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► To cite this version:

Christelle Elias, Marta C Nunes, Mitra Saadatian-Elahi. Epidemiology of community-acquired pneumonia caused by *Streptococcus pneumoniae* in older adults: a narrative review. *Current Opinion in Infectious Diseases*, 2024, 37 (2), pp.144-153. 10.1097/QCO.0000000000001005 . hal-04901076

HAL Id: hal-04901076

<https://hal.science/hal-04901076v1>

Submitted on 20 Jan 2025

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Epidemiology of community-acquired pneumonia caused by *Streptococcus pneumoniae* in older adults: a narrative review

Christelle Elias^{a,b}, Marta C. Nunes^{b,c,d} and Mitra Saadatian-Elahi^{a,b}

Purpose of review

This review covers updated perspectives on different aspects of pneumococcal community-acquired pneumonia (pCAP), including the epidemiology, clinical presentation, risk factors, antibiotic treatment, and existing preventive strategies in older adults.

Recent findings

pCAP remains the most prevalent condition among lower respiratory tract infections in the older adults according to Global Burden of Diseases 2019. Older adults can display atypical symptoms such as confusion, general clinical deterioration, new onset of and exacerbation of underlying illness that might trigger clinical suspicion of pCAP. Older adults with pCAP often experience increased disease severity and a higher risk of pulmonary complications compared with younger individuals, owing to age-related changes in immunity and a higher prevalence of comorbidities. Vaccination stands fundamental for prevention, emphasizing the need for effective immunization strategies, specifically tailored for older adults. There is a pressing need to reinforce efforts aimed at boosting pneumococcal vaccination rates.

Summary

Despite a high morbidity and mortality, the burden of pCAP, in particular hospital admission and occurrence of invasive infections, among the elderly population is not sufficiently documented. This review findings emphasize the substantial burden of pCAP in this vulnerable population, driven by factors such as advancing age and underlying comorbidities. The emergence of antibiotic-resistant pneumococcal strains further complicates treatment decisions and highlights the importance of tailored approaches for managing pCAP in older adults.

Keywords

community-acquired pneumonia, elderly, epidemiology, pneumococcus

INTRODUCTION

Streptococcus pneumoniae, commonly referred to as pneumococcus, is a gram-positive bacterium which is a normal colonizer of the nasopharynx and known for its ability to cause a wide range of illnesses, with community-acquired pneumonia being one of its most significant manifestations, especially among vulnerable populations such as children and older adults [1]. Pneumococcus is characterized by a polysaccharide capsule that surrounds the cell wall, aiding in evasion of the host immune system. Its virulence factors include adhesins, toxins, and enzymes that enable it to colonize the upper respiratory tract and invade deeper lung tissues, leading to pneumonia [2]. Pneumococci are classified into more than 100 serotypes and all licensed vaccines are based on the capsule antigen [3]. The most prevalent serotypes detected in the elderly population are 8, 3,

22F, 11A and 9N [2,4]. Pneumococcal pneumonia can result in severe morbidity and mortality, particularly in individuals with compromised immune

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Curr Opin Infect Dis 2024, 37:000–000

DOI:10.1097/QCO.0000000000001005

KEY POINTS

- *Streptococcus pneumoniae* is the most prevalent pathogen causing community-acquired pneumonia in older adults.
- Older adults are at heightened risk of contracting pneumococcal community-acquired pneumonia due to age-related changes in the immune system and an increased prevalence of underlying health conditions.
- Pneumococcal community-acquired pneumonia in older adults often leads to severe outcomes, including longer time of recovery, hospitalization and increased mortality rates, placing a substantial burden on healthcare systems.
- Pneumococcal vaccines, that is pneumococcal conjugate vaccine and pneumococcal polysaccharide vaccine, are pivotal in preventing pneumococcal disease in older adults. Increasing pneumococcal vaccine coverage remains a public health priority and the main prevention strategy.

systems or underlying health conditions such as the elderly population [5].

