

Review

# Prevalence of streptococcus pneumoniae in elderly with pneumonia: A meta-analysis and systematic review in Asia

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## ABSTRACT

**BACKGROUND:** There is currently insufficient study focusing on comprehensive studies that thoroughly assess the prevalence of *Streptococcus pneumoniae* specifically among elderly patients with pneumonia in Asia.

**OBJECTIVES:** To analyze the prevalence of *Streptococcus pneumoniae* as a causative factor of pneumonia among elderly populations in Asian countries.

**METHODS:** This meta-analysis was designed to systematically collect data from PubMed, Scopus, and Embase within the timeframe of January to February 2024. The study focused on gathering prevalence data of *Streptococcus pneumoniae* among elderly patients diagnosed with pneumonia in Asian countries. Statistical analysis employed a single-arm meta-analysis methodology to consolidate and evaluate the cumulative prevalence of *Streptococcus pneumoniae* in this specific population group.

**RESULTS:** The total sample included in our study comprised 15 articles. Through our analysis, we found that the cumulative prevalence of *Streptococcus pneumoniae* among elderly patients diagnosed with pneumonia in Asia was 9% (Event rate: 0.09; 95% CI: 0.06, 0.12; Egger's test:  $p = 0.7047$ ;  $p$  Heterogeneity  $< 0.0001$ ;  $p < 0.0001$ ).

**CONCLUSION:** *Streptococcus pneumoniae* remains a plausible causative agent of pneumonia in elderly Asian populations.

**KEYWORDS:** Pneumonia; elderly; *Streptococcus pneumoniae*; prevalence; Asia.

## INTRODUCTION

Pneumonia continues to present a significant global health challenge, characterized by lung parenchymal infections caused by various pathogens.<sup>1</sup> It ranks as the fourth leading cause of mortality worldwide.<sup>2</sup> The incidence of pneumonia among those aged 65 years and older stands at approximately 63 cases per 100,000 individuals annually.<sup>3</sup> In Indonesia, the hospital discharge rate for pneumonia is reported as 1,526 cases per 100,000 population, with hospital stays typically lasting between 6 to 10 days.<sup>4</sup> Global data from the Institute for Health Metrics and Evaluation indicate a mortality rate of 3.14% for pneumonia among individuals aged 60-79 years during the period from 2010 to 2019, doubling among elderly patients with dementia.<sup>5</sup> The prevalence and mortality rates of pneumonia in elderly patients vary significantly depending on the causative infectious agents.<sup>6</sup> Therefore, there is a critical need for studies aimed at identifying these agents in the elderly population to inform targeted and effective management and prevention strategies.

The predominant pathogen detected in elderly individuals suffering from community-acquired pneumonia (CAP) globally is *Streptococcus pneumoniae*, with *Haemophilus influenzae* and respiratory viruses also commonly implicated.<sup>7</sup> Conversely, in the adult population across Asia, pneumonia is primarily caused by

*Streptococcus pneumoniae*, respiratory viruses, and gram-negative enteric bacteria.<sup>8</sup> *Streptococcus pneumoniae* has historically been recognized as the leading etiological agent of pneumonia.<sup>9</sup> However, comprehensive studies that thoroughly evaluate the prevalence of *Streptococcus pneumoniae* specifically among elderly pneumonia patients in Asia are currently lacking. Hence, meta-analysis serves as a robust methodological tool to systematically assess *Streptococcus pneumoniae* prevalence in this demographic across diverse Asian countries. This meta-analysis was conducted to aggregate and critically analyze data spanning the last decade, aiming to discern the prevalence of *Streptococcus pneumoniae* as a causative pathogen of pneumonia in elderly populations throughout Asia. By synthesizing findings from various studies, this analysis seeks to provide a comprehensive overview of *Streptococcus pneumoniae* epidemiology in elderly pneumonia patients across different regions of Asia. The outcomes of this study are expected to significantly contribute to our understanding of *Streptococcus pneumoniae* prevalence among elderly pneumonia patients, facilitating evidence-based strategies for effective management and prevention. Moreover, these findings could guide future research directions and public health interventions aimed at mitigating the impact of pneumonia in aging populations across Asia.

## METHODS

### Study Design

The meta-analysis was conducted between January and February 2024. The methodology involved extracting data on the prevalence of *Streptococcus pneumoniae* among elderly pneumonia patients from multiple articles to determine the cumulative prevalence. The protocols adhered to a Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA)-based checklist,<sup>10</sup> and the study was registered with Prospero under the number CRD42023414897.

