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Prevalence of pertactin-deficient *Bordetella pertussis* isolates in Ontario, Canada from 2009 – 2017

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Disclosure Statement

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

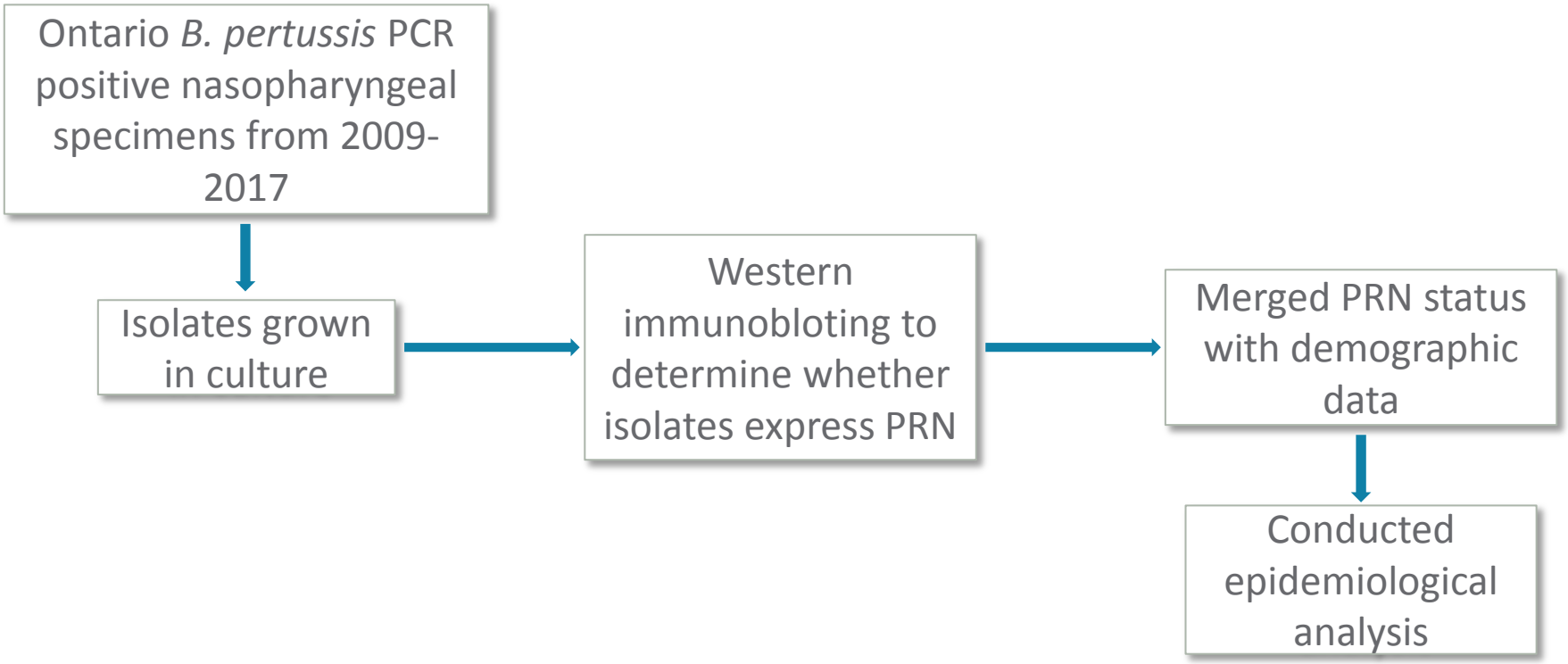
Background

- Since the introduction of acellular pertussis vaccines *B. pertussis* strains have emerged that do not express pertactin (PRN)
- Canada introduced acellular pertussis vaccine in 1997
- The proportion of PRN negative strains dramatically increased from 2011, coinciding with a global pertussis resurgence
- PRN is a component of the acellular pertussis vaccine
  - Virulence factor that plays a role in adherence
  - Possible vaccine selection pressure?
  - Vaccinated individuals have a higher likelihood of infection with PRN negative strains
  - PRN negative strains are fitter than PRN positive strains in vaccinated mice