Understanding the epidemiology, risk factors and clinical presentation of pneumococcal community-acquired pneumonia (pCAP) in older adults holds significant importance for several reasons. First and foremost, older adults, especially those aged 65 years and older, are at a heightened risk of contracting pCAP due to age-related changes in the immune system and an increased prevalence of underlying health conditions [5]. Second, pCAP in older adults often leads to severe outcomes, including hospitalization and increased mortality rates, placing a substantial burden on healthcare systems [6,7]. In-depth research into this population helps identifying strategies to reduce the burden on healthcare resources and to improve the quality of care in older adults. Furthermore, pneumococcal vaccines, i.e. pneumococcal conjugate vaccine and pneumococcal polysaccharide vaccine, play a pivotal role in preventing pneumococcal infections in the elderly [3]. More data on vaccine effectiveness, vaccination coverage are essential to guide vaccination strategies and to protect this vulnerable population. Finally, as antibiotic resistance among *Streptococcus pneumoniae* continues to emerge, monitoring changes in bacterial susceptibility patterns of pCAP in older adults is vital to ensure effective treatment protocols [3,8,9].

The global demographic landscape is undergoing a significant transformation with people enjoying longer life expectancies. Projections indicate that by 2030, approximately one in six individuals worldwide will have reached the age of 60 or

older. By 2050, the global population of individuals aged 60 and above will double and the demographic of those aged 80 years or older is set to triple [10]. Given the steady rise in the proportion of older adults on a global scale, an upsurge on the burden of pCAP can also be expected.

Contrary to the abundance of literature about pneumococcal diseases in young children, less is known about the incidence, and consequences (hospitalisation, mortality) of pCAP among older adults. This review is dedicated to summarize the clinical presentation, epidemiology, risk factors, preventive strategies and antibiotic treatment pertaining to pCAP among this population.

CLINICAL PRESENTATION

Nasal colonization is considered a prerequisite for pneumococcal diseases [11], although carriage is asymptomatic in most cases. Rates of asymptomatic carriage vary with age, environment and the presence of upper respiratory infection [12] with estimated colonization rates in adults at least 65-year-old ranging from 0 to 6% [13]. A systematic review from 2020 revealed that living in care facilities, particularly nursing homes, active smoking as well as frequent contact with children aged 6 years or less were associated with an increased prevalence of pneumococcal colonization [odds ratio (OR), 2.30; 95% confidence interval (95% CI), 1.26–4.21; OR, 1.69 (95% CI, 1.12–2.53) and OR, 1.93 (95% CI, 1.20–2.93), respectively], whereas living in urban areas was associated with a lower prevalence [OR, 0.43 (95% CI, 0.27–0.70)] [14].

Older adults are the second most susceptible age group to *S. pneumoniae* infection after the children less than 5 years old with an incidence rate exceeding 10 000 cases/100 000 population [15^{*}] and an estimated global total number of deaths for pneumococcus reaching the highest (150 000 deaths) in the 80–84 age group [15^{*}].

The clinical presentation of pCAP in older adults is characterized by a wide range of symptoms and poses challenges that are critical to address for effective diagnosis and management. Older adults may exhibit both typical respiratory symptoms, such as productive cough, and dyspnea or fever, and atypical symptoms, including confusion, delirium, falls and generalized weakness, which can often be the initial manifestations of pCAP [1]. This atypical presentation together with the presence of multiple chronic conditions that can mask or mimic pneumonia symptoms can complicate diagnosis, leading to delayed treatment, delayed recovery and potentially worse outcomes such as septic shock and respiratory failure [16].

Additionally, age-related immunosenescence may blunt the typical inflammatory response seen in younger patients, making clinical and radiological findings less pronounced. These diagnostic challenges underscore the importance of a comprehensive evaluation that includes clinical, radiological and microbiological assessments, such as chest radiographs and sputum cultures, to establish an accurate diagnosis of pCAP [17,18].

Early diagnosis and appropriate treatment of pCAP in older adults are thus paramount to improve outcomes and reduce morbidity and mortality [18]. Pneumococcal CAP should always be suspected in older adults, especially those with atypical symptoms or underlying comorbidities, and prompt initiation of empiric antibiotic therapy according to the local guidelines is crucial while awaiting diagnostic confirmation [19–21]. Timely intervention, along with comprehensive care that considers the unique challenges of this population, is essential in optimizing outcomes for older adults with pCAP.

GLOBAL EPIDEMIOLOGY

Using data from the Global Burden of Disease Study 2019, a report from 2023 estimated that the annual incidence of lower respiratory tract infections (LRTIs) worldwide was 6295 cases per 100 000 population [15[■]]. Also, the LRTI-related death rate consistently increased after the age of 65, surpassing 1000 cases per 100 000 after reaching the age of 85. While the distribution of LRTI deaths attributed to specific causes varied across age groups, *S. pneumoniae* was the leading cause of LRTI-related deaths globally, and in all age brackets. The highest number of LRTI-related deaths attributable to pneumococcus occurred in the 75–89 age group [15[■]].

