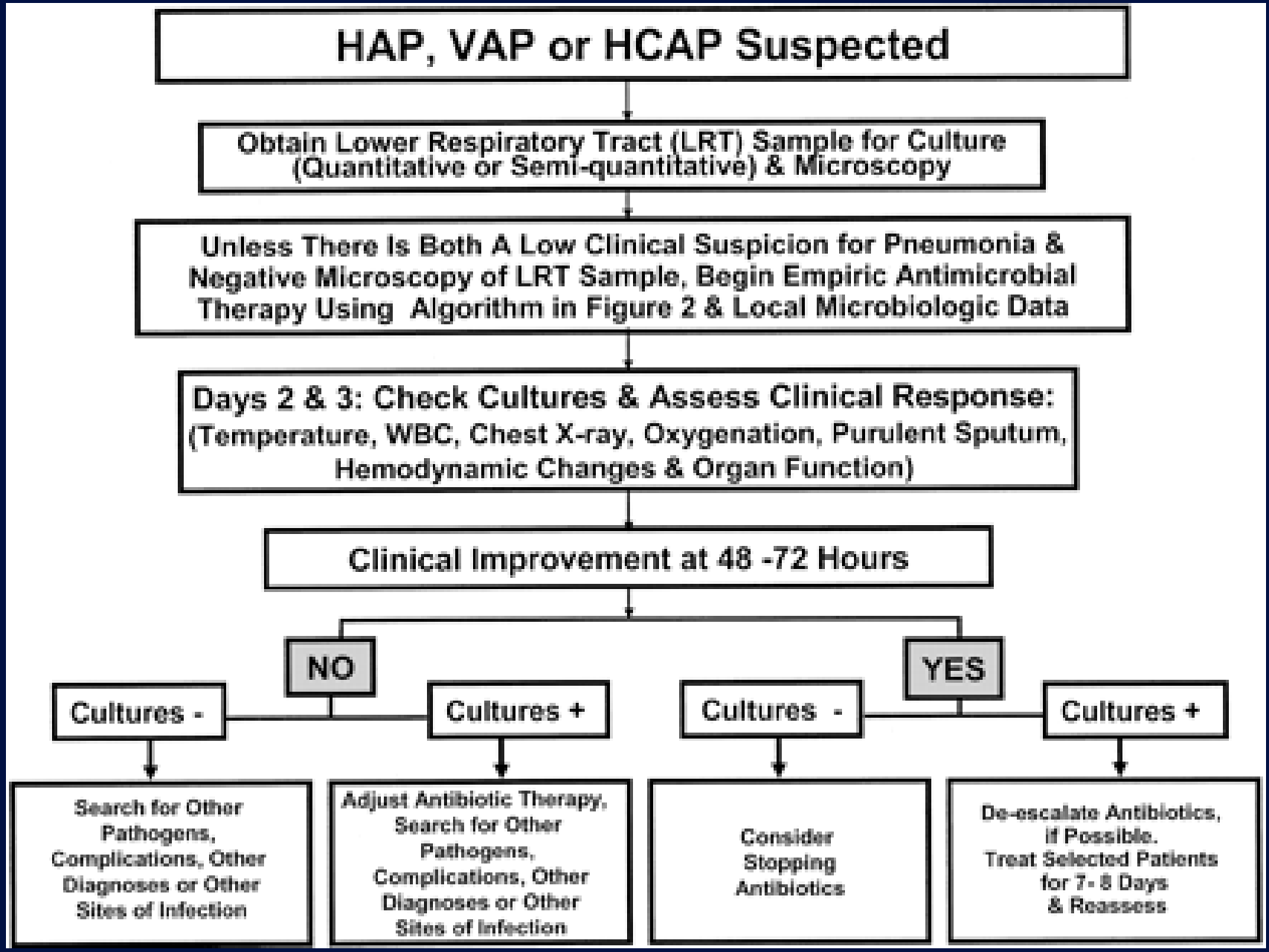


Kollef *Chest* 115:462, 1999

HAP: The Importance of Initial Empiric Antibiotic Selection

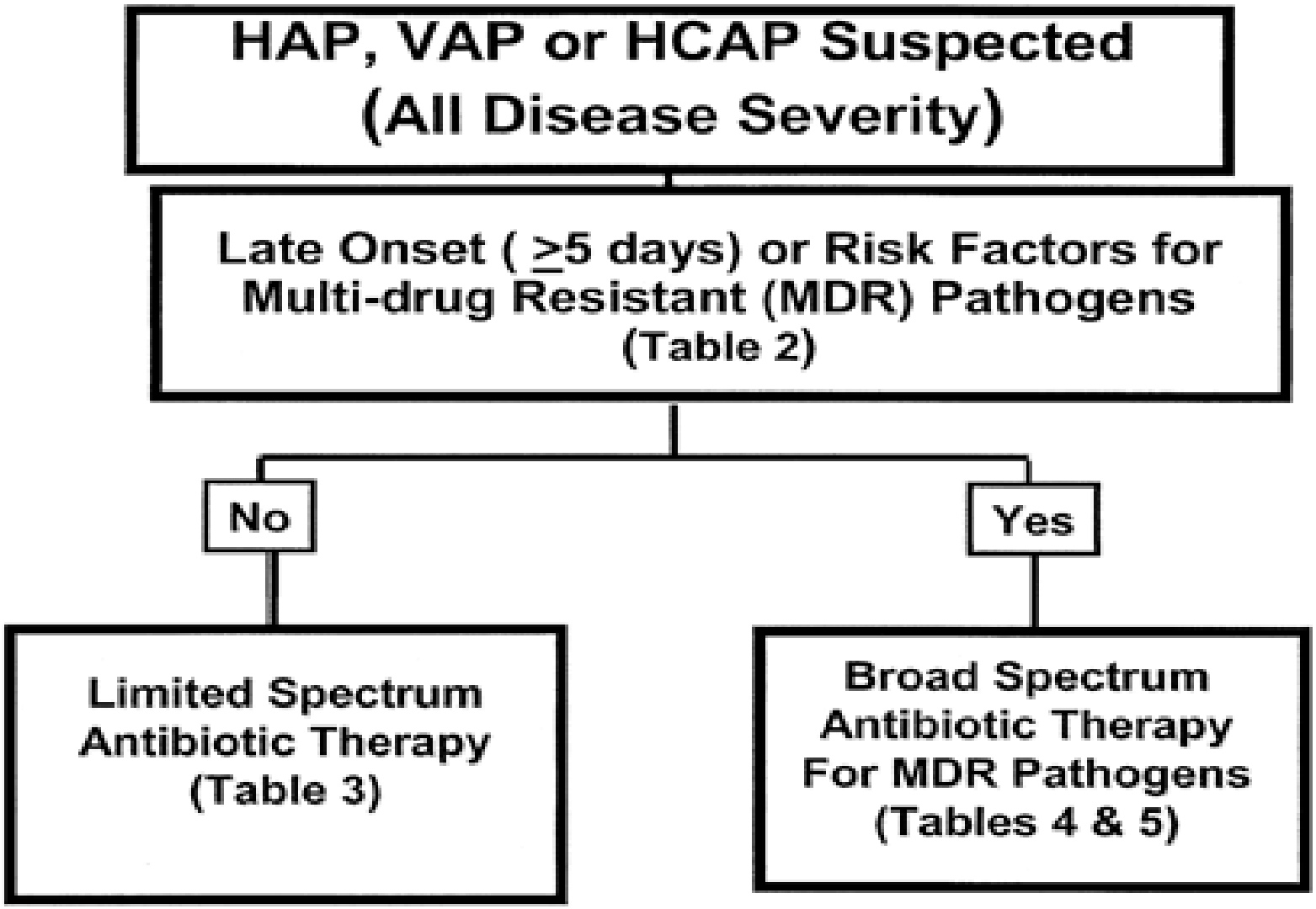


Alvarez-Lerma F. *Intensive Care Med* 1996 May;22(5):387-394.
Rello J, Gallego M, Mariscal D, et al. *Am J Respir Crit Care Med* 1997 Jul;156(1):196-200.
Luna CM, Vujacich P, Niederman MS, et al. *Chest* 1997;111(3):676-685.
Kollef MH and Ward S. *Chest* 1998 Feb;113(2):412-20.
Sanchez-Nieto JM, Torres 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

