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Acellular pertussis vaccine effectiveness and waning immunity in Alberta, Canada: 2010–2015, a Canadian Immunization Research Network (CIRN) study

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ABSTRACT

Background: Pertussis is still frequently reported in Canada. In Alberta, pertussis incidence ranged from 1.8 to 20.5 cases per 100,000 persons for 2004–2015. Most cases occurred in those aged <15 years. In Alberta, acellular formulations replaced whole-cell in 1997. We investigated pertussis vaccine effectiveness (VE) using a test-negative design (TND) study.

Methods: We included all persons who had a real-time PCR laboratory test for *Bordetella pertussis* between January 1, 2010 and August 31, 2015, in the province of Alberta, Canada. Vaccination history was obtained from Alberta's immunization repository. Vaccination status was classified as complete, incomplete, or unvaccinated, based on the province's vaccination schedule. Persons who had received ≥one dose of whole cell vaccine were excluded from analysis. Multivariable logistic regression models were used to estimate adjusted odds ratios (aOR) and 95% confidence intervals (95% CI) for pertussis infection by time since last vaccination. We adjusted for vaccination status, age, sex, neighbourhood income, urban/rural status, and the presence of a co-morbid condition. VE was calculated as [(1 − aOR) * 100].

Results: Of the 12,149 tests available, 936 (7.7%) were positive for *Bordetella pertussis*. Among the full cohort, VE was 90% (95% CI 87–92%) at 1 year, 81% (95% CI 77–85%) at 1–3 years, 76% (95% CI 68–82%) at 4–7 years, and 37% (95% CI 11–56%) at 8 or more years since a last dose of acellular pertussis vaccine.

Conclusions: Pertussis VE was highest in the first year after vaccination, then declined noticeably as years since a last vaccination increased. Our results suggest that a large number of adolescents and adults are susceptible to infection with *Bordetella pertussis*. Regular boosters throughout childhood, adolescence, and during pregnancy may be needed.

1. Background

Pertussis (whooping cough) is a highly infectious respiratory disease that is transmitted through direct contact or inhalation of airborne droplets and is caused by the bacteria *Bordetella pertussis* [1]. Pertussis infection often presents first with cold-like symptoms and mild fever, followed by serious coughing episodes that may lead to difficulty breathing, choking, and vomiting. Infants are most susceptible to serious symptoms and complications that could lead to hospitalization and, in severe cases, death [2].

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A whole-cell pertussis vaccine was first developed in the 1930s, significantly decreasing pertussis incidence upon universal use [3]. Following concerns of high rates of adverse events following vaccination, a new acellular formulation of the vaccine was developed in the 1980s [4,5]. In Alberta, acellular formulations replaced whole-cell in 1997 [6].

Pertussis is still a frequently reported disease in Canada. Since 2000, an average of almost 2500 annual cases of pertussis have been reported in Canada, with many more likely unreported [7,8]. In Alberta, pertussis incidence has ranged from 1.8 to 20.5 cases per 100,000 persons during 2004–2015, with the majority of cases reported in those aged <15 years [9]. Low and high periods of incidence have been observed to occur cyclically, with peaks in disease every few years [7,9,10].

Ongoing incidence of pertussis in Canada may be an indication of either low vaccination coverage or secondary vaccine failure. Nationally, 77% children have received all recommended preschool doses of pertussis vaccines, which is below the target of 95% [11,12] The purpose of this study was to estimate vaccine effectiveness (VE) and duration of protection of acellular pertussis vaccine in Alberta, Canada.

2. Methods

2.1. Population

In this test-negative design (TND) study, we identified all individuals who had undergone a laboratory test for pertussis between January 1, 2010 and August 31, 2015, in the Canadian province of Alberta (population 4.18 million in 2015).

Exclusions included those too young to have their vaccination status classified (under 3 months of age), those with indeterminate or inconclusive laboratory results, those with missing data required for linkage to variables of interest, and those with a history of receipt of at least one dose of whole-cell vaccine [Fig. 1].

The study was approved by the Conjoint Health Research Ethics Board of the University of Calgary (Ethics ID: REB15-0732) and funded by the Canadian Institutes of Health Research (grant # 137470; Canadian immunization Research Network, sub grant PC01 AB03), and a research agreement between the Alberta Ministry of Health and the University of Calgary (RSO 1026380).

2.2. Data sources

Alberta has a publicly funded, universally available, health care insurance system that covers at least 99% of the provincial population. Registration with the Alberta Health Care Insurance Plan (AHCIP) is mandatory for all residents of the province. The registration system for the AHCIP (Alberta Central Stakeholder Registry) contains demographic information (age, sex, postal code, urban/rural residency) about registrants as well as a unique personal identifier (ULI) that can be used for deterministic linkage across multiple administrative databases. The postal code is further linked with Canadian census data (2011) to derive neighbourhood income levels.

