

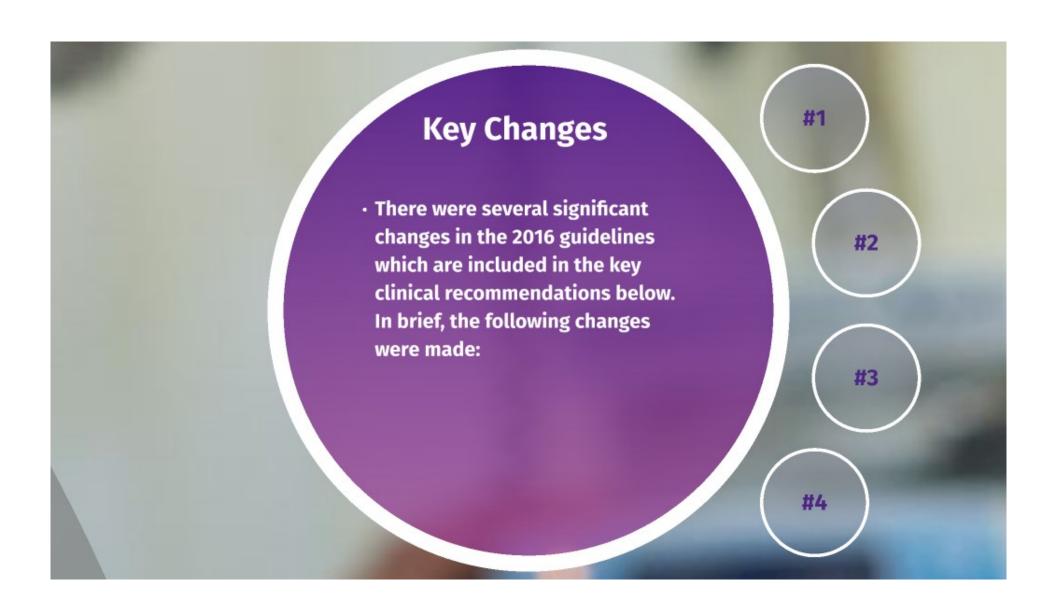
About the Guideline

- The 2016 clinical practice guidelines for management of adults with hospital-acquired pneumonia (HAP) and ventilator-associated pneumonia (VAP) were developed collaboratively by the IDSA and the ATS to provide recommendations for the diagnosis and management of adults with HAP/VAP.
- The 2016 guidelines serve as an update to the Guidelines for the Management of Adults with Hospital-acquired, Ventilator-associated, and Healthcare-associated Pneumonia published in 2005 by the IDSA and the ATS.

About the Guideline (cont'd.)

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 Hospital-acquired infections, including HAP and VAP, remain a significant complication of receiving care in a hospital setting and in the intensive care unit (ICU). The most recent guideline provides evidence-based recommendations based on updated scientific knowledge regarding the best diagnostic and treatment approaches for HAP and VAP.



1. The term healthcare-associated pneumonia (HCAP) was eliminated, and replaced with the following terms (Kalil et al. 2016):

