Control of measles and pneumococcal disease in China

by

Abram Wagner

A dissertation submitted in partial fulfillment
of the requirements for the degree of
Doctor of Philosophy
(Epidemiological Science)
in the University of Michigan
2015

Doctoral Committee:

Professor Matthew L. Boulton, Chair
Professor Bhramar Mukherjee
Clinical Associate Professor Eden V. Wells
Associate Professor Brian J. Zikmund-Fisher

© Abram Wagner, 2015

ACKNOWLEDGMENTS

I am thankful to the many mentors I had at Michigan and in China who helped me through my dissertation. My advisor, Matthew Boulton, was an amazing resource to bounce ideas off of, and I am fortunate to have received so much encouragement from him to do work in China. Eden Wells always had a positive disposition, and it was always a joy to talk to her about my research and life in general. Brian Zikmund-Fisher was instrumental in putting together my survey and always being available to work through analytical issues. And of course, my dissertation was strengthened in innumerable ways because of insights from Bhramar Mukherjee. Several consultants at CSCAR—Kathy Welch, Brady West, Missy Plegue, and Shyamala Nagaraj—were also important methodological resources for me.

I am grateful that my colleagues in China made me feel welcome there and presented me with an open environment to do research. Thanks especially to Ding Yaxing and Zhang Ying in Tianjin and Sun Xiaodong, Huang Zhuoying, Ren Jia, and Tao Lina in Shanghai. I would not have been able to do research without their connections, their expertise, and their willingness to take me in.

I am blessed with many other colleagues, friends, and families who helped me along the way. Thanks, Mom and Dad, for listening and encouraging; thanks to my siblings, Isaac, Margot, and Lucas, for being examples of diligent doctoral students; and thanks to my friends for your love and support—I especially am grateful for Steven Toth, Angela Liu, Emily DeMeo, Sonia Hegde, and Nijika Shrivastwa.

TABLE OF CONTENTS

LIST OF TABLES

TABLE

LIST OF FIGURES

FIGURE

LIST OF APPENDICES

APPENDIX

LIST OF ABBREVIATIONS

CDC	Centers for Disease Control and Prevention
CDR	Child Dependency Ratio
CI	Confidence Interval
df	Degrees of Freedom
EHR	Electronic Health Record
EPI	Expanded Program on Immunization
GEE	Generalized Estimating Equation
HBM	Health Belief Model
Hib	*Haemophilus influenzae* type b
HPV	Human Papillomavirus
IPD	Invasive pneumococcal disease
M1	Measles vaccine dose 1
MCV	Measles-containing vaccine
MCV1	Measles-containing vaccine dose 1
MCV2	Measles-containing vaccine dose 2
MCV3	Measles-containing vaccine dose 3
MMR	Measles-mumps-rubella vaccine
MMR1	Measles-mumps-rubella vaccine dose 1
MMR2	Measles-mumps-rubella vaccine dose 2

NIDMIS	National Infectious Disease Monitoring Information System
OR	Odds Ratio
PCV	Pneumococcal Conjugate Vaccine
PPS	Probability Proportionate to Size
PPSV	Pneumococcal Polysaccharide Vaccine
PV	Pneumococcal Vaccine (either PCV or PPSV)
RR	Rate Ratio
RMB	Renminbi
SD	Standard Deviation
SE	Standard Error
SIA	Supplementary Immunization Activity
SIPIS	Shanghai Immunization Program Information System
USD	United States Dollar
WHO	World Health Organization

ABSTRACT

China has made great strides in controlling most common vaccine-preventable diseases by increasing access to childhood vaccines through the government-funded Expanded Program for Immunization. Despite this success, China was unable to meet the national and WHO goal of measles elimination by 2012, and has chosen to not publicly fund newer vaccines, like the pneumococcal vaccine. Non-locals, migrants from rural to urban areas, are generally thought to be a significant contributor to the difficulty in controlling vaccine preventable diseases in China because of their higher mobility and lower socioeconomic status. Using registry and survey data, we quantified differences in disease incidence between locals and non-locals. In the first study, we characterized differences in the measles incidence rate between locals and non-locals in a Poisson regression of time series data from Tianjin. We found that non-locals had a higher rate of measles before the 2008 supplementary immunization activity (SIA), but this disparity attenuated in the two years after the first SIA and was completely eliminated after the 2010 SIA. In the second study, we used logistic regression models to examine patterns of measles and pneumococcal vaccination among children in the Shanghai immunization registry, in particular focusing on differences between locals and non-locals and on role of township-level factors. Non-locals had less timely measles vaccines and lower uptake of pneumococcal vaccines, except for the pneumococcal polysaccharide vaccine. Children residing in non-local-majority townships also had less timely administration of measles vaccines than those living in local-majority townships. For the third study, we surveyed parents in Shanghai, and compared parental perceptions of measles, pneumonia, and meningitis using a logistic regression model. Parents believed that measles and meningitis needed a vaccine more than pneumonia. Perceived prevalence of disease was not associated with vaccine necessity, and more non-locals believed the pneumonia vaccine to be necessary than locals. The findings from this dissertation help to identify the contribution of non-locals towards difficulties in controlling vaccine-preventable diseases in China, and this dissertation provides a framework for discussing what township-level variables and individual-level attitudes are associated with vaccination behaviors.

CHAPTER I

Introduction to vaccine-preventable diseases in China

Vaccine-preventable diseases have remained an important, albeit declining, source of childhood morbidity and mortality worldwide over the last few decades. As a result of improved routine immunization programs and supplemental immunization activities (SIAs), annual, global deaths among all ages from 11 vaccine-preventable diseases[1] decreased from over 4 million in 1990 to under 2.7 million in 2010 [1]. Vaccinations are an important tool for disease elimination, the absence of transmission in a defined geographical area for over 1 year [2], and worldwide eradication.

Controlling diseases becomes much more difficult in the epidemic tail, when disease circulates at low levels [3]. The population of susceptible individuals can actually increase during periods of low transmission to the point of potentiating large outbreaks in ensuing years, particularly among older adults who are typically not the focus of vaccination and other disease control programs. As morbidity decreases and people have less personal experience with disease, perceived risk of the disease decreases, and the societal support of control and elimination efforts withers. Concomitantly, the cost of surveillance per case inflates because the infected populace becomes more isolated. Stakeholders, such as policy makers and citizens, also may have concerns at this stage that resources are being diverted

[1] Invasive pneumococcal disease, invasive disease from *Haemophilus influenzae* type b, measles, influenza, rotaviral diarrhea, hepatitis A, hepatitis B, tetanus, pertussis, varicella, and diphtheria

from other primary care programs into overseeing cases of a disease that no longer represents a high morbidity in a particular region [3].

China has an extensive system of hospitals, immunization clinics, and Centers for Disease Control (CDC) which work in concert to prevent and treat vaccine-preventable diseases. Since 2003, China has been rolling out a progressively comprehensive insurance scheme, and now 95% of Chinese have some form of medical insurance to cover some costs associated with treating diseases [4]. In contrast, immunizations, which are offered at immunization clinics, are not covered by insurance, and are either completely publically funded or require payment out-of-pocket. Immunization services in China fall under the purview of CDCs. The CDC network includes a national CDC, provincial-level CDCs (including those for the provincial-level municipalities Beijing, Tianjin, Shanghai, and Chongqing), and CDCs at districts at other lower-level administrative regions within provinces. Doctors trained in preventive medicine work at the CDCs to investigate outbreaks and evaluate disease control programs, such as immunization services [5].

Some researchers have indicated that one obstacle in eliminating measles and controlling other infectious diseases in China is the rising number of internal migrants, referred to in this dissertation as the non-local population [6,7]. There are over 220 million migrants in China who do not have official residency papers, or *hukou*, which give a Chinese citizen access to local government entitlement programs, including education, health care services, and social security [8,9]. These migrants typically move from poorer and more rural areas in Western China to wealthier cities on the East Coast of China [9,10], where they may face societal discrimination [9]. Some studies have found that non-local children do have lower vaccination coverage [11–13], but research into differences in immunological protection by residency show mixed results [14,15]. Moreover, most provinces in China have had two measles supplementary immunization activities for locals and non-locals in the past decade, in addition to offering free vaccines to all children within routine services. Therefore, there are not obvious relationships among residency status, measles vaccination, and measles infection; and, in particular, previous research on measles cases in China [7,16,17] has not adequately quantified the difference in measles incidence rate by residency status.

Vaccination programs

The World Health Organization (WHO) recommends all immunization programs to include vaccinations against tuberculosis, hepatitis B, polio, diphtheria, tetanus, pertussis, *Haemophilus influenzae* type b (Hib) disease, pneumococcal disease, rotavirus, measles, rubella, and human papillomavirus (HPV) [18]. In its Expanded Program on Immunization (EPI), the government-funded program of routine immunization services, China incorporates a slightly different list of vaccines. Hepatitis A, meningococcal meningitis, Japanese encephalitis, and mumps vaccines are funded by the government in addition to the WHO-recommended list, although China does not include Hib, pneumococcal, rotavirus, or HPV vaccines on the national EPI schedule [19]. Even so, many of these vaccines are available for children at immunization clinics, but the family of the child must pay out-of-pocket for administration.

Proof of prior administration of EPI vaccines is required for school entry, and coverage of these vaccines is therefore typically high throughout China, and especially in wealthier cities in Eastern China. Even in Gansu province, a less wealthy province in Western China, 86% of infants were up-to-date with EPI vaccinations by 12 months [20].

Because of their cost and because they are not required for school entry, non-EPI vaccines have lower coverage than EPI vaccines. In a survey of electronic vaccination records from Guangzhou, only about half of children were vaccinated against rotavirus by 5 years of age [21]. A study from the Shanghai immunization information system found that, among children between the ages of 2 and 6, only 50.9% had received a Hib vaccine and a mere 11.4% had received a pneumococcal conjugate vaccine, and that both vaccines were typically delayed so as not to be co-administered with EPI vaccines [13].

In this dissertation, I focus on two vaccine-preventable infections in order to better generalize the experience of vaccinations in China beyond one particular example. Measles vaccine is a free vaccine and has been on the China EPI since 1978 [19]. Further, there has been tremendous attention placed on measles in China and worldwide for its elimination effort [22]. Conversely, the pneumococcal vaccine has only been more recently introduced to the Chinese market and it is prohibitively expensive for many Chinese. Although it has been listed on the EPI schedule of many countries, including those less developed than China [23], China has yet to publically fund this vaccine [24].

Measles

Measles has already been eliminated in the Americas, and the other five regions of the World Health Organization (WHO) have planned to eliminate measles by 2020 [25]. Elimination is possible because of measles vaccination; before the invention of the measles vaccine, 90% of people would be infected by age 20, leading to 100 million cases and 6 million deaths each year [26]. As measles vaccination coverage has increased, measles morbidity and mortality has decreased. From 1990 to 2010, for instance, deaths worldwide from measles decreased from 631,200 to 125,400 [1].

China has put forward several goals to control measles. One of the first goals, to reduce measles incidence by 90% between 1965 and 1995 [7], was achieved when incidence declined from over 1,000 cases per 100,000 in the 1960s before vaccination to 5.7 cases per 100,000 in the late 1990s [7]. Subsequent goals, to reduce measles incidence by 90% from 2000 to 2010 and to eliminate measles by 2012, a highly publicized WHO goal [27], were not reached: incidence decreased slowly from 6 cases per 100,000 in 2000 [28] to only 2.86 in 2010 [17]. Moreover, there has been a slight upswing in cases between 2011 and 2014. There has not been a convincing explanation for China's difficulty in eliminating measles, especially given that China has invested in both routine immunization services and supplementary immunization activities [17].

China approved its own measles vaccine strain in 1966, and has since used a domestically-produced vaccine as the first dose of measles vaccine [29]. A review of 70 studies showed measles vaccine efficacy of 84.0% at 9 to 11 months of age and 92.5% at 12 months of age or older [30]. Therefore, more than one dose of measles vaccine is necessary to ensure adequate herd immunity within a population, especially when the first dose is given at <12 months of age. Immunization clinics in Shanghai and Tianjin, China, currently provide 3 doses of measles-containing vaccine (MCV) for free to every child as part of its EPI: a measles-rubella combined vaccine (M1) is given to children at 8 months of age, and a measles-mumps-rubella combined vaccine (MMR) is given to children at 18-24 months of age (MMR1) and at 5 years of age (MMR2) [31]. Although most children in China are eventually vaccinated against measles, we found in a previous study in Tianjin that less than 90% of children were vaccinated on-time [32], and another study from Zhejiang province found only 70.1% of children had a timely administration of the first dose of MCV [12]. Because the amount of vaccination delay in these circumstances is substantial, vaccine timeliness is a better indicator of population-level immunity than estimating coverage regardless of the timing [33].

According to the WHO, the second dose of MCV can be given either in routine immunization services or in supplementary immunization activities (SIAs), which are mass immunization events within a defined geographical region over a short period of time and which were successful in eliminating measles in the Americas in the 1990s and early 2000s [34]. In *catch-up* SIAs, all children within a particular age group are vaccinated, typically regardless of their previous vaccination status. *Follow-up* SIAs then focus on the children born since the previous SIA [35]. Between 2004 and 2009, 25 of 31 province-level administrative regions in mainland China implemented catch-up SIAs, vaccinating 164 million children [16]. In 2010, follow-up SIA delivered 102.3 million doses nationwide [36]. In Tianjin, the 2008 catch-up SIA distributed 1.3 million doses of measles vaccine to children between the ages of 8 months and 14 years; and the 2010 follow-up SIA targeted all children aged 8 months to 4 years, and 450,000 MCV doses were administered [37].

Pneumococcal disease

Pneumococcus is responsible for a spectrum of disease, from otitis media to serious invasive disease, including pneumonia, meningitis, and septicemia [38]. Like measles, it can also be directly spread through airborne droplets, but the transmission dynamics and epidemiology of pneumococcus are complex and less well characterized than a highly communicable disease such as measles. Pneumococcal disease is often preceded by asymptomatic colonization of pneumococcus in the nasopharyngeal tract [39]. A total of 90 serotypes of pneumococcus have been discovered, and immunity is thought to be serotype specific [40]. In contrast to worldwide declines in measles mortality, mortality from invasive pneumococcal disease has remained relatively stable at over 900,000 deaths from 1990 to 2010 [1].

Unlike measles, pneumococcus is not a nationally notifiable disease in China [41]. Identification of pneumococcal cases in China faces some difficulty because its clinical presentation is similar to that of other infectious diseases, like Hib disease and meningococcal disease, and because common antibiotic overuse makes isolation of bacteria from patients difficult [42]. From a review of literature published on pneumococcus cases throughout China, Chen et al. estimated that in 2000 there were 384.45 cases of pneumococcal pneumonia per 100,000 children <5 years and 1.33 cases of pneumococcal meningitis per 100,000 children <5 years [43].

Two different pneumococcal vaccines are available at immunization clinics in China for a fee. The 23-valent pneumococcal polysaccharide vaccine (PPSV) can only be administered to children ≥2 years and it produced a T-cell independent response [40,44]. A 7-valent pneumococcal conjugate vaccine (PCV) has been available since 2008 in China [24]. It protects against fewer serotypes and is substantially more expensive than PPSV ($135 per dose of PCV compared to $24 per dose of PPSV), but it is more immunogenic and is licensed in China for infants as young as 6 weeks of age.

Health behaviors

Anthropologist Mark Nichter distinguishes between passive acceptance of and active demand for vaccinations [45]. The populace attains high vaccination coverage only after the public health sector devotes intensive resources towards promoting a certain vaccine in the former scenario, whereas in the latter, a well-informed public perceives the need for vaccination and drives demand for immunization services. With no government funding currently for pneumococcal vaccination, it is unclear which of Nichter's scenarios pneumococcal vaccination falls into. Understanding Chinese parents' perceptions about both this non-EPI vaccine and the diseases it prevents is key to developing effective interventions to increase vaccine uptake. And, if pneumococcal vaccine is added to the EPI schedule, understanding parental attitudes towards it will be important for developing programs to increase people's acceptance of the vaccine.

Vaccine decision-making can be explained by health behavior models like the Health Belief Model (HBM), which is one of the oldest [46] and most used [47] models to explain health behavior. It explains and predicts behavior by conceiving of health-related actions as an output of an individual's perceptions of both a disease and an action related to that disease. These constructs specifically include people's perceived susceptibility or vulnerability to the disease, their understanding of disease severity, a sense of the potential benefits of the action, and anticipated barriers or obstacles to performing that action [48].

The HBM has often been used to explain vaccination behaviors worldwide [46,49–51]. In China, an HBM framework has explored dysentery vaccine need [52], influenza vaccination intent [53], and influenza vaccine uptake among healthcare workers [54]. Although these studies show the usefulness of HBM to describe vaccination behaviors in China, no previous study in China has compared and contrasted perceptions towards EPI and non-EPI vaccines. It may be that people think differently about measles and pneumococcal vaccines, which have dissimilar payment mechanisms, which vary by length of time on the market, and for which people plausibly have assorted levels of experience.

Other health behavior models, such as the Theory of Planned Behavior and the Social Norms Theory, incorporate community-level behaviors, like social norms, into their predictions of individual-level behaviors. Here we can distinguish from the descriptive norm of vaccination, which is the perceived commonness or prevalence of vaccination in a community, from the subjective norm of vaccination [55,56], which is the perceived social pressure to perform or not perform this behavior [57]. Some researchers suggest that descriptive norms are better than subjective norms at predicting intent to perform a health behavior [56,58].

Multilevel models

Multilevel models, in which community-level factors are placed in models to predict individual-level outcomes, have become increasingly important in public health literature [59]. Vaccination itself offers multilevel protection: vaccines not only prevent disease in the individual, but also in an individual's social contacts through herd immunity. Neighborhood social characteristics, such as urbanicity, race/class composition, and age structure, may influence an individual's risk for disease or a parent's attitudes towards vaccination through a variety of mechanisms. Neighborhoods describe an individual's built and natural environment in which disease spreads and in which health care facilities provide preventive care. Neighborhoods' differing demographic characteristics may differentially dispose an individual to disease. For instance, neighborhoods with more children may foster the spread of infectious diseases commonly found in young children; places with many transient workers may see high incidence of diseases carried by migrants; and social norms within one community may value, or disapprove of, certain medical interventions, such as vaccination.

Previous studies have found some important links between neighborhood-level risk factors and immunization. A survey in the Netherlands in 2009 found community political preferences and socioeconomic condition to be linked to HPV uptake [60]. A study of Hawaiian kindergartners in 2002-2003 found that Census tract-level statistics, including education levels, urbanicity, and ethnic proportions, were significantly associated with up-to-date immunizations [61].

Health registries

Data for parts of this dissertation come from electronic health record (EHR) systems. I have analyzed the epidemiology of measles cases from Tianjin in the National Infectious Disease Monitoring Information System (NIDMIS), and vaccination patterns from the Shanghai Immunization Program Information System (SIPIS). China has followed a similar path as the US, by first creating state- (or province-) based registries focused on particular conditions, such as notifiable diseases or vaccinations. Over time, the US has standardized some registries so that information from different states can be communicated to the Centers for Disease Control and Prevention (CDC), but by and large, these health registries in the US are discrete entities. This type of registry can be contrasted with many EHR systems in northern Europe, where registries, like cancer registries, prescription registries, and cause-of-death registries, can be interlinked through a standard individual identifier [62].

Regardless of their complexity or ability to communicate with other systems, these registries have a number of common, important functions. Registries are a continuous repository of data which have been systematically collected. Researchers and public health officials can use registries to analyze data, with the focus on determining public health priorities, evaluating public health practices, and planning for future programs [63]. Highly functional registries not only benefit researchers at a central location but also staff at a particular health clinic—for example, by allowing for calculations of disease statistics within the clinic. This is an important incentive for participation even beyond any legal mandate to do so.

Registries can be contrasted with the carefully delineated study populations of traditional public health studies. Though theoretically a census of the population within a defined geographical region, registries are dependent on both patients interfacing with health care professionals and the health care professionals, who need to transmit the data into a central database. As patients move out of the registry catchment area, there is attrition from the registry which is not always marked within the registry database. The information collected within a registry tends to be limited. Changes in how data are collected or what questions are asked can limit temporal comparisons.

Tianjin and Shanghai

The People's Republic of China comprises 33 province-level administrative regions. Beijing, Tianjin, Shanghai, and Chongqing are 4 directly-controlled municipalities, meaning that they have the same political privileges as provinces, but are in geographically restricted areas. Though these municipalities contain populous, urban districts, adjacent suburban districts and rural counties also figure into the municipality's administration. The 3 municipalities in eastern China—Beijing, Tianjin, and Shanghai—are the wealthiest subdivisions in China, and are shown in Figure 1-1. In 2013, GDP per capita is 93,213 RMB (15,015 USD) in Beijing, 99,607 RMB in Tianjin (16,083 USD), and 90,092 RMB in Shanghai (14,547 USD) [64]. All three of substantial disparities between urban and rural populations; average disposable income in urban areas is over fifty two hundred dollars for all three municipalities, but rural net income is below thirty two hundred dollars. These cities also each have substantial non-local populations. Of the 21.1 million residents in Beijing, 8.0 million are non-locals; 4.7 million of the 14.7 million people in Tianjin are non-locals; and Shanghai's 24.1 residents include 9.8 million non-locals [64].

Aims

Overall, this dissertation seeks to answer the questions "What are the differences between locals and non-locals in disease incidence and vaccination outcomes in China?" and "What are the similarities and differences between measles and pneumococcal vaccination programs in China?" I respond to these questions in Chapters 2 through 4. In Chapter 2, we use data from the Tianjin notifiable disease registry to characterize temporal trends in measles incidence by residency (non-local versus local) and to evaluate the impact of SIAs on measles incidence. Chapter 3 explores vaccination outcomes in terms of timely M1 and MMR1 administration as well as uptake of PCV and PPSV. Specifically, we estimate the proportion of children in Shanghai with these vaccination outcomes, compare vaccination outcomes in non-locals and locals, and assess the impact of township-level characteristics on vaccination outcomes. In Chapter 4, we compare perceptions of pediatric measles and pneumococcal vaccinations among parents in Shanghai, and we characterize the associations between HBM constructs, demographic characteristics, and perceived vaccine necessity, by disease.

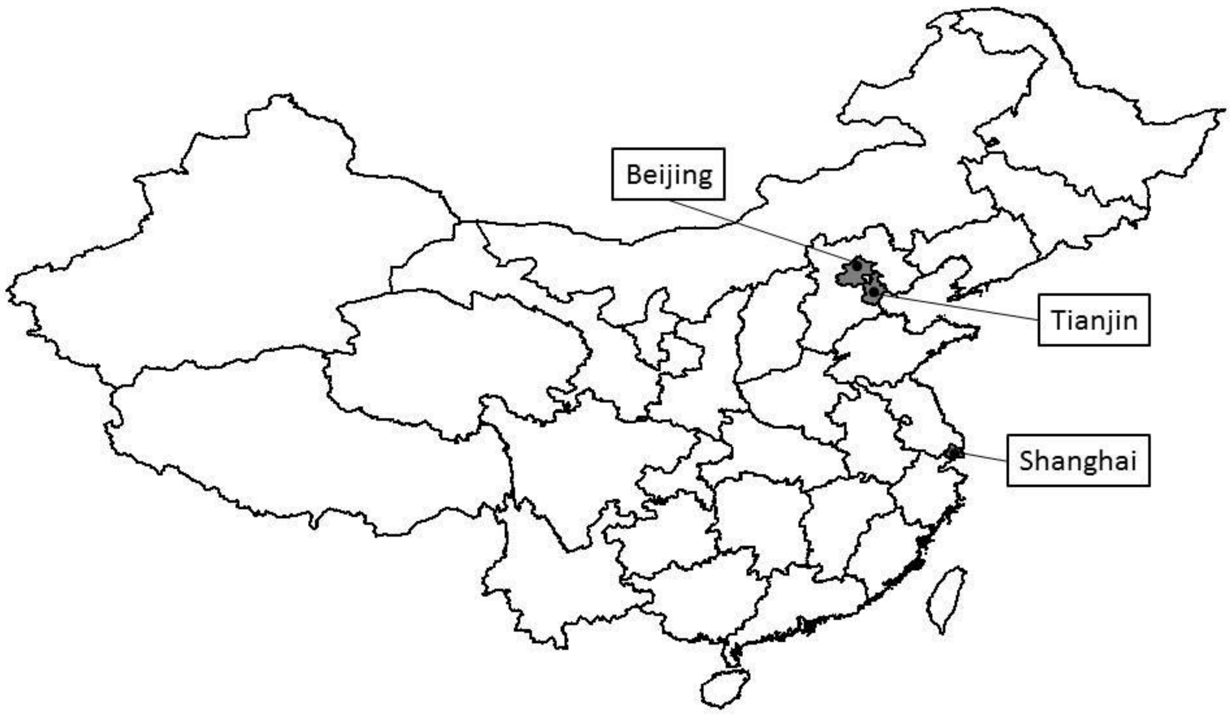


Figure 1-1. Locations of Beijing, Tianjin, and Shanghai, three province-level municipalities in Eastern China.

REFERENCES

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, et al. (2012) Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 380: 2095–2128. doi:10.1016/S0140-6736(12)61728-0.

2. World Health Organization (2013) Guidelines on verification of measles elimination in the Western Pacific Region. Geneva, Switzerland: World Health Organization.

3. Klepac P (2013) Towards the endgame and beyond: complexities and challenges for the elimination of infectious diseases. Phil Trans R Soc B 368: 20120137.

4. Blumenthal D, Hsiao W (2015) Lessons from the East - China's Rapidly Evolving Health Care System. N Engl J Med 14: 1281–1285. doi:10.1056/NEJMp1415160.

