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# Antibiotics treatment pathways and prescribing preferences in treating patients with clinically suspected hospital-acquired pneumonia using cohort pathway applications

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## Abstract

*Hospital-acquired pneumonia is the second most frequent cause of hospital-acquired infection and the leading cause of morbidity and mortality from nosocomial infections. It remains a major health concern and contributor to hospital cost. Although these negative outcomes can be reduced by the rapid initiation of appropriate antibiotic therapy, it is a challenge to choose optimal antibiotics before identifying the offending pathogen, which is empiric. The study evaluated the preferences of empirical antibiotic use and treatment pathways in patients with clinically suspected hospital-acquired pneumonia using cohort pathway application in the Observational Health Data Sciences and Informatics tools.*

## Introduction

The American Thoracic Society (ATS) and Infectious Diseases Society of America (IDSA) guideline for management of hospital-acquired pneumonia (HAP) was updated in 2016<sup>1</sup>. Initial empiric antibiotic therapy for HAP was recommended based on the risk of mortality and the factors increasing likelihood of methicillin-resistant *Staphylococcus aureus* (MRSA). Prescribing initial empiric antibiotics appropriately is important to achieve better clinical outcomes. Thus, so far the prescription prevalence and epidemiology of disease have been studied using healthcare big data, but there were concerns on data curation with heterogeneous population characteristics, medical complexity of infections and inconsistent analysis methods<sup>2</sup>. The Observational Medical Outcomes Partnership (OMOP) Common Data Model (CDM) was adopted in recent studies, but they simply showed the prescription patterns and prevalence of various medications of metabolic chronic diseases<sup>3</sup> and special population patients<sup>4</sup>. This study evaluated the preferences of empirical antibiotics and treatment pathway for clinically suspected HAP. Further, we assessed the appropriateness of antibiotics selected for suspected pathogens such as *Pseudomonas aeruginosa* potentially causing HAP based on the guideline recommendation.

## Methods

Patients in the cohort were 18 years and above, had at least one diagnosis code for pneumonia and lower respiratory infections. To make HAP cohort, the pneumonia was refined where it was occurred 72 hours after the inpatient visits with at least one exposure of antibiotics after the diagnosis. The index date of each patient was the date of the first prescription of antibiotics recommended for pneumonia. The patients had to have at least 30 days of history in the database before the index date. Exclusions were history of previous pneumonia, other infectious diseases, use of antibiotics for MRSA during prior 90 days, pregnancy and VAP after the index date. The combination treatment was defined as the minimum 3 days of overlap use. Observational Health Data Sciences and Informatics (OHDSI) tools were applied to electronic medical records of Ajou University School of Medicine (AUSOM) database from 1994 to 2017 which transformed into OMOP CDM<sup>2</sup>.

The treatment cohort pathways were analyzed retrospectively. Three pathways were prepared to evaluate the proportion of the number of patients on corresponding antibiotics; pathway 1) antibiotics recommended for initial empiric HAP therapy especially for patients not at high risk of mortality and no factors increasing the likelihood of MRSA (Figure 1 & 2), 2) antibiotics recommended for initial empiric HAP therapy for patients at any level of risk of mortality and MRSA, and 3) antibiotics recommended for CAP in addition to those for HAP in patients any risks of mortality and MRSA. Ceftriaxone, the commonly used broad spectrum antibiotic medication, was included in each pathway. Sunburst plots were generated from medication sequences. In addition, the pathway flow chart in the ATLAS v.2.7 was used to visualize the prescription preferences per each antibiotic medication in detail. The cohort pathway with cohort definition to extract antibiotics records from CDM database and the analysis code (<https://github.com/SandyRhie/antibioticsTreatmentPathway>) are available as open source at GitHub.

## Results

The 829 patients were in the target cohort and the number of patients with pathway counted 590 (71.2%, pathway 1), 669 (80.7%, pathway 2), and 757 (91.7%, pathway 3), respectively. Levofloxacin was most commonly prescribed medication as the initial choice (38.1, 25.1, and 16.4% in the order from pathway 1 to 3, respectively) and remained the only medication 14.7, 7.3, and 2.5% of the time from pathway 1 to 3, respectively. It was followed by ceftriaxone, piperacillin-tazobactam and ciprofloxacin. The above 4 medications were prescribed from 45.8 to 85.4% in pathways for treating HAP. Noticing, amikacin and tobramycin sole uses were observed which incompliant with the guideline although these were small proportions in the pathways. Moreover, two-drug combinations of ceftriaxone and clarithromycin, and piperacillin-tazobactam and ceftriaxone, and three-drug combination of piperacillin-tazobactam, meropenem and ceftriaxone was also observed for at least 3 days and more as the empiric initial choices. In the study, we have developed the cohort definition with patients of acute disease condition which may need for the short courses of antibiotic treatments using OMOP CDM. Ceftriaxone was widely used as an initial treatment, but considering it had no activity against *Pseudomonas aeruginosa*, further study are warranted. Moreover, aminoglycoside sole use and vancomycin sole uses also needed further analysis to assess the appropriateness.

