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# Pneumococcal vaccination of older adults
## Conjugate or polysaccharide?

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Pneumococcal polysaccharide vaccines have demonstrated effectiveness in prevention of invasive pneumococcal disease (IPD).[1] However, their effectiveness against non-invasive pneumococcal pneumonia or all-cause community-acquired pneumonia (CAP) has not been established; two recently published meta-analyses concluded that prevention of pneumococcal pneumonia could not be demonstrated for pneumococcal polysaccharide vaccines.[2,3] By contrast, conjugated pneumococcal vaccines have proven effective against pneumococcal pneumonia and all-cause pneumonia in infants and young children.[4-6] This success generated interest in their potential use in adults for the prevention of pneumococcal CAP, which remains a major unmet medical need.

Consequently, the United States Food and Drug Administration granted accelerated approval of the 13-valent pneumococcal conjugate vaccine (PCV13) based on immunologic non-inferiority to 23-valent pneumococcal polysaccharide vaccine (PPSV23). In their review, Drs Fedson and Guppy note that the immunogenicity of the predecessor 7-valent pneumococcal conjugate vaccine was similar to that of PPSV23, but does not describe the results of the pivotal clinical trials that supported the licensure of PCV13 for adults aged 50 y and older.[7] Functional antibody responses to PCV13 were compared with those generated by PPSV23 for the 12 shared serotypes and serotype 6A, unique to PCV13. In subjects not previously vaccinated with PPSV23, functional antibody responses to a single dose of PCV13 were not only similar (noninferior) to responses to PPSV23 for all shared serotypes, but were statistically significantly higher for 9 of the 13 serotypes.[8] This pattern was repeated in adults who had previously received a dose of PPSV23 at least 5 y earlier; functional antibody responses to PCV13 were not only similar (noninferior) to responses to PPSV23 for all shared serotypes but were statistically significantly higher for 11 of the 13 serotypes.[9]

Drs Fedson and Guppy also maintain that "repeat vaccination with PPV23 was found to be safe and effective with no evidence of hyporesponsiveness." In the PCV13 study summarized above, subjects returned for a dose of either PCV13 or PPSV23 3 to 4 y after their initial dose of PCV13 or PPSV23.[10] Prior to the second vaccination, functional antibody levels had declined in all groups. However, a second dose of PCV13 generated functional antibody responses comparable to those seen after the first dose of PCV13 for all of the serotypes and a statistically significantly higher response to the second dose for 6 of the 13 serotypes. A similar result was observed when a dose of PCV13 was followed 3 to 4 y later by a dose of PPSV23. These results contrasted to the responses seen when subjects received two doses of PPSV23 3 to 4 y apart. In these subjects, the second dose of PPSV23 elicited a response that was statistically significantly lower for 8 of the 12 serotypes shared by both vaccines when compared with the response after the first dose of PPSV23. Furthermore, responses to two doses of PCV13 were significantly higher for all 12 serotypes shared by both vaccines when compared with response in subjects who received two doses of PPSV23. These results suggest that PCV13 primed the immune system for an anamnestic response to subsequent vaccination with either PCV13 or PPSV23, and contrasts with the blunted response to repeat doses of PPSV23.

Drs Fedson and Guppy also discuss the relevance of the PCV13 serotypes for adults in countries where PCVs have been used in pediatric immunization programs. We do not argue that the indirect effects of PCV7 implementation on rates of vaccine-type IPD in adults have been profound. However, the most frequent presentation of pneumococcal disease in adults is non-invasive pneumococcal pneumonia, and drawing firm conclusions regarding the magnitude of indirect effects in adults for pneumonia is more difficult. Studies have reported contrasting results, noting either a reduction or no effect on all-cause pneumonia hospitalizations.[6,11-13] Data emerging from studies of CAP, which utilize a validated serotype-specific urinary antigen detection assay, are likely to be extremely helpful in this regard; a study recently completed in the US suggests that the PCV7 serotypes remain a notable cause of CAP in US adults 10 to 12 y post-introduction of PCV7.[14,15] Therefore, indirect effects alone may not be sufficient to tackle this significant public health burden in older adults. We contend that even in settings of high uptake of conjugate vaccine in the pediatric population there remains a need to offer direct protection to prevent pneumococcal CAP.

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Furthermore, cost-effectiveness analyses have been conducted, taking into consideration indirect effects of pediatric programs, and have shown that adult age- and risk-based recommendations for PCV13 are still expected to be cost-effective.[16-18]

## Disclosure of Potential Conflicts of Interest

Hollingsworth R and Isturiz R are employees of Pfizer Inc.

