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A scoping review protocol of patient profiles and treatable traits for community-acquired pneumonia (CAP) in the outpatient setting

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ADMINISTRATIVE INFORMATION

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Review Stage at time of this submission - Preliminary searches.

Conflicts of interest - None declared.

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Amendments - This protocol was registered with the International Platform of Registered Systematic Review and Meta-Analysis Protocols (INPLASY) on 21 November 2025 and was last updated on 21 November 2025.

INTRODUCTION

Review question / Objective What are the treatable traits and patient profiles for community-acquired pneumonia (CAP) in adults in the outpatient setting?

Background Pneumonia is a complex and heterogenous disease, ranging from mild to severe, causing a wide range of symptoms and complications dependent on the aetiological organisms as well as the patient's age and clinical history. Causative agents include viruses, bacteria (most commonly Streptococcus pneumoniae) and fungi.

Community-acquired pneumonia (CAP) is diagnosed when a patient has two or more symptoms of pneumonia combined with consistent radiographic findings with no other explanation. CAP typically presents with symptoms and signs consistent with a lower respiratory tract infection (i.e., cough, dyspnoea, pleuritic chest pain, mucopurulent sputum, myalgia, fever) and no other explanation for the illness. Older people present more frequently with confusion or worsening of pre-existing conditions, and without chest signs or fever.

CAP is common, but diagnosis by general practitioners frequently relies only on clinical features, an approach that is limited by poor sensitivity and specificity. Possible sequelae of CAP include sepsis, acute respiratory distress syndrome, and death. Recent data from the United States document 1.4 million emergency department visits, 740,000 hospitalisations, and 41,000 deaths per year for CAP; hospitalisation is required in up to 10% of patients with CAP.

Aetiology of CAP directs treatment decisions; however, identification of the causative microorganism is difficult, and available data indicate that even in the hospital setting the majority of patients do not have a pathogen identified. In the absence of an identified causative pathogen, empirical treatment of CAP should be guided by the most likely pathogen and severity of

disease, but few data are available to direct treatment of outpatients with CAP.

The 2019 American Thoracic Society (ATS)/ Infectious Diseases Society of America (IDSA) joint guidelines provide treatment recommendations for the ambulatory setting according to whether patients also have relevant comorbidities, with monotherapy (amoxicillin or doxycycline) noted for those without comorbidities, and combination therapy (amoxicillin/clavulanate (co-amoxiclav) or a cephalosporin such as cefpodoxime or cefuroxime with azithromycin) for those with comorbidities. Antibiotic pharmacokinetic/pharmacodynamic parameters, dosage, scheduling and duration of the selected therapy, must also be considered to increase the chances of clinical success.

Co-amoxiclav, a World Health Organization (WHO) AWaRe (Access, Watch, Reserve) key "Access" antibiotic, is commonly prescribed in community healthcare settings to treat various infections and combines the semisynthetic penicillin amoxicillin and the β-lactamase inhibitor clavulanate potassium. However, antibiotic resistance has become a global health crisis. The prevalence of antibiotic resistance is increasing among common CAP-causative pathogens in the community, including Streptococcus (S.) pneumoniae (notably penicillin-non-susceptible S. pneumoniae) and Haemophilus (H.) influenzae (notably ampicillin-resistant H. influenzae) two resistant strains that are WHO priority pathogens, as well as among other CAP pathogens such as Moraxella catarrhalis and Klebsiella pneumoniae. Increasing resistance trends raise concerns about antibiotic stewardship given frequent empirical antibiotic use.

Treatable traits is a concept whereby consideration of the biomedical complexity of individual patients is factored in to improve medical diagnosis and treatment of pneumonia, in essence, personalised medicine. A treatable trait is clinically important, recognisable and treatable. Treatable traits can be identified in three key domains: pulmonary issues, comorbidities (extrapulmonary domain) and risk factors/behavioural traits that contribute to the disease burden.

Rationale Given the complexity of pneumonia, encompassing varied presentation and diverse causes, along with the influence of host responses and comorbidities, a 'treatable traits' approach has the potential to improve patient care and relieve patient morbidity. A personalized approach is particularly relevant for cases that are more complicated, such as elderly patients with comorbidities, and also potentially offers a mechanism whereby patients requiring intravenous therapy might switch to oral therapy in a timely manner, thereby reducing hospital length of stay with its associated costs, and reducing the risk of nosocomial infections. As a foundation to a 'treatable traits' approach to patient care, it is necessary to evaluate what is already known and, conversely, where evidence gaps should be addressed.

