



# Predictors of pertussis outbreak in urban and rural municipalities of Saskatchewan, Canada

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## Abstract

**Objectives** Increased numbers of pertussis cases in September 2015 led to the declaration of an outbreak in the Saskatoon Health Region (SHR). SHR (population approximately 350,000) is a geographic area in central Saskatchewan consisting of both urban and rural municipalities. The purpose of this study was to describe the epidemiology and identify possible predictors of the outbreak.

**Methods** Confirmed cases of pertussis in SHR from 2010 to 2015 were extracted from the integrated Public Health Information System (iPHIS) database. Univariate and bivariate analyses and a comparison of the two outbreaks were conducted. Poisson regression modelling was used to estimate incidence rate ratios (IRRs) of factors associated with pertussis infection.

**Outcomes** Two outbreaks between 2010 and 2015. Factors associated with the 2015 outbreak were residence in rural areas (IRR = 18.67, 95% CI 11.82–29.49; 11.37, 95% CI 6.40–20.21; and 6.31, 95% CI 3.43–11.62) for Humboldt, Watrous, and Rosthern areas, respectively, compared to the City of Saskatoon, and among children 11–14 years of age (IRR = 3.11, 95% CI 1.67–5.79) compared to children under 5 years of age. Unvaccinated persons had increased risk (IRR = 1.60, 95% CI 1.07–2.38). Multiple interventions, including enhanced contact tracing, supplemental immunization clinics, and cocooning, were employed in the 2015 outbreak.

**Conclusion** Pertussis is a cyclical disease with outbreaks occurring every 3 to 5 years. Teenagers have increased risk of disease compared to younger children, likely due to waning immunity. Rural residents had a higher incidence of disease, possibly due to clusters of conscientious objectors. Control efforts require recognition of waning immunity and unvaccinated susceptibles.

## Résumé

**Objectifs** Une augmentation des cas de coqueluche en septembre 2015 a mené à la déclaration d'une flambée dans la Région sanitaire de Saskatoon (RSS). La RSS (environ 350,000 habitants) est une zone géographique du centre de la Saskatchewan qui englobe à la fois des municipalités urbaines et rurales. Nous avons voulu décrire l'épidémiologie de cette flambée et en cerner les prédicteurs possibles.

**Méthode** Les cas confirmés de coqueluche survenus dans la RSS entre 2010 et 2015 ont été extraits de la base de données du Système intégré d'information sur la santé publique (SIISP). Des analyses univariées et bivariées et une comparaison de deux flambées ont été effectuées. Par modélisation de la régression de Poisson, nous avons estimé les rapports de taux d'incidence (RTI) des facteurs associés à l'infection par la coqueluche.

**Résultats** Il y a eu deux flambées entre 2010 et 2015. Les facteurs associés à la flambée de 2015 étaient le fait de résider dans les régions rurales de Humboldt, Watrous et Rosthern, respectivement (RTI = 18,67, IC de 95 % 11,82–29,49; 11,37, IC de 95 % 6,40–20,21; et 6,31, IC de 95 % 3,43–11,62) comparativement à la Ville de Saskatoon et d'être un enfant de 11 à 14 ans (RTI = 3,11, IC de 95 % 1,67–5,79) comparativement à un enfant de moins de 5 ans. Le risque était plus élevé chez les personnes non vaccinées (RTI = 1,60, IC de 95 % 1,07–2,38). Plusieurs interventions, dont le retraçage renforcé des contacts, l'ajout de cliniques de vaccination et le cocooning, ont été employées durant la flambée de 2015.

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**Conclusion** La coqueluche est une maladie cyclique dont les flambées surviennent tous les trois à cinq ans. Les adolescents y sont plus vulnérables que les enfants plus jeunes, probablement en raison de la baisse de leur immunité. L'incidence de la maladie était plus élevée dans la population rurale, ce qui pourrait s'expliquer par la présence de grappes d'objecteurs de conscience. Pour lutter contre la coqueluche, il faut donc tenir compte de la baisse de l'immunité et des réceptifs non vaccinés.

