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Risk factors for measles in children aged 8 months–14 years in China after nationwide measles campaign: A multi-site case-control study, 2012–2013

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Abstract

Introduction: Endemic measles persists in China, despite >95% reported coverage of two measles-containing vaccine doses and nationwide campaign that vaccinated more than 100 million children in 2010. In 2011, almost half of the 9943 measles cases in China occurred in children eligible for measles vaccination. We conducted a case-control study during 2012–2013 to identify risk factors for measles infection in children aged 8 months–14 years.

Methods: Children with laboratory-confirmed measles were age- and neighborhood-matched with three controls. We interviewed parents of case and control infants on potential risk factors for measles. We calculated adjusted matched odds ratios and 95% confidence intervals of risk factors. We calculated attributable fractions for risk factors that could be interpreted as causal and vaccine efficacy (VE) for the measles containing vaccine (MCV) used in the Chinese immunization program.

Results: In all, 969 case-patients and 2845 controls were enrolled. In multivariable analysis, lack of measles vaccination both overall (mOR 22.7 [16.6, 31.1] and when stratified by region (east region, mOR 74.2 [27.3, 202]; central/western regions mOR 17.4 [12.5, 24.3]), hospital exposure (mOR 63.0, 95% CI [32.8, 121]), and migration among counties (overall mOR 3.0 [2.3, 3.9]) were

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Authors' contributions

Dr. Lixin Hao, Chao Ma, Christopher J Gregory, and Huaqing Wang designed the study and directed its implementation, including quality assurance and control. Dr. Chao Ma, Kathleen A. Wannemuehler, Qiru Su, and Zhijie An designed and implemented the study's analytic strategy. Dr. Li Li, Ning Wang, Huiming Luo and Linda Quick helped supervise the field activities. Yuanbao Liu, Hanqing He, Qing Xu, Yating Ma, Wen Yu, Ningjing Zhang lead their field investigation in the six study sites. Dr. Lisa Cairns and Lance Rodewald helped conduct the literature review and prepare the Methods and the Discussion sections of the text.

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Competing interests

The authors declare that they have no competing interests.

significant risk factors. The calculated VE was 91.9–96.1% for a single dose of MCV and 96.6–99.5% for 2 doses.

Conclusions: Lack of vaccination was the leading risk factor for measles infection, especially in children born since the 2010 supplementary immunization activity. Reducing missed vaccination opportunities, improving immunization access for migrant children, and strengthening school/kindergarten vaccine checks are needed to strengthen the routine immunization program and maintain progress toward measles elimination in China.

Keywords

Measles; Measles elimination; Case-control study; Population immunity; Risk factors; China

1. Introduction

In 2006, China endorsed an action plan to eliminate measles, consistent with the World Health Organization (WHO) Western Pacific Region's goal of measles elimination by 2012. Key components of the plan include achieving and maintaining 2-dose routine measles-containing vaccine (MCV) coverage >95% and conducting supplementary immunization activities (SIAs) to close immunity gaps in children. In China, MCV is given at age 8 months (Measles and Rubella Combined Attenuated Live Vaccine is used) and again between 18 and 23 months of age (Measles, Mumps and Rubella Combined Attenuated Live Vaccine is used), with >95% reported coverage for both doses since 2009 [1]. In 2005, the Chinese State Council (which oversees all Ministries) issued a regulation instituting a requirement that all children have their vaccination records checked at the time of entry to kindergarten and primary school, to ensure that school-age children are—or have been—vaccinated against measles. In practice, children who are not up-to-date with vaccines at the time of school entry are encouraged to be vaccinated, but not excluded from school. During 2004–2009, 27 of 31 provinces conducted unsynchronized province-wide catch-up SIAs [2]. In September 2010, China conducted a synchronized nationwide SIA, with a reported coverage of 97.52% [3], to ensure that all children born during1995–2009 had the opportunity to receive at least 1 dose of MCV regardless of prior vaccination status. As a result, measles incidence decreased dramatically, from 99.5 cases per million people in 2008 to 7.4 in 2011. The drop in reported measles incidence was observed not only in vaccine-targeted children but also among infants under vaccination age and adults [4].

Despite this success, sustained measles virus transmission continues in every province. In 2011, 9943 measles cases were reported nationally. Among these cases, 4574 (46%) were in children aged 8 months through 14 years, who were eligible to receive MCV via the routine schedule or in SIAs conducted during 2004–2010 [4,5]. To understand remaining barriers to measles elimination in China after the nationwide 2010 campaign, we conducted a multi-site case-control study during 2012–2013 to identify risk factors for measles infection among different age groups. This paper summarizes results for children aged 8 months–14 years.

2. Methods

2.1. Study location and period

Six provinces (Jiangsu, Zhejiang, Shandong, Henan, Gansu, and Yunnan) were selected because they were geographically representative and had a high incidence of measles during 2005–2010 (>40 cases per million population), sustained measles virus transmission in 2011, and a high proportion of adult or infant cases. Risk factors for measles infection in infants and adults will be reported elsewhere [6,China CDC manuscript in preparation]. These six provinces have a total population of around 394.5 million, 29.6% of the total population of China in 2010 [7]. We investigated laboratory-confirmed measles cases reported from the six provinces in 2012 and extended the study for six months to cover the 2013 peak measles season to meet the target sample size.

