## **RESEARCH PAPER**

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# Preferences for vaccination program attributes among parents of young infants in Shanghai, China

Zhuoying Huang<sup>a</sup>, Abram L. Wagner <sup>b</sup>, Muzi Lin<sup>b</sup>, Xiaodong Sun<sup>a</sup>, Brian J. Zikmund-Fisher<sup>c,d</sup>, Matthew L. Boulton<sup>b,e</sup>, Jia Ren<sup>a</sup>, and Lisa A. Prosser<sup>f</sup>

<sup>a</sup>Department of Immunization Program, Shanghai Municipal Centers for Disease Control & Prevention, Shanghai, China; <sup>b</sup>Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI, USA; <sup>c</sup>Department of Health Behavior & Health Education, School of Public Health, University of Michigan, Ann Arbor, MI, USA; <sup>d</sup>Department of Internal Medicine, Division of General Medicine, Michigan Medicine, Ann Arbor, MI, USA; <sup>e</sup>Department of Internal Medicine, Ann Arbor, MI, USA; <sup>e</sup>Department of Internal Medicine, Division of General Medicine, Michigan B. Meister Child Health Evaluation and Research Center, Department of Pediatrics and Communicable Diseases, Michigan Medicine, Ann Arbor, MI, USA

#### ABSTRACT

Compared to many other countries, China offers fewer pediatric vaccines. Future attempts to add mandatory vaccines may run counter to parents' preferences for shot-limiting. The aim of this study was to assess Chinese parents' preferences and willingness-to-pay (WTP) for programmatic attributes of vaccination services. Parents of young infants <3 months of age presenting at immunization clinics in Shanghai, China, in 2017 completed a discrete choice experiment (DCE) on vaccination program attributes: waiting time at the clinic, number of shots before 7 months, number of injections per visit, cost per visit, and location of the shot. We estimated preference utilities and WTP using logistic regression. In total, 590 completed the DCE. Caregivers expressed greater utility for less waiting time, fewer office visits, lower cost of vaccines, and fewer injections co-administered. Over the course of their child's first 6 months, parents were willing to pay 113 RMB (\$17) to avoid an additional 10 minutes of waiting at each appointment (95% confidence interval [CI]: 213, 929), 474 RMB (\$70) to avoid an additional office visit (95% CI: 241, 707), and 703 RMB (\$104) to avoid an additional injection at each appointment (95% Cl: 337, 1068). As China expands its list of publicly funded vaccines, public health officials will have to counter Chinese parents' strong preferences for limiting the total number of office visits and the number of injections administered at each visit, potentially through the use of combination vaccines.

## Introduction

Compared to most low- and middle-income countries, China has relatively fewer vaccines included in its governmentfunded Expanded Program on Immunization (EPI) which provide recommended vaccines for free. Currently, some vaccines such as the bacillus Calmette–Guerin, hepatitis B, polio, diphtheria-tetanus-pertussis (DTP), measles, and rubella vaccines are administered through China's EPI,<sup>1</sup> whereas the *Haemophilus influenzae* type b (Hib), pneumococcus, and rotavirus vaccines, which are typically included in many countries' EPI, are considered optional and are only available to purchase at an immunization clinic. In some areas of the country, the EPI will be expanding in the near future. For instance, the varicella vaccine was added to the EPI in Shanghai in August 2018.<sup>2</sup>

In China, EPI vaccines are mandatory for school entry, whereas non-EPI vaccines are voluntary.<sup>3</sup> As a result, coverage of EPI vaccines is high,<sup>4</sup> even for vaccines more recently integrated into the EPI after 2008, although there are significant differences in population-level vaccine coverage in different provinces of China.<sup>5</sup>

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The national EPI schedule is shown in Table 1. Additionally, many parents end up paying for a non-EPI vaccine during the same or separate visit as an EPI vaccine's administration: In a survey of 32 counties throughout China, 61.41% had received a non-EPI vaccine.<sup>6</sup> Parents in China are allowed to make the determination as to when their child is vaccinated with non-EPI vaccines, within the constraints dictated by manufacturer's instructions and informal guidance from immunization clinics.