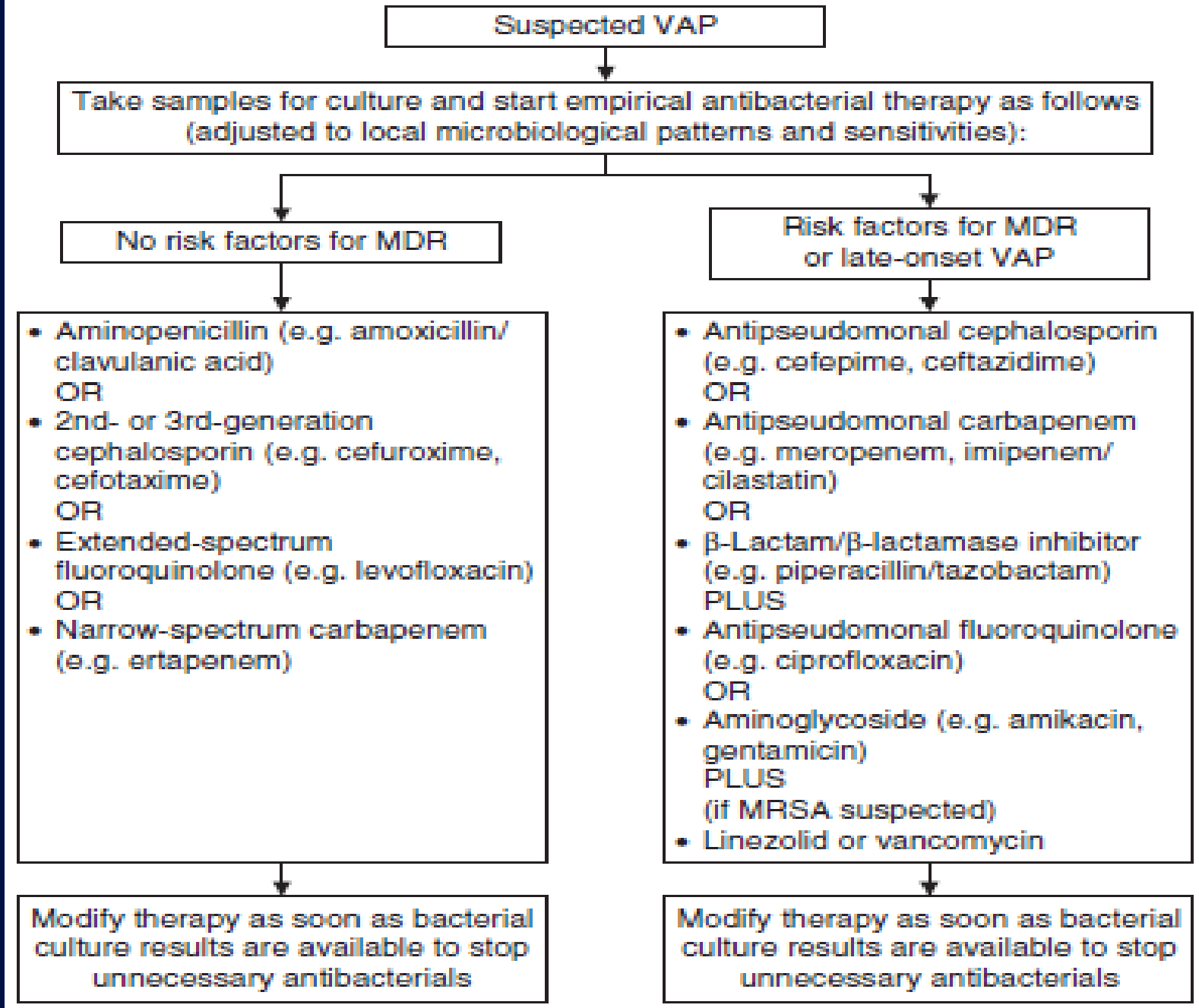


ATS/IDSA. Am J Respir Crit Care Med 2005;171:388-416

Empiric Antibiotic Therapy for HAP