**Keywords** Whooping cough · Outbreak · Disease

**Mots-clés** Coqueluche · Flambées de maladies · Maladie

## Introduction

Pertussis or whooping cough is a vaccine-preventable disease that affects the lungs and airways. It is caused by the bacteria *Bordetella pertussis*, which is endemic in Canada and known to occur year round (Public Health Agency of Canada 2002; Chan et al. 2012). It usually presents initially as a benign illness but can result in serious outcomes, including pneumonia, seizures, encephalopathy, and death, especially among infants (Galanis et al. 2006; Hartzell and Blaylock 2014).

Despite the availability of a vaccine, it remains one of the least adequately controlled vaccine-preventable diseases (Galanis et al. 2006). Additionally, outbreaks of the disease are known to occur periodically every 3 to 5 years and show a summer-autumn seasonality; despite the availability of routine childhood vaccines, this trend continues (Gabutti et al. 2015; Clark 2014; Klein et al. 2012).

Typically, a non-immune individual, irrespective of age, is susceptible to the disease; however the disease is found to occur more in naive unvaccinated infants, and these infants usually have an increased risk of adverse outcomes (Munoz and Englund 2011). However, the current epidemiology of the disease now includes previously fully vaccinated adolescents, school-aged children, and adults, not just non-immune persons as was the case previously (Galanis et al. 2006; Gabutti et al. 2015; Clark 2014; Gangarosa et al. 1998; Margaret et al. 1998).

This changing epidemiology of the disease and persistence of cyclic activity suggests waning immunity, either naturally following an infection or passively following a pertussis-containing vaccine (Cherry 2012, 2015). There is evidence that seropositivity rates for antibodies against pertussis toxin begin declining by the 5th year, necessitating a booster dose of Tetanus–diphtheria–acellular pertussis (Tdap) in adolescents/adults (Cherry 2012; McCormack 2012; Counard et al. 2008; Tafuri et al. 2013). A recent Ontario study also found a rapid decline of acellular pertussis vaccine effectiveness 4 years after the last vaccine administration (Schwartz et al. 2016). Additional evidence suggests that the duration of immunity varies between 3 and 20 years, depending on whether it is due to natural immunity (7 to 20 years), immunization with whole cell vaccine (5 to 10 years), or vaccination with acellular vaccine (3 to 5 years) (Gabutti et al. 2015; Al et al. 2007; Vickers et al. 2006).

While the outbreak declaration in September 2015 in Saskatoon Health Region is consistent with the expected cyclical pattern of outbreaks, we are not sure what the drivers of disease are in our region. We however posit that a combination of incomplete immunization of residents and waning immunity in vaccinated persons may have contributed to the observed increase in the number of reported pertussis cases from the third quarter of 2015, ultimately culminating in an outbreak declared in November 2015. The outbreak involved non-contiguous communities within Saskatoon Health Region (SHR) and required significant public health resources to control.

Saskatchewan classifies pertussis as a *Category I* communicable disease and requires laboratories and physicians to report this to the local public health department (Government of Saskatchewan 2014). In Saskatchewan, a pertussis case is defined based on a mix of clinical and laboratory criteria.<sup>1</sup>

This paper describes the epidemiology of an outbreak of pertussis in 2015 in SHR, including the public health response, determinants of at-risk populations, and actions taken to address the outbreak.

## Methods

SHR has a population of approximately 350,000 located in central Saskatchewan consisting of both urban and rural municipalities.

Using data from the integrated Public Health Information System (iPHIS), the number of pertussis cases in SHR from February 2010 to February 2016 was extracted. We described the epidemiology of cases between these two periods; however,