## References


1. Jackson LA, Neuzil KM. Pneumococcal polysaccharide vaccine. In: Plotkin SA, Orenstein WA, eds. Vaccines 5th Edition. Philadelphia, PA: Saunders, Elsevier; 2008:569-604.
2. Huss A, Scott P, Stuck AE, Trotter C, Egger M. Efficacy of pneumococcal vaccination in adults: a meta-analysis. CMAJ 2009; 180:48-58; PMID:19124790; http://dx.doi.org/10.1503/cmaj.080734
3. Moberley S, Holden J, Tatham DP, Andrews RM. Vaccines for preventing pneumococcal infection in adults. Cochrane Database Syst Rev 2013; 1:CD000422; PMID:23440780
4. Hansen J, Black S, Shinefield H, Cherian T, Benson J, Fireman B, Lewis E, Ray P, Lee J. Effectiveness of heptavalent pneumococcal conjugate vaccine in children younger than 5 years of age for prevention of pneumonia: updated analysis using World Health Organization standardized interpretation of chest radiographs. Pediatr Infect Dis J 2006; 25:779-81; PMID:16940833; http://dx.doi.org/10.1097/01.inf.0000232706.35674.2f
5. Cutts FT, Zaman SMA, Enwere G, Jaffar S, Levine OS, Okoko JB, Oluwalana C, Vaughan A, Obaro SK, Leach A, et al.; Gambian Pneumococcal Vaccine Trial Group. Efficacy of nine-valent pneumococcal conjugate vaccine against pneumonia and invasive pneumococcal disease in The Gambia: randomised, double-blind, placebo-controlled trial. Lancet 2005; 365:1139-46; PMID:15794968; http://dx.doi.org/10.1016/S0140-6736(05)71876-6
6. Griffin MR, Zhu Y, Moore MR, Whitney CG, Grijalva CG. U.S. hospitalizations for pneumonia after a decade of pneumococcal vaccination. N Engl J Med 2013; 369:155-63; PMID:23841730; http://dx.doi.org/10.1056/NEJMoa1209165
7. Fedson DS, Guppy MJ. Pneumococcal vaccination of older adults: conjugate or polysaccharide? Hum Vaccin Immunother 2013; 9: (Forthcoming); PMID:23732892; http://dx.doi.org/10.4161/hv.24692
8. Jackson LA, Gurtman A, van Cleeff M, Jansen KU, Jayawardene D, Devlin C, Scott DA, Emini EA, Gruber WC, Schmoele-Thoma B. Immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine compared to a 23-valent pneumococcal polysaccharide vaccine in pneumococcal vaccine-naive adults. Vaccine 2013; 31:3577-84; PMID:23688526; http://dx.doi.org/10.1016/j.vaccine.2013.04.085
9. Jackson LA, Gurtman A, Rice K, Pauksens K, Greenberg RN, Jones TR, Scott DA, Emini EA, Gruber WC, Schmoele-Thoma B. Immunogenicity and safety of a 13-valent pneumococcal conjugate vaccine in adults 70 years of age and older previously vaccinated with 23-valent pneumococcal polysaccharide vaccine. Vaccine 2013; 31:3585-93; PMID:23688527; http://dx.doi.org/10.1016/j.vaccine.2013.05.010
10. Jackson LA, Gurtman A, van Cleeff M, Frenck RW, Treanor J, Jansen KU, Scott DA, Emini EA, Gruber WC, Schmoele-Thoma B. Influence of initial vaccination with 13-valent pneumococcal conjugate vaccine or 23-valent pneumococcal polysaccharide vaccine on anti-pneumococcal responses following subsequent pneumococcal vaccination in adults 50 years and older. Vaccine 2013; 31:3594-602; PMID:23688525; http://dx.doi.org/10.1016/j.vaccine.2013.04.084
11. Grijalva CG, Nuorti JP, Arbogast PG, Martin SW, Edwards KM, Griffin MR. Decline in pneumonia admissions after routine childhood immunisation with pneumococcal conjugate vaccine in the USA: a time-series analysis. Lancet 2007; 369:1179-86; PMID:17416262; http://dx.doi.org/10.1016/S0140-6736(07)60564-9
12. Nelson JC, Jackson M, Yu O, Whitney CG, Bounds L, Bittner R, Zavitkovsky A, Jackson LA. Impact of the introduction of pneumococcal conjugate vaccine on rates of community acquired pneumonia in children and adults. Vaccine 2008; 26:4947-54; PMID:18662735; http://dx.doi.org/10.1016/j.vaccine.2008.07.016
13. Simonsen L, Taylor RJ, Young-Xu Y, Haber M, May L, Klugman KP. Impact of pneumococcal conjugate vaccination of infants on pneumonia and influenza hospitalization and mortality in all age groups in the United States. MBio 2011; 2:e00309-10; PMID:21264063; http://dx.doi.org/10.1128/mBio.00309-10
14. Sherwin RL, Gray S, Alexander N, et al. Distribution of PCV13-serotype Streptococcus pneumoniae in Adults Aged ≥ 50 Years Presenting to Select US Hospitals with Radiographically-Confirmed Community-Onset Pneumonia. Presented at the inaugural IDWeek. San Diego, CA. October 17-21 2012.
15. Pride MW, Huijts SM, Wu K, Souza V, Passador S, Tinder C, Song E, Elfassy A, McNeil L, Menton R, et al. Validation of an immunodiagnostic assay for detection of 13 *Streptococcus pneumoniae* serotype-specific polysaccharides in human urine. Clin Vaccine Immunol 2012; 19:1131-41; PMID:22675155; http://dx.doi.org/10.1128/CVI.00064-12
16. Smith KJ, Wateska AR, Nowalk MP, Raymund M, Lee BY, Zimmerman RK. Modeling of cost effectiveness of pneumococcal conjugate vaccination strategies in U.S. older adults. Am J Prev Med 2013; 44:373-81; PMID:23498103; http://dx.doi.org/10.1016/j.amepre.2012.11.035
17. Weycker D, Sato R, Strutton D, Edelsberg J, Atwood M, Jackson LA. Public health and economic impact of 13-valent pneumococcal conjugate vaccine in US adults aged ≥50 years. Vaccine 2012; 30:5437-44; PMID:22728289; http://dx.doi.org/10.1016/j.vaccine.2012.05.076
18. Yang HK, Chen J, O'Brien M, et al. Cost-effectiveness of Pneumococcal Vaccines for Adults in the United States. Presented at ISPOR 18th Annual International Meeting, New Orleans, LA. May 18-22 2013.