Pediatric invasive pneumococcal disease (IPD) in Ontario late after the introduction of a routine infant PCV13 program

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INTRODUCTION

An infant 13-valent conjugate vaccine (PCV13) program was introduced in Ontario, Canada in November 2010. PCV15 and PCV20 replaced PCV13 in December 2023 (Table 1). We assessed the epidemiology of invasive pneumococcal disease (IPD) among children(<18 years old) in the period from 2014 to 2023.

Table 1: Pediatric pneumococcal vaccination programs in Ontario, Canada.

Month/Year	Authorization/Program funding
2001-2009	• PCV7 authorized in 2001 and publicly funded in June 2005 • PCV10 replaced PCV7 in November 2009 • PCV13 authorized in December 2009
November 2010	• PCV13 publicly funded 3 dose vaccination program. 3 doses at 2, 4, 12 months • High risk children should get 4 doses (2, 4, 6 and 12-15 months)
2022-2024	• PCV15 authorized in July 2022, PCV20 in July 2023 • PCV15 (healthy children) and PCV20 (high-risk children) publicly funded in Ontario in December 2023 • PCV21 authorized in July 20024

OBJECTIVES

- To describe the incidence and characteristics of pediatric IPD in the period 2014-2023
- To summarize distribution of individual serotypes from IPD isolates in 2014-2023
- To describe the occurrence of IPD due to vaccine covered serotypes in vaccine-eligible children to better understand potential gaps in PCV programs

METHODS

Since 1995, TIBDN has performed population-based surveillance for IPD in Metropolitan Toronto and Peel Region (population 4.6 million in 2023).

- IPD is defined as illness associated with a sterile site culture yielding *S. pneumoniae*.
- Clinical and demographic information is collected by chart review and patient/physician interview.
- Isolates are serotyped at Canada's National Microbiology Laboratory.
- Population data are obtained from Statistics Canada.
- Pneumococcal vaccination history is recorded based on immunization records provided by parents and/or physicians. A dose of vaccine is counted if it was received at least 14 days prior to the positive culture date.

Box 1: Serotypes included in pneumococcal conjugate vaccines.

PCV7	4	6B	9V	14	18C	19F	23F																				
PCV13	4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A														
PCV15	4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A	22F	33F												
PCV20	4	6B	9V	14	18C	19F	23F	1	5	7F	3	6A	19A	22F	33F	8	10A	11A	12F	15BC							
PCV21										7F	3	6A	19A	22F	33F	8	10A	11A	12F	15BC	9N	15A	16F	17F	20	23A	23B	24F	31	35B

RESULTS

From 2014-2023, 440 pediatric (age<18y) IPD cases occurred, with clinical data available for 412 (94%), serotyping for 425 (97%).

Characteristics of children with IPD (Table 2)

- 308/440 (70%) were under 5 years of age. 155/412 (38%) had an underlying condition predisposing to IPD, and 82/412 (20%) were immunocompromised.
- Underlying conditions were more common in 5-17 year-olds than 0-4 year-olds
  - Any: 52.4% vs 31.2%, *P*<.001; Immunocompromised 36.3% vs 12.8%, *P*<.001.
- The most common underlying conditions were: leukemia, asthma, congenital cardiac disease, organ transplantation, conditions that impair ability to clear respiratory secretions.
- 45 (10%) cases required ICU admission, 29 (6.6%) had meningitis, 8 (1.8%) died.

IPD incidence (Figure 1)

- In 2022 and 2023 IPD incidence was 13.3 per 100,000/year among children aged 0-4 years, and 2.5 per 100,000/year among 5-17 year-olds, similar to 2014-2019.
- Although PCV13-type IPD appeared to be decreasing before the pandemic, the declines were not statistically significant, and PCV13 IPD persists in both age groups in 2022 and 2023.

Serotype distribution (Figure 2)

- Of the 425 cases with serotype available 104 (24.5%) were due to isolates of PCV13 STs, 56 (13.2%) PCV15/not13 STs, 122 (28.7%) PCV20/not15 STs, 92 (21.7%) PCV21/not 20 STs and 51 (12%) due to STs not included in any PCV.
- The most common serotypes were 15B/C, 22F, 19A and 3.

Proportion of isolates with serotypes included in PCVs (Figure 3)

- Between 2014-2019 and 2022-2023:
  - The proportion of isolates of STs included in PCV20 increased from 64% to 78%, *P*=.01.
  - The proportion of isolates of STs included in PCV21 did not change (85% vs 86%, *P*=.64)
  - STs in PCV20/not PCV21 increased significantly from 2.1 to 6.8% (*P*=.03),there were no significant trends on other ST groups (Figure 3B).
- In 2022-2023, 45% of isolates were of STs included in PCV15, 78% isolates were of STs included in PCV20, and 86% were of STs included in PCV21.

