



Contents lists available at ScienceDirect

## Vaccine

journal homepage: [www.elsevier.com/locate/vaccine](http://www.elsevier.com/locate/vaccine)

## Epidemiology of varicella in Haidian district, Beijing, China—2007–2015

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## ARTICLE INFO

## Article history:

Received 22 December 2016

Received in revised form 12 March 2017

Accepted 13 March 2017

Available online xxx

## Keywords:

Varicella

Chickenpox

Varicella vaccination

Surveillance

## ABSTRACT

**Background:** 1-Dose varicella vaccination was recommended for children in Beijing before November 2012. To further control school-based outbreaks and decrease incidence, a 2-dose vaccination was implemented in 2013. We described the varicella epidemiology and assessed impact of the 2-dose vaccination in Haidian district, Beijing, 2007–2015.

**Methods:** We examined the estimated incidence and disease characteristics of varicella during 2007–2015 and obtained the 1-dose vaccination coverage for children born during 2005–2013. Number of vaccine doses given was used to indirectly reflect the second-dose vaccination coverage. Overall and age-specific estimated incidences were compared between 2007–2012 and 2013–2015.

**Results:** A total of 23,497 cases were reported during 2007–2015. Of the 23,497 cases, 13,440 (57.20%) were male, and 68.40% were <20 years of age and 70.02% were students and children in kindergarten. The estimated incidence increased from 82 cases per 100,000 population in 2007 to 104 in 2011, before substantially decreasing from 86 in 2012 to 56 in 2015. The median age increased from 14 years in 2007 to 18 years in 2015. The 1-dose varicella coverage for children at  $\geq 2$  years of age gradually increased from 74.21% in 2007 to 90.06% in 2015. Compared with 2007–2012, two-fold average vaccine doses were given during 2013–2015, and the overall estimated incidence declined by 34.4%, particularly in children aged 5–9 years, with a significantly declined trend in children aged 1–9 years and older adolescents aged 15–19 years and non-significantly declined trend in adults aged  $\geq 20$  years, but a significant increasing trend in infants.

**Conclusions:** The overall incidence of varicella has decreased substantially in Haidian district since 2013, with largest decline in children aged 5–9 years. The 2-dose varicella vaccination might not lead to increase in incidence in adults. Long-term surveillance is needed to fully evaluate the long-term impact of the 2-dose varicella vaccination.

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## 1. Introduction

Varicella (chickenpox) is a highly contagious disease caused by varicella-zoster virus (VZV) primary infection. In the absence of varicella vaccination, it was a universal childhood disease [1]. Varicella vaccines (Oka strain), developed in 1970s [2], are now widely used as the most effective measure for prevention of varicella [3]. The vaccine was approved for use in Beijing in 1998 [4], but not included in routine immunization program and parents had to pay for their children's vaccination at their private fee. In recent years, with an increasing coverage rate of 1-dose varicella vaccination in Beijing, the incidence of varicella declined as other regions and countries [5–8].

To date, national varicella surveillance data through the China Information System for Disease Control and Prevention (CISDCP)—a web-based, passive infectious disease surveillance system, are not available, since varicella is not a national notifiable disease in China. In 2005, the China Ministry of Health issued the national guideline on the reporting of information related to public health emergency event [9], which defined all kinds of emergency events, including occurrence of  $\geq 10$  varicella cases in facilities population within one week. Accordingly, varicella became a key disease in Beijing, particularly in schools and kindergartens population. And in 2007, required by the Beijing Bureau of Health, all medical agencies should report varicella cases via CISDCP within 24 h [10], once clinical diagnose of varicella was made. Subsequently, there were so many varicella cases and varicella outbreaks (i.e.,  $\geq 5$  varicella cases occurred in facilities population within one week) reported to the departments of health that in response to school-based varicella outbreaks, single-dose vaccinations have been supplied free of charge to unvaccinated children in schools

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<http://dx.doi.org/10.1016/j.vaccine.2017.03.044>

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and kindergartens population in Beijing [10]. Despite the overall success of varicella vaccination, varicella outbreaks continued to occur, even among highly vaccinated population [11,12], and incidence of varicella plateaued at levels of 1.0–1.1 cases per 1000 population in Beijing between 2007 and 2010 [13], indicating the limits of control and prevention of varicella reached with the 1-dose varicella vaccination [14,15]. To further control school-based varicella outbreaks and decrease varicella incidence, in November 2012, the Beijing Center for Diseases Control and Prevention (BCDC) adapted technical guideline on varicella vaccination [16], recommending that children should receive one dose of varicella vaccine at  $\geq 18$  months of age and a second dose at 4 years of age or older. The guideline also recommended that a second catch-up dose of varicella vaccine should be given to children and adolescents, who previously had received one dose. As of July 2014, the 2-dose varicella vaccination coverage maintained 44.7% for children born in 2006–2009, ranging from 30.5% for children born in 2006 to 51.2% for children born in 2009 [14]. The implementation of the 2-dose varicella vaccination program effectively controlled outbreaks of varicella in schools and kindergartens population [14], but the impact on varicella epidemiology in Beijing is lacking.