In Alberta, pertussis is a notifiable disease [13]. Reports are captured in the provincial Communicable Disease Reporting System (CDRS), which contains records of all cases of communicable diseases notifiable by law in Alberta. Reporting is mandatory for all health care providers, including laboratories [14]. Only CDRS records with laboratory confirmation were used as cases in this study. All *B. pertussis* laboratory testing in Alberta has been performed by Alberta's provincial laboratory (ProvLab) since 2004, using a real-time polymerase chain reaction (PCR) assay. A separate collection kit and swab must be requested specifically for *B. pertussis*, and testing was not performed as part of a regular panel of tests for respiratory agents. Specimens were reported as positive for *B. pertussis* if the amplification curve was of good quality and the crossing point was $\leq$35 cycles [15]. The final classification information for specimens (positive or negative) tested for *B. pertussis* was obtained from the Data Integration for Alberta Laboratories (DIAL) system [16]. Persons who were listed in CDRS and had a positive test result identified in DIAL were classified as cases for the purpose of this study. Persons who had undergone PCR testing and for whom the test result was negative were classified as controls. If an individual had more than one PCR test within a 90-day period, only one result date was used; this was the first positive PCR date or first PCR test date if all tests were negative.

Income quintiles (one being the lowest, and five being the highest) were assigned by using the individual's postal code as of test date, and linking it with the Statistics Canada Postal Code Conversion File to obtain the 2011 Canadian National Household Survey neighbourhood income quintile based on the corresponding dissemination area [17].

Alberta's Immunization and Adverse Reaction to Immunization (Imm/ARI) repository was used to access individual vaccination records. Imm/ARI captures all vaccinations administered through public health programs in the province and has strict guidelines that promote the submission of high-quality data [9,18]. Business rules are also in place to reject and flag vaccination records that contain errors, so providers can investigate, correct, and resubmit. Pertussis-containing vaccines are administered almost exclusively by Public Health in Alberta. Imm/ARI has prospectively captured all provincial vaccination data since 2006 and has received historical data (retrospectively) from the majority of jurisdictions within the province back to 2000 or earlier. The study start year of 2010 therefore provided at least ten years of historical vaccination data for the province. Chronic disease conditions were identified through physician claims using codes from the International Classification of Disease, ninth revision (ICD-9), and through the hospital discharge database using codes from the International Classification of Disease, tenth edition, Canada (ICD-10-CA) [19,20].

2.3. Vaccination status

Vaccination status was classified as *complete*, *incomplete*, or *unvaccinated*, based on the number of age-appropriate doses within Alberta's vaccination schedule, using a 30-day grace period for scheduled doses under 2 years of age. The grace period allows infants to be up to 30 days late on vaccination before they become classified as incomplete or unvaccinated. Complete status required 1 dose by 3 months of age, 2 doses by 5 months of age, 3 doses by 7 months of age, 4 doses by 19 months of age, 5 doses by 7 years of age, and 6 doses by 16 years of age. Those with incomplete status had a history of vaccination but did not meet the criteria for number of recommended doses for their age outlined above. Doses administered <14 days prior to a laboratory test were not considered as valid doses towards vaccination status.

2.4. Statistical analysis

Multivariable logistic regression models were used to estimate crude and adjusted odds ratios (ORs) for pertussis infection by time since last vaccination. Separate (stratified) models were run considering vaccination status (complete or incomplete), age ($\leq$21 or >21 years), and calendar year (2010–2012 or 2013–2015). An additional sensitivity analysis was conducted on infants younger than three years of age. All models were adjusted for age at time of testing, sex, income quintile, urban/rural status, and the presence of a co-morbid condition. VE was calculated as $[(1 - OR) * 100\%]$.

