

# Effectiveness of three pneumococcal conjugate vaccines to prevent invasive pneumococcal disease in Quebec, Canada.

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# Disclosure Statement



- I have no affiliation (financial or otherwise) with a pharmaceutical, medical device or communications organization.

# Implementation of PCV Program in Quebec



October 2002:

- PCV-7 offered to high-risk infants and children < 5 yrs old (4 doses)

December 2004:

- PCV-7 offered to low-risk infants (3 doses, + catch-up < 5 year-old)

June-August 2009:

- switch from PCV-7 to PCV10 (PHiD-CV) (no catch-up)

January 2011:

- switch from PCV10 to PCV-13 (no catch-up)

PCV coverage (2 years of age)<sup>1</sup>

- At least 1 dose : 97%
- 3 doses : 84% (2006) to 93% (2012)

# Objective



Evaluation of the effectiveness of the three PCVs sequentially used in the context of a 2+1 doses recommendation during the period 2005-2013

# Methods

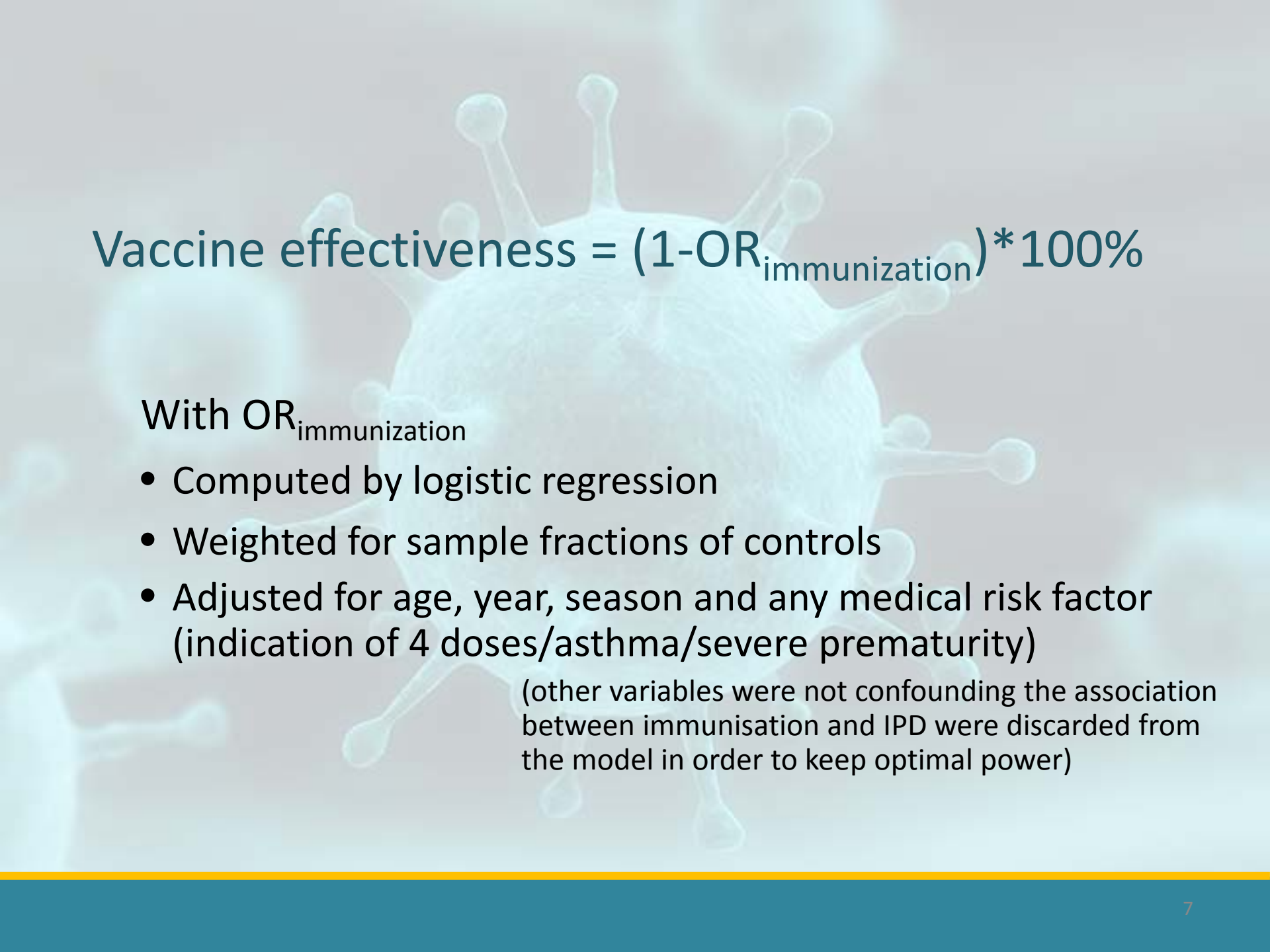
- **Frequency matched case-control study**
  - Province of Québec, Nunavik excluded, 2005-2013
  - Children 2 months to 4 years old
  - Phone survey
    - Tobacco exposure, day care, breastfeeding, season, influenza immunization, asthma, high risk medical conditions (= indications for a 4<sup>th</sup> dose), number of children and adults in the household, mother's education, household income, ethnicity, region
  - + immunization records check in medical files with parent's written authorization

