



UNIVERSITY OF CALGARY

# Pneumococcal Disease Trends in the Post-Vaccine Era in Calgary, Canada: An Interrupted Time Series Analysis

LJ Ricketson MSc, JD Kellner MD, FRCPC, for the CASPER Investigators

## Background

Invasive pneumococcal disease (IPD) most commonly affects children under 2, adults over 65-years-old, and people who have immunocompromising conditions or other underlying illnesses.

Vaccination development is difficult due to the number of pneumococcal serotypes (STs) and the ability of pneumococcus to share genetic material and evolve.

In the province of Alberta, the 7-valent pneumococcal protein conjugate vaccine (PCV7) was introduced in a 4-dose (2, 4, 6, 18 mos) universal infant program for all children born July 1, 2002 onwards. It was replaced with a 3-dose (2, 4, 12 mos) 13-valent vaccine (PCV13) universal infant program in July 2010.

We examined IPD trends from 1998 to mid-2019 (pre-COVID-19) to look at trends in overall IPD and IPD caused by vaccine serotypes following introduction of PCV7 and then PCV13.

## Methods

The Calgary Area *Streptococcus pneumoniae* Epidemiology Research team (CASPER) has been collecting data on all IPD cases presenting to Calgary hospitals and healthcare centres since January 1998.

We examined trends in IPD using an interrupted time series model examining the incidence of IPD per quarter (January to March, April to June, July to September, October to December) from 1998 to mid-2019 (pre-COVID). The time indicators correspond to quarters over this time period (e.g. January-March 1998=1998 Q1).

This model allows for a change in trend at points of intervention: the introduction of PCV7 in August 2002 and the introduction of PCV13 in July 2010.

For the PCV7 serotype model we restricted the analysis to cases of IPD caused by serotypes represented in the PCV7 vaccine (STs 4, 6B, 9V, 14, 18C, 19F, 23F).

For the pediatric model we restricted the analysis to IPD occurring in children under 18 years of age and for the adult model we restricted to only adults  $\geq 18$  years of age.

For the overall model we included all cases from 1998 to mid-2019 in all ages of people presenting to a Calgary healthcare center with IPD.

For the PCV13-only serotype model we restricted the analysis to cases of IPD caused by serotypes represented in the PCV13 but not in the PCV7 (STs 1, 3, 5, 6A, 7F, 19A).

For the PCV13 model, we included all serotypes in the PCV13 vaccine (STs 1, 3, 4, 5, 6A, 6B, 7F, 9V, 14, 18C, 19A, 19F, 23F).

The models were adjusted for autocorrelation of residuals.

## Results

IPD due to PCV7 serotypes showed a significant decline in the post-PCV7 era with a post-intervention decline of 0.04 cases per 100,000 people per quarter (95% CI -0.05 to -0.03) (P-value<0.001) (Figure 1).

After PCV7 was introduced, cases of IPD caused by any serotype in children <18 years showed non-significant trends (Figure 2).

For adult disease, the decline post-PCV7 was not significant, but there was a significant increase in disease post-PCV13 (0.03 cases per 100,000 people per quarter; 95%CI: 0.02 to 0.05)(P<0.001)(Figure 3).

For overall IPD (all serotypes, all ages) the quarterly incidence trend did not show significant change post-PCV7 but was showing a significant increase post-PCV13 (0.03 cases per 100,000 people per quarter; 95% CI: 0.01 to 0.04 (P<0.001)(Figure 4).

The rate of IPD caused by the PCV13-only serotypes trends did not show significant change in all ages in either vaccine period (Figure 5).

Trends for IPD caused by PCV13-serotypes did not show significant change in trends for all ages in either vaccine period (Figure 6).

There were increases in ST19A, ST3, ST7F disease in the post-PCV7 period as well as an outbreak of ST5 and ST8 in adults in 2006/2007.

ST3 and ST19A continue to circulate and cause IPD.

An outbreak of ST4 occurred between 2014 and 2018, causing IPD in adults, especially adults who are homeless (DOI: 10.3390/microorganisms9102116; 10.1093/ofid/ofz362).

## Results

Figure 1. Trends in PCV7-ST IPD for All Ages in Calgary, 1998 to mid-2019 (PCV7 introduced in Sep 2002 & PCV13 introduced in Aug 2010)

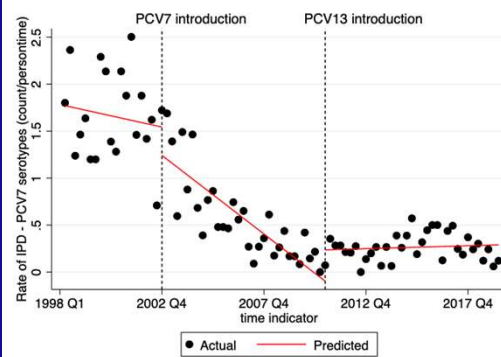


Figure 2. Trends in All ST IPD in Children (<18 years) in Calgary, 1998 to mid-2019