5. Zhang L (2009) Building a better infectious disease surveillance system for China. Saarbrücken, Germany: VDM Verlag Dr. Müller.

6. Freeman III CW (2009) China's Capacity to Manage Infectious Diseases. Freeman III CW, Lu X, editors Washington, DC: Center for Strategic and International Studies.

7. Wang L, Zeng G, Lee LA, Yang Z, Yu J, et al. (2003) Progress in Accelerated Measles Control in the People's Republic of China, 1991 – 2000. J Infect Dis 187: 252–257.

8. Liang Z (2012) Recent Migration Trends in China : Geographic and Demographic Aspects and Development. UN Expert Gr Meet New Trends Migr Demogr Asp. Available: http://www.un.org/esa/population/meetings/EGM_MigrationTrends/UN_presentatoin_Dec_2012_FINAL_SH.pdf.

9. Chan K (2012) China: internal migration. In: Ness I, Bellwood P, editors. The Encyclopedia of Global Human Migration. Wiley-Blackwell. doi:10.1002/9781444351071.wbeghm124.

10. Du Y, Park A, Wang S (2005) Migration and rural poverty in China. J Comp Econ 33: 688–709. doi:10.1016/j.jce.2005.09.001.

11. Sun M, Ma R, Zeng Y, Luo F, Zhang J, et al. (2010) Immunization status and risk factors of migrant children in densely populated areas of Beijing, China. Vaccine 28: 1264–1274. doi:10.1016/j.vaccine.2009.11.015.

12. Li Q, Hu Y, Zhong Y, Chen Y, Tang X, et al. (2014) Using the Immunization Information System to determine vaccination coverage rates among children aged 1-7 years: a

report from Zhejiang Province, China. Int J Environ Res Public Health 11: 2713–2728. doi:10.3390/ijerph110302713.

13. Wagner AL, Sun X, Montgomery JP, Huang Z, Boulton ML (2014) The Impact of Residency and Urbanicity on Haemophilus influenzae Type b and Pneumococcal Immunization in Shanghai Children: A Retrospective Cohort Study. PLoS One 9: e97800. doi:10.1371/journal.pone.0097800.

14. Wang F, Wu X, Chen Z (2010) Surveillance of measles antibody levels in local and migrant populations of Jinhua city. Dis Surveill 25: 1980–1981 [in Chinese].

15. Pang H, Zhang Z, Liu H, Xu Y (2009) Investigation of Measles, Rubella and Varicella IgG Antibody Levels Among Migrant and Native Pupils in Changning District of Shanghai. Chin J Vaccine Immun 15: 223–225 [in Chinese].

16. Ma C, An Z, Hao L, Cairns KL, Zhang Y, et al. (2011) Progress toward measles elimination in the People's Republic of China, 2000-2009. J Infect Dis 204: S447–S454. doi:10.1093/infdis/jir103.

17. Ma C, Hao L, Zhang Y, Su Q, Rodewald L, et al. (2014) Monitoring progress towards the elimination of measles in China: an analysis of measles surveillance data. Bull World Health Organ 92: 340–347. doi:10.2471/BLT.13.130195.

18. World Health Organization (2015) Summary of WHO Position Papers - Recommendations for Routine Immunization: 1–9. Available: http://www.who.int/immunization/policy/Immunization_routine_table1.pdf.

19. Zheng J, Zhou Y, Wang H, Liang X (2010) The role of the China Experts Advisory Committee on Immunization Program. Vaccine 28S: A84–A87. doi:10.1016/j.vaccine.2010.02.039.

20. Cui F-Q, Gofin R (2007) Immunization coverage and its determinants in children aged 12-23 months in Gansu, China. Vaccine 25: 664–671. doi:10.1016/j.vaccine.2006.08.027.

21. He Q, Wang M, Xu J, Zhang C, Wang H, et al. (2013) Rotavirus vaccination coverage among children aged 2-59 months: a report from Guangzhou, China. PLoS One 8: e68169. doi:10.1371/journal.pone.0068169.

22. McFarland J (2012) World Immunization Week, China.

23. GAVI Alliance (2015) Vaccine goal indicators. GAVI. Available: http://www.gavi.org/results/goal-level-indicators/vaccine-goal-indicators/.

24. Yu H, Yang W, Varma JK (2012) To save children's lives, China should adopt an initiative to speed introduction of pneumonia vaccines. Heal Aff 31: 2545–2553. doi:10.1377/hlthaff.2011.1272.

25. Durrheim DN, Crowcroft NS, Strebel PM (2014) Measles – The epidemiology of elimination. Vaccine 32: 6880–6883. doi:10.1016/j.vaccine.2014.10.061.

26. Strebel P (2008) Measles. In: Heymann D, editor. Control of Communicable Diseases Manual. Washington, DC: American Public Health Association. pp. 402–408.

27. World Health Organization (2012) Global Measles and Rubella Strategic Plan 2012-2020. Switzerland: World Health Organization.

28. Ji Y, Zhang Y, Xu S, Zhu Z, Zuo S, et al. (2009) Measles resurgence associated with continued circulation of genotype H1 viruses in China, 2005. Virol J 6: 135. doi:10.1186/1743-422X-6-135.

29. Xiang J, Chen Z (1983) Measles Vaccine in the People's Republic of China. Rev Infect Dis 5: 506–510.

30. Uzicanin A, Zimmerman L (2011) Field effectiveness of live attenuated measles-containing vaccines: a review of published literature. J Infect Dis 204: S133–S148. doi:10.1093/infdis/jir102.

31. Schulter W, Wang X, Mendoza-Aldana J, Jee Y, Diorditsa S, et al. (2013) Progress Toward Measles Elimination - Western Pacific Region, 2009-2012. MMWR Morb Mortal Wkly Rep 62: 445–447.

32. Wagner AL, Zhang Y, Montgomery JP, Ding Y, Carlson BF, et al. (2014) Timely measles vaccination in Tianjin, China: a cross-sectional study of immunization records and mothers. BMC Public Health 14: 888. doi:10.1186/1471-2458-14-888.

33. Akmatov MK, Kretzschmar M, Krämer A, Mikolajczyk RT (2008) Timeliness of vaccination and its effects on fraction of vaccinated population. Vaccine 26: 3805–3811. doi:10.1016/j.vaccine.2008.05.031.

34. Castillo-Solorzano C C, Matus CR, Flannery B, Marsigli C, Tambini G, et al. (2011) The Americas: paving the road toward global measles eradication. J Infect Dis 204 Suppl: S270–S278. doi:10.1093/infdis/jir166.

35. World Health Organization (2013) Measles. WHO Media Cent. Available: http://www.who.int/mediacentre/factsheets/fs286/en/.

36. World Health Organization (2011) News in Brief. Measles-Rubella Bull 5: 1–9.

37. Ministry of Health of the People's Republic of China (2015) Jing Jin Hu qidong mazhen qianghua mianyi xingdong. Available: http://wsb.moh.gov.cn/mohjbyfkzj/s10769/201008/48593.shtml.

38. Heymann D, Aylward R (2008) Mass vaccination in public health. In: Heymann DL, editor. Control of Communicable Diseases Manual. Washington, DC: American Public Health Association. pp. A51–A57.

39. Bogaert D, Groot R De, Hermans PWM (2004) Streptococcus pneumoniae colonisation : the key to pneumococcal disease. Lancet Infect Dis 4: 144–154.

40. CDC (2012) Pneumococcal disease. Epidemiology and Prevention of Vaccine-Preventable Diseases. pp. 233–248.

41. Wang L, Wang Y, Jin S, Wu Z, Chin D (2008) Emergence and control of infectious diseases in China. Lancet 372: 34–41. doi:10.1016/S0140-6736(08)61365-3.

42. Yang Y-H, Fu S-G, Peng H, Shen A-D, Yue S-J, et al. (1993) Abuse of antibiotics in China and its potential interference in determining the etiology of pediatric bacterial diseases. Pediatr Infect Dis J 12: 986–987. doi:10.1097/00006454-199312000-00004.

43. Chen Y, Deng W, Wang S-M, Mo Q-M, Jia H, et al. (2011) Burden of pneumonia and meningitis caused by Streptococcus pneumoniae in China among children under 5 years of age: a systematic literature review. PLoS One 6: e27333. doi:10.1371/journal.pone.0027333.

44. Shapiro ED (2012) Prevention of Pneumococcal Infection: An Evolving Story. JAMA 307: 847–849.

45. Nichter M (1995) Vaccinations in the third world: a consideration of community demand. Soc Sci Med 41: 617–632.

46. Janz NK, Becker MH (1984) The Health Belief Model: a decade later. Health Educ Q 11: 1–47.

47. Glanz K, Rimer BK, Lewis EM, editors (2002) Health Behavior and Health Education: Theory, Research, and Practice. 3rd ed. San Francisco, CA: Jossey-Bass Publishers.

48. Rosenstock IM, Strecher VJ, Becker MH (1988) Social learning theory and the Health Belief Model. Heal Educ Q 15: 175–183.

49. Brewer NT, Fazekas KI (2007) Predictors of HPV vaccine acceptability: a theory-informed, systematic review. Prev Med (Baltim) 45: 107–114. doi:10.1016/j.ypmed.2007.05.013.

50. Brewer NT, Chapman GB, Gibbons FX, Gerrard M, McCaul KD, et al. (2007) Meta-analysis of the relationship between risk perception and health behavior: the example of vaccination. Heal Psychol 26: 136–145. doi:10.1037/0278-6133.26.2.136.

51. Bish A, Yardley L, Nicoll A, Michie S (2011) Factors associated with uptake of vaccination against pandemic influenza: a systematic review. Vaccine 29: 6472–6484. doi:10.1016/j.vaccine.2011.06.107.

52. Chen X, Stanton B, Wang X, Nyamette A, Pach A, et al. (2006) Differences in perception of dysentery and enteric fever and willingness to receive vaccines among rural residents in China. Vaccine 24: 561–571. doi:10.1016/j.vaccine.2005.08.060.

53. Mok E, Yeung SH, Chan MF (2006) Prevalence of influenza vaccination and correlates of intention to be vaccinated among Hong Kong Chinese. Public Heal Nurs 23: 506–515.

54. Seale H, Kaur R, Wang Q, Yang P, Zhang Y, et al. (2011) Acceptance of a vaccine against pandemic influenza A (H1N1) virus amongst healthcare workers in Beijing, China. Vaccine 29: 1605–1610. doi:10.1016/j.vaccine.2010.12.077.

55. Wang Z, Mo PKH, Lau JTF, Lau M, Lai CHY (2013) Acceptability of HPV vaccines and perceptions related to genital warts and penile/anal cancers among men who have sex with men in Hong Kong. Vaccine 31: 4675–4681. doi:10.1016/j.vaccine.2013.06.090.

56. Liao Q, Cowling BJ, Lam WWT, Fielding R (2011) Factors affecting intention to receive and self-reported receipt of 2009 pandemic (H1N1) vaccine in Hong Kong: a longitudinal study. PLoS One 6: e17713. doi:10.1371/journal.pone.0017713.

57. Ajzen I (1991) The Theory of Planned Behavior. Organ Behav Hum Decis Process 50: 179–211.

58. Sheeran P, Orbell S (1999) Augmenting the Theory of Planned Behavior: Roles for Anticipated Regret and Descriptive Norms1. J Appl Soc Psychol 29: 2107–2142.

59. Diez-Roux A (2000) Multilevel analysis in public health research. Annu Rev Public Health 21: 171–192.

60. Rondy M, van Lier A, van de Kassteele J, Rust L, de Melker H (2010) Determinants for HPV vaccine uptake in the Netherlands: A multilevel study. Vaccine 28: 2070–2075. doi:10.1016/j.vaccine.2009.12.042.

61. Whitehead SJ, Cui KX, De AK, Ayers T, Effler P V (2007) Identifying risk factors for underimmunization by using geocoding matched to census tracts: a statewide assessment of children in Hawaii. Pediatrics 120: e535–e542. doi:10.1542/peds.2006-3296.

62. Furu K, Wettermark B, Andersen M, Martikainen JE, Almarsdottir AB, et al. (2010) The Nordic countries as a cohort for pharmacoepidemiological research. Basic Clin Pharmacol Toxicol 106: 86–94. doi:10.1111/j.1742-7843.2009.00494.x.

63. World Health Organization (2015) Public health surveillance. Heal Top: 2015. Available: http://www.who.int/topics/public_health_surveillance/en/.

64. Provincial Statistics (2013). China Data Online. Available: http://www.chinadataonline.org.

CHAPTER 2

The impact of Supplementary Immunization Activities on the epidemiology of measles in Tianjin, China

ABSTRACT

Background. Non-locals, or migrants from rural areas to wealthier cities, are often blamed for China's difficulty in controlling measles, particularly as China seeks to eliminate measles through supplementary immunization activities (SIAs). Here, we characterize temporal trends in measles incidence by residency (non-local versus local) and evaluate the impact of SIAs on measles incidence.

Methods. We tabulated daily counts of laboratory-confirmed measles cases for both locals and non-locals. These two datasets were then combined into a single dataset where each day had two observations. We conducted multivariable Poisson regression using generalized estimating equations with an exchangeable correlation structure to account for each day having two counts.

Results. From 2005 through 2013, there were 5,730 laboratory-confirmed cases of measles in Tianjin. A substantial disparity in the rate of measles between non-locals and locals is observed before the 2008 SIA (RR: 2.91, 95% CI: 2.56, 3.31), but this attenuates to non-locals having a rate of measles only 1.39 times higher between the 2008 and 2010 SIAs compared to locals (95% CI: 1.17, 1.66). There was no significant difference in the rate of measles between non-locals and locals after the 2010 SIA.

Discussion. Although we observed a reduction in measles disparities between locals and non-locals over time, persistent efforts will be needed to keep measles incidence low among non-locals in urban settings because of the continual migration of people in China.

INTRODUCTION

Measles was officially eliminated in the Americas in 2002 [1], and the other five regions of the World Health Organization (WHO) are slated for measles elimination by 2020 [2]. This remarkable success in control of a highly infectious disease has been made possible through the global adoption of measles vaccination. Prior to the advent of the measles vaccine, 90% of people were infected by age 20, resulting in 100 million cases and 6 million deaths each year [3]. As vaccination coverage has increased, the number of deaths from measles has decreased from 631,200 in 1990 to 125,400 in 2010 [4].

The Chinese government is committed to measles elimination and although the country did not meet its original elimination target of 2012, they have made steady progress in measles control. The initial goal to reduce measles incidence by 90% between 1965 and 1995 [5] was met with the decline from over 1,000 cases per 100,000 in the 1960s prior to measles vaccine availability to 5.7 cases per 100,000 in the late 1990s [5]. Subsequent goals, to reduce measles incidence by 90% from 2000 to 2010 and to eliminate measles by 2012 [6], were not realized as disease incidence gradually decreased from 6 cases per 100,000 in 2000 [7] to only 2.86 in 2010 [8], followed by a slight upswing in cases between 2011 and 2014. The exact reason(s) for China's inability to achieve sustained reductions in measles leading to elimination are not entirely clear, especially given that China has invested heavily in both routine immunization services and repeated national supplementary immunization activities [8].

China introduced its own measles-containing vaccine (MCV) to market in 1966 [9], which was subsequently integrated in 1978 into the Expanded Program on Immunization (EPI), a government-funded initiative to provide select vaccine free of charge to all children [10]. Although the national EPI schedule in China recommends two doses of MCV [10], the schedule in Tianjin and some other places differs by recommending an additional MCV dose. Currently in Tianjin, MCV1 is administered as a measles-rubella vaccine given at 8 months; MCV2, a measles-mumps-rubella vaccine (MMR) is administered at 18 to 24 months of age; and MCV3 is a second dose of MMR given at 5 years of age [10]. This third dose is important because the first dose of MCV is not as immunogenic when administered to children under 1 year of age [11]. However, the cost of giving what is generally considered an additional "throw away dose" of MCV in the first year of life is outweighed by the perceived benefits of insuring infants are immunized to measles given the high burden of disease in this age group in China [8].

According to the WHO, MCV2 can be given either as part of routine immunization services or in supplementary immunization activities (SIAs), which are mass immunization events within a defined geographical region delivered over a short period of time. The strategic use of periodic SIAs were successful in eliminating measles in the Americas in the 1990s and early 2000s [1]. In *catch-up* SIAs, all children within a particular age group are vaccinated, typically regardless of their previous vaccination status. *Follow-up* SIAs then focus on mass vaccination of children born since the previous SIA [12]. Between 2004 and 2009, 25 of 31 province-level administrative regions in mainland China implemented catch-up SIAs, collectively vaccinating 164 million children [13]. In 2010, follow-up SIA delivered 102.3 million doses nationwide within the same time period [14]. In Tianjin, the 2008 catch-up SIA administered 1.3 million doses of measles vaccine to children between the ages of 8 months and 14 years; and the 2010 follow-up SIA, which targeted all children aged 8 months to 4 years, resulted in the administration of 450,000 MCV doses [15].

The epidemiology of measles in China has been characterized by periodic regional and national outbreaks. Many researchers and Chinese public health officials suggest that these outbreaks are potentiated by the country's highly mobile population [5,8,16], who are moving from poorer and more rural areas to wealthier cities [17,18]. These internal migrants are sometimes called the floating population although we refer to them as non-locals in this paper in order to distinguish their residency status from "locals." There are over 260 million of these internal migrants in China who do not have official residency papers, or *hukou*, which accord Chinese citizens access to local government entitlement programs, including education, social security, and some health care services [18,19]. Even though non-local children are offered EPI vaccines for-free, just like local children, they nonetheless have been shown in some studies to have lower coverage of EPI vaccines than locals [20], which public health officials have attributed, at least in part, to the difficulties government immunization services encounter in trying to locate and identify children who have newly relocated to a particular area [8].

China has made a large financial investment in both funding routine measles immunization services and delivering hundreds of millions of doses of measles vaccine to children through SIAs. Despite these efforts, there has been a periodic resurgence of measles in recent years resulting in China's failure to meet its own goal of disease elimination by 2012. Lower vaccination coverage among non-locals could be an important contributing factor to sustained measles transmission and outbreaks although MCV is offered to all children in routine immunization services. Moreover, within the past decade the majority of provinces in China have had 2 SIAs, which mostly have targeted all children in the province between 8 months and 14 years of age [13]. More research is needed to fully characterize the changing epidemiology of measles in China and to quantify the difference in measles incidence by residency status, since previous research on measles cases in China [5,8,13] has not adequately addressed this question. In this paper, we use data from the Tianjin notifiable disease registry to characterize temporal trends in measles incidence by residency (non-local versus local) and to evaluate the impact of SIAs on measles incidence.

MATERIALS AND METHODS

Study population

This study used data from Tianjin, a municipality 100 km away from Beijing. It is one of the wealthiest subdivisions in China, with a GDP per capita of 99,607 RMB ($16,083) in 2013. There has been substantial migration into this city from outside areas: in 2014, 4.7 million of the 14.7 million people in Tianjin were non-locals [21]. Though Tianjin does contain populous, urban districts, adjacent suburban districts and rural counties also figure into the municipality's administration. The health infrastructure in Tianjin includes both a municipality-wide Center for Disease Control and Prevention (CDC) with jurisdiction over the entire municipality as well as district-level CDCs.

Measles is a notifiable infectious disease in China [22], and suspected cases at hospitals are reported into the National Infectious Disease Monitoring Information System (NIDMIS). These cases are investigated by staff from district-level CDCs. NIDMIS includes demographic information for each case (birth date, sex, district of residence, residency), vaccination status (unknown, ≥1 dose, or 0 doses), and date of onset of fever. We limited our analysis to cases with laboratory confirmation because of limited information on clinically-confirmed cases in the database. Laboratory-confirmed cases are required to have a positive IgM result reported from serum or other body fluid or to include report of wild-type measles virus isolated by RT-PCR [23].

Derived variables

The two municipal-wide SIAs in Tianjin occurred in December 2008 and in September 2010. We grouped cases into 3 time periods, depending on when their reported date of onset of fever was relative to the SIAs. Fevers starting on January 1, 2005, through December 4, 2008, were considered "before the 2008 SIA"; cases whose fever started on December 5, 2008 through September 20, 2010, happened "between the 2008 and 2010 SIAs"; and "after the 2010 SIA" includes all cases who had fevers starting on September 21, 2010, through December 31, 2013.

We distinguished district-level administrative regions by urbanicity, with urban areas being home to more high-income industries [24] and having better access to public services [25] than suburban and rural areas. The 7 urban districts in Tianjin are Heping, Hedong, Hexi, Nankai, Hebei, Hongqiao, and Binhai New Area; 4 districts are categorized as suburban—Jinnan, Dongli, Xiqing, and Beichen; and 2 districts (Baodi and Wuqing) as well as 3 counties (Ji, Jinghai, and Ninghe) are considered rural.

Statistical analysis

The distribution of cases was recorded by sex, urbanicity, residency, vaccination status, and time period. The rate of measles was plotted over time, with the rate calculated by dividing case counts from annual population figures which were available from the China Statistical Yearbook. Separate population figures were available each year for both locals and non-locals.

We first did an exploratory analysis of the time series of measles. Monthly case counts from January 1, 2005, to December 31, 2015, were tabulated for the total population, and separately by residency and age group (<8 months, 8 months to <15 years, 15 years and above). Subsequently, we used observed monthly case counts from January 2005 to November 2008 to forecast monthly case counts from January 2009 to December 2015 using exponential smoothing with additive error, trend, and seasonal components.

To make formal inferences about rates in locals and non-locals, we calculated daily case counts separately for these two groups. These two datasets were then combined into a single dataset where each day had two observations, one for locals and the other for non-locals. We conducted multivariable Poisson regression using generalized estimating equations with robust variation estimation and with an exchangeable correlation structure to account for each day having two counts. The natural log of the population by residency was added to the model as an offset to obtain rates. The main predictors in this model were residency, time period, and an interaction between residency and time period. This model also controlled for a lag 1 autoregressive term (AR1) and seasonality of measles. Measles seasonality was the seasonal component of a daily time series, which was decomposed into trend, seasonal, and remainder components.

The data were analyzed in R [26], and we used the STL procedure [27] and the packages *forecast* [28] and *geepack* [29].

Ethics statement

This study was limited to analyses of de-identified cases. Because it fell under standard public health surveillance activities, the University of Michigan Institutional Review Board determined that the study was exempt from regulation.

RESULTS

From Jan 1, 2005, through December 31, 2013, there were a total of 5,730 laboratory-confirmed cases of measles reported in Tianjin, China. Slightly more cases were males (57.8%) than females, a majority (72.9%) were locals, and there was an even distribution of cases from urban (31.3%), suburban (37.4%) and rural (31.3%) districts. Most of the cases (65.9%) occurred before the 2008 SIA, 28.2% of all cases occurred in the 21 months between the two SIAs, and only 6.0% after the second municipality-wide SIA.

Table 2-1 shows the distribution of demographic and vaccination characteristics overall and by residency. There was a bimodal distribution of cases by age, with most cases occurring either in children under 5 years of age, or adults over 15 years of age, the majority of whom were under 40 years of age. Compared to locals, non-local cases were more likely to be younger than 30 years of age. Additionally, most cases (54.5%) aged 8 months to <15 years were unvaccinated and more non-locals (60.3%) than locals (50.6%) in this age category had not received a measles vaccine.

The count and frequency of demographic characteristics relative to the SIAs is shown in Table 2-2. There was a shift in the geography of cases over time; before the 2008 SIA, most cases occurred in suburban (41.7%) and rural areas (33.3%), but after the 2010 SIA, only 27.1% and 15.2% occurred in these areas, respectively. Although fewer childhood cases had been vaccinated against measles between the 2008 and 2010 SIAs (22.3%) compared to before the 2008 SIA (39.7%), there was not an appreciable difference in the proportion of vaccinated children after the 2010 SIA (34.0%) compared to before the 2008 SIA.

Figure 2-1 shows a decline in the rate of measles over time, and in particular, the disparity between the rates of measles in non-locals and locals disappears by 2010. In Figure 2-2, a similar seasonal pattern is seen for both locals and non-locals. There is a difference in the configuration of measles counts over time across different age groups. For infants <8 months of age and persons ≥15 years of age, who were not vaccinated in either SIA, there was a sharp increase in the number of cases in 2010, compared to 2009, whereas for children from 8 months through 14 years of age, this increase was in line with predicted values from the time series forecast. From 2011 on, there were few cases of measles, although a slight increase was seen in 2013.

Results from the multivariable regression are presented in Table 2-3. A substantial disparity in the rate of measles between non-locals and locals is observed before the SIAs (RR: 2.91, 95% CI: 2.56, 3.31), but this attenuates to non-locals having a rate of measles

1.39 times higher during the SIAs compared to locals (95% CI: 1.17, 1.66). There was no significant difference in the rate of measles between non-locals and locals after the SIAs.

DISCUSSION

SIAs have been an important tool used worldwide to progress towards disease elimination in a cost-effective manner [1,30,31]. We found a substantial reduction in the number of measles cases in Tianjin, China following implementation of two municipality-wide SIAs. In addition to dramatically reducing the overall number of measles cases, the reductions were accompanied by a diminishing gap in measles rates between non-locals and locals, which eventually disappeared completely after the 2010 SIA. SIAs have been shown to be key in eliminating measles in the Americas [1], and reducing incidence of disease in Eastern Europe [30]. A study of 15 province-wide SIAs taking place in China during 2004-2008 found that there was on average an 88.1% decrease in measles incidence the year after an SIA compared to the average rate in the preceding five years [13]. Even in Guangxi, a less developed province in China, non-synchronous SIAs taking place in high-incidence counties over 8 years reduced measles incidence 84.7% in the entire province during this time period [32]. Especially for countries and regions with weaker capacity to reliably deliver vaccines in routine immunization services, SIAs are a cost-effective method to distribute the second dose of measles vaccines [31].

