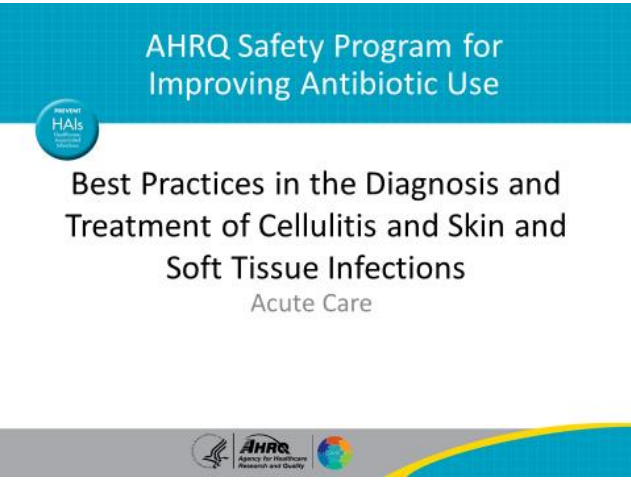
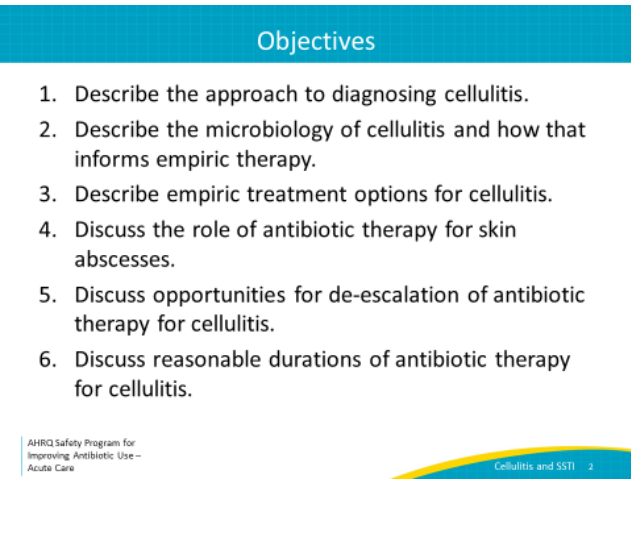


AHRQ Safety Program for Improving Antibiotic Use

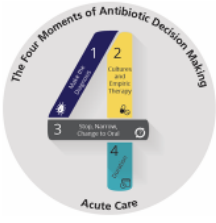
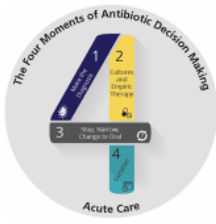



Best Practices in the Diagnosis and Treatment of Cellulitis and Skin and Soft Tissue Infections



Acute Care


Slide Title and Commentary	Slide Number and Slide
<p>Best Practices in the Diagnosis and Treatment of Cellulitis and Skin and Soft Tissue Infections Acute Care</p> <p>SAY:</p> <p>This presentation will address best practices in the diagnosis and treatment of cellulitis and skin and soft tissue infections.</p>	<p>Slide 1</p> 
<p>Objectives</p> <p>SAY:</p> <p>By the end of this presentation, participants will be able to—</p> <ul style="list-style-type: none"> • Describe the approach to diagnosing cellulitis • Describe the microbiology of cellulitis and how that informs empiric therapy • Describe empiric treatment options for cellulitis • Discuss the role of antibiotic therapy for skin abscesses • Discuss opportunities for de-escalation of antibiotic therapy for cellulitis • Discuss reasonable durations of antibiotic therapy for cellulitis 	<p>Slide 2</p> 






Slide Title and Commentary	Slide Number and Slide
<p>The Four Moments of Antibiotic Decision Making</p> <p>SAY:</p> <p>As we discuss cellulitis and skin and soft tissue infections, we will use the Four Moments of Antibiotic Decision Making framework.</p> <p>As a reminder, Moment 1 asks: Does my patient have an infection that requires antibiotics?</p> <p>Moment 2 consists of two questions and asks: Have I ordered appropriate cultures before starting antibiotics? What empiric therapy should I initiate?</p> <p>Moment 3 consists of three questions and asks: A day or more has passed since initiating antibiotics. As I have more clinical and microbiologic data available can I stop antibiotics, can I narrow antibiotics, or can I change from intravenous to oral antibiotics?</p> <p>And finally, Moment 4 asks: What duration of therapy is needed for my patient's diagnosis?</p>	<p>Slide 3</p> <p>The Four Moments of Antibiotic Decision Making</p>  <ol style="list-style-type: none"> 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? <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p>Cellulitis and SSTI 3</p>
<p>The Four Moments of Antibiotic Decision Making</p> <p>SAY:</p> <p>Moment one is: Does my patient have an infection that requires antibiotics?</p>	<p>Slide 4</p> <p>The Four Moments of Antibiotic Decision Making</p> <ol style="list-style-type: none"> 1. Does my patient have an infection that requires antibiotics?  <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p>Cellulitis and SSTI 4</p>