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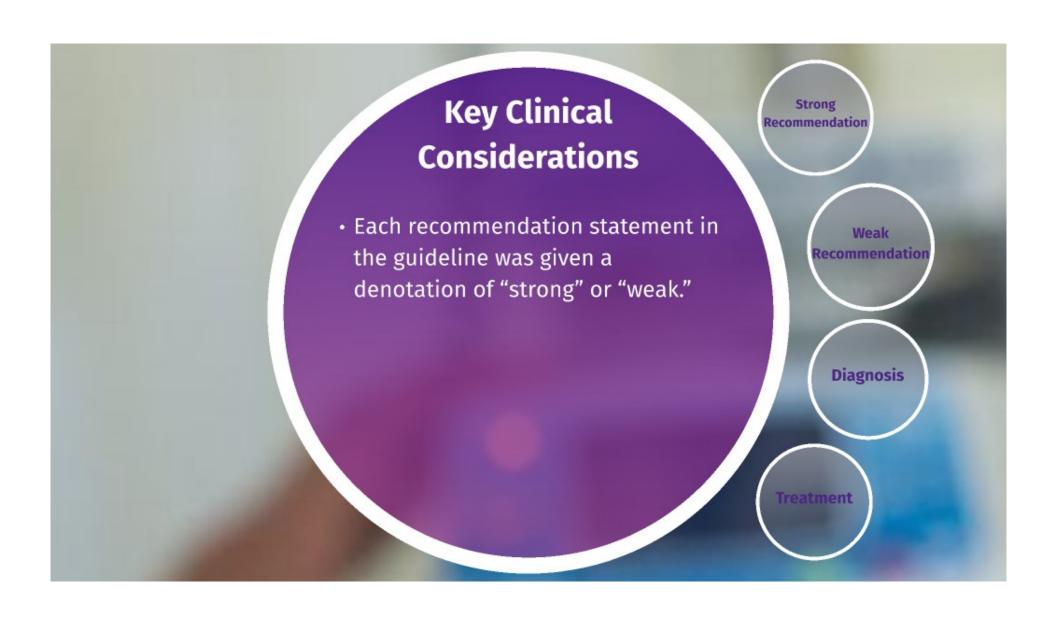
- Hospital-acquired pneumonia (HAP) an episode of pneumonia not associated with mechanical ventilation, AND
- Ventilator-associated pneumonia (VAP) HAP in a patient being mechanically ventilated.

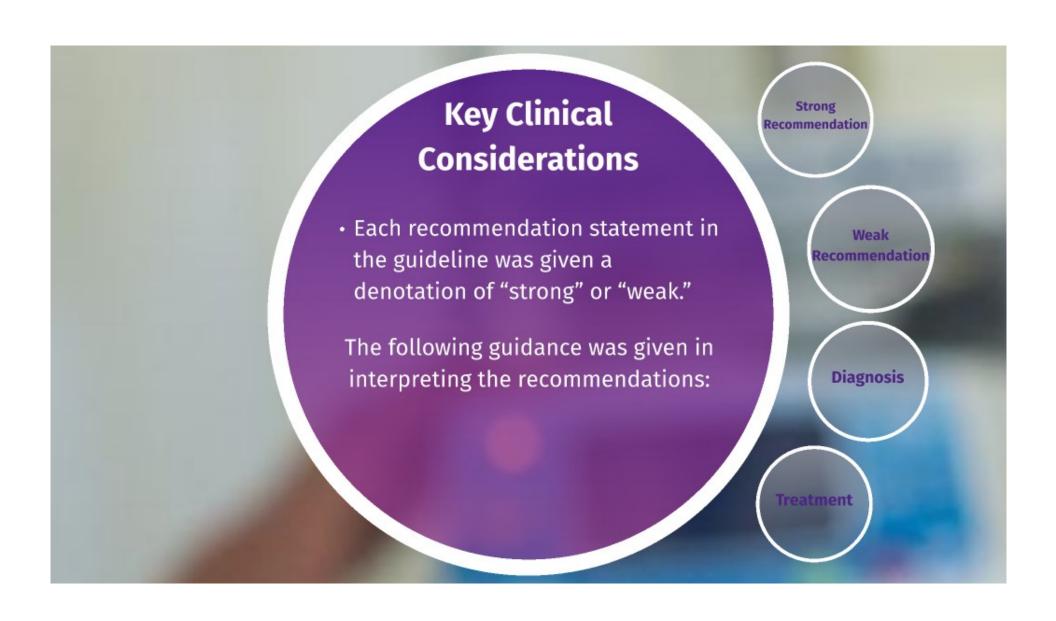
2. Recommendation that hospitals create antibiograms to guide treatment individualized to the local patterns of organisms and resistance patterns.

3. The development and use of antibiograms to decrease administration of unnecessary antibiotics, and specifically, to decrease potentially inappropriate/unnecessary double coverage of gramnegative organisms and methicillinresistant *Staphylococcus aureus* (MRSA).