Table 1. Baseline characteristics of article included in our analysis

Author	Design	Location	Type of pneumonia	Quality assessment
Choi 2021	Retrospective	South Korea	Organizing pneumonia	Moderate
Farahat et al 2021	Retrospective	Saudi Arabia	CAP	Moderate
Jung et al 2018	Retrospective	South Korea	Post operative pneumonia	Moderate
Koh et al 2015	Retrospective	South Korea	NHAP	Moderate
Lee et al 2014	Retrospective	South Korea	CAP	Moderate
Liang et al 2012	Retrospective	Taiwan	CAP, HAP	Moderate
Memish et al 2014	Cross - sectional	Saudi Arabia	CAP	Moderate
Morimoto et al 2015	Prospective	Japan	CAP	High
Nakashima et al 2022	Retrospective	Japan	CAP	High
Osman et al 2021	Retrospective	Thailand	CAP	High
Song et al 2017	Retrospective	South Korea	HAP	Moderate
Suzuki et al 2021	Retrospective	Japan	Aspiration pneumonia CAP, HAP, aspiration	Moderate
Takedani et al 2021	Retrospective	Japan	pneumonia	Moderate
Xie et al 2023	Retrospective	China	NA	High
Yamazaki et al 2016	Retrospective	Japan	NA	Moderate

Note, NA, not available; CAP, Community-acquired pneumonia; NHAP, Nursing home-acquired pneumonia; HAP, Hospital-acquired pneumonia.

### Eligibility Criteria

The inclusion criteria for the meta-analysis included observational studies such as cross-sectional, retrospective, and prospective designs that evaluated the prevalence of *Streptococcus pneumoniae* in elderly patients with pneumonia and provided complete data for calculating cumulative prevalence. Studies were excluded if they were deemed irrelevant based on their title and/or abstract, or if they were reviews, commentaries, or assessed as poor quality according to the Newcastle-Ottawa Scale.

## Quality Assessments

The quality of the articles was assessed using the Newcastle-Ottawa Scale, which evaluates three main components: the selection of study groups, the comparability of these groups, and the ascertainment of the outcome of interest. Scores range from 0 to 9 points, with 0-3 indicating low quality, 4-6 indicating moderate quality, and 7-9 indicating high quality.<sup>11</sup> The assessment was conducted by YRKAW, AAP, ASN, APS, AF, AS, GNU, MKJ, PA, VPU, ZS, and DSBS. Any discrepancies in evaluations were resolved through discussions with a senior researcher (SS).

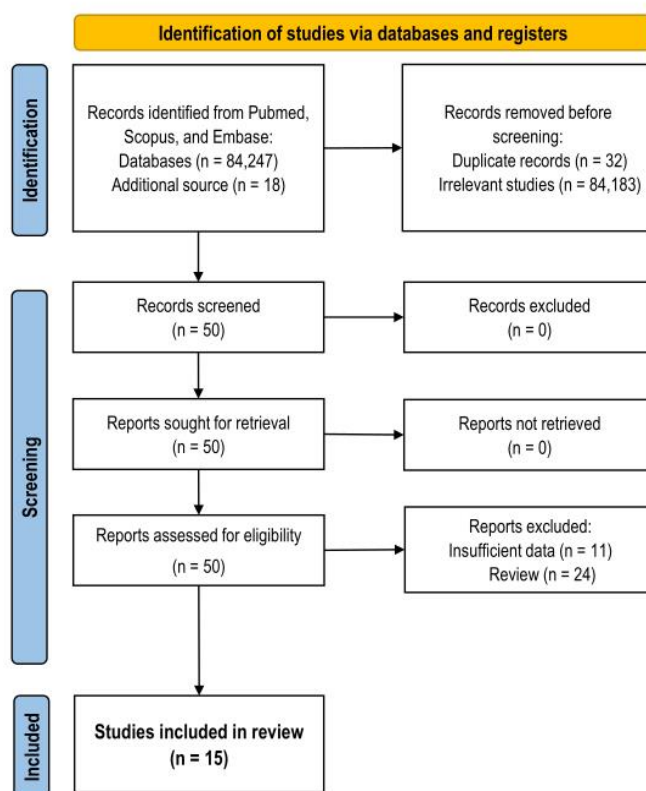


Figure 1. A flowchart of article selection in our study

## Search Strategy

The source databases for the search strategy included PubMed, Embase, and Scopus. The search was conducted up to January 5, 2024, and was limited to articles published in English. Keywords used in the search were “pneumonia” AND “elderly” AND “Streptococcus pneumoniae” AND “Asia.” Additionally, relevant articles were identified by searching through the reference lists of related articles.

## Data Extraction

Information extracted from each article included the first author's name, year of publication, country where the study was conducted, study design, type of pneumonia, quality assessment, and the prevalence of Streptococcus pneumoniae in elderly patients with pneumonia. Data extraction was carried out by YRKAW, AAP, ASN, APS, AF, AS, GNU, MKJ, PA, VPU, ZS, and DSBS. Any discrepancies in the data were resolved through discussions with a senior researcher (SS).