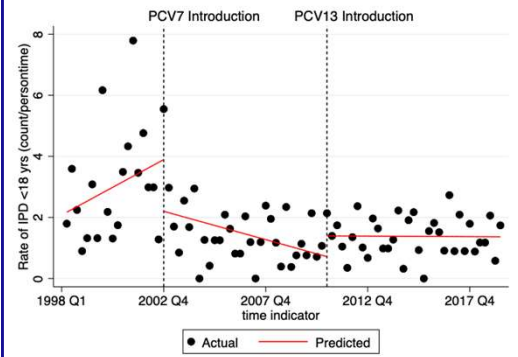


Figure 3. Trends in All ST IPD in Adults ( $\geq 18$  years) in Calgary, 1998 to mid-2019

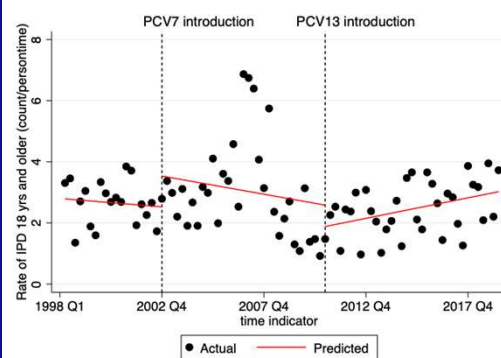


Figure 4. Trends in All ST IPD in All Ages in Calgary, 1998 to mid-2019

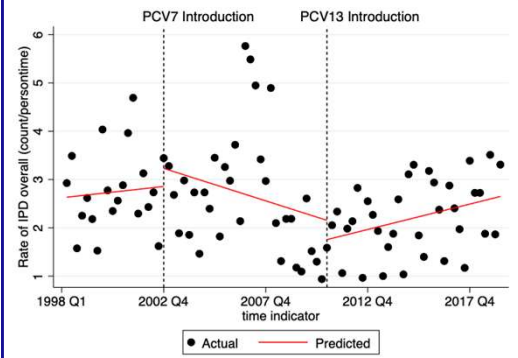


Figure 5. Trends in PCV13-Only ST (1, 3, 5, 6A, 7F, 19A) IPD in All Ages in Calgary, 1998 to mid-2019

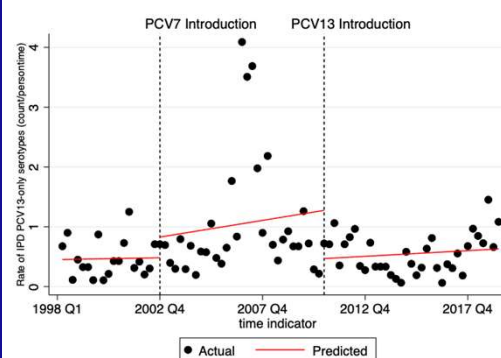
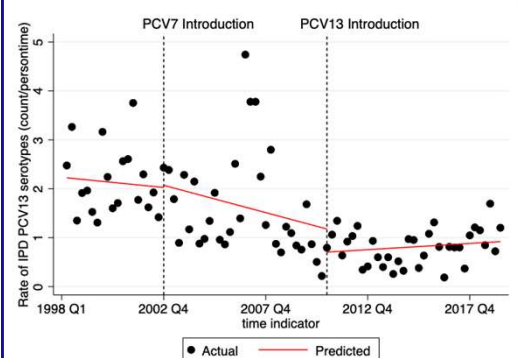


Figure 6. Trends in PCV13-ST IPD in All Ages in Calgary, 1998 to mid-2019



## Conclusions

PCV7 serotype IPD has declined, but overall IPD has not declined significantly in the PCV7/13-vaccine era.

Prior to the COVID-19 pandemic, overall and adult IPD showed an increasing trend. Changes in IPD incidence related to the COVID-19 pandemic, make it impossible to examine trends past 2019 at this time.

PCV13 serotypes, and non-vaccine serotypes, continue to cause IPD.

After PCV13 introduction there was no significant change in disease rate overall, however, there was a statistically significant increase in adult IPD, which may be partially driven by an outbreak of serotype 4 in adults that began in 2014 and ended in 2018.

An adult vaccination program including PCVs may improve IPD prevention because outbreaks of IPD in adults continue to occur.

This interrupted time series analysis included multiple time points with consistently measured data over 20 years, which improves statistical power. In contrast, the number of cases at each time point was sometimes low, which reduces statistical power.

After 2019, ITSA analysis of PCV impact would be confounded by the COVID-19 pandemic (See Kellner et al. Abstract #8, Poster Board 388).

## Acknowledgements

The authors would like to acknowledge the contributions of CASPER research staff (Shannon Pyra, Nicole McMillan and Joslyn Gray). We would also like to acknowledge Tracie Lloyd from Alberta Precision Laboratories-Calgary Laboratory Services, and the APL-Public Health Laboratory for isolate serotyping. We thank Payton Sayers for assistance with preparation of the poster.

The CASPER project and this work is funded in part by an unrestricted grant from Pfizer Canada.

Corresponding author: Dr. James D. Kellner, Jim.Kellner@ahs.ca

Access this poster online:



ACHIEVERESEARCH