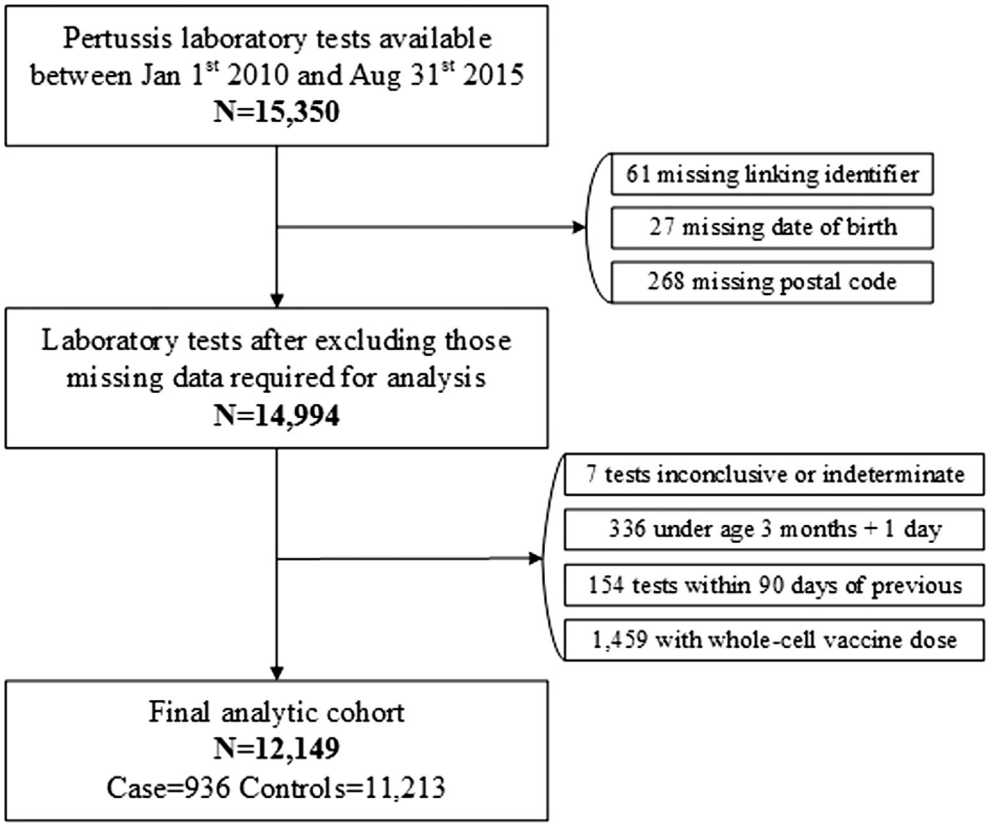


Fig. 1. Flow diagram of tests that met inclusion/exclusion criteria for analytic dataset.

A p-value of <0.05 was used to assess statistical significance, and 95% confidence intervals were provided for all parameter estimates. Data were analyzed using SAS 9.3 (SAS Institute Inc., Cary, NC 2011) and graphed in SigmaPlot 13.5 (Systat Software Inc.).

3. Results

There were 15,350 pertussis laboratory results available between January 1, 2010 and August 31, 2015 [Fig. 1]. After excluding 356 with missing information, 7 inconclusive or indeterminate laboratory tests, 336 laboratory tests for individuals aged <91 days, 154 duplicate tests within 90 days, and 1459 individuals with receipt of at least one dose of whole-cell vaccine, the final study sample consisted of 12,149 laboratory tests (from 11,877 individuals), with 936 (7.7%) testing positive for pertussis. None of the patients who tested positive for pertussis had another positive test >90 days apart.

Cases were younger (mean age of 15.9 vs. 18.9 years; $p < 0.001$), more likely to live in rural areas (47.5% vs. 32.8%; $p < 0.001$), and more likely to be in the lowest income quintile (32.6% vs. 23.7%; $p < 0.001$) [Table 1]. Controls were more likely to be complete on their pertussis vaccinations than cases (43.6% vs. 24.8%; $p < 0.001$), and more likely to have one or more co-morbidities (20.2% vs. 17.0%; $p = 0.017$). Fig. 2 shows the number of pertussis tests and percent positivity per year in our study period.

Vaccine effectiveness was highest within the first year following vaccination [VE 90%; 95%CI (87–92%)], with a noticeable decline beginning at 6 years [Fig. 3], and mild protection for those with 8 or more years since a last administered dose (VE 37%; 95%CI 11–56%) [Table 2].

Table 2 shows pertussis VE by years since last vaccination, stratified in three separate models by vaccination status, age cohort, and year of testing. VE declined by time since last vaccination in all three models. For all age groups combined, adjusted VE estimates in those with complete vaccination status was 91% (95%CI 88–94%) at 1 year, 85% (95%CI 81–89%) at 1–3 years, 80% (95%CI 72–85%) at 4–7 years, and 27% (95%CI −9 to 51%) at 8 years or more since the last administered dose of a pertussis-containing vaccine. A similar decline in pertussis VE was observed for those with incomplete vaccination status, with an adjusted VE of 84% (95%CI 74–90%) at 1 year, 71% (95%CI 59–80%) at 1–3 years, 67% (95%CI 49–79%) at 4–7 years, and 56% (95%CI 20–76%) at 8 years or more since a last administered dose. Vaccine effectiveness point estimates remained high in children under 4 years of age for each year that passed since a last pertussis dose.