Systematic scoping reviews seek to explore the scope of literature on a given topic by following a systematic approach to map and summarize the available evidence. The objective of this systematic scoping review is to identify and describe currently available literature on treatable traits for patients with CAP.

METHODS

Strategy of data synthesis A systematic search will be conducted in the MEDLINE (PubMed), Embase (Ovid), and Cochrane Library databases. The search strategy will be initially developed for MEDLINE (PubMed) and adapted for the other databases. The search strategy will be developed in conjunction with an information professional, and will involve testing combinations of keywords, controlled vocabulary terms, Boolean operators, and database-specific functionalities to ensure optimal sensitivity and specificity. It will include controlled language (MeSH, Emtree) and keywords for two main concepts: "community acquired pneumonia" and "treatable traits".

Grey literature will also be searched in the form of manual searches of abstract books from the European Respiratory Society (ERS) Congress, the Congress of the European Society of Clinical Microbiology and Infectious Diseases (ESCMID Global), and the American Thoracic Society (ATS) International Conference.

Eligibility criteria This scoping review will include primary research studies of any design published between 2015 and 2025 for articles, or between 2024 and 2025 for congress abstracts. Publications that do not present original research findings (e.g., narrative reviews, protocols, opinions, editorials, and reports) will be excluded. Community-acquired pneumonia (CAP) is defined as pneumonia acquired outside of the hospital setting. Participants may be of any sex or age. Only studies published in English will be considered. No restrictions will be applied regarding geographic location. To be eligible, studies must report data on at least one treatable

trait associated with community acquired pneumonia requiring high doses for amoxicillin in the outpatient setting. Treatable traits are defined as "a recognizable phenotypic or endotypic characteristic that can be assessed and successfully targeted by treatment to improve a clinical outcome" in a patient with CAP.

Source of evidence screening and selection The titles and abstracts of each study will be screened by two independent reviewers for assessment against the inclusion criteria. Studies that meet the inclusion criteria at the first screening round will be retrieved in full text and linked to their relevant citation within Covidence (Veritas Health Innovation Ltd. VIC, Australia), a web-based platform for review management.

For the second screening round, the full text will be assessed against the inclusion criteria by two independent reviewers, and reasons for exclusion will be recorded and reported in the systematic scoping review. Any disagreements that arise between the reviewers at each screening round will be resolved through discussion, or with a senior member of the review team. The results of the search and the study inclusion process will be reported in full in the final systematic scoping review and presented in a PRISMA-ScR flow diagram (Tricco et al. 2018).

Data will be extracted from studies included in the systematic scoping review by a reviewer using a bespoke data extraction form developed by the review team. The data extracted will include specific details about the participants, concept, context, study methods, and key findings relevant to the review question. A draft data extraction form will be created in Excel to capture agreed data categories from the included studies. The form will be tested on five records by one member of the review team, with the results reviewed by the wider team. Any amends will then be incorporated, before building the final form.

Reference

Tricco AC, Lillie E, Zarin W, O'Brien KK, Colquhoun H, Levac D, et al. PRISMA Extension for Scoping Reviews (PRISMAScR): Checklist and Explanation. Ann Intern Med. 2018;169:467–473. doi: 10.7326/M18-0850.

Data management Following the searches, a list of identified studies will be collated within EndNote (Clarivate Analytics, PA, USA). Duplicates will then be removed, before being uploaded into Covidence.

Reporting results / Analysis of the evidence A narrative summary will be developed to accompany the tabulated and / or charted results and will describe how the results relate to the review's objective and questions. A PRISMA flowchart diagram of the review will also be developed.

Presentation of the results The extracted data will be presented in diagrammatic or tabular form in a manner that aligns with the objective and questions of this systematic scoping review. A PRISMA diagram, as produced by Covidence, will be included. The tables and / or charts will report on the agreed data categories and any other elements deemed relevant.

Language restriction The review will be restricted to articles and congress abstracts published in English.

Country(ies) involved Turkey; Italy; India; UK.

Keywords Community-acquired pneumonia; treatable traits; amoxicillin; co-amoxicillin.

Dissemination plans The literature review will be summarised into a manuscript publication and published in an appropriate journal.

Contributions of each author

Author 1 - Serhat Unal - SU contributed to the conceptualisation, investigation, analysis, and interpretation of review content. SU contributed to manuscript writing, reviewed the manuscript critically for important intellectual content, and approved the final version of the manuscript.
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Author 5 - Puja Nijhara - PN contributed to the conceptualisation, investigation, analysis, and interpretation of review content. PN contributed to the writing, reviewed the manuscript critically for important intellectual content, and approved the final version of the manuscript. PN is the guarantor of this work and, as such, had full access to all the data.
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