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

Tianyan Hu[1]; Virginie Giroux[2]; Alexandra Goyette[2]; Thomas Weiss[1]; Tanaz Petigara[1]; Kwame Owusu-Edusei[1]

[1]Merck & Co., Inc., Kenilworth, NJ, USA;
[2] Merck Canada Inc., Kirkland, QC, Canada

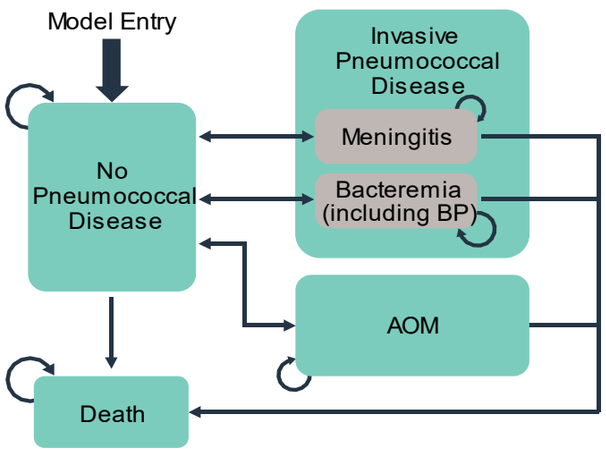
Background and Objectives

- *Streptococcus pneumoniae* causes invasive and noninvasive pneumococcal disease. The most common noninvasive syndromes are nonbacteremic pneumococcal pneumonia (NBPP) and acute otitis media (AOM)
- The introduction of pneumococcal conjugate vaccines (PCV) in infant immunization schedules has led to substantial disease reduction. However, unmet needs remain due to the serotype replacement and select vaccine serotypes that continue to persist, such as serotype 3[2]
- Merck is developing V114, an investigational 15-valent PCV that contains the PCV7, PCV10, and PCV13 serotypes as well as 2 additional serotypes, 22F and 33F
- This study quantifies the health and economic burden of IPD and AOM attributable to all 15 serotypes in V114 in a hypothetical unvaccinated birth cohort in Canada

Methods

Modeling approach: A Markov model with 4 health states – no pneumococcal disease, IPD (meningitis and bacteremia, including bacteremic pneumonia), AOM, and death (**Figure 1**) – was adapted.[3]

Figure 1. Model Structure



- A hypothetical cohort of unvaccinated newborns in 2018 in Canada was followed for 20 years to estimate cases, deaths, direct medical costs, and indirect costs for IPD and AOM. The total cohort consisted of 372,329 newborns
- 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 from 1999 were applied to all 15 serotypes in V114
  2. **Value of V114 serotypes post-PCV7 and post-PCV13 introduction (Post-PCV):**
     a) Pre-PCV7 epidemiological inputs were applied to PCV7 serotypes in V114[4]
     b) Pre-PCV13 epidemiological inputs were applied to the additional 6 PCV13 serotypes that are not in PCV7 (PCV13-PCV7)[4]
     c) Disease related to the unique V114 serotypes (22F and 33F) was estimated using the most recent epidemiological data from the post-PCV13 era (V114-PCV13)
- Epidemiologic and economic parameters were retrieved from the literature and are summarized in **Table 1**
- A limited societal perspective considered all direct medical costs, and indirect cost including productivity loss. Costs were updated to 2018 Canadian dollars and discounted at 1.5% annually
- Deterministic sensitivity analysis (DSA) was utilized to assess the impact of uncertainties around key parameters and assumptions in the pre-PCV scenario only

Table 1. Epidemiology and Economic Model Parameters

Input	Manifestation	Age Groups	Pre-PCV Scenario			Post-PCV Scenario		
			PCV7 Types	PCV13-PCV7 Types	V114-PCV13 Types	PCV7 Types	PCV13-PCV7 Types	V114-PCV13 Types
Serotype-specific incidence rate (per 100,000 person-years)	IPD[5,6,7]	<1	30.6	3.2	0.5	30.6	16.0	2.6
		1-4	20.6	2.2	0.3	20.6	12.6	1.8
		5-9	3.0	0.3	0.0	3.0	3.0	0.5
		10-14	0.9	0.1	0.0	0.9	0.8	0.2
		15-19	1.2	0.1	0.0	1.2	0.9	0.2
	AOM[8,9,10,11]	<2	28,442.2	7,855.8	362.6	28,442.2	22,377.3	769.1
		2-4	28,442.2	7,855.8	362.6	28,442.2	22,377.3	769.1
		5-19	0.0	0.0	0.0	0.0	0.0	0.0
Proportion of IPD[12]	Meningitis			15%			19%	
	Bacteremia			85%			82%	
Case fatality rate[13]	Meningitis				10%			
	Bacteremia				2%			
Direct medical cost (per episode)[14,15]	Meningitis				$18,849			
	Bacteremia				$40,207			
	AOM				$165			
Indirect cost (per episode)[16,17,18]	Meningitis				$1,375			
	Bacteremia				$359			
	AOM				$100			