2.2. Sample size and case selection

Since 1986, China's 31 mainland provinces have been divided into three groups according to economic and social development: eastern, central, and western regions [2,8]. Jiangsu, Zhejiang, and Shandong are from the more developed eastern region, and Henan, Gansu, and Yunnan from the less developed central or western region. In this multi-site case-control study, we combined the central/western region for the purpose of sample size calculation. For children aged 8 months–14 years, assuming a risk-factor prevalence in controls of 30%, 134 cases with three matched neighborhood controls in each of the eastern and central/western regions would provide a 90% power to detect an odds ratio (OR) >2 with 95% confidence. To account for possible non-participation of 10%, we sought to investigate 150 cases aged 8 months–14 years per region. All measles case-patients from the six provinces that were confirmed in a World Health Organization (WHO) Global Measles and Rubella Laboratory Network-accredited laboratory by positive IgM enzyme-linked immunosorbent assay (SERION ELISA anti-measles virus IgM, Institut Virion\Serion GmbH) or by isolation of measles virus were eligible for enrollment. Case-patients were excluded if the patient had received MCV 7–14 days before rash onset [9] or declined to participate in the study. The details of sampling and participant selection procedures are reported in a separate manuscript summarizing the results for infants aged ≤7 months [6].

2.3. Control selection

We enrolled three neighborhood controls matched to case-patients within the following age strata: 8–17 months, 18 months–5 years, 6–9 years, and 10–14 years. These age strata were selected in part to correspond to China's MCV immunization schedule, as ≥8 months for the first-dose of MCV (MCV1), and ≥18 months for the second-dose of MCV (MCV2). Controls were selected starting with the household closest to that of the case-patient, and subsequent households were visited until three eligible controls were found and enrolled. Potential controls were excluded if they did not consent to participate in the study or had a history of fever and rash in the previous 3 months; if more than one age-eligible individual lived in the household, we selected the one closest in age to the case-patient.

2.4. Data collection

Trained investigators used a standard questionnaire to conduct in-house face-to-face interviews with case-patients and controls. Variables collected included demographic characteristics, migration status, hospital exposure, MCV vaccination history, reasons for non-vaccination if appropriate, and healthcare service use and access. Receipt of MCV for both routine and SIA doses was determined by household-retained vaccination card and clinic-based vaccination records. Personal and family migration status was defined as described in the companion paper [6].

2.5. Data analysis

We completed a summary description of demographic variables and risk factors of interest for all case-patients and controls. We calculated unadjusted and adjusted matched odds ratios (mORs) and 95% confidence intervals (CIs) for risk factors for measles via conditional logistic regression overall and by region. Vaccine effectiveness (VE) was estimated using the formula VE = 1 − aMOR, where aMOR was the adjusted matched odds ratio [10]. Attributable fractions (AF) were calculated for those exposure risk factors that could be interpreted as causal, using the formula $\mathrm{AF} = P[E|D]\left(1 - \frac{1}{\mathrm{mOR}}\right)$ where $P[E|D]$ is the observed prevalence of the exposure among case-patients. Bootstrap 95% CI for the AF were calculated by sampling repeatedly with replacement n matched sets, where n is the total number of matched sets available in the analysis [11]. The 2.5th and 97.5th percentiles of 500 estimated AFs define the 95% CI.

Age categories for analysis of receipt of MCV were defined based on eligibility for routine MCV doses and measles vaccination campaigns: 8–17 months (eligible for routine MCV1), 18–23 months (time window for MCV2), 24–47 months (eligible for both routine MCV1 and MCV2, not targeted by the 2010 nationwide SIA), 48–71 months (pre-school children who are eligible for both doses of routine MCV, targeted by the 2010 SIA), and ≥72 months (school age children targeted by 2010 SIA and school entry vaccination history check). Kaplan–Meier methods [12] in R v 3.1 were used to estimate the time (age) to vaccination among case-patients and controls.

2.6. Ethical considerations

We obtained written informed consent from parents or guardians of participating children. The study protocol was reviewed and approved by both the Ethics Review Committee of the WHO Regional office for the Western Pacific (Unique ID Number: 2011.24.CHN.05.EPI), and the Ethical Review Committee of China Center for disease control and prevention (Unique ID: 201117).

3. Results

Among 2164 laboratory-confirmed measles case-patients aged 8 months–14 years reported in the six study provinces from January 2012 through June 2013, 969 (44.8%) were enrolled based on available resources for case investigation. Enrolled and non-enrolled case-patients did not differ significantly by age group ($\chi^2 = 1.125$, $p = 0.57$) or sex ($\chi^2 = 1.673$, $p = 0.196$). Overall, 73% of enrolled case-patients came from the central/western regions (Table

1). Yunnan Province contributed the largest number of case-patients (421), followed by Henan (220), Shandong (130), Zhejiang (108), Gansu (70), and Jiangsu (20). Children aged 8–17 months made up most (61%) case-patients, and 91% of all enrolled case-patients were preschool children aged <6 years (Table 1). Among all potential controls approached, 2845 age-matched controls were enrolled in the analysis, 40 refused consent for participation, and five were excluded for a history of fever and rash in the past three months.

