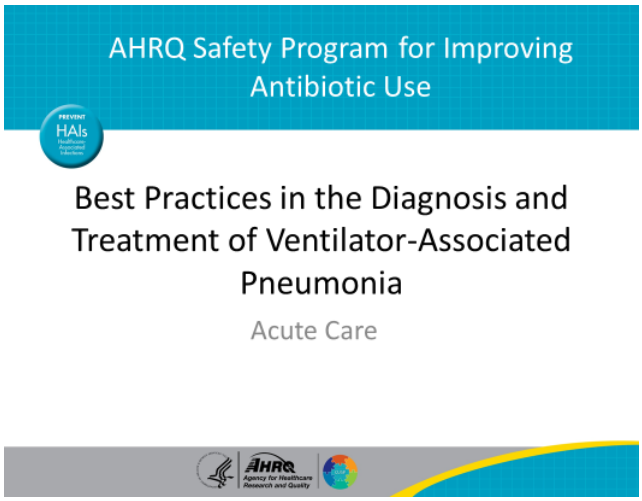
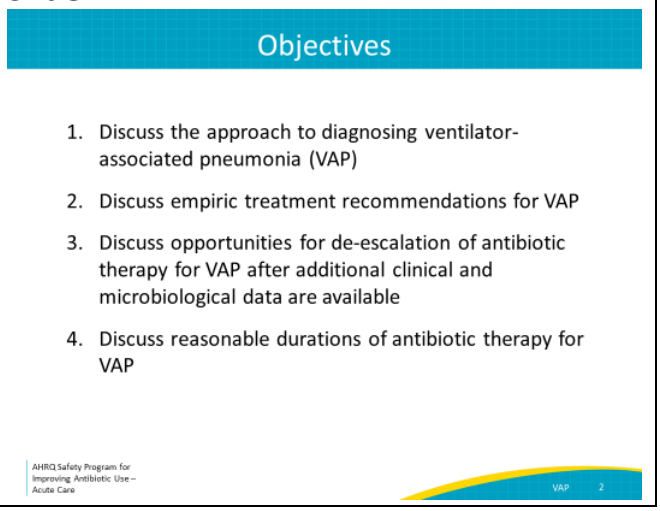
Best Practices in the Diagnosis and Treatment of Ventilator-Associated Pneumonia

Acute Care

Slide Title and Commentary	Slide Number and Slide
Best Practices in the Diagnosis and Treatment of Ventilator-Associated Pneumonia SAY: This presentation is titled "Best Practices in the Diagnosis and Treatment of Ventilator-Associated Pneumonia."	**Slide 1** 
Objectives SAY: This presentation will address: 1. The approach to diagnosing ventilator-associated pneumonia (VAP) 2. Empiric treatment recommendations for VAP 3. Opportunities for de-escalation of antibiotic therapy for VAP after additional clinical and microbiological data are available 4. Reasonable durations of antibiotic therapy for VAP	**Slide 2** 

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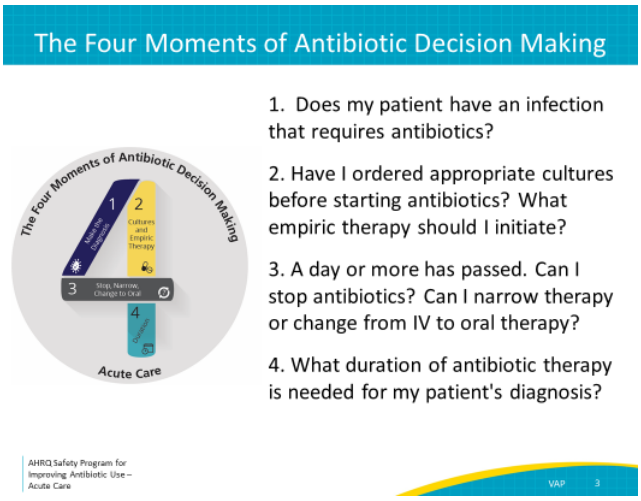
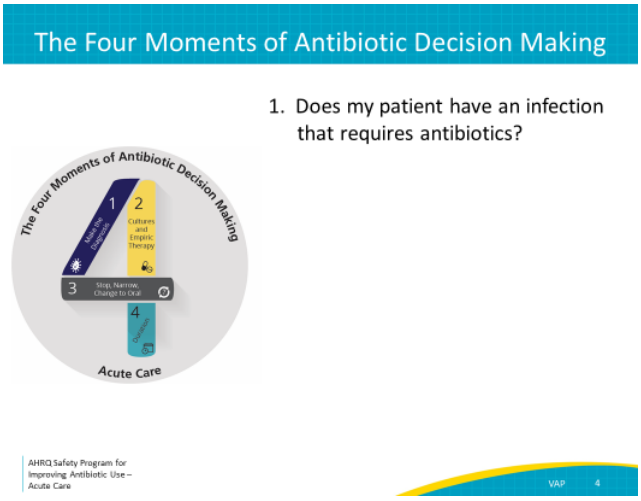
The Four Moments of Antibiotic Decision Making SAY: As we discuss the diagnosis and treatment of VAP, we will continue to use the Four Moments of Antibiotic Decision Making framework. As a reminder, Moment 1 asks: Does my patient have an infection that requires antibiotics? Moment 2 consists of two questions and asks: Have I ordered appropriate cultures before starting antibiotics? What empiric therapy should I initiate? Moment 3 consists of three questions and asks: A day or more has passed. Can I stop antibiotics? Can I narrow therapy, or change from intravenous to oral therapy? And finally, Moment 4 asks: What duration of therapy is needed for my patient's diagnosis?	**Slide 3** 
The Four Moments of Antibiotic Decision Making SAY: The first moment of the Four Moments of Antibiotic Decision Making asks the question, "Does my patient have an infection that requires antibiotics?"	**Slide 4** 

