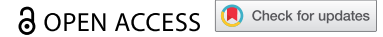


RESEARCH ARTICLE



Theories-based determinants analysis of Hib-combined vaccine hesitancy in China: A multi-group structural equation modeling

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ABSTRACT

Objectives: To explore determinants of Hib-combined vaccine hesitancy in Chinese parents, and to provide scientific intervention measures to tackle vaccine hesitancy.

Methods: 2,531 parents were recruited from local healthcare centers in Zhejiang Province by accidental sampling, and completed the self-developed online questionnaire with voluntary participation. Health Belief Model and Model of Determinants of Vaccine Hesitancy were applied to construct the framework of research. Multi-group Structural Equation Modeling was performed to explore the effects of determinants of vaccine hesitancy across various socio-economic status (SES).

Results: Hib-combined vaccine hesitancy for total sample was 2.184 ± 0.777 (95%CI: 2.153–2.214), and most of them were in low ($n = 1436$, 56.7%) level. Low SES group (2.335 ± 0.763 , 95%CI: 2.271–2.400) had significantly highest vaccine hesitancy. For total sample, Self-Efficacy and Cues to Action presented -0.517 and -0.437 of standard total effect on Vaccine Hesitancy, respectively. The Multi-group Structural Equation Model with satisfying goodness of fit in SES groups ($\chi^2 = 1616.074$, $df = 314$, $\chi^2/df = 5.147$, CFI = 0.973, TLI = 0.966, SRMR = 0.027, RMSEA = 0.041) showed that Cues to Action imposed -0.621 (95%CI: -0.867 – -0.389 , $p < .001$) of major standard total effect on Vaccine Hesitancy in low SES group, while Self-Efficacy imposed -0.560 (95%CI: -0.668 – -0.444 , $p < .001$) and -0.685 (95%CI: -0.841 – -0.454 , $p < .001$) of principal standard total effect on Vaccine Hesitancy in middle and high SES groups, respectively.

Conclusions: Hib-combined vaccine hesitancy in Chinese parents was low, and the lower the SES, the higher the vaccine hesitancy. Cues to Action and Self-Efficacy played primary role in declining vaccine hesitancy for parents at low SES, and at middle and high SES, respectively.

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Introduction

Immunization is regarded globally as one of the most successful and cost-effective public health interventions against infectious diseases, which prevents 2–3 million deaths worldwide every year.¹ In 1978, China started to conduct National Immunization Program (NIP), under the guideline of Expanded Program on Immunization (EPI) of World Health Organization (WHO), providing free immunization services for children in corresponding age to prevent six infectious diseases of measles, polio, diphtheria, tetanus, pertussis, and tuberculosis. Later, NIP vaccines list was expanded in 2007 to prevent more infectious diseases of hepatitis A & B, rubella, mumps, Japanese encephalitis, and Meningococcal meningitis for children nationwide, and to prevent epidemic hemorrhagic fever, anthrax, and leptospirosis for high-risk populations in endemic regions.

In China, the vaccines were categorized into two major kinds, i.e. First-class/NIP vaccines and Second-class/non-NIP vaccines. The former ones are provided for free by government, and citizens, especially children, get vaccinated compulsorily when absolutely necessary to prevent infectious diseases. In contrast, the latter ones are self-paid vaccines in accordance to citizens' willingness and affordability.² By 2014, 36 non-NIP vaccines were reported by Chinese CDC, including ones could

substitute for NIP vaccines, with 106 million doses non-NIP vaccines provided in total, which increased by 13.54% than the provision of 2013. However, it was still less than one third NIP vaccines administered doses.³ In addition to the factor of family income and vaccine price, there are other multiple associated factors contribute to the situation, involving vaccine characteristics and effectiveness, vaccine quality and safety, vaccine provision and availability, vaccination knowledge and awareness, health status of family members, etc.⁴ As an important supplement to NIP vaccines, non-NIP vaccines relate to not only people's health interests, but also national public health security.