4. The support of a shorter course of antibiotics for HAP/VAP with prompt de-escalation when clinically applicable.

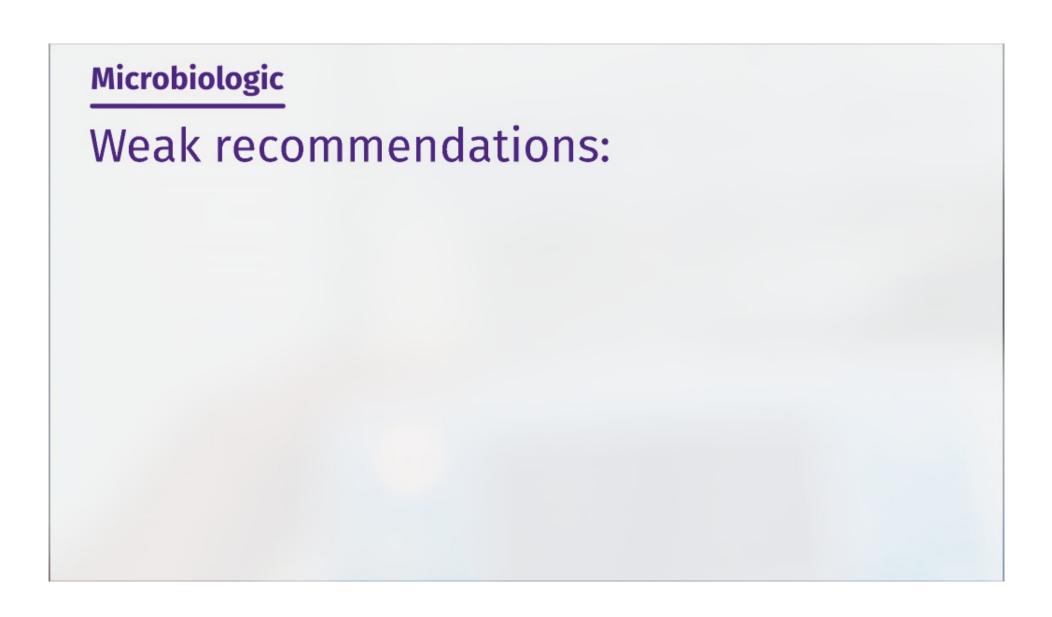






 Strong: recommended for most patients; the data supporting the recommendation is robust enough to support healthcare organizations/clinicians to use the recommendation as a quality measure in the delivery of care for patients with VAP or HAP.





Microbiologic

Weak recommendations:

1. The use of noninvasive sampling (endotracheal aspiration) with semi-quantitative cultures to diagnose VAP is preferred over invasive sampling (bronchoscopy, bronchial sampling) with quantitative cultures, or noninvasive sampling with quantitative cultures.

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- 2. If invasive sampling is obtained and culture results are below the diagnostic threshold for VAP, antibiotics should be withheld, if withholding is supported by clinical factors (i.e. alternative source of infection, clinical evidence of improvement).

Microbiologic

Weak recommendations:

- The use of noninvasive sampling (endotracheal aspiration) with semi-quantitative cultures to diagnose VAP is preferred over invasive sampling (bronchoscopy, bronchial sampling) with quantitative cultures, or noninvasive sampling with quantitative cultures.
- 2. If invasive sampling is obtained and culture results are below the diagnostic threshold for VAP, antibiotics should be withheld, if withholding is supported by clinical factors (i.e. alternative source of infection, clinical evidence of improvement).
- 3. For patients with suspected HAP (non-VAP), treatment should be guided by non-invasive microbiologic results rather than empiric treatment. Non-invasive studies include an expectorated sputum sample (either induced or spontaneous), nasotracheal suctioning, or endotracheal aspirate (in those with HAP who require mechanical ventilation).

Biomarkers Strong recommendations:

Strong recommendations:

 Procalcitonin: Use clinical criteria alone, rather than procalcitonin (PCT) and clinical criteria, to guide initiation of antibiotic therapy in patients with HAP/VAP.

