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ORIGINAL RESEARCH ARTICLE

Value Added by the Prevnar 13 Childhood Immunization Program in Alberta, Canada (2010–2015)

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Abstract
Background *Streptococcus pneumoniae* is a pathogen causing acute respiratory infections, as well as meningitis and bacteremia. The province of Alberta, Canada, began vaccinating infants against seven *S. pneumoniae* serotypes in 2002 using Prevnar 7 (PCV7). However, a 13-valent conjugate vaccine (PCV13) was introduced in 2010 to address changes in the distribution of serotypes causing disease. PCV13 targets 13 serotypes including six additional serotypes to the previously adopted PCV7.
Objective In this study, we estimate the impact of the new PCV13 immunization program on the burden of disease and related healthcare costs in Alberta.
Methods Serotype-specific passive surveillance invasive pneumococcal disease (IPD) data were drawn from the Alberta Public Health Laboratory. These data were used to estimate average annual IPD incidence of the six additional serotypes included in PCV13 during the PCV7 era (2000–2009), and after the introduction of PCV13 (2011–2015). The difference in estimated cases pre-/post-PCV13 was used to estimate associated changes in direct health service costs.
Results Following the replacement of PCV7 with PCV13 in 2010, the number of cases of IPD caused by the additional serotypes contained in PCV13 has declined significantly across all ages. The expected number of IPD cases prevented annually is an estimated 1.6 per 100,000. Direct health service costs are expected to be averted as a result of the implementation of PCV13 universal vaccination in Alberta. Indirect benefits are experienced by ages >20 years as IPD incidence significantly declines following the PCV13 infant immunization in Alberta.
Conclusion The impact on direct healthcare costs of replacing PCV7 with PCV13 in Alberta's public immunization program are estimated to be CAN$3.5 million as of 2015.

Key Points

The distribution of *Streptococcus pneumoniae* serotypes causing invasive pneumococcal disease changed over time, following the introduction of Prevnar 7. As a result, value has been added by replacing Prevnar 7 with Prevnar 13 in Alberta's childhood immunization program.

Public immunization programs should be evaluated to inform policy makers of resulting changes in disease incidence and associated healthcare costs.

1 Introduction

Streptococcus pneumoniae is a pathogen causing acute respiratory infections, as well as meningitis and bacteremia. There is a high burden of disease attributable to *S. pneumoniae* in the form of invasive pneumococcal disease (IPD), and non-invasive pneumococcal disease (NIPD).

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Invasive disease can result in a range of clinical presentations, including invasive pneumonia, meningitis, or bacteremia; sequelae can include death. NIPD is less severe and generally presents as either acute otitis media (in children only) (AOM), or non-bacteremic pneumonia.

Research has shown that conjugate polysaccharide vaccines, administered to children, have been both clinically effective [1] and cost effective at reducing the cases of pneumococcal disease via direct and indirect protection [2, 3]. Consequently, in 2002, a seven-valent conjugate vaccine, Prevnar 7 (PCV7), was introduced to protect against serotypes 4, 6B, 9V, 14, 18C, 19F and 23F, in Alberta, Canada. However, within a few years of the introduction of PCV7, changes in the distribution of *S. pneumoniae* serotypes were observed [4, 5]. This phenomenon, termed serotype replacement, reflects an emergence or increase in the frequency of cases caused by non-vaccine serotypes following the introduction of PCV7. For example, serotypes 5 and 19A showed the most dramatic increases following PCV7 in Alberta, increasing 96 % from 0.1 per 2000 to 2.25 per 100,000 in 2008 [6].

A 13-valent conjugate vaccine (PCV13) was introduced in Alberta, Canada in 2010 to address observed changes in serotype distribution. PCV13 targets 13 serotypes including six additional serotypes (1, 3, 5, 6A, 7F, 19A) to the previously adopted PCV7. The purpose of this study is to estimate the added value of adopting PCV13 relative to PCV7 as a result of reduced health service resource use between 2010 when PCV13 was introduced and the present year, 2015.

