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## Shingles in Alberta: Before and after publicly funded varicella vaccination<sup>☆</sup>

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### ABSTRACT

**Purpose:** A universal publicly funded chickenpox vaccination program was implemented in Alberta in 2002. We examine the epidemiology of medically attended shingles in Alberta from 1994 to 2010.

**Methods:** Incident shingles cases (earliest health service utilizations for ICD-9 053 or ICD-10-CA B02) and their co-morbid conditions for the 12 months prior to shingles diagnosis were identified from the records of Alberta's universal, publicly funded health-care insurance system for 1994–2010. Shingles diagnostic codes at least 180 days after the first were classified as recurrent episodes. Denominators for rates were estimated using mid-year population estimates from the Alberta Health Care Insurance Plan Registry. Annual age- and sex-specific rates were estimated. We estimated the proportion of all cases that were hospitalized. We explored the pattern of rates for sex, age-group co-morbidity and year effects and their interactions.

**Results:** Crude rates of shingles increased over the interval 1994–2010. Most persons had only a single episode of shingles; 4% of cases were hospitalized. Shingles rates were higher among females than males. While only 2% of shingles cases had one or more co-morbidities, this proportion was also higher for females than males. Prior to 2002, all age groups of both sexes experienced increasing annual rates of shingles. However, there was a sharp decline in the rate of shingles for both females and males under the age of 10 years for 2002–2010, the period in which there was publicly funded chickenpox vaccination.

**Conclusion:** The declining rates of shingles among persons under the age of 10 years are consistent with an impact of the chickenpox vaccination program. The trend of increasing rates of shingles among older persons began prior to implementation of vaccination.

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### 1. Background

Herpes zoster (shingles) results when there is reactivation of latent varicella zoster virus after a primary episode of chickenpox. Modelling studies have suggested that the introduction of mass vaccination programs against varicella might, over time, lead to an increase in rates of herpes zoster (shingles) [1] because of a lack of immunological boosting due to exposure to varicella virus. Changes

in shingles epidemiology might be apparent within 10 years of implementation of a varicella (chickenpox) vaccination program [1–5].

Varicella vaccines were licensed in Canada in 1998 but initially were not publicly funded in any province or territory. Alberta became the second Canadian province (after Prince Edward Island) to introduce a publicly funded varicella vaccination program. The publicly funded Alberta program targeted special groups (e.g., healthcare workers and children in grade 5 who did not have a prior history of chickenpox, shingles or chickenpox vaccination) beginning in spring 2001 [6]. Starting in July 2001, a single dose of chickenpox vaccine was added to the routine immunization schedule for all children one year of age (i.e., administered at age 12 months); in spring 2002 a single dose of chickenpox vaccine was also offered to all pre-schoolers born on or after January 1, 1997 (catch-up). The routine vaccination schedule for infants in Alberta has thus included a single dose of chickenpox vaccine to be given at age 12 months since 2001 and the programme gave rise to a dramatic increase in vaccine uptake. Chickenpox vaccine coverage

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was less than 5% in 2001, the last year in which vaccine was available only by private purchase. It jumped to 60% in 2002 (first year of publicly funded vaccine for routine childhood vaccination schedule). In 2005 and in every subsequent year, it exceeded 80% (Alberta Health, unpublished data). Alberta introduced a second dose of chickenpox vaccine for children aged 4–6 years into the routine childhood vaccination schedule in August 2012 [7]. It has been shown that publicly funded varicella immunization programs in Canada and the United States have resulted in a reduction in chickenpox incidence [5,6,8]. However, the impact of these programmes on shingles is less clear because the incidence of shingles began to increase before chickenpox vaccination programs were introduced [9,10]; thus programme evaluations that do not consider this may result in misleading interpretations of the observed data. It is now more than 10 years since the implementation of the Alberta publicly funded chickenpox vaccination program. We examine the epidemiology of shingles in Alberta over 1994–2010. These data span the pre-vaccine era (1994–1998), the period in which vaccine was licensed in Canada but not publicly funded in Alberta – i.e., ‘private availability’ (1999–2001), and the time since implementation of the publicly funded varicella vaccination program (2002–2010 – ‘public availability’).