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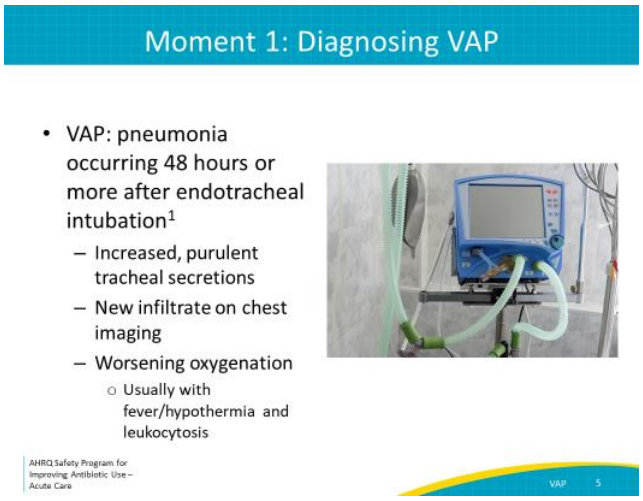
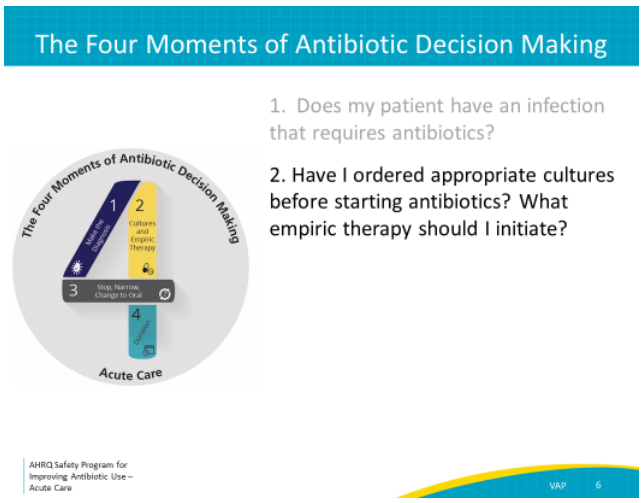
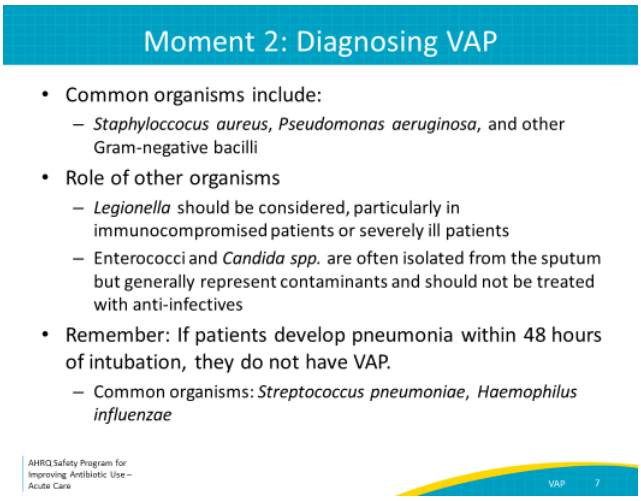
Moment 1: Diagnosing VAP SAY: VAP occurs 48 hours or more after endotracheal intubation. VAP presents with increased purulent tracheal secretions, a new infiltrate on chest imaging, and worsening oxygenation. It is also usually associated with fever or hypothermia and leukocytosis. Diagnosing VAP can be challenging because there are several reasons why a patient can have respiratory decompensation while mechanically ventilated, such as mucus plugs, pulmonary embolisms, and volume overload. Additionally, there are several reasons why a patient may have abnormalities on chest imaging, such as aspiration pneumonitis, atelectasis, and volume overload; thus, the diagnosis is not always straightforward. It is important to remember that even if antibiotics for suspected VAP are initiated, antibiotic decisions should be reviewed on a daily basis during an antibiotic time out. Also note that the clinical diagnosis for VAP differs from National Healthcare Safety Network or NHSN surveillance definitions for ventilator-associated events including infection-related ventilator-associated complications and possible VAP.	**Slide 5** 
The Four Moments of Antibiotic Decision Making SAY: During Moment 2 ask, “Have I ordered appropriate cultures before starting antibiotics? What empiric therapy should I initiate?”	**Slide 6** 

