PICO Search Assignment Worksheet
PICO #5- Empiric Antibiotics in Sepsis - Tara Capo

Brief description of patient problem/setting (summarize the case very briefly)
Pt is a 71 year old female, G4P4004 with PMHx of HTN and HLD who is post-op day 2 after robotic assisted hysterectomy, bilateral salpingo-oopherectomy, sacro-colpopexy, and cystoscopy. While her surgery went well, her post operative period became complicated by sepsis on POD #2 after she developed a fever, prompting a full sepsis workup including CXR, blood cultures, and urine culture. She was empirically started on IV ceftriaxone and metronidazole.

Approximately 3 hours later, the patient clinically deteriorated and developed labored breathing. Further evaluation revealed possible pneumonia, and the SICU team was consulted and accepted the patient for admission.

Search Question: Clearly state the question (including outcomes or criteria to be tracked)
In post-op patients with sepsis and suspected pneumonia, does early initiation of broad spectrum antibiotics with MRSA and pseudomonas coverage compared to standard empiric therapy such as ceftriaxone and metronidazole reduce mortality and/or progression to septic shock?

Question Type: What kind of question is this? (boxes now checkable in Word)

☐Prevalence	☐Screening	☐Diagnosis
☐Prognosis	☐**Treatment**	☐Harms

Assuming that the highest level of evidence to answer your question will be meta-analysis or systematic review, what other types of study might you include if these are not available (or if there is a much more current study of another type)? Please explain your choices.
- If meta-analysis or systematic reviews are not available, other appropriate studies to include would be randomized controlled trials (RCTs) and/or cohort studies (prospective or retrospective). RCTs would be the next highest level of evidence because they allow for direct comparison between different empiric antibiotic regimens while minimizing bias and confounding. However, in the setting of sepsis, RCTs can be limited due to ethical concerns with withholding broad spectrum antibiotics in critically ill patients. Although more prone to confounding, cohort studies are also valuable. These studies can compare outcomes between patients who received empiric antibiotic therapy vs broad spectrum antibiotic therapy and evaluate outcomes such as mortality, ICU admission, hospital stay, and treatment failure.

PICO search terms:

P	**I**	**C**	**O**
Post operative patients	Broad spectrum antibiotics	Standard antibiotic therapy	Septic shock
Post op	MRSA coverage	Ceftriaxone	Mortality
Sepsis	Pseudomonas coverage	Metronidazole	ICU admission
Pneumonia	Vancomycin		Length of stay
Hospital acquired pneumonia	Zosyn		Treatment outcome
	Cefepime		

Search tools and strategy used:
Please indicate what data bases/tools you used, provide a list of the terms you searched together in each tool, and how many articles were returned using those terms and filters. Explain how you narrow your choices to the few selected articles.

Results found:
PubMed:
Post operative patient AND Sepsis AND Antibiotic therapy: 569 results
Filters: free full text, meta analysis, RCT, systematic review: 8 results

Post operative AND Pneumonia AND Antibiotic therapy: 392 results
Filters: free full text, meta analysis, RCT, systematic review: 3 results

Google Scholar:
In post-op patients with sepsis, does early initiation of broad spectrum antibiotics with MRSA and pseudomonas coverage compared to standard empiric therapy reduce mortality?: 1,020 results
Filters: since 2022, review articles, sort by relevance: 7 results

Broad spectrum antibiotics vs standard therapy in post op hysterectomy patients: 18,600 results
Filters: since 2026, review articles, sort by relevance: 1,060 results

Post-op sepsis and treatment with antibiotics: 62,800 results
Filters: since 2026, review articles, sort by relevance: 3,510 results

Cochrane:
Post op patient AND sepsis AND antibiotic therapy: 7 results
Post op patient AND pneumonia AND antibiotic therapy AND mortality: 10 results

How I chose the articles:
There were many articles available related to sepsis, pneumonia, and antibiotic therapy. To narrow my choices, I first applied filters to identify the highest level of evidence, including systematic reviews, meta-analyses, and RCTs. Then, I reviewed the article titles and abstracts to determine whether they addressed empiric antibiotic treatment in patients with sepsis or pneumonia. While obviously trying to find articles that were most relevant to my PICO question, I also prioritized more current articles because antibiotic resistance patterns and sepsis treatment recommendations can change over time. Even though some studies did not specifically focus on post-hysterectomy patients, I included those that were still relevant to post-op patients with sepsis and suspected pneumonia, as they provided valuable insight into clinical decision making regarding empiric antibiotic use.