In the early development stage of vaccine, the application of traditional single vaccines shows limitations, including adverse events with higher frequency of administrations. In this respect, advanced vaccine products were developed, like combined vaccines, to break the ceiling.⁵ The main objective of combined vaccines is to protect the body from multiple diseases at a time, which demonstrate outstanding features of minimizing the frequency of injections, reducing the possibility of adverse events and hospital-acquired infections, decreasing the cost and difficulty of vaccine storage and management, declining the work time of vaccination practitioners, improving vaccine coverage, facilitating the incorporation of new

vaccines in the immunization schedule, etc.^{5–7} Due to these advantages, combined vaccines have been applied in NIP since 1978, such as DTaP, MMR, and further combined with other non-NIP vaccines latter, such as DTaP-IPV-Hib, DTaP-Hib, MCV-AC-Hib, China CDC typically reported.^{3,8} We notice that Hib vaccine is the most generally combined vaccine in non-NIP vaccines. As cases stand, Hib-combined vaccine is a sort of vaccine consisting of several antigens, including Hib, in one single formulation for preventing various diseases at once.

Haemophilus influenzae is a gram-negative coccobacillus which exists in encapsulated and non-encapsulated strains with six identified serotypes, one of which, serotype b, is responsible for approximately 95% of all invasive disease, such as pneumonia, meningitis, and etc.⁹ Hib disease could occur in any age group, but over 90% of cases of invasive Hib disease occur in children less than 5 years of age.¹⁰ WHO estimated that Hib causes about 3 million cases of serious disease and 386,000 children deaths every year, including 14% cases and 5.1% deaths of Chinese children or so.^{11,12} Randomized controlled trials and observational studies of the clinical effectiveness of Hib vaccines against pneumonia, meningitis and other forms of invasive Hib disease have demonstrated that Hib vaccine effectively protects against these diseases.^{13–15} Watt estimated that for children born in 2000, about 338,000 future Hib cases (uncertainty range 304,000–542,000) and 12,500 future Hib deaths (uncertainty range 8300–20,000) were averted by vaccination.¹⁶

WHO suggested that vaccination remains the only effective means of preventing Hib disease, and the use of Hib vaccines should be part of a comprehensive immunization strategy for children.⁹ However, although the Hib-combined vaccine synthesized advantages of combined vaccine and Hib vaccine, comparing with more than 15.6 million doses Hib-singled vaccine (the second highest non-NIP vaccine), the reported administrations of the combined vaccine were approximately 1.07 million doses in China, accounting for merely around 6.4% administrations of Hib vaccines.³ 152 countries' Hib3 coverage were higher than 80% among 194 WHO member countries in the world 2014 estimated by WHO-UNICEF, whereas 46.72% Hib2 coverage that China CDC estimated in the same year.^{3,17} By 2021, only China has not introduced Hib vaccine into the NIP among 194 WHO member counties and regions.¹⁸

Under the circumstance, parents have to make a choice between the traditional single Hib vaccine with cheaper price and relatively expensive Hib-combined vaccine with multi-advantage. Here comes “vaccine hesitancy” to parents over whether they should administer the Hib-combined vaccine for their children less than 5 years of age. Take the DTaP-IPV-Hib combined vaccine for example, if parents prefer the combined vaccine, the schedule of administration decreases from 12 doses that separated administration needed, to 4 doses following lower risk of adverse event, yet the price may not be affordable for some family. Otherwise, if parents intend to vaccinate children with single vaccines separated with other first-class vaccines, they have to put off the administration of

Hib vaccine after 6 months of age, so that children may not have access to protection before high-incidence period of Hib diseases.⁷

Vaccine hesitancy refers to delay in acceptance or refusal of vaccination despite availability of vaccination services, which is defined by Strategic Advisory Group of Experts Working Group on Vaccine Hesitancy.¹⁹ The working group drafted a “Model of Determinants of Vaccine Hesitancy” (MDVH), known as “3Cs Model” (i.e., confidence, complacency, and convenience), around three main determinants of vaccine hesitancy: (1) contextual influences, arising due to historical, socio-cultural, environmental, health system/institutional, economic or political factors; (2) individual and social group influences, arising from personal perceptions of the vaccine or social/peer environment; (3) vaccine/vaccination-specific issues, which directly related to vaccine or vaccination.¹⁹ Actually, determinants of MDVH were originated from classic models (e.g., Health Belief Model),²⁰ yet without analysis framework. Therefore, the determinants of MDVH are in fair accordance with that of Health Belief Model (HBM) which rightly consider determinants and correlations, and explore possible pathways in terms of those above-mentioned factors with specific analysis framework.