Slide Title and Commentary	Slide Number and Slide
Moment 2: Microbiologic Diagnosis SAY: Common organisms implicated in VAP include *Staphyloccocus aureus*, *Pseudomonas aeruginosa*, and other gram-negative bacilli. *Legionella* should be considered for hospitalized patients but particularly those who are immunocompromised or severely ill. Enterococci and *Candida* species are often isolated from the sputum but generally represent contaminants and should not be treated with anti-infectives in the majority of patients. It is important to remember that VAP occurs after 48 hours or more of intubation. If patients develop pneumonia before this time, they are not considered to have VAP. Patients who develop pneumonia before 48 hours of intubation are most likely infected with organisms such as *Streptococcus pneumoniae* or *Haemophilus influenzae*.	**Slide 7** 

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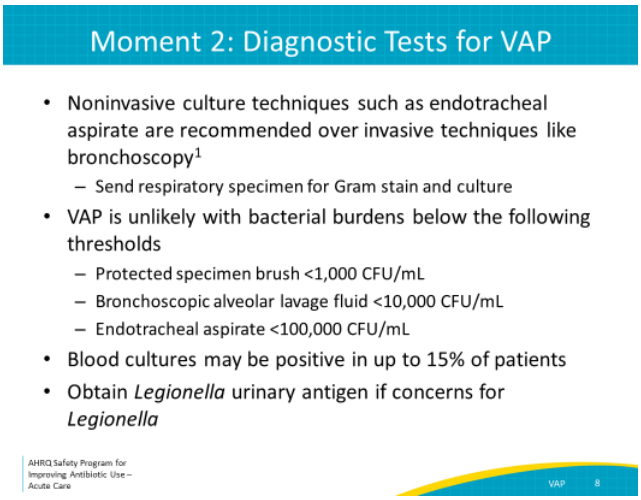
Moment 2: Obtaining Microbiologic Specimens for VAP SAY: The 2016 Infectious Diseases of America (or IDSA) and American Thoracic Society (or ATS) Clinical Practice Guidelines for management of VAP recommend use of noninvasive culture techniques such as endotracheal aspirates over invasive techniques like bronchoscopy because they can be performed more rapidly than invasive sampling, with fewer complications and resources. If cultures cannot be obtained with noninvasive sampling, invasive methods should be considered. Respiratory specimens should be sent for Gram stain and bacterial culture. VAP is unlikely when the bacterial burdens are below 1,000 CFU/mL for protected specimen brush samples, less than 10,000 CFU/mL for bronchoscopic alveolar lavage fluid, and less than 100,000 CFU/mL for endotracheal aspirates. Blood cultures may be positive in up to 15 percent of patients, so are reasonable to obtain when VAP is suspected. Hospitalized patients are at risk for *Legionella* pneumonia. A *Legionella* urinary antigen should be considered for severely ill patients or immunocompromised patients.	**Slide 8** 