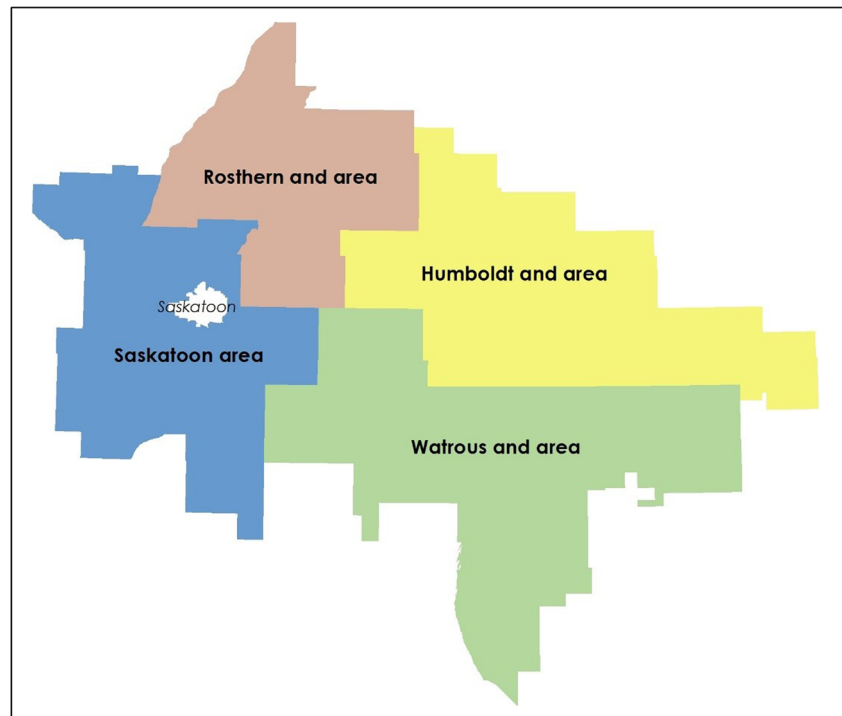
<sup>1</sup> A case is defined based either on isolation of *Bordetella pertussis* from appropriate specimen or detection of *B. pertussis* DNA from appropriate specimen and the presence of one or more of the following:

- i. Cough lasting 2 or more weeks;
- ii. Paroxysmal cough of any duration;
- iii. Cough with inspiratory whoop or ending in vomit or gagging.

A case can also be identified if there is epidemiologic linkage to a laboratory-confirmed case with the presence of one of the following:

- i. Paroxysmal cough of any duration;
- ii. Cough with inspiratory whoop or ending in vomit or gagging.

**Fig. 1** Map showing the Rural Planning Zones in Saskatoon Health Region



the analytic epidemiology component of our study was focused on the most recent pertussis outbreak that occurred from late 2015 to early 2016. Using the covered population that is a count of all persons who held Saskatchewan health coverage on June 3 of the preceding year as the denominator, we calculated the age-specific incidence rates.

A Poisson regression model was used to estimate the incidence rate ratio (IRR) with 95% confidence intervals for the 2015 pertussis cases in the rural planning zones<sup>2</sup> (RPZs) and City of Saskatoon based on the client residency and immunization status (vaccinated versus unvaccinated) (see Fig. 1 [2010 outbreak was not included in the regression model due to lack of data]). Immunization status was considered complete if a client aged between 2 and 4 months had received one pertussis-containing vaccine, two vaccines between 4 and 6 months, three pertussis-containing vaccines for client aged between 6 and 18 months, and four pertussis-containing vaccines between 18 months and 4 years. Clients aged more than 6 years and less than 18 years were deemed vaccinated if they had received five pertussis-containing vaccines, and persons older than 18 years of age were considered fully vaccinated if they have received six pertussis-containing vaccines.

We also included in the model the following age categories: persons younger than 5 years, persons between 5 and 10 years, persons between 11 and 14 years, and persons older than

14 years. We used these age classifications because it is expected that by 5 years of age, clients should have completed the primary vaccine series; clients between age 5 and 10 years should have received the fifth dose of the schedule; and in clients between 11 and 14 years, the grade 8 booster dose would have been received. Finally, clients older than 15 years were considered adults, representing the last group.

Our model included an offset term described as the log of the “at risk” population in each group, defined as the population in each RPZ age group vaccination category. Where this was not available, an estimated value for the “at risk” population was used and assumed that 70% of the population was fully vaccinated and 30% unvaccinated. The choice of 70% is based on the average coverage rate for pertussis vaccination in the health region (CommunityView Collaboration - Saskatoon Health Region Immunization *n.d.*).