HBM is the most widely used health behavior theories in the behavioral science. HBM was developed in the 1950s by social psychologists Hochbaum, Rosenstock and others to explain the failure of people participating in programs to prevent and detect disease, and was extended later to study people's behavioral responses to health-related conditions, which includes six key components: perceived threats (formed by perceived susceptibility and severity of getting disease or condition), perceived benefits of taking action, perceived barriers to taking action, cues to action, self-efficacy, and individual behavior.²¹

Consequently, the main purpose of this article is going to explore determinants of Hib-combined vaccine hesitancy of Chinese parents based on theories of MDVH and HBM with Structural Equation Model (SEM) analysis, and to provide behavioral intervention measures and approaches to tackle vaccine hesitancy and to improve the vaccine coverage in China.

Methods

Study design

A cross-sectional study was performed in all 11 cities of Zhejiang Province located in the east of China during the period between March and April of 2021. These cities were in different development stages according to the GDP of 2019. Specifically, six cities reached to GDP over 500 billion yuan were relatively developed, while the rest under 500 billion yuan of GDP were viewed as developing cities. We conducted an accidental sampling process in randomly selected 26 local healthcare centers under 20 counties (one or two healthcare centers per county) of these 11 cities, when parents who came for vaccine administration, clinical consultation or regular physical examination for their young children.

With 88.2% valid sample, 2531 parents were recruited in the study. Parents completed a self-reported questionnaire in electronic form, which was self-developed based on theories of MDVH and HBM, under the support of trained and experienced research assistants from local healthcare centers. Informed consent was obtained from all individual participants during the process of investigation, and the participation of subjects were absolutely voluntary, refusal or quitting the survey without any negative consequences.

Measures

The self-developed online questionnaire was composed of seven parts, including socio-demographic characteristics, Perceived Benefits (PBe), Perceived Barriers (PBa), Perceived Threats (PT), Self-Efficacy (SE), Cues to Action (CA), and Vaccine Hesitancy (VH).

Gender, age (≤ 30 , 31–40, > 40), education (middle school or below, high school, college/university or above), occupation (healthcare professional, non-healthcare professional), yearly family income (≤ 100 , 101–200, 201–300, > 300 thousand yuan), and city were included in the part of socio-demographic characteristics.

For items of the latent variables (Table 2) mentioned above, the 5-points Likert scale provided responses categories from “very disagreeable” to “very agreeable,” which were assigned from “1” to “5” to indicate personal inclination (opposite assignment was applied in Vaccine Hesitancy).

Statistical analysis

Description of the socio-demographic of study sample was presented in text and tabulated. Student's *t* tests and one-way ANOVAs were conducted to compare the vaccine hesitancy across socio-demographic characteristics, and LSD tests were conducted for multiple comparisons after statistically significant results showed in one-way ANOVAs. The variable of socio-economic status (SES), which comprised statistically significant socio-economic-related characteristics (i.e., education, occupation, and family income), was constructed according to the results of comparisons of vaccine hesitancy.

Confirmatory Factor Analysis (CFA) was performed to confirm the factor structure of the scale by analyzing the composite reliability of items of a latent variable, and discriminant validity between the latent variables, based on standard factor loading of each item. Pearson correlation analysis was performed to analyze correlations between latent variables. Structural equation model for total sample was constructed based on correlations between latent variables and theories of HBM and TPB to explore possible relations between latent variables, and verify the model by goodness of fit (we hypothesized that (1) Perceived benefits/Vaccine attitude, Perceived Threats, and Cues to action/Subjective norm have positive effects on Self-efficacy/Perceived behavioral control and negative effects on Vaccine Hesitancy; (2) Perceived Barriers has a negative effect on Self-efficacy/Perceived behavioral control and a positive effect on Vaccine Hesitancy; (3) Self-efficacy/Perceived behavioral control has a negative effect on Vaccine Hesitancy).

