Health and Economic Burden Associated With 15-Valent Pneumococcal Conjugate Vaccine Serotypes in Children in New Zealand

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Background and Objectives

- *Streptococcus pneumoniae* is a Gram-positive organism that causes invasive and noninvasive pneumococcal disease. Invasive pneumococcal disease (IPD) syndromes include bacteremia without focus, bacteremic pneumonia, and meningitis.[1] The most common noninvasive syndromes are non-bacteremic pneumococcal pneumonia (NBPP) and acute otitis media (AOM)
- The introduction of pneumococcal conjugate vaccines (PCV) into infant immunization schedules has led to substantial disease reduction. However, unmet needs remain due to the emergence of non-vaccine serotypes and select vaccine serotypes that continue to persist, such as serotype 3[2]
- Future pediatric PCVs must therefore include serotypes contained in currently licensed PCVs to maintain disease reduction and also expand serotype coverage to key non-vaccine serotypes that have emerged
- MSD is developing V114, an investigational 15-valent PCV that contains the PCV10 and PCV13 serotypes as well as 2 additional serotypes, 22F and 33F
- This study quantifies the health and economic burden of IPD attributable to all 15 serotypes in V114 in a hypothetical unvaccinated birth cohort in New Zealand. To demonstrate the value of continued disease protection while also expanding serotype coverage, IPD cases and costs attributable to V114 serotypes are estimated at several time points prior to and following PCV7, PCV10, and PCV13 introduction

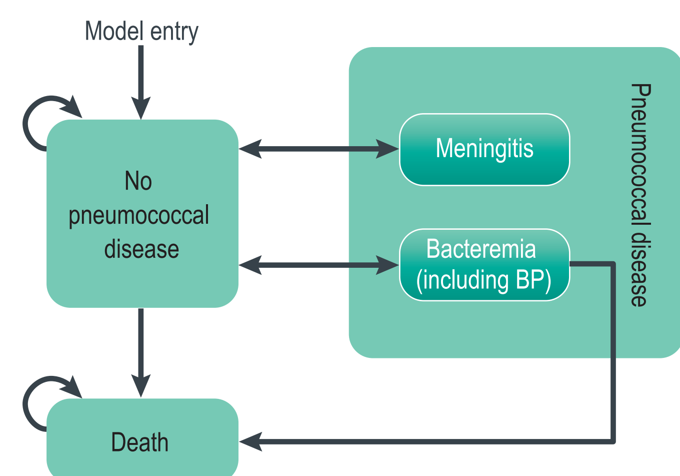
Methods

Target population: A cohort of unvaccinated newborns in 2017 in New Zealand.

Modeling approach:

- A Markov model with 3 health states – no pneumococcal disease, IPD (meningitis and bacteremia, including bacteremic pneumonia (BP)), and death (Figure 1) – was adapted.[3] Post-meningitis sequelae and NBPP were not considered in the current analysis

Figure 1. Model Structure



- A cohort of unvaccinated newborns in 2017 in New Zealand was followed for 20 years to estimate cases, deaths, direct medical costs, and indirect costs for IPD. The total cohort consisted of 59,145 newborns[4]
- Health and economic outputs were estimated under 2 scenarios:
  1. **Value of V114 serotypes prior to PCV7 introduction ("Pre-PCV"):** Pre-PCV7 disease incidence and serotype distribution were applied to all 15 serotypes in V114[5]
  2. **Value of V114 serotypes post-PCV7 and post-PCV10/PCV13 introduction ("Post-PCV"):**
     a) Pre-PCV7-era epidemiological inputs were applied to the common PCV7 serotypes in V114
     b) Pre-PCV10 epidemiological inputs were applied to the additional 3 PCV10 serotypes not in PCV7 (PCV10-PCV7) circulating in the post-PCV7 era[6]
     c) Disease related to the V114 serotypes that are in PCV10 (V114-PCV10) was estimated using recent epidemiological data from the most current time period[6]
- Epidemiologic and economic parameters were retrieved from the literature and are summarized in Table 1
- The most recent case fatality rates were retrieved from the literature to reflect current access to care and medical treatment for IPD
- Direct medical costs were estimated from the healthcare perspective. A limited societal perspective considered all direct medical costs, productivity losses due to premature death among children, and productivity losses among adult caregivers. Costs were updated to 2017 New Zealand Dollars (NZD) and discounted at 3.5% annually
- Deterministic sensitivity analysis (DSA) was utilized to assess the impact of uncertainties around key parameters and assumptions in the pre-PCV scenario only. The following assumptions were explored: incidence rate of IPD is 0.8-1.2 times the base case value, case fatality rate of IPD is 0.8-1.2 times the base case value, direct medical costs and indirect costs associated with treating meningitis and bacteremia are 0.8-1.2 times the base case value, and discount rate is either 0% or 5%

