

## Comparison of the Effectiveness of Pneumococcal and Influenza Vaccines in Preventing Pneumonia in the Elderly

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### ABSTRACT

Pneumonia in older adults remains a significant health burden due to a combination of immunosenescence, comorbidities, and exposure to respiratory pathogens. This paper summarizes evidence on pneumonia prevention with pneumococcal vaccines (PPSV23, PCV13/15/20) and influenza vaccines (IIV, RIV, and adjuvanted/high-dose/intradermal formulations) in the older population. Pneumococcal vaccines reduce the incidence of invasive pneumococcal disease and some community-acquired pneumonia, particularly with a sequential strategy (PCV followed by PPSV23) to expand serotype coverage. Influenza vaccines reduce influenza-associated pneumonia, hospitalizations, and mortality; the benefit is enhanced with improved formulations for older adults. Virus-bacterial interactions cause influenza to facilitate pneumococcal superinfection, so dual vaccination approaches provide consistent synergistic effects reducing hospitalizations and deaths to a greater extent than either vaccine alone. Key challenges include diminished immune responses and antibody durability, host heterogeneity (immunosuppression, multimorbidity), and gaps in vaccine coverage. Optimization involves selecting the vaccine type, sequence, and timing of administration (including selected revaccinations), as well as strategies to increase uptake. In conclusion, the combination of pneumococcal and influenza vaccines is a powerful basic prevention strategy for reducing pneumonia morbidity and mortality in the elderly.

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## INTRODUCTION

Pneumonia in the elderly remains a significant public health problem due to the combination of immunosenescence, comorbidities, and high exposure to respiratory pathogens. *Streptococcus pneumoniae* a gram-positive, encapsulated bacterium with >100 serotypes is the leading cause of bacterial pneumonia, with a small number of serotypes predominating in invasive disease in vulnerable groups such as the elderly. Nasopharyngeal colonization is a prerequisite for disease; phenotypic variation (transparent vs. opaque) and capsule thickness influence invasion and phagocytosis evasion capabilities, thus shaping disease epidemiology and vaccine design. In the elderly population, pneumococcal pneumonia, bacteremia, and meningitis contribute to significant morbidity and mortality, often with atypical presentations – such as confusion or worsening of chronic illness that delay diagnosis and therapy.

Influenza drives the burden of primary viral pneumonia and facilitates secondary bacterial pneumonia, including by *S. pneumoniae*. Subtype patterns influence severity in the elderly: A(H3N2) is consistently associated with more severe disease and higher hospitalization rates, while A(H1N1)pdm09 causes a significant burden in those aged >40 years but is generally less severe than A(H3N2) in the elderly; the B-Yamagata lineage is also relevant in this age group. Clinically, approximately one-third of hospitalized elderly patients with confirmed influenza may develop pneumonia, with the risk increasing with age >75 years, nursing home residence, COPD, or immunosuppression; inflammatory markers and acute respiratory failure are often present. Case reports highlight the role of bacterial co-infections (e.g., MRSA) as well as the importance of early antivirals and vigilance against superinfection.

Prevention strategies rely on complementary pneumococcal and influenza vaccination. The 23-valent pneumococcal polysaccharide vaccine (PPSV23) covers 23 serotypes with a total of 575 µg of antigen per dose; it elicits a broad but variable T-cell-independent response for non-bacteremic pneumonia and is affected by a decline in response in the elderly. Conjugate vaccines (PCV13 and newer versions such as PCV15/PCV20) bind polysaccharides to carrier proteins (e.g., CRM197), triggering T-cell-dependent responses, immune memory, and better duration of protection, as well as expanding serotype coverage. At the population level, trials and efficacy studies have shown PCV to be effective against vaccine-type pneumonia and IPD, while a sequential strategy of PCV followed by PPSV23 increases serotype coverage and protection.

Influenza vaccines are available as inactivated influenza vaccines (IIV) commonly in quadrivalent formulations—with a good safety profile in the elderly; studies using adjuvants (e.g., MF59) and immunogenicity-enhancing approaches (e.g., ssRNA) have shown potential for enhancing humoral and cellular responses. Other variants include the live attenuated influenza vaccine (LAIV) for limited age groups and the recombinant influenza vaccine (RIV) based on egg-free HA expression, which is relevant for individuals with egg allergies and allows rapid adaptation to circulating strains. Consistent with these findings, immunosenescence reduces seroprotection following standard influenza vaccination, necessitating higher-dose formulations, adjuvants, or intradermal

routes targeting skin antigen-presenting cells; these approaches have demonstrated equivalent or superior immunogenicity in the elderly with an acceptable safety profile.

## LITERATURE REVIEW

### *Overview of Pneumococcal Disease*

Pneumococcal disease is caused by *Streptococcus pneumoniae*, a gram-positive, lanceolate-shaped bacterium that colonizes the human respiratory tract. There are over 100 identified serotypes of *S. pneumoniae*, distinguished by differences in their polysaccharide capsules, which significantly influence their colonization behavior and disease-causing properties. Although most serotypes can cause disease, a small subset is responsible for the majority of invasive pneumococcal infections, such as pneumonia, particularly in vulnerable populations such as the elderly.

These bacteria typically inhabit the nasopharynx without symptoms. Carriage rates vary by age and environment typically 5–10% in healthy adults without children, 20–60% in school-age children, and up to 60% in close populations such as military personnel. The duration of carriage tends to be longer in children. Importantly, colonization is a prerequisite for disease development, but the precise relationship between carriage and innate immunity remains incompletely understood.

Capsular polysaccharides are critical virulence factors that help pneumococci evade host immune responses. Phenotypic variations including differences in capsule thickness and colony morphology (transparent vs. opaque) affect their ability to colonize mucosal surfaces and invade sterile sites such as the bloodstream. Opaque colony phenotypes are more encapsulated, aiding their survival in the blood and resistance to phagocytosis, while transparent phenotypes tend to excel at colonization.

### *Overview of Influenza in the Elderly*

Influenza remains a significant health risk for the elderly, a population that is particularly vulnerable to severe respiratory infections and pneumonia. Influenza viruses are broadly classified into four types: A, B, C, and D. Among these, Influenza A and B viruses are responsible for seasonal epidemics in humans, causing a typical flu season each year. Influenza A viruses are further divided into subtypes based on two surface proteins called hemagglutinin (H) and neuraminidase (N). There are 18 hemagglutinin subtypes (H1-H18) and 11 neuraminidase subtypes (N1-N11) identified, although only a few subtypes commonly circulate in humans, primarily A(H1N1) and A(H3N2). Influenza B viruses do not have subtypes but are classified into two main lineages: B-Victoria and B-Yamagata.

Epidemiological studies have highlighted that the elderly population (aged 60 years and older) is more frequently infected with influenza A(H3N2) and B-Yamagata lineage subtypes. This specific subtype pattern influences the severity and complications of influenza in older adults, such as susceptibility to secondary bacterial infections like pneumonia. Subtype A(H3N2) is specifically

associated with more severe disease and higher hospitalization rates in elderly patients compared to other subtypes. On the other hand, A(H1N1)pdm09 tends to affect adults aged 25-59 years more frequently but is also associated with a high disease burden in the age group over 40 years, albeit with a lesser severity compared to A(H3N2) in the elderly.

Subtype differences have implications for vaccination strategies aimed at preventing pneumonia in the elderly. Influenza vaccines are typically formulated annually to target the predicted dominant circulating strains, such as subtype A and the relevant B lineages. Recognizing that elderly individuals are primarily affected by A(H3N2) and B-Yamagata informs vaccine composition and prioritization. Furthermore, comparison with pneumococcal vaccine effectiveness is crucial because pneumococci are often the causative agent of secondary pneumonia following influenza infection. The interaction between influenza virus type and the risk of pneumococcal pneumonia emphasizes the need for an integrated vaccination strategy targeting both pathogens for optimal pneumonia prevention in the elderly.