Slide Title and Commentary	Slide Number and Slide
<p>Moment 1: Diagnosis of Cellulitis</p> <p>SAY:</p> <p>Patients with cellulitis present with redness, warmth, tenderness, and swelling of the skin with relatively sudden onset.</p> <p>Cellulitis is almost always unilateral; patients who have bilateral skin findings more likely have chronic venous stasis than infection. Fever is seen in 20–70 percent of patients before or upon presentation, 60–90 percent of patients have elevated inflammatory markers, and 35–50 percent of patients have leukocytosis.</p> <p>Development of cellulitis is generally associated with skin surface disruption due to recent trauma, tinea pedis, cutaneous ulcers, or past saphenous venectomy. In addition, impaired venous and lymphatic drainage can predispose to cellulitis.</p>	<p>Slide 5</p> <p>Moment 1: Diagnosis of Cellulitis^{1,2}</p> <ul style="list-style-type: none"> • Redness, warmth, tenderness, and swelling of skin • Relatively rapid onset/progression • Almost always unilateral • Fever in 20–70% of patients • Elevated inflammatory markers in 60–90% of patients • Leukocytosis in 35–50% of patients • Associated with skin surface disruption <ul style="list-style-type: none"> – Recent trauma – Tinea pedis – Cutaneous ulcer – Saphenous venectomy – Impaired venous and lymphatic drainage <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care Cellulitis and SSTI 5</p>
<p>Moment 1: Cellulitis Mimics</p> <p>SAY:</p> <p>Several noninfectious conditions can be confused with cellulitis.</p> <p>In one study of 145 patients hospitalized for presumed cellulitis, 41 (28%) had an alternative diagnosis. These included venous stasis dermatitis (37%), trauma-related inflammation (5%), deep vein thrombosis (5%) nonspecific dermatitis, and (5%), thrombophlebitis (5%).</p>	<p>Slide 6</p> <p>Moment 1: Cellulitis Mimics</p> <p>Several noninfectious conditions are commonly misdiagnosed as cellulitis.</p>  <p>In one study of 145 patients hospitalized for cellulitis, 41 (28%) had alternative diagnoses including:³</p> <ul style="list-style-type: none"> • Venous stasis dermatitis (37%) • Trauma-related inflammation (5%) • Deep vein thrombosis (5%) • Nonspecific dermatitis (5%) • Thrombophlebitis (5%) <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care Cellulitis and SSTI 6</p>

Slide Title and Commentary	Slide Number and Slide
<p>Moment 1: Cellulitis Mimics</p> <p>SAY:</p> <p>Venous stasis dermatitis can be distinguished from cellulitis in several ways. It is often bilateral; usually present for a long period of time; and associated with chronic skin hyperpigmentation, itchiness, scaling, pitting edema, and/or serous drainage. Patients may have pain, but it is less intense than with cellulitis and should not be associated with fever or significant leukocytosis. Venous stasis dermatitis can be treated with elevation of the extremity, compression, and topical steroids.</p>	<p>Slide 7</p> <p>Moment 1: Cellulitis Mimics</p> <ul style="list-style-type: none"> • Venous stasis dermatitis⁴ <ul style="list-style-type: none"> – Often bilateral – Usually present for a long time – Associated with chronic skin hyperpigmentation – Associated with pitting edema and/or serous drainage – Itchiness and scaling may be present – Less painful than cellulitis – No fever or significant leukocytosis – Treat with elevation, compression, topical steroids  <p><small>Reprinted with permission from Keller EC, Tomecki KJ, Alraas MC. Distinguishing cellulitis from its mimics. <i>Cleve Clin J Med.</i> 2012 Aug;79(8):547-52. Copyright © 2012 Cleveland Clinic Foundation. All rights reserved.</small></p> <p><small>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</small></p> <p><small>Cellulitis and SSTI 7</small></p>
<p>Moment 1: Cellulitis Mimics</p> <p>SAY:</p> <p>Lymphedema results from disruption of lymphatic drainage. It can be congenital but is usually related to obesity or lymph node dissection. It is usually unilateral (distal to the lymphatic disruption) and associated with diffuse nontender erythema that improves with elevation. There is minimal associated warmth. Fevers should not be present.</p> <p>Both venous stasis and lymphedema can predispose to cellulitis so the history and physical exam is important.</p> <p>Ask if there has been an acute change in symptoms that suggests a new process, new fever, or increased warmth, tenderness and erythema. Examine the extremity for evidence of new superficial cutaneous edema and/or shiny and smooth skin. These symptoms and signs suggest cellulitis.</p>	<p>Slide 8</p> <p>Moment 1: Cellulitis Mimics</p> <ul style="list-style-type: none"> • Lymphedema⁴ <ul style="list-style-type: none"> – Results from disruption of lymphatic drainage <ul style="list-style-type: none"> • Can be congenital but usually related to obesity or lymph node dissection – Usually unilateral – Diffuse nontender erythema – Erythema improves with elevation – Minimal warmth – No fever  <p><small>By Abdulrah Sarhan - Own work, CC-BY-SA-4.0. https://commons.wikimedia.org/wiki/File:148467226</small></p> <p><small>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</small></p> <p><small>Cellulitis and SSTI 8</small></p>

Slide Title and Commentary	Slide Number and Slide
<p>Moment 1: Cellulitis Mimics</p> <p>SAY:</p> <p>Patients with peripheral arterial disease can present with dependent rubor, defined as erythema that can be bright or dusky red that goes away when the leg is elevated. Dependent rubor can be associated with pain when patients have severe arterial insufficiency, but is not associated with warmth or edema.</p>	<p>Slide 9</p> <p>Moment 1: Cellulitis Mimics</p> <ul style="list-style-type: none"> • Peripheral arterial disease⁴ <ul style="list-style-type: none"> – Can present with dependent rubor <ul style="list-style-type: none"> • Erythema that goes away when the leg is elevated – Can be associated with pain when patients have severe arterial insufficiency, but not warmth or edema  <p><small>Parrin S, Dean SM. History and physical exam of chronic critical limb ischemia. In: Critical Limb Ischemia. Copyright © 2017 Springer International Publishing Switzerland. All rights reserved. Used with permission.</small></p> <p><small>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</small></p> <p><small>Cellulitis and SSTI 9</small></p>
<p>Moment 1: Cellulitis Mimics</p> <p>Other noninfectious syndromes that can be confused with cellulitis are listed on this slide. Patients with contact dermatitis can have lesions that look like cellulitis, but lesions are confined to the site of contact with the allergen. Patients will often be able to identify potential exposures such as bandages or lotions.</p> <p>The skin is generally not involved in patients with deep venous thrombosis, although they can have swelling of the extremity with associated erythema and some warmth.</p> <p>The skin surrounding the affected joint(s) in patients with gout can mimic cellulitis with warmth, erythema, and pain.</p>	<p>Slide 10</p> <p>Moment 1: Cellulitis Mimics⁴</p> <ul style="list-style-type: none"> • Contact dermatitis <ul style="list-style-type: none"> – Lesions usually confined to the site of contact with the allergen – Ask about potential exposures • Deep venous thrombosis <ul style="list-style-type: none"> – Skin not generally involved, although can have swelling of the extremity with associated erythema and some warmth • Gout <ul style="list-style-type: none"> – Skin surrounding involved joint(s) can mimic cellulitis with warmth, erythema, and pain <p><small>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</small></p> <p><small>Cellulitis and SSTI 10</small></p>