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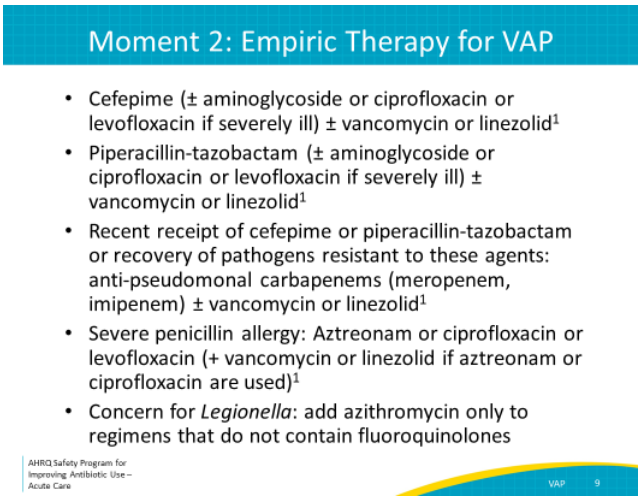
Moment 2: Empiric Therapy for VAP SAY: The 2016 IDSA/ATS Guidelines recommend that two antipseudomonal agents from different classes should be considered as empiric therapy for suspected VAP in patients at risk for antibiotic-resistant organisms. For patients without risk factors for antibiotic resistance, a single anti-pseudomonal agent can be used. One approach is to administer an agent such as cefepime or piperacillin-tazobactam as empiric therapy for suspected cases of VAP. The addition of an aminoglycoside or ciprofloxacin or levofloxacin to cefepime or piperacillin/tazobactam—or, alternatively, the use of an anti-pseudomonal carbapenem like meropenem or imipenem/cilastatin as monotherapy should be considered for severely ill patients, patients who recently received either cefepime or piperacillin-tazobactam, or patients who previously had Gram-negative organisms recovered which were resistant to either cefepime or piperacillin-tazobactam. For patients with severe penicillin allergy, consider the use of aztreonam, ciprofloxacin, or levofloxacin. If the patient is severely ill, consider adding an aminoglycoside to these agents. Vancomycin or linezolid is recommended for Gram-positive coverage unless levofloxacin is part of the regimen because neither aztreonam, aminoglycosides, nor ciprofloxacin provide Gram-positive coverage. Of note, as fluoroquinolones have coverage against *Legionella*, for patients receiving fluoroquinolone therapy, additional coverage is not needed to target *Legionella*.	**Slide 9** 