Sixty-six percent of case-patients were male compared with 53% of controls; the age distributions of case-patients and controls were similar (Table 1). Household vaccination cards were available from 88% of measles case-patients and 97% of controls. Only 45% of case-patients had received MCV1 compared with 96% of controls (Table 2). Among those eligible to receive MCV2, 90% of all controls but only 45% of case-patients (26% in the eastern region and 55% in the central/western regions) had been vaccinated. MCV coverage was particularly poor among the youngest age-groups where the majority of cases were observed. Among 9–17 month old case-patients, only 35% had received MCV1. For children eligible to receive MCV2, only 23% of 18–23 month old case-patients had received this dose (Table 2).

A personal history of migration was more frequently reported in case-patients than controls in both regions (14–26% vs. 7–11%), but was almost twice as common in the eastern region compared with the central/western regions (Table 1). A family history of migration was present in 13–24% of case-patients overall compared with 9–18% of controls. The overall frequency of family migration and the difference between case-patients and controls were greater in the eastern region than the central/western regions (Table 1). Among case-patients, 36% had visited a hospital or clinic at least once in the 8–21 days before rash onset compared with 5% of controls during the same period before interview (45% vs. 6% in the eastern region, and 32% vs. 4% in the central/western regions). Visits were further classified as inpatient (17% cases, 0% controls) and non-inpatient (18% cases, 4% controls). Case-patients more often reported a history of exposure to inpatient wards (37% vs. 4%) and infusion rooms (46% vs. 27%) than controls (data not shown). Case-patients and controls in the eastern region had higher levels of parental education and fewer siblings than case-patients and controls from the central/western regions (Table 1).

On univariate conditional logistic models analysis, case-patients were more likely not to have a vaccination card than controls (overall mOR 8.7 [5.7, 13.4]), and they were much more likely not to have received any MCV dose both overall (mOR 22.7 [16.6, 31.1] and when stratified by region (east region, mOR 74.2 [27.3, 202]; central/western regions mOR 17.4 [12.5, 24.3]) (Table 3). Among children eligible for two doses of MCV, case-patients were more likely than controls to have received only one dose (overall mOR 6.1 [4.1, 9.1]; eastern region mOR 9.5 [3.2, 28.0], central/western regions mOR 5.5 [3.6, 8.5]). For case-patients, the odds of having received no MCV doses vs. >2 doses was more than 100 times greater compared with controls (overall mOR 138 [86.3, 221]).

In addition, case-patients were more likely than controls to have visited a hospital in the 8–21 days before rash onset or interview date, and were much more likely to have inpatient visit than controls overall (mOR 63.0, 95% CI [32.8, 121]) and in both regions (Table 3). A

personal history of the child moving into the current county of residence from outside the county was a risk factor for measles with an overall mOR of 3.0 [2.3, 3.9]. Families of case-patients were more likely than families of controls to have migrated among provinces, prefectures, and counties in both regions, but this was not significant for migration among provinces in the central/western regions (mOR 1.3 [0.8, 1.9]). For all these family migration variables, the mOR for being a case-patient was two to four times higher in the east (mORs 3.9–5.8) than in the central/western regions (mORs 1.3–2.1). Common risk factors for being a case-patient among regions also included male sex and the primary caretakers being the child's parents. Additional risk factors for being a case-patient only in the east included lower level of parental education and not having siblings (Table 3).

In multivariable logistic models, significant factors associated with being a case-patient were number of MCV doses received and hospital visit in the eastern region; sex, hospital visit, and the interaction between MCV doses and mother's education in the west/central regions; and sex, hospital visit, migration from a different county, and the interaction between MCV doses and mother's education in the overall model (Table 4). Among children with mothers having primary education or less, the adjusted OR for zero doses vs. 1 dose was 12.4 (95% CI: 7.0, 21.8) and 29.3 (95% CI: 15.7, 54.7) for zero dose vs. 2 doses; among children with mothers having at least a middle-school education, the adjusted OR was 25.4 (95% CI: 16.2, 40.0) for zero dose vs. 1 dose and 214 (95% CI: 112, 410) for zero dose vs. 2 doses (Table 4). The calculated AF of measles cases for zero doses of MCV was 62% (95% CI: 59, 65) adjusting for sex, hospital visit, and migration from a different county. The AF of measles cases for any hospital visit was 32% (95% CI: 29, 36%) adjusted for any MCV doses received, sex, and migration from a different county. The AF for inpatient and non-inpatient hospital visits was 17% (95% CI: 14, 19) and 16% (95% CI: 13, 18), respectively.

Vaccine effectiveness (VE) of MCV for a single dose ranged from 91.9% to96.1% and for 2 doses from 96.6% to 99.5% (Table 4). There was an interaction between the level of maternal education and VE for both 1 and 2 MCV doses.