Slide Title and Commentary	Slide Number and Slide
<p>The Four Moments of Antibiotic Decision Making</p> <p>SAY:</p> <p>Moment two is: Have I ordered appropriate cultures before starting antibiotics? What empiric therapy should I initiate?</p>	<p>Slide 11</p> <p>The Four Moments of Antibiotic Decision Making</p> <ol style="list-style-type: none"> 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?  <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p>Cellulitis and SSTI 11</p>
<p>Moment 2: Microbiologic Diagnosis</p> <p>SAY:</p> <p>In patients with cellulitis, blood cultures are positive in less than 5 percent of cases and thus not routinely recommended. Blood cultures should be obtained in severely ill patients, immunocompromised or neutropenic patients, and patients with certain exposures (for example, salt water leading to possible <i>Vibrio</i> infection).</p> <p>Wound cultures should be obtained if purulence is present. It is best to send the actual pus, not a swab of pus, so that a Gram stain can be performed and to optimize the yield of cultures.</p> <p>There is no indication for aspiration of the cellulitis margin. Punch biopsy can be considered for unusual skin findings particularly in immunocompromised hosts but not for routine cellulitis cases.</p>	<p>Slide 12</p> <p>Moment 2: Microbiologic Diagnosis</p> <ul style="list-style-type: none"> • Blood cultures positive in < 5% of cases, not routinely recommended • Blood cultures recommended in— <ul style="list-style-type: none"> – Severely ill patients – Immunocompromised or neutropenic patients – Certain exposures (e.g., salt water leading to possible <i>Vibrio</i> infection) • If purulence is present, cultures should be obtained <ul style="list-style-type: none"> – Best to send pus, not a swab of pus • No indication for routine punch biopsy or aspiration of cellulitis margin <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p>Cellulitis and SSTI 12</p>



Slide Title and Commentary	Slide Number and Slide
<p>Moment 2: Diagnosis of Type of Cellulitis</p> <p>SAY:</p> <p>It is important to assess whether the patient has nonpurulent cellulitis, in which there <u>is no</u> evidence of fluid collection, phlegmon or abscess OR purulent cellulitis in which there <u>is</u> evidence of a fluid collection, phlegmon, or abscess associated with the cellulitis.</p>	<p>Slide 13</p> <p>Moment 2: Diagnosis of Type of Cellulitis</p> <div style="display: flex; justify-content: space-around;"> <div style="text-align: center;"> <p>Nonpurulent</p>  </div> <div style="text-align: center;"> <p>Purulent</p>  </div> </div> <p><small>Leff S, Chira S, David CG, et al. Non-suppurative cellulitis: risk factors and its association with <i>Staphylococcus aureus</i> colonization in an area of endemic, community-associated methicillin-resistant <i>S. aureus</i> infections. <i>Epidemiol Infect</i>. 2011 Apr;139(4):606-12 [Epub 2010 Jun 21]. © Cambridge University Press 2010. Reproduced with permission.</small></p> <p><small>Image courtesy of DermNetNZ.org via Creative Commons license. Attribution-NonCommercial-NoDerivs 3.0 New Zealand. https://creativecommons.org/licenses/by-nc-nd/3.0/nz/</small></p> <p><small>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</small></p> <p><small>Cellulitis and SSTI 13</small></p>

