Cost-effectiveness of 2+1 Dosing of 13-Valent Pneumococcal Conjugate Vaccine Compared With 2+1 Dosing of 10-Valent Conjugate Vaccine in Preventing Pneumococcal Disease in Canada

Stephanie R Earnshaw,[1] Cheryl L McDade,[1] Giovanni Zanotti,[2] Raymond A Farkouh,[3] David R Strutton[3]

[1] RTI Health Solutions, Research Triangle Park, NC, United States;
[2] Pfizer Canada, Inc., Kirkland, Quebec, Canada;
[3] Pfizer, Inc., Collegeville, PA, United States

INTRODUCTION

- A 7-valent pneumococcal polysaccharide-protein conjugate vaccine, Prevnar (PCV7), was licensed for use in Canada in 2001 in children.
  - The vaccine led to a dramatic decrease in *Streptococcus pneumoniae*-related diseases such as acute otitis media (AOM), pneumonia (PNE), and invasive pneumococcal disease (IPD) in Canada.[1-8]
- Two pneumococcal conjugate vaccines have recently been approved for use in infants in Canada.
  - The 10-valent pneumococcal conjugate vaccine (PCV10)[9] offers seroprotection against the original seven pneumococcal serotypes plus three additional serotypes: 1, 5, and 7F. The 10 serotypes are conjugated to three different proteins, one of which is protein D, which may provide protection against nontypeable *Haemophilus influenzae* (NTHi).[10]
  - The 13-valent pneumococcal conjugate vaccine Prevnar 13 (PCV13) provides the same seroprotection as PCV7 and contains the 10 serotypes in PCV10 plus three additional pneumococcal serotypes: 3, 6A, and 19A.[11]
- Immunization programs are determined at the province level in Canada. Quebec and Ontario previously transitioned from PCV7 to PCV10.
- PCV10 was originally approved with a 3+1 dosing schedule but was recently approved for a 2+1 dosing schedule in Europe.[12] It previously was used in Quebec with a 2+1 schedule.[9]
- As of January 2011, after Ontario and Quebec switched from PCV10 to PCV13, all provinces in Canada are using PCV13 in their immunization programs. Therefore, it is important to understand the value for money or cost-effectiveness of vaccine policies with these newer vaccines.

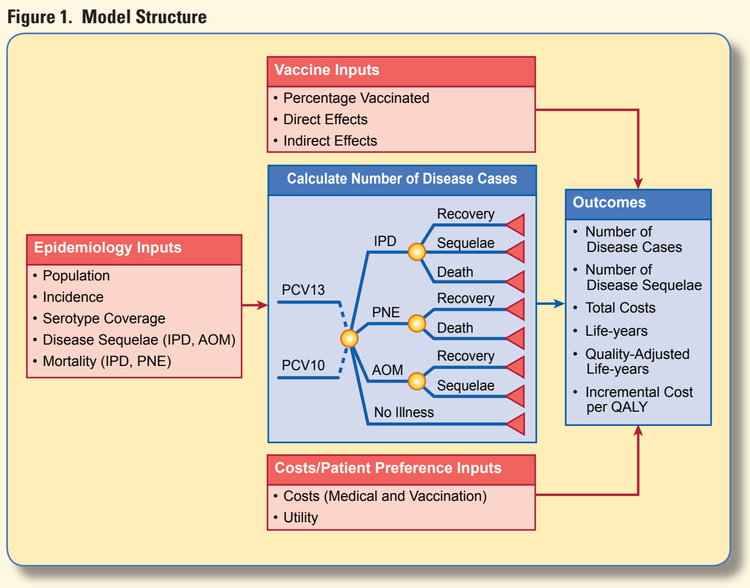
OBJECTIVE

- To compare costs and outcomes associated with the use of PCV13 compared with PCV10 across all provinces and territories in Canada, using a two-dose primary series followed by a booster dose at 12 to 15 months.