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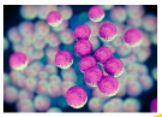
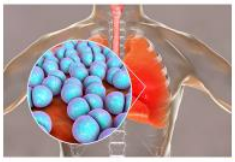
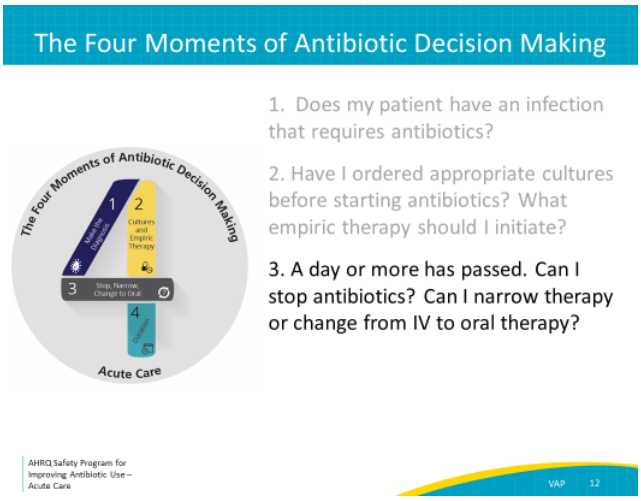
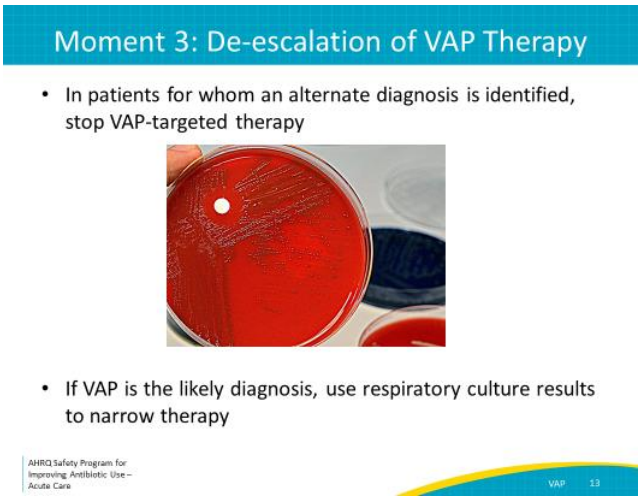
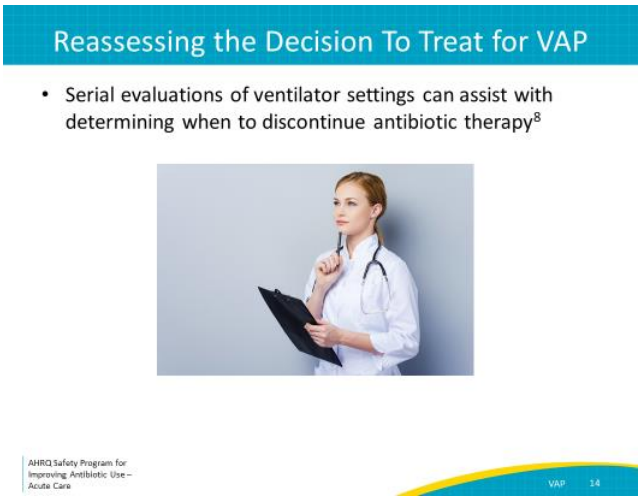
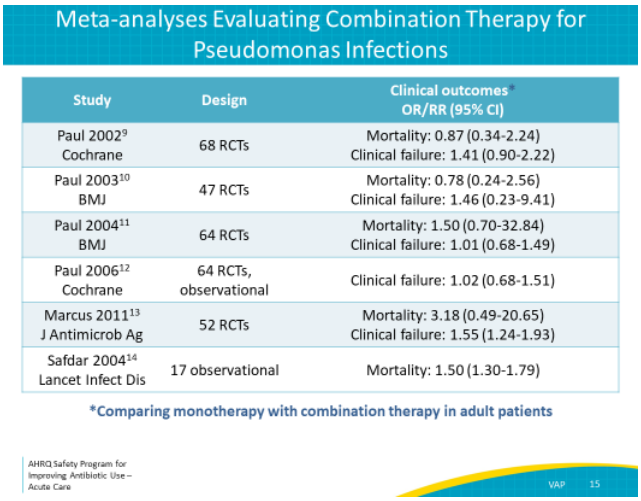
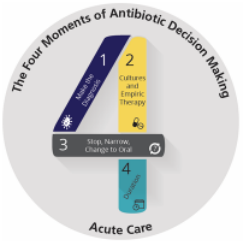
Moment 2: Empiric Therapy for VAP SAY: The 2016 IDSA/ATS guidelines recommend the addition of targeted methicillin-resistant *Staphylococcus aureus* or MRSA therapy when there is a reasonable proportion of patients colonized with MRSA locally—when at least 20 percent of *S. aureus* isolates from a unit are methicillin resistant. It can be difficult to obtain these data, and they may not reflect an individual patient's risk of MRSA colonization. Thus, other patient-level risk factors should prompt the initiation of empiric anti-MRSA VAP therapy. These include a known history of MRSA colonization or infection, intravenous drug use, the presence of necrotizing pneumonia, an ill-appearing patient with a recent stay in a nursing home or skilled nursing facility, or a patient with a prolonged hospitalization with an unknown MRSA colonization status. A meta-analysis including 32 studies and over 5,000 patients investigated the diagnostic value of MRSA nasal swab results in predicting the likelihood of MRSA pneumonia. The investigators found that the negative predictive value of the swab was 97 percent; meaning that if the swab was negative for MRSA, there was a 97 percent chance that MRSA was not the cause of pneumonia during that same hospitalization.	**Slide 10** Moment 2: Empiric Therapy for VAP • When should I add anti-MRSA coverage on an empiric basis? – High local prevalence of MRSA – Known patient history of MRSA colonization or infection[2,3] – Intravenous drug use – Necrotizing pneumonia – Ill-appearing patient with a recent stay in a nursing home or skilled nursing facility – Prolonged hospitalization with unknown MRSA colonization status  AHRQ Safety Program for Improving Antibiotic Use – Acute Care VAP 10
Vancomycin vs. Linezolid? SAY: Both vancomycin and linezolid are reasonable options for MRSA coverage for pulmonary infections. At least four meta-analyses of randomized controlled trials have shown that use of vancomycin versus linezolid for the treatment of MRSA pulmonary infections yield similar outcomes. Daptomycin is inactivated by pulmonary surfactant and is not a suitable option for the treatment of pneumonia.	**Slide 11** Vancomycin vs. Linezolid? • Both vancomycin and linezolid are reasonable options for MRSA coverage for pulmonary infections[4,5,6,7] • At least 4 meta-analyses of randomized controlled trials have shown use of vancomycin versus linezolid for the treatment of MRSA pulmonary infections yield similar outcomes • Daptomycin is inactivated by pulmonary surfactant and is not a suitable option for the treatment of pneumonia  AHRQ Safety Program for Improving Antibiotic Use – Acute Care VAP 11

Slide Title and Commentary	Slide Number and Slide
The Four Moments of Antibiotic Decision Making SAY: Moment three occurs after a day or more has passed. Ask: Can I stop antibiotics? Can I narrow therapy or change from intravenous or IV to oral therapy?	**Slide 12** 
Moment 3: De-escalation of VAP Therapy SAY: In patients for whom an alternate diagnosis is identified, stop VAP-targeted therapy. If VAP is the likely diagnosis, use respiratory culture results to direct therapy. Determine if the beta-lactam agent you started can be narrowed. If anti-MRSA coverage was added empirically, discontinue it if MRSA was not recovered. If an aminoglycoside or fluoroquinolone was added to the beta-lactam, discontinue if an appropriate beta-lactam is available for treatment. *S. aureus* and Gram-negative bacilli grow easily in culture. If these organisms are not isolated, coverage for methicillin-resistant *S. aureus* and multidrug-resistant Gram-negative bacilli can be discontinued.	**Slide 13** 