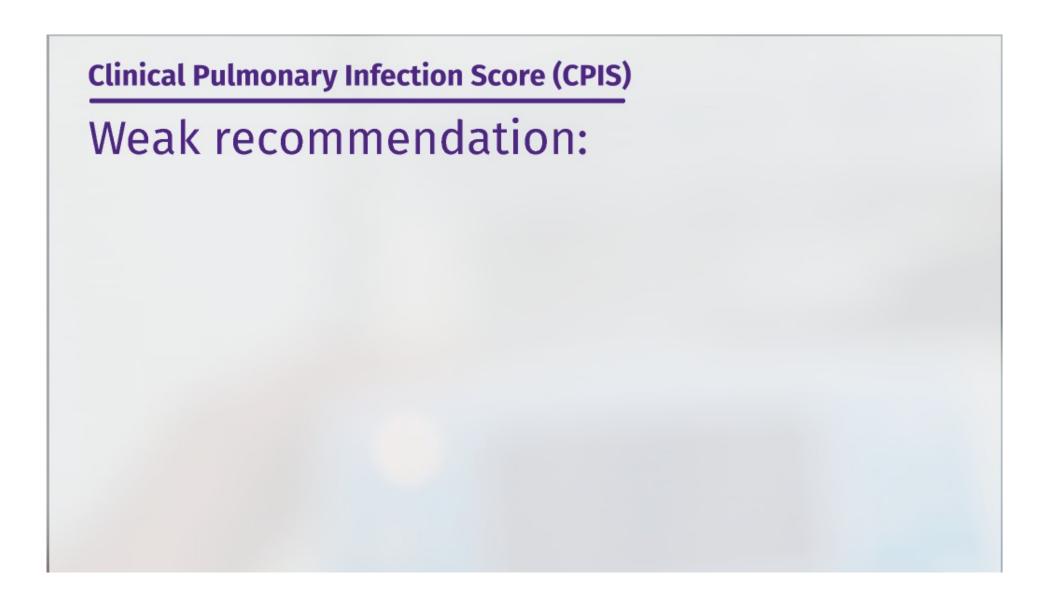
Strong recommendations:

- Procalcitonin: Use clinical criteria alone, rather than procalcitonin (PCT) and clinical criteria, to guide initiation of antibiotic therapy in patients with HAP/VAP.
- Soluble triggering receptor expressed on myeloid cells (sTREM-1):
 Use clinical criteria alone, rather than bronchoalveolar lavage fluid
 (BALF) sTREM-1 plus clinical criteria, to guide initiation of antibiotic
 therapy in patients with HAP/VAP.

Weak recommendations:

Weak recommendations:

1. Use clinical criteria alone, rather than C-reactive protein (CRP) plus clinical criteria, to guide initiation of antibiotic therapy in those with HAP/VAP.



Clinical Pulmonary Infection Score (CPIS)

Weak recommendation:

1. CPIS: Use clinical criteria alone rather than CPIS plus clinical criteria to guide initiation of antibiotic therapy for those with HAP/VAP.



Ventilator-associated tracheobronchitis (VAT)

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Weak recommendation: For patients with VAT, antibiotic therapy should not be initiated.

General recommendations for HAP/VAP

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- Antibiotic treatment should be guided by local antibiotic resistant patterns.
 - When possible, hospitals should generate and distribute local antibiograms specific to the intensive care populations. They should be updated at regular intervals and guided by each individual institution.
 - An empiric treatment regimen should be guided by antibiograms with a
 goal of targeting local distribution of pathogens and antimicrobial
 susceptibilities (Kalil et al. 2016), minimizing inappropriate antibiotic use,
 and targeting the narrowest specific pathogens for VAP and HAP.