## • Cases :

- IPD confirmed by culture/PCR from normally sterile site sample
- Notified and recruited by Public Health authorities (IPD = reportable disease)
- Reference date = date of sampling for culture.

## • Controls

- Random age and year-stratified sample of the Quebec Health Insurance Registry (RAMQ) database
  - Monthly fixed number of participants,
  - $\approx 4$  participants for each expected case
- Reference date = date of interview (or the 15th of the month).


$$\text{Vaccine effectiveness} = (1 - \text{OR}_{\text{immunization}}) * 100\%$$

With  $\text{OR}_{\text{immunization}}$

- Computed by logistic regression
- Weighted for sample fractions of controls
- Adjusted for age, year, season and any medical risk factor (indication of 4 doses/asthma/severe prematurity)

(other variables were not confounding the association between immunisation and IPD were discarded from the model in order to keep optimal power)

# Results



- 889 eligible IPD cases 2005-2013
  - 689 recruited by public health authorities
  - 667 interviewed
  - 516 (58% of those eligible) returned written authorization to check immunization records
- 3,356 randomly selected controls.
  - 2,613 interviewed
  - 1,767 (53% of those eligible) returned written authorization to check immunization records



# Vaccine effectiveness ( $\geq 1$ dose)

IPD Serotypes	Cases number			PCV-7	PCV-10	PCV-13
<b>Any serotype</b>	Total	516	V+ cases	305	34	44
			VE	<b>50%</b>	<b>72%</b>	<b>66%</b>
	V-	83	95%CI	29 to 64%	46 to 85%	29 to 83%
<b>PCV7 included + 6A (4,6B,9V,14,18C,19F,23F)</b>	Total	73	V+ cases	23	1	0
			VE	<b>90%</b>	<b>96%</b>	<b>ND</b>
	V-	49	95%CI	82 to 95%	50 to 100%	
<b>PCV10 incl. + 6A (+1,5F,7F)</b>	Total	118	V+ cases	60	2	0
			VE	<b>78%</b>	<b>97%</b>	<b>ND</b>
	V-	54	95%CI	63 to 86%	84 to 99%	
<b>PCV13 included (+3,6A,19A)</b>	Total	310	V+ cases	193	17	10
			VE	<b>63%</b>	<b>84%</b>	<b>86%</b>
	V-	71	95%CI	45 to 74%	65 to 93%	62 to 95%

VE computed by logistic regression model weighted for sampling fraction of controls and adjusted for age, year, season and underlying medical conditions including asthma and severe prematurity.

ND = Not Determined as no case was observed in vaccinated children and no controls vaccinated in the same strata.

