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## Antibiotic Stewardship in Skin and Soft Tissue Infections

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**Title:** Antibiotic Stewardship in Skin and Soft Tissue Infections

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**Abstract:**

Antibiotic use during inpatient hospitalizations have a significant impact on both patient care and healthcare costs. Vancomycin, an inhibitor of cell wall synthesis in Gram-positive bacteria, and piperacillin/tazobactam, an anti-pseudomonal penicillin with a beta-lactamase inhibitor, are two of the more commonly used antibiotics. Using data collected over a one month period in 2019 from inpatient hospitalizations, we aim to determine the most common indicated uses for vancomycin and piperacillin-tazobactam, along with the average days of therapy for their use in treating skin and soft tissue infections.

**Introduction:**

Skin and soft tissue infections (SSTIs) are characterized by microbial invasion of the skin layers and are common in various healthcare settings. Physicians primarily refer to the Infectious Diseases Society of America's (IDSA) 2014 classification of SSTIs.<sup>1</sup> The IDSA classifies them as primarily nonpurulent (cellulitis, erysipelas, and necrotizing) versus purulent (furuncles, carbuncles, and abscesses). In this classification, abscesses and cellulitis are the most prevalent. One study, conducted between 2005-2010, in the United States found a total of 2.3 million cases of SSTIs in ambulatory and inpatient settings combined.<sup>2</sup> This was higher than the rates of pneumonia and urinary tract infections during the same time period. Another study found that between 2000 and 2012, there was a 40% increase (2.4 million to 3.3 million) in cases of SSTIs.<sup>3</sup> These epidemiologic findings indicate that the disease burden of SSTIs is high and concerning and susceptible to antimicrobial stewardship interventions.

This study aims to investigate the average days of therapy (DOT) for use of vancomycin and piperacillin-tazobactam, in a local hospital, with over 800 beds, in the treatment of skin and soft tissue infections. Data was collected over a one month period of time during inpatient hospitalizations.

**Materials and Methods:**

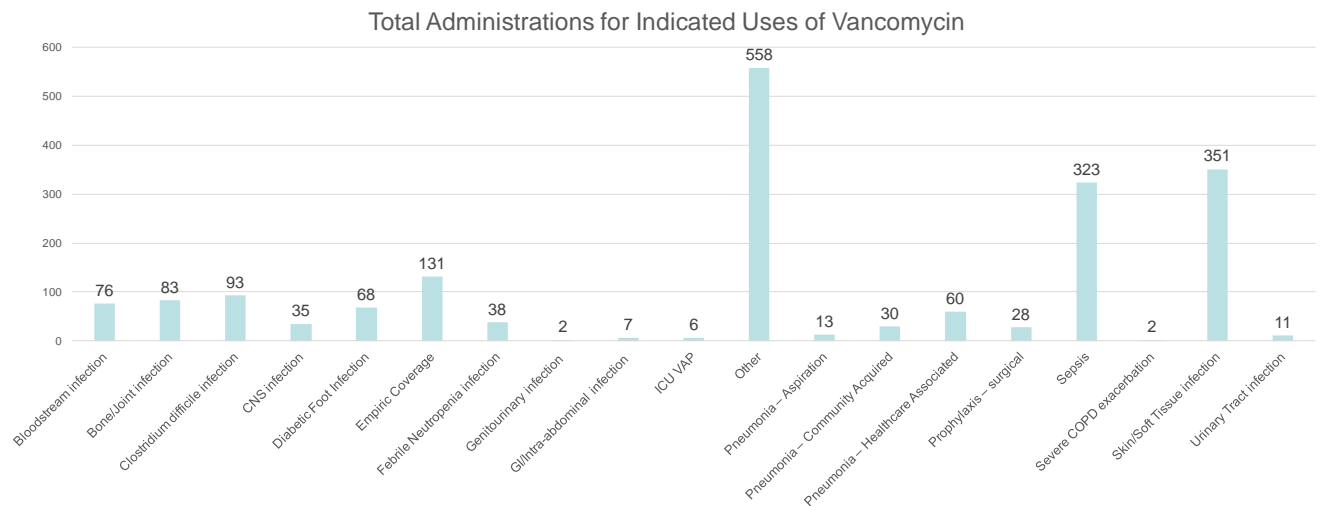
Data regarding the total administrations of all antimicrobials over a one month period (January 2019) from a local hospital in the Rio Grande Valley were obtained. Patient encounters were tracked from all hospital services. This included: the emergency room, inpatient hospitalizations, intensive care unit, among other services. The data tracked order ID, patient account numbers, the prescribing provider, administering nurse, scheduled and actual administration time, route of administration, as well as the indicated use of the antibiotic. All data was obtained via Microsoft Excel.