Community-acquired pneumonia, a major manifestation of LRTI of public health concern, is associated with high morbidity and mortality [22]. Although other pathogens including bacteria, viruses, fungi and parasites can cause CAP, *S. pneumoniae* remains the most common etiologic agent [23].

Detection of *S. pneumoniae* from clinical specimens is the only way to confirm the etiological origin of the pneumonia. Different blood and urinary tests are available, but the sensitivity rarely exceeds 70% [24]. The combination of one or more conventional and molecular methods would be ideal for identification of atypical or nonencapsulated pneumococci which would also increase sensitivity. Molecular serotyping methods are highly useful in developing countries where culture negativity is more common; however, no molecular method resolves all serotypes [25]. MALDI-TOF is

a useful tool for identification of *S. pneumoniae* but not suitable for differentiating serotypes, although it may still have utility in surveillance purposes [26]. Estimates are significantly impacted by the type of testing used for pneumococcal identification and serotyping, with lower proportions from studies using just conventional techniques compared to newer techniques like serotype-specific urinary-antigen detection (ss-UAD) and PCR. Multiplex urine immunoassays that are specific to serotypes of pneumococcal bacteria that are covered by PCV13 and/or PPSV23 have been developed. These ss-UADs find extra cases of pCAP that traditional culture or BinaxNOW *S. pneumoniae* urinary antigen test alone would miss. When compared to traditional culture methods that include serotyping isolates using the Quellung reaction, these noncultural procedures (ss-UAD or PCR) exhibit a greater sensitivity for the identification of pneumococcal infection. Because the serotypes identified by the ss-UADs used to detect pneumococcal cases will mostly correlate to the vaccine-types in PCV13 and PPSV23, respectively, studies that primarily depend on ss-UADs for the detection of pneumococcal cases may overestimate the proportion of pCAP [27[■]].

The burden of pCAP has not been described in older adults. This can be explained, at least partly, by challenges regarding the clinical definition of pCAP because clinical syndromes characterizing infections caused by various agents overlap one another. A review from 2018 investigating the burden of pCAP in European adults reported an overall incidence rate of 68–7000 per 100 000 inhabitants with substantial variations between countries, age group, study and time period [23]. Torres *et al.* [23] reported that Spain had the highest incidence rates for pCAP (166 per 100 000) and invasive pneumococcal disease (IPD) (60 per 100 000) in patients aged at least 60 and at least 65 years, respectively. The highest incidence among older adults correlates with the observed high incidence of severe pneumococcal disease and subsequent outcomes in this population. Torres *et al.* [23] reported in the CAPA cohort study (mean age: 66.83 ± 17.25 years) that serotype 3, 8 and 19A were more predominant in pCAP patients with complications, with a hospital length of stay greater than 7 days, and with respiratory failure [28]. The same study showed that compared to other serotypes, serotype 7F, 14 and 12F were associated with the highest risks of complicated pCAP [OR, 3.66 (95% CI, 1.30–10.34)], septic shock [OR, 7.63 (95% CI, 3.06–19.04)] and ICU admission [OR, 3.47 (95% CI, 1.25–9.65)], respectively [28]. In Switzerland, older age (≥50 and ≥65 years) was associated with increased hospitalization for pneumonia and pneumococcal pneumonia, longer length of