METHODS

- A decision-analytic model (Figure 1) was constructed to examine the costs and outcomes of vaccine policies that included PCV13 and PCV10 for vaccinating children against *Streptococcus pneumoniae*, which causes IPD (bacteremia and meningitis), PNE (hospitalized and ambulatory), and AOM (mild and moderate/severe).
- 34,108,000 individuals in the general Canadian population were examined.[13] Individuals from different age groups (0-2, 2-4, 5-17, 18-64, 65+ years) entered the model either vaccinated (91% of children < 2 years of age)[2] or not vaccinated.
- Individuals were followed over the remainder of their lifetimes, in which they were at risk for contracting IPD, PNE, or AOM based on their vaccination status.
  - Individuals contracting IPD had a risk of developing hearing loss (13%) and/or neurological impairment (7%).[14]
  - Individuals contracting PNE had a risk of dying if they were hospitalized.
  - Children who contracted moderate/severe AOM were at risk for requiring myringotomy (1.6%).[15]
- Costs and outcomes were presented from a Canadian health system perspective. Costs were not discounted and outcomes were discounted at 5%.[16]
- A base-case analysis was performed in which both direct and indirect effects were considered. A secondary analysis was performed in which only direct effects were considered.
- Sensitivity analyses were performed on a number of parameters.

Figure 1. Model Structure



Disease Incidence

- Incidence of pneumococcal disease (disease cases per 100,000) by age is presented in Table 1.

Serotype Coverage

- Serotype coverage for IPD for PCV10 and PCV13 was obtained from the National Centre for Streptococcus for the most current available year (2009). Isolates were collected from all Canadian territories (excluding Quebec) over the years (Table 1).
- PNE and AOM were considered from an all-cause perspective, because etiology is typically not determined for cases of mucosal disease. Thus, serotype coverage data were implicitly considered within vaccine effectiveness.

Table 1. Incidence and Serotype Coverage

Parameter	Age, Years				
	0-2	2-4	5-17	18-64	65+
Incidence (per 100,000)					
Bacteremia	14.77	10.62	6.74	43.67	87.07
Meningitis	0.52	0.37	0.24	1.54	3.07
Inpatient PNE	1,135.13	380.99	170.84	102.76	1,343.40
Outpatient PNE	874.77	460.69	514.63	55.35	63.31
Mild AOM	13,762.21	13,811.12	10,486.67	0.00	0.00
Moderate/severe AOM	2,147.86	2,155.49	1,636.65	0.00	0.00
Serotype coverage					
PCV10	0.18	0.23	0.26	0.28	0.22
PCV13	0.61	0.68	0.42	0.55	0.55

Sources: Incidence: Institut National de Sante Publique du Quebec (2010),[17] Morrow et al. (2007),[18] Nelson et al. (2008),[19] Petit et al. (2003),[20] De Wals et al. (2009)[21]; Serotype coverage: Personal communication from Gregory J Tyrell on March 21, 2011.

Mortality

- General mortality in individuals was assumed to be similar to that observed in the general Canadian population.[22]
- IPD-specific and inpatient PNE mortality was obtained from Scheifele et al. (2000)[23] and Jette et al. (2001).[24]
- Deaths due to outpatient PNE and AOM were assumed to not occur.

Direct Effects of Vaccines

- Direct effects for IPD in children younger than 2 years were for serotype-covered disease.
- Direct effects for PNE and AOM were for "all-cause" disease (disease caused by any pathogen).
- Due to the lack of data on direct effects for the newer vaccines, direct effects for PCV10 and PCV13 were calculated based on the direct effects demonstrated by PCV7 and the increase in the serotype coverage that PCV10 and PCV13 demonstrate over PCV7 (Table 2).

Indirect Effects

- Indirect effects in the presence of PCV10 and PCV13 have not yet been demonstrated. As a result, indirect effects were derived from indirect effects observed in the presence of PCV7 (Table 2) and the increase in serotype coverage that PCV10 and PCV13 demonstrate over PCV7.
- Indirect effects for individuals younger than 2 years were applied for invasive and noninvasive disease. For other age groups, indirect effects were applied only to invasive disease (exception: inpatient PNE age group 18-64 years).
- Given the results of the POET study, it is uncertain if PCV10 will generate indirect effects. The 11-valent investigational vaccine that preceded PCV10 had no statistically significant effect on pneumococcal nasopharyngeal carriage, and PCV10 has not demonstrated a consistent statistically significant reduction in nasopharyngeal carriage.[10,25-27] Therefore, in our base-case analysis, we assumed that PCV10 would not generate indirect effects.