The objective of this study is to estimate the added value of introducing PCV13 in the Alberta childhood immunization schedule over and above that gained as a result of PCV7 between the year of introduction (2010) and the current year (2015).The impact on health service resource use and costs will be estimated using real-world observational data. Given that 7 of the 13 serotypes were targeted by the previously administered PCV7, we estimated health service use and associated costs for the six new serotypes covered by PCV13 (1, 3, 5, 6A, 7F, 19A) between 2000 and 2015 based upon the observed and forecast change in vaccine serotypes following the introduction of PCV7.

2 Methods

A prospective population-based surveillance program has tracked the incidence of IPD by serotype in Alberta, Canada since 2000 [7]. Using this serotype-specific data, observed (2000–2013) and predicted (2014–2015) cases of IPD in the province were estimated, as well as the reduction in resulting health service costs.

2.1 IPD Surveillance Data and Forecast Data

The Canadian national case definition for IPD is isolation of a positive culture of *S. pneumoniae* from normally sterile body fluid, primarily blood or cerebrospinal fluid [8]. IPD is a notifiable health condition to Provincial Public Health Authorities in Alberta. This leads to all pneumococcal isolates from cases of IPD being forwarded to the Provincial Public Health Laboratory in Edmonton, Alberta for serotype analysis [7]. Details regarding the program are published elsewhere [7]. Data consisting of reported IPD cases by age, between 2000 and 2013, were obtained from the Provincial Public Health Laboratory and used in the present analysis. These data allow for identification of the seven serotypes targeted by PCV7, as well as the additional six serotypes included in PCV13, which will be referred to as 'incremental serotypes' for the remainder of this paper.

To examine the value added of PCV13 over and above PCV7, age-specific incidence and fatality rates of IPD in Alberta were estimated based on ascertained cases subdivided into seven categories (<2, 2–4, 5–9, 10–19, 20–64, 65+ years), using population data drawn from Statistics Canada, and [10].

Age-specific annual incidence rates of the incremental serotypes were estimated post-implementation based upon observed cases between 2010 and 2013. Due to the unavailability of data for 2014 and 2015, incidence rates for these additional six serotypes were forecasted based upon the trends observed in PCV7.[1]

Forecasts were made assuming the impact of PCV13 on burden of disease will follow the same trend as PCV7. As such, age-specific year-over-year percentage changes in PCV7 incidence between 2003 and 2007 were applied to incidence rates for corresponding years of vaccine introduction for the six additional serotypes included in PCV13 (year of vaccine introductions were matched (2002 and 2010), and each subsequent year was matched for the following 5 years).[2] The first observation used to predict incremental serotype incidence was the average age-specific incidence between 2009 and 2010. These forecasted incidence rates were validated by comparing predicted IPD cases between 2011 and 2013 to observed IPD cases in Alberta during this same time period.

[1] According to Hyndman and Athanasopoulus, it is best to use per-capita data rather than totals for data affected by population change. As a result, incidence rates were forecast instead of total annual cases [9].

[2] A number of functional forms were examined when analyzing the trend in PCV7 IPD incidence. However, each functional form and associated data transformation resulted in very similar predicted incremental serotype incidence and resulting costs. As a result, the simplest method assuming linear year-over-year declines in incidence was applied.

Table 1 Epidemiology and direct health service costs (2014 CAN$) [11]

	Age groups (years)					
	<2	2–4	5–9	10–19	20–64	65+
Distribution of invasive pneumococcal disease (IPD) by presenting diagnosis (%)						
Hospitalized pneumonia	74.00	74.00	88.20	62.40	66.90	81.50
Hospitalized bacteremia	14.30	14.30	6.70	24.80	26.30	15.00
Non-hospitalized bacteremia	8.90	8.90	4.10	9.60	5.10	2.90
Meningitis	2.50	2.50	1.00	3.20	1.70	0.60
Mortality (%)						
Hospitalized pneumonia	1	1	1	2	2	2
Bacteremia	2	2	2	2	15	31
Meningitis	7	7	7	7	28	28
Direct health service costs (CAN$)						
Meningitis	38,070	38,070	35,857	35,857	15,406	12,289
Hospitalized bacteremia	7124	7124	5576	5576	12,714	12,271
Non-hospitalized bacteremia	155	155	155	155	155	155
Hospitalized pneumonia	2920	2920	4690	7789	8289	8731

The IPD incidence rates were reported by presenting diagnosis, and calculated by applying the distributions of pneumococcal disease states previously calculated by Morrow et al. [11] to observed IPD annual age-specific incidence rates in Alberta (Table 1). Case fatality rates were drawn from this same study [11] and applied to Alberta IPD age-specific observed incidence rates.