stay and higher mortality [29]. In a Swedish study published in 2023, the incidence of pneumococcal disease was 12.3/100 000 in individuals aged 18–64 years, 52.1 in individuals aged 65–74 years, and 85.3 in those aged 75 years and above [30]. As age increased, the 30-day case fatality rate also rose, standing at 2.2% in individuals aged 18–64 years, 5.4% in those aged 65–74 years, and 11.7% in those aged 75 years and above. Among bacteriemic patients aged 75 and above, the 30-day case fatality rate was the highest, reaching 21.4%. Additionally, the average 30-day cost per pneumococcal infection was estimated at €4467 in the 18–64 age group, €5278 in the 65–74 age group and €5898 in individuals aged 75 years and above [30]. In Canada, mortality rates for pCAP increased with age from 3.8% (16–49 years), to 6.3% (50–64 years), and 12.0% (≥ 65 years) [24]. In the same study, adults at least 65 years of age accounted for 67% of deaths attributed to pCAP, 43% of the ICU admissions and 43% of patients requiring mechanical ventilation, while these outcome measures (in the same order) were 10, 20 and 20% in adults 16–49 years of age [24]. Likewise, among IPD cases in the United States in 2021, the mortality rate increased with age from 0.22/100 000 in the youngest adults 18–34 years to 1.71/100 000 among those 65–74 years and 2.38/100 000 among those at least 85 years of age [31]. In both Europe [23] and the United States (USA), the highest burden has been reported in individuals more than 65 years old with comorbidity [32]. In addition to the presence of comorbidities, the susceptibility of older adults could be exacerbated by the effects of immunosenescence [5]. The relationship between pneumococcal serotypes and invasive disease syndromes, as well as their level of severity and risk of hospitalisation and mortality, varies, with notable discrepancies between Europe and the US. The proportion of pCAP varied according to geographical region, with a pooled estimate of 26% from European studies compared to 11% in North America [27^{***}]. Since adding a 13-valent pneumococcal conjugate vaccine to the paediatric vaccination schedule, the UK has experienced an increase in nonvaccine serotype invasive pneumococcal disease, most notably in older persons, similarly to what is observed in other European settings. In the USA, where the prevalence of nonvaccine serotype invasive pneumococcal disease in older adults and young children has remained steady since the introduction of the same vaccine, such effects of serotype replacement have not been documented. Hence, differences in sampling methods between countries may result in disparate serotype distributions and potentially inconsistent incidence estimates of pneumococcal disease. In the USA,

monitoring encompasses both ambulatory and inpatient cases, resulting in a higher proportion of nonsevere disease, such as occult bacteraemia, than in the UK and Europe, where it is usually restricted to hospital inpatients who would represent more severe cases. Additionally, differences in transmission dynamics could be caused by different pneumococcal conjugate vaccines schedules and uptakes among countries as well as different contact patterns among generations and across settings. Increased exposure of older adults to the reservoir of pneumococci that colonise young children has been suggested to cause the well known spike in invasive pneumococcal disease in older adults around the winter holiday season. Other factors such as differences across countries in the microbiomes of individual hosts could be contributing to this effect [33].

RISK FACTORS

Age

Age is undeniably a major risk factor for pCAP in the adult population, with epidemiological trends indicating that older adults are more affected by pCAP [hazard ratio, 1.06 (95% CI, 1.05–1.07) $P < 0.001$] [34^{***}]. Studies consistently show that as individuals advance in age, their susceptibility to pCAP significantly increases, with a sharp rise in incidence observed among those aged 65 years and older [34^{***}] as presented in a large observational Spanish cohort, which reported increased risk by age [age 50–64: hazard ratio, 1 (reference); age 65–79: hazard ratio, 1.95 (95% CI, 1.77–2.16); age at least 80: hazard ratio, 4.46 (95% CI, 4.01–4.96)] [34^{***}].

Despite effective treatment options and high vaccination rates, morbidity and mortality related to pCAP in older adults are significant public health concerns, with implications for healthcare systems. Older adults with pCAP often experience increased disease severity and a higher risk of complications compared with younger individuals, owing to age-related changes in immunity and a higher prevalence of comorbidities. In addition, age was identified as a key contributor to the risk of CAP severity [35]. Adults aged 65 years or older have a substantially higher rate of hospitalization due to pneumococcal pneumonia compared to adults aged 18–64 years old (280 per 100 000 vs. 53 per 100 000, respectively) [6]. Age at least 65 years (vs. < 65 years) [OR, 2.42 (95% CI, 2.36–2.49)] was a significant risk factor for hospitalization with a diagnosis of pneumococcal pneumonia vs. hospitalization without a diagnosis of pneumococcal pneumonia. Similarly, Cavallazzi *et al.* [36] found that individuals aged

over 65 were more likely to require be admitted to ICU.

Pneumococcal CAP is a leading cause of infectious disease-related deaths in older adults [37–39]. Age at least 65 was found as an independent risk factor for in-hospital mortality [OR, 2.69 (95% CI, 2.25–3.22)] and for length of stay [OR, 1.20 (95% CI, 1.19–1.21)] in patients with a pneumococcal pneumonia diagnosis [29]. In comparison with patients aged lower than 65, hospitalization rates among pCAP patients older than 65 are notably elevated [relative risk (RR), 1.83] [36], requiring intensive medical care, extended hospital stays and poorer outcomes. Bedos *et al.* [39] reported that in-hospital pCAP mortality increased with age for 27.1% in the group older than 65 years ($P < 0.0001$) despite that 5-day in-hospital pCAP mortality was similar across age groups. And, compared to patients aged between 18 and 50 years, patients aged above 65 were more at risk of hospital death [adjusted OR, 2.86 (95% CI, 1.32–6.19)] [39]. A study conducted in the New York State (USA) reported that the mean annual age-adjusted community-setting pneumonia-associated hospitalization rate increased as age increased and those aged at least 80 years had more than 30 times the rate of community-setting pneumonia-associated hospitalization rate than those aged 20–44 years [40].