Multi-group Structural Equation Model (MSEM) was applied to investigate structural variance of latent variables across groups of statistically significant socio-demographic characteristics after measurement invariance of the scale was confirmed. Measurement invariance is the most commonly tested by fitting and comparing a series of nested models, with each model constraining an additional set of parameters to be equal across groups. If the structural constraint results in a statistically significant chi-square change/degree of freedom change between nested models, then the parameters are deemed variant across groups, i.e., the models among groups are viewed as partial invariance. Three types of nested models were reported: (1) an unconstrained model with no impositions of equality constraints (M_{u} ; configural invariance); (2) a constrained model that assumed all factor loadings being equal (measurement weights) across groups (M_{m} ; measurement invariance); (3) a constrained model that assumed all path coefficients being equal across groups based on measurement invariance (M_{s} ; structure invariance).

SPSS version 24.0 and Amos version 22.0 were used for analyzing; maximum likelihood method was used for parameter estimation in CFA and SEM; bootstrap was performed with 5,000 bootstrap samples to estimate biased-corrected 95% confidence intervals and statistical significance in MSEM; the criteria for CFA and SEM analysis were Standard Factor Loading (SFL) > 0.5 ,²² Composite Reliability (CR) > 0.7 ,²³ Average Variance Extracted (AVE) > 0.5 ,²⁴ Comparative Fit Index (CFI) > 0.9 ,²⁵ Tucker-Lewis Index (TLI) > 0.9 ,²⁶ Standardized Root Mean Square Residual (SRMS) < 0.08 ,²⁷ and Root Mean Square Error of Approximation (RMSEA) < 0.08 ,²⁸ and *p* value < 0.05 was considered as statistical significance.

Results

Socio-demographic characteristics

As shown in Table 1, among all the included sample, 1995 (78.8%) were female (mother); about half of them ($n = 1479$, 58.4%) aged from 31 to 40 years; most of them ($n = 1618$, 63.9%) came from developed cities. 1507 (59.5%) reported education of college/university or above level; 460 (18.2%) were healthcare professionals; most of them ($n = 1901$, 75.1%) reported family income ≤ 200 thousand yuan per year. 537 (21.2%) were at low SES (high school or below, non-healthcare professional, ≤ 100 thousand yuan per year), 368 (14.5%) were at high SES (college/university or above, healthcare professional, > 100 thousand yuan per year), and the rest of them ($n = 1626$, 64.3%) were at middle SES.

Vaccine hesitancy

Vaccine hesitancy for total sample was 2.184 ± 0.777 (95%CI: 2.153–2.214), 1436 (56.7%) of them had low vaccine hesitancy ($VH \leq 2$), 991 (39.2%) of them had medium vaccine hesitancy ($2 < VH \leq 3$), and the rest of them ($n = 104$, 4.1%) had high vaccine hesitancy ($VH > 3$).

As shown in Figure 1, the groups of gender, education, occupation, family income, and SES presented statistically significant different in vaccine hesitancy. Specifically, group aged > 40 years (2.298 ± 0.721 , 95%CI: 2.298–2.372) had highest

Table 1. Description of study sample ($n = 2531$).

Characteristics	<i>n</i>	%
Gender		
Male	536	21.2
Female	1995	78.8
Age		
≤30	683	27.0
31–40	1479	58.4
>40	369	14.6
City		
Developed city	1618	63.9
Developing city	913	36.1
Education		
middle school or below	477	18.9
high school	547	21.6
collage/university or above	1507	59.5
Occupation		
Healthcare professional	460	18.2
Non-healthcare professional	2071	81.8
Family income (thousand yuan/year)		
≤100	836	33.0
101–200	1065	42.1
201–300	400	15.8
>300	230	9.1
Socio-economic status		
Low	537	21.2
Middle	1626	64.3
High	368	14.5