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



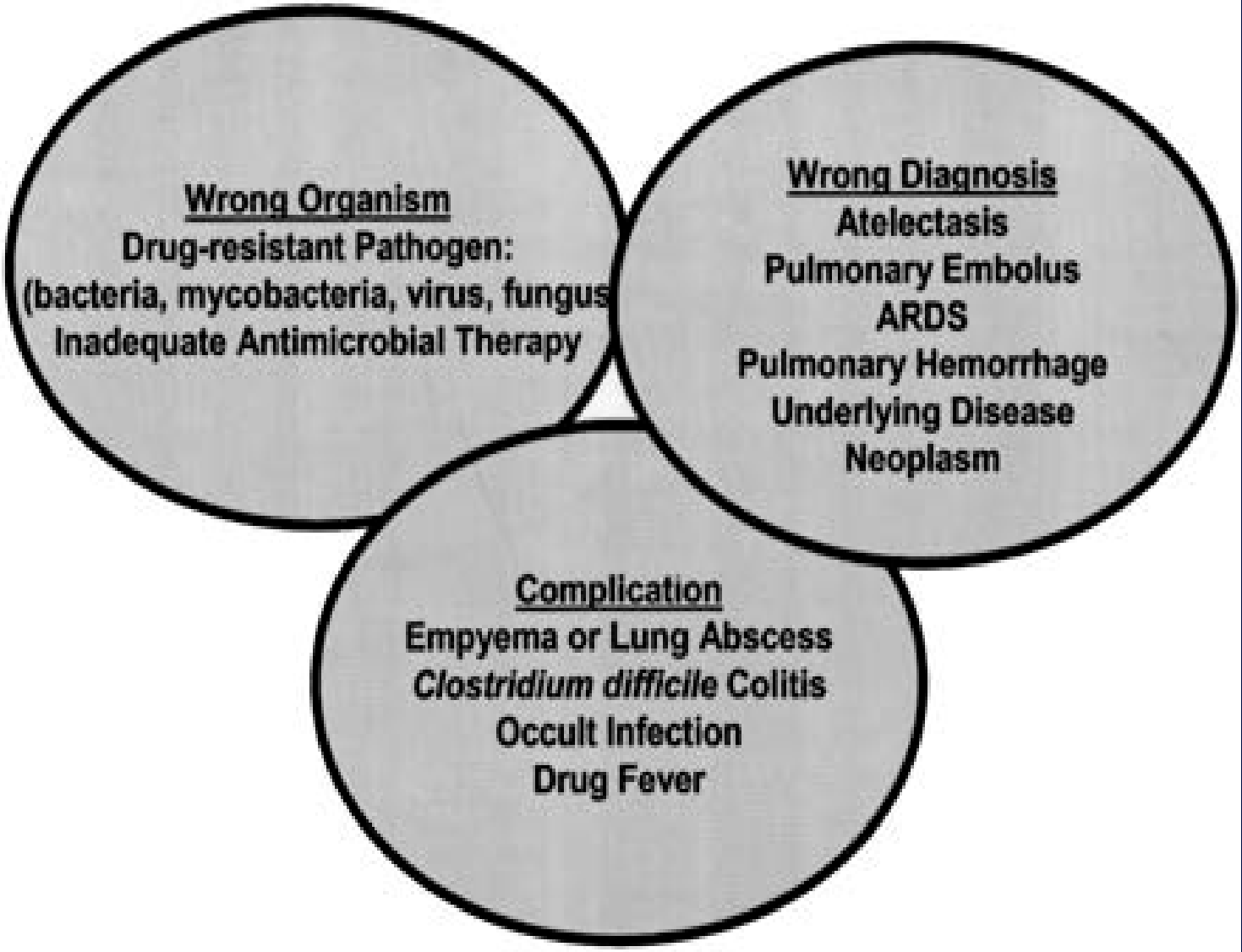
Vincent J-L, et al. Drugs 2010;70:1927-1944