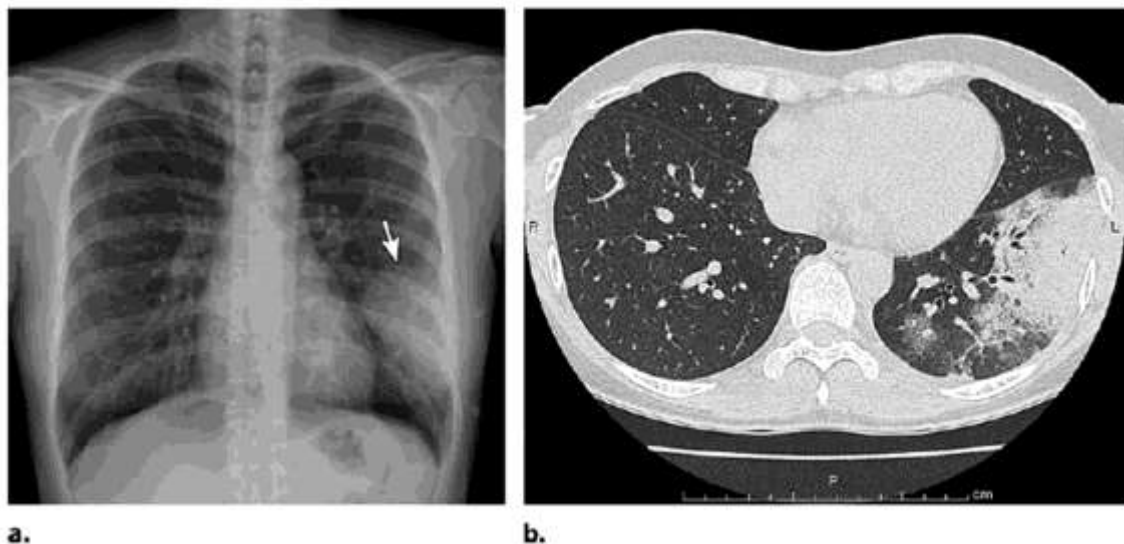


Figure 1 (a) PA chest radiograph shows sublobar consolidation in the left inferior lobe (arrow) with a round morphology. (Figure 4a is reprinted with permission from reference 100.) (b) Axial chest CT image (lung window) shows peripheral consolidation and ground-glass opacities typical of lobar pneumonia. No tree-in-bud micronodules or bronchial mucoid impaction are seen.

### ***Pneumococcal Vaccine***

Pneumococcal Polysaccharide Vaccine, commonly referred to as PPSV23 or Pneumovax 23® PPSV23 contains purified capsular polysaccharide antigens from 23 serotypes of *Streptococcus pneumoniae* responsible for most pneumococcal infections in adults. Each dose of PPSV23 contains 25 micrograms of polysaccharide antigen from each serotype, a total of 575 micrograms of antigen, along with 0.25% phenol as a preservative to maintain vaccine stability.

Unlike conjugate vaccines, which link polysaccharides to protein carriers to elicit a stronger immune response, PPSV23 is purely a polysaccharide vaccine.

This distinction is important because polysaccharide vaccines typically induce T-cell-independent immune responses, which may be less robust in certain populations, such as young children and the elderly. However, PPSV23 covers a broader range of serotypes than many conjugate vaccines, including those that cause a significant burden of invasive disease in older adults.

Structurally, the polysaccharide antigen in PPSV23 resembles the long chain of sugar molecules that make up the bacterial capsule. This capsule is crucial for pneumococcal virulence because it protects the bacteria from phagocytosis. The broad serotype coverage of the vaccine includes common and clinically important serotypes such as those associated with invasive disease and pneumonia in the elderly. Recent biochemical studies have elucidated detailed compositional elements of the pneumococcal polysaccharide, such as the presence of galactose residues, N-acetylglucosamine, and galacturonic acid, which contribute to the antigenic diversity that PPSV23 aims to address.

### *Influenza Vaccine*

Inactivated influenza vaccines (IIVs) are one of the most widely used forms of flu vaccine, particularly favored for their safety and efficacy, particularly in vulnerable populations such as the elderly. These vaccines contain killed or inactivated viral particles that are unable to cause disease but still trigger an immune response. IIVs typically come in trivalent and quadrivalent formulations, targeting three and four influenza virus types, respectively. Quadrivalent vaccines aim to offer broader protection by including an additional B virus lineage compared to trivalent variants.

The safety profile of inactivated influenza vaccines is excellent, which is particularly important given the higher risk profile in elderly individuals. Common side effects tend to be mild and transient, such as pain at the injection site, low-grade fever, and general malaise, which usually resolve within a few days. Notably, despite early concerns about protein- or egg-based vaccines triggering allergic reactions, evidence does not support a significant risk in individuals with egg allergies.

In terms of effectiveness, inactivated influenza vaccines induce a humoral immune response characterized by the production of antibodies directed against hemagglutinin, the surface protein of the influenza virus. Recent research has shown that incorporating adjuvants, such as single-stranded RNA (ssRNA) derived from viral regions, can enhance the immune response by stimulating balanced humoral and cellular immunity, as well as mucosal immunity – essential for combating respiratory viruses. This enhanced response with adjuvants also promotes the formation of memory T cells, which contribute to long-term immunity and cross-protection against various influenza strains.

From the perspective of pneumonia prevention in older adults, influenza vaccination plays a crucial role. Pneumonia, a frequent serious complication of influenza infection in older adults, can be reduced by effective immunization strategies. Comparisons between pneumococcal and influenza vaccines reveal complementary protective effects; while pneumococcal vaccines directly target pathogenic bacteria frequently implicated in pneumonia, influenza vaccines

prevent primary viral infections that often predispose patients to secondary bacterial pneumonia. Therefore, ensuring robust influenza vaccine-induced immunity indirectly reduces the incidence of pneumonia in this age group.

### *Immunogenicity of Pneumococcal Vaccine in the Elderly*

Pneumococcal vaccines, particularly the 23-valent pneumococcal polysaccharide vaccine (PPSV23) and the pneumococcal conjugate vaccine (PCV), are crucial in preventing pneumococcal diseases such as pneumonia in older adults, who are at higher risk due to decreased immune function and comorbidities. The immunogenicity of these vaccines in older adults reflects the immediate antibody response elicited after vaccination and the durability of this response over time, both of which are important considerations when evaluating the effectiveness of the vaccine compared with influenza vaccine in preventing pneumonia in this population.

Studies have shown that PPSV23 induces a sustained IgG antibody response for at least four years post-vaccination in older adults aged 65 to 70 years, with antibody levels against key serotypes maintaining higher concentrations compared to baseline even at the four-year mark. Factors such as gender and body mass index influence antibody levels, with women and individuals with a BMI above 25 showing higher post-vaccination antibody concentrations for certain serotypes. Importantly, different antibody waning trajectories exist, suggesting that some individuals experience a more rapid decline in antibody levels after two years, which has implications for the timing of revaccination strategies among older adults.

While PPSV23 elicits a T-cell-independent response leading to immediate antibody production, it does not induce immunological memory. This contrasts with PCV, which is T-cell-dependent and has the capacity to generate immunological memory, potentially resulting in longer-lasting protection. However, in immunosuppressed patients, common in the elderly population with comorbidities, the response to PCV may be diminished due to impaired T-cell function, while the PPSV23 response remains less affected because it is T-cell-independent. Some evidence suggests that while PCV elicits stronger long-term immunity in healthy individuals, the superiority of PCV over PPSV23 in the elderly or immunocompromised population is not consistently clear, emphasizing the need for a personalized vaccination approach.