Understanding parents' perceptions of the vaccine schedule is particularly important because parents often have concerns about the number and/or timing of vaccines. In previous surveys, most parents in Shanghai (64%) were concerned about vaccine co-administration, and many (31%) expressed concerns about infants <6 months receiving too many vaccines.<sup>7</sup> Parents also express concern about safety and the pain from multiple injections, even if additional injections during one visit do not produce higher rates of adverse reactions.<sup>8</sup> In one study in the United States in 1999, parents were willing to pay over \$10 to avoid pain and emotion distress from multiple injections.<sup>9</sup> Beyond parents, health-care providers also express some hesitancy in administering multiple injections.<sup>10,11</sup> One

CONTACT Abram L. Wagner 😂 awag@umich.edu 🗈 Department of Epidemiology, School of Public Health, University of Michigan, Ann Arbor, MI, USA Subject classification codes: include these here if the journal requires them © 2020 Taylor & Francis Group, LLC

### Table 1. Immunization schedule in China in 2016.

	Recommended age at administration														
Vaccine	Birth	1 m	2 m	3 m	4 m	5 m	6 m	8 m	9 m	18 m	2 y	3у	4 y	5 y	6 y
Expanded Program on Immur	nization (I	EPI) vacc	ines					-							
НерВ	1	2					3								
BCG	1														
IPV			1												
OPV				1	2								3		
DTaP				1	2	3				4					
DT															1
MR								1							
MMR										1					
JE-live or								1			2				
JE-inactivated								1, 2			3				4
MPSV-A							1		2						
MPSV-AC												1			2
HepA-live or HepA-inactivated										1					
										1	2				
Non-EPI vaccines <sup>a</sup>															
Hib			1	2											
PCV		1	2	3											
Influenza							1	2							
Rotavirus			1												
PPSV											1				
Varicella										1					

BCG: bacillus Calmette–Guérin, DT: diphtheria-tetanus, DTaP: diphtheria-tetanus-acellular pertussis, HepA: hepatitis A (2BS cell strains), HepB: hepatitis B (recombinant *Hansenula polymorpha*), IPV: inactivated polio vaccine (Types I, II, and III), JE: Japanese encephalitis (SA14-14-2 strains), MMR: measles-mumps-rubella vaccine (measles: Shanghai-191, mumps: vS<sub>79</sub> Strains, rubella: BRD II), MPSV: meningococcal polysaccharide vaccine (Group A & C), MR: measles-rubella vaccine (measles: Shanghai-191, rubella: BRD II), OPV: oral polio vaccine (Types I and III), PCV: pneumococcal conjugate vaccine (13 valent), PPSV: pneumococcal polysaccharide vaccine (23 valent), rotavirus (Lanzhou lamb rotavirus or Rotarix).

a Non-EPI vaccines are administered according to manufacturer's instructions, without official guidance from the China Experts Advisory Committee on Immunization Program.

alternative is the expanded use of combination vaccines. Although more expensive, combination vaccines save health-care providers' time and reduce the number of injections for a child.<sup>12</sup>

One methodology for studying vaccine decision-making is through discrete choice experiments (DCEs), such as conjoint analysis studies.<sup>13</sup> DCEs allow individuals to evaluate several attributes simultaneously, thereby taking into account trade-offs across attributes. Respondents choose between two profiles that have different attribute levels listed for each attribute. For instance, Hall et al.'s study from Paris, France found that the decision whether to immunize a child is influenced by various factors, such as the high cost of vaccine, uncertainty about the disease and limited trust in health providers.<sup>14</sup> burden, A previous study by Gidengil et al. in the US found that people prioritized fewer injections and to minimize costs.<sup>15</sup> A study of adult preferences for hepatitis B vaccination in Shandong province, China, examined the impact of different health facilities and the number of doses required on vaccination preferences and found that individuals willing to pay 35 RMB to increase the duration of protection from 5 to 20 y. $^{16}$ 

There is little research from low- and middle-income countries on parent's preferences around pediatric vaccination programs. The overall research goal of this study is to explore how parents in China decide to vaccinate their children using a conjoint analysis approach. We look specifically at vaccination program attributes that can influence children's primary caregivers' decisions about the vaccine, such as waiting time at the clinic, timing of shots after birth and before 7 months, cost per visit, number of injections per visit, and location of the shot.