RISK FACTORS FOR MDR-PATHOGENS CAUSING HAP

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

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

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 pulmonry 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% ($p=0.04$)

THERAPY: SUMMARY I

- 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
- 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

THERAPY: SUMMARY II

- Low risk patients
  - Single-drug, broad spectrum therapy adequate
    - Ceftriaxone (3rd generation cephalosporin)
    - Ertapenem (carbapenem)
    - Ampicillin/sulbactam (β-lactam/β -lactamase inhibitor combination)
    - Ciprofloraxin, Levofloxacin, Moxifloxacin (fluoroquinolone)
  - Therapy directed by local epidemiology and costs

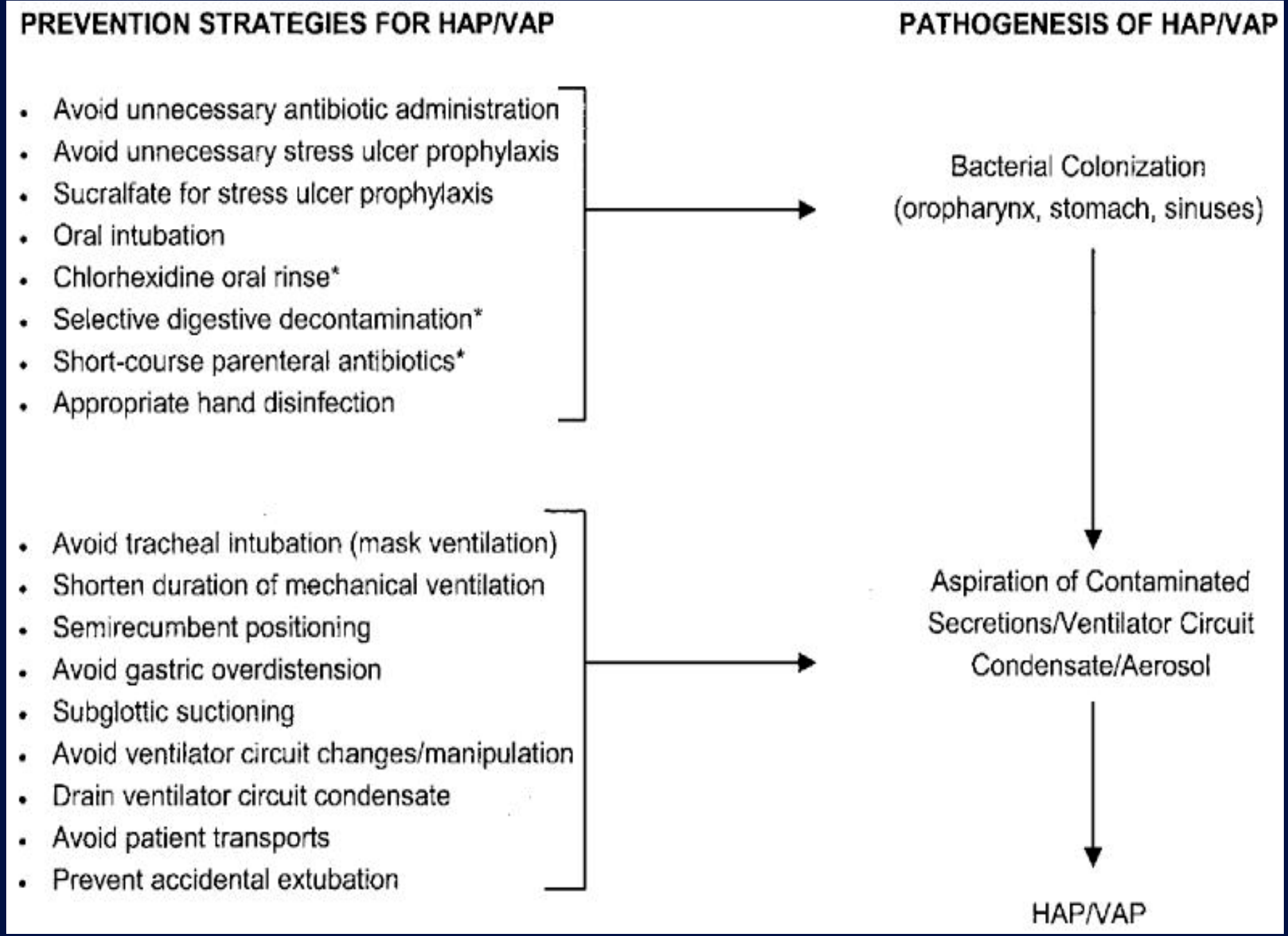
THERAPY: SUMMARY III

- High risk patients
  - Multiple-drug regimens required
  - Combine beta-lactam with aminoglycoside (preferred) or quinolone (levo or cipro)
  - Consider need for coverage of oxacillin-resistant *S. aureus*, *Legionella*

THERAPY: SUMMARY IV

- Bronchoscopy directed therapy
  - May improve outcome
    - Demonstrated by a randomized study
    - Several cohort studies have failed to demonstrated benefit
- Mortality reduced by initial use of appropriate antibiotics
- Duration of therapy, in general, should be 7-8 days

PREVENTION



Kollef M. Chest 2004;32:1396

Table 4. Pharmacologic-based strategies for VAP prevention

Strategy	Recommendation	Evidence Level	Reference(s)
Topical iseganan	No	1	51
Orodigestive decontamination (topical/topical plus intravenous antibiotics)	No recommendation	1	52, 53
Oral chlorhexidine	Yes	1	54, 55
Aerosolized antibiotics	No recommendation	1	56, 57
Intravenous antibiotics	No recommendation	1	58