Slide Title and Commentary	Slide Number and Slide
Reassessing the Decision To Treat for VAP SAY: The diagnosis of VAP can be ambiguous, and it is reasonable to initiate therapy early even when uncertain of the diagnosis. It is important, however to reassess this decision daily. If a patient initiated on therapy for presumed VAP shows rapid recovery and is able to be weaned from a ventilator within a day or two, the diagnosis of VAP is unlikely, and it is reasonable to discontinue antibiotics. Patients with stable serial ventilator settings may be able to have antibiotics discontinued early. In a study of 1,290 patients, patients with minimal and stable ventilator settings were treated with 1 to 3 days versus greater than 3 days of antibiotics. The two groups had similar comorbidities and clinical presentations. There were no differences between the groups with regards to time to extubation or mortality. Evaluating serial ventilator settings may help clinicians identify candidates for early antibiotic discontinuation.	**Slide 14** 
Meta-analyses Evaluating Combination Therapy for *Pseudomonas* Infections SAY: In the past, some have advocated for combination therapy for *Pseudomonas aeruginosa* infections based on studies where aminoglycosides were used as monotherapy. However, aminoglycoside monotherapy Is now discouraged for the treatment of infections other than urinary infections as bacteria can develop resistance to these agents relatively quickly. Additionally, aminoglycosides don't penetrate some body sites very efficiently when administered systemically, including lung tissue. Combination therapy has not been shown to improve the outcomes of patients with invasive Pseudomonal infections if a single agent with good activity against *Pseudomonas* is available.	**Slide 15** 

Slide Title and Commentary	Slide Number and Slide
Moment 3: Oral Step-Down Therapy for VAP SAY: After a patient shows clinical improvement and the ability to tolerate oral medications, switch to oral therapy. If *Pseudomonas* has been isolated in cultures, consider ciprofloxacin or levofloxacin, if susceptible. If pseudomonal coverage is not needed because *Pseudomonas* has not been isolated, consider agents like second- or third-generation oral cephalosporins or amoxicillin-clavulanate, based on culture results. If a patient has a severe penicillin allergy, consider a respiratory fluoroquinolone such as levofloxacin or moxifloxacin. If MRSA has been isolated, consider clindamycin, trimethoprim/sulfamethoxazole, or linezolid based on culture results. After the patient shows clinical improvement and the ability to tolerate oral medications, antibiotic therapy should be adjusted based on susceptibility results, if available.	**Slide 16** Moment 3: Oral Step-Down Therapy for VAP • After patient shows clinical improvement and the ability to tolerate oral medications – If pseudomonal coverage needed: consider ciprofloxacin or levofloxacin (based on susceptibility results) – If pseudomonal coverage ***not*** needed: consider second- or third-generation oral cephalosporin or amoxicillin-clavulanate (based on susceptibility results) – Severe penicillin allergy: respiratory fluoroquinolone – If MRSA coverage is needed: clindamycin, trimethoprim/sulfamethoxazole, or linezolid (based on susceptibility results) AHRQ Safety Program for Improving Antibiotic Use – Acute Care VAP 16
The Four Moments of Antibiotic Decision Making SAY: The fourth moment of antibiotic decision making is asking the question, “What duration of antibiotic therapy is needed for my patient's diagnosis?”	**Slide 17** The Four Moments of Antibiotic Decision Making  1. Does my patient have an infection that requires antibiotics? 2. Have I ordered appropriate cultures before starting antibiotics? What empiric therapy should I initiate? 3. A day or more has passed. Can I stop antibiotics? Can I narrow therapy or change from IV to oral therapy? 4. What duration of antibiotic therapy is needed for my patient's diagnosis? AHRQ Safety Program for Improving Antibiotic Use – Acute Care VAP 17

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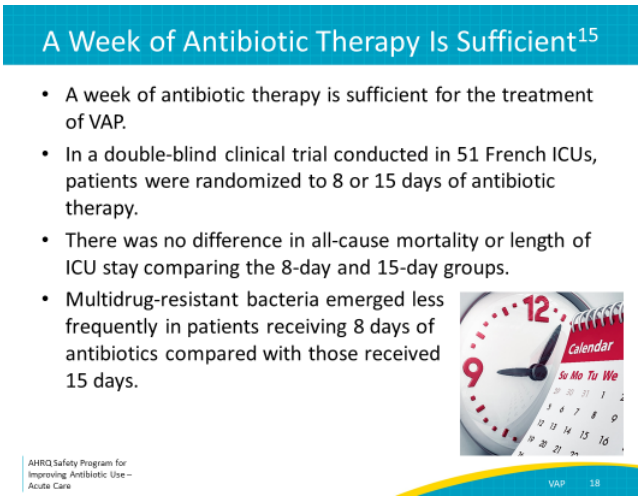
A Week of Antibiotic Therapy Is Sufficient SAY: Generally, a week of antibiotic therapy is sufficient for the treatment of VAP. In a double-blind clinical trial conducted in 51 French intensive care units or ICUs that included 401 patients with VAP, patients were randomized to 8 or 15 days of antibiotic therapy. As indicated on the survival curve, there was no difference in all-cause mortality comparing the 8-day and 15-day groups. Furthermore, there was no difference in mechanical ventilation-free days or length of ICU stay. Importantly, multidrug-resistant bacteria emerged less frequently in patients receiving 8 days of antibiotics compared with those received 15 days. Although this study did not specifically evaluate 7 days of antibiotics for VAP, most clinicians extrapolate the findings from this study to indicate that 7 days of therapy for VAP is sufficient. The IDSA/ATS guidelines recommend 7 days of antibiotic therapy for most cases of VAP.	**Slide 18** 