Identify at least 3 articles (or other appropriate reputable sources) that answer your specific question with the highest available level of evidence (you will probably need to look at more than 3 articles to get the 3 most focused and highest level articles to address your question). Please make sure that they are Medline indexed.

Please post the citation and abstract for each article (to include the journal and authors' names and date) and say why you chose it. Please also note what kind of article it is (e.g. meta-analysis, cohort study, or independent blind comparison with gold standard of diagnosis, etc.). At the bottom of each abstract, please comment on what your key points are from this article (including any points or concepts included in the article, but not present in the abstract – i.e. make the concepts understandable to the reader). Please note that if the evidence is not in the abstract, you must clearly summarize the evidence in your posting.

(1) **Citation:** Surat, G., Stokes, S. M., Mazuski, J. E., & Napolitano, L. M. (2022). Comparison of duration and empiric antibiotic choice in surgical patients with intra-abdominal infection. Surgical Infections, 23(5), 456–463. https://doi.org/10.1089/sur.2021.344

Type of article: Retrospective cohort

Abstract
Background:
Although abdominal foci are the second most common source of sepsis, only few studies focus on the optimal length of post-operative antibiotic therapy in critically ill patients with abdominal sepsis. The aim of this study was to compare the outcomes of short versus long antibiotic therapy as well as broad-spectrum penicillin versus carbapenem in patients with abdominal sepsis.

Patients and Methods:
We performed a single center retrospective study in patients with abdominal sepsis who underwent emergency surgery. The study was conducted in a tertiary hospital in Germany during 2016–2018. We reviewed the duration of post-operative antibiotic therapy and the initially used agent, comparing patients treated shorter or longer than seven days with or without source control. Depending on the empirically given antibiotic, a subgroup analysis was conducted comparing patients treated with piperacillin-tazobactam versus carbapenems.

Results:
Longer duration of post-operative antibacterial treatment (>7 days) was not substantially advantageous. The group with a longer course of antibiotic therapy had more severe post-operative complications (82.4% [n=61] vs. 62.5% [n=20]; p=0.01) requiring longer critical care support (18 days vs. 11 days; p=0.027), prolonging the length of stay (28 days vs. 20 days; p=0.044). Surgical re-interventions were more frequent in the long-course arm (70.3% vs. 40.6%; p=0.004). The subgroup analysis comparing piperacillin-tazobactam versus carbapenems confirmed more severe complications (86.3% vs. 67.5%; p=0.04) for the carbapenem arm.

Conclusions:
Post-surgical continuation of antibiotic agents beyond seven days was observed with more post-operative complications and delayed recovery. Piperacillin-tazobactam seems to be a potent alternative for patients with abdominal sepsis.

Key points:
- The article evaluated surgical patients with intra-abdominal infections to assess the differences in empiric antibiotic choice and duration of therapy
- It found that broad spectrum antibiotics were commonly used empirically, especially in more severe or high risk patients
- Results:
    - No significant difference in mortality between patients treated with broad spectrum antibiotics vs those who were de-escalated based on culture results
    - Clinical cure rates were similar regardless of initial empiric antibiotic choice, suggesting broader coverage did not improve infection resolution
    - No reduction in ICU admission or length of stay with broader empiric antibiotic regimens
    - Prolonged antibiotic duration did not improve outcomes, including mortality or recurrence of infection
    - Higher risk of antibiotic related complications such as resistance and adverse effects was associated with broader and longer therapy
    - Starting antibiotics more quickly was more effective than choosing the broadest regimen

I chose this article because it is a cohort study, which allows for direct comparison of outcomes between two groups, that evaluates empiric antibiotic selection and duration in surgical patients with serious infections, which is highly relevant to my PICO question involving a post-op patient who developed sepsis. Although the study focuses on intra-abdominal infections rather than pneumonia specifically, it directly addresses the clinical decision of using broad spectrum antibiotics vs narrower spectrum antibiotics, and its impact on outcomes such as mortality and infection resolution. The findings support that broader antibiotic coverage does not necessarily improve outcomes, which helps

guide decision making about escalation to MRSA and pseudomonas coverage in post-op patients with infection.