Table 1. Epidemiology and Economic Model Parameters

Input	Manifestation	Age Groups	PCV7 Serotypes (pre-PCV era)	PCV10-PCV7 Serotypes (pre-PCV era)	V114-PCV10 Serotypes (pre-PCV era)	PCV10-PCV7 Serotypes (post-PCV era)	V114-PCV10 Serotypes (post-PCV era)
Serotype-specific incidence rate by age group and by vaccine-type serotypes in various periods (per 100,000 person-years)	IPD[5,6]	<1	83.0	2.6	10.4	3.5	13
		1	85.0	2.6	10.6	2.5	13.2
		2-4	19.8	0.6	2.5	0.3	4.8
		5-14	2.0	0.5	0.6	0.3	4.0
		15-20	1.7	0.4	0.5	0.2	3.7
Case fatality rate (CFR)	Meningitis[6]	0-11% (CFR varies by age)					
	Bacteremia[6]	0-11% (CFR varies by age)					
Direct medical cost (per episode)	Meningitis[7]	$7,447					
	Bacteremia[7]	$8,563					
Indirect cost (per episode)	Meningitis[7]	$553					
	Bacteremia[7]	$720					

Results

Figures 2 and 3 present IPD cases attributable to V114 serotypes in the pre- and post-PCV scenarios over the 20-year time horizon in New Zealand.

- V114 serotypes cause nearly 183 and 219 IPD cases in the pre- and post-PCV scenarios, respectively. In both scenarios, a majority of cases, 83% (pre-PCV) and 69% (post-PCV), are attributable to PCV7 serotypes
- PCV10-PCV7 and V114-PCV10 serotypes cause 31 cases (17%) and 67 cases (31%) in the pre- and post-PCV scenarios, respectively. The increase of 37 IPD cases in the post-PCV scenario is mainly due to increases in ST 1 (15 cases, 40% of the increase), ST 22F and 33F (15 cases, 41% of the increase), ST 19A (9 cases, 25% of the increase), and ST 3 (5 cases, 15% of the increase)

Figure 2. IPD Cases Attributable to PCV15 Serotypes in the Pre-PCV Scenario (proportion of cases among total cases attributable to V114 serotypes in parentheses)

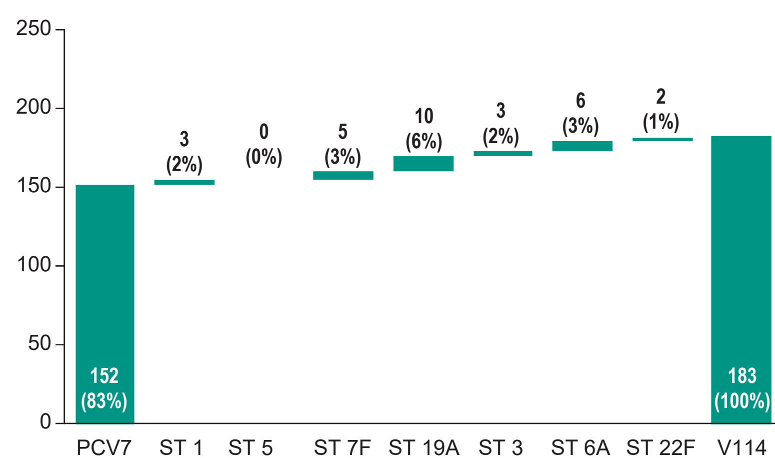


Figure 3. IPD Cases Attributable to PCV15 Serotypes in the Post-PCV Scenario (proportion of cases among total cases attributable to V114 serotypes in parentheses)

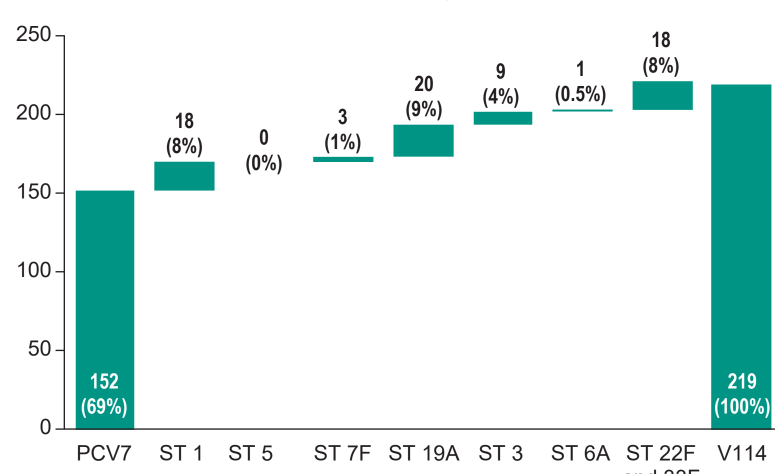


Table 2 presents discounted direct medical costs and indirect costs for IPD cases attributable to V114 serotypes.