4. Discussion

In this study, we measured acellular pertussis VE using over five years of PCR laboratory data in Alberta. Our results suggest a moderately high VE in the first few years following vaccination, with evidence of waning immunity beginning at six years since a last vaccine dose received. The indications are that young children are well protected, which means that the program is achieving its primary goal of protecting infants from the severe outcomes of pertussis, as well as aligning with the World Health Organizations position on pertussis vaccination [21]. Although we observed significant waning immunity, our analysis indicates the vaccine may still provide modest protection beyond eight years.

Despite the availability of a vaccine, pertussis remains a prevalent disease in Canada and elsewhere [7,10,11]. In our province, pertussis rates change over the calendar year and follow secular trends [22,23]. Previous work has indicated that pertussis outbreaks can impact sub-provincial regions for reasons that are still

Table 1
Characteristics of those with a positive (case) or negative (control) Bordetela pertussis test.

	Cases, n (%)	Controls, n (%)	p-value	Total, n
Age in years, mean (sd)	15.9 (18.4)	18.9 (22.1)	<0.001	18.6 (21.9)
Age				
3–11 months	100 (10.7)	1513 (13.5)	<0.001	1613
1–4 years	220 (23.5)	3074 (27.4)		3294
5–9 years	172 (18.4)	1588 (14.2)		1760
10–21 year	212 (22.7)	1263 (11.3)		1475
22–44 year	122 (13.0)	1799 (16.0)		1921
45–64 year	94 (10.0)	1481 (13.2)		1575
65+ years	16 (1.71)	495 (4.41)		511
Sex				
Female	489 (52.2)	6053 (54.0)	0.307	6542
Male	447 (47.8)	5160 (46.0)		5607
Geographic Location				
Rural	445 (47.5)	3682 (32.8)	<0.001	4127
Urban	491 (52.5)	7531 (67.2)		8022
Income Quintiles				
Q1 (lowest)	305 (32.6)	2659 (23.7)	<0.001	2964
Q2	164 (17.5)	2240 (20.0)		2404
Q3	161 (17.2)	1914 (17.1)		2075
Q4	164 (17.5)	2218 (19.8)		2382
Q5 (Highest)	142 (15.2)	2182 (19.5)		2324
Time since last vaccination				
15–364 days	62 (6.6)	2853 (25.4)	<0.001	2915
1–3 years	121 (12.9)	2323 (20.7)		2444
4–7 years	85 (9.1)	917 (8.2)		1002
8 or more years	60 (6.4)	234 (2.09)		294
Unvaccinated	608 (65.0)	4886 (43.6)		5494
Vaccination status				
Unvaccinated	608 (65.0)	4885 (43.6)	<0.001	5493
Incomplete	96 (10.3)	1442 (12.9)		1538
Complete	232 (24.8)	4886 (43.6)		5118
Co-morbidity reported				
No	777 (83.0)	8943 (79.8)	0.017	9720
Yes	159 (17.0)	2270 (20.2)		2429
Year of test				
2010–2012	267 (28.5)	4393 (39.2)	<0.001	4660
2013–2015	669 (71.5)	6820 (60.8)		7489