vaccine hesitancy ($F = 9.205, p < .001$); group with education of middle school or below ($2.317 \pm 0.726, 95\%CI: 2.251-2.382$) and high school ($2.282 \pm 0.810, 95\%CI: 2.214-2.350$) had higher vaccine hesitancy ($F = 19.096, p < .001$); non-healthcare professional ($2.214 \pm 0.779, 95\%CI: 2.181-2.248$) had higher vaccine hesitancy ($t = 4.308, p < .001$); group earned family income ≤ 100 thousand yuan per year ($2.290 \pm 0.768, 95\%CI: 2.237-2.342$) had highest vaccine hesitancy ($F = 8.527, p < .001$); group at low SES ($2.335 \pm 0.763, 95\%CI: 2.271-2.400$) had highest vaccine hesitancy ($F = 19.411, p < .001$).

Table 2. Confirmatory factor analysis.

Latent variables	Items	Standard Factor Loading	Composite Reliability
Perceived Benefits	PBe1. Combined vaccine prevents multi-disease effectively.	0.799***	0.910
	PBe2. Combined vaccine has less adverse events and more safety than traditional single vaccine.	0.865***	
	PBe3. Combined vaccine decreases frequency of administrations than traditional single vaccine.	0.861***	
	PBe4. It's necessary to administrate combined vaccine.	0.861***	
Perceived Barriers	PBa1. The knowledge of combined vaccine (type, formulation, content, etc.)	0.792***	0.929
	PBa2. The knowledge of vaccination policy (routes, methods, schedule, etc.)	0.883***	
	PBa3. The availability of combined vaccine (provide or not, provision amount, administration site amount, etc.)	0.945***	
	PBa4. The convenience of vaccination (administration hours, geographic distance, transport convenience, etc.)	0.894***	
	PBa5. The cost of combined vaccine	0.725***	
Perceived Threats	PT1. There are probabilities of getting infected of Hib for my children.	0.692***	0.867
	PT2. I'm worried about it would be serious if my children get infected of Hib.	0.905***	
	PT3. The disease would affect the body of children and even lead to disability and death.	0.875***	
Self-Efficacy	SE1. I have the ability (knowledge, time, money, etc.) to vaccinate my children with Hib-combined vaccine.	0.873***	0.913
	SE2. I'm confident to overcome barriers to vaccinate my children with Hib-combined vaccine.	0.926***	
	SE3. It's under my control to vaccinate my children with Hib-combined vaccine.	0.846***	
Cues to Action	CA1. My family and friends who benefited from the vaccine suggested me to vaccinate my children with Hib-combined vaccine.	0.910***	0.910
	CA2. Doctors suggested me to vaccinate my children with Hib-combined vaccine.	0.918***	
Vaccine Hesitancy	VH1. I'd like to pay money to vaccinate my children with a more beneficial vaccine instead of NIP vaccine.	0.811***	0.918
	VH2. I prefer combined vaccine to traditional single vaccine.	0.910***	
	VH3. I'd like to vaccinate my children with self-paid Hib-combined vaccine.	0.940***	

*** $p < .001$.

Confirmatory factor analysis

As shown in Tables 2 and 3, the standard factor loadings of all items ranged from 0.692 to 0.945 with statistical significance; Perceived benefits, Perceived Barriers, Perceived Threats, Self-Efficacy, and Cues to Action for total sample were 3.726 ± 0.797 (95%CI: 3.695–3.757), 2.983 ± 1.266 (95%CI: 2.933–3.032), 3.489 ± 0.809 (95%CI: 3.458–3.521), 3.722 ± 0.776 (95%CI: 3.692–3.752), 3.691 ± 0.800 (95%CI: 3.660–3.722), respectively; CRs and AVEs of all latent variables between 0.867 to 0.951, and 0.688 to 0.835, respectively; all square roots of AVEs of latent variables, from 0.829 to 0.914, were higher than their correlations with other latent variables (i.e., high discriminate validity) which ranged from 0.280 to 0.825 with statistical significance. As Table 4 shows, the fit indices of CFA ($\chi^2/df = 7.433$, CFI = 0.979, TLI = 0.975, SRMR = 0.022, RMSEA = 0.050) were satisfied with criteria.