Quantitative data analysis was done using Microsoft Excel and SAS version 9.4.

## Results

Two hundred and twelve pertussis cases were extracted from the iPHIS from 2010 to 2016, and during this period, two outbreaks were reported (see Table 1). Cases occurring during known outbreak years (2010 and 2015) were considered outbreak cases and the other cases occurring during the intervening years are deemed sporadic.

The age distribution in both outbreak periods ranged from 0.05 to 69.91 years during the 2010 outbreak and 0.09 to 58 years during

<sup>2</sup> These are geographic areas identified in Saskatoon Health Region and include City of Saskatoon, Saskatoon and area (i.e., bedroom communities of Saskatoon), Rosthern and area, Humboldt and area, and Watrous and area.

**Table 1** Saskatoon Health Region (SHR) pertussis cases by rural planning zones (RPZs) (Chan et al. 2012) 2010–2015

Year	Humboldt and area, n (%)	Rosthern and area, n (%)	City of Saskatoon, n (%)	Saskatoon area, n (%)	Watrous and area, n (%)	Total
2010	4 (5)	2 (3)	64 (85)	5 (7)	0 (0)	75
2011	0 (0)	1 (20)	4 (80)	0 (0)	0 (0)	5
2012	0 (0)	0 (0)	6 (100)	0 (0)	0 (0)	6
2013	0 (0)	0 (0)	3 (100)	0 (0)	0 (0)	3
2014	0 (0)	3 (33)	6 (67)	0 (0)	0 (0)	9
2015	42 (37)	15 (13)	33 (29)	6 (5)	18 (16)	114
Total	46 (22)	21 (10)	116 (55)	11 (5)	18 (8)	212

the 2015 outbreak (see Table 2). We did not observe any statistically significant differences between the 2010 and 2015 outbreaks ( $\chi^2 = 7.734$ ;  $p$  value = 0.052). During the 2010 outbreak, there were a higher proportion of cases in children aged between 11 and 14 years compared to 5–10-year-old children and there was a reversal in this trend during the 2015 outbreak (see Table 2).

The distribution of the cases during the outbreak years by area of residence identified by rural planning zones (RPZs) and the City of Saskatoon was significantly different. As shown in Appendix Fig. 3, pertussis cases started increasing in August 2015 and peaked in November 2015.

The incidence of disease was low among recently vaccinated children (under 5 years old); however, it increased steadily and peaked around the mid-teenage years (corresponding to grade 8). This was followed by a steep decline in incidence in adulthood; with younger adults generally having higher rates of disease compared to older adults (Fig. 2).

Potential predictors for pertussis included age, sex, place of residency (classified by rural planning zone and City of Saskatoon), and immunization status.

**Table 2** Descriptive statistics, pertussis outbreaks in SHR, 2010 and 2015

	2010	2015	Pr > ChiSq
Mean (years)	21.01	16.97	
Median (years)	14.06	12.7	
Range (years)	58.83	69.86	
Age group affected			0.052 <sup>a</sup>
Younger than 5 years, n (%)	13 (50)	13 (50)	
5–10 years, n (%)	7 (25)	21 (75)	
11–14 years, n (%)	20 (32)	43 (68)	
Older than 15 years, n (%)	35 (49)	37 (51)	
Gender			0.046 <sup>a</sup>
Female, n (%)	44 (47)	50 (53)	
Male, n (%)	31 (33)	64 (67)	
Rural planning zones			<0.001 <sup>a</sup>
Humboldt and area, n (%)	4 (9)	42 (91)	
Rosthern and area, n (%)	2 (12)	15 (88)	
Saskatoon area, n (%)	5 (46)	6 (54)	
Watrous and area, n (%)	0 (0)	13 (100)	
City of Saskatoon, n (%)	64 (66)	33 (34)	

<sup>a</sup> Chi-square

Statistically significant adjusted higher incidence rates of pertussis were found in the rural RPZs of Humboldt, Watrous, and Rosthern with the following incidence rate ratios (IRRs): IRR = 18.67, 95% CI 11.82–29.49; 11.37, 95% CI 6.40–20.21; and 6.31, 95% CI 3.43–11.62, respectively. These rural planning zones within the SHR are known to have communities that object to vaccination programs to varying extents. Our analysis showed that females had a non-statistically significant lower incidence rate ratio compared to males (IRR = 0.83, 95% CI 0.58–1.20). Compared to children less than 5 years of age, children aged between 5 and 10 years and older children aged 11–14 years had higher incidence rate ratios; however, only the IRR for children between 11 and 14 years was statistically significant (see Table 3).