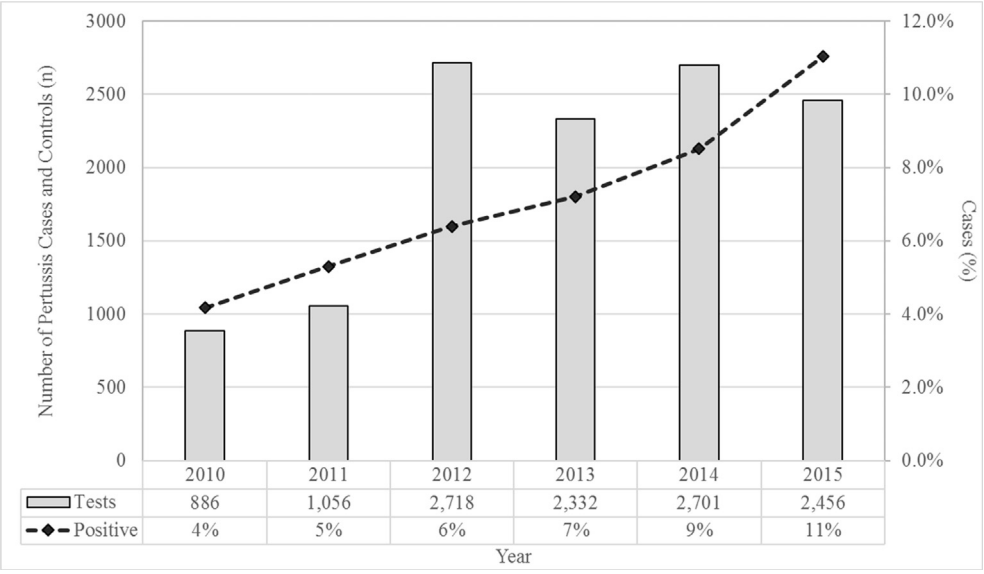
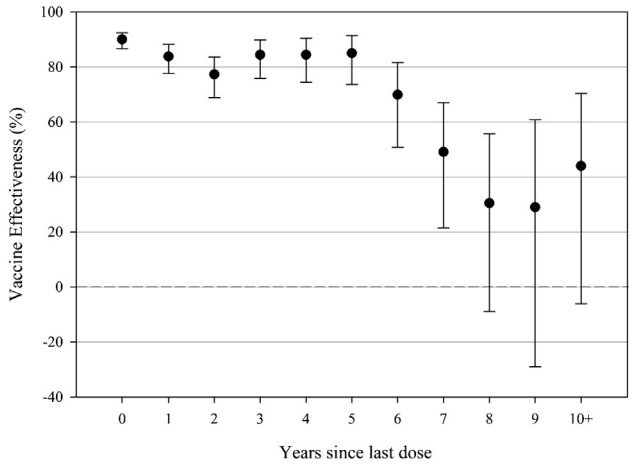


Fig. 2. Number of pertussis tests (Grey bars, left axis) and % positive (black dotted line, right axis), by year of test.

unexplained [24]. Some prior work suggests that increases in pertussis may result from incomplete historical coverage with an effective vaccine or changes in the actual disease agent [25–27].

The higher proportion of rural cases has been a consistent finding in Alberta over the past decade, likely influenced by lower vaccination coverage compared to large urban centres [8]. Cases were



[1] Adjusted for age, sex, income quintile, urban/rural status, and the presence of a co-morbid condition

Fig. 3. Pertussis vaccine effectiveness by years since last dose[1]. [1] Adjusted for age, sex, income quintile, urban/rural status, and the presence of a co-morbid condition.

also more likely to be in the lowest income quintile compared to controls, suggesting that socioeconomic factors may play a role in the distribution of pertussis in the population. Previous studies in Canada have demonstrated an association between lower income and decreased vaccination uptake, which may have contributed to the greater number of cases in the lowest income quintile we observed [28]. These findings deserve further exploration by social scientists in order to fully understand how social determinants are influencing the risk of pertussis.

The vaccine effectiveness estimate of 91% for those with complete vaccination within one year of a vaccination was higher than the VE of 80% observed in a recent, similarly designed test-negative study in Canada [29]. Both studies saw significant waning of protection over time. In our study, waning of immunity began to accelerate after 6 years since last vaccination, with only modest protection after 8 years. Other recent observational studies in North America have shown evidence that early waning of vaccine induced immunity is occurring [30–32]. Booster dose schedules should consider this rapid waning, as longer gaps between doses could leave a period of time where protection is low or non-existent.

Table 2
Pertussis VE by vaccination status and years since last vaccination in all age groups.