However, there are well recognized disadvantages to SIAs, including the future accumulation of susceptible children who were too young to have been vaccinated after the SIA. In our study, we observed a large increase in measles cases among young infants and young adults in 2010, two years after the first, municipality-wide SIA. Similarly, three years after a major SIA in Xinjiang, China, a large-scale outbreak occurred, predominantly in children born after the SIA [13]. Characterization of measles incidence for several years after an SIA is, therefore, important in order to not yield to the frequent common practice of over-ascribing success in disease control to an SIA, which instead of resulting in sustained reductions in measles incidence may instead shift the burden of disease to later birth cohorts or foster development of a biennial cycle of heightened measles transmission.

SIAs also tend to be confined in their geographic impact, in that they typically target people residing within a defined city, county, or province, which limits their effectiveness in controlling spread of disease among persons who migrate to this region after the SIA occurred. China's switch from utilizing staggered SIAs occurring at different times and regions throughout the year before 2009 to a single, synchronized national event in 2010 may be one explanation for why a local/non-local disparity in measles incidence persisted in the two years after the first SIA, but not after the second SIA. Numerous studies in China have suggested that migrants are a cause of high measles incidence [5,13,32], although it is a shortcoming that none of these previous studies quantified the rate of disease in non-locals or the disparity in rates between locals and non-locals. Moreover, beyond directly transmitting disease, unvaccinated migrants increase the pool of susceptible individuals in a population, which theoretically leads to a larger peak number of measles cases every second year [33,34]. As increased numbers of migrants move into Tianjin, NIDMIS could be used to not just measure the seasonality and incidence of measles cases but also identify high risk groups and forecast future epidemiological scenarios.

Strengths and Limitations

Because we had access to a disease information from a population-based registry and population information from the China Statistics Yearbook, we were able to compare the burden of disease between locals and non-locals, controlling for different population sizes. As China continues to focus significant resources on the elimination of endemic transmission of measles, identifying high-risk groups will likely become more logistically difficult and resource intensive[35]. Establishing linkages between NIDMIS and other databases, like immunization registries, population statistical databases, and hospital records, could increase the usefulness of NIDMIS to identify higher risk, susceptible populations and provide data to research correlates of disease. Importantly, giving hospitals access to some information within a limited geographic area could provide useful knowledge about their catchment area and increase their motivation to provide timely, comprehensive reports of disease [36].

This study uses laboratory-confirmed cases, and most measles cases in China were laboratory-confirmed by 2009 [8]. Prior to this, many cases were only clinically-confirmed (i.e. based on clinical presentation without supporting laboratory evidence), but because of the clinical similarity between measles and other febrile rash illnesses, like rubella, clinically-confirmed cases are subject to misclassification [37]. Moreover, there is no evidence to suggest that residency status, our main predictor, was related in any way to the confirmation method for measles. This lack of clinically-confirmed cases, predominantly from before 2009, could, however, attenuate our estimate of the impact of SIAs on measles incidence.

An additional limitation is the validity of population figures, particularly for non-locals. Our data on population size came from the China Statistical Yearbook, but China has changed how it estimates the size of the non-local population over time [38]. However, it is widely reported that population growth in Chinese cities over the past decade is primarily driven by migration and not through natural growth [39], which is what we observe in the population figures used in this study.

This study estimates the impact of SIAs by comparing measles incidence before and after the intervention, but a number of other conditions could affect incidence, including improved routine immunization services, which could have improved in targeting recent migrants. For example, Tianjin has introduced a program in recent years which pays immunization clinic doctors to find migrant children and enroll them at the clinic.

Conclusions

A time-series analysis of reported measles cases in Tianjin, China from January 1, 2005, to December 31, 2013, revealed a reduction in measles disparities between locals and non-locals, particularly after the occurrence of two municipality-wide SIAs. Because of the ongoing and significant internal migration of people in China, sustained efforts will be needed to keep measles incidence low among non-locals in urban settings: SIAs on a supraprovincial scale can reach future migrants to cities, mop-up SIAs can specifically target new arrivals to an area, and routine immunization services can be improved to better serve new arrivals. During the elimination period, dissemination of information from disease registries will be an important part of characterizing disease in subpopulations and evaluating control efforts.

ACKNOWLEDGMENTS

We thank the staff at the Tianjin CDC for providing us with these data, and the health care workers at the municipal and district-level CDCs for investigating the measles cases. This research was supported by a grant from the National Institutes of Health, Institute for Allergy and Infectious Diseases (5U01-AI-088671).

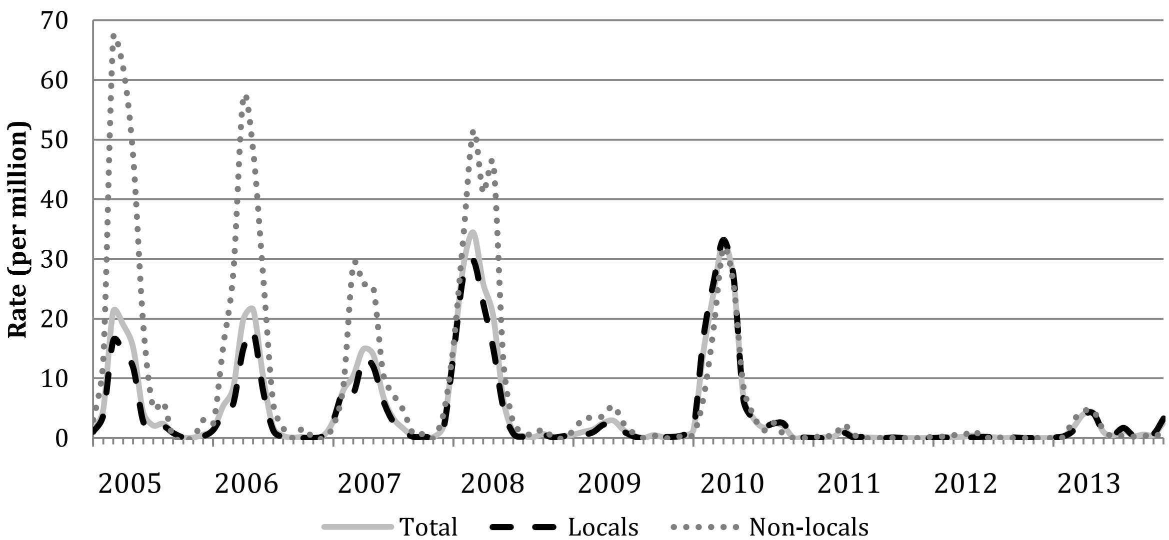


Figure 2-1. Monthly rate of measles in Tianjin, China, in the total population and by residency. Inset includes data from 2011 through 2013 on a shorter axis.

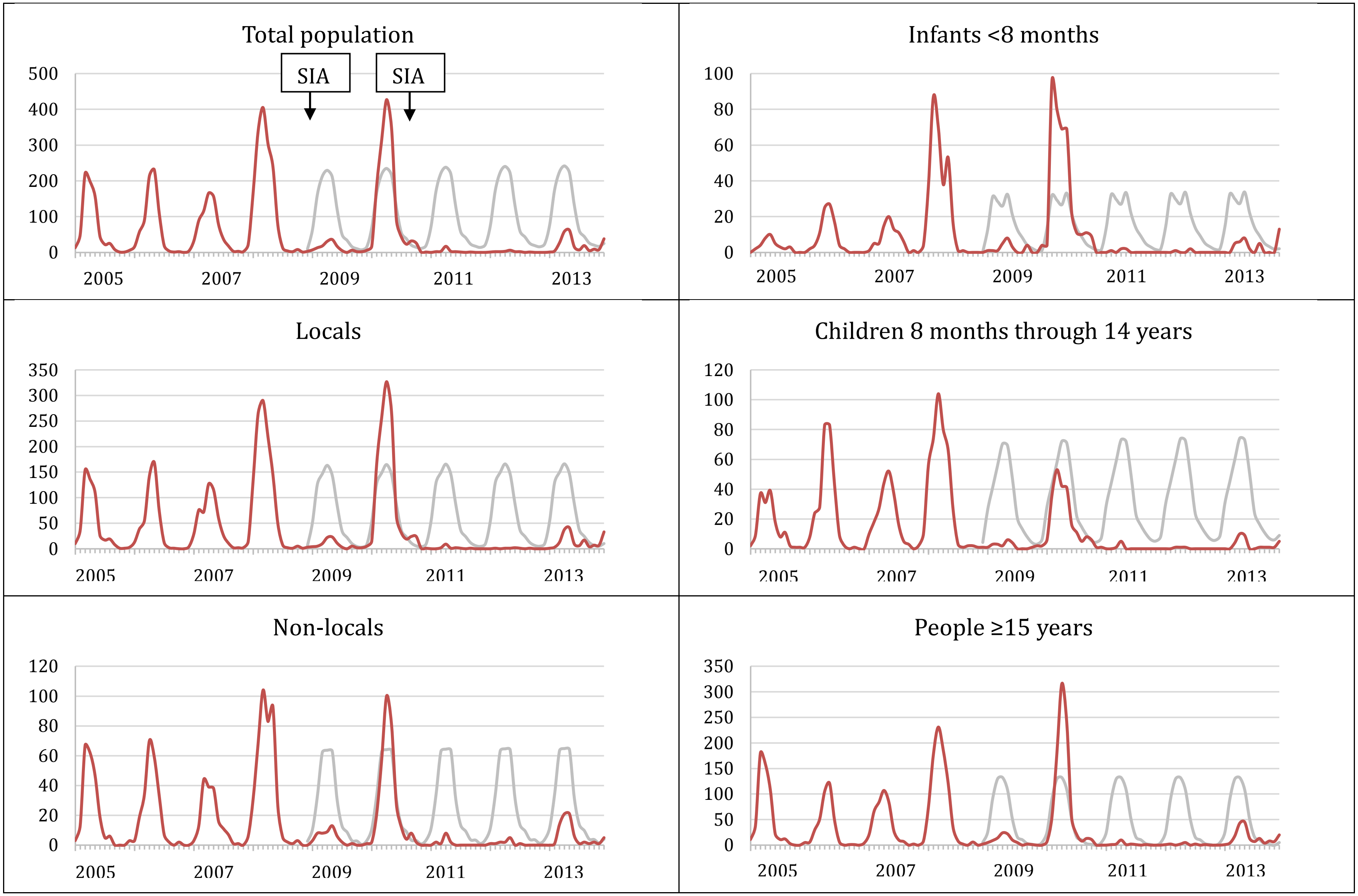


Figure 2-2. Modelled (grey line) and observed (red line) cases of measles in Tianjin, China. Black arrows indicate the timing of supplementary immunization activities (SIAs).

Table 2-1. Demographic characteristics of measles cases in Tianjin, China, from 2005 through 2013.

	Overall	**Residency**[a]	
	Overall Count (%)	Local Count (%)	Non-local Count (%)
Overall	5,730 (100%)	4,178 (100%)	1,514 (100%)
Sex			
Male	3,313 (57.8%)	2,396 (57.3%)	894 (59.0%)
Female	2,417 (42.2%)	1,782 (42.7%)	620 (41.0%)
Urbanicity			
Urban	1,796 (31.3%)	1,448 (34.7%)	331 (21.9%)
Suburban	2,141 (37.4%)	1,159 (27.7%)	968 (63.9%)
Rural	1,793 (31.3%)	1,571 (37.6%)	215 (14.2%)
Age			
<8 months	968 (16.9%)	762 (18.2%)	191 (12.6%)
8 months to <5 years	975 (17.0%)	556 (13.3%)	410 (27.1%)
5 to <15 years	397 (6.9%)	239 (5.7%)	157 (10.4%)
15 to <30 years	1,793 (31.3%)	1,225 (29.3%)	560 (37.0%)
30 years and above	1,597 (27.9%)	1,396 (33.4%)	196 (13.0%)
Time period			
Before the 2008 SIA	3,774 (65.9%)	2,687 (64.3%)	1,049 (69.3%)
Between the SIAs	1,613 (28.2%)	1,254 (30.0%)	359 (23.7%)
After the 2010 SIA	343 (6.0%)	237 (5.7%)	106 (7.0%)
Vaccination status[b]			
0 doses	749 (54.5%)	402 (50.6%)	342 (60.3%)
≥1 dose	500 (36.4%)	347 (43.7%)	153 (27.0%)
Unknown	123 (9.0%)	46 (5.8%)	72 (12.7%)

[a] 38 children with unknown residency status are excluded in these calculations.
[b] For children aged 8 months to <15 years.

Table 2-2. Distribution of measles cases from Tianjin, from 2005 through 2013, by timing relative to Supplementary Immunization Activities (SIAs).

	Before 2008 SIA Count (%)	Between SIAs Count (%)	After 2010 SIA Count (%)
Overall	3,774 (100%)	1,613 (100%)	343 (100%)
Sex			
Male	2,139 (56.7%)	984 (61.0%)	190 (55.4%)
Female	1,635 (43.3%)	629 (39.0%)	153 (44.6%)
Residency			
Local	2,687 (71.2%)	1,254 (77.7%)	237 (69.1%)
Non-local	1,049 (27.8%)	359 (22.3%)	106 (30.9%)
Urbanicity			
Urban	942 (25.0%)	656 (40.7%)	198 (57.7%)
Suburban	1,575 (41.7%)	473 (29.3%)	93 (27.1%)
Rural	1,257 (33.3%)	484 (30.0%)	52 (15.2%)
Age			
<8 months	513 (13.6%)	392 (24.3%)	63 (18.4%)
8 months to <5 years	706 (18.7%)	229 (14.2%)	40 (11.7%)
5 to <15 years	374 (9.9%)	13 (0.8%)	10 (2.9%)
15 to <30 years	1,261 (33.4%)	455 (28.2%)	77 (22.5%)
30 years and above	920 (24.4%)	524 (32.5%)	153 (44.6%)
Vaccination status[a]			
0 doses	536 (49.6%)	181 (74.8%)	32 (64.0%)
≥1 dose	429 (39.7%)	54 (22.3%)	17 (34.0%)
Unknown	115 (10.7%)	7 (2.9%)	1 (2.0%)

[a] For children aged 8 months to <15 years.

Table 2-3. Rate ratio estimates for measles by residency and timing relative to Supplementary Immunization Activities (SIAs).

	Rate Ratio (95% CI)
Non-local vs local	
Before 2008 SIA	2.91 (2.56, 3.31)
Between SIAs	1.39 (1.17, 1.66)
After 2010 SIA	0.96 (0.76, 1.22)
For Locals	
Between SIAs vs before 2008 SIA	0.80 (0.69, 0.92)
After 2010 SIA vs before 2008 SIA	0.17 (0.13, 0.21)
For Non-locals	
Between SIAs vs before 2008 SIA	0.48 (0.39, 0.59)
After 2010 SIA vs before 2008 SIA	0.33 (0.25, 0.43)

Poisson regression model using Generalized Estimating Equations controlled for seasonality, count of measles in the previous day, residency, and SIA time points.

REFERENCES

1. Castillo-Solorzano C C, Matus CR, Flannery B, Marsigli C, Tambini G, et al. (2011) The Americas: paving the road toward global measles eradication. J Infect Dis 204 Suppl: S270–S278. doi:10.1093/infdis/jir166.

2. Durrheim DN, Crowcroft NS, Strebel PM (2014) Measles – The epidemiology of elimination. Vaccine 32: 6880–6883. doi:10.1016/j.vaccine.2014.10.061.

3. Strebel P (2008) Measles. In: Heymann D, editor. Control of Communicable Diseases Manual. Washington, DC: American Public Health Association. pp. 402–408.

4. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, et al. (2012) Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 380: 2095–2128. doi:10.1016/S0140-6736(12)61728-0.

5. Wang L, Zeng G, Lee LA, Yang Z, Yu J, et al. (2003) Progress in Accelerated Measles Control in the People's Republic of China, 1991 – 2000. J Infect Dis 187: 252–257.

6. World Health Organization (2012) Global Measles and Rubella Strategic Plan 2012-2020. Switzerland: World Health Organization.

7. Ji Y, Zhang Y, Xu S, Zhu Z, Zuo S, et al. (2009) Measles resurgence associated with continued circulation of genotype H1 viruses in China, 2005. Virol J 6: 135. doi:10.1186/1743-422X-6-135.

8. Ma C, Hao L, Zhang Y, Su Q, Rodewald L, et al. (2014) Monitoring progress towards the elimination of measles in China: an analysis of measles surveillance data. Bull World Health Organ 92: 340–347. doi:10.2471/BLT.13.130195.

9. Xiang J, Chen Z (1983) Measles Vaccine in the People's Republic of China. Rev Infect Dis 5: 506–510.

10. Zheng J, Zhou Y, Wang H, Liang X (2010) The role of the China Experts Advisory Committee on Immunization Program. Vaccine 28S: A84–A87. doi:10.1016/j.vaccine.2010.02.039.

11. Uzicanin A, Zimmerman L (2011) Field effectiveness of live attenuated measles-containing vaccines: a review of published literature. J Infect Dis 204: S133–S148. doi:10.1093/infdis/jir102.

12. World Health Organization (2013) Measles. WHO Media Cent. Available: http://www.who.int/mediacentre/factsheets/fs286/en/.

13. Ma C, An Z, Hao L, Cairns KL, Zhang Y, et al. (2011) Progress toward measles elimination in the People's Republic of China, 2000-2009. J Infect Dis 204: S447–S454. doi:10.1093/infdis/jir103.

14. World Health Organization (2011) News in Brief. Measles-Rubella Bull 5: 1–9.

15. Ministry of Health of the People's Republic of China (2015) Jing Jin Hu qidong mazhen qianghua mianyi xingdong. Available: http://wsb.moh.gov.cn/mohjbyfkzj/s10769/201008/48593.shtml.

16. Freeman III CW (2009) China's Capacity to Manage Infectious Diseases. Freeman III CW, Lu X, editors Washington, DC: Center for Strategic and International Studies.

17. Du Y, Park A, Wang S (2005) Migration and rural poverty in China. J Comp Econ 33: 688–709. doi:10.1016/j.jce.2005.09.001.

18. Chan K (2012) China: internal migration. In: Ness I, Bellwood P, editors. The Encyclopedia of Global Human Migration. Wiley-Blackwell. doi:10.1002/9781444351071.wbeghm124.

19. Gong P, Liang S, Carlton EJ, Jiang Q, Wu J, et al. (2012) Urbanisation and health in China. Lancet 379: 843–852. doi:10.1016/S0140-6736(11)61878-3.Urbanisation.

20. Sun M, Ma R, Zeng Y, Luo F, Zhang J, et al. (2010) Immunization status and risk factors of migrant children in densely populated areas of Beijing, China. Vaccine 28: 1264–1274. doi:10.1016/j.vaccine.2009.11.015.

21. Provincial Statistics (2013). China Data Online. Available: http://www.chinadataonline.org.

22. Standing Committee of the People's Republic of China (2004) Law of the People's Republic of China on Prevention and Treatment of Infectious Diseases. Available: http://www.npc.gov.cn/englishnpc/Law/2007-12/12/content_1383919.htm.

23. World Health Organization (2007) Manual for the laboratory diagnosis of measles and rubella virus infection Second edition. Second. Geneva, Switzerland: World Health Organization.

24. Chen W, Peng X (2012) Household registration system, economic opportunity, and the income gap between urban and rural residents in China. Econ Surv 2: 100–104 [in Chinese]. doi:10.15931/j.cnki.1006-1096.2012.02.030.

25. Li H, Wang Q, Shi W, Deng Z, Wang H (2015) Residential clustering and spatial access to public services in Shanghai. Habitat Int 46: 119–129. doi:10.1016/j.habitatint.2014.11.003.

26. R Core Team (2014) R: A Language and Environment for Statistical Computing. Available: http://www.r-project.org.

27. Cleveland RB, Cleveland WS, McRae JE, Terpenning I (1990) STL: A Seasonal-Trend Decomposition Procedure Based on Loess. J Off Stat 6: 3–73.

28. Hyndman RJ, Khandakar Y (2008) Automatic time series forecasting: the forecast package for R. J Stat Softw 26: 1–22.

29. Højsgaard S, Halekoh U, Yan J (2006) The R Package geepack for Generalized Estimating Equations. J Stat Softw 15: 1–11.

30. Khetsuriani N, Deshevoi S, Goel A, Spika J, Martin R, et al. (2011) Supplementary immunization activities to achieve measles elimination: Experience of the European region. J Infect Dis 204. doi:10.1093/infdis/jir074.

31. Dayan GH, Cairns L, Sangrujee N, Mtonga A, Nguyen V, et al. (2004) Cost-effectiveness of three different vaccination strategies against measles in Zambian children. Vaccine 22: 475–484. doi:10.1016/j.vaccine.2003.07.007.

32. Zhuo J, Geng W, Hoekstra EJ, Zhong G, Liang X, et al. (2011) Impact of supplementary immunization activities in measles-endemic areas: A case study from Guangxi, China. J Infect Dis 204: 455–462. doi:10.1093/infdis/jir063.

33. Marguta R, Parisi A, Parisi A (2015) Impact of human mobility on the periodicities and mechanisms underlying measles dynamics. J R Soc Interface 12: 20141317.

34. Uziel A, Stone L (2012) Determinants of periodicity in seasonally driven epidemics. J Theor Biol 305: 88–95. doi:10.1016/j.jtbi.2012.02.031.

35. Klepac P (2013) Towards the endgame and beyond: complexities and challenges for the elimination of infectious diseases. Phil Trans R Soc B 368: 20120137.

36. Zhang L (2009) Building a better infectious disease surveillance system for China. Saarbrücken, Germany: VDM Verlag Dr. Müller.

37. Sniadack DH, Mendoza-Aldana J, Jee Y, Bayutas B, Lorenzo-Mariano KM (2011) Progress and challenges for measles elimination by 2012 in the Western Pacific Region. J Infect Dis 204: 439–446. doi:10.1093/infdis/jir148.

38. Martina M, Lan W, Miles T, Durfee D (2011) Factbox: China's 2010 Census. Reuters. Available: http://www.reuters.com/article/2011/04/28/us-china-census-factbox-idUSTRE73R0XM20110428. Accessed 21 March 2015.

39. Cox W (2011) China: Urbanizing and moving East: 2010 Census. NewGeography.com. Available: http://www.newgeography.com/content/002218-china-urbanizing-and-moving-east-2010-census.

CHAPTER 3

Measles and pneumococcal immunization of Shanghai children: Assessing timeliness and predictors for vaccination

ABSTRACT

Background. Measles and pneumococcal vaccines are important tools to reduce morbidity and mortality in Chinese children, but delayed measles vaccination is a recognized problem in China and uptake of pneumococcal vaccines is limited by expense. Additionally, immunization services in large cities in China have difficulty reaching non-locals, migrants coming from outside the city. This study has three aims: to estimate the proportion of children in Shanghai with timely measles vaccinations and with the two different pneumococcal vaccinations; to compare vaccination outcomes in non-locals and locals; and to assess the impact of township-level characteristics on vaccination outcomes.

Methods. Individual-level data from a cohort in the Shanghai Immunization Program Information System were linked to township-level data from the 2010 China Census. We used a generalized estimating equations framework with logistic regression models to assess individual- and township-level predictors of vaccination outcomes.

Results. Non-locals had lower vaccination levels than locals. Non-locals had 0.44 times the odds of timely M1 (95% 0.42, 0.47), 0.27 times the odds of timely MMR1 (95% CI: 0.25, 0.30), 0.36 times the odds of PCV1 by 8 months of age (95% CI: 0.31, 0.41), and 0.73 times the odds of PCV1 by 4 years of age (95% CI: 0.67, 0.80), compared to locals. For local children born in 2007, a higher proportion of non-locals in the township was associated with less timely measles vaccinations but greater odds of pneumococcal vaccination.

Discussion. Untimely measles vaccination and extremely low uptake of pneumococcal vaccination impede successful control of these infectious diseases in Shanghai. Because non-locals have worse outcomes than locals, they should be especially targeted for vaccination, and immunization information systems can track the progress in eliminating disparities.

INTRODUCTION

Measles and pneumococcal pneumonia followed only TB and malaria as the leading causes of infectious disease mortality worldwide in 1990 [1]. In the ensuing two decades, annual mortality from invasive pneumococcal disease (IPD), which comprises pneumonia, meningitis, and septicemia, has remained relatively stable at over 900,000 deaths in contrast to the substantial decrease in measles mortality, from 631,200 deaths in 1990 to 125,400 deaths in 2010 [1]. Although the global epidemiology of these two vaccine preventable diseases are markedly different [2], the World Health Organization (WHO) recommends inclusion of vaccines for both diseases in all countries' national immunization programs [3], and they would likely be two of the largest sources of infectious disease mortality worldwide in young children if it were not for vaccination programs.

China first approved the use of a measles vaccine in 1966 [4]. Because measles is so infectious and the measles vaccination is known to be less effective at younger ages [5], multiple doses of vaccine are necessary to ensure adequate herd immunity, especially when the first dose is given at <12 months of age [6]. In Shanghai, 3 doses of measles vaccine are provided for free to every child as part of the government-funded Expanded Program on Immunization (EPI): a measles-rubella combined vaccine (M1) is administered to children at 8 months of age, and a measles-mumps-rubella combined vaccine (MMR) is given to children at 18-24 months of age (MMR1) and again at 5 years of age (MMR2) [7]. As a result of increasing measles vaccine coverage, measles incidence in China has declined from over 1,000 cases per 100,000 in the 1960s to 5.7 cases per 100,000 in the late 1990s [8]. Although China has mobilized to eliminate measles [9], it did not reach a goal of elimination by 2012, which was pushed back to 2020 [10,11]. Difficulty in controlling measles has been explained by increased numbers of migrants in China [8,12], as well as untimely measles vaccination. Although most children in China are eventually vaccinated against measles, previous studies have found that less than 90% of children have a timely administration of M1 [13,14]. With such substantial delay in vaccination, vaccine timeliness is a better indicator of population-level immunity than estimates of coverage that do not consider timing [15].