## Conclusion

The appropriateness of antibiotic selected and the prescription preferences for clinically suspected HAP were assessed using the real world data. Broad spectrum antibiotics without activity against *Pseudomonas aeruginosa* and the combination regimens with inadequate coverage for potential causative pathogens were observed.

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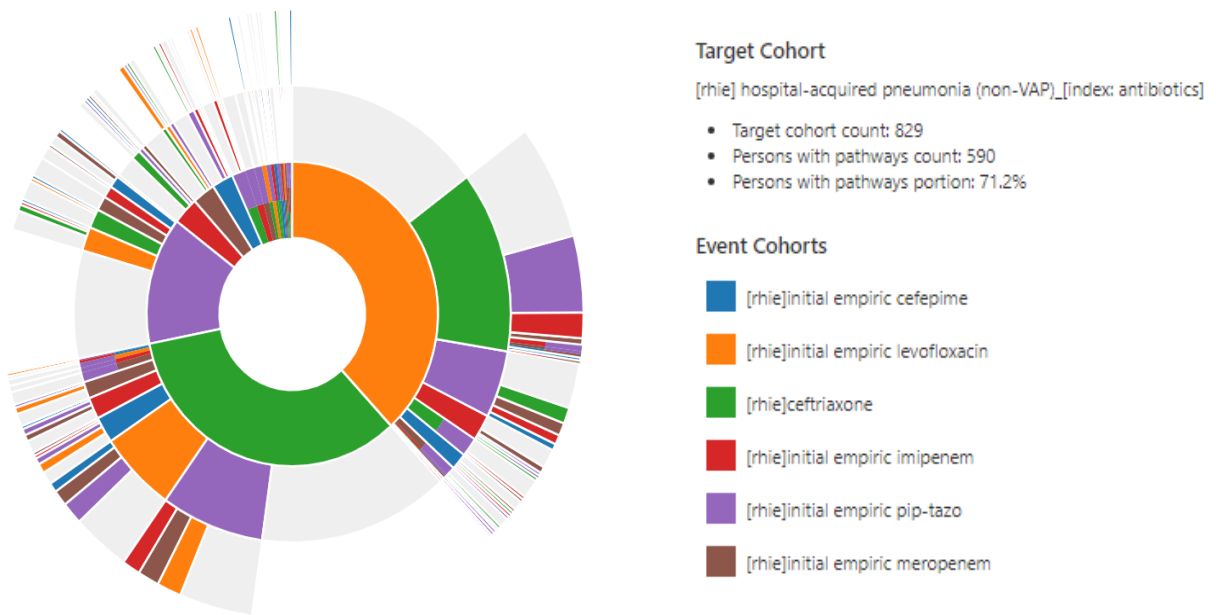


Figure 1. Treatment pathway for hospital-acquired pneumonia in pathway 1. The inner circle shows the first relevant medications that the patients were prescribed; the second circle shows the second medication, and up to the third choices of antibiotics.

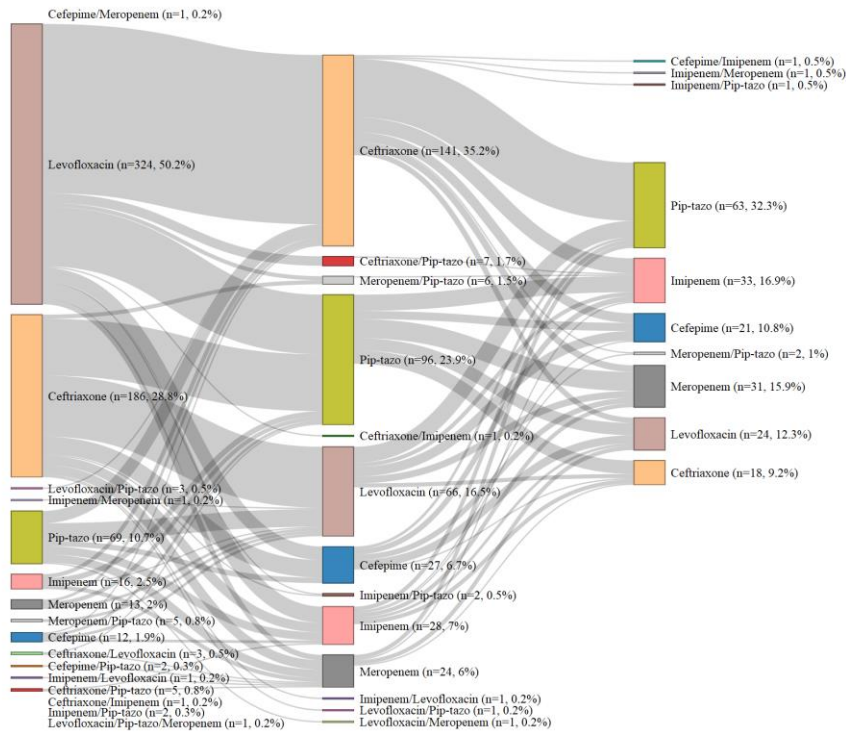


Figure 2. Pathway flow chart for proportion of antibiotics selected empirically in pathway 1.