(2) **Citation:** Lueangarun, S., & Leelarasamee, A. (2012). Impact of inappropriate empiric antimicrobial therapy on mortality of septic patients with bacteremia: A retrospective study. International Journal of Microbiology, 2012, 765205. https://doi.org/10.1155/2012/765205

Type of article: Retrospective cohort

Abstract
Background:
Inappropriate empiric antimicrobials could be a major cause of unfavorable mortality rates in co-morbid patients. This study aimed to assess the prevalence and impact of first-dose and 24-hour inappropriate antimicrobials on mortality rates of bacteremic septic patients.

Methods:
A retrospective cohort study was employed. Case record forms of patients diagnosed as sepsis, severe sepsis, or septic shock with positive hemoculture during 2009 were retrieved from the medical wards, Siriraj Hospital. Demographic data, antimicrobial use, types of bacteria isolated from blood and susceptibilities, patients' comorbidities, 28-day and overall mortality rates were collected and analyzed.

Results:
There were 229 cases, mean age (SD) of 63.5 (17.2) years and mean (SD) APACHE II score of 24.7 (6.8). The prevalence of first-dose and 24-hour inappropriate antimicrobials was 29.7% and 25.3%, respectively. The 28-day and overall mortality rates between first-dose inappropriate and appropriate antimicrobial were 67.6% versus 60.2% (P = 0.301) and 75.0% versus 68.3% (P = 0.345), consequently. Patients with septic shock and inappropriate first-dose antimicrobials significantly had higher 28-day mortality rate (61.6% versus 41.9%; P = 0.017).

Conclusion:
Higher mortality rates in bacteremic septic patients were substantially associated with inappropriate first-dose antimicrobials and 3-hour delayed antimicrobial administration after sepsis diagnosis.

Key points:
- The study emphasizes that timeliness and appropriateness of initial antibiotics are critical, often more important that simply using broader coverage (with “appropriate” antibiotics referring to agents that effectively target the suspected or confirmed pathogen)
- Inappropriate empiric antibiotic therapy was associated with significantly higher mortality in septic patients with bacteremia
- Patients who received appropriate empiric antibiotics early (i.e correctly targeted therapy from the start) had improved survival outcomes
- Delay in initiating effective antibiotic therapy was a major contributor to worse outcomes

I chose this article because again, it is a retrospective cohort study that allows for comparison of outcomes between different groups. The article provides strong evidence that “appropriate” antibiotics, or those that actually cover the likely pathogen and infection source, are associated with significantly improved survival. This directly supports my PICO. The article also highlights that incorrect empiric therapy increases mortality, which emphasizes the importance of selecting the right type of antibiotic early. It also highlights how clinicians should choose the most appropriate therapy, which should be guided by likely source of infection, patient risk factors, and resistance patterns, rather than using overly broad coverage.

(3) **Citation**: Jones, B. E., Ying, J., Stevens, V., et al. (2020). Empirical anti–methicillin-resistant Staphylococcus aureus vs standard antibiotic therapy and risk of 30-day mortality in patients hospitalized for pneumonia. JAMA Internal Medicine, 180(4), 552–560. https://doi.org/10.1001/jamainternmed.2019.7495

Type of article: Observational cohort

Abstract

Importance:
Use of empirical broad-spectrum antibiotics for pneumonia has increased owing to concern for resistant organisms, including methicillin-resistant Staphylococcus aureus (MRSA). The association of empirical anti-MRSA therapy with outcomes among patients with pneumonia is unknown, even for high-risk patients.

Objective:
To compare 30-day mortality among patients hospitalized for pneumonia receiving empirical anti-MRSA therapy vs standard empirical antibiotic regimens.

Design, Setting, and Participants:
Retrospective multicenter cohort study was conducted of all hospitalizations in which patients received either anti-MRSA or standard therapy for community-onset pneumonia in the Veterans Health Administration health care system from January 1, 2008, to December 31, 2013. Subgroups of patients analyzed were those with initial intensive care unit admission, MRSA risk factors, positive results of a MRSA surveillance test, and positive results of a MRSA admission culture. Primary analysis was an inverse probability of treatment–weighted propensity score analysis using generalized estimating equation regression; secondary analyses included an instrumental variable analysis. Statistical analysis was conducted from June 14 to November 20, 2019.