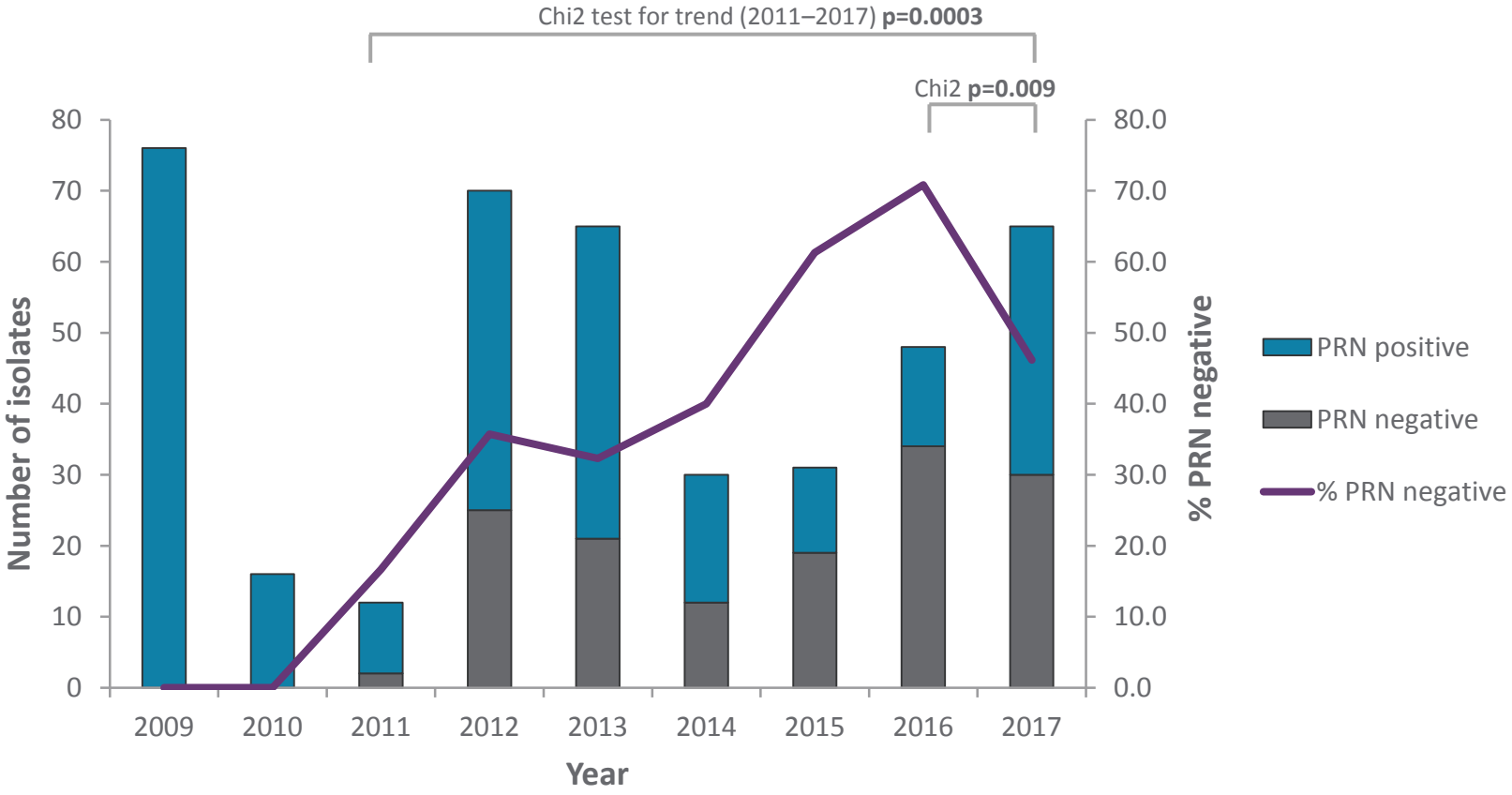
Martin et al., CID 2015; Safarachi et al., Vaccine 2015; Hegerle et al., Vaccine 2014

