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Cost-effectiveness of pneumococcal conjugate vaccination in immunocompromised adults

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ABSTRACT

Objective: Pneumococcal disease is a significant problem in immunocompromised persons, particularly in HIV-infected individuals. The CDC recently updated pneumococcal vaccination recommendations for immunocompromised adults, adding the 13-valent pneumococcal conjugate vaccine (PCV13) to the previously recommended 23-valent pneumococcal polysaccharide vaccine (PPSV23). This analysis estimates the cost-effectiveness of pneumococcal vaccination strategies in HIV-infected individuals and in the broader immunocompromised adult group.
Design: Markov model-based cost-effectiveness analysis.
Methods: The model considered immunocompromised persons aged 19–64 years and accounted for childhood PCV13 herd immunity; in a separate analysis, an HIV-infected subgroup was considered. PCV13 effectiveness was estimated by an expert panel; PPSV23 protection was modeled relative to PCV13 effectiveness. We assumed that both vaccines prevented invasive pneumococcal disease, but only PCV13 prevented nonbacteremic pneumonia.
Results: In all immunocompromised individuals, a single PCV13 cost $70,937 per quality adjusted life year (QALY) gained compared to no vaccination; current recommendations cost $136,724/QALY. In HIV patients, with a longer life expectancy (22.5 years), current recommendations cost $89,391/QALY compared to a single PCV13. Results were sensitive to variation of life expectancy and vaccine effectiveness. The prior recommendation was not favored in any scenario.
Conclusions: One dose of PCV13 is more cost-effective for immunocompromised individuals than previous vaccination recommendations and may be more economically reasonable than current recommendations, depending on life expectancy and vaccine effectiveness in the immunocompromised.

1. Introduction

Streptococcus pneumoniae illness epidemiology is strikingly different between the general population and individuals with immunocompromising conditions. While invasive pneumococcal disease (IPD) incidence is low among young adults (3.8 cases per 100,000) and rises nearly 10-fold among adults over age 65 years (36.4/100,000), incidence increases dramatically among immunocompromised adults with hematological cancer or HIV infection (173–186/100,000) [1]. Previously, the Advisory Committee on Immunization Practices (ACIP) recommended two doses of 23-valent pneumococcal polysaccharide vaccine (PPSV23) at least five years apart for immunocompromised individuals [2]. In June 2012, the ACIP issued new recommendations for immunocompromised adults, adding the 13-valent pneumococcal conjugate vaccine (PCV13) to the previously recommended PPSV23 [1].

The rationale for this change has 4 major components. First, comparable or greater antibody responses to PCV13 relative to PPSV23 were found in immunocompetent adults, indicating a reasonable likelihood of clinical benefit [3]. Interestingly, PCV13 antibody response was less when given 1 year after PPSV23 than when given *de novo*, which not seen when PCV13 immunization followed another PCV13 dose [3]. Second, the previously used 7-valent conjugate vaccine (PCV7), given in 2 doses 4 weeks apart, was 75% effective in preventing IPD in HIV infected adults not on highly active antiretroviral therapy in Malawi [4], and provided similar antibody responses compared to PPSV23 in US and European HIV patients [5,6]. In addition, when given vaccines in series, greater antibody responses were seen when PPSV23 was given after PCV7 and blunted response was not observed when PCV7 was given 5 years after PPSV23 [4,6]. Third, PPSV23 efficacy in preventing pneumococcal disease in the immunocompromised is questionable, with many experts believing it ineffective in this group [7]. Despite conflicting evidence on PPSV23 efficacy in HIV patients

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[8,9], the ACIP concluded that benefits of PPSV23 use outweighed its risks [1]. Finally, the strong indirect (herd immunity) effects due to childhood PCV7 observed in most population groups have not carried through to the immunocompromised, with high IPD rates from PCV7 serotypes seen in HIV-infected persons [10]. Also, PCV13 serotypes caused 50% of IPD in the immunocompromised in 2010, with an additional 21% caused by serotypes contained only in PPSV23 [1]. Substantial replacement disease occurred in immunocompromised persons after widespread PCV7 use, especially an increase in serotype 19A [11]. The new recommendation includes both vaccines because PPSV23 contains 11 *S. pneumoniae* serotypes not found in PCV13, and PPSV23's known IPD protection in most populations [1].

PCV13 costs considerably more than PPSV23. An analysis from the UK found PCV13 use for persons with immunocompromising and other high-risk conditions unlikely to be cost effective [12]. The CDC also performed a cost-effectiveness analysis, but only examined the new vaccination recommendation for the immunocompromised compared to the prior recommendation [1,13]. Given doubts regarding PPSV23 effectiveness in the immunocompromised, the cost effectiveness of using only PCV13 in this group is germane. Here we consider several vaccination strategies, specifically examining the cost-effectiveness of the previous ACIP recommendation (two PPSV23 vaccines separated by at least 5 years), the current ACIP recommendation using both PCV13 and PPSV23, and regimens using only PCV13.