Table 2. Direct and Indirect Effects

	Bacteremia	Meningitis	Inpatient PNE	Outpatient PNE	Mild AOM	Moderate/ Severe AOM
Direct effects						
PCV10	0.94	0.94	0.05	0.01	0.01	0.07
PCV13	0.94	0.94	0.19	0.04	0.05	0.11
Indirect effects						
PCV7						
0-2	0.68	0.68	0.07	0.16	0.21	0.15
3-4	0.68	0.68	0.00	0.00	0.00	0.00
5-17	0.39	0.39	0.00	0.00	0.00	0.00
18-64	0.47	0.47	0.26	0.00	0.00	0.00
65+	0.36	0.36	0.00	0.00	0.00	0.00

Sources: Direct effects: Adapted from Black et al. (2006),[28] Ray et al. (2006),[29] Black et al. (2002),[30] Fireman et al. (2003),[31] Prymula et al. (2006)[10]; Indirect effects: Ray et al. (2006),[29] Hansen et al. (2006),[32] Zhou et al. (2007).[33]

Costs

- Direct medical costs were assumed to include diagnostics, physician time, hospitalization, prescriptions, and over-the-counter medications as needed (Table 3).
- Costs were reported in 2010 Canadian dollars.
- Vaccine acquisition cost per dose was assumed to be $86.26 for PCV13. Acquisition cost per dose for PCV10 was assumed to be equivalent to PCV13.
- Administration cost per dose was estimated as $7.84.[34,35]

Table 3. Direct Medical Costs

Parameter	Age, Years				
	0-2	2-4	5-17	18-64	65+
Bacteremia	$10,578.71	$3,379.85	$9,768.95	$13,559.64	$11,913.26
Meningitis	$48,382.04	$24,615.09	$61,114.72	$22,409.11	$11,782.22
Inpatient PNE	$3,450.13	$2,149.73	$10,305.00	$9,606.02	$8,370.61
Outpatient PNE	$138.18	$69.09	$184.24	$126.66	$103.63
Mild AOM	$95.30	$47.65	$71.47	$0.00	$0.00
Moderate/severe AOM	$95.30	$47.65	$71.47	$0.00	$0.00

Sources: Morrow et al. (2007),[18] Statistics Canada (2011).[35]

Utilities

- General health utility (0.90) was obtained for the general Canadian population from the Canadian Community Health Survey.[36]
- Utility decrements due to neurological impairment and hearing loss were obtained from Morrow et al. (2007)[18] and were assumed to be 0.6 and 0.8, respectively.

RESULTS

Base-Case Analysis

- Use of PCV13 may prevent 44,504 more cases of disease than PCV10 in the overall Canadian population over a 1-year time horizon (Figure 2).
- Total direct medical costs, including the cost of the vaccine, may be reduced by $132.8 million when vaccinating with PCV13 compared with PCV10 (Table 4).
- Because PCV13 generated better outcomes (life-years, quality-adjusted life-years [QALYs], illness avoided, death avoided) while generating savings to the system, it was shown to dominate PCV10 in the incremental analysis.
- For each child vaccinated with PCV13 instead of PCV10, $305 may be saved by the health care system.