Ventilator-associated pneumonia

Empiric antibiotic treatment

*Risk factors for multi-drug resistant (MDR) pathogens (Kalil et al. 2016)

Rick factors for MIDR VAR

- IV antibiotic therapy in prior 90 days
- Septic shock at time of VAP
- Adult respiratory distress syndrome (ARDS) preceding VAP
- Hospitalization of five or more days preceding onset of VAP
- Acute renal replacement therapy prior to VAP onset

Risk factors for MDR HAP

- IV antibiotic therapy in prior 90 days

Risk factors for MRSA VAP or HAP

- IV antibiotic therapy in prior 90 days

Risk factors for MDR Pseudomonas VAP or HAP

- IV antibiotic therapy in prior 90 days

Empiric antibiotic treatment

1. For empiric treatment of VAP include coverage for Staphylococcus aureus (S. aureus), Pseudomonas aeruginosa and other gramnegative bacilli (strong recommendation).

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 Include coverage for methicillin-resistant S. aureus (MRSA) for patients at risk for multi-drug resistant (MDR) organisms*, where local distribution of S. aureus is > 10% to 20% MRSA, and in units where MRSA prevalence is unknown; otherwise, cover for methicillin-sensitive S. aureus (MSSA) only (weak recommendation).

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continue ->

Empiric antibiotic treatment

 If coverage for MRSA is indicated, include either vancomycin or linezolid (strong recommendation).

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Recommended dosing:

Empiric antibiotic treatment

 If coverage for MRSA is indicated, include either vancomycin or linezolid (strong recommendation).

Recommended dosing:

- Vancomycin 15 mg/kg IV every 8–12 hours (consider a one-time loading dose of 25–30 mg/kg for severe illness).
- Linezolid 600 mg IV every 12 hours.

Empiric antibiotic treatment

 Treat with an agent active against MSSA if no MRSA risk factors are identified; use piperacillin-tazobactam, cefepime, levofloxacin, imipenem, or meropenem (weak recommendation).

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Recommended dosing:

- Piperacillin-tazobactam 4.5 g IV every 6 hours
- Cefepime 2 g IV every 8 hours
- Levofloxacin 750 mg IV daily
- Imipenem 500 mg IV every 6 hours
- Meropenem 1 g IV every 8 hours
- Although nafcillin, oxacillin, or cefazolin are preferred agents for MSSA, they are not necessary for treatment of VAP if one of the above agents is used (Kalil et al. 2016).

Empiric antibiotic treatment

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continue ->

Empiric antibiotic treatment

 For patients with suspected VAP caused by Pseudomonas aeruginosa and risk factors for infection with multi-drug resistant (MDR) organisms, include double coverage for Pseudomonas with two agents from two different classes of antibiotics with anti-pseudomonal activity (weak recommendation).

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 - It is recommended that double coverage for pseudomonas should be considered for patients with structural lung disease (bronchiectasis, cystic fibrosis) and an increased risk of gram-negative infection (Kalil et al. 2016).

Empiric antibiotic treatment

 For patients without risk for MDR organisms, and for patients in ICUs that report a ≤ 10% resistance rate to the chosen agent, monotherapy with one anti-pseudomonal agent is sufficient (weak recommendation).

Empiric antibiotic treatment

- For patients without risk for MDR organisms, and for patients in ICUs that report a ≤ 10% resistance rate to the chosen agent, monotherapy with one anti-pseudomonal agent is sufficient (weak recommendation).
 - Beta-lactam-based anti-pseudomonal agents
 - Piperacillin-tazobactam 4.5 g IV every 6 hours

OR

· Cefepime 2 g IV every 8 hours; or ceftazidime 2 g IV every 8 hours

OR

· Imipenem 500 mg IV every 6 hours; or meropenem 1 g IV every 8 hours

OR

· Aztreonam 2 g IV every 8 hours

Empiric antibiotic treatment

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· Imipenem 500 mg IV every 6 hours; or meropenem 1 g IV every 8 hours

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continue ->

Empiric antibiotic treatment

- Non-βeta-lactam-based anti-pseudomonal agents
 - · Ciprofloxacin 400 mg IV every 8 hours; or levofloxacin 750 mg IV every 24 hours.