2.2 Costing Model

Using actual (2011–2013) IPD surveillance data and predicted IPD incidence (2014–2015), an economic model was developed to compare the direct medical costs averted resulting from replacing PCV7 with PCV13. The changes in incidence of *S. pneumoniae* disease caused by the six additional (incremental) serotypes and associated health service resource use were estimated.

We adopted a direct payer perspective, including costs related to direct medical services associated with IPD for incremental serotypes. Changes in costs resulting from direct and indirect vaccine protection were taken into account from 2011 to 2015. There is no cost difference between PCV7 and PCV13, and therefore is not included in this analysis. The changes in frequency of IPD and associated cost impact following the introduction of Prevnar 13 are estimated using Microsoft Excel 2012.

2.2.1 Method for Calculation of Direct Medical Costs Averted as a Result of PCV13

The number of cases averted were estimated as the difference between the average incremental serotype incidence during the PCV7 era (pre-PCV13 between 2000 and 2009), and following the replacement of PCV7 with PCV13 (post-PCV13 between 2011and 2015). Because of differences in medical service costs across disease state and age, cases averted were calculated according to age-specific rates of IPD caused by incremental serotypes and presenting diagnosis, as well as IPD-related mortality.

Direct health service costs were then applied to age-specific numbers of IPD cases by presenting diagnosis (pneumonia, bacteremia, meningitis), and number of deaths from incremental serotypes.[3] The estimated cost associated with a case fatality is CAN$34,789, taken from a study on end-of-life care for patients suffering from infection [12]. All costs were adjusted to reflect 2014 Canadian dollars using the Canadian Consumer Price Index, and 2015 cost estimates are discounted using a 3 % discount rate.

As with a previous publication [6], the costs averted were estimated by first calculating the difference between the average annual incidence of incremental serotypes while PCV7 was being administered (pre-PCV13, between 2000 and 2009), and following the replacement of PCV7 with PCV13 (post-PCV13, between 2011 and 2015), by presenting diagnosis. We excluded the first year of the vaccination program (2010) to allow for a wash-out period. Second, the difference in estimated annual incidence was then multiplied by the number of Albertan's in each age category to estimate the average number of cases pre- and post-PCV13 implementation. Cases averted were calculated as the difference between the estimated average

[3] Direct health service costs include the cost of hospitalization and outpatient costs. Costs of health care vary across age and disease presentations. The direct costs accounted for in this analysis include health service costs resulting from hospitalization for IPD outpatient care, as well as any subsequent hospitalizations. These costs of treatment and sequelae for survivors of IPD are taken from Morrow et al. (Table 1) [11].

number of incremental serotype cases pre- and post-PCV13. July 2013 population data, which represent the midpoint between 2011 and 2015, were used to generate an estimate of the total cases pre- and post-PCV13 implementation. Third, to calculate the annual total PCV13 costs averted, we multiplied the estimated total cases averted in Alberta per year by the average cost per case. The average cost per case was previously estimated by Morrow et al. and was used in the present study (Table 1) [11].

2.3 Direct and Indirect Vaccine Protection

In 2010, at the time of universal PCV13 vaccination in Alberta, only children reaching 2 months of age were targeted. Children older than 2 months were not offered the vaccine unless they belonged to a high-risk group [13]. In this study, the measure of direct vaccine protection against IPD is the difference between annual incidence before and after vaccine introduction by presenting diagnosis for children vaccinated.

Indirect protection is assumed to apply to the non-vaccinated population as a result of the decreased circulation of the disease. This is evidenced by a decrease in annual incidence of IPD following the vaccine introduction [4, 5, 14]. Indirect protection was estimated as the difference between the annual incidence of unvaccinated people across the 5-year post-vaccination program (ages 10 years and older), by presenting diagnosis, pre- and post-PCV13. The youngest age considered for evidence of indirect protection was 10 years, since by 2015 children with direct protection will be between the ages of 5 and 9 years.