Furthermore, the risk of pCAP-related mortality is often compounded by the presence of underlying

health conditions and comorbidities commonly seen in older adults [7,41]. In contrast, one study with a median population age of 80 years, revealed that compared with other respiratory bacterial pathogens, pneumococcus was associated with a lower risk [OR, 0.41 (95% CI, 0.35–0.48)] of dying from pneumonia [37].

Immunosenescence, a natural consequence of ageing, leads to a gradual decline in immune function, leading to reduced pathogen recognition, diminished antibody production and impaired cell-mediated immunity [42] making older adults more vulnerable to infections like pCAP [43,44]. Furthermore, ageing often coincides with the presence of comorbidities which further elevates the risk of pCAP [34^{***},38,45].

Underlying health conditions and comorbidities

Among the various comorbidities, as depicted in Fig. 1, according to a large population-based study of Ochoa-Gondar *et al.* [34^{***}] in person aged at least 50 years, HIV infection stands out as a strong risk factor [OR, 5.16 (95% CI, 3.57–7.46)] for pCAP hospitalization in older adults together with chronic obstructive pulmonary disease COPD [OR, 2.66 (95% CI, 2.47–2.86)] given its high prevalence in the elderly population and the association with impaired lung function [37,41]. Cardiovascular

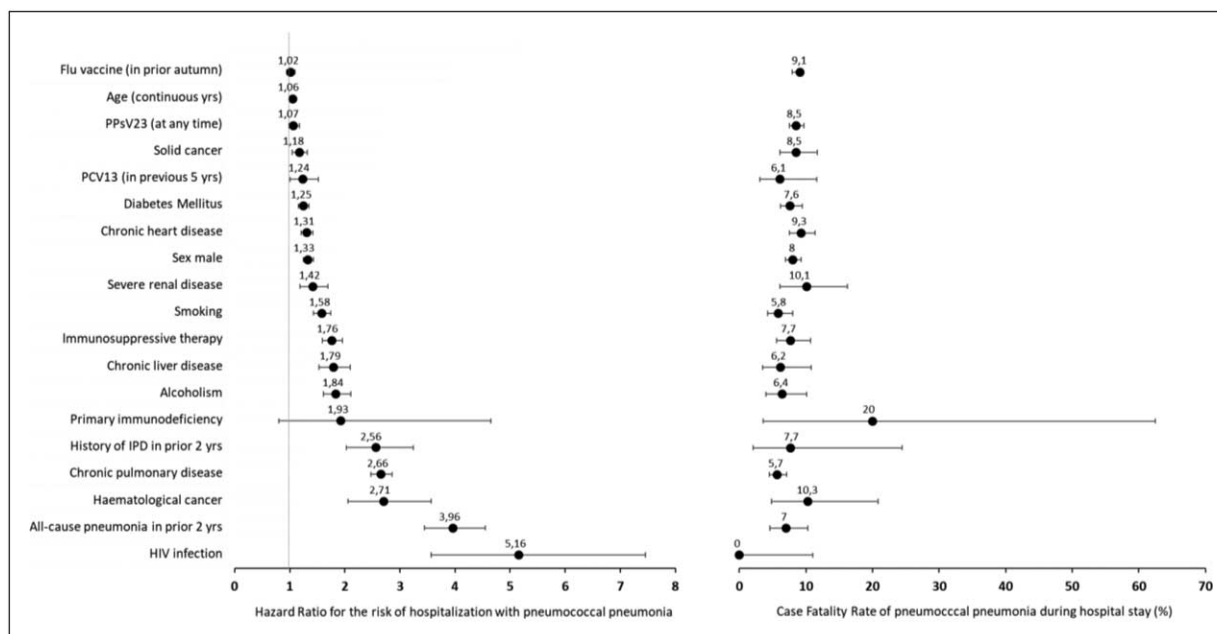


FIGURE 1. Forest plot of hazard ratios for the risk of hospitalization with pneumococcal pneumonia, and case-fatality rates of pneumococcal pneumonia during the hospital stay, in adults ≥ 50 years old by distinct specific underlying conditions [34^{***}]. IPD, invasive pneumococcal disease; PCV13, 13-valent pneumococcal conjugate vaccine; PPsV23, 23-valent pneumococcal polysaccharide vaccine.