When the immunization status was considered, we found that persons who were unvaccinated or incompletely vaccinated were at a higher risk of pertussis (IRR = 1.60, 95% CI: 1.07–2.38) (see Table 3).

**Public health response**

The declaration of the outbreak allowed Population and Public Health to expand their response to prioritize identified clusters in the communities. One such response was to leverage the existing influenza immunization clinics in the affected communities to provide pertussis-containing vaccine to clients who were not fully vaccinated. Others include the extension of hours of clinic service and drop-in clinics in these communities (see Appendix Fig. 4). Because of the outbreak, Tdap vaccine was offered to all pregnant women at 26 weeks or greater regardless of previous immunization status (Saskatchewan Ministry of Health n.d.). Cocooning in the post-delivery stage is part of routine pertussis intervention in the Region.

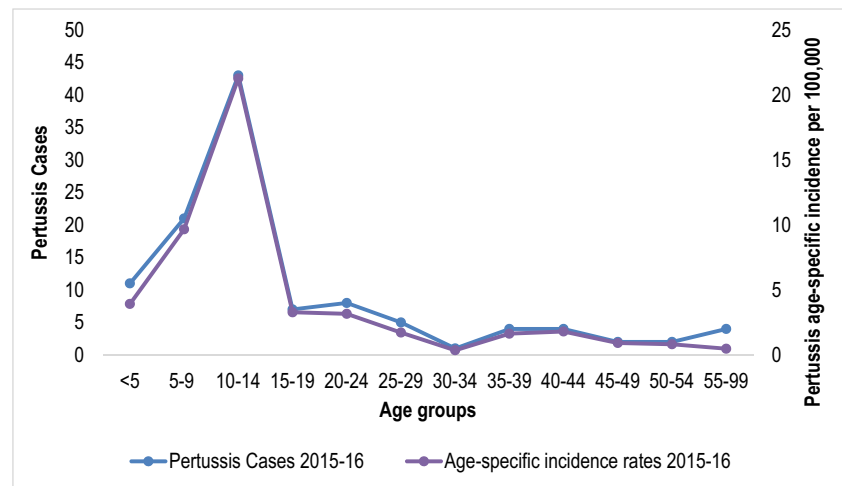
Ongoing communication was provided to health care practitioners in the Region and the various community groups, including churches, schools, daycares, and sport teams, where case(s) were identified. Appendix Fig. 4 shows the timelines of the public health outbreak response.

Intensive contact tracing with confirmed cases included the identification of all contacts as per the guidelines in the Provincial Communicable Disease Control Manual (Government of Saskatchewan 2010). All close contacts were notified of their exposure and provided with information on pertussis. They were all assessed for early symptoms, immunization status, and susceptibility of disease (i.e., infants, pregnant in last trimester, and healthcare workers) and were referred to physicians as appropriate for testing, assessment, prophylaxis, or treatment.

Robust epidemiology support was provided by the Public Health Observatory using GIS and social network analysis in real time to identify important drivers of the outbreak and inform targeted intervention.

Following exhaustive work and with no new reported cases after two incubation periods, the outbreak was declared over on the 16th of March 2016.

**Fig. 2** Age distribution and age-specific incidence of pertussis cases, Saskatoon Health Region, 2015 ( $n = 114$ )



## Discussion

The results from Saskatoon Health Region are consistent with published literature suggesting a 4- to 6-year cyclical trend in the occurrence of pertussis outbreaks (Klein et al. 2012; Davis 2005). Differences were observed in the geographical distribution of the disease between the 2015 outbreak and the usual annual disease distribution where sporadic disease tends to occur more within the bounds of the City of Saskatoon.