Slide Title and Commentary	Slide Number and Slide				
<p>Moment 2: Purulent Versus Nonpurulent</p> <p>SAY:</p> <p>The microbiologic etiology of cellulitis can be predicted by the type of cellulitis.</p> <p>Nonpurulent cellulitis is primarily caused by beta-hemolytic strep—usually group A streptococcus, but sometimes group B, C, or G streptococcus. All beta-hemolytic streptococci are penicillin susceptible; however, clindamycin resistance occurs in 10–20 percent of B, C, and G streptococcal infections.</p> <p>Methicillin-susceptible <i>Streptococcus aureus</i> or MSSA is estimated to be the cause of nonpurulent cellulitis in only about 10 percent of cases. Because MSSA is such an uncommon cause of nonpurulent cellulitis, some treat these infections with regimens that do not cover <i>S. aureus</i> such as intravenous or IV penicillin if they require IV therapy, or oral amoxicillin. In the United States, many clinicians elect to cover for MSSA using IV cefazolin or ampicillin/sulbactam, or an oral first-generation cephalosporin or amoxicillin/clavulanate.</p> <p>Purulent cellulitis is primarily caused by <i>S. aureus</i>, including MRSA. Debridement of any associated abscess should occur whenever possible; ultrasound may be helpful to detect abscess or phlegmon in cases where physical exam is equivocal. Empiric treatment should include coverage for MRSA. Oral options include trimethoprim/sulfamethoxazole, doxycycline, and clindamycin, although if using clindamycin it is important to assess local susceptibility data given recent large increases in resistance in many areas.</p> <p>More severe cases should be treated with IV therapy such as vancomycin or linezolid. It is important to use linezolid judiciously to prevent increases in resistance, particularly now that it is more accessible from a cost standpoint.</p>	<p>Slide 14</p> <div data-bbox="863 273 1464 724" style="border: 1px solid black; padding: 10px;"> <p style="text-align: center; background-color: #0070C0; color: white; padding: 5px;">Moment 2: Nonpurulent Versus Purulent</p> <table border="1" style="width: 100%; border-collapse: collapse;"> <thead> <tr> <th style="background-color: #D9E1F2; padding: 5px;">Nonpurulent</th> <th style="background-color: #D9E1F2; padding: 5px;">Purulent</th> </tr> </thead> <tbody> <tr> <td style="padding: 5px;"> <ul style="list-style-type: none"> • Caused by beta-hemolytic strep⁵ <ul style="list-style-type: none"> – Usually group A strep – Sometimes group B, C, G – All are penicillin susceptible <ul style="list-style-type: none"> • Clindamycin resistance 10–20% in B, C, G • MSSA estimated to be the cause of only ~10% of cases • Treatment: <ul style="list-style-type: none"> – Penicillin G IV or amoxicillin PO – Cefazolin or ampicillin/sulbactam IV – Oral first-generation cephalosporin or amoxicillin/clavulanate PO </td> <td style="padding: 5px;"> <ul style="list-style-type: none"> • Caused by <i>S. aureus</i> <ul style="list-style-type: none"> – Risk for MRSA • Debridement required whenever possible • Ultrasound may be helpful to detect abscess or phlegmon in cases where physical exam is equivocal • Treatment: Cover for MRSA <ul style="list-style-type: none"> – Trimethoprim/sulfamethoxazole (TMP/SMX), doxycycline, clindamycin* – Vancomycin or linezolid for more severe cases <p style="font-size: small; margin-top: 5px;">*When using clindamycin, check local resistance.</p> </td> </tr> </tbody> </table> <p style="font-size: x-small; margin-top: 10px;">AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p style="text-align: right; font-size: x-small; margin-top: 5px;">Cellulitis and SSTI 14</p> </div>	Nonpurulent	Purulent	<ul style="list-style-type: none"> • Caused by beta-hemolytic strep⁵ <ul style="list-style-type: none"> – Usually group A strep – Sometimes group B, C, G – All are penicillin susceptible <ul style="list-style-type: none"> • Clindamycin resistance 10–20% in B, C, G • MSSA estimated to be the cause of only ~10% of cases • Treatment: <ul style="list-style-type: none"> – Penicillin G IV or amoxicillin PO – Cefazolin or ampicillin/sulbactam IV – Oral first-generation cephalosporin or amoxicillin/clavulanate PO 	<ul style="list-style-type: none"> • Caused by <i>S. aureus</i> <ul style="list-style-type: none"> – Risk for MRSA • Debridement required whenever possible • Ultrasound may be helpful to detect abscess or phlegmon in cases where physical exam is equivocal • Treatment: Cover for MRSA <ul style="list-style-type: none"> – Trimethoprim/sulfamethoxazole (TMP/SMX), doxycycline, clindamycin* – Vancomycin or linezolid for more severe cases <p style="font-size: small; margin-top: 5px;">*When using clindamycin, check local resistance.</p>
Nonpurulent	Purulent				
<ul style="list-style-type: none"> • Caused by beta-hemolytic strep⁵ <ul style="list-style-type: none"> – Usually group A strep – Sometimes group B, C, G – All are penicillin susceptible <ul style="list-style-type: none"> • Clindamycin resistance 10–20% in B, C, G • MSSA estimated to be the cause of only ~10% of cases • Treatment: <ul style="list-style-type: none"> – Penicillin G IV or amoxicillin PO – Cefazolin or ampicillin/sulbactam IV – Oral first-generation cephalosporin or amoxicillin/clavulanate PO 	<ul style="list-style-type: none"> • Caused by <i>S. aureus</i> <ul style="list-style-type: none"> – Risk for MRSA • Debridement required whenever possible • Ultrasound may be helpful to detect abscess or phlegmon in cases where physical exam is equivocal • Treatment: Cover for MRSA <ul style="list-style-type: none"> – Trimethoprim/sulfamethoxazole (TMP/SMX), doxycycline, clindamycin* – Vancomycin or linezolid for more severe cases <p style="font-size: small; margin-top: 5px;">*When using clindamycin, check local resistance.</p>				

Slide Title and Commentary	Slide Number and Slide
<p>Moment 2: Etiology of Nonpurulent Cellulitis in the MRSA Era Is NOT MRSA</p> <p>SAY:</p> <p>A common clinical concern is whether nonpurulent cellulitis is caused by MRSA, given the increase in MRSA skin and soft tissue infections seen in the early 2000s. A 2017 randomized controlled trial in 500 outpatients older than 12 years with uncomplicated, nonpurulent cellulitis compared a regimen without MRSA activity to one with MRSA activity.</p> <p>Patients received either cephalexin or cephalexin and trimethoprim/sulfamethoxazole for 7 days. All patients had ultrasounds of the lesion to confirm no abscess was present.</p> <p>The proportions of patients with prior MRSA infection (4%) and diabetes (~10%) were comparable in both arms. Clinical cure rates in patients who complied with the protocol were similar: 86 percent in the cephalexin only group versus 84 percent in the cephalexin plus trim/sulfa group.</p> <p>The finding that clinical cure was high with therapy directed only at beta-hemolytic strep and MSSA, and that additional MRSA coverage offered no benefit, is highly suggestive that the addition of MRSA coverage is not needed in patients with nonpurulent cellulitis.</p>	<p>Slide 15</p> <p>Moment 2: Etiology of Nonpurulent Cellulitis in the MRSA Era Is NOT MRSA</p> <ul style="list-style-type: none"> • Randomized controlled trial (RCT) of outpatients older than 12 years with uncomplicated cellulitis 2009–2012⁶ <ul style="list-style-type: none"> – All patients had ultrasound to confirm no abscess present • Patients received either cephalexin or cephalexin and trimethoprim/sulfamethoxazole for 7 days • Proportions of patients with prior MRSA infection (4%) and diabetes (~10%) similar in both arms • Clinical cure in patients who complied with the protocol: 86% in cephalexin group vs 84% in the combination group <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p>Cellulitis and SSTI 15</p>