Objective and Methods

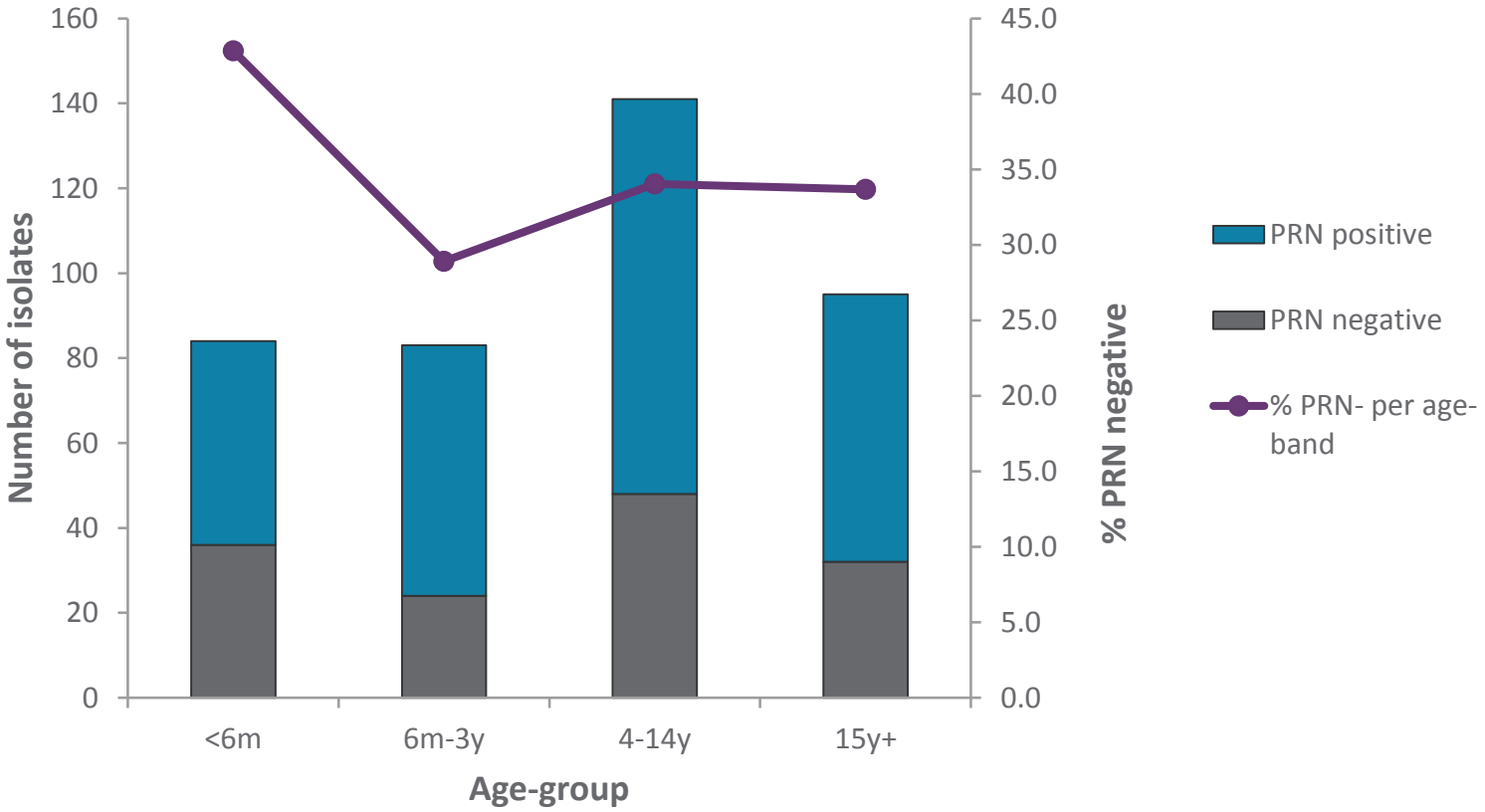
<u>Objective:</u> To measure trends in the prevalence of PRN negative strains in Ontario overall and by demographic characteristics