## Materials and methods

#### Study population

Between May and September 2017, caregivers accompanying infants <3 months at public immunization clinics in Shanghai, China, were enrolled. We sampled clinics based on the population of the surrounding township, according to a probabilityproportionate-to-size (PPS) method. We selected caregivers from a convenience sample, with the inclusion criterion being a parent or grandparent of a child <3 months of age. All participants had to be at least 18 y of age. Participants completed one of the two versions of a questionnaire, one version focused on vaccine attributes, the other (detailed in this manuscript) focused on vaccination program attributes.

We estimated a required sample size of 410 based on a previously proposed rule of thumb<sup>17</sup> and a design effect of 1.6384 (estimated from an intracluster coefficient of 0.0456 from a previous study on vaccine attitudes<sup>7,18</sup> and with 15 individuals in each cluster).

The dataset is publicly available at a figshare repository (https://doi.org/10.6084/m9.figshare.6463304).

## Attributes and survey design

Participants provided demographic information, including their relation to the child, monthly family income, education, and residency status (i.e., Shanghai local or a non-local – a more recent migrant).

We selected attributes based on consideration from previous DCE studies,<sup>15</sup> along with a qualitative study from Shanghai about parents' preferences for vaccination.<sup>19</sup> Based on this information, the final attribute list included waiting time at

Table 2. Attributes and attribute levels in a discrete choice experiment of vaccination program attributes.

Attribute	Levels		
Waiting time at clinic	60 minutes		
	90 minutes		
	20 minutes		
	40 minutes		
Timing of shots after birth and before 7	3 visits: 2, 4, 6		
months	5 visits: 2, 3, 4, 5, 6		
	7 visits: 2, 3, 3.5, 4, 4.5, 5, 6		
	8 visits: 2, 3, 3.5, 4, 4.5, 5, 5.5. 6		
Cost per visit	100 RMB		
	200 RMB		
	400 RMB		
	800 RMB		
Number of injections per visit	1		
	2		
	3		
	4		
Location of shot	Government-run immunization		
	clinic		
	Private hospital		

the clinic, timing of shots, cost per visit, number of injections per visit, and location of vaccination (Table 2). Timing of shots and the number of injections were based on a consideration of the current immunization schedule (Table 1). Cost was based on the typical range of immunization costs in Shanghai (ranging from 59 RMB [9 USD] for [domestic Hib] to 858 RMB [129 USD] for [imported PCV7]).

The attribute, number of office visits, was designed based on variation in schedules in China. During the period of time PCV7 was available on the market in China (2007 to 2015), the manufacturer's instructions explicitly indicated that it was not to be co-administered with any other vaccine although those instructions did not apply in other countries. Local immunization clinics in China responded by developing ad hoc PCV vaccination schedules (e.g. usually administering at 3.5, 4.5, 5.5, and 12–15 months). The rotavirus vaccine, which is a different formulation than the vaccine typically used in other countries, is usually administered at 2 months or after. The variation in these potential schedules was simplified into the attribute levels shown in Table 2.

It would not have been logistically feasible for participants to respond to all possible choices in a full factorial design given that four attributes had four levels each and one had two levels.<sup>20</sup> Therefore, we used an ad hoc program in SAS to develop 16 different choice profiles through a more efficient fractional factorial design. For ease of administering the survey and printing off the questionnaire, these were separated into four groups. To each group was added an additional choice that was deemed to be relatively simple for the participant to respond to in order to introduce them to the DCE format. In summary, each respondent was given five different choice sets and was told to make a choice between two profiles in each set (for a forced-choice design).

## Statistical analysis

We fit a conditional logistic regression model to test the significance of individual attributes on decision-making.<sup>13</sup> The individual's choice between two alternatives was the response variable, with the attribute levels related to that choice set being the independent variables. The analysis used survey procedures clustered at the levels of individual and township immunization clinics. We calculated marginal willingness-to-pay (WTP) from the beta estimates of the adjusted model, with the relevant variable divided by the total cost attribute.<sup>13</sup> We calculated confidence intervals for marginal WTP amounts using the delta method.<sup>21</sup>

As a sensitivity analysis, we limited the analysis to just mothers and to individuals with varying socioeconomic levels (education or income). Significance was assessed at an alpha = 0.05 level and 95% confidence intervals (CI) are presented. We conducted analyses in SAS version 9.4 (SAS Institute, Cary, NC, USA).

# Results

In total, 1,285 individuals were approached to participate, and 1,188 (92.5%) agreed. Study participants responded to 1 of 2 DCEs, with 590 participating in this DCE of vaccination program attributes.