Figure 2. Base-Case Number of Disease Cases

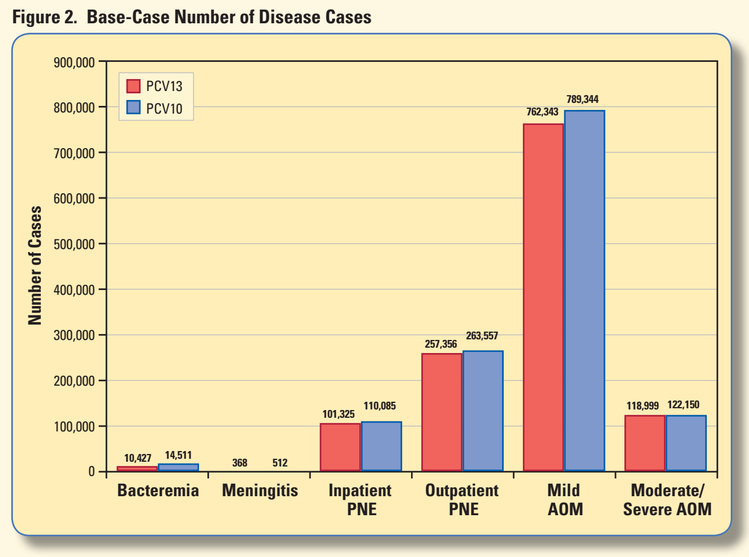


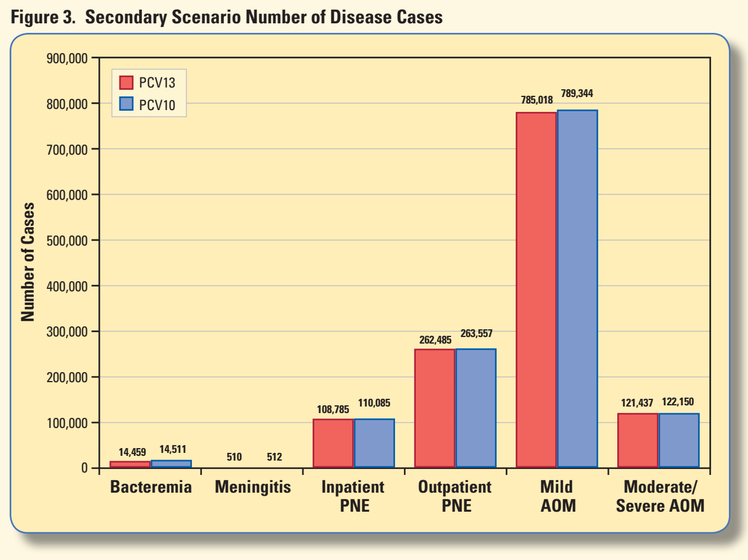
Table 4. Incremental Analysis

Outcome	Base-Case Scenario	Secondary Scenario
Total life-years	15,283	287.45
Total QALYs	13,828	257.70
Annual number of sequelae		
Myringotomy	–49	–11
Neurological impairment	–10.1	–0.1
Hearing loss	–18.7	–0.2
Death	–879.44	–13.97
Annual direct medical costs	–$132,823,511	–$5,759,017
Cost per QALY	PCV13 dominates PCV10	PCV13 dominates PCV10

Secondary Scenario Analysis

- Similar results were found in the secondary analysis.
- In this scenario, the use of PCV13 versus PCV10 would prevent 6,629 more cases of disease in the overall Canadian population and reduce costs by $5.7 million over a 1-year time horizon (Figure 3 and Table 4).
- When only direct effects were considered, PCV13 dominated from a cost-effectiveness perspective. For each child vaccinated with PCV13 instead of PCV10, $13 may be saved by the health care system.

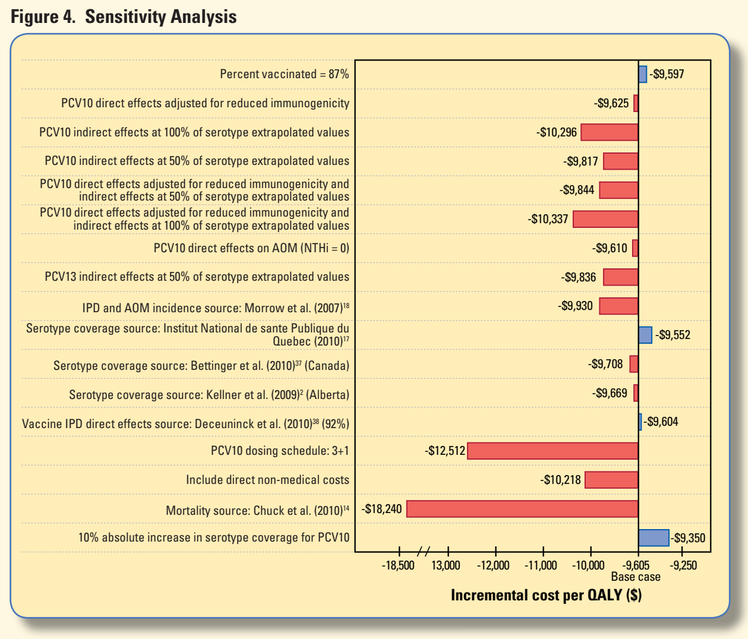
Figure 3. Secondary Scenario Number of Disease Cases



Sensitivity Analysis

- One-way and scenario analyses showed that changes in various parameters had little impact on results in that the use of PCV13 dominated the use of PCV10 in all analyses (Figure 4).

Figure 4. Sensitivity Analysis



CONCLUSIONS

- Use of PCV13 may be cost-saving compared with PCV10, given the most recently available epidemiology of disease and the potential effects of PCV10 and PCV13.

REFERENCES

Please see handout for a complete reference list.

CONTACT INFORMATION

Stephanie Earnshaw, PhD
Vice President, US Health Economics

RTI Health Solutions
200 Park Offices Drive
Research Triangle Park, NC 27709

Phone: +1.919.485.2730
Fax: +1.919.541.7222
E-mail: searnshaw@rti.org

Presented at: ISPOR 14th Annual European Congress
November 5-8, 2011
Madrid, Spain