Probability of MCV1 and MCV2 vaccination by age for case-patients and controls up to age 36 months is shown in Fig. 1. By age 12 months, >90% of controls had received MCV1 compared with ~40% of case-patients. At 24 months, the upper limit of the recommended age for MCV2 in China, there was a >70% probability of vaccination with MCV2 for controls compared with <40% for case-patients. Fewer than 50% of eligible case-patients had received MCV2 even by age 36 months compared with >80% of controls. Reasons for missing MCV vaccination in the routine system and in the 2010 SIA are given in Table 5. Parental report of contraindication to vaccine was the most frequent cause in both regions: 44–56% for MCV1 and 24–26% for MCV2. Other reasons included parental report that parents were too busy, absent from residence, or unaware that the child needed vaccination. Among case-patients, multivariable analysis demonstrated associations between lack of vaccination and age 8–17 months (mOR 4.0 [2.4, 6.6]), age 18–71 months (mOR 1.8 [1.1, 3.1]), and county-to-county migration (mOR 2.2 [1.5, 3.1]) (Table 6).

4. Discussion

In this matched case-control study among children of measles-vaccine target age, we have shown that the Chinese MCV is highly effective and that three significant risk factors exist for acquisition of measles: (1) failing to vaccinate young children in a timely manner, (2) hospital exposure, and (3) migrating into a new community. Furthermore, we have shown that failure to vaccinate in a timely manner was associated with missed immunization opportunities and migration.

Children in this study were all age-eligible for MCV through China's Expanded Program on Immunization (EPI). Compared with analysis of measles passive surveillance data, the matched case-control study design also has advantages, including the ability to identify and quantify specific risk factors, determine the fraction of cases that can be attributed to a risk factor, and to more directly measure VE. The risk factors for measles identified in this study are consistent with evaluations in other countries [13–18], and in China [2,4,19,20]. The age distribution of case-patients shows an accumulation of susceptible children after this SIA. Few measles cases in school-age children might indicate the impact of the SIA; children who were of school age when this study was conducted had been the age-target of the SIA. Rare acquisition of measles among school-age children might also show the impact of the school vaccination record check and referral requirements that have been part of the Chinese immunization program's legal framework since 2005.

Although failure to vaccinate was responsible for most measles infection in children, almost one in three infections in this age group could be attributed to exposure in hospitals. High nosocomial transmission and delay of timely receipt of MCV might be acting synergistically. Hospitals are well known as important sites for transmission of measles, in part because people ill with measles are often brought to hospitals for evaluation and treatment, and measles is highly transmissible in the early stages when symptoms are non-specific. As outlined in a global review, there have been a large number of articles worldwide that have described transmission from healthcare workers to patients or other staff members [21]. Nosocomial transmission among patients and health care workers emerges as a risk factor when a country nears the elimination of measles [21] and remains a risk factor after measles elimination [22].

Missed opportunities to immunize have challenged elimination efforts and immunization programs for decades [23]. The measles resurgence in the United States during 1989–1991 was largely a result of missed opportunities to immunize [24]. Several types of missed opportunities have been defined: (1) use of false contraindications to vaccination, (2) failure to provide at an immunization visit all of the recommended vaccines due at that visit, and (3) failure to vaccinate at healthcare encounters other than vaccination visits. In this study, the most frequent type of missed opportunity was for contraindications to MCV. Our study did not evaluate the validity of the contraindications, but because there are very few absolute contraindications to MCV, many of these contraindications were likely false. However, contraindications to vaccination vary by country, and official contraindications for MCV have been broader in China than in other countries [25,26]. A recent measles importation to the United States from China supports this possibility [27]. Additionally, egg allergy has

been listed as a contraindication to MCV in China, and some clinics screen for egg allergy before vaccination. Egg allergy as a contraindication is not limited to China [28]. A commonly occurring false contraindication to vaccination globally is mild illness, such as diarrhea, runny nose, or low-grade fever.

China is undergoing large and rapid urbanization, with many families migrating with young children for employment opportunities. Although the EPI system in China officially allows all age-eligible children to receive free vaccines regardless of residency status, it is challenging for an immunization clinic to be aware of children who are new to an area. As a result, children of migrant workers have lower coverage, as shown in our case-control study, as well as in other studies [29].

Of the three major risk factors identified in our study, none of them or their antecedents lend themselves to simple strategies that will rapidly reduce the number of measles cases. Changing longstanding provider practices takes time and is not always possible. Working with hospitals and hospital infection-control organizations to ensure that healthcare workers are fully vaccinated against measles and that hospital infection control policies are adequate for measles also takes time. Developing a systematic means to identify children new to an area in a timely manner is a large challenge. However, addressing these three risk factors has the potential to not only facilitate measles elimination but also to strengthen the routine immunization program. These risk factors transcend measles vaccination and almost certainly apply to other vaccines in the routine immunization schedule and for improved infection control of non-vaccine-preventable diseases as well.

That relatively few school-age children acquire measles in China may be due to the impact of the 2010 measles SIA. Of critical importance, however, is that children born after the SIA are about to enter kindergarten in China. Strengthening the school entry check and referral system to determine that all school children have 2 documented doses of measles- and rubella-containing vaccine could provide a fail-safe mechanism to prevent persistence of susceptibility to measles after age 5 years. Such a mechanism could ensure that children with missed opportunities for receipt of MCV and other vaccines or who migrated into a new community are protected before entering school. In the presence of pockets of unvaccinated children, schools can function as efficient locations for measles transmission and have been well-documented sources for outbreaks [30].

