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The Epidemiology of Measles in Tianjin, China, 2005–2014

Xiexiu Wang¹, Matthew L. Boulton², JoLynn P. Montgomery², Bradley Carlson², Ying Zhang¹, Brenda Gillespie³, Abram L. Wagner², Yaxing Ding¹, Xiaoyan Luo¹, and Tian Hong¹

¹ Tianjin Centers for Disease Control and Prevention, Tianjin, 300011, People's Republic of China

² Department of Epidemiology, University of Michigan, Ann Arbor, MI 48109, USA

³ Department of Biostatistics, University of Michigan, Ann Arbor, MI 48109, USA

Abstract

Background—Measles incidence in China has declined over the last decade and elimination is targeted by 2020. Despite increases in routine immunization services and supplementary immunization activities (SIAs), periodic outbreaks continue to occur. In this paper, we examine measles epidemiology during 2005 to 2014 in Tianjin, China.

Methods—Measles case data were extracted from a web-based communicable disease surveillance system. We examined the socio-demographic characteristics of measles case-patients, including age, sex, urbanicity, residency status, and vaccination history. Demographic characteristics of cases were compared to the general population.

Results—From January 1, 2005 through December 31, 2014, 12,466 measles cases in Tianjin were reported. Among cases, 7,179 (57.6%) were male, and 5,287 (42.4%) were female. Over time, more cases occurred in adults, and for the 2,711 cases in 2014, the majority were either infants <1 year (558, 20.58%) or adults ≥20 years (2,043, 75.36%). Municipal-wide SIAs in Tianjin occurred in 2008 and 2010 with reductions in measles cases the following year for both (189 cases in 2009, and 37 cases in 2011). The number of cases rebounded to pre-SIA levels or higher within 1–3 years following each SIA: 1,990 cases in 2010 and 2,711 cases in 2014. Vaccination status was reported as “none” or “unknown” for 84% of all reported measles cases.

Conclusions—Despite the general decline in cases, measles outbreaks continue to occur. Although the SIAs reduce numbers in their immediate aftermath, case counts rebound 1–3 years after the intervention. Continued monitoring of cases through disease surveillance activities accompanied by targeted immunization activities, including to adults, can help ensure progress toward elimination.

Corresponding Author: Matthew L. Boulton MD, MPH, University of Michigan, Department of Epidemiology, 1415 Washington Heights, 5208 SPH II, Ann Arbor, MI 48109, USA, Phone: (734) 936-1623, Fax: (734) 936-2084, mboulton@umich.edu.

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Potential conflicts of interest

The authors declare no conflict of interest.

Keywords

Measles; Epidemiology; China; Immunization

Introduction

In 2005, the World Health Organization (WHO) committed to achieving measles elimination in the Western Pacific Region (WPR) by 2012 [1]. Although that goal was unrealized, China and other countries in the region have nonetheless made impressive progress in measles control, and the WPR is on track to eliminate measles by 2020 [2]. The WPR experienced a greater than 95% reduction in measles between 2000 and 2011 with reported cases falling from 177,052 to 8,524, representing a historic low [1] with much of this improvement attributable to China, home to approximately 75% of the region's population. While China had the overwhelming majority of cases, they also achieved the most dramatic declines from 131,441 in 2008 to 6,183 cases in 2012 [2,3].

China's success at controlling measles transmission is attributable to a combination of factors including increased measles vaccination rates and improvements in measles surveillance [4]. China has provided a measles vaccine free of charge through their Expanded Program on Immunization (EPI) starting in 1978 [5], and in 1986, a second measles dose was added to the EPI [6]. Estimated coverage of 2 doses of measles-containing vaccine in children has exceeded 90% since 2006 [2,7], although a 2009 study in Beijing migrant children showed lower coverage (around 88%) [8]. In addition to focusing on routine vaccination and immunization verification prior to school entry, China has carried out a number of large-scale measles supplementary immunization activities (SIAs) in an attempt to vaccinate hard-to-reach communities, high risk counties, and under or unvaccinated children [4]. Approximately 168 million people were vaccinated for measles from 2004-2009 in 25 province-wide SIAs [4], and a nation-wide, synchronous SIA vaccinated 102 million children in 2012 [9], with the specific ages targeted in each SIA varying by province. However, despite consistently high coverage, serial SIAs delivering vaccination to millions of children, and historically-low case counts, measles has yet to be eliminated and periodic outbreaks continue to occur [10]. China reported a resurgence in the number of cases to 52,628 in 2014, almost double the number in 2013 and representing a 6-year high [3]. The rebound in measles incidence underscores the importance of sustained control interventions against this highly communicable disease.

