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Pneumococcal Community-Acquired Pneumonia (CAP) in Adults: Epidemiology, Pathophysiology, and Updated Vaccination Guidance

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A B S T R A C T

On October 23, 2024, the Centers for Disease Control and Prevention recommended a major change in its guidelines for pneumococcal vaccination in adults, lowering the recommended age of vaccination from 65 to 50 years. The rationale is based on the opportunity to protect adults from pneumococcal disease when risk of infection substantially increases. This review discusses recent epidemiologic and clinical data regarding pneumococcal disease in adults (focusing on *Streptococcus pneumoniae* community-acquired pneumonia), the current Centers for Disease Control and Prevention vaccination recommendations in adults, adverse events/contraindications, and the role of nurse practitioners and others in advocating for pneumococcal vaccination in adults to promote public health.

Microbiology of *Streptococcus pneumoniae*

Comprehension of the microbiologic properties of *Streptococcus pneumoniae* is a necessity for nurse practitioners (NPs) and other clinicians because this knowledge is vital to understanding the pathophysiology caused by the bacteria and mechanisms of action of related vaccines. *S pneumoniae* are Gram-positive, lancet-shaped, encapsulated bacteria that exhibit α-hemolysis under aerobic conditions and β-hemolysis under anaerobic conditions.[1] They are human-adapted pathogens that colonize the nasopharynx in ~20% to 30% of healthy adults. The organism evades immune clearance by recruiting human factor H, a complement regulatory protein, and by producing a polysaccharide capsule that inhibits phagocytosis.[2]

The pneumococcal genome is ~2 megabase-pairs with ~70% constituting a conserved core genome and the remainder forming an accessory genome that varies among strains. Genetically related groups, or clonal complexes, have spread globally, and some display reduced susceptibility to penicillin. Whole-genome sequencing reveals high variability in certain surface proteins, such as pneumococcal surface protein A, which influences virulence, immune evasion, and potential as vaccine targets.[1]

The polysaccharide capsule is the key virulence factor and the primary target for current vaccines.[2] More than 100 distinct capsular serotypes have been identified, each differing in structure, colonization capacity, and invasive potential. Certain serotypes (eg, 1 and 7F) are highly invasive but uncommon in healthy carriers, whereas others (eg, 19F and 23F) are frequently found in asymptomatic colonization.[1] Serotype distribution is influenced by strain competition, with some gaining an advantage in colonization success.

Vaccination, particularly in children, has altered pneumococcal epidemiology by reducing vaccine-type strains but increasing the prevalence of nonvaccine serotypes and nontypeable strains. The diversity of the accessory genome supports rapid adaptation to interventions, underscoring the need for surveillance to detect serotype replacement, antimicrobial resistance, and genomic changes that may impact future vaccine strategies.[1]

Pathophysiology of *S. pneumoniae* Associated Community-Acquired Pneumonia

Pneumonia is the leading infectious cause of hospitalization and death among adults in the United States (US) and occurs when a pathogen infects the lower respiratory tract, triggering an infection and inflammatory response that results in respiratory (eg, cough and dyspnea) and systemic symptoms (eg, fever).[2] Severe cases can lead to sepsis, acute respiratory distress syndrome, and death.[3]

Community-acquired pneumonia (CAP) refers to pneumonia contracted outside of hospital settings or in patients not hospitalized within the 48 hours before diagnosis. Since 2019, CAP also includes cases previously classified as health care–associated pneumonia occurring after recent hospitalization or in nursing facilities. CAP excludes hospital-acquired pneumonia developing after more than 48 hours of hospitalization and ventilator-associated pneumonia occurring during mechanical ventilation.[3] The severity of pneumococcal CAP is due to significant

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inflammatory response induced by the activation of complement pathways and cytokine release by cell-wall proteins, autolysin, the capsular polysaccharides, and DNA released by bacterial end-products.[2]