Limitations of this case control study have been described in detail [6], and include the underreporting of measles cases, the possibility that results from these provinces might not generalize to all of China, and the chance that excluding controls with fever and rash from the study could bias the study toward increasing the association between previous hospital exposure and measles infection. In addition, parents of measles cases might be more likely to recall hospital visits. Why maternal education levels modified the calculated VE of both 1 and 2 doses of MCV is unclear. It is possible that women from lower education levels more frequently had previous natural measles infection and subsequently higher maternal antibody levels that interfered with the immune response to MCV in their children or that children from women with higher education levels had a more robust immunological response to vaccination. Neighboring matching of cases with controls, utilized to reduce the risk of

differential exposure to measles virus given the low level of recent disease transmission in China, limits the ability to look at residence as a risk-factor for infection. This also likely lead to an underestimation of the association between migration status and infection, as recent migrants in eastern China tend to predominately cluster in certain neighborhoods.

The findings and conclusions support recommendations to (1) study the reasons for missed immunization opportunities to eliminate them, (2) evaluate and strengthen the school vaccination record check to ensure that all school children have 2 MCV doses, (3) work with local Centers for Disease Control and Prevention and hospital infection control organizations to implement or strengthen policies that reduce nosocomial transmission of measles through staff vaccination and implementation of measles and fever and rash management protocols, and (4) identify good practices for conducting outreach to children of migrating workers in China and ensure that immunization clinics do not restrict access to services for non-local children.

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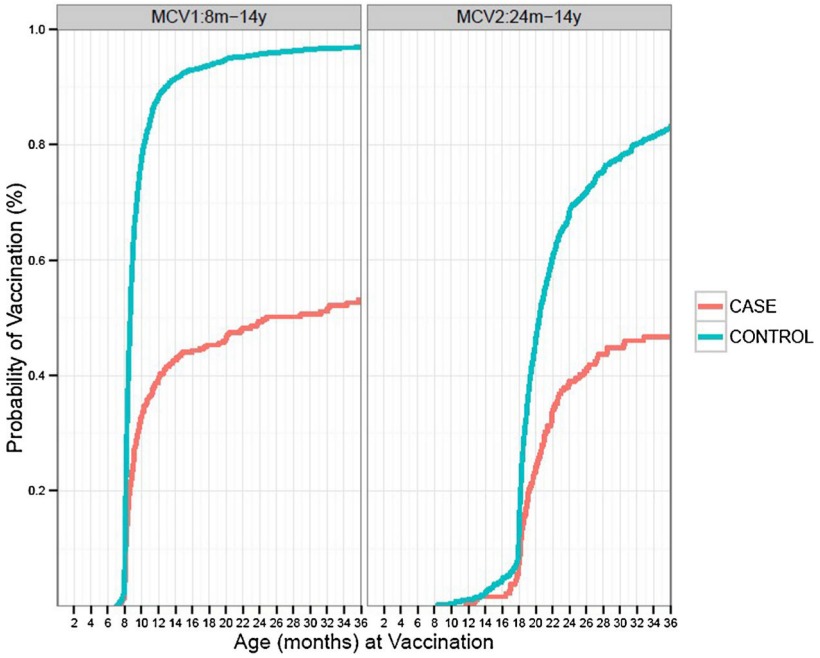

Fig. 1.

Probability of vaccination by age with measles-containing vaccine in children aged 8–36 months, matched case–control study—China, 2012–2013. Abbreviations: MCV1, first dose of measles-containing vaccine; MCV2, second dose of measles-containing vaccine

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Table 1

Summary characteristics for children aged 8–179 months enrolled in measles case-control study—China, 2012–2013.

Variable Description	Eastern region, *N* (%)		Central/western regions, *N* (%)		Total, *N* (%)	
	Cases (*n* = 258)	Controls (*n* = 761)	Cases (*n* = 711)	Controls (*n* = 2084)	Cases (*n* = 969)	Controls (*n* = 2845)
Sex (male)	178(69)	402 (53)	463(65)	1103(53)	641 (66)	1505(53)
Age (months)						
8–17	163(63)	447 (59)	431(61)	1110(53)	594 (61)	1557(55)
18–71	75 (29)	253 (33)	215(30)	767 (37)	290 (30)	1020(36)
72–119	12(5)	36 (5)	43 (6)	150(7)	55 (6)	186(7)
120–179	8 (3)	25 (3)	22 (3)	57 (3)	30 (3)	82 (3)
Vaccination card (yes)	237 (93)	745 (98)	606 (87)	1971 (96)	843 (88)	2716(97)
Total number ofMCV doses						
0 doses	183(71)	25 (3)	437(61)	193 (9)	620 (64)	218(8)
1 doses	49(19)	380 (50)	176(25)	1007(48)	225 (23)	1387(49)
≥2 doses	26(10)	356 (47)	98(14)	884 (42)	124(13)	1240(44)
Schooling status						
Preschool	211 (82)	615(81)	555(81)	1591 (79)	766(81)	2206 (80)
Kindergarten	29(11)	90(12)	69(10)	227(11)	98(10)	317(11)
Primary school	17(7)	52 (7)	56 (8)	176(9)	73 (8)	228 (8)
Middle school	1 (0)	4(1)	4(1)	5 (0)	5(1)	9 (0)
Out of school (school age)	0	0	2 (0)	11 (1)	2 (0)	11 (0)
Mother’s education						
≤ Primary school	47(18)	89(12)	252 (36)	646(31)	299 (31)	735 (26)
Middle school	188(74)	593 (78)	416 (59)	1321 (64)	604 (63)	1914(68)
≥College	20 (8)	76(10)	34 (5)	89 (4)	54 (6)	165(6)
Father’s education						
≤ Primary school	27(11)	47 (6)	194(28)	533 (26)	221(23)	580(21)
Middle school	208(81)	612 (80)	467 (67)	1399(68)	675 (70)	2011(71)
≥College	22 (9)	102(13)	40 (6)	124(6)	62 (6)	226 (8)
Type of house						
Multistory building	109 (42)	353 (46)	272 (38)	813(39)	381 (39)	1166(41)