The data was sorted by antibiotic used and then tallies were made of the various indicated uses for the chosen antimicrobial. The tallies were organized into a bar graph of total administrations for indicated uses of the medication. After this, we sorted by indications, and measured the days of therapy for administration of the two medications by skin and soft tissue infections. Days of therapy accounted for multiple administrations in one day. To clarify, multiple administrations were counted as one day of therapy.

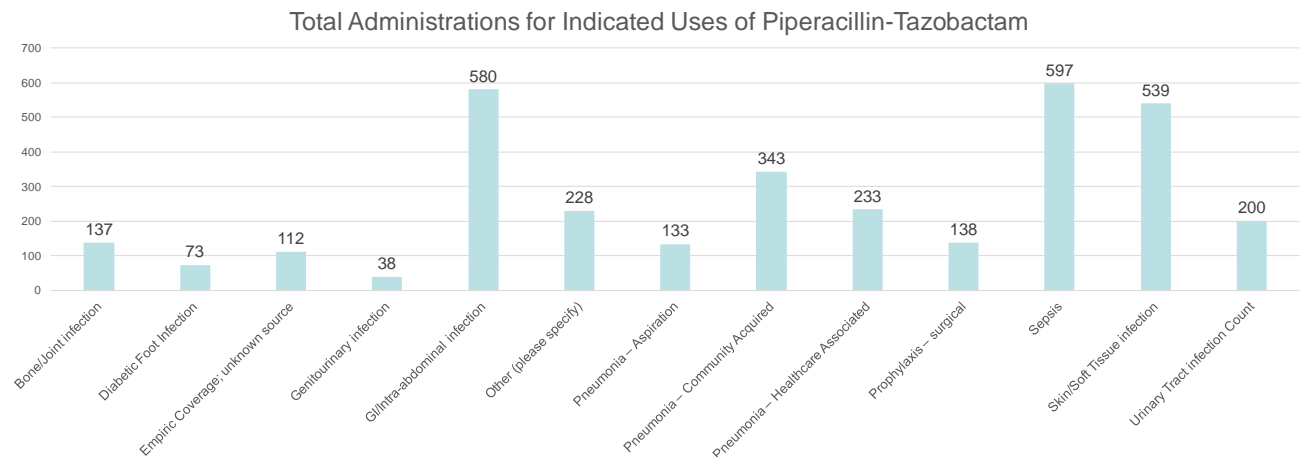
## Results:

Table 1.

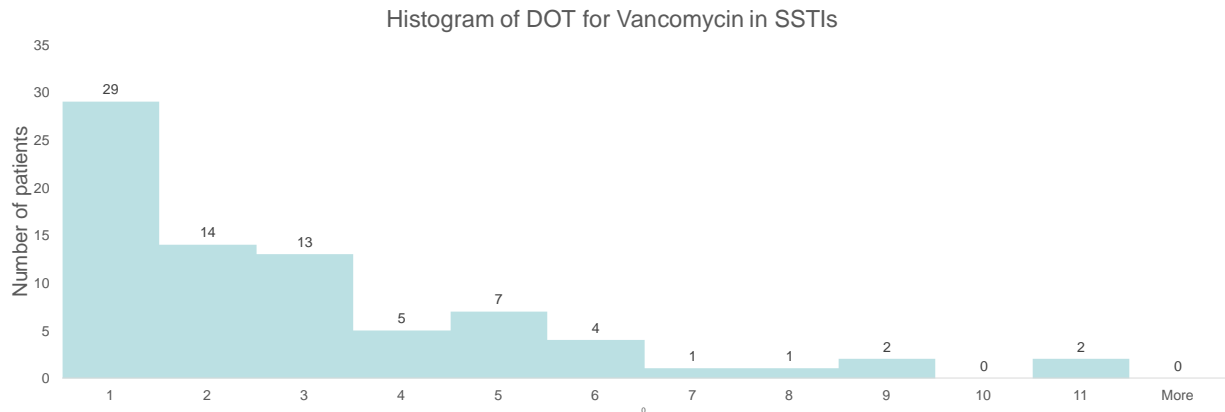
Antibiotic	Drug specific day of therapy	Day of therapy per 1,000 patient days
Piperacillin-tazobactam	1561	79.7
Vancomycin	1194	61