As opposed to sporadic cases of disease, outbreak years show higher incidence rates in areas of SHR that have pockets of communities with conscientious objectors to immunization. As opposed to the last known outbreak in 2010 when the cocooning strategy was being developed, the 2015 outbreak benefitted from early and enhanced contact tracing in conjunction with the provincial cocooning strategy, and this may have led to lower case

counts in urban area during the 2015 outbreak. The cocooning strategy is an approach providing indirect protection of infants too young to be vaccinated through the immunization of household and close contacts (Munoz and Englund 2011; MacDonald et al. 2014).

The most recent outbreak (2015) had more cases among 11 to 15 year olds and a higher age-specific incidence in this age group relative to 2010. Increased incidence was also observed in the regression model in this age group relative to persons younger than 5 years of age and this was the only group where we found a statistically significant increase in the incidence rate ratio. This age group was likely to have received their last pertussis-containing vaccine more than 3 years prior to onset of symptoms and diagnosis and this may be due to the waning of immunity. A recent Ontario study demonstrated the impact of waning immunity on development of pertussis (Schwartz et al. 2016).

The impact of this outbreak on the health care system cannot be overstated, as it required a redistribution of services and increased time for public health management and support. This is in addition to associated costs incurred for clinic and acute care services.

While our data analysis shows some important results, it is not without limitations. First, we had a limited sample size of 212 pertussis cases (2010–2015). Of these cases, 114 were from the 2015 outbreak and these were included in the regression analysis. There were some cases for which we could not confirm evidence of immunization, assumed to be unvaccinated, and these were excluded from our analysis. This subset with missing data was three cases, comprising less than 10% of the total, so we do not expect this to influence the results significantly. Additionally, we used estimated values for the “at risk” population in about an eighth of the population groups; however, we do not expect this to impact on our estimates because the estimated “at risk” populations closely approximate the recorded “at risk” populations.

When pertussis control efforts are being designed, adequate consideration should recognize the role of rapid declines in the effectiveness of pertussis vaccine resulting in waning levels of immunity in vaccinated persons and unvaccinated susceptibles.

**Table 3** Incidence rate ratios and 95% confidence intervals for pertussis outbreak associated with place of residence and other factors in Saskatoon Health Region 2015

Parameter	IRR	95% CI	Chi-square	Pr > ChiSq
Place of residence				
City of Saskatoon	1	Reference		
Humboldt and area	18.67	11.82–29.49	157.41	$P < 0.0001$
Rosthern and area	6.31	3.43–11.62	34.93	$P < 0.0001$
Saskatoon area	0.85	0.36–2.03	0.14	$P = 0.711$
Watrous and area	11.37	6.40–20.21	68.61	$P < 0.0001$
Age categories				
Less than 5 years	1	Reference		
Adults	0.17	0.09–0.32	30.51	$P < 0.0001$
5–10 year olds	1.50	0.75–3.0	1.29	$P = 0.256$
11–14 year olds	3.11	1.67–5.79	12.87	$P = 0.0003$
Gender				
Male	1	Reference		
Female	0.83	0.58–1.20	0.95	$P = 0.329$
Immunization status				
Vaccinated	1	Reference		
Unvaccinated/incompletely vaccinated	1.60	1.07–2.38	5.20	$P = 0.023$