## 2. Methods

Alberta has a universal publicly funded health care insurance system. Over 99% of Albertans are covered by this programme and the registration file for this programme includes demographic information about registrants as well as a unique personal identifier that can be used to link the registration file to other administrative health databases [9]. Medically attended shingles cases were identified over the interval 1994–2010 for each calendar year using data from physician visits and hospital admissions. The databases employed included the Supplemental enhanced service event system (SESE – physician claims) [6], the Alberta communicable disease reporting system (CDRS), and the morbidity and ambulatory care reporting (MACAR) databases held by the Alberta Ministry of Health. MACAR includes data from both hospital inpatients (hospital morbidity inpatient database) and from hospital emergency department visits and outpatient procedures. The first dated health service utilization for ICD-9-CM code of 053 or ICD-10-CA code of B02 was classified as incident. Diagnostic codes at least 180 days after the first were classified as recurrent episodes. For each year, we estimated the proportion of cases that had one or more of selected co-morbidities (thought most likely to be related to immunosuppression from condition or treatment for the condition) in the 12 months prior to the incident shingles diagnosis. Co-morbidities were identified using linkage by personal health number to multiple chronic disease databases (Table 1). Denominators for rates were estimated using mid-year population estimates from the Alberta Health Care Insurance Plan Registry [11] which have been shown to be a reliable population data source [12]. Annual age- and sex-specific rates were estimated. We estimated the proportion of all cases that were hospitalized and that had co-morbidities by age-group for each year and sex. Shingles rates were modelled with a Poisson model. Denominators for the modelled rates used the mid-year population estimates linking individuals to co-morbidity status determined by any of the listed co-morbidities during that calendar year. We explored the pattern of rates for sex, age, co-morbidity and year effects and their interactions. Of a priori interest were the three time periods related to varicella vaccine accessibility in Alberta. In the pre-licensure period (1994–1998) vaccine was not available in Canada. During the private availability (1999–2001) period, vaccine was available but not publicly funded, thus available only to persons who had to pay.

**Table 1**

Co-morbidities of interest by databases used to identify them.

Condition	Databases used
HIV/AIDS	CDRS
Neoplasms including in situ, those of uncertain or unknown behaviour, and all malignant neoplasms excluding non-melanoma skin cancers	Alberta cancer registry
Agranulocytosis (ICD-9-CM 284.0–284.9, 288.0–288.2 or ICD-10-CA D70)	SESE, MACAR (hospital morbidity inpatient database)
Immune system disorders (ICD-9-CM 279.0–279.9 or ICD-10-CA D80–89)	SESE, MACAR (hospital morbidity inpatient database)
Cystic fibrosis ICD-9-CM 277.0, ICD-10-CA-E84)	SESE, MACAR (hospital morbidity inpatient database)

In the public availability period (2002–2010), vaccine was publicly funded. The independent variables in the Poisson model included: linear trends within each time period (1994–1998, 1999–2001, 2002–2010), sex, age-group (<10 years, 10–44 years, 45–64 years, 65 years or older), co-morbidity status (any vs. none) and two-way interaction terms (age-group  $\times$  sex, age-group  $\times$  co-morbidity, time-period  $\times$  age-group, time-period  $\times$  sex, sex  $\times$  co-morbidity). An alpha level of 0.05 was used to test for significance of interaction terms. As the two-way interactions for co-morbidity  $\times$  age-group and for co-morbidity  $\times$  sex were significant at 0.05, a three way interaction term (age-group  $\times$  sex  $\times$  co-morbidity) was added to the model. The goodness of fit statistic (deviance goodness of fit 1.6) indicated this was an appropriate model. There was no difference between the pre-licensure and private availability period, so these periods were pooled for the final model without affecting model fit. In sensitivity analysis, we modelled only first episodes of shingles to determine the impact of modelling numbers of episodes rather than numbers of individual persons. Secular trends are described using locally weighted scatter plot smoothing (LOESS) curves [13]. SAS 9.2 (SAS Institute Inc, Cary, NC) was used for all data manipulation and analysis, except the LOESS which was carried out using SigmaPlot 11.0 (Systat Software, San Jose, CA).

### 2.1. Ethics

The study was approved by the Conjoint Health Research Ethics Board of the University of Calgary (E 23776, E17522).

## 3. Results

Fig. 1 shows that crude rates of medically attended shingles episodes increased over the interval 1994–2010. The crude rate for 1994 was 3.5 per 1000 person-years. This increased to 3.8/1000 person-years in 1998, to 4.0/1000 person-years by 2001 and to 4.5/1000 person-years by 2010.

Most patients (90%) had only a single episode of shingles; 8% had 2 episodes and 2% had more than 2 episodes (data not shown).

As can be seen in Table 2, for the overall interval 1994–2010, 59% of medically attended shingles episodes (cases) occurred among females. Rates were higher among females than males over the entire interval, and increased more rapidly for females than males (Fig. 2).

Less than 2% of shingles cases had one or more co-morbidities in the 12 months prior to shingles diagnosis and this proportion remained stable throughout all three periods studied (Table 2). A slightly higher proportion of female than male cases had a co-morbidity and this pattern was also stable over all three periods studied (data not shown).

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