PRN expression in Ontario by year 2009-2017 (N=413)

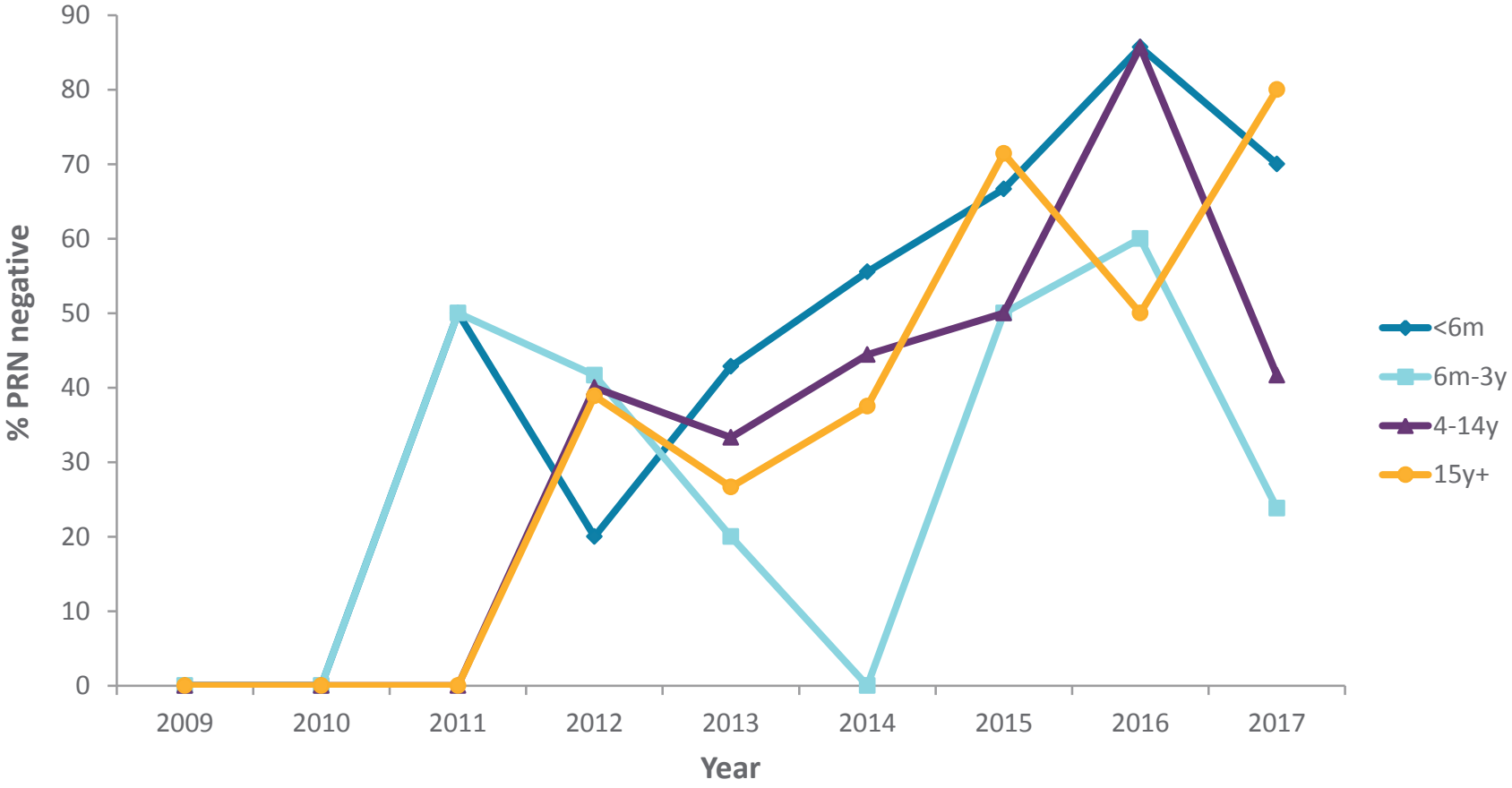


PRN expression in Ontario by age-group 2009-2017 (n=403)



The proportion of PRN negative isolates does not differ significantly by age-group (Pearson's chi-square p=0.29)

Proportion of PRN- isolates in Ontario
by year and age-group



Association between age-band, year and PRN expression using logistic regression

Variable	Odds ratio for PRN negative strain (OR)			
	Crude OR	95% CI	aOR*	95% CI
Age				
<6 months	1.0 (ref)	--	1.0 (ref)	--
6 months-3 years	0.54	0.29, 1.03	**0.39**	**0.19, 0.83**
4-14 years	0.69	0.40, 1.20	0.73	0.39, 1.39
15 years+	0.68	0.37, 1.24	0.76	0.38, 1.53
Year				
2009	0	0, infinity	0	0, infinity
2010	0	0, infinity	0	0, infinity
2011	1.0 (ref)	--	1.0 (ref)	--
2012	2.78	0.56, 13.69	2.78	0.56, 13.79
2013	2.33	0.47, 11.61	2.30	0.46, 11.56
2014	3.33	0.62, 17.97	3.18	0.58, 17.32
2015	**7.92**	**1.47, 42.54**	**7.46**	**1.37, 40.61**
2016	**11.43**	**2.21, 59.09**	**13.31**	**2.53, 70.05**
2017	4.29	0.87, 21.11	4.85	0.97, 24.22

*Odds ratios adjusted for age and year

PRN expression in Ontario by vaccine eligibility 2009-2017

Excluding infants <6 months (n=248)

PRN expression	Whole-cell primed (born <1997)	Acellular primed (born ≥1997)	Chi-square p-value
PRN- isolates	26	78	0.70
PRN+ isolates	33	111	
Total	**59**	**189**	

Excluding infants <2 months (n=286)

PRN expression	Whole-cell primed (born <1997)	Acellular primed (born ≥1997)	Chi-square p-value
PRN- isolates	26	99	0.95
PRN+ isolates	33	128	
Total	**59**	**227**	