	Pertussis Positive #vaccinated/total	Pertussis Negative #vaccinated/total	Crude VE	Adjusted VE
Full cohort				
15–364 d	62/670	2853/7739	82.5 (77.2–86.6)‡	89.9 (86.6–92.4)‡
1–3 yr	121/729	2323/7209	58.1 (48.8–65.8)‡	81.4 (76.7–85.2)‡
4–7 yr	85/693	917/5803	25.5 (5.5–41.3)†	75.9 (68.1–81.7)‡
8+ yr	60/668	234/5120	−106 (−177 to −53.3)‡	37.1 (10.7–55.7)†
Incomplete vaccination				
15–364 d	17/625	574/6067	75.5 (60–85)‡	84.1 (73.7–90.3)‡
1–3 yr	39/647	619/6112	46 (24.5–61.4)‡	71.1 (58.9–79.6)‡
4–7 yr	26/634	241/5734	2.8 (−47.2 to 35.9)	67.4 (49.1–79.1)‡
8+ yr	14/622	104/5597	−25 (−121 to 29.3)	55.9 (19.6–75.9)†
Complete				
15–364 d	45/653	2296/7182	84.2 (78.6–88.4)‡	91.3 (88–93.7)‡
1–3 yr	82/690	1743/6629	62.2 (52.1–70.2)‡	85.1 (80.5–88.6)‡
4–7 yr	59/667	702/5588	32.5 (10.7–48.9)†	79.6 (71.8–85.2)‡
8+ yr	46/654	144/5030	−157 (−262 to −82.3)‡	27 (−9.20 to 51.2)
Under 22 years of age				
15–364 d	60/444	2746/4125	92.2 (89.6–94.1) ‡	89.9 (86.5–92.4) ‡
1–3 yr	116/500	2187/3566	81 (76.3–84.7) ‡	82 (77.3–85.8) ‡
4–7 yr	84/468	902/2281	66.6 (57–74) ‡	76.5 (68.8–82.3) ‡
8+ yr	60/444	224/1603	3.8 (−30.7 to 29.2)	38.8 (12.7–57.1) †
Over 21 years of age				
15–364 d	2/226	107/3614	70.7 (−19.3 to 92.8)	70.6 (−20.3 to 92.8)
1–3 yr	5/229	136/3643	42.4 (−42 to 76.7)	40.9 (−46.3 to 76.1)
4–7 yr	1/225	15/3522	−4.4 (−694 to 86.3)	0 (−666 to 86.9)
8+ yr	0/224	10/3517	n/a	n/a
Under 4 years of age				
15–364 d	52/245	2289/3178	89.5 (85.6–92.4)‡	88 (83.4–91.4)‡
1 yr	20/213	608/1497	84.8 (75.7–90.5)‡	83.1 (72.8–89.5)‡
2 yr	7/200	238/1127	86.5 (70.8–93.7)‡	84.6 (66.7–92.9)‡
3 yr	1/194	28/917	83.5 (−21.6 to 97.8)	80.9 (−41.7 to 97.4)
Year 2010–2012				
15–364 d	21/211	1127/3170	80 (68.4–87.3)‡	89.7 (83.2–93.7)‡
1–3 yr	30/220	836/2879	61.4 (42.8–74)‡	83.1 (73.8–89.1)‡
4–7 yr	15/205	319/2362	49.4 (13.3–70.5)†	79.9 (63.6–88.9)‡
8+ yr	11/201	68/2111	−73.9 (−235 to 9.6)	24.1 (−59.9 to 64)
Year 2013–2015				
15–364 d	41/459	1726/4569	83.8 (77.6–88.3)‡	90.7 (86.8–93.4)‡
1–3 yr	91/509	1487/4330	58.4 (47.3–67.1)‡	82.2 (76.7–86.4)‡
4–7 yr	70/488	598/3441	20.4 (−4.1 to 39.1)	77.2 (68.4–83.6)‡
8+ yr	49/467	166/3009	−101 (−181 to −43.6)‡	48 (21.9–65.4)†

Adjusted for age, sex, income quintile, urban/rural status, and the presence of a co-morbid condition.
† $p < 0.05$.
‡ $p < 0.001$.

Canada's pertussis vaccination coverage and disease reduction targets have a strong emphasis on infants, as the majority of hospitalizations and deaths occur in those under 1 year of age, with three pertussis vaccination doses scheduled (2, 4, 6 months) during this period for all jurisdictions [33,34]. We found the vaccine to be highly effective in preventing pertussis cases in those younger than 4 years of age, prior to the 4- to 6-year recommended booster in Canadian jurisdictions. The waning immunity observed is primarily a concern in the older age groups, as the gap between scheduled doses is greater than the younger age cohorts we analyzed. The pertussis dose scheduled at 4–6 years of age is vital for preventing significant vaccine waning in early school-aged children, as the next scheduled booster in the majority of jurisdictions in Canada does not occur until teenage years in schools [33].

Infants younger than two months of age, who are at greatest risk for severe outcomes from pertussis infection, must rely on maternal antibodies and herd immunity for protection. Pregnant women with more than 7 years since a last vaccination may not be able to pass on sufficient passive immunity to their babies, as they themselves are unlikely to be protected against pertussis infection if relying on immunity from immunization during their own childhood. The National Advisory Committee on Immunization (NACI) recommended in March 2018 that pregnant women be immunized with a combined tetanus-diphtheria-acellular pertussis vaccine (Tdap) during every pregnancy, regardless of vaccination history [35]. In light of this recommendation, further study should be undertaken to determine the impact on VE after infant doses.

4.1. Limitations

Vaccination data completeness in Edmonton (an area containing ~25% of the provincial population), is considered to be inferior to the rest of the province prior to the year 2006. With our study period beginning in 2010, it is possible some Edmonton residents may have been missing vaccination data as early as 4 years prior to a pertussis test. This misclassification may have impacted our VE estimates.