## Study covariates

The primary outcome in our study was the cumulative prevalence of Streptococcus pneumoniae in elderly patients with pneumonia. This measure provided a comprehensive understanding of prevalence rates across different studies, enabling a more accurate and consolidated assessment of the burden of Streptococcus pneumoniae in this population.

### Statistical Analysis

The data were presented as event rates. Potential publication bias was assessed using Egger's test and visualized with a funnel plot.<sup>12</sup> Heterogeneity was evaluated using the I-squared statistic and the p-value from the Q statistic. A random-effects model was applied in the presence of heterogeneity, whereas a fixed-effects model was used when no heterogeneity was detected.<sup>13</sup> The main findings were evaluated using a single-arm meta-analysis, with results considered statistically significant if  $p < 0.05$ . Effect sizes were expressed as event rates with 95% confidence intervals and presented in a forest plot.<sup>14</sup> All analyses were performed using Comprehensive Meta-Analysis Software version 4.

## RESULTS

### Article selection

The initial search on PubMed, Scopus, and Embase yielded 84,247 articles, with an additional 18 articles identified from the reference lists of related articles. After removing 32 duplicates, 84,183 articles were excluded due to irrelevant titles and/or abstracts. Subsequently, 50 articles underwent full-text review. Among these, 11 articles were excluded due to insufficient data, and 24 articles were excluded because they were reviews. Ultimately, the final sample included 15 articles.<sup>6,15-28</sup> Figure 1 illustrates the article selection process in this study. The baseline characteristics of the articles included in our analysis are presented in Table 1.

### The cumulative prevalence of Streptococcus pneumoniae in elderly pneumonia patients in Asia

The total sample comprised 15 articles. Our analysis determined that the cumulative prevalence of Streptococcus pneumoniae among elderly patients with pneumonia in Asia was 9% (Event rate: 0.09; 95% CI: 0.06, 0.12; Egger's test:  $p = 0.7047$ ;  $p$  Heterogeneity  $< 0.0001$ ;  $p < 0.0001$ ) (Figure 2).

### Heterogeneity among studies & potential publication bias

In our analysis, we observed that the p-value for Egger's test was 0.7047, indicating no significant publication bias. Additionally, our assessment using the Q statistic revealed a p-value for heterogeneity of  $< 0.0001$ , demonstrating substantial heterogeneity among the included studies. Therefore, we employed a random-effects model to accommodate this heterogeneity in our analysis.

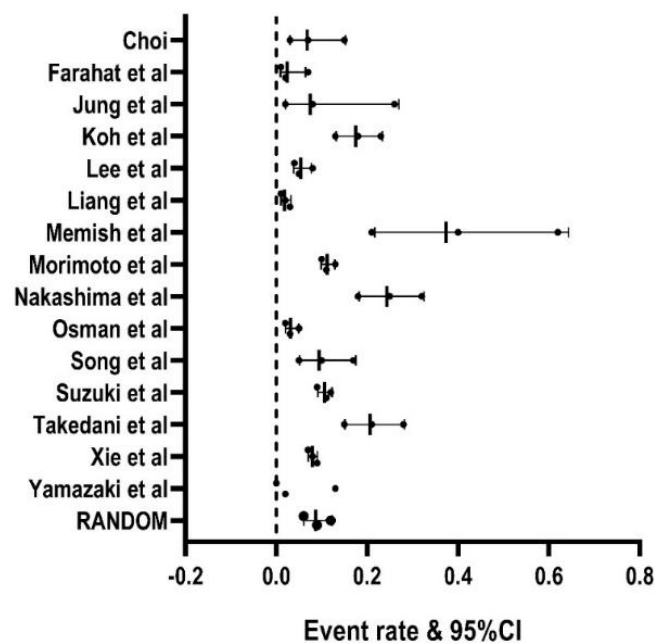


Figure 2. A forest plot of the prevalence of streptococcus pneumoniae in elderly with pneumonia in Asia (Event rate: 0.09; 95%CI: 0.06, 0.12;  $p$ Egger: 0.7047;  $p$ Heterogeneity $<0.0001$ ;  $p<0.0001$ )