The city of Tianjin, one of four province-level municipalities in China, has mirrored measles incidence trends countrywide, and the use of a highly functional immunization information system in combination with ongoing measles surveillance by the Tianjin Centers for Disease Control (CDC) makes them an ideal municipality for characterizing the epidemiology of measles during the elimination phase. Tianjin is located 120 km southeast of Beijing and has a population of approximately 14 million people. Currently, Tianjin uses a 3-dose measles vaccine schedule, with a recommendation for children to be immunized at 8 months, at 18-24 months, and again at 4-6 years. Large-scale SIAs were conducted in Tianjin in December 2008 and again in September 2010. The 2008 SIA targeted children ages 8

months to 15 years and vaccinated 1.2 million children and the 2010 SIA targeted children ages 8 months to 4 years and vaccinated approximately 450,000 children [11]. Estimates of SIA coverage from official reports are quite high, for example 96% in Beijing for the 2010 SIA, although some subpopulations may have had lower uptake of the vaccine during these interventions. For example a survey of migrants in Beijing found only 83.4% of migrant children were vaccinated in the 2010 SIA [12].

Elimination of endemic transmission of measles in China will require a better understanding of who is acquiring measles. Because vaccination is the cornerstone of measles control efforts, detailed information about measles cases is needed in order to evaluate current vaccination programs and inform the development of more targeted vaccination interventions, either through routine immunization services or SIAs. In this paper, we examine the epidemiology of measles over a 10 year period from 2005 to 2014 in Tianjin, China.

Methods

This study describes measles cases reported to the Tianjin CDC from 2005 through 2014. Measles case data were extracted from the China Information System for Disease Control and Prevention (CISDCP), a web-based communicable disease surveillance system that allows for reporting of communicable disease information from local CDCs, hospitals and other health agencies. Health care providers in China are required to report cases of 37 infectious diseases, including measles, to a public health authority under provision of the Law of the People's Republic of China on Prevention and Treatment of Infectious Diseases [13]. China's central public health authority consists of a network of CDCs, headed by the national China CDC in Beijing. Province-level CDCs, including the Tianjin CDC, have jurisdiction over their own area, and approximately 3,000 smaller CDCs at the district and local levels report to provincial CDCs. When a diagnosis of measles is made, health care providers report case information to their local CDC via the CISDCP web portal. Once case-based information has been entered, all levels of CDC within the appropriate jurisdiction (local, district, provincial, and national) have access to the case information and provide coordinated investigative follow-up [14]. The WHO-recommended measles case definition, which China adheres to, includes clinical and laboratory criteria for diagnosis, and both were used to define confirmed cases [15].

We examined the socio-demographic characteristics of measles case-patients in Tianjin from 2005-2014. The CISDCP surveillance report for each measles case consists of basic demographic information (age, sex, occupation, district, and residency status), measles disease summary information, and vaccination history, which includes the number of doses administered for cases in 2009 and later. When presenting results, we divided cases into 3 age categories: infants <1 year of age, children 1 through 19 years of age, and adults 20 years of age where appropriate.

The municipality of Tianjin is divided up into 16 districts. Among the districts, 7 have been classified as Urban (Heping, Hedong, Hexi, Nankai, Hebei, Hongqiao, Binhai New Area), 4 as Suburban (Jinnan, Dongli, Xiqing, Beichen), and 5 as Rural (Baodi, Wuqing, Ji, Jinghai,

Ninghe). The classifications are based on a district's social, economic, and political structures [16,17]. Within each district, residents may be locals or non-locals. A non-local is someone whose official residency, or *hukou*, is located outside of Tianjin but who is currently residing within the municipality.

Analyses included descriptive statistics such as case counts and proportions. The demographic characteristics of cases were compared to information about the general population from the Tianjin Municipal Statistics Bureau [18]. Statistical tests were not run for these comparisons since the case data and population-level data encompass the entire population, not samples. Data were analyzed using SAS software, version 9.3 (SAS Institute, Inc, Cary NC, USA).