Epidemiology of *S. pneumoniae* Associated CAP

Pneumococci are significant contributors to global mortality and morbidity from a wide range of infections ranging from relatively mild respiratory tract issues (eg, otitis and sinusitis) to severe invasive pneumococcal diseases (eg, meningitis and pneumonia). Although CAP is often managed in outpatient settings, ~10% of patients require hospitalization, leading to ~1.4 million emergency department visits, 740,000 hospitalizations, 41,000 deaths, and $7.7 billion in in-patient costs annually in the US.[3] The hospitalization rate for CAP is ~24.8 per 10,000 person-years for all adults, with a higher rate of 63.0 per 10,000 person-years among those >65 years old, costing an estimated $9 billion annually.[2] The 30-day mortality rate after hospitalization for CAP ranges from 2.8% for adults <60 years to 26.8% for those ≥60 years with comorbid conditions.[3]

In hospitalized and ambulatory adult patients with radiologically confirmed pneumonia, the strongest risk factor for CAP is older age (≥65 years). Other significant risk factors include impaired mucociliary clearance (eg, smoking), underlying lung diseases (eg, asthma and chronic obstructive pulmonary disease), poor oral health, poor nutritional status, functional impairment, environmental exposures (eg, metals, dust, fumes), and immunosuppressive therapy.[3]

In 2016, pneumococcal infections were estimated to cause 1.18 million deaths around the world, with the highest mortality rates in younger children. Epidemiologic data have supported a seasonal cyclic characteristic of the disease, with incidence rates being higher in the winter and early spring months.[2] Mortality from *S. pneumoniae*—associated CAP in adults <65 years (18%) and ≥65 years (23%) is considerable.[4] The World Health Organization has identified pneumococci as a priority pathogen due to increasing antimicrobial resistance, necessitating new antibiotic development.[1]

The overall rate of confirmed *S. pneumoniae* for adults ≥65 years is 36.4 per 100,000, with infection occurring through respiratory droplets inhaled from nasopharyngeal colonies, causing infection of the lower airways.[2] Recent data suggest 15% of cases of pneumonia in the US are related to *S. pneumoniae* infection, with a 5% mortality rate across all age-groups.[2] However, older adults (≥65 years old) may have higher rates of death associated with infection complications.[5] This article focuses on pneumonia related to infections from *S. pneumoniae;* however, Table 1 lists other pathogens which are causative for pneumonia.[6]

Signs, Symptoms, and Diagnosis of *S. pneumoniae* Associated CAP

Pneumonia is diagnosed through a combination of clinical signs and symptoms, such as fever, abnormal leukocyte counts, new or increased cough, and dyspnea, along with radiographic findings such as air space density.[3] Among hospitalized patients with CAP, common symptoms include new or worsening cough, sputum production, and dyspnea.[2,3] However, no single sign or symptom is highly sensitive or specific for diagnosing CAP, and in older adults, generalized weakness, alterations in mentation, and a general sense of malaise may be initial signs.[2] A meta-analysis found the absence of abnormal vital signs can help rule out CAP, whereas specific findings such as egophony and dullness to percussion, although rare, have high specificity.[7] Despite this, many patients with CAP do not exhibit auscultatory findings, highlighting the need for radiographic evaluation to confirm the diagnosis.[3]

Table 1
Nonpneumococcal Pathogens That are Causative Agents for Pneumonia[6]

Bacterial Infections
• *Mycoplasma pneumoniae*
• *Chlamydia pneumoniae*
• *Haemophilus influenza*
• *Legionella*
• *Bordetella pertussis* (whooping cough)
• *Chlamydia psittaci* (psittacosis)
Fungal Infections
Viral Infections
• Coronavirus disease 2019
• Human metapneumovirus
• Human parainfluenza virus
• Influenza
• Respiratory syncytial virus
• Rhinovirus
• Advenovirus
• Varicella
• Measles

Chest radiography is typically the initial diagnostic test, but its sensitivity and specificity vary.[2] For the best-quality images, a chest radiograph should be taken with both posterior-anterior and lateral projections. If chest radiography does not show evidence of CAP but pneumonia is suspected, chest computed tomography is recommended because it can identify opacities not visible on radiographs and evaluate for alternative diagnoses such as pulmonary embolism. Common radiographic findings in CAP include air space opacities or infiltrates, and less common findings include pleural effusion, cavitation, and mass-like appearances. The variability in diagnostic accuracy has led to substantial overdiagnosis of CAP, with many patients treated for CAP not meeting diagnostic criteria (cf, Ebell et al.[7]). Therefore, patients with CAP symptoms and radiographic results should undergo further evaluation to rule out other causes of their symptoms.