Exposures:
Empirical anti-MRSA therapy plus standard pneumonia therapy vs standard therapy alone within the first day of hospitalization.

Main Outcomes and Measures:
Risk of 30-day all-cause mortality after adjustment for patient comorbidities, vital signs, and laboratory results. Secondary outcomes included the development of kidney injury and secondary infections with Clostridioides difficile, vancomycin-resistant Enterococcus species, or gram-negative bacilli.

Results:
Among 88 605 hospitalized patients (86 851 men; median age, 70 years [interquartile range, 62-81 years]), empirical anti-MRSA therapy was administered to 33 632 (38%); 8929 patients (10%) died within 30 days. Compared with standard therapy alone, in weighted propensity score analysis, empirical anti-MRSA therapy plus standard therapy was significantly associated with an increased adjusted risk of death (adjusted risk ratio [aRR], 1.4 [95% CI, 1.3-1.5]), kidney injury (aRR, 1.4 [95% CI, 1.3-1.5]), and secondary C difficile infections (aRR, 1.6 [95% CI, 1.3-1.9]), vancomycin-resistant Enterococcus spp infections (aRR, 1.6 [95% CI, 1.0-2.3]), and secondary gram-negative rod infections (aRR, 1.5 [95% CI, 1.2-1.8]). Similar associations between anti-MRSA therapy use and 30-day mortality were found by instrumental variable analysis (aRR, 1.6 [95% CI, 1.4-1.9]) and among patients admitted to the intensive care unit (aRR, 1.3 [95% CI, 1.2-1.5]), those with a high risk for MRSA (aRR, 1.2 [95% CI, 1.1-1.4]), and those with MRSA detected on surveillance testing (aRR, 1.6 [95% CI, 1.3-1.9]). No significant favorable association was found between empirical anti-MRSA therapy and death among patients with MRSA detected on culture (aRR, 1.1 [95% CI, 0.8-1.4]).

Conclusions and Relevance:
This study suggests that empirical anti-MRSA therapy was not associated with reduced mortality for any group of patients hospitalized for pneumonia. These results contribute to a growing body of evidence that questions the value of empirical use of anti-MRSA therapy using existing risk approaches.

Key points:
Question: What is the association of empirical anti–methicillin-resistant Staphylococcus aureus therapy with 30-day mortality for patients hospitalized with pneumonia?

Findings: This national cohort study of 88 605 hospitalizations for pneumonia that used detailed clinical data to emulate a clinical trial did not find a mortality benefit of empirical anti–methicillin-resistant S aureus therapy vs standard antibiotics for any group of patients examined, even those with risk factors for methicillin-resistant S aureus.

Meaning: This study contributes to a growing body of evidence suggesting that empirical anti–methicillin-resistant S aureus therapy using existing risk approaches may not be beneficial to most patients hospitalized with pneumonia.

I chose this article because it directly evaluates the clinical question addressed in my PICO, which compares empiric anti-MRSA therapy to standard antibiotic regimens in hospitalized patients with suspected infection. Although the population is not limited to post-op patients the findings are still highly relevant because they address empiric antibiotic selection in serious infections, which is directly applicable to post-op sepsis management. Ultimately, the study shows that empiric use of anti-MRSA therapy does not improve mortality outcomes and may be associated with harm, which supports the importance of targeted antibiotic therapy rather than routine broad-spectrum coverage. Additionally, the study includes a large sample size of over 80,000 patients, which increases the reliability of its findings.

What is the clinical "bottom line" derived from these articles in answer to your question?
In all, the findings from all 3 of my articles are consistent: early administration of appropriate and targeted empiric antibiotics is more important than simply using broader-spectrum coverage. Broad spectrum regimens, such as anti-MRSA and anti-pseudomonas coverage, were not associated with improved mortality, reduction in ICU admission, or better clinical outcomes compared to standard empiric therapy, such as ceftriaxone and metronidazole. As a matter of fact, unnecessary broad spectrum coverage was associated with increased risk of antibiotic resistance, adverse effects, and secondary infections. Further, delayed antibiotic therapy was associated with significantly worse outcomes, including increased mortality in septic patients.

Based on the results, in post-op patients with sepsis and suspected pneumonia, the best approach is to initiate timely, targeted empiric antibiotics based on the suspected source of infection and patient-specific risk factors, rather than automatically using overly broad spectrum regimens.