diseases, such as congestive heart failure, diabetes mellitus and chronic kidney and liver disease, further elevate the risk of pCAP [34²²,37,38,41,45,46]. Immunocompromising conditions, including HIV infection and other malignancies such as patients with bone marrow transplant, acute and chronic leukemia, multiple myeloma or genetic disorders affecting the immune system, markedly increase vulnerability to pCAP [34²²] and severe pCAP [47,48]. These conditions not only elevate the risk of pCAP but also contribute to immunosuppression which affects the course and outcomes of pCAP cases, leading to increased morbidity and mortality.

Neurological conditions such as dementia can contribute to impaired swallowing and aspiration, predisposing the senior population to an increased risk of dying from pneumonia in the hospital [OR, 1.43 (95% CI, 1.32–1.55)] [37].

Lifestyle factors like smoking and excessive alcohol consumption, which can persist into older age, remain consistent contributors to risk [37,49,50]. A study showed that current cigarette smoking was associated with increased risk of septic shock in pCAP patients [OR, 1.06 (95% CI, 1.02–1.10), $P=0.001$] [49]. A Spanish study in people over 50 years in Catalonia showed that smoking is associated with an increased risk of pneumococcal disease [OR, 2.09 (95% CI, 2.07–2.10)], although the same study reported that smoking was associated with a lower risk of pneumococcal diseases for people aged at least 65 years as compared with people aged 50–64 years [51].

Moreover, it is known that there is an association and interaction between viral infections and bacterial respiratory tract pathogens supporting the notion that respiratory viruses may enhance carriage acquisition and pneumococcal transmission also in older adults [12,47]. A particular association with influenza virus infection, including both seasonal and pandemic influenza, with subsequent development of pneumococcal infections have been highlighted and the underlying mechanisms well documented in both experimental animal models and human studies [7].

Social determinants and living conditions

Social determinants and living conditions play a pivotal role as risk factors for pCAP in the elderly, where socioeconomic status emerges as a critical factor, with lower income levels, limited access to healthcare, and inadequate housing conditions amplifying the risk of pCAP in older adults [40]. Wu *et al.* [40] reported that the mean annual age-adjusted rate generally increased as area-based poverty level increased. Furthermore, insufficient social

support networks and isolation in the elderly population contribute to delayed diagnosis and suboptimal healthcare-seeking behavior, potentially exacerbating the severity and outcomes of pCAP cases. Among the participants of the study of Barnes *et al.* [52] (mean age = 76.5 years), 9.8% ($n=684$) were considered lonely only, 20.6% ($n=1439$) socially isolated only, 9.1% ($n=639$) both lonely and socially isolated, and adjusted results reported that participants who were both lonely and socially isolated had significantly higher rates of emergency room visits.

Moreover, inequities in access to pneumococcal vaccination among older adults from disadvantaged backgrounds further emphasize the impact of social determinants on pCAP risk [53].

Exposure to healthcare settings and long-term care facilities

Healthcare settings and long-term care facilities (LTCF), while intended to provide care, often facilitate the transmission of respiratory infections, including pCAP, among vulnerable older adults. Indeed, studies have shown that LTCF, where residents often live in close quarters, are particularly conducive to outbreaks of infectious diseases, with higher infection rates reported in such environments [37,38,41,54]. A review from Henig *et al.* [1] showed that the incidence of pneumonia among residents of LTCFs was higher than in elderly persons who live at home. The median reported annual incidence of pneumonia among LTCF residents was 365 cases per 1000 persons (range, 99–912) approximately 11 times the incidence reported among patients from the community older than 75 years of age (34 per 1000 persons) [1]. Moreover, frequent interactions with healthcare professionals and shared healthcare resources can lead to increased transmission of pneumococcus and therefore to an increased exposure to potential carriers of pneumococcal pneumonia [55].