Pneumococcal Vaccination in Adults

Decades ago, polysaccharide-based vaccines targeting the pneumococcal capsule were introduced, starting with a 14-valent vaccine and later expanding to a 23-valent pneumococcal polysaccharide vaccine (PPSV23) in 1983, which is still in use for adults. However, these vaccines were not sufficiently immunogenic in high-risk pediatric groups and did not induce a T cell–dependent response.[1,8,9] Although efficacy data are conflicting regarding PPSV23, research supported up to a 64% efficacy rate with the vaccine.[10]

Pneumococcal conjugate vaccines (PCVs), which link the capsular polysaccharide to a protein, have been developed to target up to 20 pneumococcal serotypes (PCV20). The introduction of PCVs, such as PCV7 in 2000 and, later, PCV10 and PCV13, has significantly reduced invasive pneumococcal disease in vaccinated children. However, an increase in nonvaccine serotypes (NVTs) has been observed in unvaccinated populations, such as older adults.[1] PCVs in use in the US include PCV15 (Vaxneuvance, Merck), PCV20 (Prevnar 20, Pfizer), and PCV21 (Capvaxine, Merck).[10-12] A noted advantage of the PCV is longer-lasting activity. However, because PCV15, PCV20, and PCV21 are considered newer vaccines, their long-term efficacy data are evolving. The PCV13 vaccine has been shown in prelicensure studies to protect adults ≥65 years from pneumococcal pneumonia by 38% to 71% and PCV13-type invasive pneumococcal disease by 47% to 75%.[13,14] PCV21 contains 8 new pneumococcal

serotypes not included in PCV15, PCV20, or PPSV23, expanding its potential coverage. However, it does not include certain serotypes (eg, serotype 4) included in other pneumococcal vaccines.

Recent advancements include the development of 15-valent (PCV15) and 20-valent (PCV20) vaccines, with ongoing trials for vaccines targeting 24 serotypes. All PCVs are administered as an intramuscular injection; however, the PPSV23 vaccine can be administered either through intramuscular or subcutaneous injection.[15] The preferred intramuscular administration site in adults is the nondominant deltoid.[16]

Current Recommendations for Pneumococcal Vaccination in Adults

On October 23, 2024, the Director of the Centers for Disease Control and Prevention (CDC) endorsed the CDC Advisory Committee on Immunization Practices recommendation for lowering the age of pneumococcal vaccination from 65 to 50.[17,18] The rationale for the change was that lowering the age "gives more adults the opportunity to protect themselves from pneumococcal disease at the age when risk of infection substantially increases."[17]

Epidemiologic data strongly suggest this recommendation is evidence-based. A retrospective cohort study found a significantly higher rate ratio of *S. pneumoniae*—associated invasive pneumococcal disease and pneumonia in adults ≥50 years compared with those 18 to 49 years old.[19] Vaccination is also recommended for adults ages 19 to 64 with high-risk medical conditions.[16] Table 2 summarizes the preexisting medical conditions included in this recommendation.[16] Data suggest these individuals are at much greater risk of infection and death.[19]

The pneumococcal vaccine schedule for adults >50 years old and those aged 19 to 64 with high-risk medical conditions is complex and highly dependent on prior vaccination history. Therefore, when prescribing or making clinical decisions regarding correct selection and scheduling of pneumococcal vaccines, the CDC recommends NPs, nurses, and other clinicians use the PneumoRecs VaxAdvisor App for Vaccine,[20] which is available as a downloadable app for iOS and Android or as a website (https://www2a.cdc.gov/vaccines/m/pneumo/pneumo.html). This app provides pneumococcal vaccination guidance for providers based on a patient's age, potential specific high-risk conditions, and pneumococcal vaccination history.[20] In turn, this app can help "eliminate the challenge of interpreting and synthesizing multiple pneumococcal vaccination recommendation statements" and does not collect patient's personal information.[20]