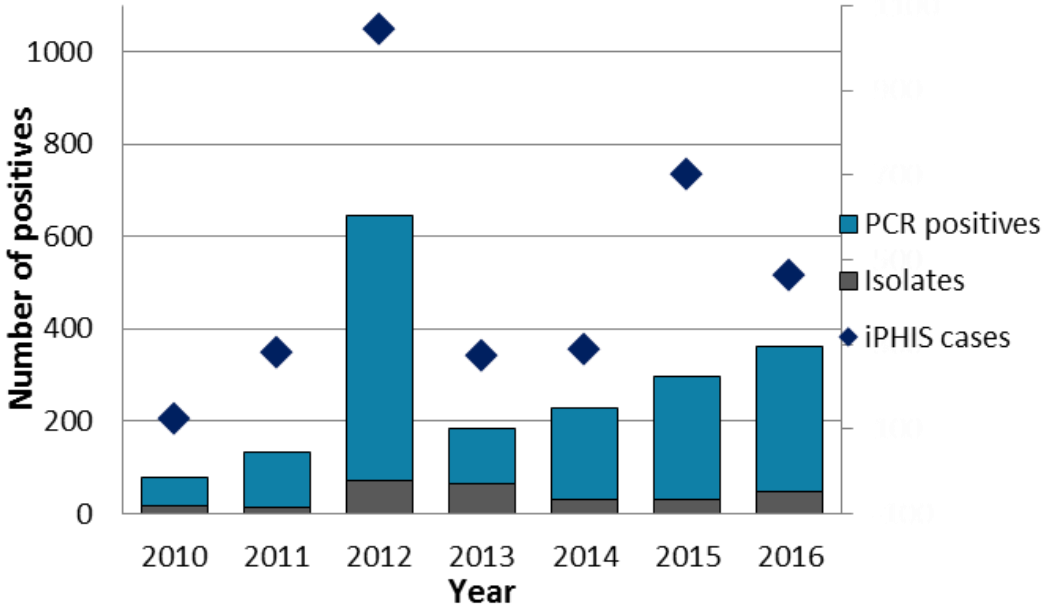
Discussion

- This is the first Canadian study to characterize PRN expression epidemiologically
- Increase in PRN negative isolates from 2011, decrease in 2017
  - Different than US pattern, similar to Japan (decrease since 2014)
- PRN deficiency was not associated with vaccine eligibility
- Decreased odds of PRN deficiency for those 6 months-3 years compared to those <6 months
    - This age-group is recently vaccinated, VE should be high
    - Is higher VE protective against PRN negative strains?
    - Perhaps study isolates are from unvaccinated children?

Martin et al., CID 2015

Limitations

- Limited sample size
  - ~18% of PCR positive lab specimens
  - Many more cases reported to public health
  - Substantial underreporting of pertussis in Ontario
- Ecological
  - We do not know which of the cases are vaccinated



Crowcroft et al., PLOS ONE 2018

Future directions and conclusions

- Further studies, including whole-genome sequencing would enhance our understanding of the evolution of PRN negative isolates
- Larger studies that include vaccination status are required to understand the implications of PRN- isolates on vaccine effectiveness

Thank you!