## Vaccine effectiveness ( $\geq 1$ dose)

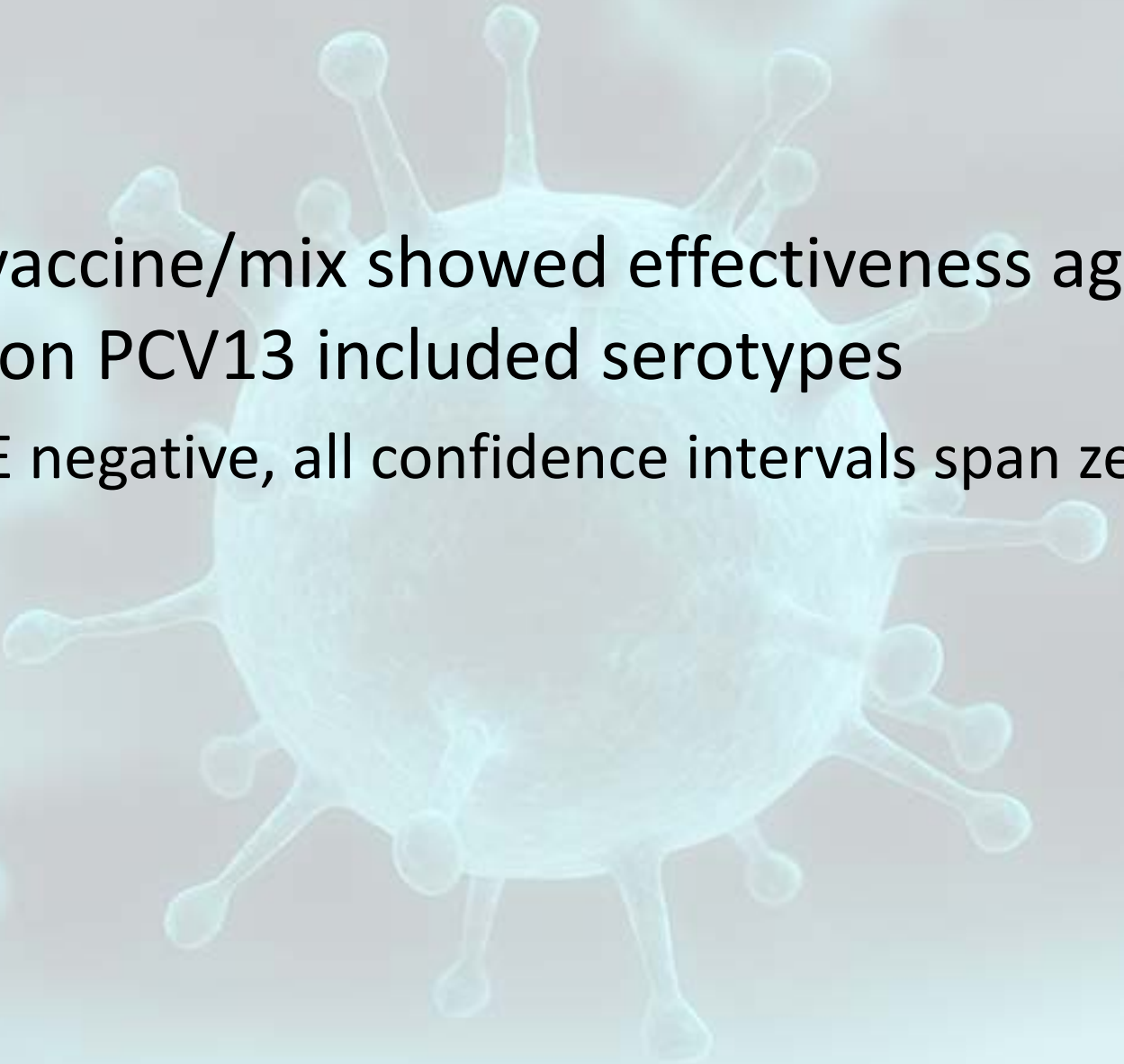
IPD Serotypes	Cases number			PCV-7	PCV-10	PCV-13
Serotype 19A	Total	167	V+ cases	113	13	9
	V-	16	VE	<b>42%</b>	<b>71%</b>	<b>74%</b>
			95%CI	-9 to 69%	24 to 89%	11 to 92%
Serotype 7F	Total	38	V+ cases	30	1	0
	V-	5	VE	<b>15%</b>	<b>93%</b>	<b>ND</b>
			95%CI	-161 to 72	23 to 99%	

VE computed by logistic regression model weighted for sampling fraction of controls and adjusted for age, year, season and underlying medical conditions including asthma and severe prematurity.

ND = Not Determined as no case was observed in vaccinated children and no controls vaccinated in the same strata.