For most adults who have never received a PCV, one dose of a modern conjugate vaccine (eg, PCV20 or PCV21) is usually enough to complete pneumococcal conjugate vaccination because these vaccines cover a broad set of serotypes and do not require a follow-up polysaccharide dose.[16] This one-dose approach is the current CDC Advisory Committee on Immunization Practices default for PCV-naïve adults aged ≥50 years and for many adults with risk conditions; it also applies in many situations where someone received a prior PPSV23 only (PCV given ≥1 year after PPSV23).[16] If PCV15 is chosen instead of PCV20/21, it should be followed by one dose of PPSV23 (typically ≥1 year later for most adults) because PCV15 does not include as many serotypes as PCV20/21.[16]

For individuals who previously received earlier conjugates (eg, PCV13), current guidance recommends giving a single dose of PCV20 or PCV21 at the recommended interval to complete conjugate protection rather than repeating multiple conjugate doses.[16] Multiple-product schedules are used only when necessary to broaden serotype coverage (eg, PCV15 followed by PPSV23) or to complete an older vaccine series started before newer PCVs were available.[16]

Adverse Events and Contraindications of Pneumococcal Vaccines

The most common adverse events and contraindications associated with pneumococcal vaccination (see Table 3)[16,21,22] vary depending mostly on the type of vaccine administered, with some overlap between the vaccines. The CDC suggests through its clinical data assessment that the most common adverse events are self-limiting and subside ≤48 hours.[21,23-27] NPs, nurses, and other clinicians are encouraged to report all adverse events associated with any vaccination to the Vaccine Adverse Event Reporting System (https://vaers.hhs.gov) and to research potential adverse events and contraindications of the pneumococcal vaccines by

Table 2
High-Risk Medical Conditions in Adults Necessitating Pneumococcal Vaccination[16]

- Alcoholism
- Cerebrospinal fluid leak
- Chronic liver disease
- Chronic lung disease, including chronic obstructive pulmonary disease and asthma
- Chronic heart disease, including congestive heart failure and cardiomyopathies
- Cigarette smoking
- Cochlear implant
- Diabetes mellitus
- Congenital or acquired asplenia[a]
- Congenital or acquired immunodeficiency[a]
- Chronic renal failure[a]
- Malignancy[a]
- Hodgkin disease[a]
- HIV infection[a]
- Iatrogenic immunosuppression from radiation therapy and chronic systemic corticosteroids[a]
- Lymphoma[a]
- Leukemia[a]
- Multiple myeloma[a]
- Nephrotic syndrome[a]
- Solid organ transplant[a]
- Sickle cell disease or hemoglobinopathies[a]

[a] Indicates immunocompromising conditions.

Table 3
Common Adverse Events and Contraindications With Pneumococcal Vaccines in Adults[16,21,22]

Vaccination	Common Adverse Events
PCV15, PCV20, or PCV21	Erythema, edema, pain, and tenderness at the site of injection
	Pyrexia and rigors
	Anorexia
	Fatigue/tiredness
	Headache
	Myalgia/joint pain
PPSV23	Erythema and pain at the site of injection
	Fatigue/tiredness
	Pyrexia
	Myalgias
	Contraindications
PCV20	Severe allergy to any component of the vaccine or diphtheria-toxoid containing vaccine; immunocompromised individuals may have a decreased immune response
PCV21	Immunocompromised individuals may have a decreased immune response
PPSV23	Severe allergy to any component of the vaccine or diphtheria-toxoid containing vaccine; use with caution in patients with severely compromised pulmonary and cardiovascular function, as any systemic reaction can lead to significant risk

Pregnancy is not a contraindication to pneumococcal vaccination. Pregnant woman at high-risk should be vaccinated (Table 2).

appraising vaccine product inserts via the US Food and Drug Administration (https://www.fda.gov/vaccines-blood-biologics/vaccines).