Slide Title and Commentary	Slide Number and Slide
<p>Skin Abscesses With Minimal Cellulitis</p> <p>SAY:</p> <p>Another clinical concern is the role of antibiotics in treatment of skin abscesses with minimal associated cellulitis. The primary treatment for cutaneous abscesses is drainage, and the role of adjunctive antibiotic therapy after drainage has been uncertain.</p> <p>A recent study suggests a modest benefit of antibiotic therapy for adult outpatients with drained abscesses at least 2 cm in diameter.</p> <p>In the study, 617 patients received trimethoprim/sulfamethoxazole and 630 patients received placebo for 7 days. Baseline patient and lesion characteristics were similar—8 percent had prior methicillin-resistant <i>S. aureus</i> or MRSA infection, 11 percent had diabetes, the median abscess diameter was 2.5 cm, and <i>S. aureus</i> was isolated in more than 60 percent of cases (predominantly MRSA). Clinical cure in the evaluable population was 95 percent for trim/sulfa and 86 percent for placebo with a p-value of < 0.001. However, trim/sulfa was associated with adverse events in approximately 10 percent of patients.</p> <p>Overall, clinical cure was high in both groups. Clinicians should weigh the higher proportion of cure with antibiotics with the potential for antibiotic side effects when making the decision about prescribing antibiotics for patients with uncomplicated skin abscesses.</p>	<p>Slide 16</p> <p style="background-color: #00A0C0; color: white; padding: 5px; text-align: center;">Skin Abscesses With Minimal Cellulitis</p> <ul style="list-style-type: none"> • The primary treatment for cutaneous abscesses is drainage • The role of adjunctive antibiotic therapy after drainage is unclear • A recent study suggests modest benefit for adult outpatients with drained abscesses ≥ 2 cm⁷ <ul style="list-style-type: none"> – 617 patients received trimethoprim/sulfamethoxazole and 630 patients received placebo for 7 days – Baseline patient and lesion characteristics similar <ul style="list-style-type: none"> • 8% with prior MRSA infection • 11% with diabetes • Median abscess dimension 2.5 cm • <i>S. aureus</i> isolated in > 60% of cases (mainly MRSA) – Clinical cure in evaluable population: 95% for TMP/SMX and 86% for placebo (p < 0.001) – TMP/SMX associated with adverse events in ~10% of patients <div style="font-size: small; margin-top: 10px;"> <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p style="text-align: right;">Cellulitis and SSTI 16</p> </div>

Slide Title and Commentary	Slide Number and Slide
<p>Indications for Antibiotics in Skin Abscesses</p> <p>SAY:</p> <p>There are certain patients and conditions in which antibiotics should be strongly considered in patients with skin abscesses. These include patients with signs and symptoms of systemic illness; underlying immunosuppression, including diabetes, AIDS, and active malignancy; extremes of age; location of abscess in areas that makes complete drainage difficult or that can be associated with septic phlebitis of a major vessel; lack of response to initial incision and drainage, or I&D; and more extensive surrounding cellulitis. Note that many patients admitted to the hospital for these infections will meet these criteria.</p>	<p>Slide 17</p> <p>Indications for Antibiotics in Skin Abscesses</p> <ul style="list-style-type: none"> • Signs and symptoms of systemic illness • Underlying immunosuppression <ul style="list-style-type: none"> – Diabetes, AIDS, malignancy • Extremes of age • Location of abscess in area that makes complete drainage difficult or that can be associated with septic phlebitis of a major vessel • Lack of response to initial incision & drainage • Extensive surrounding cellulitis <p><small>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</small></p> <p><small>Cellulitis and SSTI 17</small></p>
<p>Moment 2: Gram-Negative Coverage in Cellulitis</p> <p>SAY:</p> <p>Gram-negative organisms are generally not the cause of either purulent or nonpurulent cellulitis; thus, routine Gram-negative coverage is not needed in the normal host with cellulitis. Patients with diabetes who have cellulitis also do not need Gram-negative coverage in most cases. For patients with cellulitis associated with a diabetic ulcer, several publications have shown that Gram-positive organisms are the most common colonizing organisms with the exceptions of longstanding ulcers and/or prior receipt of multiple antibiotic courses. Gram-negative coverage can be considered in these patients.</p> <p>Other indications for Gram-negative coverage include critically ill patients, neutropenic or severely immunocompromised patients, concern for necrotizing infection, peri-rectal infections, bites, cellulitis associated with aquatic injuries, and severe surgical site infections involving the groin or abdominal wall.</p>	<p>Slide 18</p> <p>Moment 2: Gram-Negative Coverage in Cellulitis</p> <ul style="list-style-type: none"> • Gram-negative organisms are generally not the cause of either purulent or nonpurulent cellulitis; thus, routine Gram-negative coverage is not indicated in the normal host⁸ • Patients with diabetes who have cellulitis do not need Gram-negative coverage in most cases <ul style="list-style-type: none"> – Consider if associated with an ulcer that may have become colonized with a Gram-negative organism • Other indications for Gram-negative coverage: <ul style="list-style-type: none"> – Severely ill patient – Neutropenic or severely immunocompromised patient – Concern for necrotizing infection – Peri-rectal infection – Bites – Aquatic injury – Severe surgical site infection involving the groin or abdominal wall <p><small>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</small></p> <p><small>Cellulitis and SSTI 18</small></p>