This study was reviewed by the University of Michigan Institutional Review Board and deemed to be exempt from human subjects regulation because it was part of standard public health activities.

Results

From January 1, 2005 through December 31, 2014, 12,466 cases of measles in Tianjin were reported into the CISDCP. Table 1 describes the demographic characteristics of cases. Among cases, 7,179 (57.6%) were male, translating to an average rate of 9.1 cases per 100,000 males per year, and 5,287 (42.4%) were female—an average rate of 7.7 cases per 100,000 females per year. In general, males were more likely than females to acquire measles, especially among very young children (67% male compared to 33% female in children <1 year of age). Urban districts contain 52% of the population of Tianjin and reported 43% of cases, suburban districts have 19.5% of the population and 25% of cases, while rural districts have 28.2% of the population but 31.9% of cases. The non-local population comprised 26% of measles cases from 2005 through 2014 and constituted approximately 31.8% of the overall population in Tianjin in 2013.

Vaccination status was reported as “none” or “unknown” for 84% of all reported measles cases (Table 2). The proportion of cases with an unknown vaccination status increased by age. For infants, 5.0% had an unknown vaccinations status, compared to 33.1% and 69.8% of case-patients age 1-19 years and 20 years and older, respectively. The vast majority (85.3%) of infant cases had records confirming no receipt of a vaccine, compared to 30.3% of cases aged 1-19 years and 19.7% of adult cases. Few cases in any age group had a documented dose of MCV: 9.8% of infants, 36.7% of cases 1-19 years, and 10.5% of adult cases. Since 2009, when CISDCP first starting collecting information on a second MCV dose, 1.5% of cases had 2 doses of MCV, including 14.4% of children 1-19 years, and 0.7% of adults 20 years.

The number of measles cases increased from 1,617 in 2005 to 2,540 in 2008 (Table 2). Municipal-wide SIAs in Tianjin occurred in 2008 and 2010, and in the year after the SIA, there was a substantial reduction in the number of measles cases (189 cases in 2009, and 37 cases in 2011). However, the number of cases rebounded to pre-SIA levels or even higher

within 1-3 years following each SIA; in 2010 there were 1,990 cases, and 2014 had 2,711 measles cases (Figure 1).

Measles cases ranged in age from a single congenital case at birth to 84 years of age (mean 19.7 years, standard deviation 15.4). Nearly a quarter of all measles cases (24%) occurred in children under 1 year of age. Children aged 1-19 years represented 21.6% of the cases, and adults bore more the greatest burden of disease (54.3%). Following the 2 SIAs, increasingly more cases occurred in adults. For example in 2005, just over half (53.68%) of the 1,617 cases were in adults whereas by 2014 the majority (75.36%) of the 2,711 cases were in adults 20 years of age (Table 2).

To examine the proportion of cases by age group, we compared them to the proportion of people in each age group in the general population for those years with more than 300 cases. Figure 2 is visually illustrative of the age distribution of cases for each year and shows the early childhood burden of disease as well as a prominent swell in the proportion of adult cases, which is disproportionately greater than their fraction in the general population. In particular, the number of cases in adults increases from 2010 to 2014, the period after the 2 SIAs.

Discussion

Measles continues to be endemically transmitted in Tianjin, China, albeit at progressively lower levels, following a series of SIAs intended to increase childhood vaccination levels in pursuit of national disease elimination. Despite the general decline in numbers, the highly communicable nature of measles continues to result in recurrent outbreaks and a sequence of cyclical peaks and valleys in reported cases. Although the SIAs appear to knock down case counts in their immediate aftermath, overall case counts have tended to rebound to pre-SIA levels or higher 1-3 years after the intervention; this phenomenon has been previously documented in China [4].

The socio-demographic profile of cases, including residence, differs from that of the general population. Although the proportion of cases with rural residence is roughly commensurate with the proportion of the population living in rural areas, this is not true of urban and suburban cases. Urban areas represented a smaller proportion of cases compared to their population proportion while suburban areas represented a disproportionately larger number of cases. Despite broad disease control efforts in Tianjin, including municipal-wide SIAs, the measles risk in suburban areas seems heightened, possibly as a result of suburban areas drawing in a disproportionate number of migrants from rural areas. Rapidly urbanizing settings in many lower and middle income countries show similar patterns of suburban crowding in the presence of limited infrastructure to support comprehensive measles control effort [17,19].