Public Health Ontario

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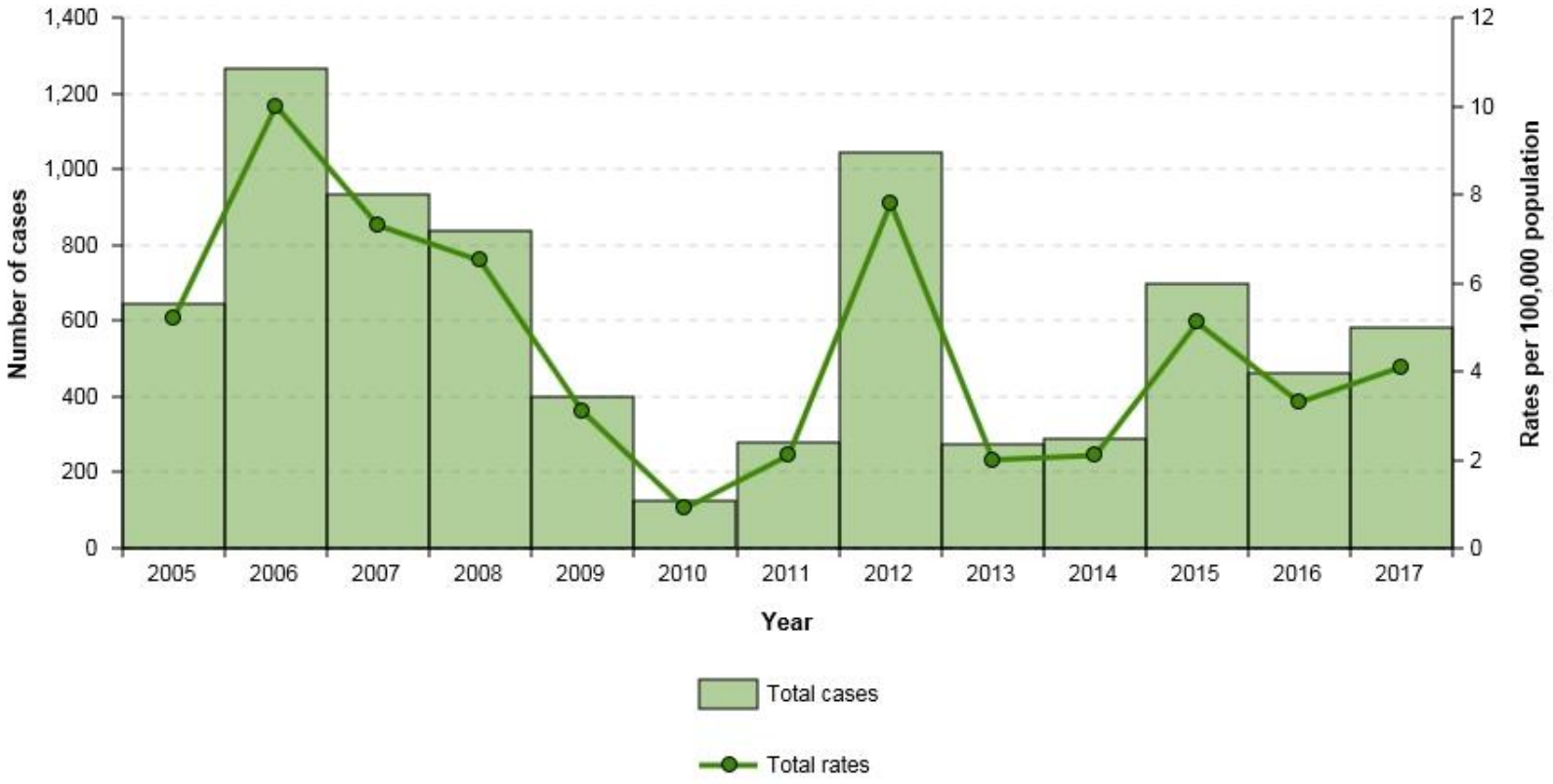