Slide Title and Commentary	Slide Number and Slide
<p>Moment 2: Nonantibiotic Therapy</p> <p>SAY:</p> <p>We often forget that successful treatment of cellulitis requires more than just antibiotics. Most importantly, patients must elevate the affected extremity.</p> <p>In addition, it is important to assess for and treat tinea pedis, if it is found. If the cellulitis is associated with venous stasis or lymphedema, these conditions must be managed at the same time.</p>	<p>Slide 19</p> <p>Moment 2: Nonantibiotic Therapy</p> <ul style="list-style-type: none"> • Elevate the affected extremity • Assess for and treat tinea pedis • Manage venous stasis and lymphedema  <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p>Cellulitis and SSTI 19</p>
<p>The Four Moments of Antibiotic Decision Making</p> <p>SAY:</p> <p>Moment 3 occurs after a day or more has passed. Ask yourself: Can I stop antibiotics? Can I narrow therapy or change from IV to oral therapy?</p>	<p>Slide 20</p> <p>The Four Moments of Antibiotic Decision Making</p> <ol style="list-style-type: none"> 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?  <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p>Cellulitis and SSTI 20</p>

Slide Title and Commentary	Slide Number and Slide																				
<p>Moment 3: Narrowing and Converting to Oral Therapy</p> <p>SAY:</p> <p>When deciding whether to narrow or stop therapy for cellulitis, you should assess whether the patient is improving. It is important not to equate an increase or lack of change in the size of margins of erythema after a few doses of antibiotics with antibiotic failure. Toxin production can cause extensive local inflammation, and its persistence or extension over the first 2 days of therapy does not, by itself, indicate antibiotic failure. However, the erythema should become less intense and systemic symptoms such as fever should improve in 48 to 72 hours.</p> <p>The graph on the slide shows the results of a study of the natural history of cellulitis on days 1, 2, and 3 of antibiotic therapy (moving left to right). The blue bars show the proportions of patients with cessation of lesion spread. The red bars show improvement in local inflammation. The green bars show both cessation of lesion spread and improvement in inflammation. The purple bars show defervescence.</p> <p>Note that only about half of patients have cessation of lesion spread on day 1 of therapy. This proportion increases to more than 90 percent by day 2–3. Similar findings can be noted for improvement of local inflammation. But, when these variables are combined in the third green bar, overall improvement is generally not seen until day 3 of therapy. Finally, note that many patients remain febrile until day 3.</p>	<p>Slide 21</p> <p>Moment 3: Narrowing and Converting to Oral Therapy</p> <ul style="list-style-type: none"> An increase or lack of change in the size of the margins of erythema is not indicative of antibiotic failure⁹ <ul style="list-style-type: none"> Toxin production can cause extensive local inflammation Persistence or extension of erythema does not indicate antibiotic failure Erythema should become less intense Systemic symptoms such as fever should improve by 48–72 hours <table border="1"> <caption>Approximate data from the bar chart on Slide 21</caption> <thead> <tr> <th>Day</th> <th>Cessation of lesion spread (%)</th> <th>Improvement of local inflammation (%)</th> <th>Cessation of lesion spread and improvement of local inflammation (%)</th> <th>Defervescence (%)</th> </tr> </thead> <tbody> <tr> <td>Day 1</td> <td>~50</td> <td>~45</td> <td>~35</td> <td>~35</td> </tr> <tr> <td>Day 2</td> <td>~90</td> <td>~85</td> <td>~80</td> <td>~60</td> </tr> <tr> <td>Day 3</td> <td>~95</td> <td>~90</td> <td>~90</td> <td>~85</td> </tr> </tbody> </table> <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p>Cellulitis and SSTI 21</p>	Day	Cessation of lesion spread (%)	Improvement of local inflammation (%)	Cessation of lesion spread and improvement of local inflammation (%)	Defervescence (%)	Day 1	~50	~45	~35	~35	Day 2	~90	~85	~80	~60	Day 3	~95	~90	~90	~85
Day	Cessation of lesion spread (%)	Improvement of local inflammation (%)	Cessation of lesion spread and improvement of local inflammation (%)	Defervescence (%)																	
Day 1	~50	~45	~35	~35																	
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Day 3	~95	~90	~90	~85																	

Slide Title and Commentary	Slide Number and Slide
<p>Moment 3: Narrowing and Converting to Oral Therapy</p> <p>SAY:</p> <p>If patients are demonstrating improvement by day 3, most can be converted to oral therapy and have therapy narrowed if initial broad-spectrum therapy was started. For example, therapy specifically directed at Gram-negative organisms can be stopped unless there is evidence of Gram-negative infection. If vancomycin was started, it can usually be switched to an oral agent based on the cellulitis type as described previously.</p> <p>Potential regimens for nonpurulent cellulitis are an oral beta-lactam or, for patients with severe penicillin allergy, clindamycin. For patients with purulent cellulitis and culture data, convert to oral therapy based on these results. For patients without culture data, convert to TMP/SMX or doxycycline. If clindamycin susceptibilities are high in your area or you know that the organism is susceptible, it can be considered as an option for MRSA treatment, although it is more associated with <i>Clostridioides difficile</i> infection than other options. Linezolid can be considered for more severe infections but as we discussed previously, widespread use will likely lead to a rise in resistance so it should be used judiciously.</p> <p>You should consider extending IV therapy in obese patients if there is concern that adequate tissue levels cannot be obtained.</p> <p>If a patient is not improving by day 3, it is important to reassess. Consider imaging to assess for a new or persistent abscess and/or a change in antibiotic therapy.</p>	<p>Slide 22</p> <p>Moment 3: Narrowing and Converting to Oral Therapy</p> <ul style="list-style-type: none"> • Most patients can be converted to oral therapy and have therapy narrowed after 3 days. <ul style="list-style-type: none"> – Stop therapy specifically directed at Gram-negative organisms unless there is evidence of Gram-negative infection – Convert vancomycin therapy to an oral regimen based on cellulitis type <ul style="list-style-type: none"> • Nonpurulent cellulitis: beta-lactam (penicillin allergy: clindamycin) • Purulent cellulitis: TMP/SMX, doxycycline, linezolid • Consider extending IV therapy in obese patients if there is concern that adequate tissue levels cannot be obtained <p><small>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</small></p> <p><small>Cellulitis and SSTI 22</small></p>