Structural equation model for total sample

As shown in Figure 2, Tables 4 and 5, the fit indices ($\chi^2/df = 7.394$, CFI = 0.979, TLI = 0.975, SRMR = 0.023, RMSEA = 0.050) of SEM for total sample were satisfied with criteria. Latent variables of Self-Efficacy (Standard Total Effect (STE) and Standard Direct Effect (SDE) = -0.516, 95%CI: -0.645–0.388, $p < .001$), Cues to Action (SDE = -0.115 (95%CI: -0.251–0.090, $p = .003$), Standard Indirect Effect (SIE) = -0.322 (95%CI: -0.439–0.231, $p < .001$), STE = -0.437, 95%CI: -0.550–0.314, $p < .001$), Perceived Threats (SDE = -0.199 (95%CI: -0.281–0.130, $p < .001$), SIE = -0.106 (95%CI: -0.153–0.067, $p < .001$), STE = -0.305, 95%CI: -0.381–0.233, $p < .001$), Perceived Benefits (SDE = -0.132 (95%CI: -0.214–0.053, $p = .003$), SIE = -0.069 (95%CI: -0.128–0.017, $p = .009$),

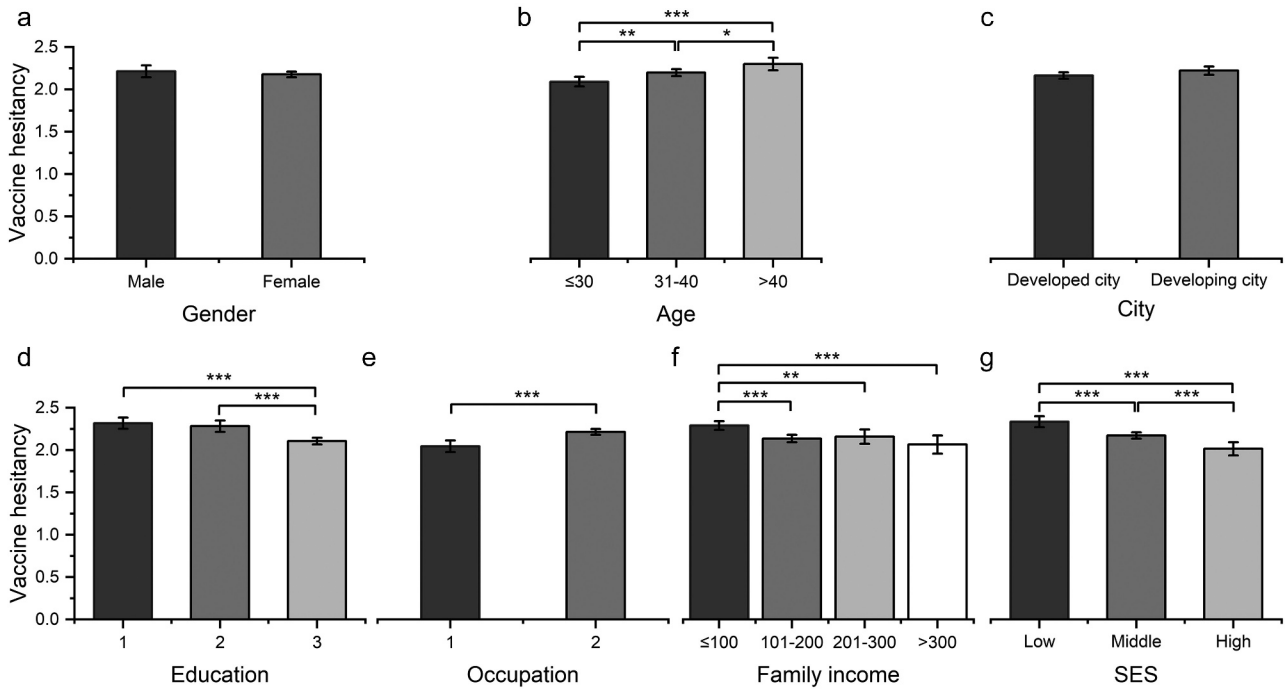


Figure 1. Comparisons of vaccine hesitancy across gender, age, city, education, occupation, family income, and SES. The error bars indicated 95% confidential interval; group 1, 2, and 3 in figure D represented middle school or below, high school, and college/university or above, respectively; group 1 and 2 in figure E represented healthcare professional and non-healthcare professional, respectively; * $p < .05$, ** $p < .01$, *** $p < .001$