Specific stress ulcer prophylaxis regimen	No	1	60
Short-course antibiotic therapy (when clinically applicable)	Yes	1	61–63
Routine antibiotic cycling/rotation/heterogeneity[a]	No	2	64–66
Restricted (conservative) blood transfusion	Yes	2	67–69
Vaccines (influenza, pneumococcal)[b]	Yes	1	71, 72

VAP, ventilator-associated pneumonia.

[a]May be useful in specific clinical circumstances (as an adjunct to controlling an outbreak of a multidrug-resistant bacterial infection); [b]general recommendation without specific evidence for VAP. Evidence levels: 1, supported by randomized trials; 2, supported by prospective or retrospective cohort studies; 3, supported by case series.

Morrow LE, Kollef MH. Crit Care Med 2010;38[suppl]:S352-352

Table 5. Nonpharmacologic-based strategies for VAP prevention

Strategy	Recommendation	Evidence Level	Reference
Use of noninvasive mask ventilation	Yes	1	75–77
Avoid reintubation	Yes	2	78
Avoid patient transports	Yes	2	79
Orotracheal intubation preferred	Yes	1	80
Orogastric intubation preferred	Yes	2	81
Routine ventilator circuit changes	No	1	82, 83
Use of heat-moisture exchanger	Yes	1	85–87
Closed endotracheal suctioning	Yes	1	90, 91
Subglottic secretion drainage	Yes	1	93–95
Shortening the duration of mechanical ventilation	Yes	1	99, 100
Adequate intensive care unit staffing	Yes	2	101, 102
Silver-coated endotracheal tube	Yes	1	104, 105
Polyurethane endotracheal tube cuff	Yes	1	106, 107
Semierect positioning	Yes	1	108, 109
Rotational beds	Yes	1	110–112
Chest physiotherapy	No	1	113–115
Early tracheostomy	No recommendation	1	116–118
Use of protocols/bundles	Yes	2	119–121

VAP, ventilator-associated pneumonia.

Evidence levels: 1, supported by randomized trials; 2, supported by prospective or retrospective cohort studies; 3, supported by case series.