3 Results

3.1 Health Impacts

The estimated health resource use and associated costs are based upon the underlying annual incidence rates of *S. pneumoniae* caused by serotypes contained in PCV13. The annual incidence per 100,000 caused by PCV7 serotypes in Alberta decreased from a high of roughly 7.5 in 2000 to approximately 0.78 in 2010 (Fig. 2). The annual incidence of incremental serotypes, on the other hand, increased from 1.8 per 100,000 in 2000 to 3.4 in the year of vaccine introduction (2010). There was an outbreak of serotypes 5 and 19A in Alberta in 2006 and 2007.

The total incidence of incremental vaccine serotypes from 2011 to 2015 will have declined by an estimated 1.6 cases by 2015, assuming PCV13 follows a similar trend to PCV7 following vaccine introduction (Fig. 1). Estimated age-specific IPD incidence can be found in Table 2.

The health impacts of serotypes 5 and 19A are expected to be significantly reduced by 2015 as a result of PCV13 (Fig. 2).

Children aged <4 years, and adults aged 20 years and older had the highest incidence of IPD caused by incremental serotypes before vaccine introduction (Table 2).[4] Direct protection is expected to result in a nearly complete decline in incidence for children younger than 4 years. Those aged 10–19 years had low incidence prior to vaccine introduction, and therefore are not expected to decline as dramatically as other ages. Adults are expected to see significant declines from 2.8 cases per 100,000 in 2010 to 1.4 cases per 100,000 5 years after the vaccine is introduced. Overall, we predict that between 2011 and 2015 PCV13 serotypes will decrease by 69 % from 3.43 per 100,000 in 2010 to 1.6 per 100,000 in 2015. The annual number of IPD cases averted per 100,000, caused by incremental serotypes, ranges from 0.3 in ages 10–19 years to 6.6 in ages <2 years.

3.2 Direct Service Cost Impacts

The direct health service costs averted by the health ministry as a result of the observed declines in incremental serotypes are expected to amount to over CAN$699,000 per year in Alberta, or CAN$3.5 million over the 5 years after PCV13 immunization program implementation (Table 3). The greatest savings in health service costs are found in the adult age categories. Specifically, on net, those aged 20–64 years averted costs of CAN$546,000 annually, or an estimated CAN$2.7 million over the 5 years post-vaccination. The next most significant savings were the elderly with indirect protection resulting in CAN$101,000 saved annually, or CAN$502,000 over the 5 years post-vaccination. Direct protection resulted in CAN$51,000 saved annually for ages ≤19 years, amounting to CAN$255,000 over the 5 years post-vaccination.

The costs attributed to serotype 5 and 19A account for 68 % of the costs averted as a result of the vaccine (CAN$2.4 million) (Table 4). The benefits are mostly accrued to those aged 20–64 years (CAN$2.3 million), who tend to experience the greatest burden of disease caused by these two serotypes.

4 Discussion

In this study, we analyzed the expected cost impact to the health system from replacing PCV7 with PCV13 in Alberta's childhood vaccination strategy. As such, we

[4] Detailed incidence disaggregated by disease state available upon request.

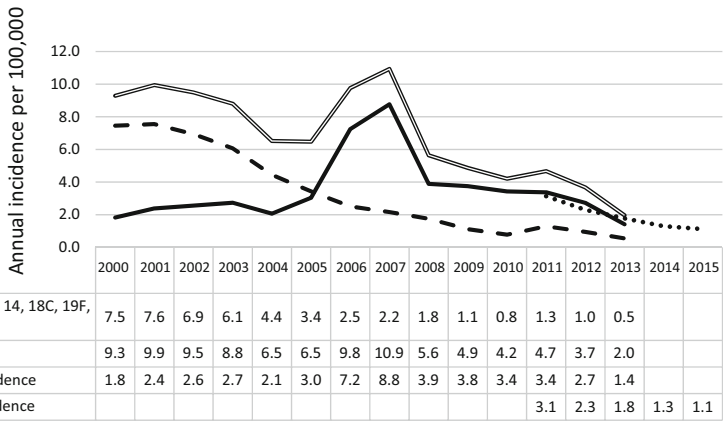

Fig. 1 Incidence of IPD caused by incremental vaccine serotypes. *IPD* invasive pneumococcal disease, *PCV7* Prevnar 7, a seven-valent conjugate vaccine