Although early immunogenicity of pneumococcal vaccines is good in older adults, antibody levels often begin to wane as early as three years after vaccination. Revaccination, typically recommended after a five-year interval, can restore antibody levels comparable to those of primary vaccination. However, the clinical efficacy of revaccination in preventing pneumococcal disease has not been definitively established. Furthermore, the quality of functional antibodies, such as opsonophageal activity, can decline with age and influence protection independently of antibody quantity. These immunosenescence-related changes emphasize the importance of monitoring antibody responses and exploring vaccines that induce T-cell-dependent immunity to achieve more durable protection in the elderly population.

### ***Immunogenicity of Influenza Vaccine in the Elderly***

Influenza vaccination plays a crucial role in preventing pneumonia and its complications among the elderly, who are particularly vulnerable due to age-related waning immunity. The immune response elicited by influenza vaccines, often measured by the degree of seroprotection—the proportion of vaccinated individuals who achieve antibody titers considered protective—tends to be reduced in older adults compared with younger populations. This factor is crucial for understanding the relative effectiveness of influenza vaccines in preventing pneumonia in the elderly.

The degree of seroprotection following influenza vaccination in elderly individuals can vary significantly depending on the type of vaccine, the use of adjuvants, and individual patient factors such as comorbidities and pre-existing immunity. Studies have shown that standard-dose influenza vaccines sometimes produce lower antibody responses in this age group, prompting the development and use of enhanced vaccines, such as high-dose formulations and adjuvants, aimed at increasing immunogenicity. For example, the MF59 adjuvanted influenza vaccine has demonstrated improved seroprotection and consequently reduced rates of pneumonia and influenza hospitalizations among the elderly, as evidenced by meta-analyses showing vaccine efficacy ranging from 25% to over 50% against pneumonia-related hospitalizations.

Comparatively, pneumococcal vaccination also contributes significantly to pneumonia prevention in the elderly population, but these two vaccines target different pathogens—viruses versus bacteria—that cause pneumonia. Influenza infection often precedes or exacerbates secondary bacterial infections such as pneumococcal pneumonia, underscoring the importance of both vaccines in a synergistic prevention strategy. Influenza vaccine directly reduces the risk of viral pneumonia and may indirectly reduce the incidence of bacterial pneumonia by preventing influenza-associated epithelial damage and modulating immunity that predisposes patients to bacterial superinfection.

### ***Clinical Effectiveness of Pneumococcal Vaccine***

The clinical effectiveness of pneumococcal vaccines plays a crucial role in preventing invasive pneumococcal disease (IPD), particularly among the elderly population at higher risk. Pneumococcal disease remains a significant cause of morbidity and mortality worldwide, particularly in adults aged 65 years and older. Existing vaccines include the 13-valent pneumococcal conjugate vaccine (PCV13) and the 23-valent pneumococcal polysaccharide vaccine (PPSV23). Both vaccines aim to stimulate an immune response against multiple serotypes of *Streptococcus pneumoniae*, the bacteria responsible for pneumococcal infections.

Evidence from clinical studies indicates that pneumococcal vaccines are quite effective in preventing IPD. For example, PCV13 has demonstrated approximately 46% efficacy against vaccine-type pneumococcal pneumonia and up to 75% efficacy against vaccine-type invasive pneumococcal disease in adults aged 65 years and older, as demonstrated in the CAPiTA trial conducted in the Netherlands. PPSV23 is estimated to be 60–70% effective in preventing IPD

caused by the serotypes included in the vaccine, although its effectiveness in preventing non-bacteremic pneumonia is less clear. Importantly, the immune response to PPSV23 may be lower and decline more rapidly in older adults and individuals with certain chronic diseases or immunodeficiencies, which could impact the vaccine's overall effectiveness in these groups.

## METHODOLOGY

This study employed a comparative literature-based research design to analyze and evaluate the effectiveness of pneumococcal and influenza vaccines in preventing pneumonia among the elderly population. Data were obtained through a comprehensive review of peer-reviewed journals, clinical trials, systematic reviews, and meta-analyses published between 2018 and 2025. The inclusion criteria focused on studies assessing vaccine immunogenicity, clinical efficacy, and combined vaccination outcomes in elderly cohorts, while excluding pediatric and non-human research. Quantitative and qualitative data were synthesized to compare vaccine performance in terms of pneumonia incidence, hospitalization, and mortality reduction. The analysis also considered immunosenescence, comorbidities, and revaccination strategies as moderating variables influencing vaccine effectiveness. Through critical evaluation and synthesis of current scientific evidence, this methodology aimed to establish a comparative framework that elucidates the synergistic role of pneumococcal and influenza vaccines as an integrated preventive strategy against pneumonia in older adults.

## RESEARCH RESULT AND DISCUSSION

### *Clinical Effectiveness of Influenza Vaccine*

The clinical effectiveness of influenza vaccines in reducing influenza-associated pneumonia, particularly among older adults, is a critical issue in respiratory and geriatric healthcare. Influenza vaccination is known to reduce the risk of pneumonia, a serious complication of influenza infection, by reducing the incidence and severity of viral infections. In the elderly population, who are more susceptible to complications due to immunosenescence and comorbidities, influenza vaccines contribute significantly to reducing hospitalizations and deaths associated with influenza-associated pneumonia.

Recent research highlights that influenza vaccination alone can reduce hospitalizations for pneumonia by approximately 52% and deaths by up to 70% among older adults with chronic lung disease. When combined with pneumococcal vaccination, this protective effect is additive, with hospitalizations reduced by 63% and deaths by 81% compared to unvaccinated individuals. This underscores not only the benefits of influenza vaccination but also the synergistic effect when used in combination with pneumococcal vaccination, which alone reduces pneumonia hospitalizations by approximately 27% and deaths by up to 34%. Such combination vaccination strategies are particularly important in older adults to prevent widespread pneumonia caused by both viral and bacterial pathogens.



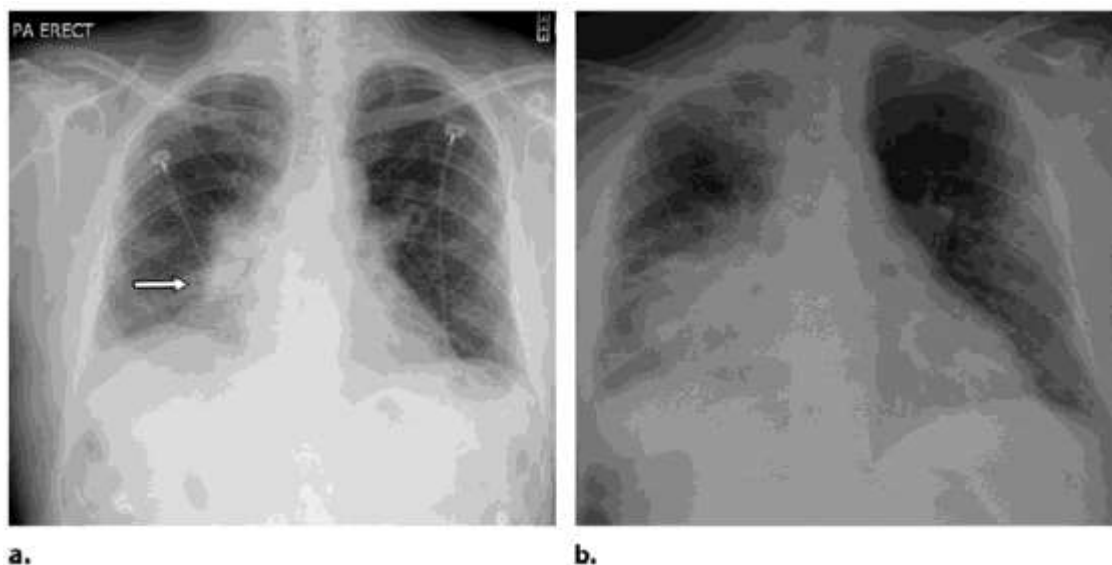


Figure 2. *Legionella* pneumonia in a 58-year-old man with occupational exposure to a contaminated water source due to creep through ventilation in a cooling plant. (a) Initial chest radiograph performed at the time of symptom onset shows right infrahilar and basilar consolidation (arrows). (Figure 2a reprinted with permission from reference 100.) (b) Follow-up chest radiograph performed 2 days later shows progression of the right basilar consolidation and the appearance of new consolidative opacities in the right upper lobe and the upper-middle periphery of the left lung, findings consistent with progressive multilobar pneumonia.