OF

Amikacin 15-20 mg/kg IV every 24 hours; or gentamicin 5-7 mg/kg IV every 24 hours;
 or tobramycin 5-7 mg/kg IV every 24 hours

OR

Colistin 5 mg/kg IV × 1 (loading dose), followed by 2.5 mg × (1.5 × CrCl + 30) IV every
 12 hours (maintenance dose); or polymyxin B 2.5-3m g/kg/day divided in two daily
 IV doses

Empiric antibiotic treatment

4. Avoid aminoglycosides and colistin in patients with VAP if an alternative agent has adequate gram-negative coverage (Kalil et al. 2016) (weak recommendation).

- 4. Avoid aminoglycosides and colistin in patients with VAP if an alternative agent has adequate gram-negative coverage (Kalil et al. 2016) (weak recommendation).
- 5. Consider using both inhaled and systemic antibiotics for those patients with VAP caused by gram-negative bacilli definitively known to be susceptible only to aminoglycosides or polymyxins (colistin or polymyxin B) (weak recommendation).

Empiric antibiotic treatment

1. When selecting antibiotics for empiric coverage of HAP, include coverage for *S. aureus* (strong recommendation).

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- When selecting antibiotics for empiric coverage of HAP, include coverage for S. aureus (strong recommendation).
 - If coverage for only MSSA is indicated, use piperacillintazobactam, cefepime, levofloxacin, imipenem, or meropenem (weak recommendation).
 - Recommended dosing:
 - Piperacillin-tazobactam 4.5 g IV every 6 hours
 - Cefepime 2 g IV every 8 hours
 - Levofloxacin 750 mg IV daily
 - Imipenem 500 mg IV every 6 hours
 - Meropenem 1 g IV every 8 hours

Empiric antibiotic treatment

2. Provide antibiotic coverage for MRSA for those at high risk for MRSA, including patients that have had intravenous antibiotic therapy in the past 90 days, have been treated in a unit with > 20% MRSA prevalence or unknown prevalence, or for those with a high risk of mortality (mechanical ventilation or septic shock) (weak recommendation).

- 2. Provide antibiotic coverage for MRSA for those at high risk for MRSA, including patients that have had intravenous antibiotic therapy in the past 90 days, have been treated in a unit with > 20% MRSA prevalence or unknown prevalence, or for those with a high risk of mortality (mechanical ventilation or septic shock) (weak recommendation).
 - For those requiring coverage for MRSA, vancomycin or linezolid should be utilized (strong recommendation).

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 - For those requiring coverage for MRSA, vancomycin or linezolid should be utilized (strong recommendation).

continue ->

Empiric antibiotic treatment

· Recommended dosing:

- Recommended dosing:
 - Vancomycin 15 mg/kg IV every 8–12 hours (consider a one-time loading dose of 25–30 mg/kg for severe illness)
 - Linezolid 600 mg IV every 12 hours

Empiric antibiotic treatment

- Recommended dosing:
 - Vancomycin 15 mg/kg IV every 8–12 hours (consider a one-time loading dose of 25–30 mg/kg for severe illness)
 - Linezolid 600 mg IV every 12 hours

Also include agent active against MSSA

- Piperacillin-tazobactam 4.5 g IV every 6 hours
- Cefepime 2 g IV every 8 hours
- · Ceftazidime 2 g IV every 8 hours
- · Levofloxacin 750 mg IV daily
- · Ciprofloxacin 400 mg IV every 8 hours
- · Imipenem 500 mg IV every 6 hours
- · Meropenem 1 g IV every 8 hours
- · Aztreonam 2 g IV every 8 hours

Empiric antibiotic treatment

Empiric antibiotic treatment

3. When choosing an empiric agent, include coverage for *P. aeruginosa* and other gram-negative bacilli (strong recommendation).

Empiric antibiotic treatment

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4. Include double coverage for Pseudomonas with 2 agents from 2 different classes for patients with a history of antibiotic therapy in the previous 90 days, and those at high risk for mortality (mechanical ventilation, septic shock) (weak recommendation).