Although the misclassification of cases as controls is possible, the likelihood was low as we used PCR for the whole duration of the study, which would detect infection for a longer period of time than traditional testing [36].

In the >21 years age group, very few pertussis cases were vaccinated with acellular vaccine, leading to unstable estimates and the inability to provide a VE point estimate in the 8 or more years since a last dose strata. This was a result of excluding whole-cell vaccine recipients, who were over-represented in the older age group.

The test-negative design using routinely submitted specimens without a case definition has not been validated for pertussis. Further investigation by comparing results from pertussis VE studies using different methodologies is required.

4.2. Conclusion

We have observed that the pertussis vaccine affords moderately high protection to those within the first six years of an administered dose. However, significant waning of protection began thereafter, with mild to no protection beyond 8 years since a last vaccination. Regular boosters throughout childhood, adolescence, and during pregnancy may be needed.

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Declaration of Competing Interest

Dr. Mahmud (SSM) reports grants from Merk, grants from GlaxoSmithKline, grants and personal fees from Sanofi Pasteur, grants from Pfizer, grants from Roche-Assurex, during the conduct of the study. All other authors have no conflicts.

Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.vaccine.2019.05.067.

References

[1] Public Health Agency of Canada (PHAC). Pathogen Safety Data Sheets: Infectious Substances – Bordetella pertussis; 2010 [updated 2011-08-19; cited 2018]. Available from: https://www.canada.ca/en/public-health/services/laboratory-biosafety-biosecurity/pathogen-safety-data-sheets-risk-assessment/bordetella-pertussis.html.
[2] Public Health Agency of Canada (PHAC). Pertussis (whooping cough); 2014. Available from: https://www.canada.ca/en/public-health/services/immunization/vaccine-preventable-diseases/pertussis-whooping-cough.html.
[3] Cherry JD. The history of pertussis (whooping cough); 1906–2015: facts, myths, and misconceptions. Curr Epidemiol Rep 2015;2(2):120–30.
[4] Ad Hoc Group For The Study Of Pertussis V. Placebo-controlled trial of two acellular pertussis vaccines In Sweden—protective efficacy and adverse events. Lancet 1988;331(8592):955–60.
[5] Cody CL, Baraff LJ, Cherry JD, Marcy SM, Manclark CR. Nature and rates of adverse reactions associated with DTP and DT immunizations in infants and children. Pediatrics 1981;68(5):650–60.
[6] Alberta Health. History of biologicals administered in Alberta. In: Health Alberta, editor; 2017.
[7] Public Health Agency of Canada (PHAC). Canadian Notifiable Disease Surveillance System (CNDSS); 2018.
[8] Crowcroft NS, Johnson C, Chen C, Li Y, Marchand-Austin A, Bolotin S, et al. Under-reporting of pertussis in Ontario: a Canadian Immunization Research Network (CIRN) study using capture-recapture. PLoS ONE 2018;13(5):e0195984.
[9] Liu XC, Bell CA, Simmonds KA, Svenson LW, Fathima S, Drews SJ, et al. Epidemiology of pertussis in Alberta, Canada 2004–2015. BMC Public Health 2017;17(1):539.
[10] Centers for Disease Control and Prevention (CDC). Pertussis Surveillance and Reporting; 2017. Available from: https://www.cdc.gov/pertussis/surv-reporting.html.
[11] Alberta Health. Interactive Health Data Application; 2018. Available from: http://www.ahw.gov.ab.ca/IHDA_Retrieval/.
[12] Public Health Agency of Canada (PHAC). Vaccine coverage in Canadian children: Highlights from the 2013 childhood National Immunization Coverage Survey (cNICS); 2013. Available from: https://www.canada.ca/en/public-health/services/publications/healthy-living/vaccine-coverage-canadian-children-highlights-2013-childhood-national-immunization-coverage-survey.html.
[13] Alberta Health. Notifiable disease and diseases under surveillance list; 2015.
[14] Government of Alberta. Public health act. Edmonton (Alberta): Alberta Queen's Printer; 2000.
[15] Reischl U, Lehn N, Sanden GN, Loeffelholz MJ. Real-time PCR assay targeting IS481 of Bordetella pertussis and molecular basis for detecting Bordetella holmesii. J Clin Microbiol 2001;39(5):1963–6.
[16] Fathima Sumana, Ferrato Christina, Lee Bonita E, Simmonds Kimberley, Yan Lin, Mukhi Shamir N, et al. Bordetella pertussisin sporadic and outbreak settings in Alberta, Canada, July 2004 – December 2012. BMC Infect Dis 2014;14(1). , http://bmcinfectdis.biomedcentral.com/articles/10.1186/1471-2334-14-48. https://doi.org/10.1186/1471-2334-14-48.
[17] Statistics Canada. Postal CodeOM Conversion File (PCCF), Reference Guide; 2017. Available from: https://www150.statcan.gc.ca/n1/pub/92-154-g/92-154-g2017001-eng.htm.
[18] Alberta Health. Immunization data submission and response guidelines; 2017.
[19] Feudtner C, Christakis DA, Connell FA. Pediatric deaths attributable to complex chronic conditions: a population-based study of Washington State, 1980–1997. Pediatrics 2000;106(Suppl. 1):205–9.
[20] Alberta Health. Overview of administrative health databases. In: Health Alberta, editor; 2017.
[21] World Health Organization (WHO). Pertussis vaccines: WHO position paper – September 2015;90(35):433–60. Available from: http://www.who.int/wer/2015/wer9035/en/.