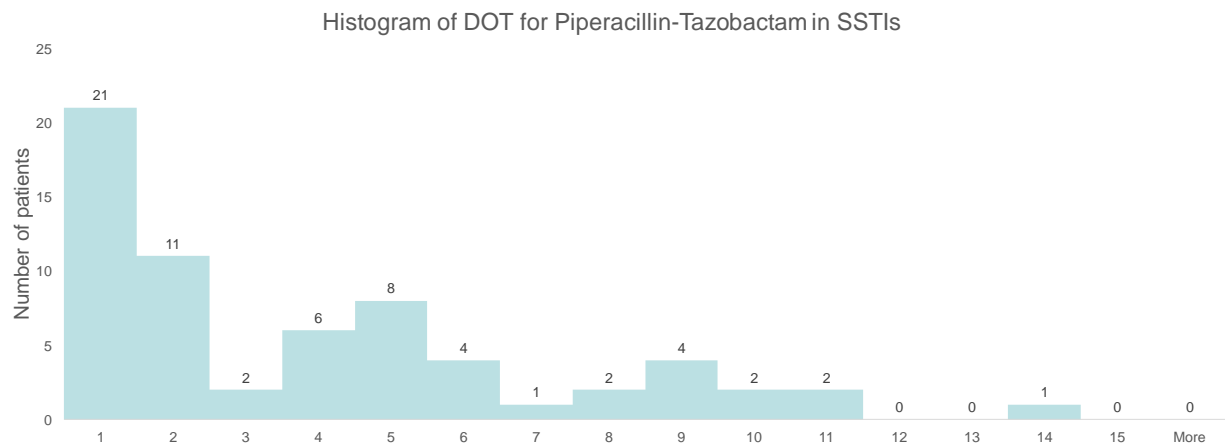
**Figure 1.** Total tally of administrations for vancomycin show that the highest indicated uses are listed as other, skin/soft tissue infections, and sepsis, in descending order.



**Figure 2.** Total tally of administrations for piperacillin/tazobactam show that the highest indicated uses are listed as sepsis, GI/intra-abdominal infections, and skin/soft tissue infections, in descending order.



**Figure 3.** Histogram of calculated days of therapy for vancomycin in the treatment of SSTIs showed and an average DOT of 2.97 days.



**Figure 4.** Histogram of calculated days of therapy for piperacillin-tazobactam in the treatment of SSTIs showed and an average DOT of 3.94 days.

### Discussion:

Among the antimicrobials used in the one-month period studied, table 1 indicates that piperacillin-tazobactam and vancomycin had a drug-specific day of therapy of 1561 and 1194, respectively. This was the first and second highest days of therapy tallied among the antimicrobials, with ceftriaxone coming in at third with 1022 days of therapy. The days of therapy were adjusted per 1,000 patient days and found to be 61 and 79.7 for vancomycin and piperacillin-tazobactam, respectively. Given their high utilization rates, among various antimicrobials, our initial interest in studying these two particular medications was reaffirmed. The antimicrobials studied included antibiotics, antivirals, and antifungals. Moreover, the high usage of vancomycin and piperacillin-tazobactam makes sense considering that the data was collected in a hospital setting. Vancomycin, which is primarily given intravenously, with oral vancomycin only indicated in the treatment of clostridioides infection, and piperacillin-tazobactam also being administered intravenously. Intravenous administration necessitates care from a healthcare worker. Data collected in an outpatient setting would likely show vastly different results.