In contrast to measles vaccines, pneumococcal vaccines (PVs) have only recently been introduced into China [16]. Two PVs are available at immunization clinics for a fee: the 23-valent pneumococcal polysaccharide vaccine (PPSV) since 1996 and the 7-valent pneumococcal conjugate vaccine (PCV) since 2008 [16]. Although PCV (135 USD/dose) is more expensive than PPSV (24 USD/dose), it is more immunogenic, and can be administered to children as young as 6 weeks, compared to PPSV which is only available for children ≥2 years [17]. Coverage of PVs is still relatively low in China [18], and promoting their dissemination does not appear to be a government priority [16], even though the vaccine could reduce the substantial burden of pneumococcal disease among children in China. Chen et al. estimated that in 2000 there were 384.45 cases of pneumococcal pneumonia per 100,000 children <5 years and 1.33 cases of pneumococcal meningitis per 100,000 children <5 years [19].

Several studies have shown that vaccination coverage is lower in non-locals, migrants from rural to urban areas, than locals, including coverage for pneumococcus and measles [18,20,13]. Of the 23 million residents in Shanghai, 9 million are non-locals who do not have the official residency papers, or *hukou*, which give a Chinese citizen access to some social welfare programs [21]. Children are, however, offered EPI vaccines for-free in China regardless of their residency status.

Non-locals often cluster together in neighborhoods [22], and this demographic clustering, along with other social characteristics associated with neighborhoods, could influence an individual's attitudes towards vaccination through a variety of mechanisms. Neighborhoods represent the environment in which disease spreads and in which health care facilities provide preventive care. For instance, neighborhoods with more children may more frequently foster the spread of infectious diseases commonly found in young children; places with many transient workers may experience a higher incidence of diseases carried in by the migrants; and a community's social norms, which are influenced by the demographic structure of that community, may value, or alternatively, disapprove of vaccination. Previous studies in the Netherlands [23] and in Hawaii [24] have found some important links between neighborhood-level risk factors, such as socioeconomic condition and racial distribution, and immunization status. In Shanghai townships, a neighborhood administrative division with over 100,000 people on average, not only have distinguishing demographic characteristics but also have a shared experience of immunization services because people within a township attend the same immunization clinic.

The influence of township-level characteristic on vaccination characteristics has not been well-studied in China, and quantifying vaccination disparities between non-locals and locals within the context of the township where they actually reside is important in identifying pockets of susceptible populations and in evaluating whether immunization programs are equitably reaching diverse groups of people. Moreover, programs for different vaccinations are not likely to be equally successful, particularly for immunizations which have varying levels of governmental priority, national attention, and payment methods, as do the measles and pneumococcal vaccines. This study explores vaccination outcomes in terms of timely M1 and MMR1 administration as well as uptake of PCV and PPSV at milestone ages. Specifically, we estimate the proportion of children in Shanghai with these vaccination outcomes, compare vaccination outcomes between non-locals and locals, and assess the impact of township-level characteristics on vaccination outcomes.

MATERIALS AND METHODS

Study population

We used a single-stage cluster design to explore pediatric vaccination outcomes in Shanghai. Townships were selected by a probability proportionate to size (PPS) systematic selection procedure using population of children 0 to 14 years of age from the China 2010 Census as the population size. In each selected township, we sampled every child born between January 1, 2000, and July 4, 2014. From a preliminary analysis of older data, we determined that 24 clusters were needed to discriminate between proportions of 92.4%

and 79.5%, the estimated values of MMR timeliness for locals and non-locals, respectively, given an intracluster correlation coefficient of 0.133. Figure 3-1 shows the location of the selected townships in Shanghai.

Because each vaccination outcome that we examined involves a different age group, our analysis uses 4 pools of children drawn from this first sample. For timely M1, we included children over 8 months of age, and excluded children with no M1 record given that measles vaccination coverage is very high in China [13,25], and no recorded measles vaccination could be indicative of attrition from the dataset or a contraindication to vaccination. Similarly, for timely MMR1, all children over 18 months of age who had a record of MMR1 administration were included. In examining PCV1 receipt by 8 months of age, we limited the analysis to children at least 8 months of age who were born in 2008 or after because the vaccine was not released in China until that year. For PV by 4 years of age, we included all children over 4 years of age, and stratified analyses based on whether they had received PCV compared to no PV or whether they had received PPSV compared to no PV.

Data sources

This study combines individual-level data from a cohort in the Shanghai Immunization Program Information System (SIPIS) and township-level data from the 2010 China Census. SIPIS includes information on children's birthdate, sex, residency status (local vs non-local), the township immunization clinic where they received their latest vaccination, and dates of any vaccinations. Urbanicity was defined by the location of the township; Huangpu, Xuhui, Changning, Jing'an, Putuo, Zhabei, Hongkou, and Yangpu comprise the urban districts; and the suburban districts are Minhang, Baoshan, Jiading, Pudong, Jinshan, Songjiang, Qingpu, Fengxian, and Chongming.

Timely M1 was defined as a measles vaccine or measles-rubella vaccine administered when the child was between 8 and 9 months of age, and MMR1 was considered timely if administered when the child was between 18 and 24 months of age. Vaccinations after these ages were considered untimely. The outcome, PCV1 by 8 months of age, compares children who had a dose administered by 8 months of age to children with no PCV by 8 months. Finally, PV by 4 years of age divides children older than 4 years of age into 3 outcome categories: those with no PV before 4 years, those with PCV administered before 4 years, and those with PPSV administered before 4 years.

The China 2010 Census provided information about township residency composition, and child dependency ratio (CDR). The township residency composition was derived from the proportion of non-locals living in the township, i.e. one minus the proportion of the total population of registered permanent residents in the total resident population of the township. The child dependency ratio (CDR) was calculated as the total population between the ages of 0 to 14 years divided by the total population between the ages of 15 and 65, multiplied by 100. In the multivariable regressions, the township residency composition was categorized based on which residency group, local or non-local, formed the majority of the population. The CDR was dichotomized at the median.

Statistical analysis

Frequencies and proportions were calculated for each of the individual-level explanatory and outcome variables, and these proportions were compared by residency status. The mean and median were used to describe the distribution of the township-level variables before they were categorized.

For each model, we fit a multilevel model through a generalized estimating equation (GEE) framework with a binomial distribution and logit link. To account for each intra-township correlation, we specified an exchangeable correlation matrix at the township level. The explanatory variables in each model were specified *a priori* and were generally the same for each outcome in order to facilitate comparisons across different vaccinations. These variables included residency, urbanicity, township proportion non-local, and township CDR. To evaluate trends over time and to account for more complete records in SIPIS in recent years, both birth year centered at 2007 and a piecewise linear term after birth year 2007 were included in the models. Because PCV1 by 8 months of age only included children who were born in 2008 or after, the piecewise linear term was not included. Interactions were included for residency and 3 other variables: birth year, the piecewise linear term after birth year 2007, and township residency composition. Because of the differential probabilities of selection based on population size, we included population of children aged between 0 and 14 in the township as quartiles in the regression. We calculated estimates and standard errors for the OR of locals compared to non-locals in different strata by combining main and interaction coefficients Plots of odds ratios comparing non-locals to locals by township residency composition and at different birth years were constructed to facilitate interpretation of models. The precision of results was evaluated through 95% confidence intervals. All analyses were performed with R version 3.0.3 [26], including the packages *geepack* [27], *plotrix* [28], and *ggplot2* [29].

Ethics statement

This study was exempted from ethical approval by the University of Michigan Institutional Review Board and a Shanghai CDC ethics committee because it was limited to analysis of previously de-identified data.

RESULTS

A sample of 416,750 young children was drawn from SIPIS for the study. The majority of children in the sample were non-locals (61.2%), male (53.1%), and lived in Shanghai's suburban district (87.9%). Starting with the 2007 year, at which point SIPIS was widely used throughout the city, over 35,000 children born in each subsequent year were selected into the study (Table 3-1) with 24 townships represented in the sample. The CDR ranged from 7.9 to 15.5 in the sample, with a median of 10.6. The proportion of non-locals in the townships varied between 17% and 74%, and the median was 66% (Table 3-2).

Table 3-3 shows the distribution of vaccination outcomes in the total sample and by residency. The proportion of children with timely M1 was 83.6% and with timely MMR1 was 87.2%. Very few children had PCV1 administered by 8 months (3.7%) or 4 years (7.3%). Locals had more timely measles vaccinations and greater uptake of PCV, but PPSV1 coverage was higher among non-locals (32.2%) than locals (27.7%) at 4 years of age.

Findings from the multivariable regressions are shown in Table 3-4. For children born in 2007 who lived in local-majority townships, non-locals had lower odds of timely measles vaccinations and lower odds of PCV administration by 8 months or 4 years than locals. The odds of PPSV1 by 4 years of age were similar for locals and non-locals.

Local children had worse vaccination outcomes in non-local majority townships than in local-majority townships, except for PCV1 by 4 years of age (OR: 1.94; 95% CI: 1.80, 2.10). And the interaction terms between individual residency status and township residency composition reveal that living in non-local-majority townships leads to differentially worse vaccination outcomes for non-locals than for locals. For instance, non-locals have 0.84 times the odds of timely M1 compared to locals, when living in non-local-majority townships (95% CI: 0.80, 0.88).

The ORs comparing non-locals and locals across select years and different township settings are graphically depicted in Figure 3-2. Except for MMR1 timeliness, the disparity in vaccination outcomes between non-locals and locals decreased over time. Additionally, there is less of a difference between non-locals and locals in local-majority townships than in non-local-majority townships.

People living in townships with an above-median CDR had less timely M1 (OR: 0.93; 95% CI: 0.91, 0.96) and MMR1 (OR: 0.87; 95% CI: 0.84, 0.90) than those from townships with a below-median CDR. The opposite direction of association was seen for pneumococcal vaccinations. The odds of PCV1 by 8 months of age (OR: 1.25, 95% CI: 1.19, 1.32), PCV1 by 4 years of age (OR: 2.40, 95% CI: 2.29, 2.52) and PPSV1 by 4 years of age (OR: 1.32, 95% CI: 1.28, 1.37) were higher for those living in townships with an above-median CDR compared to those from townships with a below-median CDR.

DISCUSSION

Before widespread vaccination in China, 3 to 4 million cases of measles [30] and almost 700,000 cases of IPD [19] occurred each year. Measles and pneumococcal vaccine programs have great potential to reduce morbidity, especially in young children, but we found that many children in Shanghai were vaccinated late; timeliness of measles vaccinations was below herd immunity thresholds, and the few children who did receive a pneumococcal vaccine usually were vaccinated after they were 8 months of age. These vaccination patterns mean that young infants in China are still at risk for highly infectious diseases, even though vaccines are available.

Our findings that less than 90% received timely vaccination in Shanghai was similar to what we previously found in Tianjin, another large municipality in China [14]. One other study in China, in Zhejiang, a province which borders Shanghai, found relatively lower timely M1; there, only 70.1% of children had timely M1 [13]. Timeliness of MMR1 was similar in our study and in studies from developed countries: Dannetun et al. found MMR1 timeliness between 80% and 90% in 3 different cohorts in Sweden [31], and about 90.4% of American parents who did not intentionally delay vaccination had timely MMR1 according to the 2003 National Immunization Survey [32]. In each case, timely coverage of measles vaccinations is below critical vaccination coverage levels [33]. In spite of several studies suggesting that there is high coverage of measles and other EPI vaccines [13,14,34], this lack of vaccine timeliness in China, could be one explanation for the difficulty in eliminating vaccine-preventable diseases as evidenced by China inability to meet with 2012 measles elimination target [12].

We found very low uptake of PCV. Corroborating our findings is a survey of parents across all provinces in mainland China, which found that only 9.9% of children had received this vaccine [35]. In contrast, in the 73 countries eligible for financial support from the GAVI Alliance, uptake of the third dose of PCV, a more stringent standard than what we or Zheng et al. investigated, was 19% [36]. It is concerning that China, which is too wealthy to be eligible for GAVI funding, has lower coverage than these countries many of which are presumably poorer and have fewer resources to devote to immunization programs. Although academics and Chinese public health officials have called for China to introduce PCV as a government-funded vaccine [16], Che et al. indicated that this may not be cost-effective [37] and it does not appear to be a current government priority to increase PCV uptake. However, to eliminate disparities between different socioeconomic or demographic groups, government funding is likely to be necessary, and newer, higher-valent vaccines than the 7-valent PCV may be more cost-effective in China.

Urbanicity in China is correlated with many other factors, with more urban areas characterized as economically developed and their residents having better psychological and physical health compared to counterparts in less urban areas [38]. We found M1 and MMR1 timeliness, as well as PPSV administration, to be higher in suburban districts compared to urban districts. This positive association may indicate higher levels of immunization system performance in suburban districts or suburban residents expressing more positive social norms towards paid vaccines. Conversely, PCV1 administration, by both 8 months and 4 years, is lower in suburban districts compared to urban districts, indicating more sensitivity to higher prices in the economically less-developed suburban districts.

Vaccination outcomes, except for PPSV uptake, were lower in non-locals than locals. Considering that there is substantial clustering of people by residency within China, these low vaccination levels indicate that there may be particular difficulty in controlling the spread of measles and pneumococcal disease within the non-local population. Moreover, non-locals had even worse outcomes in non-local-majority townships compared to local-majority townships. This disparity may result from other factors associated with non-local-majority townships, such as low socioeconomic status, or it may be because different types of migrants live in different settings within Shanghai [39]. For instance, more prosperous migrants may move to areas with fewer non-locals.

Regarding CDR, there was a clear delineation between patterns for M1 and MMR1 timeliness and for pneumococcal vaccinations. A larger CDR was associated with worse timeliness; because a larger CDR indicates a larger concentration of children in the township, this could make it difficult for township immunization clinics to organize services so that children are vaccinated within a constrained time period. However, a larger CDR was associated with greater propensity for pneumococcal vaccination, suggesting that a greater number of children in someone's living area may be accompanied by a commensurate increase in social norm that prompts parents to seek vaccination for their child.

Strengths and limitations

This study has a number of limitations. We used immunization information system data from Shanghai to calculate vaccination coverage which limited us to data since the year 2000, but data before 2008 were sparse and SIPIS was not comprehensively used throughout the city until after 2010. Although absolute numbers may be biased and may overestimate vaccination outcomes, especially for earlier years, the relative comparison between outcomes should be reasonably unbiased, as the degree of missing data should follow a similar pattern for all vaccines considered. Additionally, attrition is a problem, because children who move away from Shanghai may still be present in the dataset. We did not pursue sensitivity analyses comparing a full dataset and a smaller dataset with children for whom we know records exist at a given age, because the methods of limiting the dataset could also plausibly be related to both the explanatory variables and vaccination outcomes, and thus create a collider bias. Finally, the SIPIS dataset includes few individual-level variables. Income, education, and personal beliefs towards health care services could confound the relationship between residency status or township characteristics and vaccination outcomes. However, this study population does form a representative sample of children in Shanghai, and we were able to observe characteristics associated with rare outcomes (like PCV uptake) because of the large sample size.

Conclusions

Although limited in their ability to obtain data on individual-level behaviors, immunization information systems have the goal to not only collect data, but also analyze it and use it to evaluate and improve public health practices [40,41]. As an information system becomes more comprehensive, it can become better at predicting areas with low vaccination coverage, hot spots for potential disease outbreaks, clinics which have difficulties in organizing immunization services, and populations that are, or are not, willing to obtain novel immunizations. As China increases efforts to eliminate measles, it should ensure that immunization services as a whole improve; vaccination against measles should not be the only end goal, but it should be a means and opportunity to improve programs that provide immunizations against other diseases [42]. To this end, both measles vaccination timeliness and pneumococcal vaccination could be used as standard indicators of different but equally important aspects of immunization program performance.

ACKNOWLEDGMENTS

Data for the China 2010 Census was obtained from the China Data Center through the University of Michigan Asia Library. We are thankful to the staff at the Shanghai CDC for obtaining the dataset and familiarizing us with SIPIS. This research was funded by the University of Michigan Office of Global Public Health and by a Rackham International Research Award.

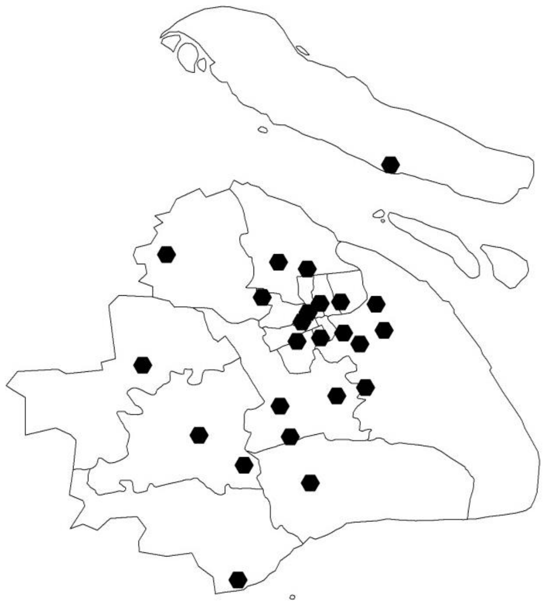


Figure 3-1. Map of 24 townships in Shanghai selected into sample.

Table 3-1. Distribution of demographic characteristics overall and by residency status within a sample of children from the Shanghai Immunization Program Information System.

		Locals	Non-locals
	Count (%[a])	Count (%[b])	Count (%[b])
Overall	416,750 (100%)	161,801(38.8%)	254,949 (61.2%)
Sex			
Male	221,283 (53.1%)	83,452 (37.7%)	137,831 (62.3%)
Female	195,269 (46.9%)	78,252 (40.1%)	117,017 (59.9%)
Birth year			
2000	5,428 (1.3%)	3,873 (71.4%)	1,555 (28.7%)
2001	5,669 (1.4%)	3,719 (65.6%)	1,950 (34.4%)
2002	6,951 (1.7%)	4,222 (60.7%)	2,729 (39.3%)
2003	7,224 (1.7%)	3,704 (51.3%)	3,520 (48.7%)
2004	11,341 (2.7%)	5,266 (46.4%)	6,075 (53.6%)
2005	21,185 (5.1%)	8,883 (41.9%)	12,302 (58.1%)
2006	30,478 (7.3%)	11,695 (38.4%)	18,783 (61.6%)
2007	37,995 (9.1%)	15,146 (39.9%)	22,849 (60.1%)
2008	40,953 (9.8%)	14,269 (34.8%)	26,684 (65.2%)
2009	41,415 (9.9%)	13,769 (33.3%)	27,646 (66.8%)
2010	44,560 (10.7%)	16,103 (36.1%)	28,457 (63.9%)
2011	46,117 (11.1%)	16,216 (35.2%)	29,901 (64.8%)
2012	53,928 (12.9%)	19,932 (37.0%)	33,996 (63.0%)
2013	47,132 (11.3%)	17,752 (37.7%)	29,380 (62.3%)
2014	16,374 (3.9%)	7,252 (44.3%)	9,122 (55.7%)
Urbanicity			
Urban	50,628 (12.2%)	27,292 (53.9%)	23,336 (46.1%)
Suburban	366,122 (87.9%)	134,509 (36.7%)	231,613 (63.3%)

Notes:

[a] Proportion of children with that characteristic.

[b] Proportion of children with that characteristic who are local or non-local.

Table 3-2. Distribution of the child-dependency ratio (CDR) and proportion non-local in the townships within a sample of young children from the Shanghai Immunization Program Information System.

	Range	Mean (SD)	Median
CDR	7.9 – 15.5	11.3 (1.8)	10.6
Proportion non-local	0.17 – 0.74	0.60 (0.13)	0.66

Table 3-3. Distribution of vaccination outcomes overall and by residency status within a sample of children from the Shanghai Immunization Program Information System.

			Locals	**Non-locals**
	Number	Proportion	Proportion	Proportion
Timely M1	339,483	83.6%	89.7%	79.6%
Timely MMR1	276,405	87.2%	92.1%	83.8%
PCV1 by 8 months	266,100	3.7%	6.6%	2.1%
PV by 4 years	230,195			
PCV1		7.3%	11.3%	4.6%
PPSV1		30.4%	27.7%	32.2%

Notes:
M1, measles vaccine dose 1; MMR1, measles-mumps-rubella vaccine dose 1; PCV1, pneumococcal conjugate vaccine dose 1; PV, pneumococcal vaccine; PPSV1, pneumococcal polysaccharide vaccine

Table 3-4. Odds ratios and 95% confidence intervals of five different vaccination outcomes according to generalized estimating equations (GEE) regressions from a sample of young children from the Shanghai Immunization Program Information System.

	Timely M1	Timely MMR1	PCV1 by 8 mo.	PCV1 vs no PV	PPSV1 vs no PV
	n=339,483	n=276,405	n=266,100	n=160,273	n=213,486
Main effects					
Non-local vs local	0.44 (0.42, 0.47)	0.27 (0.25, 0.30)	0.36 (0.31, 0.41)	0.73 (0.67, 0.80)	0.99 (0.94, 1.04)
Birth year (centered at 2007)	0.99 (0.98, 1.01)	1.57 (1.55, 1.60)	1.32 (1.29, 1.34)	1.36 (1.33, 1.38)	1.23 (1.21, 1.24)
Change after birth year 2007	1.06 (1.04, 1.08)	1.26 (1.21, 1.31)		0.67 (0.64, 0.69)	0.69 (0.67, 0.71)
Suburban vs urban district	1.07 (1.04, 1.11)	1.21 (1.14, 1.28)	0.55 (0.51, 0.59)	0.30 (0.28, 0.32)	2.37 (2.26, 2.49)
Township residency composition (non-local majority vs local majority)	0.89 (0.85, 0.93)	0.31 (0.29, 0.34)	0.64 (0.59, 0.70)	1.94 (1.80, 2.10)	0.80 (0.76, 0.84)
Township CDR (above vs below median)	0.93 (0.91, 0.96)	0.87 (0.84, 0.90)	1.25 (1.19, 1.32)	2.40 (2.29, 2.52)	1.32 (1.28, 1.37)
Township population					
2nd vs 1st quartile	1.17 (1.14, 1.21)	1.95 (1.85, 2.05)	0.74 (0.69, 0.80)	0.46 (0.42, 0.49)	0.75 (0.72, 0.79)
3rd vs 1st quartile	0.87 (0.84, 0.90)	1.48 (1.41, 1.55)	1.00 (0.92, 1.08)	0.89 (0.83, 0.95)	0.52 (0.50, 0.55)
4th vs 1st quartile	0.79 (0.77, 0.82)	1.80 (1.71, 1.90)	1.27 (1.17, 1.39)	0.51 (0.47, 0.55)	1.00 (0.96, 1.05)
Interactions					
Non-local*birth year	1.08 (1.06, 1.09)	0.85 (0.83, 0.86)	1.08 (1.05, 1.11)	1.10 (1.07, 1.13)	1.11 (1.09, 1.13)
Non-local*change after birth year 2007	1.00 (0.97, 1.02)	1.20 (1.15, 1.25)		0.93 (0.88, 0.98)	1.05 (1.01, 1.08)
Non-local*non-local-majority township	0.84 (0.80, 0.88)	1.08 (1.00, 1.17)	0.63 (0.57, 0.69)	0.54 (0.49, 0.58)	0.82 (0.78, 0.86)

Notes:
CDR, child dependency ratio; M1, measles dose 1; mo., month; MMR1, measles-mumps-rubella dose 1; PCV1, pneumococcal conjugate vaccine dose 1; PV, pneumococcal vaccine; PPSV1, pneumococcal polysaccharide vaccine dose 1.