[22] Fathima S, Ferrato C, Lee BE, Simmonds K, Yan L, Mukhi SN, et al. Bordetella pertussis in sporadic and outbreak settings in Alberta, Canada, July 2004-December 2012. BMC Infect Dis 2014;14:48.
[23] Simmonds K, Fathima S, Chui L, Lovgren M, Shook P, Shuel M, et al. Dominance of two genotypes of Bordetella pertussis during a period of increased pertussis activity in Alberta, Canada: January to August 2012. Int J Infect Dis 2014;29:223–5.
[24] Fisman DN, Tang P, Hauck T, Richardson S, Drews SJ, Low DE, et al. Pertussis resurgence in Toronto, Canada: a population-based study including test-incidence feedback modeling. BMC Public Health 2011;11:694.
[25] Guiso N. Bordetella pertussis: why is it still circulating? J Infect 2014;68(Suppl 1):S119–24.
[26] Riolo MA, King AA, Rohani P. Can vaccine legacy explain the British pertussis resurgence? Vaccine 2013;31(49):5903–8.
[27] Canadian Immunization Research Network (CIRN). A multiprovincial approach to evaluating pertussis vaccine effectiveness in Canada using administrative data; 2018. Available from: http://cirnetwork.ca/research-study/a-multiprovincial-approach-to-evaluating-pertussis-vaccine-effectiveness-in-canada-using-administrative-data/.
[28] Gilbert NL, Gilmour H, Wilson SE, Cantin L. Determinants of non-vaccination and incomplete vaccination in Canadian toddlers. Hum Vaccin Immunother 2017;13(6):1–7.
[29] Schwartz KL, Kwong JCS, Deeks SL, Campitelli MA, Jamieson FB, Marchand-Austin A, et al. Effectiveness of pertussis vaccination and duration of immunity. CMAJ 2016;188(16):E399–406.
[30] Klein NP, Bartlett J, Rowhani-Rahbar A, Fireman B, Baxter R. Waning protection after fifth dose of acellular pertussis vaccine in children. N Engl J Med 2012;367(11):1012–9.
[31] Misegades LK, Winter K, Harriman K, Talarico J, Messonnier NE, Clark TA, et al. Association of childhood pertussis with receipt of 5 doses of pertussis vaccine by time since last vaccine dose, California, 2010. JAMA 2012;308(20):2126–32.
[32] Tartof SY, Lewis M, Kenyon C, White K, Osborn A, Liko J, et al. Waning immunity to pertussis following 5 doses of DTaP. Pediatrics 2013;131(4):e1047–52.
[33] Public Health Agency of Canada (PHAC). Canada's provincial and territorial routine (and catch-up) vaccination routine schedule programs for infants and children; 2018. Available from: https://www.canada.ca/en/public-health/services/provincial-territorial-immunization-information/provincial-territorial-routine-vaccination-programs-infants-children.html.
[34] Public Health Agency of Canada (PHAC). Vaccination coverage goals and vaccine preventable disease reduction targets by 2025; 2018. Available from: https://www.canada.ca/en/public-health/services/immunization-vaccine-priorities/national-immunization-strategy/vaccination-coverage-goals-vaccine-preventable-diseases-reduction-targets-2025.html#2.0.
[35] National Advisory Committee on Immunization (NACI). Update on immunization in pregnancy with tetanus toxoid, reduced diphtheria toxoid and reduced acellular pertussis (Tdap) vaccine; 2018.
[36] Palmer CM, McCall B, Jarvinen K, Nissen MD. Bordetella pertussis PCR positivity, following onset of illness in children under 5 years of age. Commun Dis Intell Q Rep 2007;31(2):202–5.