Studies from other regions of China have attributed the continued high levels of measles transmission, at least in part, to a highly mobile fraction of the population that we referred to as the non-local population [8,12,20,21]. Theoretically, this could characterize the suburban cases as many suburban areas support an exceptionally large number of construction and

industrial jobs which are the main occupations of the non-local population [16]. Although non-locals are obviously contributing to measles transmission in Tianjin, the proportion of non-local cases is actually smaller than the proportion of the population they represent. Importantly, local vs non-local status has become increasingly difficult to distinguish as the number of internal migrants in China climbs, but case demographics do not appear to support the notion that the non-local population is disproportionately responsible for the measles burden in Tianjin [6]. Immunization outreach activities to this hard-to-reach population should clearly continue in order to target new residents who may not have received vaccines in their province of origin.

More males than females contracted measles in Tianjin, and while there are more males in Tianjin's general population, the difference persists beyond the population proportions; this sex differential is especially pronounced among infants. Historically, case fatality rates were reported to be slightly higher for males of all ages, but longer-term post-measles mortality rates may be higher among females [22–25]; more recent studies describe similar rates of complication among male and female patients [22,26,27]. The difference found in this study may be due to social, rather than biological, differences such as care seeking patterns and behaviors, with male children being less likely to be vaccinated, more likely to seek medical care when sick, or having a different set of exposure risk due to congregate settings or occupation. In the most recently published data on pediatric measles vaccination in Tianjin, males had a significantly lower measles vaccine series completion compared to females, but this difference was very slight (79.1% in males versus 78.5% in females), and not a major factor in the wide disparity we see in measles cases by sex [7].

The WHO recommends a 2-dose schedule because measles is so highly infectious and because there is the chance of vaccine failure [2]. However, we were unable to draw many conclusions about trends in vaccine dosing because of the large number of people with unknown vaccination status and because information about the second dose of measles-containing vaccine was only added in 2009. Given that many cases in this study had an unknown vaccination status, it is challenging to accurately describe the relationship between vaccination and disease. For children 1 through 19 years of age, an age range of vaccine eligibility with a majority of cases of known vaccination status, approximately half of the cases with a known vaccination status were vaccinated. This finding follows the theoretical expectation that half of cases will be vaccinated if a vaccine is 90% efficacious and if 90% of the population is vaccinated [28]. Mapping the theoretical distribution of previously-vaccinated cases onto adults is more difficult because a larger proportion of cases in this age group have unknown vaccination status; electronic records of vaccination and widespread use of vaccination booklets did not occur until more recently. Because comprehensive vaccination information on adults is currently not available in China, population-level seroprevalence studies could assist with characterizing susceptibility to measles among adult populations. However, the large burden of disease among young adults, which we see in this study, suggests that an SIA targeting adults aged 20–40 years could be useful. Previous research on measles elimination in the Americas has shown that SIAs for adults have been important in closing immunity gaps and moving towards elimination [29]. Moreover, given that the WHO WPR has also adopted a resolution for members to accelerate control of

rubella, combining measles and rubella vaccines in SIAs for adults and other age groups would be a cost-effective mechanism to regionally eliminate both diseases [30].

The high burden of measles disease in infants, who are mostly too young to receive measles containing vaccine, is concerning since infants are at highest risk of serious complications from measles, including death [22]. It has been estimated that 99% of age-eligible children in Tianjin have received two doses of measles vaccine [7], although this is certainly much lower in certain migrant groups. Efforts aimed at maintaining very high childhood routine vaccination rates in Tianjin should continue since, theoretically, 95% of a homogenous population needs to have immunity to prevent outbreaks [31], although disease elimination is possible with lower coverage in the presence sustained routine immunization combined with targeted SIAs. The large number of cases in adults, which may be proportionally increasing over time, is concerning and potentially implicates adults as having a central role in ongoing transmission of measles including back transmission to susceptible infants. The disproportionately large number of adult cases is consistent with findings from a study in Shaanxi Province, China that found a large proportion of cases to be younger than 8 months and older than 27 years of age [32]. Future longitudinal studies of individuals by birth year could collect data on vaccination coverage and strategy (i.e., SIAs and MCVs in routine immunization services) and on measles attack rates. This strategy has been used in the Americas [33], and findings from this study could inform why certain age groups have higher attack rates than others.