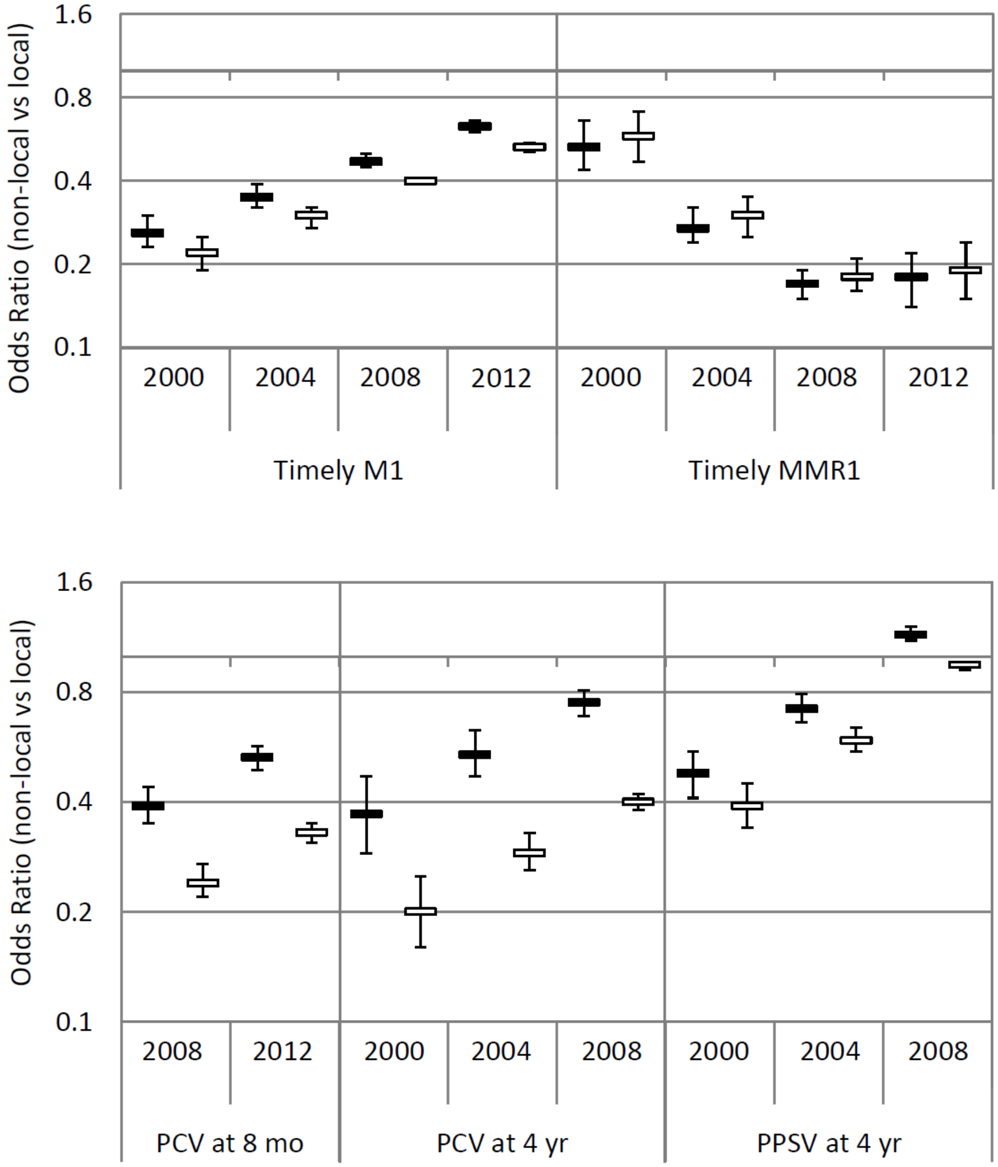
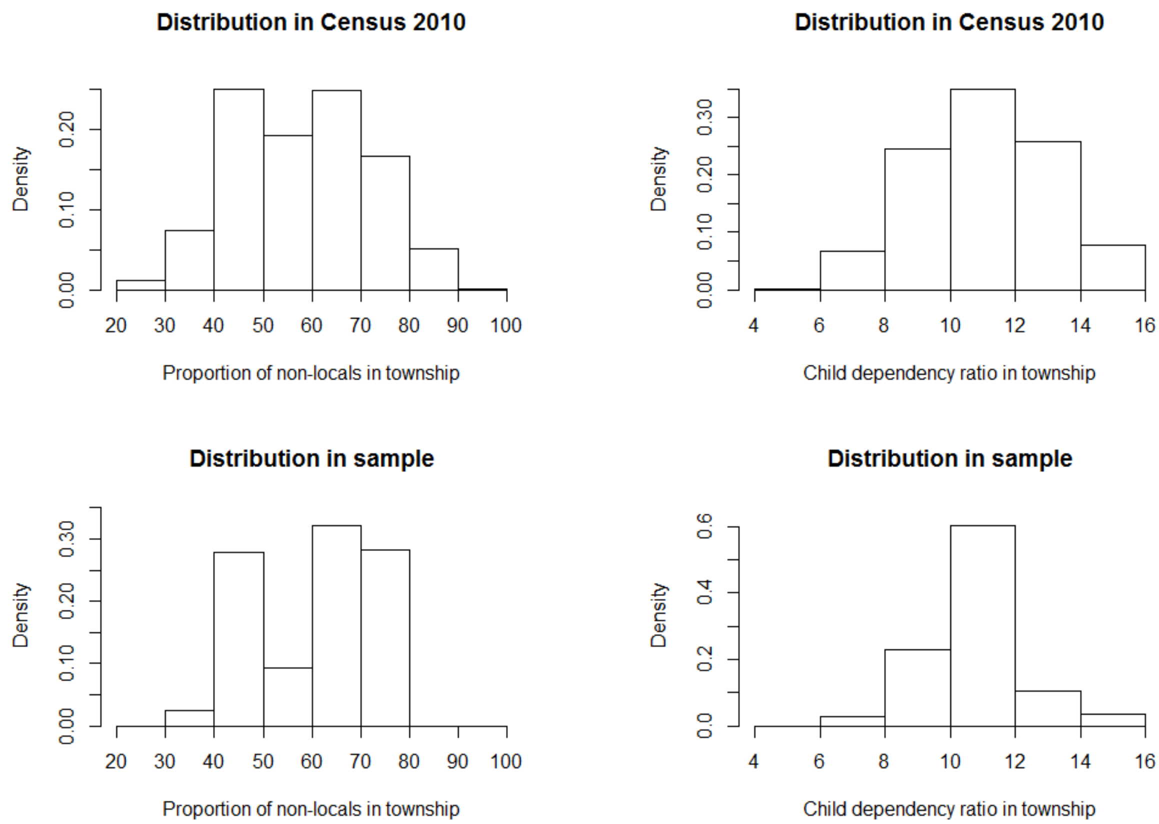


Figure 3-2. Odds ratios and 95% confidence intervals comparing vaccination outcomes in non-locals vs locals by birth year and township residency composition (black boxes indicate local-majority townships, white boxes non-local-majority townships). M1, measles vaccine dose 1; MMR1, measles-mumps-rubella vaccine dose 1; PCV, pneumococcal conjugate vaccine; PPSV, pneumococcal polysaccharide vaccine.



Supplemental Figure 3-S1. Comparison of the distributions of proportion non-locals in township and child dependency ratio in township in the China Census 2010 and in a sample of young children from the Shanghai Immunization Program Information System.

REFERENCES

1. Lozano R, Naghavi M, Foreman K, Lim S, Shibuya K, et al. (2012) Global and regional mortality from 235 causes of death for 20 age groups in 1990 and 2010: a systematic analysis for the Global Burden of Disease Study 2010. Lancet 380: 2095–2128. doi:10.1016/S0140-6736(12)61728-0.

2. Hinman A (1999) Eradication of vaccine-preventable diseases. Annu Rev Public Heal 20: 211–229.

3. Duclos P, Okwo-Bele J-M, Gacic-Dobo M, Cherian T (2009) Global immunization: status, progress, challenges and future. BMC Int Health Hum Rights 9 Suppl 1: S2. doi:10.1186/1472-698X-9-S1-S2.

4. Xiang J, Chen Z (1983) Measles Vaccine in the People's Republic of China. Rev Infect Dis 5: 506–510.

5. Uzicanin A, Zimmerman L (2011) Field effectiveness of live attenuated measles-containing vaccines: a review of published literature. J Infect Dis 204: S133–S148. doi:10.1093/infdis/jir102.

6. World Health Organization (2009) Measles vaccines: WHO position paper. Wkly Epidemiol Rec 84: 349–360.

7. Schulter W, Wang X, Mendoza-Aldana J, Jee Y, Diorditsa S, et al. (2013) Progress Toward Measles Elimination - Western Pacific Region, 2009-2012. MMWR Morb Mortal Wkly Rep 62: 445–447.

8. Wang L, Zeng G, Lee LA, Yang Z, Yu J, et al. (2003) Progress in Accelerated Measles Control in the People's Republic of China, 1991 – 2000. J Infect Dis 187: 252–257.

9. McFarland J (2012) World Immunization Week, China. Our Glob Voices. Available: http://blogs.cdc.gov/global/2012/04/27/world-immunization-week-china/.

10. World Health Organization (2012) Global Measles and Rubella Strategic Plan 2012-2020. Switzerland: World Health Organization.

11. Durrheim DN, Crowcroft NS, Strebel PM (2014) Measles – The epidemiology of elimination. Vaccine 32: 6880–6883. doi:10.1016/j.vaccine.2014.10.061.

12. Ma C, Hao L, Zhang Y, Su Q, Rodewald L, et al. (2014) Monitoring progress towards the elimination of measles in China: an analysis of measles surveillance data. Bull World Health Organ 92: 340–347. doi:10.2471/BLT.13.130195.

13. Li Q, Hu Y, Zhong Y, Chen Y, Tang X, et al. (2014) Using the Immunization Information System to determine vaccination coverage rates among children aged 1-7 years: a report from Zhejiang Province, China. Int J Environ Res Public Health 11: 2713–2728. doi:10.3390/ijerph110302713.

14. Wagner AL, Zhang Y, Montgomery JP, Ding Y, Carlson BF, et al. (2014) Timely measles vaccination in Tianjin, China: a cross-sectional study of immunization records and mothers. BMC Public Health 14: 888. doi:10.1186/1471-2458-14-888.

15. Akmatov MK, Kretzschmar M, Krämer A, Mikolajczyk RT (2008) Timeliness of vaccination and its effects on fraction of vaccinated population. Vaccine 26: 3805–3811. doi:10.1016/j.vaccine.2008.05.031.

16. Yu H, Yang W, Varma JK (2012) To save children's lives, China should adopt an initiative to speed introduction of pneumonia vaccines. Heal Aff 31: 2545–2553. doi:10.1377/hlthaff.2011.1272.

17. CDC (2012) Pneumococcal disease. Epidemiology and Prevention of Vaccine-Preventable Diseases. pp. 233–248.

18. Wagner AL, Sun X, Montgomery JP, Huang Z, Boulton ML (2014) The Impact of Residency and Urbanicity on Haemophilus influenzae Type b and Pneumococcal Immunization in Shanghai Children: A Retrospective Cohort Study. PLoS One 9: e97800. doi:10.1371/journal.pone.0097800.

19. Chen Y, Deng W, Wang S-M, Mo Q-M, Jia H, et al. (2011) Burden of pneumonia and meningitis caused by Streptococcus pneumoniae in China among children under 5 years of age: a systematic literature review. PLoS One 6: e27333. doi:10.1371/journal.pone.0027333.

20. Sun M, Ma R, Zeng Y, Luo F, Zhang J, et al. (2010) Immunization status and risk factors of migrant children in densely populated areas of Beijing, China. Vaccine 28: 1264–1274. doi:10.1016/j.vaccine.2009.11.015.

21. Chan K (2012) China: internal migration. In: Ness I, Bellwood P, editors. The Encyclopedia of Global Human Migration. Wiley-Blackwell. doi:10.1002/9781444351071.wbeghm124.

22. Zhang L (2001) Strangers in the City: Reconfigurations of Space, Power, and Social Netowrks within China's Floating Population. Stanford, CA: Stanford University Press.

23. Rondy M, van Lier A, van de Kassteele J, Rust L, de Melker H (2010) Determinants for HPV vaccine uptake in the Netherlands: A multilevel study. Vaccine 28: 2070–2075. doi:10.1016/j.vaccine.2009.12.042.

24. Whitehead SJ, Cui KX, De AK, Ayers T, Effler P V (2007) Identifying risk factors for underimmunization by using geocoding matched to census tracts: a statewide assessment of children in Hawaii. Pediatrics 120: e535–e542. doi:10.1542/peds.2006-3296.

25. Wagner AL, Ding Y, Montgomery JP, Boulton ML (2012) Measles Vaccination Delays among Children 8 months to 7 years in Tianjin, China. Department of Epidemiology Poster Session [Poster]. Ann Arbor, MI.

26. R Core Team (2014) R: A Language and Environment for Statistical Computing. Available: http://www.r-project.org.

27. Højsgaard S, Halekoh U, Yan J (2006) The R Package geepack for Generalized Estimating Equations. J Stat Softw 15: 1–11.

28. Lemon J (2006) Plotrix: a package in the red light district of R. R-News 6: 8–12.

29. Wickham H (2009) ggplot2: elegant graphics for data analysis. Springer New York.

30. World Health Organization Western Pacific Region (2012) Measles. Available: http://www.wpro.who.int/china/mediacentre/factsheets/measles/en/.

31. Dannetun E, Tegnell A, Hermansson G (2004) Timeliness of MMR vaccination—influence on vaccination coverage. Vaccine 22: 4228–4232. doi:10.1016/j.vaccine.2004.04.018.

32. Smith PJ, Humiston SG, Vannice KS (2010) The Association Between Intentional Delay of Vaccine Administration and Timely Childhood Vaccination Coverage. Public Heal Rep 125: 534–541.

33. Gay NJ (2004) The theory of measles elimination: implications for the design of elimination strategies. J Infect Dis 189 Suppl: S27–S35. doi:10.1086/381592.

34. Montgomery JP, Zhang Y, Carlson B, Ewing S, Wang X, et al. (n.d.) Measles Vaccine Coverage and Series Completion among Children 0 to 8 Years of Age in Tianjin, China. Pediatr Infect Dis J. doi:10.1097/INF.0000000000000562.

35. Zheng J, Cao L, Guo S, A K, Wang L, et al. (2012) Survey of the current situation of category 2 vaccines in Chinese children aged 1 to 2 years. Chin J Vaccine Immun 18: 233–237 [in Chinese].

36. GAVI Alliance (2015) Vaccine goal indicators. GAVI. Available: http://www.gavi.org/results/goal-level-indicators/vaccine-goal-indicators/.

37. Che D, Zhou H, He J, Wu B (2014) Modeling the impact of the 7-valent pneumococcal conjugate vaccine in Chinese infants: an economic analysis of a compulsory vaccination. BMC Health Serv Res 14: 56. doi:10.1186/1472-6963-14-56.

38. Liu H, Li Z (2011) Social Change and Psychological Well-being in Urban and Rural China. Asia Heal Policy Progr 23.

39. Lu Z, Song S (2006) Rural-urban migration and wage determination: The case of Tianjin, China. China Econ Rev 17: 337–345. doi:10.1016/j.chieco.2006.04.007.

40. World Health Organization (2015) Public health surveillance. Heal Top: 2015. Available: http://www.who.int/topics/public_health_surveillance/en/.

41. Groom H, Hopkins DP, Pabst LJ, Morgan JM, Patel M, et al. (2014) Immunization Information Systems to Increase Vaccination Rates: A Community Guide Systematic Review. J Public Health Manag Pract 97227: 1–22. doi:10.1097/PHH.0000000000000069.

42. Strebel P, Cochi S, Grabowsky M, Bilous J, Hersh BS, et al. (2003) The unfinished measles immunization agenda. J Infect Dis 187 Suppl: S1–S7. doi:10.1086/368226.

CHAPTER 4

Parental perceptions of measles, pneumonia, and meningitis vaccines: a cross-sectional survey in Shanghai, China

ABSTRACT

Background. In China, the measles vaccine is offered for free whereas the pneumococcal vaccine is a for-fee vaccine. This difference has the potential to influence how caregivers evaluate whether a vaccine is important or necessary. Yet other factors, such as health beliefs (e.g., regarding vaccine effectiveness or disease prevalence) or experience (e.g., disease experience or nonlocal vs local residency) are also relevant. This study compares parental perceptions of different diseases (measles, pneumonia and meningitis); and characterizes associations between Health Belief Model constructs and both pneumococcal vaccine uptake and perceived vaccine necessity.

Methods. Caregivers of infants and young children between 8 months and 7 years of age from Shanghai (n=619) completed a written survey on their perceptions of measles, pneumonia, and meningitis. We used logistic regression models to assess predictors of pneumococcal vaccine uptake and vaccine necessity.

Results. Only 25.2% of children had received a pneumococcal vaccine, although most caregivers believed that pneumonia (80.8%) and meningitis (92.4%), as well as measles (93.2%), vaccines were serious enough to warrant a vaccine. Perceived safety was strongly associated with both pneumococcal vaccine uptake and perceived vaccine necessity, and

non-locals had 1.70 times higher odds of pneumonia vaccine necessity than non-locals (95% CI: 1.01, 2.88).

Conclusion. Most factors had a similar relationship with vaccine necessity, regardless of disease, indicating a common mechanism for how Chinese parents decided what vaccines are necessary. Because more parents believed meningitis needed a vaccine than pneumonia, health care workers should emphasize pneumococcal vaccination's ability to protect against meningitis.

INTRODUCTION

The provision of free vaccines through the government-funded Expanded Program on Immunization (EPI) has been a successful mechanism to control many infectious diseases [1,2]. The EPI in China started in 1978 with funding for the tuberculosis, polio, measles, pertussis, diphtheria, and tetanus vaccines. Since then, it has expanded to include hepatitides A and B, meningococcal meningitis, Japanese encephalitis, rubella, and mumps vaccines [1].

Immunization clinics in China also offer non-EPI vaccines to children for a fee, including influenza, varicella, *Haemophilus influenzae* type b (Hib), rotavirus, and pneumococcal vaccines, among others. The pneumococcal vaccine in particular is a prime candidate for inclusion on the EPI schedule given the burden of pneumococcal disease [3]. It has been introduced in many low-income countries with support from Gavi [4], and it could prevent some of the 261,000 cases and 11,000 deaths due to pneumococcal pneumonia and meningitis in Chinese children under 5 years of age [5].

Non-EPI vaccines have lower childhood coverage than EPI vaccines in China [6] because they are not required for school entry and are expensive for parents [7]; for example, 7-valent pneumococcal conjugate vaccine costs approximately 135 USD per dose and 23-valent pneumococcal polysaccharide vaccine is approximately 24 USD per dose. Given the current lack of government funding for pneumococcal vaccination, understanding Chinese parents' perceptions about this non-EPI vaccine and the diseases it prevents is key to developing effective interventions to increase vaccine uptake. And, if pneumococcal vaccine is added to the EPI schedule, understanding parental perceptions of it will be important for developing effective programs to increase people's acceptance of the vaccine.

Vaccine decision-making can be explained by health behavior models like the Health Belief Model (HBM) [8], which can conceive of vaccination behaviors as an output of an individual's perceptions of both a disease and its related vaccine [9]. These constructs specifically include people's perceived susceptibility or vulnerability to the disease, their understanding of disease severity, a sense of the potential benefits of vaccination, and anticipated barriers to vaccination [9]. Vaccine decision-making can also be influenced by demographic characteristics, such as residency and urbanicity. Non-locals or migrants from rural areas to urban cities [10], have less access to governmental entitlement programs than locals [10,11], but still receive EPI vaccines for free; and urban districts represent historical business areas, whereas suburban districts are more industrial [12] and have less access to public services [13].

Although previous studies in China have shown the usefulness of an HBM framework for understanding perceived dysentery vaccine need [14], influenza vaccination intent [15], and influenza vaccine uptake among healthcare workers [16], no previous study in China has contrasted perceptions towards EPI and non-EPI vaccines. It may be that people think differently about vaccines, such as the measles and pneumococcal vaccines, which have divergent payment mechanisms, which vary by length of time on the market, and for which people plausibly have different levels of personal experience. In this study, we compare perceptions of pediatric measles and pneumococcal vaccinations among parents in Shanghai, and we characterize the associations between HBM constructs and both pneumococcal vaccine uptake and perceived vaccine necessity.

MATERIALS AND METHODS

Study population

In this cross-sectional study which took place during May and June of 2014, we invited caregivers of young children at immunization clinics in Shanghai to participate in a brief survey, which focused on their perceptions of vaccines for measles, pneumonia, and meningitis. We selected caregivers into the study through two-stage, stratified, cluster sampling, calculating the sample size to detect a 10% difference in an outcome (81% vs 91%), with an intraclass correlation coefficient of 0.024 and a within-cluster sample size of 20. Clusters in this sample refer to townships, which are administrative regions below districts in China and which are each served by an immunization clinic. Townships were selected by a probability proportionate to size (PPS) systematic selection procedure with population of children 0 to 14 years of age from the China 2010 Census as the population size. Figure 4-1 shows the location of the township immunization clinics in Shanghai used for data collection.

Within each township immunization clinic, we selected a convenience sample of 20 to 30 caregivers who accompanied their child for a vaccination visit. The sole eligibility criterion was that the child was between 8 months and 7 years of age, meaning they were old enough to receive the measles and pneumococcal vaccines. We attempted to sample an equal number of locals and non-locals at each clinic. The analysis included sampling weights so that our study population resembled the population structure of locals and non-locals in Shanghai.

All potential participants gave informed consent prior to participation, and completed the survey at the immunization clinic. The survey took approximately 20 minutes to complete, and participants were given an incentive of 30 RMB (5 USD). The study protocol was approved by the Health Sciences & Behavioral Sciences Institutional Review Board at the University of Michigan and an ethical review committee at the Shanghai Centers for Disease Control and Prevention.

Questionnaire

The questionnaire collected information on caregiver perceptions of pediatric vaccines, in general, and measles and pneumococcal vaccines, more specifically. The questions were informed by previous literature on beliefs and perceptions of vaccine-preventable diseases [17–22], as well as a qualitative, pilot research project undertaken by the lead author on 23 parents and grandparents at immunization clinics in Tianjin, China, during the summer of 2013 [23]. For a portion of the questionnaire, the same questions were asked about all three diseases (hereafter indicated as [disease type]): measles, pneumonia, or meningitis.

Outcome variables

The first outcome considered was pneumococcal vaccine uptake, which was administration of either pneumococcal conjugate vaccine or pneumococcal polysaccharide vaccine. Because coverage of measles vaccine, which is part of the EPI, approaches 100% in China, we chose another outcome to allow us to compare how people make decisions about both measles and pneumococcal vaccines. This outcome, "vaccine necessity," was the response to the question "Do you think that [disease type] is a serious enough disease to warrant a vaccine?"

Predictor variables

We included one question to measure each HBM construct, which were measured on a 5-point Likert scale. Perceived prevalence of the disease from the question "How common is [disease type] in your community?". We measured perceived prevalence instead of the typical construct of perceived susceptibility because of feedback from the qualitative interviews. Previous studies have also made this substitution [24,25] and have found strong correlations between these two concepts [26,27].

The vaccine-related questions were asked twice, once for the measles vaccine and once for the pneumococcus vaccine (hereafter indicated as [measles / pneumococcus]). Perceived effectiveness of vaccine from the question, "How effective do you think the [measles / pneumococcus] vaccine is in preventing all cases of [disease type]?"; and perceived safety of the vaccine from the question, "How safe is the [measles / pneumococcus] vaccine?". Perceived effectiveness of vaccine and perceived safety of vaccine represent the HBM constructs of perceived benefits and barriers to a health-related action, respectively.

We also included questions on disease experience and descriptive norm of vaccination, which are not HBM constructs but which were identified as important in the qualitative research project [23]. Experience with the disease was a binary variable, with the "yes" option being a positive response to any of the following questions: "Have you ever personally contracted [disease type]?"; "Has your child ever contracted [disease type]?"; and "Has any close family member of friend of yours ever contracted [disease type]?". Finally, perceived norm of vaccination was derived from the question, "Among your social group, how many children do you think are vaccinated against [measles / pneumococcus]?".

Local or non-local status was based on a previously completed field in the child's vaccination booklet. Urbanicity was based on the location of the clinic: the urban districts include Huangpu, Xuhui, Changning, Jing'an, Putuo, Zhabei, Hongkou, Yangpu; and the suburban districts are Minhang, Baoshan, Jiading, Pudong, Jinshan, Songjiang, Qingpu, Fengxian. We did not include socioeconomic variables in the model over concerns that they would be mediators of the relationship between residency or urbanicity and the outcome, but a sensitivity analysis with education included did not significantly change any parameter estimates.

Statistical analysis

For a descriptive analysis, we used the non-parametric Kruskal-Wallis one-way analysis of variance to test for a significant difference in means for the Likert scale variables (df=2). A Chi-Square test of independence, with the Rao-Scott adjustment to account for the survey design, compared proportions for categorical variables (df=2, except for caregiver relation, which had df=4).

For pneumococcal vaccine uptake, two logistic regression models with survey adjustments were run—one for pneumonia-specific perceptions and the other for meningitis-specific perceptions.

To compare how perceptions about measles, pneumonia, and meningitis were differently associated with the outcome vaccine necessity, we created a long-form dataset wherein each individual had 3 observations, one for their perception of each of the three diseases assessed. To account for each individual yielding three separate observations, we used a generalized estimating equation (GEE) with a binomial distribution and logit link and specified an unstructured correlation matrix at the individual level. An interaction term of each predictor variable and a dummy variable for the disease of that particular observation was also entered into this model. Significance of the interaction across the 3 disease types was assessed by a Wald chi-square test (df=2, except for caregiver relation, which had df=4). Significance was assessed at an α level of 0.05 for all tests, and the precision of odds ratios (OR) was evaluated with 95% confidence intervals (CI). All analyses were weighted based on participants' probability of selection with respect to urbanicity and residency, and we used SAS version 9.3 (SAS Institute Inc., Cary, North Carolina).

RESULTS

Out of 734 caregivers approached, 619 caregivers (84.3%) of children who were between 8 months and 7 years of age participated in the survey (Figure 4-2); nearly two-thirds (64.5%) were mothers of the child, one-quarter (27.6%) were fathers; and 7.8% were other family members, mostly grandmothers. Slightly more than half of the children

(51.3%) were male; and 31.3% resided in Shanghai's urban districts (Table 4-1). Approximately one-quarter (25.2%) of children had received a pneumococcal vaccine, and nearly all (98.8%) had been administered a measles vaccine.

All caregiver perception and experience variables were significantly different across the three diseases (Table 4-2). Over 90% of caregivers judged measles and meningitis serious enough to warrant a vaccine, whereas just over 80% thought pneumonia warranted a vaccine. More caregivers (43.3%) had experience with pneumonia, compared with 18.6% for measles and only 7.1% for meningitis. Caregivers believed that meningitis was more severe (mean 4.35) than measles (4.07) or pneumonia (4.11); and the perceived prevalence of disease was higher for pneumonia (3.15) than measles (2.30) or meningitis (2.28).

Perceived necessity of a pneumonia vaccine was the strongest predictor of pneumococcal vaccine uptake in the model with pneumonia-specific perceptions (OR: 2.67, 95% CI: 1.27, 5.63) (Table 4.3). Perceived safety of vaccination was a significant predictor in the models for both pneumonia-specific (OR: 2.39, 95% CI: 1.57, 3.63) and meningitis-specific perceptions (OR: 2.12, 95% CI: 1.24, 3.63).