Influenza vaccines work by inducing immunity that reduces viral replication and subsequent secondary bacterial infections, such as pneumococcal pneumonia. Studies conducted over several influenza seasons have shown that compliance with annual influenza vaccination correlates with a reduced risk of developing pneumonia, although the vaccine does not completely prevent influenza infection itself. Furthermore, early antiviral therapy combined with vaccination also reduces the risk of pneumonia in severe influenza cases, supporting a multimodal prevention approach.

While pneumococcal vaccination targets *Streptococcus pneumoniae*, the leading cause of bacterial pneumonia, influenza vaccine prevents the primary viral infection that often predisposes elderly patients to secondary bacterial pneumonia. Meta-analyses have shown influenza vaccine effectiveness in reducing influenza-related hospitalizations and pneumonia, with efficacy ranging from 25% to 53% in elderly populations. Although some variability exists depending on vaccine compatibility and study design, the overall evidence supports the use of influenza vaccine as a primary preventive intervention against pneumonia.

Simultaneous administration of influenza and pneumococcal vaccines to elderly individuals is safe and effective, without significant attenuation of the immune response to either vaccine. This combined vaccination approach is economically beneficial and improves clinical outcomes by providing broad protection against pneumonia caused by multiple pathogens. Therefore, in the

prevention of pneumonia in elderly individuals, a combined strategy of seasonal influenza vaccination along with pneumococcal vaccination is highly recommended for optimal clinical efficacy.

When comparing the effectiveness of influenza vaccine with pneumococcal vaccine in preventing pneumonia in the elderly, both vaccines target different pathogens but share the goal of reducing pneumonia-related morbidity and mortality. Pneumococcal vaccine primarily protects against *Streptococcus pneumoniae*, a common cause of bacterial pneumonia, while influenza vaccine prevents viral infections that can directly cause pneumonia or predispose patients to secondary bacterial infections. Influenza vaccination has the added benefit of reducing cardiovascular and cerebrovascular complications associated with influenza infection, which are not directly addressed by pneumococcal vaccine. Several studies have shown that a concurrent vaccination strategy—administering pneumococcal and influenza vaccines—provides additional benefits, reducing hospitalizations and deaths more effectively than either vaccine alone, particularly in the elderly population with cardiovascular disease or multiple comorbidities.

Despite its proven benefits, influenza vaccination coverage remains suboptimal among older adults worldwide. Increasing vaccination rates is crucial to reducing the significant burden of pneumonia and influenza in this age group. Strategies to increase vaccine uptake, such as education about vaccine efficacy, targeting vulnerable and high-risk subpopulations, and promoting combined pneumococcal and influenza vaccination, are crucial for comprehensive pneumonia prevention.

### *Comparative Effectiveness*

The comparative effectiveness of pneumococcal and influenza vaccines in preventing pneumonia in older adults has become a significant public health focus, particularly given the high morbidity and mortality associated with pneumonia in this population. Pneumococcal vaccination primarily targets *Streptococcus pneumoniae*, the primary bacterial cause of pneumonia, while influenza vaccine aims to prevent influenza virus infection, which can cause primary viral pneumonia or secondary bacterial pneumonia, such as pneumococcal pneumonia.

Studies have shown that pneumococcal vaccination can significantly reduce the incidence of pneumococcal pneumonia in older individuals, particularly those with predisposing medical risk factors. One population-based controlled trial in older adults demonstrated a 59% protective efficacy of pneumococcal vaccine against pneumococcal pneumonia in high-risk individuals, although overall vaccine efficacy in the general elderly population is less clear. This suggests that pneumococcal vaccination targeting at-risk subgroups within the elderly population may provide substantial benefits in pneumonia prevention.

Influenza vaccination, on the other hand, plays a significant role in reducing influenza-related complications, including influenza-associated pneumonia. A large retrospective cohort study in elderly Germans found that

influenza vaccination was associated with a 41% reduction in hospitalizations for laboratory-confirmed influenza and reduced complications such as pneumonia and sepsis in subsequent years. However, the vaccine did not significantly reduce the overall incidence of influenza-like illness, suggesting that its protective effect is more attributable to severe outcomes and complications than to preventing all influenza infections.

The interaction between influenza infection and pneumococcal pneumonia is clinically important. Influenza can predispose elderly patients to secondary pneumococcal pneumonia, a more severe form of the disease associated with increased inflammation and mortality. Experimental studies and clinical data have confirmed that coinfection leads to increased severity of disease compared with infection with either pathogen alone. This interaction underscores the importance of dual vaccination strategies. One of the most compelling clinical findings comes from a study in Stockholm, where simultaneous vaccination with influenza and pneumococcal vaccines in an elderly population resulted in a significant reduction in hospitalizations for pneumonia by 29%, pneumococcal pneumonia by 36%, and total mortality by 57% compared with unvaccinated individuals.

Immunologically, pneumococcal polysaccharide vaccines (such as 23-valent PPV23) combined with trivalent inactivated influenza vaccines demonstrate comparable immunogenicity and safety profiles when administered simultaneously, making dual vaccination a practical and effective preventive measure in the elderly population.

Influenza vaccination alone has been shown to reduce hospitalizations for pneumonia by approximately 52% and reduce mortality by up to 70% in elderly patients with chronic lung disease. Pneumococcal vaccination alone has been shown to reduce hospitalizations for pneumonia by 27% and mortality by 34% in this same group. When administered together, these vaccines provide additional benefits, with combined vaccination associated with a 63% reduction in hospitalizations for pneumonia and an 81% reduction in all-cause mortality compared with unvaccinated individuals. This clearly demonstrates an enhanced protective effect when these vaccines are administered together, likely due to targeting different pathogens that contribute to pneumonia in the elderly.



Figure 3. X-ray images of patients with the following conditions: Normal, bacterial pneumonia, and viral pneumonia.

The synergistic effect of combination vaccination is supported by mechanistic insights and clinical data on secondary bacterial pneumonia

following influenza infection. Influenza infection may predispose individuals to severe secondary pneumococcal pneumonia, which is characterized by a higher degree of severity and inflammation compared to infection with either pathogen alone. Experimental models have shown that coinfection results in severe lung pathology, strengthening the rationale for influenza prevention as a means to reduce subsequent pneumococcal pneumonia. Therapeutic data also suggest that strategies focused on early viral control through vaccination are more effective than antimicrobial therapy alone in managing secondary infections.