Slide Title and Commentary	Slide Number and Slide
<p>The Four Moments of Antibiotic Decision Making</p> <p>SAY:</p> <p>The last moment you must consider is: What duration of antibiotic therapy is needed for your patient's diagnosis?</p>	<p>Slide 23</p> <p>The Four Moments of Antibiotic Decision Making</p> <ol style="list-style-type: none"> 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? <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p>Cellulitis and SSTI 23</p>
<p>Moment 4: Duration of Therapy for Uncomplicated Cellulitis</p> <p>SAY:</p> <p>Most cases of cellulitis can be treated with 5–7 days of antibiotics. This recommendation is supported by evidence from clinical trials showing that shorter course therapy is as effective as longer courses.</p> <p>For example, a randomized controlled trial compared 5 versus 10 days of therapy. Patients with bacteremia, severe sepsis, deep soft tissue infection, bites, infection requiring debridement, or diabetic foot infection were excluded. All patients received antibiotics for 5 days and then were randomized to placebo versus 5 more days of therapy.</p> <p>Of note, patients could still have warmth, erythema, tenderness, and edema at the time of randomization, but it had to be improving. The primary outcome was resolution by day 14 and no recurrence by day 28. Ninety-eight percent of patients in both groups were treated successfully.</p>	<p>Slide 24</p> <p>Moment 4: Duration of Therapy for Uncomplicated Cellulitis</p> <ul style="list-style-type: none"> • RCT of 5 vs. 10 days of therapy¹⁰ • Exclusions: bacteremia, severe sepsis, deep soft tissue infection, bites, infection requiring debridement, diabetic foot • All patients received antibiotics for 5 days <ul style="list-style-type: none"> – Randomized to placebo vs. 5 more days and at least minimal improvement (could still have warmth, erythema, tenderness, edema) – Primary outcome: resolution by day 14 and no recurrence by day 28 • 98% of patients in both groups treated successfully <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p>Cellulitis and SSTI 24</p>

Slide Title and Commentary	Slide Number and Slide
<p>Moment 4: Duration of Therapy for Acute Bacterial Skin and Skin Structure Infection</p> <p>SAY:</p> <p>Another randomized controlled trial included patients with more severe infections including cellulitis/erysipelas, major cutaneous abscess, or wound infection surrounded by erythema. Patients received either tedizolid once a day for 6 days or linezolid twice a day for 10 days. Exclusions included uncomplicated infection, associated with a vascular catheter site, thrombophlebitis, or nonclean surgery.</p> <p>Two hundred seventy-four patients had cellulitis/erysipelas, 198 had major cutaneous abscess, and 198 had wound infection with comparable numbers in each arm of the study</p> <p>Cure at investigator assessment 7–14 days after treatment was the same in both groups: 85 percent versus 86 percent. This study is supportive of use of a 5–7 day course of therapy for cellulitis and other skin structure infections with source control. While tedizolid and linezolid were the agents studied, it would be reasonable to extrapolate the findings of this study to patients who receive other agents. Most cases of cellulitis or cutaneous abscesses can be treated with a total of 5–7 days.</p>	<p>Slide 25</p> <p>Moment 4: Duration of Therapy for Skin and Skin Soft Tissue Infection</p> <ul style="list-style-type: none"> • RCT of tedizolid for 6 days vs. linezolid for 10 days for treatment of cellulitis/erysipelas, major cutaneous abscess, or wound infection surrounded by erythema¹³ • Exclusions: uncomplicated infection, associated with a vascular catheter site, thrombophlebitis, or non-clean surgery • Syndrome <ul style="list-style-type: none"> – Cellulitis/erysipelas: 274 patients – Major cutaneous abscess: 198 patients – Wound infection: 198 patients • Cure at investigator assessment 7–14 days after treatment: 85% vs 86% <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> <p>Cellulitis and SSTI 25</p>

Slide Title and Commentary	Slide Number and Slide
<p>Improving Prescribing for Cellulitis and Skin and Soft Tissue Infections at Your Hospital</p> <p>SAY:</p> <p>It is not uncommon for clinicians to prescribe broader-than-necessary antibiotic regimens for longer-than-needed durations for patients with cellulitis and skin and soft tissue infections. These infections often don't have associated culture data to make prescribing decisions easier and, as we have discussed, their physical manifestations such as erythema may take a few days to resolve. We have seen data in this presentation that should provide reassurance to clinicians to modify longstanding prescribing practices.</p> <p>Developing or modifying clinical guidelines for these infections, and making sure guidelines, treatment algorithms, and orders sets are available at the point of care is critical to prompt prescribing changes.</p> <p>Further, it is helpful to expand the discussion of management of cellulitis and skin and soft tissue infections across all disciplines that care for these patients such as the emergency department, medicine, surgery, orthopedic surgery, and plastic surgery.</p> <p>Finally, using the Four Moments of Antibiotic Decision Making framework, support colleagues in making evidence-based decisions about antibiotic and management plans for these infections.</p>	<p>Slide 26</p> <p>Improving Prescribing for Cellulitis and Skin and Soft Tissue Infections at Your Hospital</p> <ul style="list-style-type: none"> • Changing practices of antibiotic prescribing for cellulitis and skin and soft tissue infections can be challenging • Some reasons may include frequent lack of culture data to guide decisions and the persistence of clinical signs and symptoms on exam • Approaches to change prescribing practices include¹² <ul style="list-style-type: none"> – Development of clinical guidelines, protocols, and order set that are available at the point of care – Engagement of all clinicians who treat these infections <ul style="list-style-type: none"> • Emergency department, medicine, surgery, orthopedic surgery, plastic surgery – Use of the Four Moments of Antibiotic Decision Making framework to support colleagues in making evidence-based treatment and management plans <p><small>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</small></p> <p style="text-align: right;"><small>Cellulitis and SSTI 26</small></p>