Results from the multivariable model of vaccine necessity are shown in Table 4-4. An increase in perceived norm of vaccination was associated with 1.97 times greater odds of measles vaccine necessity (95% CI: 1.50, 2.59) and 1.53 times greater odds of pneumonia vaccine necessity (95% CI: 1.23, 1.91). Perceived safety of vaccination was positively associated with measles (OR: 2.35; 95% CI: 1.26, 4.38), pneumonia (OR: 1.62; 95% CI: 1.04, 2.52), and meningitis vaccine necessity (OR: 2.11, 95% CI: 1.31, 3.40). Perceived prevalence of disease was not associated with necessity for vaccination against measles, pneumonia, or meningitis.

The strength of the associations between most explanatory variables and vaccine necessity did not vary significantly by disease. However, the relationship between perceived effectiveness of vaccination and necessity of vaccination did vary by disease (P=0.0088); for pneumonia this was a positive association (OR: 4.05; 95% CI: 2.61, 6.31), whereas for measles and meningitis there was no association. There was also a significant interaction between urbanicity and disease (P=0.0016); people living in suburban districts were more likely to consider the pneumonia vaccine necessary (OR: 1.74; 95% CI: 1.01, 3.00), whereas the opposite relationship (OR: 0.37; 95% CI: 0.15, 0.92) was found for the measles vaccine. Additionally, although the interaction term for residency was not significant, non-locals had higher odds of pneumonia vaccine necessity than locals (OR: 1.70; 95% CI: 1.01, 2.88), whereas there was not a significant association between residency and either measles or meningitis vaccine necessity.

DISCUSSION

In this cross-sectional survey of parents in Shanghai, only a minority of children had been administered a pneumococcal vaccine, even though most of their caregivers believed that pediatric pneumonia and meningitis vaccines were necessary. Moreover, whereas over 90% of caregivers thought measles and meningitis were serious enough to warrant a vaccine, just over 80% held similar beliefs for pneumonia. Previous studies have also shown that parents generally do not consider pneumonia vaccines as important as other vaccines. In the Netherlands, Hak et al. found that fewer parents had a positive attitude towards pneumonia vaccines than other vaccines, such as those for hepatitis B or tuberculosis [28]. Bedford and Lansley similarly reported that fewer British parents would accept a pneumococcal vaccine than a meningococcal vaccine. They postulated that this difference in acceptance came from parents associating meningococcus with meningitis and pneumococcus with pneumonia, and subsequently believing that meningitis was more clinically severe than pneumonia [29], which is corroborated by our study in comparing perceptions of pneumococcal meningitis and pneumococcal pneumonia.

In this study, perceived vaccine necessity but not perceived prevalence of pneumonia was positively associated with pneumococcal vaccine uptake. Both our study and a study on pediatric dysentery vaccination by Chen et al. did not observe a relationship between perceived prevalence and vaccine need [14], suggesting that, for Chinese parents, perceptions about a disease's threat primarily derive from their thoughts about severity and is not necessarily based on their understanding of how common the disease is within the community. It is possible that Chinese parents may view the threat of diseases in a fundamentally different way compared to parents in other countries because the one-child policy results in a lot of attention and focus from parents on one child [30]. Chinese parents' consideration with their child's safety may explain why pneumonia vaccine necessity, a measure of disease severity, was a strong predictor of pneumococcal vaccine uptake and why perceived vaccine safety was strongly and positively associated with all vaccine outcomes that we considered.

Besides perceived safety of vaccination, necessity of pneumonia vaccination was also associated with pneumococcal vaccine uptake. Vaccine necessity could be an important mediator in the pathway between disease perceptions and vaccine uptake, and we may observe stronger associations between disease perceptions and vaccine necessity than disease perceptions and vaccine uptake because vaccine necessity is more proximal to these perceptions. The lack of significant associations between perceptions of meningitis and pneumococcal vaccination could result from caregivers not being aware that pneumococcal vaccines can protect against some forms of meningitis.

Most of the HBM constructs and other beliefs under consideration had a similar relationship with vaccine necessity, regardless of disease. This indicates that there was a common mechanism underlying how Chinese parents decided what vaccines are necessary, given their perceptions about the disease and the vaccine. However, the strength of the relationship between perceived effectiveness of vaccination and vaccine necessity did differ by disease. For measles, perceived effectiveness of vaccination was not an important determinant of vaccine necessity, perhaps because measles vaccine is mandatory. In contrast, because the pneumococcal vaccine requires payment from caregivers, parents may only perceive their children to need it if the vaccine is effective. We may not see any association for meningitis because the pneumococcal vaccine in China is marketed as a pneumonia vaccine, not a meningitis vaccine, and we conjecture that caregivers have little understanding of how the pneumococcal vaccine can prevent some forms of meningitis.

That measles vaccine is an EPI vaccine but pneumococcal vaccine is not prevented us from considering other factors that could influence vaccine uptake in other countries. First, measles vaccine is free in Shanghai but pneumococcal vaccine requires payment. This likely had a significant impact on decisions; in a 7-country survey of parents, support for a vaccine decreased by 14% if the vaccine required the parent to pay out-of-pocket [31]. Second, China has focused tremendous effort on measles elimination, and hundreds of millions of children have been vaccinated against measles during supplementary immunization activities within the past decade [32]. These efforts could lead to the Chinese public receiving more information about measles than about pneumonia or meningitis.

Non-locals and suburban dwellers have a number of different experiences and attributes which distinguish them from their local or urban counterparts. They may have different experiences with disease, given disparities in treatment or ability to interface with health care providers. Notably, quality and density of health care diminishes outside of urban areas in cities [13], and non-locals access health care services much less than locals [33]. Previous studies have shown that non-locals have lower vaccination coverage than locals, and suburban children have worse vaccination outcomes than those in urban districts, for both EPI and non-EPI vaccines [6,34,35]. Yet we found that non-locals and suburban dwellers had greater odds of considering pneumonia vaccines as necessary compared to locals and urban dwellers. That these subpopulations think that pneumonia vaccines are necessary but do not receive could result from the cost of these expensive vaccines, and financial incentives from the government may be necessary to increase vaccination coverage, particularly in these poorer populations where there is a demand for vaccination.

This study provides a framework for developing a better understanding of the context driving demand for a vaccine. As Nichter notes, there is a difference between passive acceptance of and active demand for vaccinations [36]. With passive acceptance, the populace attains high vaccination coverage only after the public health sector devotes intensive resources towards promoting a certain vaccine. By contrast, in the latter, a well-informed public perceives the need for vaccination and drives demand for immunization services. In our survey, perceived necessity of vaccination by caregivers was higher for measles and meningitis than it was for pneumonia. This implies that even if pneumonia vaccination were added to the EPI schedule, active demand could be lower than for other vaccines. As a result, uptake would be driven by pressure from the public health sector and not from caregivers demanding the vaccine.

Strengths and Limitations

The study has both important strengths and limitations. One strength was the purposeful sampling of people by urbanicity and by residency to account for the important demographic groups in Shanghai. However, within each township, we selected a convenience sample from each immunization clinic. This means that the study population is biased towards a population with more positive views towards immunization services. Additionally, we only used one item to measure each HBM construct, and therefore could not minimize measurement error by formulating latent constructs.

This study evaluated perceptions of meningitis and pneumococcal vaccinations, but a Hib vaccine and meningococcal vaccine are also available in China to protect against these diseases. The etiology of pneumonia and meningitis in China is poorly understood [5,37,38], but it is likely that Hib results in comparable rates of pneumonia morbidity and mortality as pneumococcus [5,39] and that the cause of meningitis morbidity in China is somewhat equally divided between meningococcus and pneumococcus [5,40]. A caregiver's perception of vaccine necessity could therefore be colored by the other vaccines already on the market, and we hypothesize that caregivers would be less apt to consider a vaccine necessary if they also thought that that disease could be caused by a number of different infections.

Conclusions

Given the enormous toll of pneumococcal disease in China [3,5], widespread pneumococcal vaccination could improve child health and save lives. China has spent tremendous resources on measles elimination [32], but measles elimination efforts should could be combined with other immunization initiatives [41], such as educating parents about the benefits of pneumococcal vaccination. In particular, because more people thought that a meningitis vaccine was necessary than a pneumonia vaccine, promotional materials for pneumococcal vaccines could focus disease severity and on meningitis, the more severe clinical presentation of pneumococcal disease.

Future studies could take a longitudinal look at attitudes towards a disease, the desire to obtain a vaccine, and, finally, actual vaccination. Additionally, both the relationship between the patient and the provider and how the provider approaches talking about vaccination are important [42], warranting further research on health care workers in China. As more vaccines are introduced into the EPI schedule in China, providers will be an important conduit of information about the risk of disease and the safety and effectiveness of vaccination.

ACKNOWLEDGMENTS

This research was funded by the University of Michigan Office of Global Public Health and by a Rackham International Research Award. This study was possible thanks to the parents and grandparents who participated and to the health department staff who coordinated site visits and interviews.

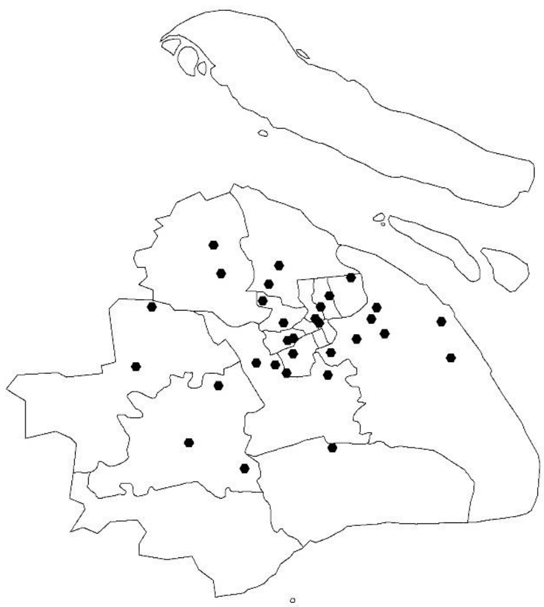


Figure 4-1. Map of 31 township clinics used in the study on perceptions of pediatric vaccinations in Shanghai, summer 2014. Chongming county encompasses islands to the north of the mainland and was not included as part of the sample.

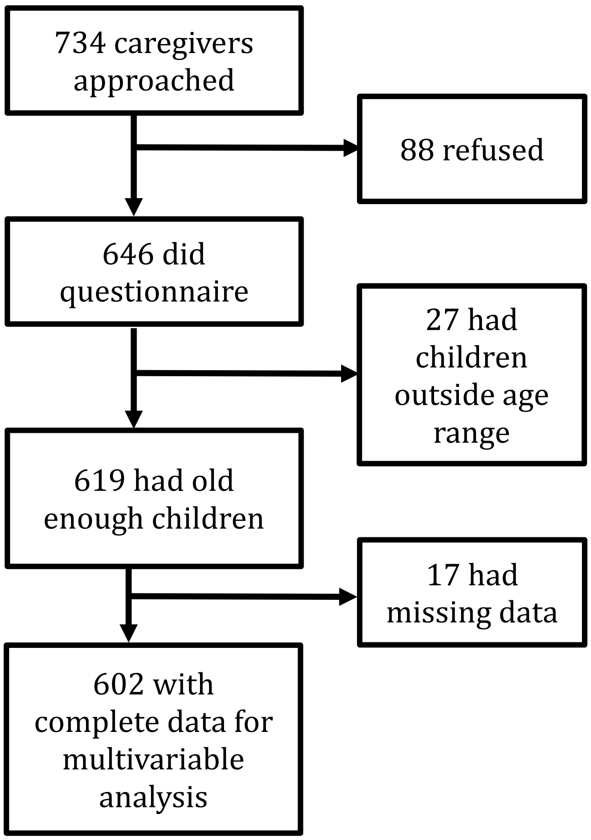


Figure 4-2. Flowchart of caregivers enrolled into study on perceptions of pediatric vaccinations in Shanghai, summer 2014.

Table 4-1. Demographic characteristics of 619 children and their caregivers from Shanghai, 2014.

Characteristic	Category	Count[a]	Proportion[b] (%)	Lower 95% CL[b] (%)	Upper 95% CL[b] (%)
Caregiver relation	Mother	405	64.5	59.8	69.3
	Father	156	27.6	23.1	32.2
	Other	57	7.8	5.5	10.1
Parent's age[c]	<28 years	105	23.1	18.3	27.9
	28 to <31 years	142	28.0	23.3	32.8
	31 to <34 years	129	24.5	19.9	29.1
	≥35 years	144	24.3	19.9	28.8
Caregiver's education	≤Middle school	142	24.2	19.9	28.6
	≤High school	93	17.8	13.8	21.8
	Some college	153	23.3	19.4	27.3
	College graduate	227	34.6	30.1	39.2
Family monthly income	<4,000 RMB	109	19.1	15.1	23.1
	4,000 to <6,000 RMB	142	23.9	19.6	28.2
	6,000 to <10,000 RMB	156	26.8	22.4	31.2
	≥10,000 RMB	208	30.2	25.9	34.5
Child's sex	Male	324	51.3	46.4	56.2
	Female	292	48.7	43.8	53.6
Child's residency	Local	315	43.2	38.5	47.8
	Non-local	303	56.8	52.2	61.5
Township urbanicity	Urban	203	31.3	26.9	35.7
	Suburban	415	68.7	64.3	73.1
Pneumococcal vaccination	Yes	170	25.2	21.0	29.3
	No	448	74.8	70.7	79.0
Measles vaccination	Yes	609	98.8	98.0	99.7
	No	9	1.2	0.3	2.0

Notes:
CL, confidence limit.
[a] Unweighted.
[b] Weighted. Proportion does not include missing values.
[c] Only for mothers and fathers.

Table 4-2. Perceptions of measles, pneumonia, and meningitis disease and vaccination among caregivers in Shanghai, 2014.

	Measles			Pneumonia			Meningitis			
	N	Estimate	SE	N	Estimate	SE	N	Estimate	SE	P-value*
Vaccine necessity (%)	609	93.2	1.15	610	80.8	1.89	613	92.4	1.34	<0.0001
Perceived severity	618	4.07	0.040	618	4.11	0.039	616	4.35	0.035	<0.0001
Perceived prevalence	616	2.30	0.043	618	3.15	0.047	617	2.28	0.037	<0.0001
Disease experience (%)	618	18.6	1.96	618	43.3	2.44	618	7.1	1.40	<0.0001
Perceived norm	614	4.03	0.045	612	3.35	0.051	612	3.35	0.051	<0.0001
Perceived effectiveness	615	3.81	0.033	615	3.58	0.032	616	3.56	0.035	<0.0001
Perceived safety	617	3.92	0.036	617	3.81	0.034	617	3.81	0.034	0.0404

Notes:
SE, standard error.
* For Likert scale variables, the P-value is the Kruskal-Wallis test. For dichotomous variables, the P-value is from the Rao-Scott Chi-Square Test.

Table 4-3. The relationship between both pneumonia-specific and meningitis-specific perceptions and pneumococcal vaccine uptake according to multivariate logistic regression models from a study of 602 caregivers in Shanghai, 2014.

	Pneumonia OR (95% CI)	Meningitis OR (95% CI)
Perceived vaccine necessity	2.67 (1.27, 5.63)	1.45 (0.52, 3.99)
Perceived prevalence	1.10 (0.84, 1.44)	0.97 (0.73, 1.31)
Disease experience		
Yes vs No	1.16 (0.70, 1.94)	1.32 (0.55, 3.17)
Perceived norm	1.16 (0.92, 1.46)	1.21 (0.96, 1.53)
Perceived effectiveness	0.91 (0.61, 1.35)	0.95 (0.61, 1.47)
Perceived safety	2.39 (1.57, 3.63)	2.12 (1.24, 3.63)
Residency		
Non-local vs local	1.01 (0.63, 1.60)	0.97 (0.62, 1.52)
Urbanicity		
Outer vs inner district	1.10 (0.69, 1.78)	1.31 (0.82, 2.08)
Caregiver relation		
Father vs mother	0.71 (0.41, 1.24)	0.67 (0.39, 1.17)
Other vs mother	1.54 (0.71, 3.32)	1.20 (0.56, 2.53)

Notes:
OR: odds ratio; CI: confidence interval

Table 4-4. Results from a single, multivariable logistic regression model of necessity of vaccination for three diseases from a study of 602 caregivers in Shanghai, 2014.

	Measles OR (95% CI)	Pneumonia OR (95% CI)	Meningitis OR (95% CI)	P-value[a]
Perceived prevalence	1.25 (0.85, 1.83)	1.18 (0.91, 1.53)	1.08 (0.65, 1.80)	0.9022
Disease experience				0.2576
Yes vs No	1.48 (0.58, 3.78)	0.76 (0.46, 1.26)	0.34 (0.10, 1.10)	
Perceived norm	1.97 (1.50, 2.59)	1.53 (1.23, 1.91)	1.13 (0.80, 1.61)	0.0753
Perceived effectiveness	1.31 (0.69, 2.49)	4.05 (2.61, 6.31)	1.17 (0.57, 2.42)	0.0088
Perceived safety	2.35 (1.26, 4.38)	1.62 (1.04, 2.52)	2.11 (1.31, 3.40)	0.5349
Residency				0.4511
Non-local vs local	1.77 (0.84, 3.73)	1.70 (1.01, 2.88)	1.06 (0.48, 2.36)	
Urbanicity				0.0016
Suburban vs urban	0.37 (0.15, 0.92)	1.74 (1.01, 3.00)	0.79 (0.32, 1.95)	
Caregiver relation				0.1886
Father vs mother	0.38 (0.17, 0.84)	1.21 (0.64, 2.27)	1.07 (0.44, 2.56)	
Other vs mother	0.20 (0.06, 0.65)	0.50 (0.21, 1.17)	0.45 (0.14, 1.48)	

Notes:
OR: odds ratio; CI: confidence interval
[a] Wald chi-square test for overall interaction (df=2, except for caregiver relation, which had df=4)

REFERENCES

1. Zheng J, Zhou Y, Wang H, Liang X (2010) The role of the China Experts Advisory Committee on Immunization Program. Vaccine 28S: A84–A87. doi:10.1016/j.vaccine.2010.02.039.

2. Wang L, Wang Y, Jin S, Wu Z, Chin D (2008) Emergence and control of infectious diseases in China. Lancet 372: 34–41. doi:10.1016/S0140-6736(08)61365-3.

3. Yu H, Yang W, Varma JK (2012) To save children's lives, China should adopt an initiative to speed introduction of pneumonia vaccines. Heal Aff 31: 2545–2553. doi:10.1377/hlthaff.2011.1272.

4. GAVI Alliance (2015) Vaccine goal indicators. GAVI. Available: http://www.gavi.org/results/goal-level-indicators/vaccine-goal-indicators/.

5. Chen Y, Deng W, Wang S-M, Mo Q-M, Jia H, et al. (2011) Burden of pneumonia and meningitis caused by Streptococcus pneumoniae in China among children under 5 years of age: a systematic literature review. PLoS One 6: e27333. doi:10.1371/journal.pone.0027333.

6. Wagner AL, Sun X, Montgomery JP, Huang Z, Boulton ML (2014) The Impact of Residency and Urbanicity on Haemophilus influenzae Type b and Pneumococcal Immunization in Shanghai Children: A Retrospective Cohort Study. PLoS One 9: e97800. doi:10.1371/journal.pone.0097800.

7. Xie J, Dow WH (2005) Longitudinal study of child immunization determinants in China. Soc Sci Med 61: 601–611. doi:10.1016/j.socscimed.2004.12.016.

8. Janz NK, Becker MH (1984) The Health Belief Model: a decade later. Health Educ Q 11: 1–47.

9. Rosenstock IM, Strecher VJ, Becker MH (1988) Social learning theory and the Health Belief Model. Heal Educ Q 15: 175–183.

10. Chan K (2012) China: internal migration. In: Ness I, Bellwood P, editors. The Encyclopedia of Global Human Migration. Wiley-Blackwell. doi:10.1002/9781444351071.wbeghm124.

11. Gong P, Liang S, Carlton EJ, Jiang Q, Wu J, et al. (2012) Urbanisation and health in China. Lancet 379: 843–852. doi:10.1016/S0140-6736(11)61878-3.Urbanisation.

12. Yang S, Wang C, Wang M (2014) Synergistic evolution of Shanghai urban economic development transition and social spatial structure. In: Wang MY, Kee P, Gao J, editors. Transforming Chinese Cities. New York, NY: Routledge. pp. 48–74.

13. Li H, Wang Q, Shi W, Deng Z, Wang H (2015) Residential clustering and spatial access to public services in Shanghai. Habitat Int 46: 119–129. doi:10.1016/j.habitatint.2014.11.003.

14. Chen X, Stanton B, Wang X, Nyamette A, Pach A, et al. (2006) Differences in perception of dysentery and enteric fever and willingness to receive vaccines among rural residents in China. Vaccine 24: 561–571. doi:10.1016/j.vaccine.2005.08.060.

15. Mok E, Yeung SH, Chan MF (2006) Prevalence of influenza vaccination and correlates of intention to be vaccinated among Hong Kong Chinese. Public Heal Nurs 23: 506–515.

16. Seale H, Kaur R, Wang Q, Yang P, Zhang Y, et al. (2011) Acceptance of a vaccine against pandemic influenza A (H1N1) virus amongst healthcare workers in Beijing, China. Vaccine 29: 1605–1610. doi:10.1016/j.vaccine.2010.12.077.

17. Bond L, Nolan T (2011) Making sense of perceptions of risk of diseases and vaccinations: a qualitative study combining models of health beliefs, decision-making and risk perception. BMC Public Health 11: 943. doi:10.1186/1471-2458-11-943.

18. Smith PJ, Humiston SG, Marcuse EK, Zhao Z, Dorell CG, et al. (2011) Parental delay or refusal of vaccine doses, childhood vaccination coverage at 24 months of age, and the Health Belief Model. Public Heal Rep 126: 135–146.

19. Timmermans DRM, Henneman L, Hirasing RA, van der Wal G (2008) Parents' perceived vulnerability and perceived control in preventing Meningococcal C infection: a large-scale interview study about vaccination. BMC Public Health 8: 45. doi:10.1186/1471-2458-8-45.

20. Ruijs WLM, Hautvast JLA, van Ansem WJC, van Ijzendoorn G, van der Velden K, et al. (2012) How orthodox protestant parents decide on the vaccination of their children: a qualitative study. BMC Public Health 12: 408. doi:10.1186/1471-2458-12-408.

21. Harmsen IA, Mollema L, Ruiter RA, Paulussen TG, de Melker HE, et al. (2013) Why parents refuse childhood vaccination: a qualitative study using online focus groups. BMC Public Health 13: 1183. doi:10.1186/1471-2458-13-1183.

22. Harmsen IA, Doorman GG, Mollema L, Ruiter RA, Kok G, et al. (2013) Parental information-seeking behaviour in childhood vaccinations. BMC Public Health 13: 1219. doi:10.1186/1471-2458-13-1219.

23. Wagner AL (2015) Attitudes towards pediatric vaccines among caregivers in Tianjin, China: a qualitative study. doi:10.13140/RG.2.1.2862.2881.

24. Butraporn P, Pach A (2004) The health belief model and factors relating to potential use of a vaccine for shigellosis in Kaeng Koi district, Saraburi province, Thailand. J Heal Popul Nutr 22: 170–181.

25. Brown A, Moodie C (2009) The influence of tobacco marketing on adolescent smoking intentions via normative beliefs. Health Educ Res 24: 721–733. doi:10.1093/her/cyp007.

26. Park JS, Grow JM (2008) The Social Reality of Depression : DTC Advertising of Antidepressants and Perceptions of the Prevalence and Lifetime Risk of Depression. J Bus Ethics 79: 379–393. doi:10.1007/sl0551-007-9403-7.

27. Windschitl PD, Martin R, Flugstad AR (2002) Context and the interpretation of likelihood information: The role of intergroup comparisons on perceived vulnerability. J Pers Soc Psychol 82: 742–755. doi:10.1037//0022-3514.82.5.742.

28. Hak E, Schönbeck Y, De Melker H, Van Essen GA, Sanders EAM (2005) Negative attitude of highly educated parents and health care workers towards future vaccinations in the Dutch childhood vaccination program. Vaccine 23: 3103–3107. doi:10.1016/j.vaccine.2005.01.074.

29. Bedford H, Lansley M (2007) More vaccines for children? Parents' views. Vaccine 25: 7818–7823. doi:10.1016/j.vaccine.2007.08.057.

30. Gong Y, Stanton BF, Von Seidlen L, Feng X, Nyamette A (2004) Perceptions of Shigella and of Shigella vaccine among rural Chinese: compatibility with Western models of behavioral change. Southeast Asian J Trop Med Public Health 35: 97–108.

31. Bakhache P, Rodrigo C, Davie S, Ahuja A, Sudovar B, et al. (2013) Health care providers' and parents' attitudes toward administration of new infant vaccines--a multinational survey. Eur J Pediatr 172: 485–492. doi:10.1007/s00431-012-1904-4.

32. World Health Organization (2011) News in Brief. Measles-Rubella Bull 5: 1–9.

33. Gong P, Liang S, Carlton EJ, Jiang Q, Wu J, et al. (2012) Urbanisation and health in China. Lancet 379: 843–852. doi:10.1016/S0140-6736(11)61878-3.

34. Sun M, Ma R, Zeng Y, Luo F, Zhang J, et al. (2010) Immunization status and risk factors of migrant children in densely populated areas of Beijing, China. Vaccine 28: 1264–1274. doi:10.1016/j.vaccine.2009.11.015.