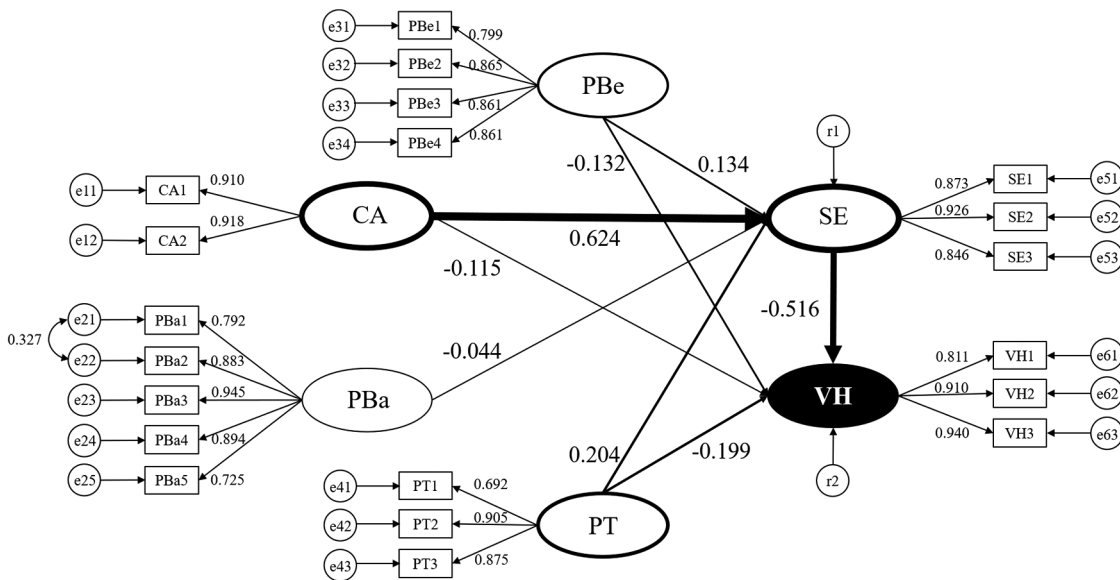


Figure 2. Structural equation model for total sample. The width of the ellipse and arrow in the structural model indicated the effect of factors, one-way straight arrows in structural model indicated the effect path of each factor with standardized regression weights, one-way straight arrows in measurement model indicated measurement loadings of each item in the scale, one-way straight arrows indicated the effect path of each factor with standardized regression weights, two-way arrows indicated correlations between coefficients; e=measurement errors, r =residuals; correlations between CA, PBA, PBe, and PT were statistically significant, but didn't show in the figure; all parameters were statistically significant ($p < 0.05$)

STE = -0.201, 95%CI: -0.307-0.102, $p < .001$), and Perceived Barriers (STE and SIE = 0.023, 95%CI: 0.010-0.040, $p < .001$) all presented statistically significant, direct and/or indirect effects on Vaccine Hesitancy with R -square 0.819. As a result, Self-Efficacy partially mediated between Cues to Action, Perceived Threats, Perceived Benefits and Vaccine Hesitancy, respectively.

Multi-group structural equation model

As shown in Table 6, the fit indices of MSEMs for SES groups (CFI = 0.963 to 0.977, TLI = 0.954 to 0.971, SRMR = 0.025 to 0.033, RMSEA = 0.052 to 0.071) were satisfied with criteria; chi-square change/degree of freedom change for SES ($\Delta\chi^2/\Delta df = 27.572/28$, $p = .487$) was statistically insignificant

Table 3. Values and Average Variance Extracted (AVE) of latent variables, and matrix of Pearson correlation coefficients between latent variables.