Morrow LE, Kollef MH. Crit Care Med 2010;38[suppl]:S352-352

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

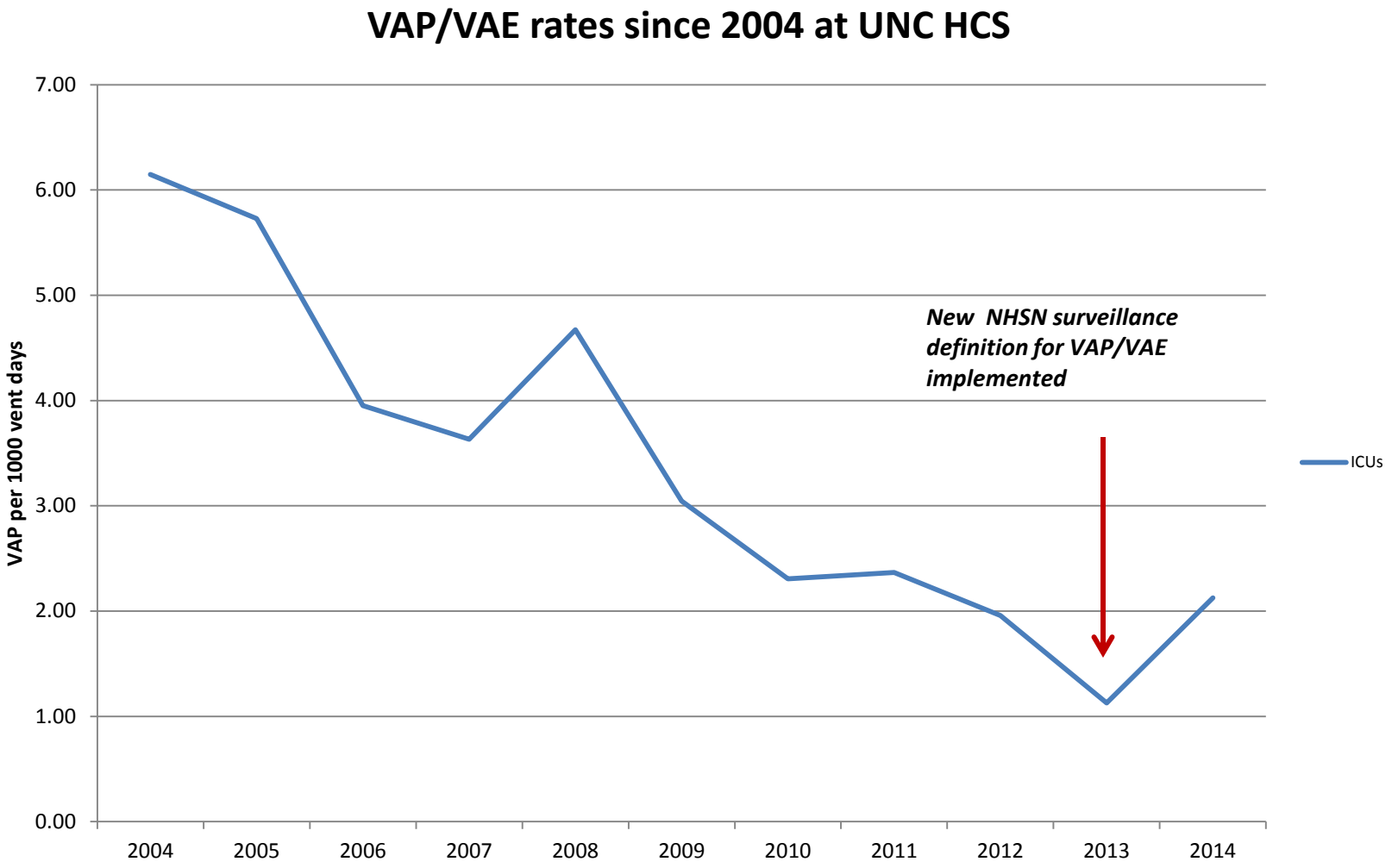
- Interventions that decrease duration of mechanical ventilation, length of stay, and/or mortality but for which insufficient data on possible risks are available
  - Selective decontamination of the oropharynx to decrease microbial burden of the aerodigestive tract {I}
- Interventions that may lower 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}

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 in 2014.*

CONCLUSIONS

- 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
- 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