PCV vaccination status (Table 3)

- Of 425 cases of pediatric IPD with isolates of known STs, 376 were eligible for PCV7, PCV10 or PCV13 and 313/376 had vaccination data available: 77.6% (243/313) were completely vaccinated (N=206) or were up-to-date for age (N=37), 15% (47/313) had ≥1 missed dose, and 7.3% (23/313) were unvaccinated.
- The proportion of children with complete/up-to-date vaccination was 70% (47/67) among vaccine-eligible children with infection due to vaccine covered serotypes, compared to 80% (196/246) of vaccine eligible children who were infected with non-vaccine strains (*P*=0.1).

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RESULTS

Table 2: Characteristics of children with IPD, TIBDN, 2014-2023

	0-4 years N=288	5-17 years N=124	All N=412	P-value
Sex at birth, female	116 (40%)	51 (41%)	167 (40.5%)	0.87
Clinical presentation				
Bacteremic pneumonia	110 (38%)	59 (48%)	169 (41%)	0.20
Primary bacteremia	132 (46%)	43 (35%)	175 (43%)	
Meningitis	19 (6.6%)	10 (8.1%)	29 (7.0%)	
Other	27 (9.4%)	12 (9.7%)	39 (9.5%)	
At least one underlying illness[1]	90 (31%)	65 (52%)	155 (38%)	<0.001
Asthma	17 (5.9%)	14 (11%)	31 (7.5%)	
Cardiac	18 (6.2%)	3 (2.4%)	21 (5.1%)	
Lung	6 (2.1%)	3 (2.4%)	9 (2.2%)	
Condition that increases the risk of aspiration	12 (4.2%)	4 (3.2%)	16 (3.9%)	
Renal	6 (2.1%)	7 (5.6%)	13 (3.2%)	
Trisomy 21	7 (2.4%)	1 (0.8%)	8 (1.9%)	
Other[2]	9 (3.1%)	4 (3.2)	13 (3.2)	
Immunocompromised	37 (13%)	45 (36%)	82 (20%)	<0.001
Leukemia	14 (4.9%)	16 (13%)	30 (7.3%)	
Organ transplantation	6 (2.1%)	11 (8.9%)	17 (4.1%)	
Sickle cell disease	5 (1.7%)	6 (4.8%)	11 (2.7%)	
Nephrotic syndrome	4 (1.4%)	3 (2.4%)	7 (1.7%)	
Solid organ cancer on chemotherapy	1 (0.3%)	6 (4.8%)	7 (1.7%)	
Other immunocompromised[3]	6 (2.1%)	9 (7.3%)	15 (3.6%)	
Hospitalized	257 (89%)	120 (97%)	377 (92%)	0.01
Required ICU admission	28 (9.7%)	17 (14%)	45 (11%)	0.23
Died	4 (1.4%)	4 (3.2%)	8 (2.0%)	0.10

[1] Underlying illness predisposing to IPD includes conditions per NACI recommendations, as well conditions such as prematurity, metabolic diseases.
[2] Liver disease (N=4), Metabolic disease (N=4), diabetis mellitus (N=2), prematurity (N=2), CSF leak (N=1)
[3] Lymphoma (N=1), other hemoglobinopathy (N=1), Chronic renal failure (N=2), Lupus (N=3), other autoimmune (N=2), asplenia (N=3),congenital immunodeficiency (N=3)

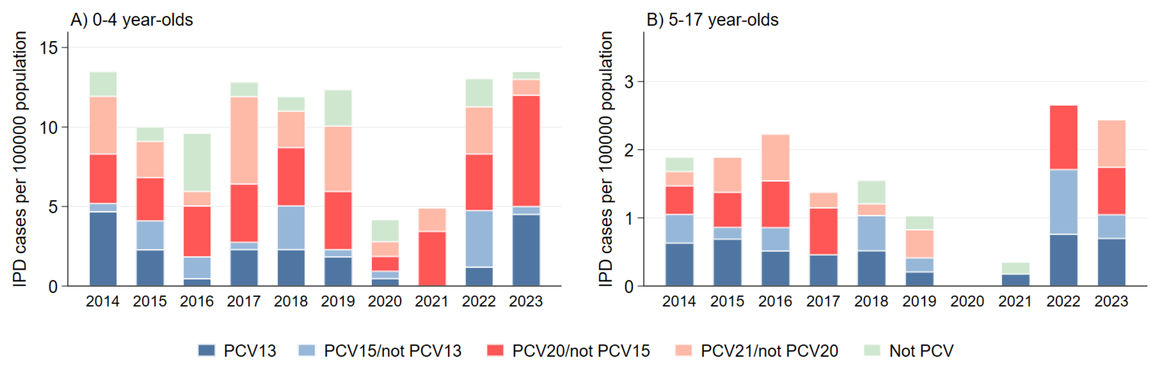

Figure 1: Annual IPD incidence by PCV serotype groups, 2014-2023. A) 0-4 year-olds, B) 5-17 year-olds.