35. Li Q, Hu Y, Zhong Y, Chen Y, Tang X, et al. (2014) Using the Immunization Information System to determine vaccination coverage rates among children aged 1-7 years: a report from Zhejiang Province, China. Int J Environ Res Public Health 11: 2713–2728. doi:10.3390/ijerph110302713.

36. Nichter M (1995) Vaccinations in the third world: a consideration of community demand. Soc Sci Med 41: 617–632.

37. Che D, Zhou H, He J, Wu B (2014) Modeling the impact of the 7-valent pneumococcal conjugate vaccine in Chinese infants: an economic analysis of a compulsory vaccination. BMC Health Serv Res 14: 56. doi:10.1186/1472-6963-14-56.

38. Yang Y-H, Fu S-G, Peng H, Shen A-D, Yue S-J, et al. (1993) Abuse of antibiotics in China and its potential interference in determining the etiology of pediatric bacterial diseases. Pediatr Infect Dis J 12: 986–987. doi:10.1097/00006454-199312000-00004.

39. Watt JP, Wolfson LJ, O'Brien KL, Henkle E, Deloria-Knoll M, et al. (2009) Burden of disease caused by Haemophilus influenzae type b in children younger than 5 years: global estimates. Lancet 374: 903–911. doi:10.1016/S0140-6736(09)61203-4.

40. Zhang X, Shao Z, Zhu Y, Xu L, Xu X, et al. (2008) Genetic characteristics of serogroup A meningococci circulating in China, 1956-2005. Clin Microbiol Infect 14: 555–561.

41. Griffiths UK, Mounier-Jack S, Oliveira-Cruz V, Balabanova D, Hanvoravongchai P, et al. (2011) How can measles eradication strengthen health care systems? J Infect Dis 204: S78–S81. doi:10.1093/infdis/jir090.

42. Benin A, Wisler-Scher D, Colson E (2006) Qualitative analysis of mothers' decision-making about vaccines for infants: the importance of trust. Pediatrics 117: 1532–1541. doi:10.1542/peds.2005-1728.

CHAPTER 5

Conclusions

In this concluding chapter, I will review the important findings of my dissertation's three studies within the context of existing literature. Then, I will focus on a discussion of the role of non-locals in vaccine-preventable disease transmission. After a discussion of the limitations and strengths of the analyses, this chapter concludes with a discussion of future research directions.

Overall, this dissertation focuses on two vaccine-preventable infections in order to better generalize the experience of vaccinations in China beyond one particular example. Measles vaccine is a free and has been on the EPI in China since 1978 [1]. There has been tremendous attention placed on measles in China and worldwide for its elimination effort [2]. Conversely, the pneumococcal vaccine has only been more recently introduced to the Chinese market and it is prohibitively expensive for many Chinese. Although it has been listed on the EPI schedule of many countries, including those less developed than China [3], China has resisted calls to publically fund this vaccine [4]. Overall, we answer the questions "What are the differences between locals and non-locals in disease incidence and vaccination outcomes in China?" and "What are the similarities and differences between measles and pneumococcal vaccination programs in China?"

Study 1 Review

In this study, we used data from the Tianjin notifiable disease registry to characterize temporal trends in measles incidence by residency (non-local versus local) and to evaluate the impact of SIAs on measles incidence. Before 2008, the rate of measles in non-locals was much higher than in locals in Tianjin, but after two SIAs within two years, there were fewer cases of measles and the disparity between locals and non-locals was eliminated. Previous studies have found SIAs to be important for reducing incidence in the Americas[5], in Eastern Europe[6], and in China [7]. Many previous studies have measured the impact of an SIA by comparing rates in the years before the SIA compared to the year after [7], but we caution against this practice. After an SIA, a new cohort of children is born, and this population of susceptible individuals can potentiate future outbreaks. In our study we observed an increase in measles cases among young infants and young adults in 2010, two years after the first municipality-wide SIA. A similar pattern was found three years after an SIA in Xinjiang, China [7]. Evaluation of measles incidence for several years after an SIA is therefore important to not ascribe too much success to an SIA, which instead of comprehensively reducing measles incidence may have shifted the burden of disease to later birth cohorts or established a biennial cycle of measles transmission.

An additional reason that could explain increases in measles incidence after an SIA is the accumulation of susceptibles through migration [8,9]. Migrants may be unvaccinated, particularly if their place of origin did not have an SIA. China's switch from implementing disparately-timed SIAs before 2009 to a synchronized national event in 2010 may be one explanation for why we still saw a disparity in measles incidence by residency in the two years after the first SIA, but not after the second SIA.

Study 2 Review

This study explored vaccination outcomes in terms of timely M1 and MMR1 administration as well as uptake of PCV and PPSV by certain milestone ages. Specifically, we estimate the proportion of children in Shanghai with these vaccination outcomes, compare vaccination outcomes in non-locals and locals, and assess the impact of township-level characteristics on vaccination outcomes.

Timeliness of measles vaccinations was 90%, below herd immunity thresholds. This is similar to what we previously described in Tianjin [10], and what has been found by others in Zhejiang, China [11], in the US [12], and in Sweden [13]. In each case, timeliness of measles vaccine administration was below levels sufficient to interrupt transmission of disease [14]. The lack of timeliness in measles vaccinations, in spite of several studies suggesting that there is high coverage of measles and other EPI vaccines [10,11,15], could be one explanation for the difficulty in eliminating vaccine-preventable diseases in China [16]; for example, China missed the 2012 measles elimination target [16].

China has resisted funding pneumococcal vaccination despite calls to do so [4], and in spite of a general recommendation from the WHO for all countries to publically fund the vaccine [17]. We accordingly found pneumococcal vaccination to be extremely low. Another study in China also found low uptake of pneumococcal vaccination [18], which sharply contrasts with the 73 countries eligible for financial support from the GAVI Alliance. In these countries, 19% of children had the third dose of PCV, a more stringent standard than what we investigated [3]. It is concerning that China, which is too wealthy to be eligible for GAVI funding, has lower coverage than these countries. This indicates that the drive for higher coverage of vaccines in China is tied to public funding, not individual initiative to get vaccinated.

Townships, administrative divisions which in Shanghai have on average over 100,000 residents, also play a role in vaccination. Not only do these places represent the social milieu of parents who get their child a vaccine, but parents within a township share an immunization clinic. We found distinct trends in vaccination when considering our township-level factors of urbanicity, township residency composition, and CDR. Our explanation for these patterns follows. Urbanicity in China is correlated with many other factors, with more urban areas being more economically developed and their residents having better psychological and physical health compared to counterparts in less urban areas [19]. That PCV1 coverage is lower in outer districts compared to inner districts indicates more sensitivity to higher prices in the economically less-developed outer districts. Residency composition may point to social norms. In our third aim, we found that non-locals have higher perceived need of pneumonia vaccination, and so locals living near more non-locals may accordingly have higher uptake as a result of this norm. Our last township-level factor, CDR, measures the relative number of children in a township. A higher CDR was associated with worse timeliness of measles, perhaps because more children make it difficult for township immunization clinics to organize services so that children are vaccinated within a constrained time period. Future research could directly compare these township-level factors to directly-measured vaccination norms.

Study 3 Review

Our third study compared perceptions of pediatric measles and pneumococcal vaccinations among parents in Shanghai, and characterized the associations between HBM constructs, demographic characteristics, and perceived vaccine necessity, by disease. We found that people were more likely to think measles and meningitis vaccines were necessary than pneumonia vaccines. Previous studies in the Netherlands [20] and in the United Kingdom [21] have echoed this sentiment that parents do not consider pneumonia vaccines as important as other vaccines. Moreover, we found that perceptions of disease severity, but not disease prevalence, influenced perceptions of vaccine need. A study on pediatric dysentery vaccination in China also found this pattern [22]. Because disease severity was more important than disease prevalence when parents thought about which vaccines were necessary for vaccination, and because our study participants thought that meningitis was more severe than pneumonia, we encourage immunization clinics to emphasize meningitis prevention when promoting pneumococcal vaccination.

Vaccination and disease among non-locals

Many previous studies have indicated that non-locals, also known as migrants or the floating population, contribute to high measles incidence in China [7,23,24]. Non-locals have a number of different experiences and attributes which distinguish them from their local counterparts. They may have different experiences with disease, given disparities in treatment and ability to interface with health care providers. Notably, quality and density of health care diminishes outside of urban areas in cities where non-locals tend to cluster [25], and non-locals access health care services much less than locals [26]. Lower vaccination coverage among non-locals could be contributing to complications in eliminating measles, but most provinces in China have had 2 SIAs in the past decade in addition to offering free vaccines to all residents in routine services. Therefore, there are not obvious relationships among residency status, measles vaccination, and measles infection. A substantial focus across the three aims of this dissertation was to quantify discrepancies between locals and non-locals and to see if there are measurable differences in infection, vaccination, or vaccine attitudes by residency.

We did see differences by residency for all three outcomes considered, but we also observed trends over time. For instance, we saw higher rates of measles in non-locals than locals before the 2008 SIA in Tianjin, but this disparity attenuated in the two years that followed and was completely eliminated in the years after that. This finding contrasts with a study from Fujian, China [27], where the contribution of non-locals to measles incidence actually increased in the years after an SIA compared to before. However, the Fujian study observed cases from a larger catchment area than our study of Tianjin. Additionally, rapid, and potentially differential, urbanization in Fujian and in our study makes comparisons across time difficult without adequate census information.

We observed that non-locals had worse measles vaccination timeliness and PCV uptake than locals. Considering that non-locals tend to live in neighborhoods with other non-locals [28], low timeliness of measles vaccinations, particularly among young, non-local infants means there may be a large pool of susceptibles in certain neighborhoods, and the preponderance of this population is not reflected in overall estimates of measles vaccine coverage. Low coverage of PCV in these young, non-local infants is also troubling because the clinical presentations of pneumococcal pneumonia and pneumococcal meningitis is especially severe at these ages [29]. However, we did find that PPSV uptake was greater in non-locals than locals. This enthusiasm for vaccination was corroborated in our cross-sectional survey of Shanghai parents, where we found that perceived necessity of pneumococcal vaccination was higher in non-locals than locals. Because PPSV is a less expensive pneumococcal vaccine than PCV, lower uptake of PCV in non-locals relative to locals is probably due to worse financial circumstances in non-locals and not less willingness to actually get vaccinated.

A number of strategies could increase the overall health of the population while working to remove differences between locals and non-locals. For measles vaccine, which is free and mandatory, catch-up and follow-up SIAs offer an opportunity for everyone within a restricted age set to get a vaccine, regardless of their vaccination status. Because people are constantly moving across China, SIAs simultaneously occurring in multiple provinces can vaccinate people who later move across borders. Other SIA approaches are also available. Mop-up SIAs, which target high-risk groups, could be implemented to specifically target new migrants to an area, and would accordingly cost less. Ensuring that new migrants are enrolled at immunization clinics and other locations, like schools or community population registers, could facilitate enumerating this population. Being able to contact non-locals for SIAs is crucial, as past research has found that migrant participation in SIAs is lower than overall numbers [30]. Another SIA option would be a speed-up SIA, in which young adults are vaccinated. This approach was previously used in Europe [6] and in the Americas [5]. Because we also see a high burden of disease in Chinese young adults, a speed-up SIA could reduce incidence of disease in this population as well as cocoon their young children from infection.

In contrast to measles vaccination, pneumococcal vaccination requires payment, which may particularly be a barrier for non-locals. It has been previously found that migrants are less willing to pay for PCV than locals in China [31], though we found that non-locals perceived that pneumonia vaccines were more necessary than locals. It follows that uptake of pneumococcal vaccines, particular PCV, is lower in non-locals and locals not because of decreased demand, but because they do not have the financial stability to do so. That non-locals do have higher coverage of PPSV, an arguably inferior vaccination which is unable to be administered to the youngest and most vulnerable children [32], is another sign that non-locals are willing to receive a vaccination, though not necessarily willing to pay a high cost for it. Overall, because of the substantial burden of pneumococcal vaccination for non-locals, to ensure equitable coverage of vaccine for both locals and non-locals would require government funding.

Strengths and Limitations

Like all research, this study has both strengths and limitations. In terms of limitations, , this dissertation was limited by residency classification. This classification came from official documents, like a vaccination booklet or registry database, but as more Chinese people migrate into cities, discerning finer distinctions between different migrant groups could better identify high-risk groups. Moreover, the composition of migrants likely has changed over time, and it is therefore difficult to compare secular trends using this crude demographic distinction. It is my hope that this dissertation can encourage future researchers to be cognizant of the limitations in defining people as being a “non-local,” “migrant,” or member of the “floating population.”

The first two aims of this dissertation used registry data, which means that the analysis was limited to the available information from the registry and not necessary all relevant risk factors. The use of the registry also means that we did not have direct measures of the overall population size: only measles cases, and not healthy controls, are listed in NIDMIS, and SIPIS may be subject to attrition as people move out of the city. We were able, however, to link these datasets to population information from the China Census and China Statistical Yearbook. The use of population information from an outside source, rather than limiting ourselves to data collected within a single study, permitted us to better approximate population parameters and reduce selection bias that would result from people selecting to participate in the study.

Expanding the registries to encompass other information could be beneficial, although it is more important for there to be a limited amount of high-quality information than larger variety of information which may have an unacceptably high proportion of missing data. Nevertheless, establishing linkages between NIDMIS and other databases, like immunization registries, population statistical databases, and hospital records, could increase the usefulness of NIDMIS to identify susceptible populations and to research correlates of disease. Importantly, giving hospitals access to some information within a limited geographic area could increase hospitals' knowledge about their catchment area and increase their likelihood of providing timely, comprehensive reports of disease [33].

The first two aims used datasets with longitudinal information: registries collect data over time. My last aim was cross-sectional. There are limitations to both approaches. First, registries collect information on a large amount of people, resulting in statistically significant results for many associations that I studied. However, statistical significance of a relationship does not mean that that association is causal, or even important. In the future, looking at findings from a variety of studies will better allow us to identify what are the important factors affecting vaccination and disease incidence in the Chinese population. Second, for the longitudinal analyses, various trends could influence the associations we see beyond what we are able to directly measure. For example, decreases in measles incidence over time could be related to the SIAs, gradual improvements in routine immunization services, or changes in how measles cases were reported into the registry. Similarly, SIPIS has improved its completeness in collecting data over time. Third, for the cross-sectional study of parental perceptions, perception and vaccination outcome were measured at the same time, and we are not able to temporally separate the two. This potentially means that there is reverse causation bias in this study.

In the second and third aim, we compared measles and pneumococcal vaccinations in order to better understand immunization services in China. That measles vaccine is an EPI vaccine but pneumococcal vaccine is not has also made us unable to consider other factors that likely influence vaccine uptake in other countries. First, measles vaccine is free in Shanghai but pneumococcal vaccine requires payment. In a 7-country survey of parents, support for a vaccine decreased by 14% if the vaccine required the parent to pay out-of-pocket [34]. Second, China has focused tremendous effort on measles elimination, and hundreds of millions of children have been vaccinated against measles during supplementary immunization activities within the past decade [35]. These efforts likely lead to the Chinese public receiving more information about measles than about pneumonia or meningitis, which can both be prevented through the pneumococcal vaccine.

Future work

Future work could build upon research from my dissertation. In the first part of my dissertation, I used a time-series analysis to quantify the incidence rate of measles over time, but a spatial statistics approach could also inform us of the geographical distribution of this highly infectious disease.

One consideration in my dissertation was how to classify children by residency. The approach I have used was to identify locals and non-locals based on the designation from their residency papers, which is present in official documentation like vaccination booklets and other immunization clinic records. However, additional factors—like socioeconomic status, which province non-locals came from, how long they have resided in the current city, and how often they return to their home province—could likely influence health seeking behavior. Future research could conceive of a classification scheme for residency which predicts vaccination attitudes and vaccination outcomes better than the binary distinction between locals and non-locals. For example, certain non-locals, like those who have lived in urban areas for much of their lives, may be more similar to locals than other non-locals. Identifying a more precise high-risk group for low vaccination coverage could lead to more targeted interventions.

Using this residency classification, I could develop a refined model to evaluate whether disparities in attitudes between different residency groups contribute to variation in pneumococcal vaccination uptake. For my dissertation, I used standard regression models, but with a mediation analysis using a structural equation model, residency could be the main predictor, HBM constructs could be the mediating attitudes and perceptions, and pneumococcal vaccination could be the outcome.

Another future analysis could better characterize associations between community-level factors and attitudes towards vaccination. Because health behaviors could be influenced by a number of social norms, understanding what community-level factors contribute to vaccination attitudes could pinpoint areas for targeted behavioral interventions and identify regions in the city which may potentiate future outbreaks of vaccine-preventable diseases.

REFERENCES

1. Zheng J, Zhou Y, Wang H, Liang X (2010) The role of the China Experts Advisory Committee on Immunization Program. Vaccine 28S: A84–A87. doi:10.1016/j.vaccine.2010.02.039.

2. McFarland J (2012) World Immunization Week, China.

3. GAVI Alliance (2015) Vaccine goal indicators. GAVI. Available: http://www.gavi.org/results/goal-level-indicators/vaccine-goal-indicators/.

4. Yu H, Yang W, Varma JK (2012) To save children's lives, China should adopt an initiative to speed introduction of pneumonia vaccines. Heal Aff 31: 2545–2553. doi:10.1377/hlthaff.2011.1272.

5. Castillo-Solorzano C C, Matus CR, Flannery B, Marsigli C, Tambini G, et al. (2011) The Americas: paving the road toward global measles eradication. J Infect Dis 204 Suppl: S270–S278. doi:10.1093/infdis/jir166.

6. Khetsuriani N, Deshevoi S, Goel A, Spika J, Martin R, et al. (2011) Supplementary immunization activities to achieve measles elimination: Experience of the European region. J Infect Dis 204. doi:10.1093/infdis/jir074.

7. Ma C, An Z, Hao L, Cairns KL, Zhang Y, et al. (2011) Progress toward measles elimination in the People's Republic of China, 2000-2009. J Infect Dis 204: S447–S454. doi:10.1093/infdis/jir103.

8. Marguta R, Parisi A, Parisi A (2015) Impact of human mobility on the periodicities and mechanisms underlying measles dynamics. J R Soc Interface 12: 20141317.

9. Uziel A, Stone L (2012) Determinants of periodicity in seasonally driven epidemics. J Theor Biol 305: 88–95. doi:10.1016/j.jtbi.2012.02.031.

10. Wagner AL, Zhang Y, Montgomery JP, Ding Y, Carlson BF, et al. (2014) Timely measles vaccination in Tianjin, China: a cross-sectional study of immunization records and mothers. BMC Public Health 14: 888. doi:10.1186/1471-2458-14-888.

11. Li Q, Hu Y, Zhong Y, Chen Y, Tang X, et al. (2014) Using the Immunization Information System to determine vaccination coverage rates among children aged 1-7 years: a report from Zhejiang Province, China. Int J Environ Res Public Health 11: 2713–2728. doi:10.3390/ijerph110302713.

12. Smith PJ, Humiston SG, Vannice KS (2010) The Association Between Intentional Delay of Vaccine Administration and Timely Childhood Vaccination Coverage. Public Heal Rep 125: 534–541.

13. Dannetun E, Tegnell A, Hermansson G (2004) Timeliness of MMR vaccination—influence on vaccination coverage. Vaccine 22: 4228–4232. doi:10.1016/j.vaccine.2004.04.018.

14. Gay NJ (2004) The theory of measles elimination: implications for the design of elimination strategies. J Infect Dis 189 Suppl: S27–S35. doi:10.1086/381592.

15. Montgomery JP, Zhang Y, Carlson B, Ewing S, Wang X, et al. (n.d.) Measles Vaccine Coverage and Series Completion among Children 0 to 8 Years of Age in Tianjin, China. Pediatr Infect Dis J. doi:10.1097/INF.0000000000000562.

16. Ma C, Hao L, Zhang Y, Su Q, Rodewald L, et al. (2014) Monitoring progress towards the elimination of measles in China: an analysis of measles surveillance data. Bull World Health Organ 92: 340–347. doi:10.2471/BLT.13.130195.

17. WHO (2012) Pneumococcal vaccines: WHO position paper - 2012. Wkly Epidemiol Rec 87: 129–144.

18. Zheng J, Cao L, Guo S, A K, Wang L, et al. (2012) Survey of the current situation of category 2 vaccines in Chinese children aged 1 to 2 years. Chin J Vaccine Immun 18: 233–237 [in Chinese].

19. Liu H, Li Z (2011) Social Change and Psychological Well-being in Urban and Rural China. Asia Heal Policy Progr 23.

20. Hak E, Schönbeck Y, De Melker H, Van Essen GA, Sanders EAM (2005) Negative attitude of highly educated parents and health care workers towards future vaccinations in the Dutch childhood vaccination program. Vaccine 23: 3103–3107. doi:10.1016/j.vaccine.2005.01.074.

21. Bedford H, Lansley M (2007) More vaccines for children? Parents' views. Vaccine 25: 7818–7823. doi:10.1016/j.vaccine.2007.08.057.

22. Chen X, Stanton B, Wang X, Nyamette A, Pach A, et al. (2006) Differences in perception of dysentery and enteric fever and willingness to receive vaccines among rural residents in China. Vaccine 24: 561–571. doi:10.1016/j.vaccine.2005.08.060.

23. Wang L, Zeng G, Lee LA, Yang Z, Yu J, et al. (2003) Progress in Accelerated Measles Control in the People's Republic of China, 1991 – 2000. J Infect Dis 187: 252–257.

24. Zhuo J, Geng W, Hoekstra EJ, Zhong G, Liang X, et al. (2011) Impact of supplementary immunization activities in measles-endemic areas: A case study from Guangxi, China. J Infect Dis 204: 455–462. doi:10.1093/infdis/jir063.

25. Li H, Wang Q, Shi W, Deng Z, Wang H (2015) Residential clustering and spatial access to public services in Shanghai. Habitat Int 46: 119–129. doi:10.1016/j.habitatint.2014.11.003.

26. Gong P, Liang S, Carlton EJ, Jiang Q, Wu J, et al. (2012) Urbanisation and health in China. Lancet 379: 843–852. doi:10.1016/S0140-6736(11)61878-3.

27. Pan WY, Cai ZK, Chen JL, Zhou Y, Huang LF, et al. (2014) Epidemiological characteristics of measles in non-target population before and after measles vaccine Supplementary Immunization Activities in Fujian Province China. Chin J Biol 27: 932–939. doi:10.13200/j.cnki.cjb.000455.

28. Zhang L (2001) Strangers in the City: Reconfigurations of Space, Power, and Social Netowrks within China's Floating Population. Stanford, CA: Stanford University Press.

29. Greenwood B (1999) The Epidemiology of Pneumococcal Infection in Children in the Developing World. Philos Trans Biol Sci 354: 777–785.

30. Hu X, Xiao S, Chen B, Sa Z (2012) Gaps in the 2010 measles SIA coverage among migrant children in Beijing: Evidence from a parental survey. Vaccine 30: 5721–5725. doi:10.1016/j.vaccine.2012.07.007.

31. Hou Z, Jie Chang, Yue D, Fang H, Meng Q, et al. (2014) Determinants of willingness to pay for self-paid vaccines in China. Vaccine 32: 4471–4477. doi:10.1016/j.vaccine.2014.06.047.

32. CDC (2012) Pneumococcal disease. Epidemiology and Prevention of Vaccine-Preventable Diseases. pp. 233–248.

33. Zhang L (2009) Building a better infectious disease surveillance system for China. Saarbrücken, Germany: VDM Verlag Dr. Müller.

34. Bakhache P, Rodrigo C, Davie S, Ahuja A, Sudovar B, et al. (2013) Health care providers' and parents' attitudes toward administration of new infant vaccines--a multinational survey. Eur J Pediatr 172: 485–492. doi:10.1007/s00431-012-1904-4.

35. World Health Organization (2011) News in Brief. Measles-Rubella Bull 5: 1–9.

APPENDIX A

English Questionnaire

ID Number __ __ __ __ __

Individual questionnaire

You are invited to participate in a survey of parents. This survey is sponsored by the Shanghai Centers for Disease Control and Prevention and the University of Michigan in the United States. In total, over 600 parents of young children will be selected from across Shanghai. This survey will research parents' attitudes towards vaccination, particularly vaccines requiring payment. This information will help guide interventions for increasing vaccination coverage. Your response will be anonymous and your decision to participate in this survey or not will not affect your treatment at this clinic. This survey should take 20 minutes, and you will receive 30 renminbi for completing every question on this survey.

We first want to ask about the child you brought to the clinic today.

1. What is your relationship to the child?
   - 1☐ Mother
   - 2☐ Father
   - 3☐ Other (Please describe ______________________)

2. What is the birthdate of the child you brought to the clinic today?

   ___ ___ ___ ___ - ___ ___ - ___ ___
   Y Y Y Y M M D D

3. What is the sex of the child you brought to the clinic today?
   - 1☐ Male
   - 2☐ Female

Next we want to ask you some questions about the immunization clinic and about vaccinations that require payments.

4. How long have you known the doctors at your immunization clinic?

   ____ years ____ months

5. When deciding on whether to get a vaccine you must pay for, how trustworthy are recommendations from your doctors at the immunization clinic?

Not at all trustworthy				Extremely trustworthy
1☐	2☐	3☐	4☐	5☐

6. When deciding on whether to get a vaccine you must pay for, how important is it for you to look online for information about vaccines yourself?

Not at all important				Extremely important
1☐	2☐	3☐	4☐	5☐

7. When deciding on whether to get a vaccine you must pay for, how important is it for you to consult family and friends?