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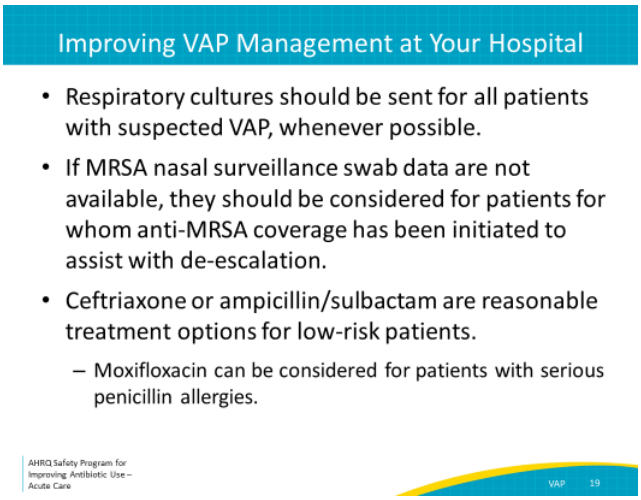
Improving VAP Management at Your Hospital SAY: The diagnosis of VAP causes significant clinical challenge given that respiratory symptoms can be multifactorial. Antibiotic stewardship teams and providers can take steps to minimize inappropriate treatment and optimize treatment for patients with true pneumonia. First, ensuring respiratory cultures are sent for all patients with suspected VAP whenever possible is critical to streamline therapy and discontinue antibiotics that are no longer needed. Even if MRSA nasal surveillance swab data are not routinely obtained in your hospital, they should be considered for patients for whom anti-MRSA coverage has been initiated to assist with de-escalation—particularly for providers uncomfortable discontinuing MRSA coverage in these settings. Patients who are otherwise healthy with suspected pneumonia that has occurred within 72 hours of hospitalization are more likely to be infected with common respiratory pathogens like *Streptococcus pneumoniae* or *Haemophilus influenzae* and unlikely to be infected with *Pseudomonas*. Ceftriaxone or ampicillin/sulbactam is a reasonable treatment option for these patients. Moxifloxacin can be considered for these low-risk patients if they have serious penicillin allergies. Finally, continued emphasis on shorter courses of therapy for VAP —7 days—is often needed because providers may be unaware of studies supporting this duration. A process should be put in place to ensure that an end date is noted in the medical record before patients are transferred out of the intensive care unit to the floor.	**Slide 19** 

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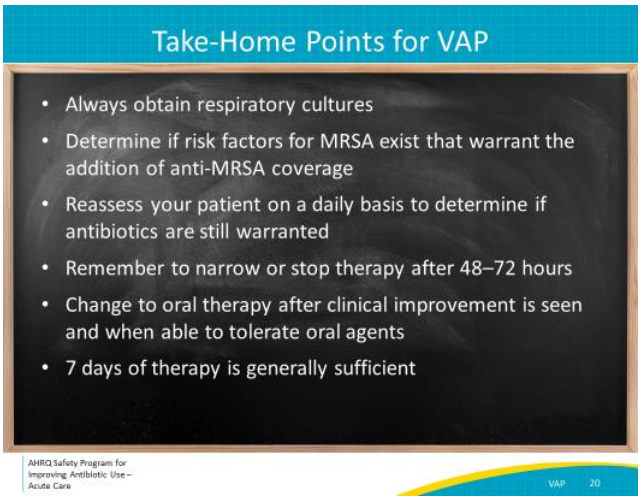
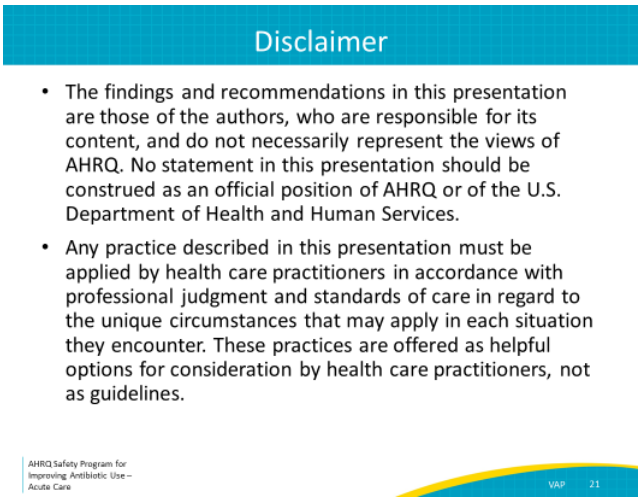
Take Home Points for VAP SAY: To summarize some important take-home points for VAP: • Always obtain a respiratory sample for Gram stain and culture. • Determine if risk factors for MRSA exist that warrant the addition of anti-MRSA coverage • As the diagnosis of VAP is challenging, reassess your patient on a daily basis to determine if antibiotics are still warranted • Remember to narrow or stop therapy after 48–72 hours • Change to oral therapy after clinical improvement is observed and when able to tolerate oral agents • Seven days of therapy is generally sufficient	**Slide 20** 
Disclaimer SAY: The findings and recommendations in this presentation are those of the authors, who are responsible for its content, and do not necessarily represent the views of AHRQ. No statement in this presentation should be construed as an official position of AHRQ or of the U.S. Department of Health and Human Services. Any practice described in this presentation must be applied by health care practitioners in accordance with professional judgment and standards of care in regard to the unique circumstances that may apply in each situation they encounter. These practices are offered as helpful options for consideration by health care practitioners, not as guidelines.	**Slide 21** 