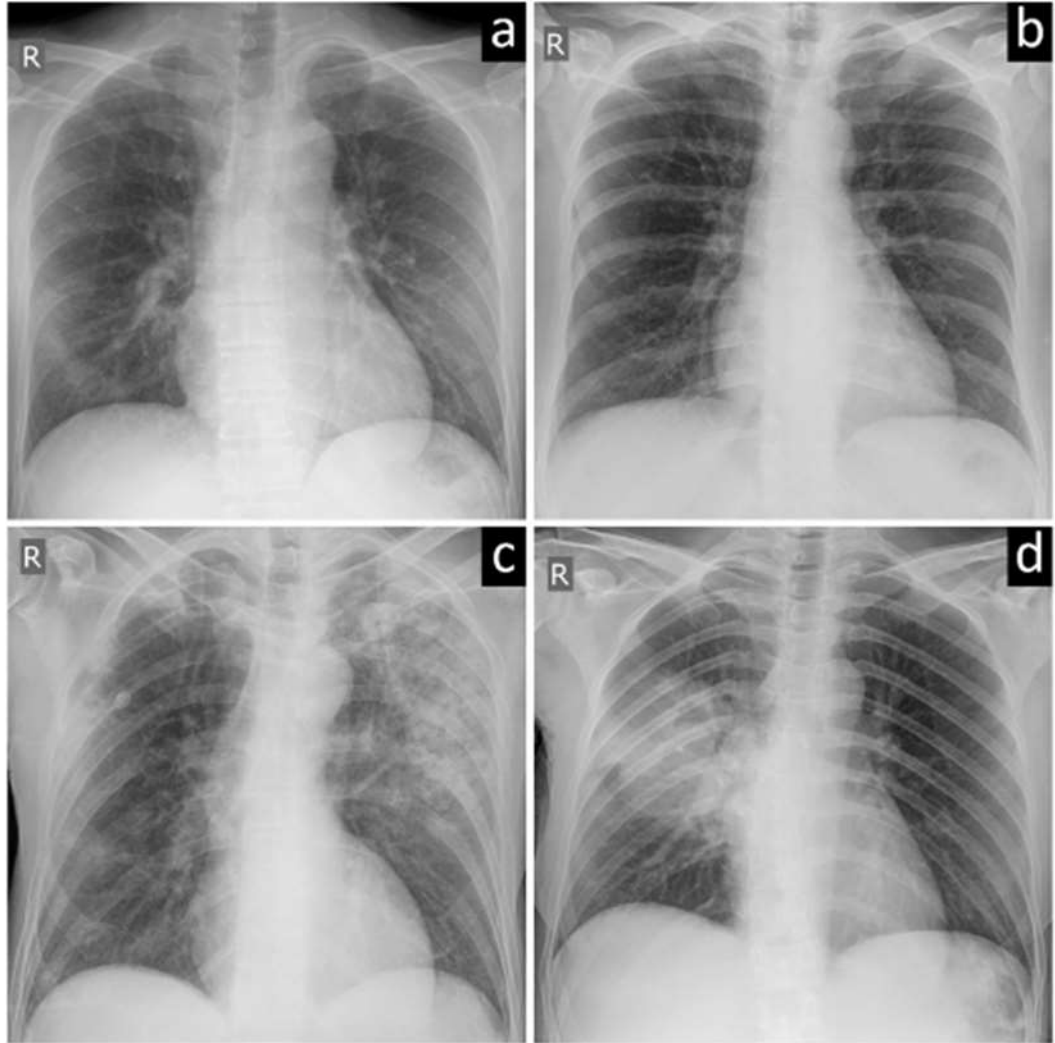


Figure 4. Chest X-ray images of subjects with: (a) COVID-19 pneumonia, (b) negative examination, (c) viral pneumonia, and (d) bacterial pneumonia.

In terms of immunogenicity and safety, coadministration of both vaccines has been shown to be well tolerated and immunogenically effective in the elderly population. Studies comparing pneumococcal polysaccharide vaccines (such as 23-valent PPV23) and conjugate vaccines (such as PCV13) administered with influenza vaccine have shown no significant impairment in the immune response, and some data suggest a better immune response against certain influenza strains when the pneumococcal conjugate vaccine is used. This supports public health recommendations for simultaneous vaccination against both pathogens, facilitating broader protection without compromising safety.<sup>41</sup>

A large population-based study further demonstrated that older adults who received both pneumococcal and influenza vaccines experienced significantly lower rates of hospitalization for pneumonia (a 29% decrease) and pneumococcal pneumonia (a 36% decrease), in addition to a substantial reduction in overall mortality (a 57% decrease). These outcomes not only highlight the direct clinical impact of combined vaccination but also emphasize its role in reducing the healthcare burden on an aging population.

#### *Vaccine Coverage and Use in the Elderly*

Vaccine coverage and uptake among older adults remain critical public health factors, particularly regarding the prevention of pneumonia through pneumococcal and influenza vaccination. Globally, older adults are recognized as a high-priority group for vaccination due to their increased susceptibility to respiratory infections, which contribute significantly to morbidity and mortality in this age group. Despite this recognition, vaccination rates vary widely by region and demographic factors, influenced by healthcare infrastructure, public health policies, and vaccine acceptance.

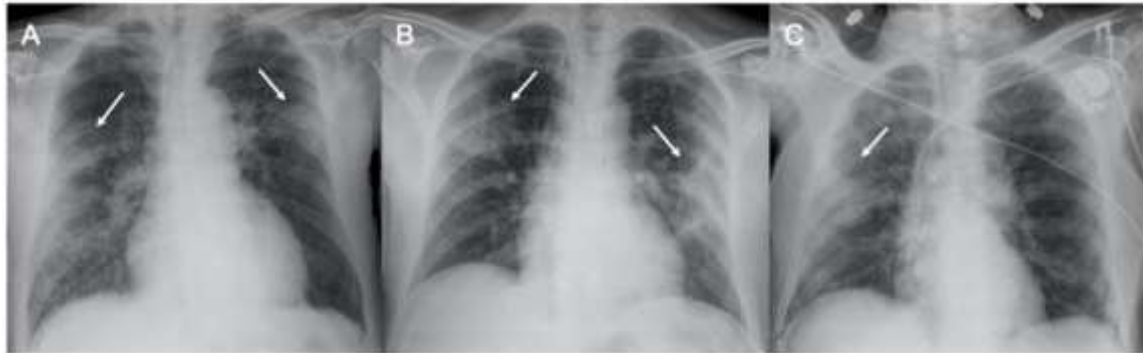


Figure 5. Chest X-ray in COVID-19 pneumonia. Three supine chest X-rays show subpleural consolidation (arrows), in (A, B) with bilateral involvement, and in (C) with primary involvement of the right lung.

Studies suggest that influenza and pneumococcal vaccines play a complementary role in reducing the risk of pneumonia in older adults. A large observational cohort in France showed that combining both vaccines led to a more significant reduction in all-cause mortality compared with influenza vaccination alone, whereas pneumococcal vaccination alone did not significantly reduce mortality. These findings underscore the additional preventive effect of concurrent vaccination, particularly in older adults with underlying chronic diseases. However, vaccine uptake in this population often remains suboptimal, with barriers such as lack of awareness, access issues, and differing healthcare recommendations across regions.