Table 2 Incremental serotype (1, 3, 5, 6A, 7F, 19A) invasive pneumococcal disease (IPD) incidence per 100,000

Year	Age groups (years)						
	<2	2–4	5–9	10–19	20–64	65+	Total
PCV7							
2000	0.0	0.9	0.9	0.2	2.1	4.1	1.8
2001	9.3	6.9	2.4	1.3	1.5	6.1	2.4
2002	9.3	3.4	0.5	0.9	2.1	7.5	2.6
2003	10.4	4.3	1.0	1.1	2.6	4.9	2.7
2004	10.0	2.6	0.0	0.0	1.5	7.8	2.1
2005	8.4	1.7	1.0	1.1	3.0	6.4	3.0
2006	11.6	5.6	1.0	1.7	8.9	7.6	7.2
2007	16.4	7.0	0.5	1.7	10.9	8.3	8.8
2008	13.4	3.0	0.5	0.2	4.1	7.0	3.9
2009	16.9	3.7	3.3	0.4	3.1	8.9	3.8
PCV13							
2010	12.8	5.6	2.3	0.0	2.8	8.9	3.4
2011	5.7	6.7	2.4	0.3	3.2	7.4	3.0
2012	2.2	4.2	2.8	0.3	2.4	6.9	2.2
2013	1.9	2.5	0.8	0.0	2.0	6.3	1.7
2014[a]	0.8	0.9	3.2	0.1	1.8	2.7	1.2
2015[a]	0.4	0.6	0.8	0.2	1.4	3.7	1.1
Annual average cases averted (2000–2009 vs 2011–2015)	6.6	1.2	−0.2	0.3	2.0	2.1	1.6
Annual average lives saved (2000–2009 vs 2011–2015)	0.08	0.01	0.00	0.01	0.11	0.13	0.09
Percentage change (2009–2010 vs 2015)	−97 %	−86 %	−71 %	−23 %	−51 %	−58 %	−69 %

[a] Forecasted results

estimated the total value added as a result of exchanging PCV7 for PCV13 to be CAN$3.5 million as of this year (2015). This estimate of costs averted is based upon observed declines in incremental serotype incidence (between 2011 and 2013), as well as predicted declines in 2014 and 2015.

Between 2011 and 2015 we estimate PCV13 incremental serotypes to have decreased by 69 % from 3.6 per 100,000 in 2009–2010 to 1.1 per 100,000 in 2015. The number of IPD cases averted is an estimated 1.6 per 100,000, or 65 cases in Alberta per year (Table 2). Ages <2 years are expected to experience upwards of 6.7 IPD cases averted per 100,000, while ages 20 years and older are predicted to experience between 2.0 and 2.1 IPD cases averted per 100,000.

While explicit assumptions regarding efficacy of PCV13 are not made in this analysis, it is expected that PCV13 will be as effective as PCV7; it has been shown that immunogenic response to PCV13 vaccine is comparable to PCV7 [15]. As a result, we assume that the decline in the