PREVENTIVE MEASURES

Vaccination against *S. pneumoniae* is a pivotal preventive measure for pCAP in older adults, given their heightened vulnerability to severe respiratory infections. Pneumococcal vaccines aim to safeguard this population from the most prevalent serotypes of *S. pneumoniae* [56]. Two main types of pneumococcal vaccines are currently available: the pneumococcal polysaccharide vaccine (PPSV23) and pneumococcal conjugate vaccines (PCV10, PCV13, PCV15 & PCV20). PPSV23 targets 23 pneumococcal serotypes and has been widely used in older adults

for decades, while PCV10, PCV13, PCV15 and PCV20 cover 10, 13, 15 and 20 serotypes, respectively.

Pneumococcal vaccines have a significant impact in preventing pCAP, reducing invasive pneumococcal diseases, hospitalization rates and averting severe complications, such as bacteremia and pleural effusion [57–61]. These vaccines have also shown effectiveness in preventing mortality associated with pCAP in the elderly, underscoring their life-saving potential [62]. A study from Canada, focusing on the impact of pneumococcal vaccination on pneumonia-related hospitalizations spanning from 1992 to 2014, delineated various phases: the prevaccine era, availability of PCV7 for private purchase, public funding for PCV7, the replacement of PCV7 with PCV10, and finally, the shift to PCV13. The findings demonstrated a significant reduction in hospitalizations for pneumonia, with declines of 34, 38 and 45% after the initiation of public funding for PCV7, PCV10 and PCV13, respectively [24].

In a review from 2022, data from The Community Acquired Pneumonia immunization Trial in Adults (CAPIA), a randomized, double-blind clinical trial in 84 496 participants aged at least 65 years in the Netherlands, demonstrated a 45.6% (95% CI, 21.8–62.5) efficacy of PCV13 against first episodes of CAP associated with vaccine serotypes (VT) and 75.0% (95% CI, 41.4–90.8) against first episodes of VT invasive pneumococcal disease per protocol [63^{***}]. PCV13 efficacy estimates were 49.3% (95% CI, 26.2–67.1) for adults aged 65–74 years and 40.5% (95% CI, 3.3–65.9) for adults aged 75–84 years [63^{***}]. PCV13 effectiveness for serotype 3 was 60.0% (95% CI, 5.2–84.8) against first episodes of radiologically confirmed CAP and 61.5% (95% CI, 17.6–83.4) against all episodes of clinical CAP [64].

Data from the systematic review of Berild *et al.* [62] reported a pooled vaccine efficacy estimate of 64% (95% CI, 35–80) against pneumococcal pneumonia (any serotype) derived from a randomized controlled trial on PPSV23 in adults aged above 60, while cohort studies indicated a pooled vaccine effectiveness of 48% (95% CI, 25–63) and a vaccine effectiveness of 53% (95% CI, 33–68) in a single case-control study. PPSV23 also appears to remain effective in reducing nonbacteraemic pneumonia for up to 5 years after vaccination when administered to individuals under the age of 75 [62]. However, despite the clear benefits, vaccine coverage among older adults remains suboptimal due to several challenges. Indeed, a recent observational study in France from Wyplosz *et al.* estimated that only 4.5% of 4 045 021 at-risk adults were up to date with their pneumococcal vaccination. Interestingly, the odds of having at least one dose of pneumococcal

vaccine was 1.12 ($P < 0.0001$) in patients 75 and above compared with patients under 65 [65^{***}].

To date, no mandatory pneumococcal vaccination has been implemented in European countries in older adults and recommendations differ across Europe, with clear discrepancies between countries [66]. This patchwork of policies may lead to unbalanced vaccine coverage rates. Also, in seven European countries, older adults have to pay for pneumococcal vaccination, even if pneumococcal vaccination has been recommended. Access issues, including financial constraints, and limited vaccine availability, hinder vaccination efforts [67,68]. Moreover, vaccine hesitancy and misconceptions about vaccine safety and efficacy contribute to suboptimal coverage rates, emphasizing the importance of public health campaigns and healthcare provider education to address these concerns [69,70]. For instance, the prevalence of vaccination hesitancy among 65–75 year old reached 35% in France in 2016 [71]. To maximize the impact of pneumococcal vaccination in older populations, comprehensive strategies are needed to enhance vaccine access, promote awareness, and address vaccine hesitancy, ultimately reducing the burden of pCAP and its associated morbidity and mortality in this vulnerable group [70,72].

Finally, a recent modelling study from Germany showed a rising incidence of invasive pneumococcal disease in adults, primarily caused by serotypes covered in PCV20, suggesting that introduction of PCV20 holds significant promise in providing comprehensive protection against pneumococcal disease among older adults [73].