Most respondents were either mothers (381, 66%) or fathers (188, 33%) of an infant <3 months; four were grandparents. About half of the sample was college educated, with a bachelor's degree (212, 36%) or graduate degree (62, 11%), and 17% (98) had a middle school education or less. About half (271, 46%) of participants were locals, and the rest were non-locals, or migrants from outside of the city, originating from urban (105, 18%) or rural (209, 36%) areas (Table 3).

Table 4 shows the results of the DCE. Caregivers expressed a greater preference for government-run vs private clinics, less waiting time, fewer office visits in their child's first 6 months, lower cost of vaccines, and fewer injections administered at one visit. In particular, respondents indicated a strong preference for minimizing the number of shots administered at one office visit (for each additional shot, OR: 0.69, 95% CI: 0.65, 0.75).

Over the course of their child's first 6 months, parents were willing to pay 113 RMB (\$17) to avoid an additional 10 minutes of waiting at each appointment (95% CI: 213, 929), 474 RMB (\$70) to avoid an additional office visit (95% CI: 241, 707), and 703 RMB (\$104) to avoid an additional injection at each appointment (95% CI: 337, 1068).

 
 Table 3. Demographic distribution of caregivers in a study of vaccination program preferences in Shanghai, China, 2017.

Group	Category	Count (%)
Caregiver's relationship	Mother	381 (66%)
5	Father	188 (33%)
	Grandparent	4 (1%)
Urbanicity	Urban	180 (30%)
	Inner suburbs	299 (51%)
	Outer suburbs	111 (19%)
Residency	Local	271 (46%)
	Urban non-local	105 (18%)
	Rural non-local	209 (36%)
Education	≤Middle school	98 (17%)
	High school	81 (14%)
	Vocational	131 (22%)
	College	212 (36%)
	Graduate school	62 (11%)
Monthly family income	<5,000 RMB	84 (15%)
	5,000-7,499 RMB	123 (21%)
	7,500–9,999 RMB	94 (16%)
	10,000–14,999 RMB	107 (19%)
	≥15,000 RMB	167 (29%)

Table 4. Results of the discrete choice experiment of vaccination program preferences among parents in Shanghai, China, 2017.

		Preference utilities	Willingness to pay			
Attribute	Comparison	OR (95% CI)	RMB	USD		
Provider	Private vs public	0.74 (0.67, 0.82)	571 (213, 929)	85 (32, 138)		
Minutes waiting	10-minute increments	0.94 (0.93, 0.96)	113 (50, 176)	17 (7, 26)		
Number of visits	1 additional visit	0.78 (0.76, 0.80)	474 (241, 707)	70 (36, 105)		
Number of shots at once	1 additional shot	0.69 (0.65, 0.74)	703 (337, 1068)	104 (50, 159)		
Cost	100 RMB increments	0.95 (0.93, 0.97)				

CI: confidence interval, OR: odds ratio, RMB: renminbi, USD: US dollar.

We did not observe differences in results when limiting to just mothers or to individuals with lower income or lower education levels (results not shown).

## Discussion

Understanding parental preferences about vaccines and vaccination programs will become increasingly important as China incorporates more vaccines into their recommended schedule. We found that parents in Shanghai have a strong aversion to co-administration of vaccines and are willing to pay more for fewer shots or fewer visits. This is particularly challenging given the increasing number of recommended vaccines since delivering age-appropriate doses typically relies heavily on co-administration. This may also indicate that the adoption of combination vaccines (like pentavalent vaccine) may be one strategy for mitigating the number of shots or visits parents must attend to, while providing the same level of immune protection.

The finding that parents have an aversion to more vaccine injections in one visit or more office visits within the child's first few months of life is not surprising and has been confirmed in previous literature outside of China. For example, in their study in the US in 2010, Gidengil et al. found that parents were WTP \$9.95 to avoid an additional injection.<sup>15</sup> Our estimate (\$113) is much higher because it estimates total costs within a 6-month period and not just in one office visit. Regardless, this number speaks to parents' strong preferences for minimizing the required number of injections for their child.<sup>7</sup> The use of combination vaccines limits the number of injections a child receives and minimizes delay in coverage. However, these vaccines can be expensive (the pentavalent combination vaccine in Shanghai costs 600 RMB or \$90 per dose), and some vaccines, like pneumococcal conjugate vaccines, are not available in combination with other antigens.