Variable Description	Eastern region, *N* (%)		Central/western regions, *N* (%)		Total, *N* (%)	
	Cases (*n* = 258)	Controls (*n* = 761)	Cases (*n* = 711)	Controls (*n* = 2084)	Cases (*n* = 969)	Controls (*n* = 2845)
Single story house	137(53)	381 (50)	386 (55)	1174(57)	523 (54)	1555(55)
Dormitory	7 (3)	20 (3)	14(2)	24(1)	21 (2)	44(2)
Other	5 (2)	7(1)	36 (5)	56 (3)	41 (4)	63 (2)
No. siblings						
0	144(56)	520 (69)	303 (43)	928 (45)	447 (46)	1448(51)
1	89 (34)	197(26)	279 (39)	821 (40)	368 (38)	1018(36)
≥2	25(10)	42 (6)	127(18)	318(15)	152(16)	360(13)
Primary caretaker						
Parents	231 (90)	614(81)	596 (84)	1677(81)	827 (86)	2291 (81)
Other	27(10)	145(19)	110(16)	389(19)	137(14)	534(19)
History of migration in child[a] (Yes)	66 (26)	83(11)	94(14)	144(7)	160(17)	227 (8)
History of family migration[a]						
From different province	72 (28)	131 (17)	53 (7)	133 (6)	125(13)	264 (9)
From different prefecture	82 (32)	156(21)	111 (16)	265(13)	193 (20)	421 (15)
From different county	87 (34)	178(23)	143 (20)	329(16)	230 (24)	507(18)
Hospital visit in last 8–21 days (yes)	116(45)	46 (6)	222 (32)	86 (4)	338 (36)	132(5)
Type of visit						
Inpatient: 8–21 days	50(19)	3 (0)	113(16)	7 (0)	163(17)	10(0)
Non-inpatient: 8–21 days	66 (26)	43 (6)	109(16)	79(4)	175(18)	122(4)
No Visit	141 (55)	708 (94)	469 (68)	1933 (96)	610 (64)	2641 (95)

[a]Migration status was defined by either a personal history of the child having at least one previous residence outside of the current county of residence or a family history of ever having migrated from a different county, prefecture, or province to the current place of residence.

Table 2

Measles-containing vaccine (MCV) coverage for children aged 9–179 months in case-control study—China, 2012–2013[a].

MCV dose by age group (months)	Eastern region number (% vaccinated)		Central/western regions number (% vaccinated)		Total number (% vaccinated)	
	Case	Control	Case	Control	Case	Control
MCV1						
9–17	27 (28)	393 (98)	102(38)	923 (95)	129(35)	1316(96)
18–23	2 (13)	59 (98)	32 (67)	202 (99)	34 (54)	261 (98)
24–47	11 (29)	125 (98)	52 (57)	359 (97)	63 (48)	484 (98)
48–71	11 (61)	64 (97)	25(61)	146(96)	36(61)	210(96)
≥72	12 (67)	58 (98)	39 (70)	173 (92)	51 (69)	231(93)
Sub-total	63 (34)	699 (98)	250 (49)	1803(96)	313 (45)	2502 (96)
MCV2						
9–17						
18–23	2 (14)	40 (70)	9(27)	139(86)	11(23)	179(82)
24–47	7 (20)	110(90)	30 (56)	305 (93)	37 (42)	415 (92)
48–71	4(22)	59 (91)	16(55)	123(92)	20(43)	182(92)
≥72	8 (57)	53(100)	27 (79)	142(90)	35 (73)	195 (93)
Sub-total	21 (26)	262 (88)	82 (55)	709 (91)	103(45)	971 (90)

[a]In China, MCV1 is scheduled at age 8 months. We therefore analyzed vaccination status for children aged 9 months and older.

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Table 3

Characteristics associated with measles in children aged 8–179 months stratified by geographic area, matched case–control study—China, 2012–2013.