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Recommended regimens:

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Use two of the following, but avoid two β -lactams:

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- Cefepime or ceftazidime 2 g IV every 8 hours
- Levofloxacin 750 mg IV daily
- Ciprofloxacin 400 mg IV every 8 hours
- Imipenem 500 mg IV every 6 hours

- Meropenem 1 g IV every 8 hours
- Amikacin 15-20 mg/kg IV daily
- Gentamicin 5-7 mg/kg IV daily
- Tobramycin 5-7 mg/kg IV daily
- Aztreonam 2 g IV every 8 hours

Empiric antibiotic treatment

Recommended regimens:

Use two of the following, but avoid two β -lactams:

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- Imipenem 500 mg IV every 6 hours

- Meropenem 1 g IV every 8 hours
- Amikacin 15-20 mg/kg IV daily
- Gentamicin 5-7 mg/kg IV daily
- Tobramycin 5-7 mg/kg IV daily
- Aztreonam 2 g IV every 8 hours

PLUS, one of the following:

- Vancomycin 15 mg /kg IV every 8–12 hours, with goal to target 15–20 mg/mL trough level (consider a one-time loading dose of 25–30 mg/kg IV for severe illness)
- Linezolid 600 mg IV every 12 hours

Empiric antibiotic treatment

Empiric antibiotic treatment

5. The use of aminoglycoside as a single agent against *Pseudomonas* is not recommended (strong recommendation).

Empiric antibiotic treatment

Empiric antibiotic treatment

 Double coverage for pseudomonas should be considered for patients with structural lung disease (bronchiectasis, cystic fibrosis), as they have increased risk of gram-negative infection (Kalil et al. 2016).

Optimization of pharmacokinetics/ pharmacodynamics in patients with HAP/VAP

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 To guide antibiotic dosing in patients with HAP/VAP, use pharmacokinetic/ pharmacodynamic data rather than the manufacturer's prescribing information (weak recommendations).

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- To guide antibiotic dosing in patients with HAP/VAP, use pharmacokinetic/ pharmacodynamic data rather than the manufacturer's prescribing information (weak recommendations).
 - Pharmacokinetic and pharmacodynamic dosing optimization refers to utilizing antibiotic drug concentrations in blood, extended and continuous infusions and weight-based dosing for certain antibiotics (Kalil et al. 2016).

1. MRSA

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Vancomycin or linezolid (strong recommendation)

2. P. aeruginosa

 Antibiotic choice should be guided by individualized organism susceptibilities (strong recommendation).

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- Use monotherapy for patients that are not in septic shock, those at low risk for death, and those with known antibiotic susceptibilities (strong recommendation).

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- Use monotherapy for patients that are not in septic shock, those at low risk for death, and those with known antibiotic susceptibilities (strong recommendation).
- Double coverage should be used for pseudomonas when the results of antibiotic susceptibilities are known, and when the patient is in septic shock, or has a high risk of death. Use two antibiotics to which isolates are susceptible (weak recommendation).

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- Monotherapy with an aminoglycoside is not recommended (strong recommendation).

3. Extended-spectrum β-lactamase (ESBL) producing gramnegative bacilli

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 - Definitive treatment should be based on antimicrobial susceptibilities and risk factors (allergies, co-morbidities that may increase risk of adverse effects) (strong recommendations).

4. Acinetobacter species

 Use carbapenem or ampicillin/sulbactam if the isolate is susceptible (weak recommendation)

- Use carbapenem or ampicillin/sulbactam if the isolate is susceptible (weak recommendation)
- If the isolate is susceptible only to polymyxins, use IV polymyxin
 (colistin or polymyxin B) (strong recommendation) and inhaled colistin
 as adjuvant therapy (weak recommendation).

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- If the isolate is susceptible only to polymyxins, use IV polymyxin
 (colistin or polymyxin B) (strong recommendation) and inhaled colistin
 as adjuvant therapy (weak recommendation).
- Use colistin alone rather than colistin and adjuvant rifampicin for patients with Acinetobacter that is sensitive only to colistin (weak recommendation).