If parents are unable to obtain combination vaccines, strong preferences for not co-administering multiple vaccine doses could lead parents to delay vaccination. This practice has become common in some areas of the United States; a study of infant vaccination schedules in Portland, Oregon, found that parents who limited the number of injections their child received to only one or two doses increased from 2.5% in 2009.<sup>22</sup> These trends in delaying vaccination

increase the population of susceptible infants and could theoretically impact the incidence of disease within the community.

Our study also found that parents have a strong preference for obtaining vaccines at public rather than private clinics. We sampled parents from public clinics; however, the use of private clinics to distribute vaccines is quite low in China. For the treatment of disease, the use of private clinics varies across different groups of people.<sup>23</sup> Although our study specified that the distance between home and the public or private clinic should be the same for the parents' decisionmaking, parents may perceive private clinics to be farther away or more difficult to reach, which could have also impacted their choice in this study, and which has been shown in other studies to affect the choice of clinic in China.<sup>23</sup>

### Policy and programmatic implications

The Chinese EPI does not include three vaccines which are recommended by the WHO: rotavirus, Hib, and PCV.<sup>24</sup> For two of these vaccines (rotavirus and Hib), domestically produced vaccines are available, but PCV is only produced by a foreign manufacturer. Location of the manufacturer could impact policy decisions, since, up until now, China has only used domestic vaccines in its EPI schedule,<sup>25</sup> except the inactivated polio vaccine (IPV), which currently has a limited domestic supply. Additionally, the lack of robust epidemiological data has also limited understanding of the epidemiology of rotavirus, Hib, and pneumococcus within China and the related burden of disease, although some recent reviews have attempted to establish the relevance of these conditions within the country.<sup>26-28</sup> Experts have called on the Chinese government to fund the Hib and pneumococcal vaccines to limit morbidity and mortality in young children.<sup>25</sup> Our study brings up an added complication for any future vaccine introduction in China: parents profess strong beliefs in limiting the number of vaccine doses their children receive.

## Strengths and limitations

By using a sampling frame from almost all districts in Shanghai, we were able to generate a representative sample of parents within the city. We caution against generalizing our results in areas beyond Shanghai, given substantive differences between people living in rural and urban areas of China. Vaccination behaviors also differ across the region (for example, more children receive non-EPI vaccines in higher-income areas of China than in lowerincome areas).<sup>6</sup> Because we sampled from immunization clinics, we also are biased toward individuals who are accepting of vaccines. However, vaccines are mandatory for school entry in China. By providing vaccines free to all children, regardless of their residency, immunization clinics in urban areas of China are highly attended. It is important to note, however, that one study has estimated that about 12% of children from non-local families do not attend public immunization clinics.<sup>29</sup>

### Conclusions

China has had remarkable success in reducing the incidence of vaccine-preventable diseases, and more vaccines will likely be added to their publicly funded immunization schedule in the future. This study found that parents in Shanghai have a strong aversion to co-administration of vaccines, accompanied by a willingness-to-pay for fewer shots or fewer visits which indicates that combination vaccines (like pentavalent vaccine) may be a strategy for mitigating the number of shots or visits parents must attend to, while conferring the same level of immune protection. It will be important for doctors to retain their role as respected and trusted sources of health information using best practices to vaccinate children in a timely manner to insure sustained high levels of childhood vaccination and protection from disease.

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### Author contributions

ZH, ALW, and ML analyzed the data and wrote the first draft of the paper. XS, BJZ, MLB, and LAP conceived the study idea and revised the manuscript for important intellectual content. JR supervised data collection and revised the manuscript for important intellectual content. All authors agree to the paper as submitted for publication.

# **Disclosure of potential conflicts of interests**

No potential conflicts of interest were disclosed.

## **Ethical considerations**

The research protocol was approved by the Health Sciences and Behavioral Sciences Institutional Review Board at the University of Michigan (#HUM00125379) and the ethical review committee at the Shanghai Centers for Disease Control and Prevention (#2017–2). All participants provided oral informed consent. After completing the interview, participants were given a small gift (such as an umbrella or blanket) to compensate for the time spent on completing the survey.

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## ORCID

Abram L. Wagner (b) http://orcid.org/0000-0003-4691-7802

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