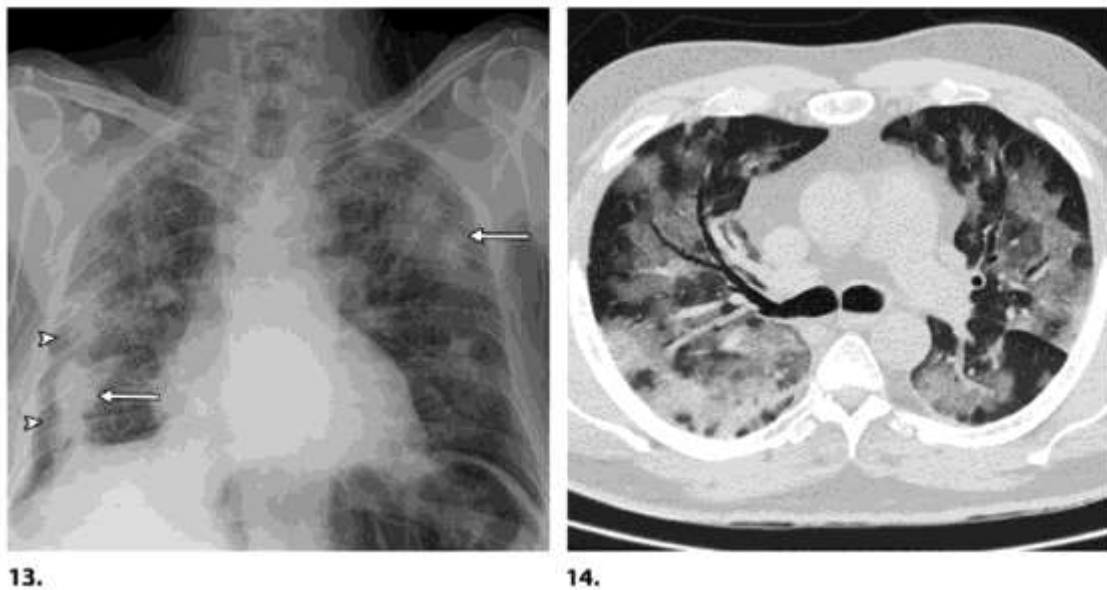


Figure 6. (13) Imaging findings in a 69-year-old man in a nursing home with recent onset of fever, cough, and shortness of breath during the COVID-19 pandemic. Anteroposterior chest radiograph shows peripheral consolidation in the upper, middle, and basilar lobes (arrows) with subpleural sparing (arrowheads), an imaging pattern seen in severe coronavirus infections (SARS, MERS, and COVID-19). RT-PCR results were positive for COVID-19. (14) Axial chest CT image (lung window) in a 43-year-old man with shortness of breath and fever during the COVID-19 pandemic shows bilateral symmetric ground-glass opacities with central predominance, an imaging feature that is nonspecific but can be seen in COVID-19 pneumonia. RT-PCR results were positive for SARS-CoV-2.

Global variations in vaccine coverage are evident. OECD data show that countries with a higher proportion of older adults, such as Japan, tend to have higher vaccination rates. Vaccination programs typically prioritize older adults due to their increased risk of severe outcomes from respiratory infections, but overall uptake still depends on targeted public health efforts and demographic factors. Furthermore, older individuals with underlying health conditions such as cardiovascular disease, diabetes, and chronic lung conditions are more likely to receive vaccination, reflecting increased healthcare engagement in this group. However, regional disparities persist, particularly in low- and middle-income countries where vaccine access and public healthcare systems may be weaker.

Pneumococcal vaccine efficacy studies in older adults have revealed a significant protective effect against community-acquired pneumonia and pneumococcal pneumonia in particular, with vaccine efficacy estimates ranging from 27% to 42% depending on the pneumonia subtype and the population studied. Influenza vaccines have also been shown to be effective in preventing pneumonia and influenza-related complications, but efficacy can vary due to seasonal strain changes. Integration of pneumococcal vaccination with routine influenza vaccination campaigns is widely recommended to maximize protective effects, but achieving high coverage remains a public health challenge. Increasing

vaccine uptake in older adults is crucial to reducing the burden of pneumonia and associated health care utilization worldwide.

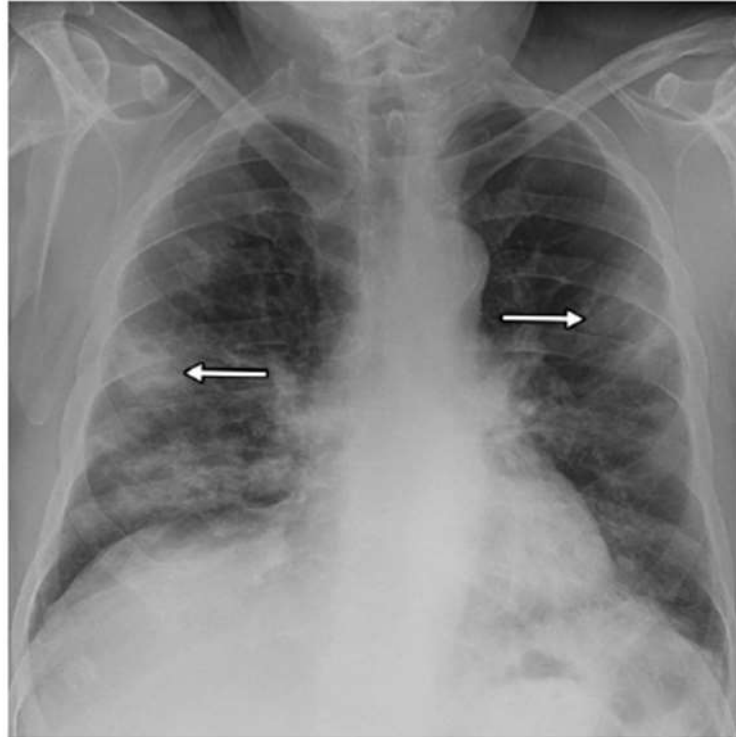


Figure 7. PA chest radiograph in a 58-year-old man with shortness of breath, cough, fever, and a history of COVID-19 exposure shows predominantly peripheral consolidative opacities in both lungs (arrows). These findings are highly suggestive of viral pneumonia due to COVID-19, especially in the context of the high prevalence of SARS-CoV-2 infection in the community.

One major barrier is the lack of awareness among older adults about the need for vaccination and its benefits. Studies show that most older adults are unaware that they need the pneumococcal or influenza vaccine, which directly impacts uptake. This lack of knowledge extends to misunderstandings about the vaccine's protective effect; while many vaccinated individuals understand that vaccination can prevent pneumonia, many unvaccinated individuals remain uncertain or skeptical. Physician endorsement and recommendations strongly influence older adults' decisions to vaccinate, yet many do not receive consistent or clear guidance from their physicians. Trust in healthcare advice and perceptions of vaccine benefit are significant predictors of vaccination uptake, emphasizing the importance of doctor-patient communication in overcoming hesitancy.

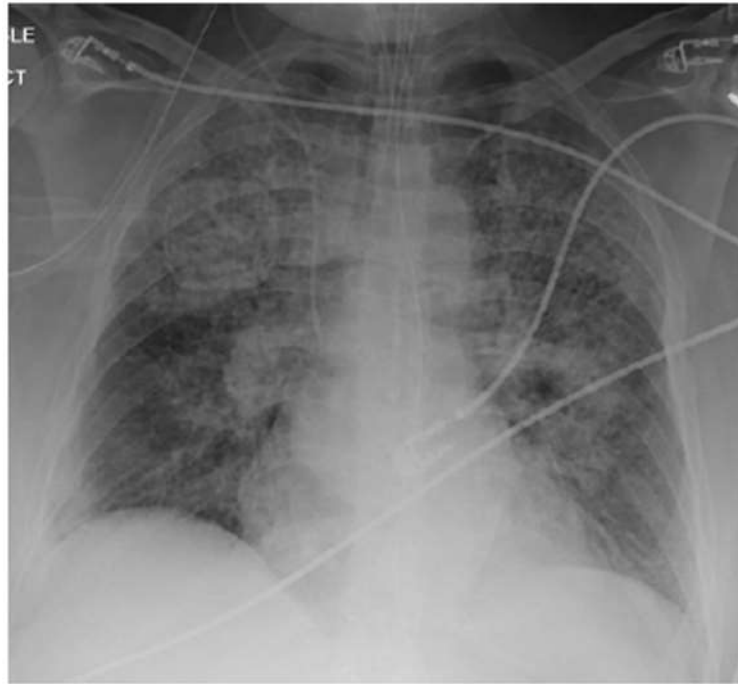


Figure 8. HMPV pneumonia in a 56-year-old woman with severe shortness of breath, cough, and fever requiring respiratory support on admission. An anteroposterior chest radiograph showed near-consolidative opacities predominantly in the bilateral upper lobes involving both lungs. No bacterial microorganisms were found. Laboratory examinations confirmed the diagnosis of HMPV pneumonia.