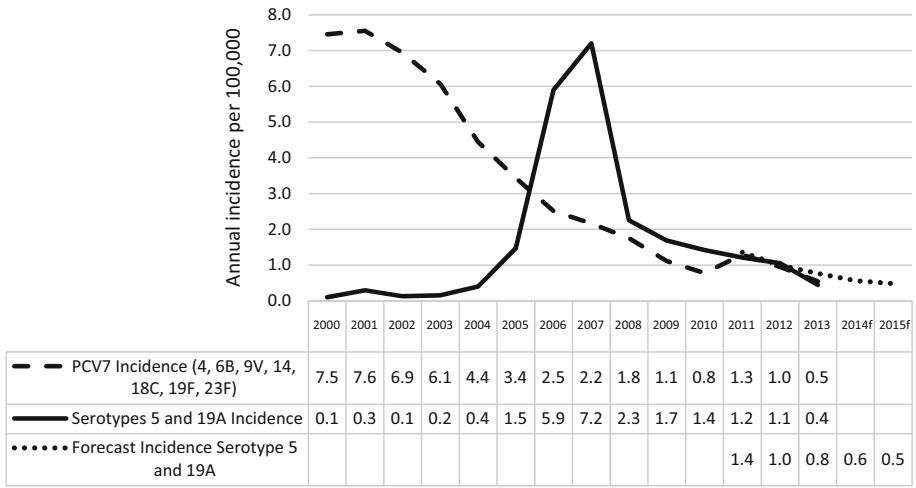

Fig. 2 Incidence of IPD caused by serotypes 5 and 19A. *f* Forecasted, *IPD* invasive pneumococcal disease, *PCV7* Prevnar 7, a seven-valent conjugate vaccine

Table 3 Health service costs averted ($CAN) (2000–2009 vs 2011–2015) for incremental serotypes (1, 3, 5, 6A, 7F, 19A)

	Age groups (years)						
	<2	2–4	5–9	10–19	20–64	65+	Total
Annual average cost pre-PCV13 vaccine (2000–2009)	$50,714	$27,868	$14,014	$31,763	$1,080,470	$324,038	$1,528,866
Annual average cost post-PCV13 (2011–2015)	$18,966	$19,042	$15,796	$19,192	$534,187	$223,052	$830,234
Annual difference in average cost pre/post-PCV13	$31,748	$8,826	($1782)	$12,571	$546,283	$100,986	$698,632
Total cumulative cost averted post-PCV13	$157,814	$43,872	($8859)	$62,488	$2,715,505	$501,990	$3,472,810

Values in parentheses represent negative values

Table 4 Predicted health service costs averted (CAN$) (2000–2009 vs 2011–2015) for serotypes 5, 19A

	Age groups (years)						
	<2	2–4	5–9	10–19	20–64	65+	Total
Annual average cost pre-PCV13 vaccine (2000-2009)	$26,974	$12,818	$4849	$13,290	$640,383	$79,888	$778,201
Annual average cost post-PCV13 (2011–2015)	$9242	$11,049	$6795	$4729	$180,482	$84,593	$296,891
Annual difference in average cost pre/post-PCV13	$17,732	$1769	($1946)	$8561	$459,901	($4705)	$481,311
Total cumulative cost averted post-PCV13 (5 years)	$88,142	$8793	($9672)	$42,554	$2,286,109	($23,390)	$2,392,535

Values in parentheses represent negative values

incidence of incremental serotypes will follow a similar trend to the seven serotypes targeted by PCV7. These declines are in part due to high efficacy, in addition to strong indirect protection (herd effects). Declines in incidence following PCV7 were experienced not only by infants immunized (direct protection), but also by populations not immunized (indirect protection). Direct protection as a result of PCV13 is anticipated to result in CAN$19,000 saved annually for ages <10 years, amounting to CAN$100,000 over the 5 years post-vaccination. Those aged 20–64 years as well as those 65+ years are found to have benefited from the PCV13 childhood immunization program through indirect protection in the same way that was experienced as a result of PCV7. Specifically, cases averted in ages 20–64 years are expected to decline from 2.8 in 2010 to 1.4 in 2015, amounting to an estimated CAN$2.7 million averted over the 5 years post-vaccination. Similarly, it is estimated that incidence rates for those aged 65 years and older will decline from 8.9 per 100,000 in 2010 to 3.7 per 100,000 in 2015, resulting in CAN$502,000 in direct medical costs averted by 2015.

