Critical Care Pharmacy Collaborative Practice to Optimize Management of Severe Community Onset Pneumonia

PURPOSE: The purpose of this study is to improve management and outcome of severe community-onset pneumonia through the advancement of the pharmacy practice model in the Medical Intensive Care Unit (MICU).

BACKGROUND: Approximately 10% of patients hospitalized for community-onset pneumonia require admission to an intensive care unit (ICU), which is associated with a mortality rate of up to 37%. Standard-of-care diagnostic tests have a low sensitivity for bacterial pathogens and are insufficient for detecting viral pathogens. This diagnostic uncertainty in pneumonia has contributed to inappropriate and excess antimicrobial treatment. Treating viral pneumonia with antimicrobials puts patients at an unnecessary risk of adverse drug events, and treatment courses lasting longer than 3 days has been associated with an increased risk of a subsequent multi-drug resistant infections. Several new diagnostic laboratory tests are available and can assist clinicians in the appropriate diagnosis and treatment of bacterial and viral pneumonia. However, literature using a combination of all diagnostic tools is lacking. This study aims to address this gap by implementing an advanced pharmacy model for antimicrobial stewardship (AMS) that utilizes Influenza PCR, Biofire® Respiratory Viral Panel, Legionella urine antigen test, and procalcitonin for severe community-onset pneumonia in the Medical Intensive Care Unit (MICU).

METHODS: This study is a quasi-experiment of severe community-onset pneumonia in the MICU before and after implementation of an advanced AMS pharmacy model at Henry Ford Hospital. Patients will be included in this study if they are at least 18 years old, admitted from the community with pneumonia symptom onset within 48 hours of admission requiring ICU admission, and receive empiric antibiotics. Patients will be excluded from this study if they meet any of the following criteria: documented lung abscesses, empyema, or loculated pleural effusion; comfort care measures only, cystic fibrosis, transferred from outside hospitals, pregnancy, or are receiving definitive antimicrobial treatment for a previously diagnosed infection. The intervention will begin in November 2017 and patients will be included in this study from the start of implementation until March 2018. Patients from October 2016 to March 2017 who meet the same inclusion criteria will be evaluated for pre-implementation comparison. Deep vein thrombosis (DVT) prophylaxis will be used as a non-equivalent dependent variable for this study. Severity of illness will be evaluated using the Pneumonia Severity Index (PSI), Quick SOFA score for Sepsis, SIRS criteria, and Charlson Comorbidity Index. The primary outcome will be days of antimicrobial therapy and secondary outcomes include diagnostic yield, length of hospitalization and ICU stay, inpatient all-cause mortality, re-treatment for pneumonia, re-admission to the ICU, and *Clostridium difficile* infection during the hospitalization. Antimicrobial de-escalation will be assessed for de-escalation, escalation, and discontinuation. Resource utilization and ancillary testing will also be evaluated before and after implementation.

DATA ANALYSIS: Continuous, nonparametric variables will be analyzed and compared using the Mann-Whitney U test and reported as medians and interquartile range. Nominal variables will be reported as percentages and compared using the $\chi 2$ test. All tests with P values <0.05 will be considered significant. Factors that are associated with the decision to deescalate/discontinue antibiotics will be evaluated via logistic regression. Variables in the bivariate analysis with a P value <0.2 and clinical rationale will be included in a multivariable regression model that will be restricted to a subject-to-variable ratio of 10:1. For the primary analysis, this study assumes an effect size of 25% or a two day reduction in antimicrobial therapy, which is consistent with internal data and published literature. Sample size was calculated to meet an 80% power and a two-sided alpha of 0.05, which requires 72 subjects in each arm. Based on preliminary evaluation of ICU pneumonia admissions, we anticipate 30 to 40 eligible patients per month, or 150 to 200 patients per study period.