- Use carbapenem or ampicillin/sulbactam if the isolate is susceptible (weak recommendation)
- If the isolate is susceptible only to polymyxins, use IV polymyxin
 (colistin or polymyxin B) (strong recommendation) and inhaled colistin
 as adjuvant therapy (weak recommendation).
- Use colistin alone rather than colistin and adjuvant rifampicin for patients with Acinetobacter that is sensitive only to colistin (weak recommendation).
- · The use of tigecycline is not recommended (strong recommendation).

5. Carbapenem-resistant pathogens

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Length of therapy for HAP/VAP

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Length of therapy for HAP/VAP

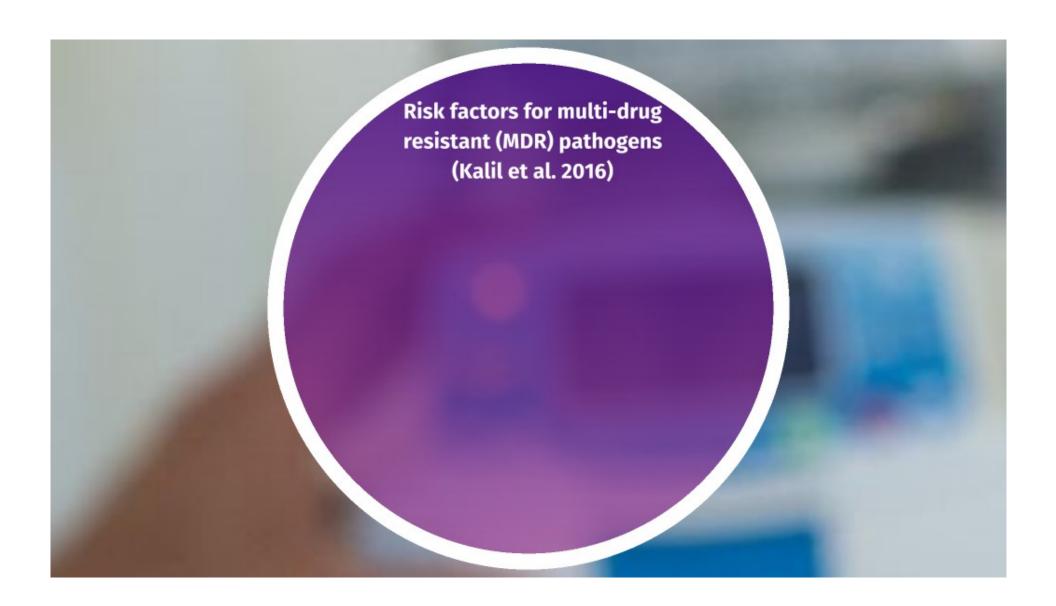
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- For patients with HAP/VAP, antibiotic therapy should be deescalated to the narrowest possible therapy rather than continued with broad-spectrum coverage of a fixed duration (weak recommendation).
- 3. Use PCT along with clinical criteria to guide decisions regarding discontinuation of antibiotic therapy, rather than clinical criteria alone (weak recommendation).

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- For patients with HAP/VAP, antibiotic therapy should be deescalated to the narrowest possible therapy rather than continued with broad-spectrum coverage of a fixed duration (weak recommendation).
- 3. Use PCT along with clinical criteria to guide decisions regarding discontinuation of antibiotic therapy, rather than clinical criteria alone (weak recommendation).
- 4. The use of CPIS to guide discontinuation of antibiotic therapy is not recommended (weak recommendation).













Risk factors for multi-drug resistant (MDR) pathogens (Kalil et al. 2016) **Risk factors for MDR VAP** · IV antibiotic therapy in prior 90 days · Septic shock at time of VAP Adult respiratory distress syndrome (ARDS) preceding VAP · Hospitalization of five or more days preceding onset of VAP Acute renal replacement therapy prior to VAP onset **Risk factors for MDR HAP** · IV antibiotic therapy in prior 90 days Risk factors for MRSA VAP or HAP • IV antibiotic therapy in prior 90 days

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