Serotypes 5 and 19A were found to significantly increase following PCV7, from 0.1 per 100,000 in 2000 to 1.7 per 100,000 in 2009. An outbreak in 2006 and 2007 resulted in rates as high as 5.9 per 100,000 [7]. This outbreak mostly affected children aged <2 years, with incidence of 11 per 100,000, as well as adults aged 20–64 years with 9.4 cases per 100,000. The inclusion of these serotypes in PCV13 is predicted to result in significant declines in incidence, and resulting costs. Of the costs

averted due to PCV13, an estimated CAN$2.4 million is attributed to serotypes 5 and 19A. Those ages that experienced the most significant burden of illness from these serotypes are predicted to experience the most significant declines in incidence and related direct health service costs. In particular, incidence in ages 20–64 years is predicted to decline from 0.9 in 2010 to 0.53 in 2015, and result in costs averted of more than CAN$2.3 million over the 5 years. Ages 65 years and above are not predicted to experience the same cost reductions despite predicted declines from 4.3 to 1.1 per 100,000 between 2010 and 2015. This is due to very similar average incidence over the two time periods, as there was <1 case per 100,000 each of the years prior to 2006. The same is true for ages 5–9 years as a spike in cases of 19A in 2009 and 2010 resulted in a higher baseline incidence rate used for forecasting. Meanwhile, there was <1 case per 100,000 for each of the years between 2002 and 2008.

Streptococcus pneumoniae comprises more than 90 serotypes, as characterized by select features exhibited within the bacteria's cell wall. These bacteria are known to be very pliant and can easily modify their external structure, and therefore change serotype. Selection pressures such as the presence of antibiotics (antibiotic resistance) and vaccine coverage are believed to cause a shift in pneumococcal serotypes [16]. However, little is known about 'normal' colonization (i.e., without any selection pressures), or about serotype replacement as a result of the conjugate vaccine in the absence of antibiotics [16]. The microbiology regarding *S. pneumoniae* and how PCV7 may have led to the replacement (increased frequency) of serotypes is not well understood. The current body of evidence concerning the association between PCV7 and serotype replacement has been generated through observational studies; numerous surveillance programs internationally have reported serotype replacement following PCV7 [17]. However, these increases in IPD cases were found to be less than the reductions in IPD due to PCV7 [17]. In general, it was found that changes in the distribution of serotypes causing disease were evident within 3 years [17, 18]. We find slight increases in IPD caused by non-PCV13 serotypes; however, the increase is roughly half of what was observed 3 years after the introduction of PCV7. In a previous study, we estimated that post-PCV7 serotype replacement would result in a 30 % reduction in costs averted as a result of the vaccine [6]. Given that serotype replacement post-PCV13 is expected to be less than post-PCV7, our cost estimates may overstate the costs averted by at most CAN$1million, resulting in a minimum total health service cost averted of CAN$2.5 million.

Results from this study should be considered with regard for study limitations. First, future serotype replacement was excluded from the present analysis because it is uncertain which serotypes will increase as a result of PCV13. The science regarding the causality and predictability of the change in distribution of serotypes is not well developed, and therefore excluded. The costs estimated in this study may overestimate the actual costs averted if serotype replacement does occur in the future. Second, there is some uncertainty concerning the estimated changes in incidence for ages 5–9 years and 10–19 years because of small incidence rates and associated variation year over year. For example, for ages 5–9 years, an increase from two cases to four cases in the 2 years preceding the new PCV13 immunization program resulted in the average incidence (and related cost) post-vaccination being larger than pre-vaccination. The results for these age groups should be interpreted with caution. Third, our 2013 observed incidence data is incomplete, as we have only obtained data until the end of November. As a result, the actual data for 2013 understates the true incidence for this year. However, using forecast 2013 incidence rates in this analysis changed the estimated costs averted by less than CAN$65,000 annually, suggesting that potential missed cases from December 2013 would have little impact on the results. Fourth, disease incidence may be affected by multiple factors, including not only the immunization program, but also demographic changes, or trends in the variety and virulence of the infectious disease itself. Lastly, NIPD has not been included in this study due to the lack of incidence data on cases of NIPD.

5 Conclusion

The direct health costs averted from replacing PCV7 with PCV13 in Alberta are estimated to amount to CAN$3.5 million between 2011 and 2015 as a result of the additional six serotypes (1, 3, 5, 6A, 7F, 19A) included in PCV13.

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Compliance with Ethical Standards

The hypothetical model developed in this study was based upon anonymous publicly available invasive pneumococcal data.

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