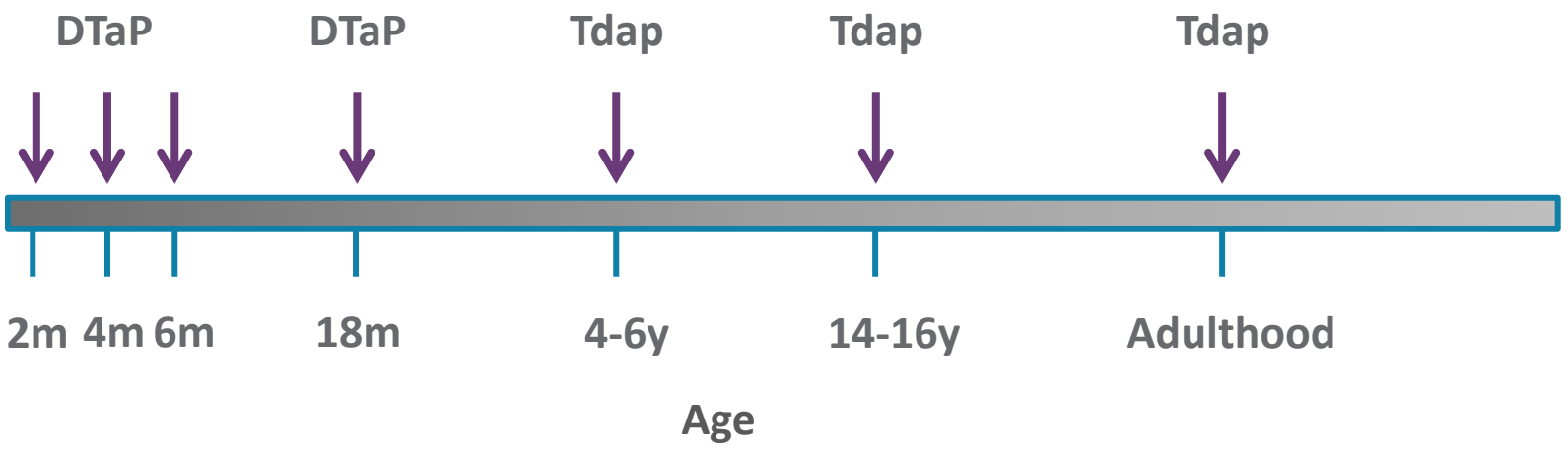
Pertussis in Ontario, 2005 - 2017



