

Role of Pneumococcal Vaccination in Chronic Lung Diseases

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Disease Burden

Chronic pulmonary diseases, as mainly defined by asthma, bronchiectasis, chronic obstructive lung disease (COPD), interstitial lung disease, pulmonary hypertension etc., represent the third leading cause of death in United States and account for more than 143,382 deaths in 2011.¹ The prevalence of chronic obstructive pulmonary disease (COPD) in India is estimated to be 31.4–57.1% over 60 years of age.¹

Infectious Complications in Chronic Lung Diseases

Pneumococcal pneumonia is a frequent complication in patients with chronic pulmonary disease.

Mortality is a frequent outcome in these cases, regardless of whether the patients have developed invasive disease.² In patients with severe and very severe COPD, respiratory failure and pneumonia are the leading causes of morbidity and mortality.³ The relative risk (adjusted for age, race and other comorbidities) of IPD, and mortality in IPD, is significantly higher [5.6 (3.2 - 9.9) and 2.8 (1.9 - 4.0) respectively] in patients with COPD, as compared to otherwise healthy adults.⁴ In the sputum examination of 91 patients (> 40 years old) with acute exacerbations of COPD, *S. pneumoniae* was isolated in 10% cases.⁶ The sputum isolation of *S pneumoniae* increases significantly when the COPD exacerbation comes after 2 months of previous episode.⁷ An association has also been shown between the presence of a new strain of *S. pneumoniae* and a significantly increased risk of an exacerbation

in COPD patients.⁸ Vaccination against *S. pneumoniae* can reduce the risk of mortality especially from more serious infections in both immunocompetent and immunocompromised patients.

Clinical and immunogenicity data of pneumococcal vaccines in lung diseases

A review of 7 RCTs suggests that while it is possible that injectable polyvalent pneumococcal vaccines may provide some protection against morbidity in persons with COPD, no significant effect was shown for reduction in pneumonia (odds ratio 0.72; 95% CI 0.51 to 1.01), acute exacerbation (OR 0.58; 95% CI 0.30 to 1.13), hospital admissions or emergency department visits and all-cause mortality (OR 0.94; 95% CI 0.67 to 1.33).⁹

In a randomized, open-label trial 120 patients with COPD were randomized to PPV23 (63 subjects) or PCV7 (57 subjects). Adjusted for baseline levels, post vaccination IgG was higher in the PCV7 group than the PPV23 group for all seven serotypes, reaching statistical significance for five (P=0.05). PCV7 resulted in a higher OPA for six of seven serotypes (statistically greater for four) compared with PPV23.¹⁰

National and global recommendations for use of pneumococcal vaccines in chronic lung diseases

Pneumococcal vaccination is recommended for use in patients with chronic lung diseases including COPD by various respiratory societies like Global Initiative For Chronic Obstructive Lung Disease

(GOLD 2013), Joint Indian Chest Society (ICS) and National College of Chest Physicians (NCCP) 2013, Swiss Respiratory Society 2013, National Institute for Health & Clinical Excellence (NICE 2010) guidelines, British Columbia Medical Association (2011) etc.¹¹⁻¹⁵ The Portuguese Respiratory Society (2014)¹⁶ recommended the sequential administration of PCV13 and PPV23 in adults > 50 years with chronic respiratory diseases including chronic asthma under inhaled corticosteroid. The Spanish Society of Pneumology and Thoracic Surgery (2013)¹⁷ in a joint consensus document recommended the use of PCV13 in chronic respiratory disease including COPD, asthma and interstitial lung disease). The Philippine society for microbiology and infectious diseases and Royal College of Physicians of Thailand also recommended the use of PCV13 in patients with chronic lung disease.^{18,19} The Centers for Disease Control and Prevention's (CDC) Advisory Committee on Immunization Practices (ACIP 2014) recommends the use of PCV13 in chronic lung diseases if some other risk factor is present (e.g. on the basis of medical, occupational, lifestyle, or other indications).²⁰

ACIP Recommendations Revised²¹

On June 20, 2012, ACIP recommended use of PCV13 for adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia,

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Table 1: New ACIP recommendations for the use of PCV13 and PPV23²¹

Pneumococcal vaccine-naïve persons	
Adults aged ≥65 years who have not previously received pneumococcal vaccine or whose previous vaccination history is unknown	One dose PCV13 followed by a dose of PPV23 PPV23 should be given 6–12 months after PCV13 If PPV23 cannot be given during this time window, the dose of PPV23 should be given during the next visit The two vaccines should not be co-administered, and the minimum acceptable interval between PCV13 and PPSV23 is 8 weeks
Previous vaccination with PPSV23	
Adults aged ≥65 years who have previously received ≥1 doses of PPV23	Should receive a dose of PCV13 if they have not yet received it A dose of PCV13 should be given ≥1 year after PPV23. For those for whom an additional dose of PPV23 is indicated, it should be given 6–12 months after PCV13 and ≥5 years after the most recent dose of PPV23

cerebrospinal fluid leak, or cochlear implants (high risk). The ACIP decision to recommend PCV13 use (routinely) among older adults was deferred until data became available on the efficacy of PCV13 against non-invasive pneumococcal pneumonia among adults.

A randomized placebo-controlled trial (CAlPiTA trial) was conducted in the Netherlands amongst approximately 85,000 adults aged ≥65 years during 2008–2013 to verify and describe further the clinical benefit of PCV13 in the prevention of pneumococcal pneumonia. The results of the CAlPiTA trial demonstrated 45.6% (95% confidence interval [CI] = 21.8%–62.5%) efficacy of PCV13 against vaccine-type pneumococcal pneumonia, 45.0% (CI = 14.2%–65.3%) efficacy against vaccine-type nonbacteremic pneumococcal

pneumonia, and 75.0% (CI = 41.4%–90.8%) efficacy against vaccine-type IPD among adults aged ≥65 years.

In June 2014, the results of CAlPiTA trial became available and were presented to ACIP. The evidence supporting PCV13 vaccination of adults was evaluated using the Grading of Recommendations, Assessment, Development, and Evaluation (GRADE) framework and determined to be type 2 (moderate level of evidence); the recommendation was categorized as a Category A recommendation. So finally on August 13, 2014, ACIP recommended routine use of PCV13 among adults aged ≥65 years.

So now ACIP recommends that both PCV13 and PPV23 should be routinely administered in series to all adults aged ≥65 years. The recommendations for routine PCV13 use among adults aged ≥65 years will be re-evaluated in 2018 and revised as needed. ACIP recommendations for use of PCV13 (high risk) in adults aged ≥19 years with immunocompromising conditions, functional or anatomic asplenia, cerebrospinal fluid leak, or cochlear implants remain unchanged.

The recommendations for usage of both the vaccines are mentioned below as well as in Table 1.

The new ACIP recommendations now support the usage of PCV13 as a routine vaccine in the adult population for prevention of pneumococcal disease. CDC believes that the implementation of PCV13 is cost effective for the immediate future. Clinicians now have guidance on the use of PCV13 in adults 65+ as well as in adults with immunocompromised conditions. ACIP recommendation and MMWR document can serve as a valuable reference to other vaccine technical committees as they consider their own policy decisions

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