Haidian—a district of municipality of Beijing, lying towards the northwestern part of urban core, covers about 430 square kilometers, and its population accounts for approximately 17% of population of Beijing. In this paper, we examined the varicella surveillance data of Haidian district during 2007–2015, and aimed to describe the varicella epidemiology and to assess impact of the 2-dose varicella vaccination program on epidemiology of varicella.

## 2. Material and methods

### 2.1. Characteristics of the study population

In Haidian district, there were an estimated 3500 thousand long-term resident population, with an approximate 8.4‰ of annual birth rate, and an estimated of 80 thousand children in kindergarten and 270 thousand students in elementary, middle, and high schools. Usually children or students were recess at home rather than being in kindergarten or at school during the summer holiday (from mid-July to August) and winter holiday (from mid-January to February) each year.

### 2.2. Case definition, varicella surveillance system and data collection

A varicella case is an illness with acute onset of generalized maculopapulovesicular rash without other apparent cause [10]. Surveillance of varicella in Haidian district is passive, and laboratory confirmation is not required. Before January 1, 2007, varicella was not a reportable disease in Beijing. Since 2007, all practitioners in medical agencies in Beijing have been required to report varicella cases electronically via CISDCP within 24 h, once clinical diagnosis of varicella was made. If varicella cases reported occurred among facilities population, such as students or children in kindergarten, the health-care providers at community-health service agency in corresponding jurisdiction would conduct epidemiological investigations and implement varicella control measures, including exclusion of case patients, vaccination of persons without evidence of immunity (i.e., not vaccinated or without prior varicella disease), disinfection of surroundings, educational interventions, etc.

Data of varicella cases with disease onset from January 1, 2007 to December 31, 2015, were derived from CISDCP for analysis. The information of varicella cases collected was as follows: name, gender, date of birth, occupation, address, date of disease onset.

Varicella cases were categorized into 6 age groups based on the age of varicella disease onset: <1, 1–4, 5–9, 10–14, 15–19 and  $\geq 20$  years of age. Based on the address of varicella cases, the place of residence was classified as rural or urban.

This study was part of routine notifiable-diseases surveillance in Haidian district, Beijing, not research. Ethical approval was not required.

### 2.3. Varicella vaccines and estimation of varicella vaccination coverage

During 2007–2015, there were three or four brands of varicella vaccines (Oka strain, all with the plaque-forming units  $\geq 10^{3.3}$  per dose) available for each year in Haidian district. And only the domestic varicella vaccines, which were manufactured by 4 Chinese biological products companies (i.e., Changchun Kengen Biological Products Co, Ltd, Jilin, Shanghai Institute of Biological Products Co, Ltd, Shanghai, Changchun Biken Biological Products Company, Jilin, and Changchun Changsheng Life Science Limited, Jilin), were used from 2012 to 2015.

Before 2013, a single-dose varicella vaccination was recommended for children  $\geq 12$  months in Haidian district, and from 2013 following the BCDC's guideline [16], a second-dose varicella vaccine was recommended for children at  $\geq 4$  years of age, in addition to the first dose administered at  $\geq 18$  months of age. Data on 1-dose varicella vaccination coverage (without adjustment for prior varicella disease) for children born during 2005–2013 were obtained from the Beijing Childhood Immunization Information System (established in 2008), in which the vaccination information (including date of vaccination, vaccine type) and demographics of children 0–6 years of age were electronically recorded. As proportion of children received the second-dose varicella vaccines was lacking, number of varicella vaccines given, collected from the vaccination service agencies each year, was used to indirectly reflect the second-dose varicella vaccination coverage. To reflect of the change of varicella vaccination, the years 2007–2015 were classified as 2 time periods: 2007–2012 as period before the 2-dose varicella vaccination implemented, and 2013–2015 as period of the implementation of the 2-dose varicella vaccination program.

### 2.4. Statistical analysis

Overall and age-specific estimated incidence rates of varicella were calculated annually from 2007 to 2015 by dividing the aggregate number of varicella cases by the corresponding aggregate population with use of census data from the Haidian district Bureau of Statistics. Demographic characteristics of varicella cases were analyzed. Seasonal trend was assessed through examination of the number of varicella cases among different occupational population (i.e., all cases, cases among students, cases among children in kindergarten, and cases among non-student adults, preschool children and infants) by month during which varicella cases occurred. To account for change of proportion of age and gender over time, when comparing the data from 2007 to 2012 with data from 2013 to 2015, the standardized estimated incidences were also calculated for each period by dividing the number of cases by the corresponding standardized population, which were directly standardized by using group sizes of population in 2011 (which was obtained from the National Population Census initiated every five years by the government) as the weighting scheme.

Pearson chi-squared test or chi-squared test for trend was used to compare proportions or trend of incidences, and rank-sum test (Mann-Whitney U) was used to compare medians. All statistical analyses were performed with SPSS software (version 13.0; SPSS, Inc., Chicago, IL). 2-sided *P* values were reported with a significance level of *P* < 0.05.

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