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 Canada: V114 serotypes caused 580 and 911 IPD cases in the pre- and post-PCV scenarios, respectively. A majority of cases, 89% (pre-PCV) and 57% (post-PCV), were attributable to PCV7 serotypes

- PCV13-PCV7 types caused an additional 285 IPD cases in the post-PCV scenario, primarily due to increases in ST3 (32 cases, which account for 11% of the increase), ST7F (70 cases, 25% of the increase), and ST19A (171 cases, 60% of the increase)
- Cases caused by 22F and 33F increased from 1% (pre-PCV) to 6% (post-PCV) of all IPD cases attributable to V114 serotypes

Figure 2. IPD Cases Attributable to V114 Serotypes in the Pre-PCV Scenario (% of Cases Among Total Cases Attributable to V114 Serotypes)

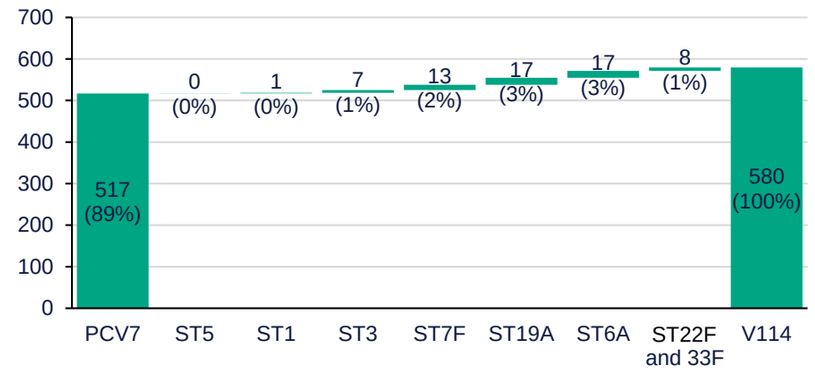


Figure 3. IPD Cases Attributable to V114 Serotypes in the Post-PCV Scenario (% of Cases Among Total Cases Attributable to V114 Serotypes)

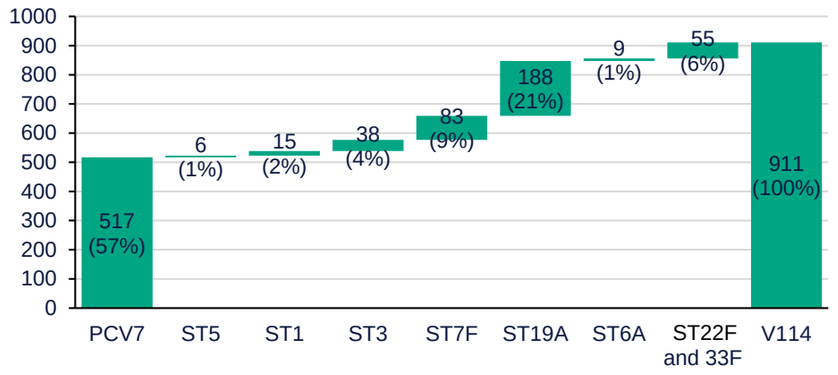


Figure 4. AOM Cases Attributable to V114 Serotypes in the Pre-PCV Scenario (% of Cases Among Total Cases Attributable to V114 Serotypes)

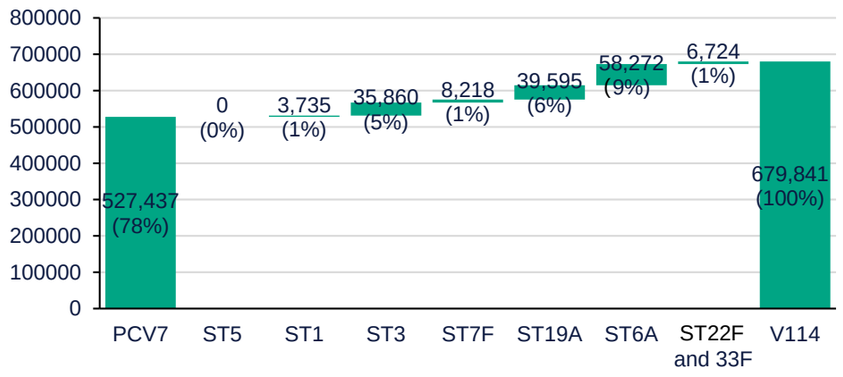
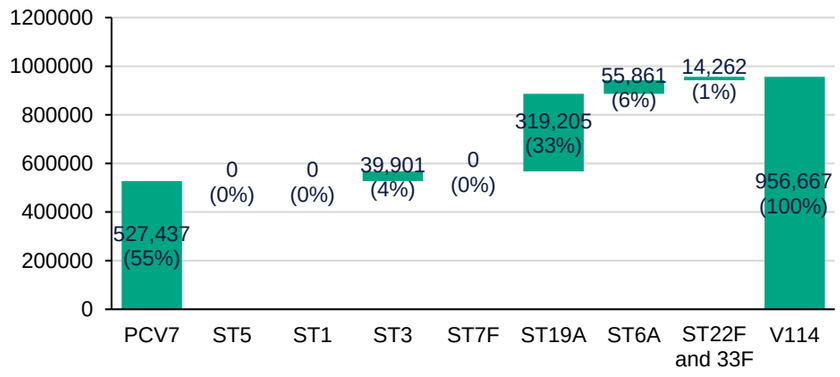