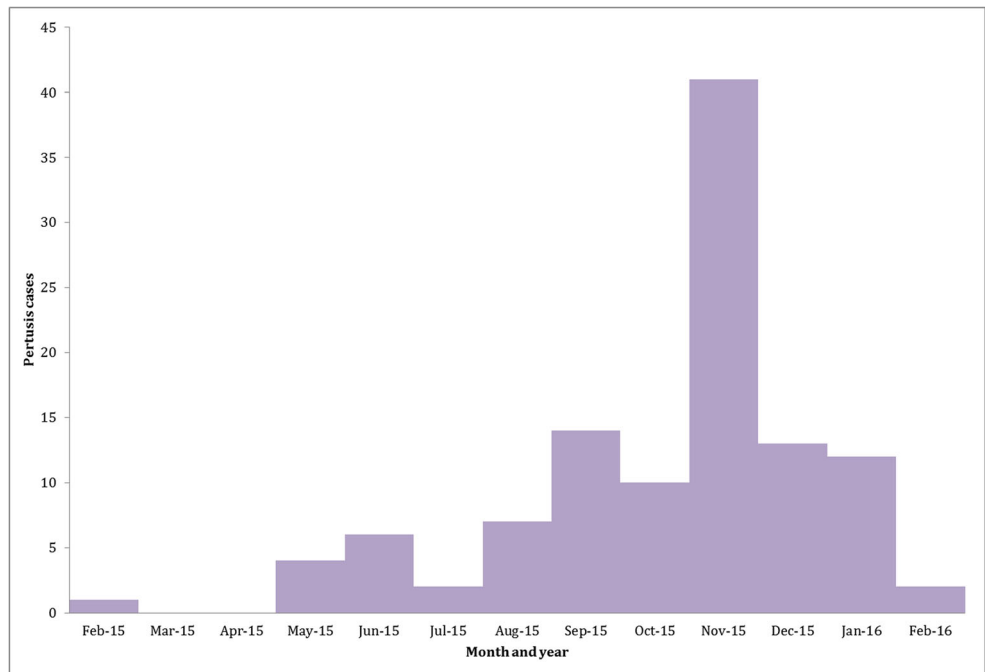
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**Compliance with ethical standards**

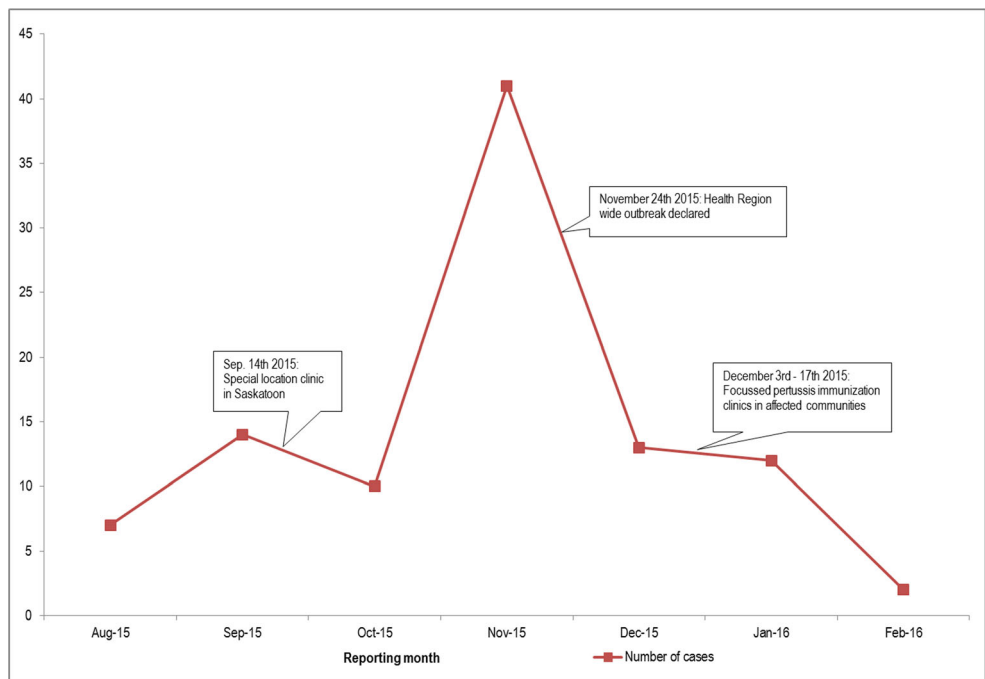
**Conflict of interest** The authors declare that they have no conflict of interest.

**Appendix**

**Fig. 3** Epidemic curve of the pertussis outbreak in Saskatoon Health Region, 2015 ( $n = 114$ )



**Fig. 4** Graph showing timelines of public health response to 2015 pertussis outbreak in SHR



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