The Role of NPs, Nurses, and Other Clinicians

NPs, nurses, and other clinicians are meeting a critical gap in public health, helping to improve access to preventative primary care services and, consequently, reducing health inequities[28] in the administration of pneumococcal vaccines to adults. A 2021 survey conducted by the American Association of Nurse Practitioners found 90% of nurse practitioners has spoken to their patients about the COVID-19 vaccine.[29] NPs, nurses, and other clinicians need to use that same advocacy, skill, knowledge, and tenacity in following the most recently updated CDC recommendations for prescribing, recommending, and safely administering pneumococcal vaccinations. This can be achieved through both primary and secondary prevention strategies.

Primary prevention roles involve proactive measures to prevent the onset of CAP. NPs and nurses are at the forefront of patient education, informing adults about the importance of pneumococcal vaccination, especially for those $\geq$50 years or with underlying health conditions. They assess patients' vaccination histories, identify those at risk, and recommend appropriate vaccines. Clinicians also ensure the correct administration of vaccines, adhering to guidelines on dosage, intervals, and coadministration with other vaccines. By maintaining up-to-date knowledge on vaccine recommendations and leveraging tools like the CDC's PneumoRecs VaxAdvisor app, they provide tailored vaccination plans. Equally important is thorough documentation in the electronic health record of both patient education and vaccine administration, particularly when addressing individuals at increased risk of CAP or discussing concerns related to vaccine hesitancy, to ensure continuity of care and facilitate informed clinical decision-making.

Secondary prevention focuses on reducing the impact of pneumococcal disease in those already affected or at high risk. Clinicians monitor patients with chronic illnesses or immunocompromised conditions, ensuring they receive timely booster doses and follow-up care. They also manage and document adverse events, providing immediate care and reporting to vaccine safety monitoring systems. In cases of outbreaks or increased disease incidence, NPs and nurses may conduct targeted vaccination campaigns in high-risk communities.

Beyond vaccine administration, NPs and nurses advocate for vaccination through public health initiatives, community outreach, and collaboration with health care providers to increase vaccination rates. They address vaccine hesitancy by dispelling myths and providing evidence-based information, fostering trust and compliance among patients. Their comprehensive approach ensures that pneumococcal vaccines are effectively used to protect adult populations from serious infections.

Summary and Conclusion

This article provides a summary of recent epidemiologic and clinical data regarding pneumococcal disease with a focus on *S. pneumoniae*—associated CAP in adults, the current CDC recommendations for pneumococcal vaccination in adults, and adverse events and contraindications associated with the pneumococcal vaccines. Although the efficacy and safety of the PCV and PPSV23 vaccines are supported, it is paramount to evaluate patients for adequate indications, potential contraindications, and the occurrence of adverse events. Familiarity with the common contraindications and adverse events associated with pneumococcal vaccines is requisite to their safe prescribing. Likewise, strong applicable knowledge in the use of the PneumoRecs VaxAdvisor App for Vaccine Providers, Vaccine Adverse Event Reporting System, and Food and Drug Administration resources on vaccines and biologics enhances care outcomes. By building strong relationships within communities, NPs, nurses, and other clinicians can help to address needs in vulnerable populations and further advance the advocacy for initiatives that improve public health.

Nurse scholars should continue to evaluate clinical and public health data and play a role in evolving clinical guidelines and recommendations for pneumococcal vaccination. Finally, nurse educators should ensure they are providing undergraduate and graduate nurse learners with the most current vaccination guidelines and recommendations, equip them with skills to help overcome vaccine hesitancy in patients,[30] and pursue roles that allow for the development of public health advocacy.

CRediT authorship contribution statement

Christopher W. Blackwell: Writing – review & editing, Writing – original draft, Validation, Supervision, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization. **Humberto López Castillo:** Writing – review & editing, Writing – original draft, Methodology, Formal analysis, Data curation, Conceptualization. **Frances Armstrong:** Writing – review & editing, Writing – original draft, Validation, Resources, Methodology, Investigation, Formal analysis, Data curation, Conceptualization.

Declaration of Competing Interest

In compliance with standard ethical guidelines, the authors report no relationships with business or industry that may pose a conflict of interest.

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