Figure 5. AOM Cases Attributable to V114 Serotypes in the Post-PCV Scenario (% of Cases Among Total Cases Attributable to V114 Serotypes)



Figures 4 and **5** present AOM cases attributable to V114 serotypes in the pre- and post-PCV scenarios over the 20-year time horizon in Canada.

- V114 serotypes caused nearly 680,000 and 957,000 AOM cases in the pre- and post-PCV scenarios, respectively. A majority of cases, 78% (pre-PCV) and 55% (post-PCV), are attributable to PCV7 serotypes
- PCV13-PCV7 types caused an additional 269,287 AOM cases in the post-PCV scenario, primarily due to increases in ST19A (279,610 cases)
- Cases caused by 22F and 33F increased from the pre-PCV to post-PCV scenario but remain 1% of all AOM cases attributable to V114 serotypes

Total discounted medical costs and indirect costs were estimated to be approximately $205 million over 20 years in the pre-PCV scenario and increased to $296 million in the post-PCV scenario

DSA results: The results of DSA analysis suggested that discounted total cost was sensitive to uncertainties around all key parameters, especially the incidence. When the incidence rate varied by 20%, discounted total costs for IPD and AOM attributable to various serotypes varied by 20%.

Limitations

- Post-meningitis sequelae and pneumonia were not considered in the current analysis
- The analysis did not include direct nonmedical costs, such as transportation costs
- The health and economic burden was only estimated for 1 hypothetical birth cohort in Canada, which was followed for 20 years. Therefore, the model underestimates the true health and economic burden associated with 15-valent pneumococcal conjugate vaccine serotypes in children in Canada

Conclusions

- PCV7 serotypes caused most pneumococcal disease-related morbidity and costs in both the pre-PCV and post-PCV scenarios
- Three additional serotypes not covered by PCV7 (7F) or PCV10 (3 and 19A) were associated with substantial morbidity and costs after the introduction of PCV7
- Serotypes, such as ST22F and 33F, are associated with additional morbidity and costs
- Investigational PCVs for infants must continue to retain serotypes in currently licensed vaccines to maintain disease reduction while expanding coverage to emerging disease-causing serotypes, such as those covered by V114 but not by PCV10 or PCV13

https://go.aws/2XK4dNx

References

1. Thorrington D, et al. *BMC Med*. 2018;16(1):13.
2. Ladhani SN, et al. *Lancet Infect Dis*. 2018;18(4):441-451.
3. Rubin JL, et al. *Vaccine*. 2010;28(48):7634-7643.
4. Moore MR, et al. *Lancet Infect Dis*. 2015;15(3):301-309.
5. Public Health Agency of Canada. Reported Cases From 1991 to 2016 in Canada: Notifiable Diseases Online.
6. Scheifele D, et al. *Clin Infect Dis*. 2000;31(1):58-64.
7. National Laboratory Surveillance of Invasive Streptococcal Disease in Canada: Annual Summary 2013 and 2016.
8. Wilson M, et al. *Infect Dis Ther*. 2018;7(3):353-371.
9. Kaur R, et al. *Pediatrics*. 2017;140(3):e20170181.
10. Wald ER, et al. *Pediatr Infect Dis J*. 2001;20(11): 1039-1042.
11. Pichichero M, et al. *Lancet Respir Dis*. 2018.
12. Bettinger JA, et al. *Vaccine*. 2010;28(9):2130-2136.
13. Sadarangani M, et al. ISPPD 2018: Clinical Features and Outcomes of Invasive Pneumococcal Disease in Canada Between 1991 and 2015 (IMPACT network).
14. Wilson M, et al. *Infect Dis Ther*. 2018;7(3):353-371.
15. Statistics Canada consumer price index for health care. Available from: https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1810000408#timeframe.
16. Morrow A, et al. *Can J Infect Dis Med Microbiol*. 2007;18(2):121-127.
17. Statistics Canada consumer price index. Available from: https://www150.statcan.gc.ca/t1/tbl1/en/cv.action?pid=1810000501#timeframe.
18. Delgleize et al. *BMC Open*. 2016.

e-Poster presented at the 12th International Symposium on Pneumococci and Pneumococcal Diseases (ISPPD), June 20–24 2020.