	Eastern region		Central/western regions		Total	
	Number of matched set	mOR (95% CI)	Number of matched sets	mOR (95% CI)	Number of matched set:	mOR (95% CI)
Demographic variables						
Sex (male:female)	258	2.0 (1.5, 2.8)	711	1.7 (1.4, 2.0)	969	1.8 (1.5, 2.1)
Mother's education	255		701		956	
≤ Primary school: college+		2.8 (1.3, 5.9)		1.1 (0.7,1.9)		1.5 (1.0, 2.3)
Middle school: college+		1.5 (0.8, 2.7)		0.8 (0.5,1.3)		1.0 (0.7,1.5)
Father's education	257		700		957	
≤ Primary school: college+		4.0 (1.8, 8.8)		1.2 (0.8, 2.0)		1.7 (1.2, 2.6)
Middle school: college+		2.0 (1.1,3.5)		1.1 (0.7,1.7)		1.4 (1.0,1.9)
Type of house	258		708		966	
Multistory: single story		0.6 (0.4,1.0)		1.0 (0.8,1.4)		0.9 (0.7,1.2)
Others: single story		3.1 (0.5,18.8)		3.3 (1.8, 6.3)		3.2 (1.7, 5.8)
Any siblings (yes:no)	258	0.4 (0.2, 0.7)	708	0.7 (0.5,1.0)	966	0.6 (0.5, 0.8)
Care taker (parents:other)	258	2.3 (1.4,3.8)	704	1.3 (1.0,1.7)	962	1.5 (1.2, 1.9)
MCV vaccination history						
Vaccination card (no:yes)	255	7.0 (2.7,18.0)	699	9.2 (5.7,15.0)	954	8.7 (5.7, 13.4)
MCV total doses (missing=no)	258		711		969	
0 doses: 1 dose		74.2 (27.3, 202)		17.4(12.5, 24.3)		22.7(16.6,31.1)
0 doses: ≥2 doses		702(172, 2869)		96.7 (58.4,160)		138(86.3, 221)
1 dose: ≥2 doses		9.5 (3.2, 28.0)		5.5 (3.6, 8.5)		6.1 (4.1, 9.1)
Migration history						
History ofmigration in child (yes:no)	254	3.9 (2.5, 6.0)	688	2.6 (1.9,3.6)	942	3.0 (2.3, 3.9)
Family migration between provinces (yes:no)	256	5.8 (3.1,10.7)	710	1.3 (0.8,1.9)	966	2.1 (1.5, 2.9)
Family migrating between prefecture (Yes:No)	256	4.8 (2.7, 8.4)	710	1.8 (1.2, 2.7)	966	2.6 (1.9, 3.6)
Family migrating between county (yes:no)	256	3.9 (2.3, 6.6)	710	2.1 (1.5,3.1)	966	2.6 (1.9, 3.5)
Hospital exposure in last 8–21 days	257		686		943	
All visit: No visit		13.1 (8.4, 20.6)		14.8(10.5,21.1)		14.2(10.8,18.7)
Inpatient visit: No visit		67.0 (20.5, 220)		61.3(28.1,134)		63.0(32.8,121)

	Eastern region		Central/western regions		Total	
	Number of matched set	mOR (95% CI)	Number of matched sets	mOR (95% CI)	Number of matched set:	mOR (95% CI)
Non-inpatient visit: no visit		8.2 (5.0,13.3)		8.0 (5.4,11.9)		8.1 (5.9, 10.9)

CI, confidence interval; mOR, matched odds-ratio; MCV, measles-containing vaccine.

Table 4

Adjusted odds ratios for case status and vaccine efficacy estimates from multivariable model, children aged 8–179 months—China, 2012–2013.

	Eastern region			Central/western regions		Total	
	Comparison	**mOR[a] (95% CI)**	**VE[b] (95% CI)**	**mOR[a] (95% CI)**	**VE[b] (95% CI)**	**mOR[a] (95% CI)**	**VE[b] (95% CI)**
Doses × mothers education interaction	Doses 0 vs. 1: primary	**130(17.2,984)**	99.2 (94.2,99.9)	**8.5 (4.7,15.2)**	88.2 (78.7,93.4)	**12.4(7.0,21.8)**	91.9(85.8,95.4)
	Doses 0 vs. 1: middle/college	**52.5 (16.4,168)**	98.1 (93.9,99.4)	**21.8(13.1,36.1)**	95.4 (92.4,97.2)	**25.4(16.2,40.0)**	96.1 (93.8,97.5)
	Doses 0 vs. 2: primary	**264 (28.9,2424)**	99.6 (96.5,100)	**20.5 (10.8,38.9)**	95.1 (90.8,97.4)	**29.3 (15.7,54.7)**	96.6 (93.6,98.2)
	Doses 0 vs. 2: middle/college	**340 (72.0,1609)**	99.7 (98.6,99.9)	**216(102,456)**	99.5 (99.0,99.8)	**214(112,410)**	99.5 (99.1,99.8)
Visit type	Visit type: inpatient vs. no visit	**46.4 (6.7,321)**		**35.2(13.9,89.0)**		**36.9(16.4,83.4)**	
	Visit type: non-inpatient vs. no visit	**7.4 (3.1,17.8)**		**7.0 (4.1,12.1)**		**6.7 (4.3,10.4)**	
Sex	Male vs. female	1.0 (0.5,1.9)		**1.7 (1.2,2.2)**		**1.5 (1.2,2.0)**	
Migrate county	Yes vs. no	2.6 (0.8,7.9)		1.6 (0.8,3.0)		**1.8 (1.1,3.2)**	

CI, confidence interval; mOR, matched odds-ration; VE, vaccine efficacy.