- Total discounted medical costs and indirect costs are estimated to be approximately $5,866 thousand over 20 years in the pre-PCV scenario and $5,784 thousand in the post-PCV scenario
- PCV7 serotypes account for the majority of costs – 84% and 79% of the total costs in the pre-PCV and post-PCV scenarios, respectively
- Total costs associated with PCV10-PCV7 and V114-PCV10 serotypes are $877 thousand and $1,226 thousand in the pre-PCV and post-PCV scenarios, respectively. The increase of $338 thousand in total costs in the post-PCV scenario is mainly attributable to the increase in ST 22F and 33F ($263 thousand, 78% of the increase), ST 1 ($213 thousand, 63% of the increase), ST 3 ($45 thousand, 13% of the increase), and ST 19A ($54 thousand, 16% of the increase)

Table 2. Discounted Direct and Indirect Costs Associated With IPD New Zealand (in thousands, 2017 NZD, proportion of each vaccine type serotype among total V114 in parentheses)

	Pre-PCV Scenario			Post-PCV Scenario		
	Total Costs	Direct Costs	Indirect Costs	Total Costs	Direct Costs	Indirect Costs
PCV7 serotypes	$4,979 (85%)	$1,171 (84%)	$3,808 (85%)	$4,558 (79%)	$1,140 (76%)	$3,419 (80%)
PCV10-PCV7 serotypes						
ST 5	$0 (0%)	$0 (0%)	$0 (0%)	$0 (0%)	$0 (0%)	$0 (0%)
ST 1	$67 (1%)	$20 (1%)	$47 (1%)	$281 (5%)	$109 (7%)	$171 (4%)
ST 7F	$149 (3%)	$38 (3%)	$11 (2%)	$100 (2%)	$19 (1%)	$81 (2%)
V114-PCV10 serotypes						
ST 3	$83 (1%)	$23 (2%)	$60 (1%)	$128 (2%)	$37 (2%)	$91 (2%)
ST 6A	$195 (3%)	$46 (3%)	$148 (3%)	$7 (0%)	$2 (0%)	$5 (0%)
ST 19A	$338 (6%)	$80 (6%)	$259 (6%)	$392 (7%)	$94 (6%)	$229 (7%)
ST 22F and 33F	$55 (1%)	$15 (1%)	$40 (1%)	$318 (5%)	$93 (6%)	$224 (5%)
V114 not PCV7 serotypes	$887 (15%)	$223 (16%)	$665 (15%)	$1,226 (21%)	$354 (24%)	$817 (20%)
Total V114 serotypes	$5,866 (100%)	$1,394 (100%)	$4,472 (100%)	$5,784 (100%)	$1,494 (100%)	$4,290 (100%)

Table 3 presents results from DSA to assess the impact of uncertainties on key parameters in the pre-PCV scenario only. The discounted total cost is sensitive to uncertainties around all key parameters, especially the discount rate. When the discount rate is 0%, discounted total costs for IPD attributable to various serotypes increase by 286%-295%.

Table 3. DSA Results (costs in thousands, 2017 NZD)

	Discounted Total Costs (percentage change from base case in parentheses)		
	PCV7 Serotypes	PCV10 not PCV7 Serotypes	V114 not PCV10 Serotypes
Base case	$4,979	$216	$671
Incidence -20%	$3,983 (-20%)	$173 (-20%)	$537 (-20%)
Incidence +20%	$5,975 (20%)	$259 (20%)	$805 (20%)
CFR -20%	$4,243 (-15%)	$186 (-14%)	$709 (6%)
CFR +20%	$5,715 (15%)	$247 (14%)	$769 (15%)
Cost -20%	$4,726 (-5%)	$203 (-6%)	$636 (-5%)
Cost +20%	$5,233 (5%)	$229 (6%)	$707 (5%)
Discount factor 0%	$19,675 (295%)	$834 (286%)	$2,636 (293%)
Discount factor 5%	$3,339 (-33%)	$145 (-33%)	$450 (-33%)

Limitations

- Post-meningitis sequelae and pneumonia were not considered in the current analysis
- The analysis did not include direct nonmedical costs

Conclusions

- PCV7 serotypes caused most pneumococcal disease-related morbidity and costs in both the pre-PCV and post-PCV scenarios
- Three V114 serotypes not contained in PCV10 (ST 1, 3, and 19A) were associated with substantial morbidity and costs after the introduction of PCV7
- Emerging serotypes, such as ST 22F and 33F, are associated with additional morbidity and costs
- Investigational PCVs for infants must continue to retain serotypes in currently licensed PCVs to maintain disease reduction while expanding coverage to disease-causing serotypes, such as those contained in V114 but not in PCV10

References

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Presented at Virtual ISPOR Asia Pacific 2020; September 14-16, 2020.

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