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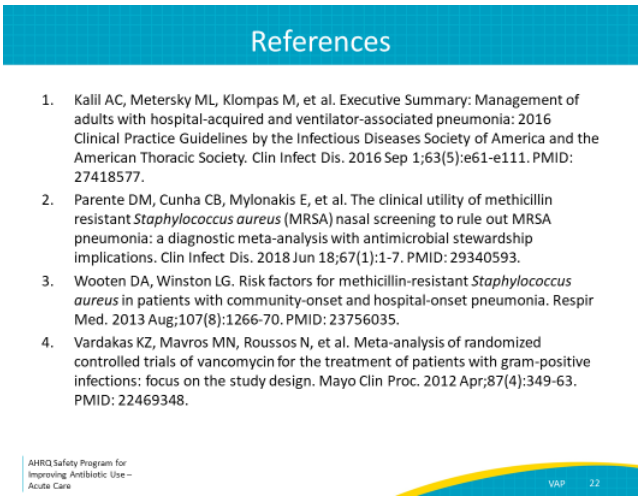
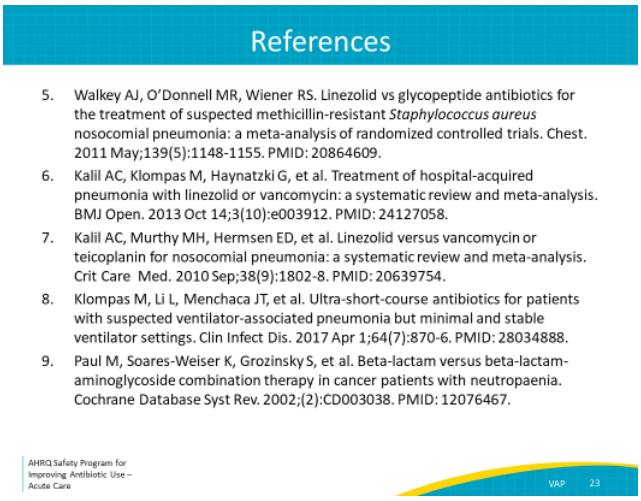
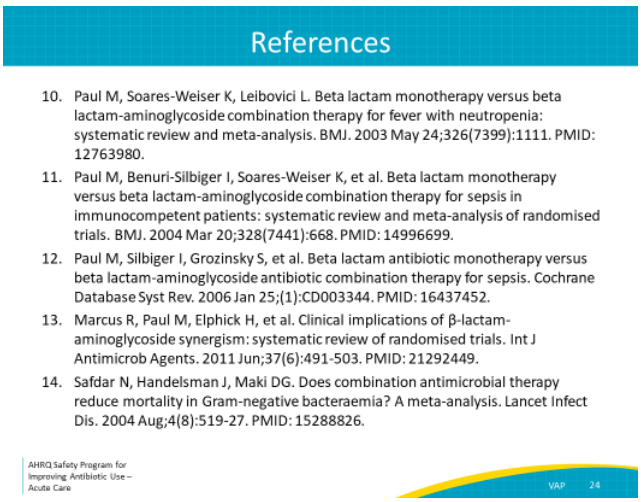
References	**Slide 22** 
References	**Slide 23** 
References	**Slide 24** 

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References 4	**Slide 25**