Results from figure 1 show that for vancomycin, “other,” skin and soft tissue infections, and sepsis were the top three indicated uses. This correlates with guidelines. For skin and soft tissue infections, the IDSA’s 2014 guidelines recommend vancomycin plus piperacillin/tazobactam in the empiric treatment of nonpurulent infections.<sup>1</sup> Nonpurulent infections would include necrotizing infections, cellulitis, and erysipelas. Vancomycin coverage includes methicillin-susceptible and resistant staph aureus but with no activity against gram-negative aerobes or anaerobes. Increased use of vancomycin likely points to providers concern about MRSA infections. This figure also illustrates a study limitation: the category of “other” had the highest indicated use and is also vague. This is concerning and warrants a more granular study. In the future, we may investigate with a random sampling of the “other” uses and take a more detailed look to see what those indications included. This category should also be the targeted of a potential quality improvement project. As it currently stands, “other” is simply too vague.

Results from figure 2 show that for piperacillin-tazobactam, the highest indicated uses were for sepsis, intraabdominal infections, and skin and soft tissue infections. Again, piperacillin-tazobactam (plus vancomycin) is used for empiric treatment of severe nonpurulent skin and soft tissue infections. Moreover, this combination is also recommended for treatment of polymicrobial skin infections by the IDSA’s guidelines as well.<sup>1</sup> Of note, is the use of piperacillin-tazobactam in the treatment of sepsis. Piperacillin-tazobactam covers both gram positives and negatives, as well as anaerobes, and is frequently used in the treatment of sepsis. Sepsis is defined as a systemic inflammatory response due to infection that can lead to organ dysfunction and death. One retrospective study found that rates of sepsis increased from 13 to 78 cases per 100,00 between 1998 and 2009.<sup>4</sup> Per the CDC, each year at least 1.7 million adults develop sepsis in America and nearly 270,000 die as a result of it.<sup>5</sup> Sepsis clearly makes a significant impact on the lives of patients. However, precise definitions of sepsis are not unanimously accepted by differing physicians and their professional groups. The Society of Critical Care Medicine (SCCM) released a “Surviving Sepsis Campaign” in 2016.<sup>6</sup> On the other hand, the Infectious Diseases Society of America (IDSA) does not endorse the SCCM’s guidelines for sepsis out of concern that the SCCM recommendations will lead to overtreatment and overuse of broad spectrum antibiotics.<sup>7</sup> At this particular hospital, the nursing staff has a sepsis protocol that is activated when the condition is suspected in hopes of leading to better patient outcomes. This potentially life-threatening condition, its treatment and relationship with antibiotic stewardship clearly warrants further study.

Figures 3 and 4 findings show that that the average days of therapy for use of vancomycin and piperacillin-tazobactam in the treatment of SSTIs was 2.97 and 3.94 days, respectively. Of note, one retrospective chart review in 2018 found that among hospitalized patients with nonnecrotizing skin and soft tissue infections, the duration of antibiotic treatment was 2 days (with a range of 1-18 days) and an adherence to IDSA guidelines of 70.2%.<sup>8</sup> IDSA guidelines recommend that duration of antibiotics should be 5 days for treatment of cellulitis and increased if the clinical presentation is not improving. This previous study, and the IDSA guideline, are in-line with the findings in our project for these two medications. We intend to compare the average days of therapy for other indications (e.g., sepsis) and compare to national averages. Our study limitations include the limited, one-month duration of the data set. Of concern is a large category of prescriptions labeled as “other” which can be explored further to understand prescription patterns. We plan to expand this work using data from a 12-month period in the same hospital.

of 1-18 days) with an adherence to IDSA guidelines of 70.2%. We intend to compare the average DOT for different indications (e.g., sepsis) and compare to national averages. We hope to interpret this data in the context of guideline recommendations on duration of intravenous therapy for SSTIs, and evaluate what differences may exist between guidelines and clinical practice. Our study limitations include the limited, one-month duration of the data set. Of concern is a large category of prescriptions labeled as “other” which can be explored further to understand prescription patterns. Additionally, limitations may also include days of therapy as a measurement itself. There has been some concern with days of therapy, given inaccuracy with patients with renal failure or in drugs with long half-lives. Some have suggested “exposure days” as a more accurate measure than days of therapy.

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