## DISCUSSION

Our analysis indicated that the combined prevalence of *Streptococcus pneumoniae* among elderly patients with pneumonia in Asia was 9% (Event rate: 0.09; 95% CI: 0.06, 0.12; p Egger: 0.7047; p Heterogeneity < 0.0001; p < 0.0001). This figure was lower compared to previous studies reporting approximately 13.3% in Asia and 19.3% in Europe.<sup>7,29</sup> The higher prevalence in those studies may be attributed to their inclusion of larger study populations, encompassing all adults with pneumonia, and the European study's use of unadjusted proportions for calculation.<sup>7,29</sup> Geographic and racial variations likely contributed to pathogen variance, influenced by differences in host genetics, innate and adaptive immunity, as well as cultural and behavioral factors such as diet, hygiene, and environmental exposures.<sup>7,29</sup> Furthermore, changes in elderly patient defenses, such as impaired mucociliary clearance, decreased chest wall motility, and reduced lung compliance, heightened the risk of infection and complicated pathogen identification via sputum examination due to cough reflex dysfunction.<sup>30</sup> Intracellular pathogens like *Legionella pneumophila*, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae*, and *Chlamydia psittaci* were frequently identified in these cases.<sup>31</sup> Comorbidities such as stroke may have also increased susceptibility to multi-drug-resistant bacterial infections.<sup>32</sup> Finally, our study's reliance solely on culture results potentially underestimated *Streptococcus pneumoniae* cases, highlighting the possibility of missed diagnoses that could have been identified through urine antigen testing, Polymerase Chain Reaction (PCR), or cases where the etiology remained unidentified due to the absence of specific testing methods.

This study had several significant clinical implications. Firstly, it highlighted the high prevalence of pneumonia in the elderly caused by *Streptococcus* bacteria. This provided new insights into pneumonia among the elderly, where *Streptococcus pneumoniae* is a common cause of CAP in Western European countries and developing nations. In contrast, Gram-negative bacteria are more frequently associated with pneumonia in the elderly in Asia, contributing to higher mortality rates.<sup>6</sup> Secondly, the study underscored the importance of evaluating pneumonia in the elderly population due to their heightened susceptibility to infections by multidrug-resistant organisms, which can lead to more severe outcomes.<sup>6</sup> Thirdly, the study emphasized that *Streptococcus pneumoniae* remains a significant cause of pneumonia in the elderly, with presentations, etiologies, clinical courses, and outcomes differing from those in younger adults.<sup>6</sup> Lastly, the findings underscored the importance of reliable estimates regarding the contribution of *Streptococcus pneumoniae* to the total burden of CAP, particularly in projecting the health and economic benefits of pneumococcal immunization programs.<sup>33</sup>

This study encountered several limitations that warrant consideration. Firstly, a predominant number of the included studies were retrospective, which may have introduced recall bias due to reliance on historical data and patient records. Secondly, the quality assessment of these studies generally yielded moderate ratings, indicating variability in methodological rigor and potential impacts on data reliability. Thirdly, the geographic scope was limited to Japan, Korea, Saudi Arabia, China, Thailand, and Taiwan, thereby potentially not fully representing the diverse epidemiological landscape across all Asian countries. This geographic variation could influence the distribution and prevalence of *Streptococcus pneumoniae* in the region. Fourthly, diagnostic tests may not always detect *Streptococcus pneumoniae* in infected patients, which could lead to underestimations in prevalence rates. Lastly, since the analysis relied on published studies, the presence of publication bias must be acknowledged, as studies with positive or significant findings are more likely to be published, potentially biasing overall conclusions.

## CONCLUSION

In conclusion, our study found that *Streptococcus pneumoniae* contributes to a cumulative prevalence of 9% among elderly pneumonia patients in Asia. While this bacterium is identified as a potential cause of pneumonia in this demographic, it is just one among several pathogens. Further research is necessary to deepen our understanding of the evolving landscape of pneumonia etiology in elderly populations across Asia.

**ETHICS APPROVAL AND CONSENT TO PARTICIPATE**

None.

**CONFLICTS OF INTEREST:**

We have no conflict of interest

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We have no source of funding

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None.

**AUTHOR CONTRIBUTION**

Conceptualization: SS; Data Curation: YRKAW, AAP, ASN, APS, AF, AS, GNU, MKJ, PA, VPU, ZS, and DSBS; Formal Analysis: YRKAW, AAP, ASN, APS, AF, AS, GNU, MKJ, PA, VPU, ZS, and DSBS; Investigation: YRKAW, AAP, ASN, APS, AF, AS, GNU, MKJ, PA, VPU, ZS, and DSBS; Project Administration: YRKAW; Resources: YRKAW; Methodology: YRKAW; SS; Software: YRKAW; SS; Visualization: YRKAW; SS; Supervision: SS; Validation: SS; Writing – Original Draft Preparation: YRKAW, AAP, ASN, APS, AF, AS, GNU, MKJ, PA, VPU, ZS, and DSBS; Writing – Review & Editing: SS. All authors have critically reviewed and approved the final draft and are responsible for the content and similarity index of the manuscript.

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