ANTIBIOTIC TREATMENT AND ANTIBIOTIC RESISTANCE

Antibiotic resistance, especially in the context of pneumococcal infections, is a growing concern that poses significant challenges in the management of pCAP among older adults. Recent publications underscore the emergence of antibiotic-resistant pneumococcal isolates as a pressing issue in healthcare leading to increased treatment failure rates, prolonged hospital stays, and higher mortality among older individuals [74–76]. A 2019 worldwide cross-sectional study on the prevalence and risk factors evaluation for drug-resistant *S. pneumoniae* pneumonia (median age = 70 years IQR 54–81); asthma was associated with penicillin resistance [OR, 5.85 (95% CI, 1.85–18.43)] and macrolide resistance [OR, 3.36 (95% CI, 1.06–10.61)], liver disease with tetracycline resistance [OR, 4.57 (95% CI, 1.24–16.81)] and noncystic fibrosis bronchiectasis with penicillin resistance [OR, 4.00 (95% CI,

1.02–15.64)] [77]. Also, resistant types, often associated with serotype replacement and the proliferation of nonvaccine serotypes, limit the effectiveness of traditional antibiotics, complicating treatment decisions for clinicians [21]. Studies have also shown that the use of broad-spectrum antibiotic therapy to treat pCAP in the elderly is associated with an increased incidence of *Clostridium difficile* infections [OR, 5.79 (95% CI, 1.86–27.51), $P = 0.008$] [75].

Macrolide resistance, particularly concerning among pneumococcal isolates, has ignited discussions regarding the reconsideration of macrolide monotherapy [46,74,77]. Controversy surrounds the choice between beta-lactam/macrolide combination therapy and fluoroquinolones alone, particularly for outpatients with underlying health conditions, hospitalized patients at risk of antibiotic-resistant pathogens, or those with severe CAP [20]. Intriguingly, a retrospective study in France uncovered no compelling evidence to suggest that patients infected with macrolide-resistant pathogens have worse outcomes when treated with guideline-compliant therapy [39]. Notably, despite the increasing prevalence of resistance, international recommendations continue to endorse the utilization of macrolides, often as part of combination therapy, primarily due to their nonantimicrobial anti-inflammatory properties [35,78,79]. Furthermore, there is a growing consensus in favor of employing beta-lactam/macrolide therapy for individuals battling Coronavirus Disease 2019 (COVID-19) pneumonia and suspected co-infection with pneumococcus, especially in cases of severe illness [35]. Finally, reducing the emergence of antimicrobial resistance by implementing an extended vaccination approach is also another preventive strategy that yielded encouraging outcomes [80].

CONCLUSION

We have highlighted critical insights into the epidemiology and management of pCAP in older adults. Despite that this review covers studies mostly conducted in high income countries, key findings underscore the substantial burden of pCAP in this vulnerable population, driven by factors such as advancing age and underlying comorbidities. The emergence of antibiotic-resistant pneumococcal strains further complicates treatment decisions and highlights the importance of tailored approaches for managing pCAP in older adults.

Preventive strategies, including public health campaigns, vaccination recommendations and education, have emerged as crucial tools in reducing the burden of pCAP in older adults. The integration of

pneumococcal conjugate vaccines alongside polysaccharide vaccines in vaccination schedules has shown promise in enhancing protection. The use of pneumococcal vaccination, particularly together with influenza vaccination has been shown to be effective in reducing influenza morbidity and associated pneumonia, while preventing pneumonia and reducing a potential poor prognosis [41,81]. It is therefore not surprising that pneumococcal vaccination, in addition to being part of pneumococcal prevention strategies, has been considered in pandemic influenza preparedness planning [12,44].

In light of these findings, it is evident that a multidimensional approach, encompassing research, surveillance, and targeted prevention, is essential in mitigating the impact of pCAP on older adults and improving their overall health outcomes.

Acknowledgements

The authors thank Juliette Dessemon, Cédric Dananché, Philippe Vanhems as well as Vincent Cottin, Gilles Leboucher, Sylvain Gaujard, Pierre Krolak-Salmon and Geraldine Martin-Gaujard for their important input to the topic.

Financial support and sponsorship

Pfizer sponsored scientific meetings leading to this review. The sponsor had no role in study design, data acquisition and interpretation, manuscript writing and decision to publish.

Conflicts of interest

C.E. declares no conflicts of interest.

M.C.N. and M.S.E. report research funding from Pfizer.

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