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Risk Factors for Multidrug-Resistant Organism Infections in Patients With Lower Respiratory Tract Infections: A Systematic Review and Meta-Analysis

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ADMINISTRATIVE INFORMATION

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 19 August 2026 and was last updated on 19 August 2026.

INTRODUCTION

Review question / Objective This systematic review and meta-analysis aims to comprehensively evaluate the impact of antibiotic utilisation patterns, comorbidity status and invasive procedures on the risk of MDRO infections in patients with LRTIs, thereby providing evidence-based guidance for clinical risk stratification and individualised anti-infective therapy.This study aimed to systematically assess potential factors associated with MDRO infection among patients diagnosed with LRTIs.

Condition being studied Multidrug-resistant organism (MDRO) infections are a leading cause of poor prognosis in patients with lower respiratory tract infections (LRTIs), yet systematic evaluation of relevant risk factors remains insufficient.

METHODS

Participant or population Participants: Patients aged ≥18 years with LRTIs, including CAP, HAP, VAP, acute exacerbations of COPD, bronchiectasis with infection, post-stroke pneumonia, post-traumatic pneumonia and pneumonia following solid organ transplantation.

Intervention Patients without MDRO infection or patients infected with non-MDRO pathogens.

Comparator Randomized controlled.

Study designs to be included A total of 20 observational studies were included in this meta-analysis.

Eligibility criteria Based on the PICO framework for systematic reviews and meta-analyses, the following inclusion criteria were predefined. (1) Participants: Patients aged ≥18 years with LRTIs, including CAP, HAP, VAP, acute exacerbations of COPD, bronchiectasis with infection, post-stroke pneumonia, post-traumatic pneumonia and pneumonia following solid organ transplantation. (2) Exposures: Antibiotic utilisation patterns, including prior antibiotic exposure, multiple

antibiotic exposure, specific antibiotic classes and duration of antibiotic exposure; comorbidities, including neurological disorders, chronic respiratory diseases, liver diseases and malnutrition; and invasive procedures, including mechanical ventilation, endotracheal intubation, tracheostomy and reoperation. (3) Comparators: Patients without MDRO infection or patients infected with non-MDRO pathogens. (4) Outcomes: MDRO infection, with multidrug resistance defined according to internationally recognised standards (e.g. definitions established by the US Centers for Disease Control and Prevention, the European Centre for Disease Prevention and Control or Magiorakos et al.). Variations in MDRO definitions across regions, study periods and pathogen species were acknowledged as a potential source of misclassification bias. (5) Study design: Cohort studies, case-control studies or cross-sectional studies. (6) Data reporting: Studies reporting multivariable-adjusted ORs with corresponding 95% confidence intervals (CIs) or providing raw data sufficient to calculate these effect estimates. Where adjusted and unadjusted effect estimates were both available, adjusted estimates were preferentially extracted.

The exclusion criteria were as follows. (1) Ineligible populations: Studies involving predominantly immunocompromised populations, including patients with human immunodeficiency virus infection, active malignancy treated with chemotherapy and organ transplantation requiring long-term immunosuppressive therapy, and studies involving patients with cystic fibrosis were excluded. Immunocompromised patients have distinct immune status, pathogen spectra and infection mechanisms compared with general LRTI populations. Therefore, including these populations would have increased clinical heterogeneity, although their exclusion may limit external validity. (2) Duplicate publications: For multiple publications from the same cohort, only the study with the most complete data or the largest sample size was included.

Information sources To comprehensively identify studies investigating risk factors for MDRO infections in patients with LRTIs, the following five electronic databases were systematically searched: PubMed, Web of Science, the Cochrane Library, Embase and Scopus. The search period covered the period from database inception to 1 March 2026. Searches were restricted to English-language publications. The search strategy combined Medical Subject Headings/Emtree terms with free-text keywords, structured around four core concepts: (1) LRTIs (including pneumonia, CAP, HAP, VAP, bronchiectasis and COPD); (2) MDROs (including multidrug-resistant, extensively drug-resistant, carbapenem-resistant, methicillin-resistant Staphylococcus aureus, extended-spectrum β-lactamase–producing Enterobacteriaceae, Pseudomonas aeruginosa and Acinetobacter baumannii); (3) risk factors (including risk factor, predictor, prognosis, multivariate analysis, logistic regression and odds ratio [OR]); and (4) observational study designs (including cohort studies, case-control studies and cross-sectional studies). Detailed search strategies for each database are presented in Supplementary Table 1.