The final stages of measles elimination will likely prove to be the most difficult for China. The number of cases in children is decreasing, in no small part due to successful and intensive vaccination campaigns, but the burden of disease in adults and infants persists and has actually increased in some age groups. Continued monitoring of cases through disease surveillance activities and ongoing intensive and targeted immunization activities can help Tianjin, like all of China, to make progress toward their goal of measles elimination. Additional programs, such as targeted adult immunization (as is recommended by the US CDC [34]) might be considered for Tianjin and China to assist with elimination efforts.

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Highlights

- Despite a gradual decline in reported measles cases outbreaks continue to occur.
- Males were more likely than females to acquire measles, especially among very young children.
- Non-locals are contributing to measles transmission but the proportion of non-local cases is actually smaller than the proportion of the population they represent.
- Although SIAs successfully reduce cases in the immediate aftermath, numbers rebound 1-3 years following these resource intensive interventions.

Figure 1.
Number of Measles Cases by Month in Tianjin China; 2005 - 2014

Figure 2.
Proportion of measles cases by age in years with more than 300 cases, Tianjin China 2005-2014.

Table 1

Demographic Characteristics of Measles Cases, Tianjin Province, 2005-2014

		Count	Proportion of Cases	Proportion of Tianjin Population*
Sex (n=12,466)	Female	5287	42.4%	46.4%
	Male	7179	57.6%	53.6%
Age in Years (n=12,466)	< 1	2997	24.0%	0.6%
	1 to 4	1033	8.3%	3.1%
	5 to 9	552	4.4%	3.7%
	10 to 14	271	2.2%	2.8%
	15 to 19	844	6.8%	5.1%
	20 to 24	1278	10.3%	11.9%
	25 to 29	1692	13.1%	10.5%
	30 to 34	1630	13.1%	8.2%
	35 to 39	1140	9.1%	7.5%
	40 to 44	619	5.0%	7.1%
	45 to 49	252	2.0%	9.5%
	50 to 54	104	0.8%	7.7%
	55 to 59	42	0.3%	8.4%
	>= 60	12	0.1%	14.0%
District Type (n=12,448)	Urban	5350	43.0%	52.1%
	Suburban	3123	25.1%	19.5%
	Rural	3975	31.9%	28.4%
Residency Status ** (n=11,931)	Non-Local	3097	26.0%	31.8%
	Local	8834	74.0%	68.2%

* Population proportions are based on 2014 population data from the China Information System for Disease Control and Prevention.

** Residency Status data from the Tianjin Statistics Bureau. "Tianjin statistical yearbook 2013." China Statistics Press: Beijing (2014).

Table 2

Cases by Age Group and Year

		Age			
		<1 Year	1 to 19 Years	20 Years	Total
Year	2005	204 (12.62%)	545 (33.70%)	868 (53.68%)	1617
	2006	294 (20.36%)	549 (38.02%)	601 (41.62%)	1444
	2007	408 (24.77%)	558 (33.88%)	681 (41.35%)	1647
	2008	733 (28.86%)	676 (26.61%)	1131 (44.53%)	2540
	2009	57 (30.16%)	26 (13.76%)	106 (56.08%)	189
	2010	676 (33.97%)	200 (10.05%)	1114 (55.98%)	1990
	2011	8 (21.62%)	6 (16.22%)	23 (62.16%)	37
	2012	3 (14.29%)	4 (19.05%)	14 (66.67%)	21
	2013	56 (20.74%)	26 (9.63%)	188 (69.63%)	270
	2014	558 (20.58%)	110 (4.06%)	2043 (75.36%)	2711
Number of Measles Vaccine Doses	None	2567 (85.3%)	832 (30.3%)	1320 (19.7%)	4719
	1	293 (9.7%)	954 (34.7%)	678 (10.1%)	1925
	Unknown	150 (5.0%)	909 (33.1%)	4683 (69.8%)	5742
Total		2997 (24.04%)	2700 (21.66%)	6769 (54.30%)	12466

* 2 or more doses have only been recorded since 2009.