# Predictors for individual patient antibiotic treatment effect in hospitalized community-acquired pneumonia patients

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## INTRODUCTION

•Antibiotic therapy is the cornerstone of community-acquired pneumonia (CAP) management. There is no consensus for the need of atypical coverage in moderate-severe CAP patients. Current research remains unsuccessful at predicting which patients benefit from atypical coverage.
•The concept of individualized medicine has extended to recognizing the heterogeneity of each individual patient.
•Our objective was to identify **clinical predictors** of antibiotic treatment effects in non-ICU hospitalized CAP patients.

## METHODS

•**Design:** post-hoc analysis of three prospective cohorts (two from the Netherlands (CAP-START and CAPiTA) and one from Spain (Bellvitge)) of CAP patients.
•**Patients:** adults, hospitalized for at least 24 hours in a non-ICU ward and having received either beta-lactam monotherapy (BL), beta-lactam + macrolide (BLM), or fluoroquinolone-based (FQL) as empiric antibiotic treatment.
•**Predictors:** Through an extensive research in PubMed we selected a list of candidate clinical treatment effect predictors from previously published studies on CAP.
•**Analysis:** Candidate clinical predictors were analyzed by a two-step approach mixed-effects logistic and linear regression models, by including interactions of the predictors with empiric antibiotic choice (BL, BLM, or FQL) using 30-day mortality and length of hospital stay (LOS) as outcomes in different models, adjusted for confounders .

## RESULTS

**A total of 8,562 patients were included:**

**2,184 (25.5%) from CAPiTA cohort**

**2,154 (25.2%) from CAP-START cohort**

**4,224 (49.3%) from Bellvitge cohort.**

**Empiric antibiotic treatment received:**

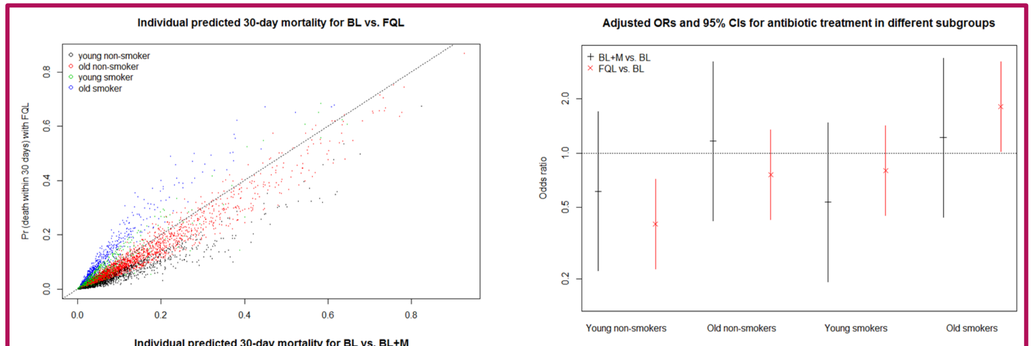
**Beta-lactams (BL) 4,399 (51.4%)**

**Fluoroquinolones (FQL) 3,373 (39.4%)**

**Beta-lactams + Macrolides (BLM) 790 (9.2%)**

**Interaction effect estimates with significant clinical predictors from the second step models OR**

| | All patients | BH - P value | Rx CAP | CAPiTA | CAP-START | Bellvitge |
|---|---|---|---|---|---|---|
| ***30-day mortality*** | | | | | | |
| Age*FQL | 1.67 (1.23-2.29) | 0.034 | 1.75 | 1.62 | 2.61 | 1.62 |
| Smoker*FQL | 2.36 (0.40-2.99) | 0.046 | 2.93 | 1.77 | 1.45 | 3.97 |
| ***Length of Hospital Stay*** | | | | | | |
| Age*BLM | 1.14 (1.06 – 1.22) | 0.008 | 1.11 | 1.78 | 1.07 | 0.93 |




***LEGEND:***
***A.*** *Individual predicted 30-day mortality comparing patients who receive BL vs. FQL as empiric treatment.*
***B.*** *Individual predicted 30-day mortality comparing patients who receive BL vs. BLM as empiric treatment.*
***C.*** *Adjusted Odds Ratio with 95% C.I. for 30-day mortality in different subgroups of patients, divided for their group age and smoke habit.*

**Predictors analysed:** age, gender, smoking habit, living in an elderly home, pneumococcal vaccination, influenza vaccination, admission during influenza season , outpatient antibiotic treatment, cardiovascular disease, COPD, immunodeficiency, duration of symptoms , cough, purulent sputum, gastrointestinal symptoms, headache, pleuritic chest pain, chills, confusion, fever , hypotension, heart rate > 125 bpm, respiratory failure, leucocytes count , serum sodium concentration, bilateral infiltrate on chest X-ray, pleural effusion on chest X-ray, positivity of *S. pneumoniae* urinary antigen test, PSI score.

## CONCLUSIONS

• In conclusion, it is plausible that older age influences the response to specific antibiotic treatment, as we found a relationship with both the use of FQL and increased 30-day mortality and BLM use and LOS in older patients.
•Current smoking was also associated with a decreased response to FQL.
•Future trials evaluating antibiotic strategies for CAP could assess the treatment effects in patients of different age categories and smoking status.