Source: https://www.publichealthontario.ca/en/DataAndAnalytics/pages/rdto.aspx#/42

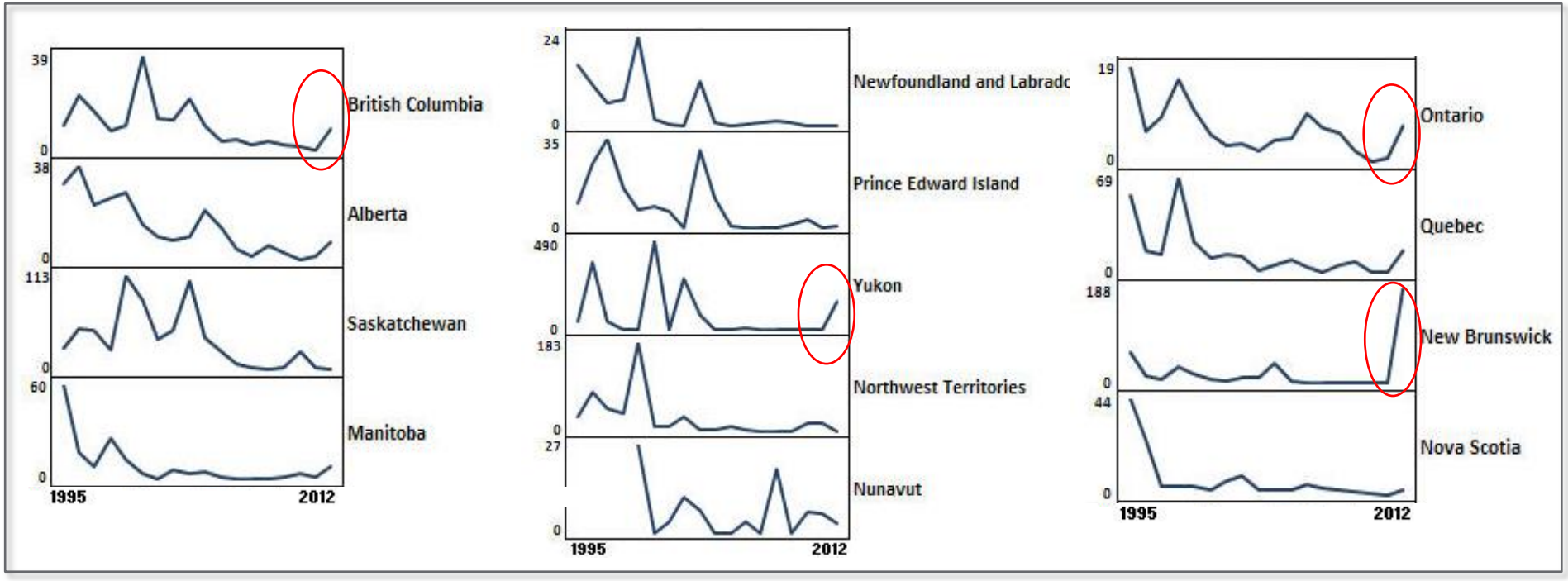
Pertussis vaccination schedule: Ontario



DTaP = Diphtheria and Tetanus toxoids, acellular Pertussis vaccine

Tdap = Tetanus toxoid, reduced diphtheria toxoid and reduced acellular pertussis vaccine

Asynchronous activity across Canada



Source: Smith et al., CCDR 2014