Not at all important				Extremely important
1☐	2☐	3☐	4☐	5☐

8. When deciding on whether to get a vaccine you must pay for, how important is it for you to consult parents in your social group?

Not at all important				Extremely important
1☐	2☐	3☐	4☐	5☐

9. How worried are you with giving your child two or more vaccines at the same time?

Not at all worried				Extremely worried
1☐	2☐	3☐	4☐	5☐

10. How worried are you with giving your child vaccines when the child is under 6 months?

Not at all worried				Extremely worried
1☐	2☐	3☐	4☐	5☐

11. How important is it for you to give your child vaccines on time?

Not at all important				Extremely important
1☐	2☐	3☐	4☐	5☐

12. What is the largest number of vaccine shots that you are willing to give your child during the same clinic visit?
   - 0☐ None
   - 1☐ 1
   - 2☐ 2
   - 3☐ 3
   - 4☐ More than 3
   - 5☐ As many as recommended by the doctor

13. How often are you willing to come to the immunization clinic to get your child a vaccine if recommended to do so?
    - 0☐ As often as needed
    - 1☐ Once a week
    - 2☐ A couple of times each month
    - 3☐ Once a month
    - 4☐ Every other month
    - 5☐ A few times a year at most

14. How important is it for you to get **every** vaccine recommended by your doctor?

Not at all important				Extremely important
1☐	2☐	3☐	4☐	5☐

15. How trustworthy is **traditional Chinese medicine** to cure infectious disease?

Not at all trustworthy				Extremely trustworthy
1☐	2☐	3☐	4☐	5☐

16. How trustworthy is **Western medicine** to cure infectious disease?

Not at all trustworthy				Extremely trustworthy
1☐	2☐	3☐	4☐	5☐

17. Do you think that the effectiveness of Chinese-made vaccines is different than the effectiveness of foreign-made vaccines?
    1☐ Yes
    2☐ No
    3☐ I do not know

18. How effective are foreign-made vaccines in Chinese children?

Not at all effective				Extremely effective
1☐	2☐	3☐	4☐	5☐

19. How effective are Chinese-made vaccines in Chinese children?

Not at all effective				Extremely effective
1☐	2☐	3☐	4☐	5☐

20. Do you think that the safety of Chinese-made vaccines is different than the safety of foreign-made vaccines?
    1☐ Yes
    2☐ No
    3☐ I do not know

21. How safe are foreign vaccines in Chinese children?

Not at all safe				Extremely safe
1☐	2☐	3☐	4☐	5☐

22. How safe are Chinese-made vaccines in Chinese children?

Not at all safe				Extremely safe
1☐	2☐	3☐	4☐	5☐

23. When deciding on whether to get a vaccine you must pay for, which of these statements best applies to you?
    1☐ My child receives all vaccines that require payment at the earliest time that these vaccines are recommended.
    2☐ My child receives all vaccines that require payment, but I may choose to delay when my child gets at least some of these vaccines.
    3☐ I may choose to refuse one or more of these vaccines that require payment.
    4☐ I refuse all vaccines that require payment.

Next, we are going to ask you about two different diseases and their associated vaccines: measles and pneumococcus.

24. Do you know what measles is?
   1☐ Yes
   2☐ No

MEASLES

Measles virus causes rash, cough, runny nose, eye irritation, and fever. It can lead to ear infection, pneumonia, seizures (jerking and staring), brain damage, and death.

25. Have you ever personally contracted measles?
   1☐ Yes
   2☐ No
   3☐ I do not know

26. Has your child ever contracted measles?
   1☐ Yes
   2☐ No
   3☐ I do not know

27. Has any close family member or friend of yours ever contracted measles?
   1☐ Yes
   2☐ No
   3☐ I do not know

28. How **serious** of a disease do you think is measles?

Not at all serious				Extremely serious
1☐	2☐	3☐	4☐	5☐

29. Do you think that measles is a serious enough disease to warrant a vaccine?
   1☐ Yes
   2☐ No

30. How **common** is measles in your community?

Not at all common				Extremely common
1☐	2☐	3☐	4☐	5☐

31. How **effective** do you think the measles vaccine is in preventing all cases of measles?

Not at all effective				Extremely effective
1☐	2☐	3☐	4☐	5☐

ID Number __ __ __ __ __

32. Among your social group, **how many children** do you think are vaccinated against measles?

None		About half		All
1☐	2☐	3☐	4☐	5☐

33. How **safe** is the measles vaccine?

Not at all safe				Extremely safe
1☐	2☐	3☐	4☐	5☐

34. After getting a measles vaccine, how likely is your child to get **a mild reaction**, like a mild fever?

Not at all likely				Extremely likely
1☐	2☐	3☐	4☐	5☐

35. After getting a measles vaccine, how likely is your child to get **a moderate or major reaction**, like a seizure?

Not at all likely				Extremely likely
1☐	2☐	3☐	4☐	5☐

36. Do you know what pneumonia is?
    1☐ Yes
    2☐ No

37. Do you know what meningitis is?
    1☐ Yes
    2☐ No

PNEUMOCOCCUS

Pneumococcal disease is caused by infection with *Streptococcus pneumoniae* bacteria. These bacteria can spread from person to person through close contact. Pneumococcal disease can lead to severe health problems, including pneumonia, blood infections, and meningitis. Meningitis is an infection of the covering of the brain. Pneumococcal meningitis is fairly rare, but it leads to other health problems, including deafness and brain damage.

38. Have you ever personally contracted pneumonia?
    1☐ Yes
    2☐ No
    3☐ I do not know

39. Has your child ever contracted pneumonia?
    1☐ Yes
    2☐ No
    3☐ I do not know

40. Has any close family member or friend of yours ever contracted pneumonia?
    1☐ Yes
    2☐ No
    3☐ I do not know

41. How **serious** of a disease do you think is pneumonia?

Not at all serious				Extremely serious
1☐	2☐	3☐	4☐	5☐

42. Do you think that pneumonia is a serious enough disease to warrant a vaccine?
    1☐ Yes
    2☐ No

43. How **common** is pneumonia in your community?

Not at all common				Extremely common
1☐	2☐	3☐	4☐	5☐

44. How **effective** do you think the pneumococcus vaccine is in preventing all cases of pneumonia?

Not at all effective				Extremely effective
1☐	2☐	3☐	4☐	5☐

45. Have you ever personally contracted meningitis?
1☐ Yes
2☐ No
3☐ I do not know

46. Has your child ever contracted meningitis?
1☐ Yes
2☐ No
3☐ I do not know

47. Has any close family member or friend of yours ever contracted meningitis?
1☐ Yes
2☐ No
3☐ I do not know

48. How **serious** of a disease do you think is meningitis?

Not at all serious				Extremely serious
1☐	2☐	3☐	4☐	5☐

49. Do you think that meningitis is a serious enough disease to warrant a vaccine?
1☐ Yes
2☐ No

50. How **common** is meningitis in your community?

Not at all common				Extremely common
1☐	2☐	3☐	4☐	5☐

51. How **effective** do you think the pneumococcus vaccine is in preventing all cases of meningitis?

Not at all effective				Extremely effective
1☐	2☐	3☐	4☐	5☐

52. Among your social group, **how many children** do you think are vaccinated against pneumococcus?

None		About half		All
1☐	2☐	3☐	4☐	5☐

53. How **safe** is the pneumococcus vaccine?

Not at all safe				Extremely safe
1☐	2☐	3☐	4☐	5☐

54. After getting a pneumococcus vaccine, how likely is your child to get **a mild reaction**, like a mild fever?

Not at all likely				Extremely likely
1☐	2☐	3☐	4☐	5☐

55. After getting a pneumococcus vaccine, how likely is your child to get **a moderate or major reaction**, like a seizure?

Not at all likely				Extremely likely
1☐	2☐	3☐	4☐	5☐

56. How much are you willing to pay for the 7-valent pneumococcus vaccine (called PCV7)?

0☐ 0 yuan
1☐ 50 yuan
2☐ 100 yuan
3☐ 200 yuan
4☐ 500 yuan
5☐ 700 yuan
6☐ Over 700 yuan

The last set of questions are about you.

57. How often do you work each week?
   1☐ I currently do not work
   2☐ 1 day
   3☐ 2 days
   4☐ 3 days
   5☐ 4 days
   6☐ 5 days
   7☐ More than 5 days

58. What is your family's monthly income?
   1☐ <2, 000 元
   2☐ 2, 000 to 3, 999 元
   3☐ 4, 000 to 5, 999 元
   4☐ 6, 000 to 9, 999 元
   5☐ 10, 000 to 19, 999 元
   6☐ Over 20, 000 元

59. What is your highest education level?
   1☐ None
   2☐ Elementary
   3☐ Middle school
   4☐ High school
   5☐ Some college
   6☐ College or above

60. What is your residency?
   1☐ Same city and same district
   2☐ Same city, different district
   3☐ Different city

61. How long have you lived in this city?
   0☐ My entire life

   ____ years ____ months

62. How long do you plan on staying in this city?
   0☐ Indefinitely

   ____ years ____ months

63. What is your home city?
  - 0☐ Shanghai
  - 1☐ Somewhere other than Shanghai:

    _____________ Province

If your home city is Shanghai, you do not need to answer the following question, and you have finished the survey. Please answer the following question if your home city is not Shanghai.

64. How often do you return to your home city?
  - 1☐ More than once a year
  - 2☐ Once a year
  - 3☐ Once every couple years
  - 4☐ Fewer than once every couple years
  - 5☐ Never

Thank you very much for your participation! Please return this form to a staff member. Have your vaccination booklet available and they will record some information about vaccinations that your child has received.

ID Number __ __ __ __ __

The following information should be filled out by staff members looking at the child's vaccination booklet. Please give the questionnaire and your child's vaccination booklet to the staff members, and wait while they fill out these last questions.

65. What measles vaccinations (including MM, MR, or MMR) has the child received?

Type of vaccine	Date of vaccination
1☐ Measles 2☐ MR 3☐ MMR 4☐ MM	___ ___ ___ ___ - ___ ___ - ___ ___ Y Y Y Y M M D D
1☐ Measles 2☐ MR 3☐ MMR 4☐ MM	___ ___ ___ ___ - ___ ___ - ___ ___ Y Y Y Y M M D D
1☐ Measles 2☐ MR 3☐ MMR 4☐ MM	___ ___ ___ ___ - ___ ___ - ___ ___ Y Y Y Y M M D D
1☐ Measles 2☐ MR 3☐ MMR 4☐ MM	___ ___ ___ ___ - ___ ___ - ___ ___ Y Y Y Y M M D D
1☐ Measles 2☐ MR 3☐ MMR 4☐ MM	___ ___ ___ ___ - ___ ___ - ___ ___ Y Y Y Y M M D D

66. What pneumococcal vaccinations (including PCV7 and PPSV23) has the child received?

Type of vaccine	Date of vaccination
1☐ PCV7 2☐ PPSV23	___ ___ ___ ___ - ___ ___ - ___ ___
1☐ PCV7 2☐ PPSV23	___ ___ ___ ___ - ___ ___ - ___ ___
1☐ PCV7 2☐ PPSV23	___ ___ ___ ___ - ___ ___ - ___ ___
1☐ PCV7 2☐ PPSV23	___ ___ ___ ___ - ___ ___ - ___ ___

APPENDIX B

Chinese Questionnaire

ID ___ ___ ___ ___ ___

个人问卷

我们邀请您参与的这项调查由上海市疾病预防控制中心和美国密歇根大学赞助。我们将从上海全市选出 600 位家长参与本调查。本调查旨在研究家长对疫苗、尤其是自费疫苗的态度。这些信息将有助于提高疫苗的接种率。本调查匿名，不会影响您在此接种门诊得到的服务。此问卷将花费您 20 分钟左右的时间。如果您完成了整份问卷，将会收到人民币 30 元或同等价值的小礼品作为奖励。

首先我们想了解一下您的孩子的相关信息。

1. 您和孩子的关系？
   1☐ 妈妈
   2☐ 爸爸
   3☐ 其他 (请描述 ______________________)

2. 您孩子的出生日期是？

   ___ ___ ___ ___ - ___ ___ - ___ ___

3. 您孩子的性别？
   1☐ 男
   2☐ 女

接下来我们要问您有关接种门诊和自费疫苗的问题。本调查中涉及的自费疫苗包括肺炎疫苗、流感疫苗、轮状病毒疫苗和水痘疫苗。

4. 您认识今天在接种门诊的为您预检登记的医生多久了？

   ___ ___ ___ ___ - ___ ___

5. 在决定是否自费注射疫苗时，您相信接种门诊的医生的建议吗?

完全不相信	基本不相信	不确定	基本相信	非常相信
1☐	2☐	3☐	4☐	5☐

6. 在决定是否自费注射疫苗时，您认为上网查找有关疫苗的讯息有多重要?

完全不重要	基本不重要	不确定	基本重要	非常重要
1☐	2☐	3☐	4☐	5☐

7. 在决定是否自费注射疫苗时，您觉得咨询家人和朋友的意见有多重要?

完全不重要	基本不重要	不确定	基本重要	非常重要
1☐	2☐	3☐	4☐	5☐

8. 在决定是否自费注射疫苗时，您觉得咨询您的社交圈内其他家长的意见有多重要?

完全不重要	基本不重要	不确定	基本重要	非常重要
1☐	2☐	3☐	4☐	5☐

9. 您是否担心给孩子同时注射两支或以上疫苗?

完全不担心	基本不担心	不确定	有点担心	非常担心
1☐	2☐	3☐	4☐	5☐

10. 您是否担心给六个月以下的孩子注射疫苗?

完全不担心	基本不担心	不确定	有点担心	非常担心
1☐	2☐	3☐	4☐	5☐

11. 您觉得及时给孩子注射疫苗有多重要?

完全不重要	基本不重要	不确定	基本重要	非常重要
1☐	2☐	3☐	4☐	5☐

12. 您愿意给孩子同时注射多少支疫苗?

0☐ 0
1☐ 1
2☐ 2
3☐ 3
4☐ 大于 3
5☐ 医生推荐的数量

13. 如果接种门诊医生建议您带孩子去接种门诊注射疫苗，您可以承受的最高频率是什么?

0☐ 需要的时候去
1☐ 1 个星期 1 次
2☐ 1 个月 2 次
3☐ 1 个月 1 次
4☐ 每 2 个月 1 次
5☐ 1 年去几次

14. 您觉得医生建议注射的**每种**疫苗都很重要吗?

完全不重要	基本不重要	不确定	基本重要	非常重要
1☐	2☐	3☐	4☐	5☐

15. 您相信**中医**可以治愈流行病吗?

完全不相信	基本不相信	不确定	基本相信	非常相信
1☐	2☐	3☐	4☐	5☐

16. 您相信**西医**可以治愈流行病吗?

完全不相信	基本不相信	不确定	基本相信	非常相信
1☐	2☐	3☐	4☐	5☐

17. 您认为国产疫苗跟进口疫苗效果一样吗?

1☐ 是
2☐ 否
3☐ 不确定

18. 您认为**进口疫苗**对中国儿童有效果吗?

完全无效	基本无效	不确定	基本有效	完全有效
1☐	2☐	3☐	4☐	5☐

ID ___ ___ ___ ___ ___

19. 您认为**国产疫苗**对中国儿童有效果吗?

完全无效	基本无效	不确定	基本有效	完全有效
1☐	2☐	3☐	4☐	5☐

20. 您认为国产疫苗跟进口疫苗一样安全吗?

1☐ 是
2☐ 否
3☐ 不确定

21. 您认为**进口疫苗**对中国儿童安全吗?

非常不安全	基本不安全	不确定	基本安全	非常安全
1☐	2☐	3☐	4☐	5☐

22. 您认为**国产疫苗**对中国儿童安全吗?

非常不安全	基本不安全	不确定	基本安全	非常安全
1☐	2☐	3☐	4☐	5☐

23. 当决定是否注射自费疫苗时，以下哪些情况最符合您?

1☐ 我的孩子应该尽早注射全部自费疫苗
2☐ 我的孩子接受全部建议的自费疫苗，但是我决定延迟给孩子注射一部分疫苗
3☐ 我可能决定拒绝一部分种类或剂次的自费疫苗
4☐ 我拒绝全部自费疫苗

接下来，我们将问您两种不同的疾病以及这些疾病相关的疫苗：麻疹和肺炎球菌。

24. 您知道麻疹吗?

1☐ 知道
2☐ 不知道

麻疹

麻疹病毒可引起皮疹、咳嗽、流鼻涕、眼睛刺激和发烧。它会导致耳部感染、肺炎、癫痫发作（抽搐和目光呆滞）、脑损伤和死亡。

25. **您自己**有没有患过麻疹?

1☐ 有
2☐ 没有
3☐ 不知道

26. **您的孩子**有没有患过麻疹?

1☐ 有
2☐ 没有
3☐ 不知道

ID ___ ___ ___ ___ ___

27. 您的**亲戚或朋友**有没有患过麻疹?

1☐ 有
2☐ 没有
3☐ 不知道

28. 您认为麻疹**有多严重**?

完全不严重	基本不严重	不确定	比较严重	非常严重
1☐	2☐	3☐	4☐	5☐

29. 您认为麻疹是否严重到需要注射疫苗来预防?

1☐ 是
2☐ 否

30. 麻疹在您的社区有**多常见**?

非常不常见	比较不常见	不确定	比较常见	非常常见
1☐	2☐	3☐	4☐	5☐

31. 您觉得麻疹疫苗对于预防全部的麻疹病例的**效果如何**?

完全无效	基本无效	不确定	基本有效	完全有效
1☐	2☐	3☐	4☐	5☐

32. 在您的社交圈中，您认为有**多少儿童**注射麻疹疫苗?

没有人	少数有	大概一半	多数有	全部
1☐	2☐	3☐	4☐	5☐

33. 麻疹疫苗**安全**吗?

非常不安全	基本不安全	不确定	基本安全	非常安全
1☐	2☐	3☐	4☐	5☐

34. 如果孩子注射麻疹疫苗，您觉得孩子是否会有**轻微的不良反应**，例如轻微的发烧?

几乎不会	不太可能会	不确定	有可能会	肯定会
1☐	2☐	3☐	4☐	5☐

35. 如果孩子注射麻疹疫苗，您觉得孩子是否会有**中度或严重的不良反应**，例如癫痫?

几乎不会	不太可能会	不确定	有可能会	肯定会
1☐	2☐	3☐	4☐	5☐

36. 您知道肺炎吗?

1☐ 知道
2☐ 不知道

37. 您知道脑膜炎吗?

1☐ 知道
2☐ 不知道

肺炎球菌疾病

肺炎球菌通过亲密接触在人与人之间传播。肺炎球菌疾病可导致严重的健康问题，包括肺炎、血液感染和脑膜炎。脑膜炎是指脑膜受感染。虽然肺炎球菌脑膜炎非常罕见，但是却会引起包括耳聋和脑损伤在内的其他健康问题。

38. **您自己**有没有患过肺炎?

1☐ 有
2☐ 没有
3☐ 不知道

39. **您的孩子**有没有患过肺炎?

1☐ 有
2☐ 没有
3☐ 不知道

40. 您的**亲戚或朋友**有没有患过肺炎?

1☐ 有
2☐ 没有
3☐ 不知道

41. 您认为肺炎**有多严重**?

完全不严重	基本不严重	不确定	比较严重	非常严重
1☐	2☐	3☐	4☐	5☐

42. 您认为肺炎是否严重到需要接种疫苗来预防?

1☐ 是
2☐ 否

43. 肺炎在您的社区有**多常见**?

非常不常见	基本不常见	不确定	比较常见	非常常见
1☐	2☐	3☐	4☐	5☐

44. 您觉得肺炎球菌疫苗对于预防全部的肺炎病例的**效果如何?**

完全无效	基本无效	不确定	基本有效	完全有效
1☐	2☐	3☐	4☐	5☐

45. **您自己**有没有患过脑膜炎?

1☐ 有
2☐ 没有
3☐ 不知道

46. **您的孩子**有没有患过脑膜炎?

1☐ 有
2☐ 没有
3☐ 不知道

47. 您的**亲戚或朋友**有没有患过脑膜炎?

1☐ 有
2☐ 没有
3☐ 不知道

48. 您认为脑膜炎**有多严重**?

非常不严重	比较不严重	不确定	比较严重	非常严重
1☐	2☐	3☐	4☐	5☐

49. 您认为脑膜炎是否严重到需要注射疫苗来预防?

1☐ 是
2☐ 否

50. 脑膜炎在您的社区有**多常见**?

非常不常见	基本不常见	不确定	比较常见	非常常见
1☐	2☐	3☐	4☐	5☐

51. 您觉得肺炎球菌疫苗对于预防全部的脑膜炎病例的**效果如何?**

完全无效	基本无效	不确定	基本有效	完全有效
1☐	2☐	3☐	4☐	5☐

52. 在您的社交圈中，您认为有**多少儿童**接种过肺炎球菌疫苗?

没有人	少数有	大概一半	多数有	全部
1☐	2☐	3☐	4☐	5☐

53. 您认为肺炎疫苗**安全**吗?

非常不安全	基本不安全	不确定	基本安全	非常安全
1☐	2☐	3☐	4☐	5☐

54. 如果孩子注射肺炎疫苗，您觉得孩子是否会有**轻微的不良反应**，例如轻微的发烧?

几乎不会	不太可能会	不确定	有可能会	肯定会
1☐	2☐	3☐	4☐	5☐

55. 如果孩子注射肺炎球菌疫苗，您觉得孩子是否会有**中度或严重的不良反应**，例如癫痫?

几乎不会	不太可能会	不确定	有可能会	肯定会
1☐	2☐	3☐	4☐	5☐

56. 您愿意为 7 价肺炎球菌疫苗支付的费用是多少?

0☐ 0 元
1☐ 50 元
2☐ 100 元
3☐ 200 元
4☐ 500 元
5☐ 700 元
6☐ 多于 700 元

ID ___ ___ ___ ___ ___

最后一组问题是关于您自己的。

57. 您一个星期工作多久?

1 ☐ 现在没有工作
2 ☐ 1 天
3 ☐ 2 天
4 ☐ 3 天
5 ☐ 4 天
6 ☐ 5 天
7 ☐ 多于 5 天

58. 您家庭的月收入是多少?

1 ☐ <2, 000 元
2 ☐ 2, 000-3, 999 元
3 ☐ 4, 000-5, 999 元
4 ☐ 6, 000-9, 999 元
5 ☐ 10, 000-19, 999 元
6 ☐ 多于 20, 000 元

59. 您的学历是?

1 ☐ 无
2 ☐ 小学
3 ☐ 初中
4 ☐ 高中
5 ☐ 大专
6 ☐ 大学或研究生

59B. 您的年龄: ______________

60. 您的户籍所在地是?

1 ☐ 上海，在我现在住的区县
2 ☐ 上海，其它区县
3 ☐ 其它省

61. 您在上海生活的时间多久?

0 ☐ 至今一直居住于上海
1 ☐ ___ ___ ___ ___ - ___ ___

62. 您计划在上海生活多长时间?

0 ☐ 没有搬迁计划
1 ☐ ___ ___ ___ ___ - ___ ___

63. 您的家乡是在哪个省?

0☐ 上海
1☐ 其他地方:

______________ 省

如果您的家乡是上海市，您不需要回答以下的问题，您已经完成这份问卷。如果您的家乡不是上海市，请回答以下的问题。

64. 您多久回一次您的家乡?

1☐ 一年几次
2☐ 一年一次
3☐ 每两年一次
4☐ 每几年一次
5☐ 从来没有

非常感谢您的参与。请将此表格交回工作人员并提供您孩子的预防接种证，他们会记录您孩子接种疫苗的一些信息。

ID ___ ___ ___ ___ ___

以下有关孩子的疫苗接种记录由工作人员填写。

这位孩子出生日期是？ ___ ___ ___ ___ - ___ ___ - ___ ___

这位孩子是？ 1☐ 本地 2☐ 外来

65. 这位孩子注射了哪一些含麻疹成分疫苗（麻疹，麻疹-风疹联合疫苗，麻疹-腮腺炎-风疹联合疫苗，麻疹-腮腺炎联合疫苗)?

	疫苗种类	注射日期
1☐ 2☐ 3☐ 4☐	麻疹 麻风 麻腮风 麻腮	___ ___ ___ ___ - ___ ___ - ___ ___
1☐ 2☐ 3☐ 4☐	麻疹 麻风 麻腮风 麻腮	___ ___ ___ ___ - ___ ___ - ___ ___
1☐ 2☐ 3☐ 4☐	麻疹 麻风 麻腮风 麻腮	___ ___ ___ ___ - ___ ___ - ___ ___
1☐ 2☐ 3☐ 4☐	麻疹 麻风 麻腮风 麻腮	___ ___ ___ ___ - ___ ___ - ___ ___
1☐ 2☐ 3☐ 4☐	麻疹 麻风 麻腮风 麻腮	___ ___ ___ ___ - ___ ___ - ___ ___

66. 这位孩子注射了哪一些肺炎球菌疫苗（7 价肺炎球菌结合疫苗，23 价肺炎球菌多糖疫苗）？

	疫苗种类	注射日期
1☐ 2☐	7 价肺炎球菌结合疫苗 23 价肺炎球菌多糖疫苗	___ ___ ___ ___ - ___ ___ - ___ ___
1☐ 2☐	7 价肺炎球菌结合疫苗 23 价肺炎球菌多糖疫苗	___ ___ ___ ___ - ___ ___ - ___ ___
1☐ 2☐	7 价肺炎球菌结合疫苗 23 价肺炎球菌多糖疫苗	___ ___ ___ ___ - ___ ___ - ___ ___
1☐ 2☐	7 价肺炎球菌结合疫苗 23 价肺炎球菌多糖疫苗	___ ___ ___ ___ - ___ ___ - ___ ___