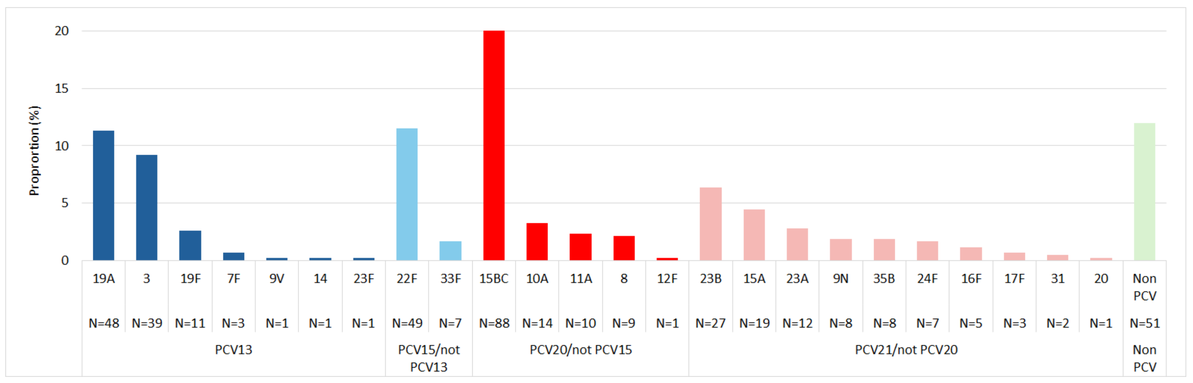

Figure 2: Serotype distribution of isolates causing IPD in children, TIBDN 2014-2023.

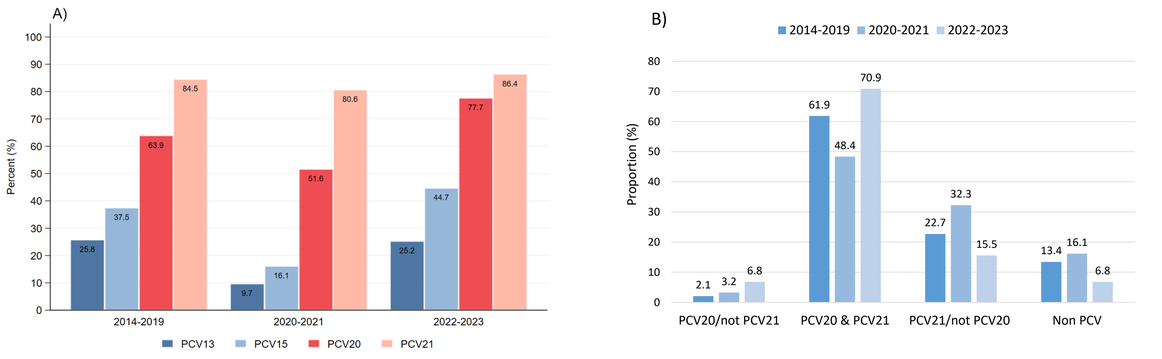

Figure 3: A) Proportion of IPD isolates with serotypes included in PCV13, PCV15, PCV20 and PCV21. B) Proportion of isolates with serotypes included/not included in PCV20 and PCV21.

Table 3: PCV vaccination status among children with IPD, TIBDN, 2014-2023

	IPD due to vaccine covered STs			IPD due to other serotypes		
	0-4 years N=66	5-17 years N=38	All N=104	0-4 years N=233	5-17 years N=88	All N=321
Vaccination status[1]						
Vaccination complete or up-to-date for age	37	10	47	155	41	196
Not vaccinated	7	3	10	8	5	13
Incomplete vaccination	7	3	10	28	9	37
Not eligible for relevant vaccine	10	19	29	5	15	20
Unknown vaccination status	5	3	8	37	18	55
Percent with complete/up-to-date vaccination[2]	73%	63%	70%	81%	75%	80%

[1] *Complete vaccination:* received at least three PCV doses, with at least one dose received after 12 months of age, or two PCV doses with both received after 12 months of age; *Up-to-date:* PCV doses were up to date for age but vaccination not complete ; *Incomplete:* at least 1 PCV dose received but not up-to-date for age; *Unvaccinated:* Eligible for PCV but no PCV dose received; *Unknown:* Eligible for PCV but detailed vaccination history is not available. Children were eligible for a vaccine based on their age and underlying illness relative to the introduction of particular vaccines.
[2] Proportion among eligible and those with known vaccination history

CONCLUSION

Post PCV13 implementation, overall IPD incidence has stabilized, with increased disease due to PCV15 and PCV20 STs; some PCV13 disease persists. Disease in 2022/3 may reflect a rebound from the pandemic, or the new normal for IPD. Higher-valency vaccines should significantly reduce IPD, particularly in younger children.