2. Methods

We used a Markov state-transition model to estimate the cost effectiveness of 6 vaccination strategies in immunocompromised persons aged 19–64 years: no vaccine, a single PPSV23, two PPSV23 doses separated by 5 years (the previous CDC recommendation [2]), a single PCV13 alone, two PCV13 doses separated by 5 years, and the current CDC recommendation for PPSV23 naïve patients, PCV13 followed by PPSV23 at least 8 weeks later then a second PPSV23 in 5 years [1]. In a sensitivity analysis, we also examined the recommended strategy for patients previously vaccinated with PPSV23, PCV13 at least 1 year after the PPSV23, then a second PPSV23 vaccination 5 years after the first. To account for changes in both duration and quality of life, we used quality adjusted life years (QALYs), the product of time in a health state and that state's quality of life utility, which can range from 0 (death) to 1 (perfect health).

In the model, hypothetical cohorts of immunocompromised persons could become ill due to nonbacteremic pneumococcal pneumonia or invasive pneumococcal disease during each yearly cycle of the model. Once ill, they could recover, become disabled, or die. If they became disabled, they could not return to a non-disabled state. Patients could die from pneumococcal illness, or due to other causes based on the cohort's life expectancy.

The model considered, over a 15-year time horizon, immunocompromised persons aged 19–64 years with an average life expectancy of 11.7 years, based on SEER data on the 5-year cause-specific survival for all malignant cancers [14]. We used CDC definitions for immunocompromising conditions, which include HIV infection, Hodgkin disease, leukemia, lymphoma, myeloma, generalized malignancy, chronic renal failure, nephrotic syndrome, solid organ or bone marrow transplant, immunoglobulin deficiency, asplenia, sickle cell disease, or current immunosuppressive therapy (including radiation, systemic steroids, or chemotherapy) [1]. In a separate analysis, we only considered HIV positive individuals, who have a 22.5-year life expectancy (95% CI 22.2–22.7 years) [15]. In each cohort, life expectancy was used to calculate yearly mortality risk, which was applied over the 15-year time horizon of the model. A 15-year time horizon assumes no vaccination health effects after 15 years.

Invasive pneumococcal disease rates for the immunocompromised were obtained from 2007 to 2008 CDC Active Bacterial Core surveillance (ABCs) data [16], which also supplied case-fatality rate and IPD serotype distribution data (Table 1, top). Meningitis risk given IPD was used as a proxy for disability risk given IPD, understanding that not all meningitis patients are disabled but some with non-meningitis IPD are. NPP rates were calculated from National Hospital Discharge Survey data [17] under the assumption that 30% of all hospitalized pneumonia cases are caused by pneumococci (Table 1, bottom) [18,19]. As previously, we assumed that the serotype distribution of NPP was similar to IPD and that NPP and IPD case rate ratios were the same among comorbidity groups [16]. Disability after hospitalized NPP was modeled as 50% of the IPD value and varied widely in sensitivity analyses. Indirect (herd immunity) effects due to childhood PCV13 use were modeled as both changes in pneumococcal illness rates and in serotype distributions among disease cases, as previously described [16].

In the immunocompromised, PPSV23 has limited effectiveness, with many experts feeling it is not protective [7]. PCV13 may be more effective in these patients, albeit based on limited evidence [4,5,8,9]. We used PCV13 effectiveness in the immunocompromised as estimated by a pneumococcal disease expert panel using the modified Delphi technique (Table 2). Since PPSV23 effectiveness in the immunocompromised is controversial, we modeled PPSV23 effectiveness as a value relative to PCV13 effectiveness against IPD, examining how effective the vaccines would need to be for strategies to be considered cost-effective. In the model, both vaccines were assumed to be effective against their respective serotypes in preventing IPD, but only PCV13 prevented nonbacteremic pneumococcal pneumonia (NPP), consistent with published data [20–22]. As we have previously described [16], pneumococcal disease risk was modeled as a function of the projected infection risk and accounting for the indirect effects of childhood PCV13, the projected likelihood of infection from a vaccine serotype, the probability of vaccination, and the probability

Table 1
Characteristics of pneumococcal disease in the immunocompromised.

	Ages 19–49	Ages 50–59	Ages 60–69	Ages 70–79	Ages 80+
Invasive pneumococcal disease					
Invasive disease rate (per 100,000)	71.85	67.08	58.52	54.1	64.3
PPSV23 vaccine serotype coverage (%)	78.0%	73.3%	74.1%	65.8%	62.9%
PCV13 vaccine serotype coverage (%)	51.9%	48.3%	48.7%	40.8%	40.8%
Probability of outcome given invasive disease					
Meningitis	6.8%	7.2%	6.2%	3.8%	2.1%
Mortality	7.0%	10.5%	11.3%	11.6%	19.7%

	Ages 19–44	Ages 45–64	Ages 65+
Hospitalized nonbacteremic pneumococcal pneumonia			
Rate (per 100,000)	204.3	343.6	868.0

Source: CDC Acute Bacterial Core surveillance data, 2007–2008.