Slide Title and Commentary	Slide Number and Slide
<p>Take-Home Messages</p> <p>SAY:</p> <p>To summarize this discussion, first make the right diagnosis! Cellulitis is generally of sudden onset, unilateral, and associated with significant warmth, erythema, fever, and evidence of inflammation (e.g., elevated WBC and inflammatory markers). Consider mimics of cellulitis before giving antibiotics to all patients with “red” extremities.</p> <p>Distinguish between nonpurulent and purulent cellulitis and treat based on the expected microbiology of these different syndromes.</p> <p>Patients should be improving by day 3 but may have some residual signs and symptoms. Lack of complete resolution does NOT mean that antibiotics are not working.</p> <p>Five- to seven-day courses of therapy work for most cases of cellulitis.</p> <p>There are many opportunities for stewardship in improving empiric therapy for cellulitis and avoiding prolonged courses of therapy. Think about areas for improvement in your practice and in your hospital.</p>	<p>Slide 27</p> <div data-bbox="852 258 1479 674"> <p style="text-align: center;">Take-Home Messages</p> <ul style="list-style-type: none"> • Make the right diagnosis! • Distinguish between nonpurulent and purulent cellulitis <ul style="list-style-type: none"> – Treat based on the expected microbiology of these different syndromes • Patients should be improving by day 3 <ul style="list-style-type: none"> – Lack of complete resolution does NOT mean that treatment is not working • Five- to seven-day courses of therapy work for most cases of cellulitis • There are many opportunities for stewardship in improving empiric therapy for cellulitis and avoiding prolonged courses of therapy </div> <div data-bbox="873 684 992 722" style="font-size: small;"> <p>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</p> </div> <div data-bbox="1240 695 1479 730" style="text-align: right; font-size: small;"> <p>Cellulitis and SSTI 27</p> </div>

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<p>Disclaimer</p> <p>SAY:</p> <p>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.</p> <p>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.</p>	<p>Slide 28</p> <p style="text-align: center;">Disclaimer</p> <ul style="list-style-type: none"> 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. <p><small>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</small></p> <p style="text-align: right;"><small>Cellulitis and SSTI 28</small></p>
<p>References</p>	<p>Slide 29</p> <p style="text-align: center;">References</p> <ol style="list-style-type: none"> Hirschmann JV, Raugi GJ. Lower limb cellulitis and its mimics: Part 1. <i>J Am Acad Dermatol.</i> 2012;Aug;67(2):163.e1-12. PMID: 22794815. Bystritsky R, Chambers H. Cellulitis and soft tissue infections. <i>Ann Intern Med.</i> 2018 Feb 6;168(3):TC17-32. PMID: 29404597. David CV, Chira S, Eells SJ, et al. Diagnostic accuracy in patients admitted to hospitals with cellulitis. <i>Dermatol Online J.</i> 2011 Mar 15;17(3):1. PMID: 21426867. Keller EC, Tomecki KJ, Alraies MC. Distinguishing cellulitis from its mimics. <i>Cleve Clin J Med.</i> 2012 Aug;79(8):547-52. PMID: 22854433. Jeng A, Beheshti M, Nathan R. The role of beta-hemolytic streptococci in causing diffuse, nonculturable cellulitis: a prospective investigation. <i>Medicine (Baltimore).</i> 2010 Jul;89(4):217-26. PMID: 20616661. Moran GJ, Krishnadasan A, Mower WR, et al. Effect of cephalexin plus trimethoprim-sulfamethoxazole vs cephalexin alone on clinical cure of uncomplicated cellulitis: a randomized clinical trial. <i>JAMA.</i> 2017 May; 317(20):2088-96. PMID: 28535235. <p><small>AHRQ Safety Program for Improving Antibiotic Use – Acute Care</small></p> <p style="text-align: right;"><small>Cellulitis and SSTI 29</small></p>

Slide Title and Commentary	Slide Number and Slide
<p>References</p>	<p>Slide 30</p> <p style="text-align: center;">References</p> <ol style="list-style-type: none"> 7. Talan DA, Mower WR, Krishnadasan A, et al. Trimethoprim-sulfamethoxazole versus placebo for uncomplicated skin abscess. <i>N Engl J Med</i>. 2016 Mar 3;374(9):823-32. PMID: 26962903. 8. Stevens DL, Bisno AL, Chambers HF, et al. Practice Guidelines for the diagnosis and management of skin and soft tissue infections: 2014 update by the Infectious Diseases Society of America. <i>Clin Infect Dis</i>. 2014 Jul 15;59(2):e10-52. PMID: 24973422. 9. Bruun T, Oppegaard O, Hufthammer KO, et al. Early response in cellulitis: a prospective study of dynamics and predictors. <i>Clin Infect Dis</i>. 2016 Oct 15;63(8):1034-41. PMID: 27402819. 10. Hepburn MJ, Dooley DP, Skidmore PJ, et al. Comparison of short-course (5 days) and standard (10 days) treatment for uncomplicated cellulitis. <i>Arch Intern Med</i>. 2004 Aug 9;164(15):1669-74. PMID: 15302637. <p style="font-size: small;">AHRQ Safety Program for Improving Antibiotic Use – Acute Care Cellulitis and SSTI 30</p>
<p>References</p>	<p>Slide 31</p> <p style="text-align: center;">References</p> <ol style="list-style-type: none"> 11. Prokocimer P, De Anda C, Fang E, et al. Tedizolid phosphate vs linezolid for treatment of acute bacterial skin and skin structure infections: the ESTABLISH-1 randomized trial. <i>JAMA</i>. 2013 Feb 13;309(6):559-69. PMID: 23403680. 12. Jenkins TC, Knepper BC, Sabel AL, et al. Decreased antibiotic utilization after implementation of a guideline for inpatient cellulitis and cutaneous abscess. <i>Arch Intern Med</i>. 2011 Jun 27;171(12):1072-9. PMID: 21357799. <p style="font-size: small;">AHRQ Safety Program for Improving Antibiotic Use – Acute Care Cellulitis and SSTI 31</p>