Research Protocol

**Title:** GDE2025 – Community-acquired pneumonia (CAP) Treatment Pathways Study

List of Abbreviations

* GDE: Guideline Driven Evidence
* OHDSI: Observational Health Data Sciences and Informatics
* HADES: Health Analytics Data-to-Evidence Suite
* CAP: community-acquired pneumonia

# Responsible Parties

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# Amendments and Updates

# Rationale and Background

# Community-acquired pneumonia (CAP) is a leading cause of morbidity and mortality worldwide, particularly among vulnerable populations such as the elderly, young children, and individuals with comorbidities [1-2]. Despite advances in diagnostic tools and therapeutic options, CAP remains a significant public health challenge due to its variable etiology, clinical presentation, and outcomes [3-4]. Antibiotic therapy is the cornerstone of CAP management, yet treatment patterns vary widely across healthcare settings, influenced by local guidelines, resistance patterns, and patient-specific factors [5-6]. Understanding these treatment patterns is critical for optimizing care and addressing emerging challenges such as antimicrobial resistance and treatment failure.

# CAP is associated with substantial clinical and economic burdens globally. In Europe, CAP incidence varies by age, gender, and country, with higher rates observed in individuals aged ≥65 years and those with chronic comorbidities [7]. Mortality rates range from <1% in outpatient settings to as high as 48% among hospitalized patients, particularly those requiring intensive care unit (ICU) admission [7-9]. Similar trends are observed in North America and Asia-Pacific regions, where CAP contributes significantly to hospitalizations and healthcare costs [10-11].

# Empiric antibiotic therapy for CAP is guided by clinical severity, patient comorbidities, and local resistance patterns. Current guidelines recommend monotherapy with macrolides or doxycycline for low-risk outpatients, while combination therapy with beta-lactams and macrolides or fluoroquinolones is preferred for hospitalized patients [12-13]. However, adherence to these guidelines remains suboptimal in many settings. For instance, studies have reported widespread use of broad-spectrum antibiotics, such as third-generation cephalosporins and fluoroquinolones, even in low-risk patients, raising concerns about unnecessary exposure and resistance development [14-15]. Conversely, inadequate antibiotic coverage in high-risk patients can lead to treatment failure and adverse outcomes [16].

# Despite the availability of evidence-based guidelines, their implementation in clinical practice is inconsistent. Factors such as clinician preferences, local prescribing habits, and patient characteristics contribute to variability in antibiotic selection [17-18]. For example, a study in Germany highlighted significant regional differences in CAP treatment patterns, which could not be fully explained by clinical or sociodemographic factors [19]. Similarly, in the United States, broad-spectrum antibiotic use for outpatient CAP has declined over time but remains common, particularly among patients with comorbidities [20]. These findings suggest that targeted interventions, such as antimicrobial stewardship programs and decision-support tools, are needed to improve guideline adherence and optimize antibiotic prescribing [21-22].

# While numerous studies have evaluated the efficacy of specific antibiotic regimens for CAP, there is limited real-world evidence on treatment patterns across diverse healthcare settings. Existing research often focuses on hospitalized patients, leaving gaps in understanding outpatient management and transitions between care settings [23-24]. Addressing these gaps is essential for developing strategies to improve care delivery, reduce antimicrobial resistance, and enhance patient outcomes.

# This study aims to conduct a retrospective analysis of observational healthcare data to characterize antibiotic treatment patterns for CAP. By examining real-world prescribing practices and their alignment with clinical guidelines, the study seeks to identify opportunities for improving antibiotic stewardship and optimizing CAP management.

# Study Objectives

1. Characterize the baseline characteristics of patients with community-acquired pneumonia
2. Characterize patterns of antibiotic treatment in patients with community-acquired pneumonia

# Research Methods

### Study Design/Data Source(s)

This will be a retrospective cohort study of databases in the OHDSI Evidence Network. Only databases that pass data diagnostics and contain the relevant concept sets and visit types will be invited to participate.

### Study Population (“Indication”)

Adults (≥18 years) with community-acquired pneumonia diagnosed in outpatient setting during the study period from 1/1/2010 to present will be included for analysis.

We will study first episode of pneumonia in patient history. We will exclude patients who have had a diagnosis of tuberculosis a year prior as well as non-CAP pneumonias (ventilator associated, influenza, congenital, aspiration, viral or fungal pneumonia) on the index date.

We will stratify patients into those who proceeded to be hospitalized. We will also stratify the study into three time periods: 01/01/2010 – 01/01/2020 (pre-pandemic), 01/01/2020 – 31/12/2022 (COVID-19 pandemic) and >01/01/2023 (post-pandemic).

### Exposures/Outcomes (“Outcome”)

We will use several drug class cohorts stratified by route of administration (oral and injectable): corticosteroids, cephalosporins stratified by generation, penicillins, macrolides, tetracyclines, trimetoprim, carbapenems, lincosamides, aminoglycosides and fluroquinolones. Full list of cohorts is available here: <https://github.com/aostropolets/CAPTreatmentPatterns/blob/main/inst/Cohorts.csv>

### Covariates

Baseline characteristics include default characteristics: age group and mean, sex, race/ethnicity, previous medications, diagnoses, procedures and measurements.

# Data Analysis Plan

### General

Various standardized analytics available in the OHDSI Community will be used to conduct this Characterization study. The Strategus pipeline will be used to call the following Health Analytics Data-to-Evidence Suite (HADES) packages: Characterization, CohortIncidence, and TreatmentPatterns. R package dependencies will be versioned using the renv R package. Source code will be versioned using git and stored in the study GitHub repository (<https://github.com/OHDSI/CAPTreatmentPatterns/tree/main>).

### Data Characterization

#### Cohort Diagnostics

The CohortDiagnostics package will be executed for all indication and outcome cohorts to evaluate developed phenotypes. This will be an iterative process as outlined by the Phenotype Development group within the OHDSI Community.

#### Cohort Features

The Characterization package will be used to extract the features of patients including demographic data (age group/mean, sex, race, ethnicity), prior conditions/drug exposures/procedures/measurements/devices/observations, and risk scores (e.g., Charlson comorbidity index, DCSI, CHADS2VASC score).

#### Treatment Pathways

The TreatmentPatterns package will be used to identify the sequence antibiotic treatment after pneumonia diagnosis for each target cohort. We will employ the following design choices for the analyses:

1. indexDateOffset = 0
2. minEraDuration = 1 day
3. eraCollapseSize = 7 days
4. CombinationWindow = 1 day
5. MinPostCombinationDuration = 1 day
6. filterTreatment: “All”
7. maxPathLength: 5

Treatment patterns will also be stratified by the age of patients at the index date (step = 10 years).

# Strengths and Limitations of the Research Methods

When complete, this study will provide one of the largest characterizations of treatment patterns in community-acquired pneumonia. Limitations include lack of blood/sputum/other specimens culture results and general limitations of coding.

# Protection of Human Subjects

Each participating institution will seek IRB approval for this study as dictated by local governance.

# Plans for Disseminating and Communicating Study Results

The results will be shared and discussed among the study participants and broader OHDSI community during the weekly Tuesday community calls. This work will be presented at conferences (such as OHDSI Global Symposium) and published as a manuscript.

# References:

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