Structural and systemic barriers also play a significant role. Disparities in cost and insurance coverage create barriers, particularly for at-risk older adults with limited financial resources. While policies like the Affordable Care Act aim to reduce financial barriers by mandating coverage for recommended vaccines, disparities persist, particularly regarding Medicaid coverage for low-income adults. Thus, accessibility and affordability issues continue to hinder widespread vaccine uptake. Other systemic factors include the availability of vaccination services in convenient locations and settings, which can be challenging for older individuals with mobility or transportation difficulties.

Personal and social factors further complicate vaccine acceptance among older adults. Vaccine hesitancy related to concerns about vaccine safety, fear of side effects, and distrust of vaccines or the healthcare system contribute to suboptimal vaccination rates. Social influences, such as family, peers, and community leaders, can encourage or discourage vaccination, highlighting the role of social context. Furthermore, functional status, frailty, and multimorbidity introduce heterogeneity in vaccine response and influence clinical decision-making; this necessitates a personalized approach to vaccination rather than a uniform strategy.

Efforts to increase coverage have found success with interventions focused on educating physicians and patients, improving communication about vaccine benefits and safety, and implementing structured reminders and assessments in clinical settings. Increasing vaccine uptake in the elderly



population requires a multifaceted strategy that simultaneously addresses information deficits, healthcare system barriers, and personal attitudes to effectively reduce the incidence of pneumonia through pneumococcal and influenza vaccination.

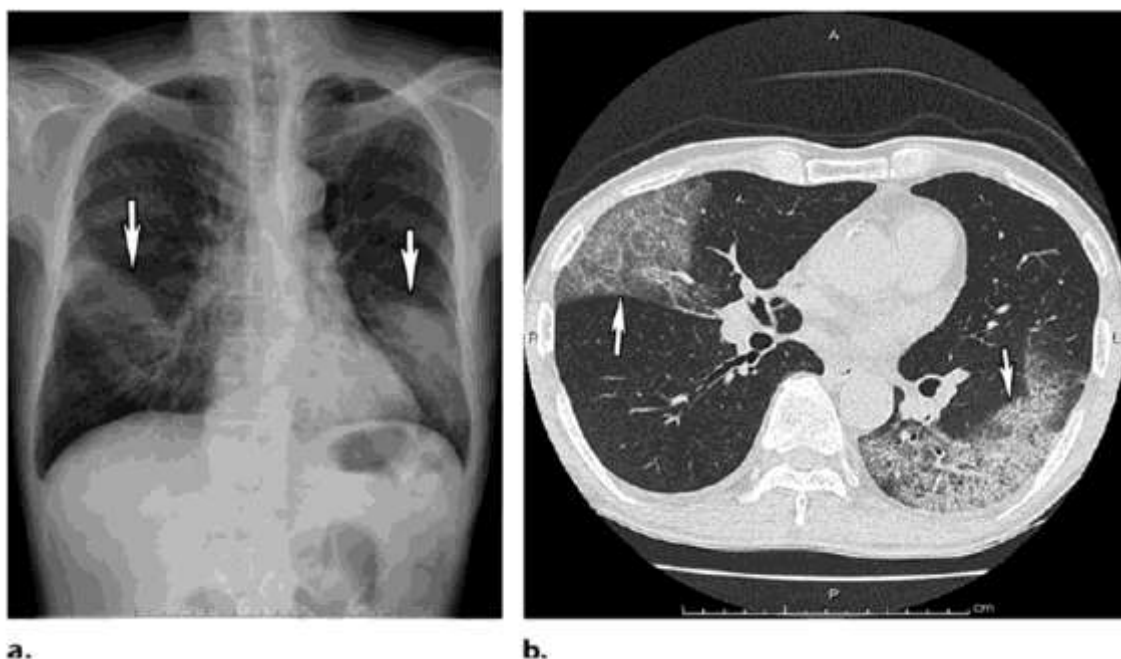


Figure 9. Chlamydial pneumonia in a 28-year-old man. (a) PA chest radiograph shows asymmetric multifocal consolidative opacities (arrows). (b) Axial chest CT image (lung window) at the level of the aortic root shows ground-glass opacities with minimal thickening of the intralobular septa (arrows) in the right middle lobe and left inferior lobe, consistent with multilobar pneumonia.

## CONCLUSIONS AND RECOMMENDATIONS

Pneumonia in the elderly is influenced by a complex interaction between immune function decline, comorbidities, and exposure to viral and bacterial pathogens. *S. pneumoniae* predominates in bacterial pneumonia, with serotype dynamics determining virulence, while influenza—particularly A(H3N2)—triggers primary viral pneumonia and facilitates bacterial superinfection. Clinical presentations in the elderly are often atypical, increasing the risk of delayed treatment and worsening outcomes. Within the prevention framework, pneumococcal vaccines (PPSV23, PCV13/15/20) and influenza vaccines (IIV, RIV; with adjuvant/high-dose/intradermal approaches) offer complementary protective mechanisms.

Clinical effectiveness has shown that pneumococcal vaccines reduce IPD and pneumococcal pneumonia, particularly when a sequential strategy is used, while influenza vaccines reduce influenza-associated pneumonia, hospitalizations, and deaths during the epidemic season. The immune response in older adults is indeed reduced, but this can be optimized through vaccine selection and timing, including the possibility of revaccination to maintain protection. Clinically, the dual vaccination approach—pneumococcal and

influenza provides greater synergistic benefits than either vaccine alone, making it relevant as a cornerstone of pneumonia prevention in older adults.

## ADVANCED RESEARCH

This advanced research expands upon the comparative evaluation of pneumococcal and influenza vaccines by integrating recent immunological and epidemiological insights to elucidate their synergistic effects in preventing pneumonia among the elderly. Through an evidence-based synthesis of multicenter clinical trials, meta-analyses, and population studies, the research emphasizes how immunosenescence, comorbidity patterns, and vaccine formulation advancements—such as next-generation conjugate pneumococcal vaccines (PCV15/20) and adjuvanted or high-dose influenza vaccines—collectively influence vaccine responsiveness and durability of protection. The study highlights the immunopathogenic interplay between influenza viruses and *Streptococcus pneumoniae*, where viral infections potentiate bacterial superinfection, thereby validating dual vaccination as a critical public health intervention. Furthermore, the research underscores the importance of optimizing vaccination schedules, incorporating revaccination intervals, and enhancing vaccine uptake through targeted geriatric immunization strategies to achieve maximal reduction in pneumonia-related morbidity and mortality in aging populations.