## VPC10, VPC13 and MIXED SCHEDULE, ≥2 doses

IPD Serotypes	Cases number			PCV-10	PCV-10/13	PCV-13
Any serotype	Total	516	V+ cases	26	16	41
	V-	83	VE	<b>75%</b>	<b>66%</b>	<b>65%</b>
			95%CI	<b>51 to 87%</b>	<b>23 to 85%</b>	<b>29 to 83%</b>
Serotype 19A	Total	167	V+ cases	11	3	9
	V-	16	VE	<b>71%</b>	<b>78%</b>	<b>68%</b>
			95%CI	<b>16 to 90%</b>	<b>2 to 95%</b>	<b>-13 to 91%</b>
PCV13 included	Total	310	V+ cases	12	3	9
	V-	71	VE	<b>85%</b>	<b>89%</b>	<b>85%</b>
			95%CI	<b>66 to 94%</b>	<b>58 to 97%</b>	<b>55 to 94%</b>

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- No vaccine/mix showed effectiveness against all non PCV13 included serotypes
    - VE negative, all confidence intervals span zero

# 19A cases in children immunized with PCV10 or PCV13 in Quebec

- **PCV10: 13 cases (2009-2012)**
  - in children without any risk factor
  - after 1st dose : 2 cases, age 3 and 4 months
  - after 2<sup>nd</sup> dose : 7 cases, age 5 to 13 months old
  - after 3rd dose : 4 cases, age 16 to 32 months
- **PCV13: 9 cases (2011-2013)**
  - in children without any risk factor
  - after 2<sup>nd</sup> dose : 9 cases, at age 9 to 12 month-old
    - before the booster dose could be administered

# PCVs effectiveness comparison in other studies

## Comparison of 3 PCVs effectiveness against all IPD (VE $\geq 1$ dose)

Vaccine	Serotype	Quebec (2+1)	Others (3+1)
PCV-7	all	<b>50% (29 to 64)</b>	<b>72% (65 to 78)<sup>1</sup></b>
PCV-10	all	<b>72% (46 to 85)</b>	<b>65% (11 to 86)<sup>3</sup></b>
PCV-13	all	<b>66% (29 to 83)</b>	<b>59% (49-70)<sup>6</sup></b>

# PCVs effectiveness comparison in other studies

## Comparison of 3 PCVs effectiveness against included serotypes (VE $\geq 1$ dose)

Vaccine	Serotype	Quebec 2+1	Others 2+/1	Others 3+1
PCV-7	7 incl.	<b>90%(82-100)</b>		<b>96%(93-98)/ /81%(57-92) <sup>1</sup></b>
PCV-10	10 incl.	<b>97%(84-99)</b>	<b>92% (58-100) <sup>2</sup></b>	<b>100 %(83-100) <sup>2</sup> 84 %(66-92) <sup>4</sup> 100% (74-100) <sup>3</sup></b>
PCV-13	13 incl.	<b>86% (62 -95)</b>	<b>75% (58-84) <sup>5</sup></b>	<b>89 %(79-94) <sup>6</sup></b>

## Comparison of 3 PCVs effectiveness against 19A serotype in different studies (VE $\geq 1$ dose)

Vaccine	Serotype	Quebec 2+1	Others 2+/1	Others 3+1
PCV-7	19A	<b>42%(-9-69)</b>		<b>26%(-45-62)<sup>1</sup></b>
PCV-10	19A	<b>71%(24-89)</b>		<b>82% (11-96)<sup>4</sup></b>
PCV-13	19A	<b>74%(11-92)</b>	<b>67 %(33-84) <sup>5</sup></b>	<b>90% (76-96)<sup>6</sup></b>





- **Mixed schedule PCV10/PCV13**

- Similar protection as compared with a PCV10-only or a PCV13-only schedule
- May be a promising cost-effective avenue

# Limitations

- Case-control study
  - Baseline IPD risk may be different in vaccinated and unvaccinated children.
  - Unmeasured confounders / residual confounding
  - Only 58% of eligible IPD cases fully participated
- Limited power
  - Population :  $\approx 80,000$  births per year
  - Truncation of the observation on December 31st 2013
    - » Long-term VE estimates unavailable yet for PCV13

# Conclusion



- PCV10 and PCV13 seem to be more effective than PCV7
- Cross-protection against 19A ensured by PCV10
- No difference in protection was seen between a PCV10-only, a PCV13-only, or a mixed PCV10+PCV13 schedule.