Main outcome(s) Twenty studies were included. Antibiotic exposure may be associated with increased MDRO infection risk (OR = 4.39, 95% confidence interval [CI]: 2.50–7.71, I^2 = 89.9%); subgroup analysis revealed significant associations for exposure within 30 days (OR = 3.97, 95% CI: 2.35–6.70, I^2 = 0%) and 90 days (OR = 2.38, 95% CI: 1.71–3.31, I^2 = 0%). Nine studies did not clearly report the time window of antibiotic exposure and were therefore interpreted narratively rather than as a distinct clinical subgroup. Comorbidities may be associated with MDRO infection risk (OR = 2.69, 95% CI: 2.21–3.27, I^2 = 1.2%), with neurological disorders/stroke showing the highest risk (OR = 3.16, 95% CI: 1.74–5.73). Invasive procedures may be associated with MDRO infection risk (OR = 7.33, 95% CI: 3.46–15.52, I^2 = 82.7%), with reoperation demonstrating particularly high risk (OR = 13.49, 95% CI: 6.42–28.36).

Quality assessment / Risk of bias analysis The Quality in Prognosis Studies (QUIPS) tool was used to assess the risk of bias in the included studies[11]. This instrument encompasses six domains: (1) study participation – whether the inclusion and exclusion criteria were clearly defined and the patients were consecutively enrolled; (2) study attrition – whether loss to follow-up was fully reported, with rates <20%; (3) prognostic factor measurement – whether risk factors were clearly defined and reliably measured; (4) outcome measurement – whether MDRO definitions conformed to international standards; (5) study confounding – whether multivariate analysis was performed with adjustment for major confounders; and (6) statistical analysis and reporting – whether statistical methods were appropriate and effect estimates with 95% CIs were fully reported.

Each domain was rated as having a low, moderate or high risk of bias based on the extent to which specific criteria were fulfilled. Overall risk of bias was evaluated according to Furlan et al.[12]:

studies with five or more domains rated as low risk were classified as having a low overall risk of bias, studies with two or more domains rated as high risk were classified as having a high overall risk of bias and all other studies were classified as having a moderate overall risk of bias.

Strategy of data synthesis Statistical analyses were performed using Stata 17.0 software. Effect sizes were presented as ORs with 95% CIs. Heterogeneity was assessed using Cochran's Q test and the I^2 statistic: $I^2 \leq 25\%$ indicated low heterogeneity, 25% 50% indicated high heterogeneity. Random-effects models were used when clinical or statistical heterogeneity was expected. Pre-specified subgroup analyses were performed according to antibiotic exposure time windows (30 and 90 days), comorbidity types and invasive procedure types. Studies with unclear antibiotic exposure timing were not treated as a clinically homogeneous subgroup; their findings were described narratively. Sensitivity analyses were conducted using the leave-one-out method to assess the impact of individual studies on pooled estimates. Publication bias was assessed using funnel plots and, where the number of studies was sufficient, Egger's and Begg's tests. Considering that some analyses included fewer than 10 studies, publication-bias assessments were interpreted cautiously. All tests were two-sided, and $P < 0.05$ was considered statistically significant.

Subgroup analysis Pre-specified subgroup analyses were performed according to antibiotic exposure time windows (30 and 90 days), comorbidity types and invasive procedure types. Studies with unclear antibiotic exposure timing were not treated as a clinically homogeneous subgroup; their findings were described narratively.

Sensitivity analysis Sensitivity analyses were conducted using the leave-one-out method to assess the impact of individual studies on pooled estimates.

Country(ies) involved China.

Keywords pneumonia; respiratory tract infections; cross infection; drug resistance, multiple, bacterial.

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