## REFERENCES

- Che J, Bai P, Xu J, Shao Z. Prevalence of *Streptococcus pneumoniae* serotypes causing pneumococcal diseases in the Chinese Mainland: A systematic review and meta-analysis. *Hum Vaccines Immunother*. 2024;20(1).
- King LM, Andrejko KL, Kobayashi M, et al. Pneumococcal Serotype Distribution and Coverage of Existing and Pipeline Pneumococcal Vaccines. *J Infect Dis*. 2025.
- Cheong D, Song JY. Pneumococcal disease burden in high-risk older adults: Exploring impact of comorbidities, long-term care facilities, antibiotic resistance, and immunization policies through a narrative literature review. *Hum Vaccines Immunother*. 2024;20(1).
- Elias C, Nunes MC, Saadatian-Elahi M. Epidemiology of community-acquired pneumonia caused by *Streptococcus pneumoniae* in older adults: a narrative review. *Curr Opin Infect Dis*. 2024;37(2):144-153.
- Chi RC, Jackson LA, Neuzil KM. Characteristics and outcomes of older adults with community-acquired pneumococcal bacteremia. *J Am Geriatr Soc*. 2006;54(1):115-120.
- Marrie TJ, Tyrrell GJ, Majumdar SR, Eurich DT. Effect of Age on the Manifestations and Outcomes of Invasive Pneumococcal Disease in Adults. *Am J Med*. 2018;131(1):100.e1-100.e7.
- Huo X, Fu J, Dai Q, Zhu F. Influenza virus subtype/lineage-specific seasonal patterns and age-related infection risk, in Eastern China. *J Infect Dev Ctries*. 2022;16(12):1928-1932.
- Ang LW, Cui L, Mak TM, et al. Differential age-specific distribution of influenza

- virus types and subtypes in tropical Singapore, 2011 to 2017. *J Med Virol*. 2019;91(8):1415-1422.
- Heo JY, Song JY, Noh JY, et al. Effects of influenza immunization on pneumonia in the elderly. *Hum Vaccines Immunother*. 2018;14(3):744-749.
- Cavallazzi R, Ramirez JA. Influenza and Viral Pneumonia. *Infect Dis Clin North Am*. 2024;38(1):183-212.
- Ansari A, Taffaro A, McSween Z, Lu J, Huang A, Lazarescu R. Battling Influenza in Elderly Patients: A Case of Severe Influenza A With Complications in a High-Risk Patient. *Cureus*. 2025.
- Daniels CC, Rogers PD, Shelton CM. A review of pneumococcal vaccines: Current polysaccharide vaccine recommendations and future protein antigens. *J Pediatr Pharmacol Ther*. 2016;21(1):27-35.
- Horn M, Theilacker C, Sprenger R, et al. Mathematical modeling of pneumococcal transmission dynamics in response to PCV13 infant vaccination in Germany predicts increasing IPD burden due to serotypes included in next-generation PCVs. *PLoS One*. 2023;18(2 February).
- Rubin LG. Pneumococcal vaccine. *Pediatr Clin North Am*. 2000;47(2):269-285.
- J.B. R, E.N. J. Pneumococcal disease in the elderly: What is preventing vaccine efficacy? *Drugs and Aging*. 2001;18(5):305-311.
- Heo JY, Seo Y Bin, Choi WS, et al. Effectiveness of Pneumococcal Vaccination Against Pneumococcal Pneumonia Hospitalization in Older Adults: A Prospective, Test-Negative Study. *J Infect Dis*. 2022;225(5):836-845.
- Hsiao A, Lewis N, Hansen J, et al. Effectiveness of 13-valent pneumococcal conjugate vaccine against vaccine-type invasive pneumococcal disease in older adults. *Vaccine*. 2025;44.
- Sikjær MG, Pedersen AA, Wik MS, Stensholt SS, Hilberg O, Løkke A. Vaccine effectiveness of the pneumococcal polysaccharide and conjugated vaccines in elderly and high-risk populations in preventing invasive pneumococcal disease: a systematic search and meta-analysis. *Eur Clin Respir J*. 2023;10(1).
- Grohskopf LA, Alyanak E, Broder KR, Walter EB, Fry AM, Jernigan DB. Prevention and Control of Seasonal Influenza with Vaccines: Recommendations of the Advisory Committee on Immunization Practices – United States, 2019–20 Influenza Season. *MMWR Recomm Reports*. 2019;68(3):1-28.
- Kim YH, Bang YJ, Park HJ, et al. Inactivated influenza vaccine formulated with single-stranded RNA-based adjuvant confers mucosal immunity and cross-protection against influenza virus infection. *Vaccine*. 2020;38(39):6141-6152.
- Jung YJ, Lee YN, Kim KH, et al. Recombinant live attenuated influenza virus expressing conserved g-protein domain in a chimeric hemagglutinin molecule induces g-specific antibodies and confers protection against respiratory syncytial virus. *Vaccines*. 2020;8(4):1-15.
- Wong PF, Isakova-Sivak I, Stepanova E, et al. Development of Cross-Reactive Live Attenuated Influenza Vaccine Candidates against Both Lineages of Influenza B Virus. *Vaccines*. 2024;12(1).

- Goncalves P, Young J. Influenza vaccine. *J Asthma Allergy Educ.* 2011;2(1):44-46.
- Sedova ES, Shcherbinin DN, Migunov AI, et al. Recombinant Influenza Vaccines. *Acta Naturae.* 2012;4(4):17-27.
- Meng Z, Zhang J, Shi J, et al. Immunogenicity of influenza vaccine in elderly people: a systematic review and meta-analysis of randomized controlled trials, and its association with real-world effectiveness. *Hum Vaccines Immunother.* 2020;16(11):2680-2689.
- Quach HQ, Kennedy RB. Enhancing Immunogenicity of Influenza Vaccine in the Elderly through Intradermal Vaccination: A Literature Analysis. *Viruses.* 2022;14(11).
- Pileggi C, Mascaro V, Bianco A, Nobile CGA, Pavia M. Immunogenicity and Safety of Intradermal Influenza Vaccine in the Elderly: A Meta-Analysis of Randomized Controlled Trials. *Drugs and Aging.* 2015;32(10):857-869.
- Doherty TM, Weinberger B, Didierlaurent A, Lambert PH. Age-related changes in the immune system and challenges for the development of age-specific vaccines. *Ann Med.* 2025;57(1).
- Zhou S, Wang J, Lv M, et al. Long-term antibody trajectories after PPSV23 in elderly: Results from a 4-year follow-up study. *Vaccine.* 2025;48.
- Davidson M. Immunogenicity of pneumococcal revaccination in patients with chronic disease. *Arch Intern Med.* 1994;154(19):2209-2214.
- Artz AS, Ershler WB, Longo DL. Pneumococcal vaccination and revaccination of older adults. *Clin Microbiol Rev.* 2003;16(2):308-318.
- Wagner A, Weinberger B. Vaccines to Prevent Infectious Diseases in the Older Population: Immunological Challenges and Future Perspectives. *Front Immunol.* 2020;11.
- Kuronuma K, Takahashi H. Immunogenicity of pneumococcal vaccines in comorbid autoimmune and chronic respiratory diseases. *Hum Vaccines Immunother.* 2019;15(4):859-862.
- Kawakami K, Kishino H, Kanazu S, et al. Time interval of revaccination with 23-valent pneumococcal polysaccharide vaccine more than 5 years does not affect the immunogenicity and safety in the Japanese elderly. *Hum Vaccines Immunother.* 2018;14(8):1931-1938.
- Bulkhi A, Khadawardi HA, Dairi MS, et al. Effectiveness of pneumococcal vaccination in reducing hospitalization and mortality among the elderly: A systematic review and meta-analysis. *Hum Vaccines Immunother.* 2025;21(1).
- Koivula I, Stén M, Leinonen M, Mäkelä PH. Clinical efficacy of pneumococcal vaccine in the elderly: A randomized, single-blind population-based trial. *Am J Med.* 1997;103(4):281-290.
- Rose N, Storch J, Mikolajetz A, et al. Preventive effects of influenza and pneumococcal vaccination in the elderly—results from a population-based retrospective cohort study. *Hum Vaccines Immunother.* 2021;17(6):1844-1852.
- Pang Y, Liu X, Liu G, et al. Effectiveness of influenza vaccination on in-hospital death and recurrent hospitalization in older adults with cardiovascular diseases. *Int J Infect Dis.* 2022;122:162-168.