[a]Adjusted matched odds ratio, adjusted for the other variables listed. mOR significantly > 1 are given in bold type.

[b]Adjusted vaccine effectiveness, VE = 1 − mOR.

Table 5

Reasons for missing receipt of measles-containing vaccine (MCV) among children aged 9–179 months in case-control study—China, 2012–2013.

Reason	Eastern region number (% reporting this reason)			Central/western regions number (% reporting this reason)		
	MCV1 (197[a])	MCV2 (95[a])	2010 campaign (77[a])	MCV1 (462[a])	MCV2 (139[a])	2010 campaign (94[a])
Caretaker knowledge and attitudes						
Caretaker believes child not yet vaccination age	4(2)	12(13)	1(1)	20 (4)	9 (6)	0 (0)
Fear of adverse effects	5 (3)	5 (5)	3 (4)	15(3)	3(2)	1(1)
Parents believe disease not serious	5 (3)	6 (6)	1(1)	17(4)	2(1)	1(1)
Parents do not believe vaccine effective	2(1)	2 (2)	1(1)	4(1)	1(1)	1(1)
Parents think children will not get the disease	8 (4)	5 (5)	2 (3)	13(3)	5 (4)	3(3)
Parents think natural measles infection better	0 (0)	0(0)	0 (0)	2 (0)	1(1)	0 (0)
Parents do not know child needs vaccine	8 (4)	4 (4)	6(8)	21 (5)	15(11)	5(5)
Child already vaccinated	0 (0)	3 (3)	19(25)	0 (0)	3(2)	9 (10)
Child had measles before	0 (0)	0(0)	0 (0)	1 (0)	1(1)	0 (0)
Religion/cultural beliefs	4(2)	2 (2)	0 (0)	3(1)	2(1)	0 (0)
Caretaker barriers to accessing vaccination services						
Parent forgot the scheduled date of vaccination	8 (4)	11(12)	1(1)	16(3)	7 (5)	0 (0)
Temporarily absent from residence	10(5)	2 (2)	3 (4)	24 (5)	18(13)	15(16)
Parent too busy/no time	15(8)	20 (21)	2 (3)	31 (7)	24(17)	16(17)
Child has no local registration	8 (4)	3 (3)	1(1)	8 (2)	1(1)	1(1)
Immunization services/systems barriers						
Contraindication to vaccination	110(56)	25 (26)	12(16)	203 (44)	34 (24)	26 (28)
Vaccine site unable to provide vaccination on time	5 (3)	2 (2)	0 (0)	10(2)	3(2)	1(1)
Immunization site too far/difficult to reach	2(1)	1(1)	0 (0)	12(3)	4 (3)	3(3)
Shortage ofvaccine/vaccine not available	0 (0)	0(0)	0 (0)	4(1)	0 (0)	0 (0)
Vaccine fee/parents need to pay	0 (0)	0(0)	0 (0)	3(1)	0 (0)	0 (0)
Poor service at vaccination site	0 (0)	0(0)	0 (0)	1 (0)	1(1)	0 (0)
Other reasons	26 (13)	15(16)	31 (40)	83 (18)	8 (6)	13(14)

MCV1, first dose of measles-containing vaccine; MCV2, second dose of measles-containing vaccine.

[a]Total number of missed doses. For each unvaccinated antigen, up to three reasons can be given.

Table 6

Adjusted odds ratios for lack of vaccination among measles cases from multivariable model, children aged 8–179 months—China, 2012–2013.

Comparison		Eastern mOR[a] (95% CI)	Central/western mOR[a] (95% CI)	All mOR[a] (95% CI)
Age	8–17 months vs. 6–14 years	**5.8(2.1,15.9)**	**3.3 (1.8, 6.0)**	**4.0 (2.4, 6.6)**
	18–71 months vs. 6–14 years	**3.8(1.3,11.0)**	1.3 (0.7, 2.4)	**1.8 (1.1, 3.1)**
Mother's education	Middle/college vs. primary	0.5 (0.2, 1.2)	1.4 (1.0, 2.0)	1.2 (0.9,1.7)
Migrate county	Yes vs. no	1.0 (0.5, 1.8)	**3.1 (1.9,4.8)**	**2.2 (1.5, 3.1)**
Hospital visit	Yes vs. no	1.5 (0.8, 2.7)	1.4 (0.9, 2.0)	1.4 (1.0,1.9)
Region	East vs. central/western			1.3 (0.9,1.8)

Abbreviations: CI, confidence interval; mOR, matched odds-ratios.

[a]Adjusted matched odds ratio, adjusted for the other variables listed. Adjusted OR significantly >1 are given in bold type.