Latent variables	Mean	SD	PBe	PBa	PT	SE	CA	VH	AVE
Perceived Benefits	3.726	0.797	0.847						0.717
Perceived Barriers	2.983	1.266	-0.326***	0.851					0.725
Perceive Threats	3.489	0.810	0.645***	-0.280***	0.829				0.688
Self-Efficacy	3.722	0.776	0.764***	-0.335***	0.716***	0.882			0.778
Cues to Action	3.691	0.800	0.794***	-0.308***	0.683***	0.825***	0.914		0.835
Vaccine Hesitancy	2.184	0.777	-0.740***	0.325***	-0.696***	-0.822***	0.774***	0.889	0.790

SD=Standard Deviation; the bold font in the diagonal of the table is the square root of AVE; *** $p < .001$.

Table 4. Goodness of fit indices of Confirmatory Factor Analysis (CFA) and structural equation model for total sample.

Model	χ^2	df	χ^2/df	CFI	TLI	SRMR	RMSEA
CFA	1144.611***	154	7.433	0.979	0.975	0.022	0.050
M_t	1146.139***	155	7.394	0.979	0.975	0.023	0.050

M_t =model for total sample; *** $p < .001$.

Table 5. Parameters of structural model of structural equation model for total sample.

Path	B	β	STE	R ²
CA to SE	0.588***	0.624***	-0.437	
CA to VH	-0.099**	-0.115**		
PT to SE	0.194***	0.204***	-0.305	
PT to VH	-0.172***	-0.199***		
PBe to SE	0.134***	0.134***	-0.201	
PBe to VH	-0.120***	-0.132***		
PBa to SE	-0.032***	-0.044***	0.023	
SE to VH	-0.471***	-0.516***	-0.516	0.856
VH				0.819

B=unstandardized regression weight, β =standardized regression weight; ** $p < .01$, *** $p < .001$.

Table 6. Measurement and structural invariance of multi-group structural equation models across SES groups.

Model	χ^2	df	χ^2/df	CFI	TLI	SRMR	RMSEA	$\Delta\chi^2/\Delta df$
M_1	382.550***	155	2.468	0.976	0.971	0.029	0.052	
M_2	861.536***	155	5.558	0.977	0.972	0.025	0.053	
M_3	439.992***	155	2.839	0.963	0.954	0.033	0.071	
M_u	1684.522***	465	3.623	0.975	0.969	0.029	0.032	
M_m	1712.094***	493	3.473	0.975	0.971	0.030	0.031	27.572/28
M_s	1768.964***	509	3.475	0.974	0.971	0.031	0.031	56.870/16***

M_1 =model for low SES group, M_2 =model for middle SES group, M_3 =model for high SES group, M_u =unconstrained model, M_m =model for measurement weights constrained, M_s =model for measurement and structural weights constrained; *** $p < .001$.

after constrained measurement weights based on M_u , which demonstrated group-invariance in measurement models in MSEM, and M_m could be deemed as the same model as M_u , so that the scale was suitable for different SES groups; chi-square change/degree of freedom change for a SES ($\Delta\chi^2/\Delta df = 56.870/16$, $p < .001$) was statistically significant after constrained structural weights based on M_m , which indicated SES moderated relations between latent variables in MSEM, so that the cross-validity of structure models brought about variance of path coefficients between SES groups.

As shown in Figure 3, MSEM across SES groups with different structure of latent variables and without parameters constrained were constructed after structural variance was presented, and the fit indices for SES groups ($\chi^2 = 1323.969$, $df = 276$, $\chi^2/df = 4.797$, CFI = 0.975, TLI = 0.969, SRMR = 0.027, RMSEA = 0.039) were satisfied with criteria. As Table 7

shows, in low SES group, Cues to Action imposed STE -0.621 (95%CI: -0.867 – 0.389 , $p < .001$) on Vaccine Hesitancy; in middle and high SES groups, Self-Efficacy imposed STE -0.560 (95%CI: -0.668 – 0.444 , $p < .001$), and -0.685 (95%CI: -0.841 – 0.454 , $p < .001$) on Vaccine Hesitancy, respectively. The effect Cues to Action exerted on Self-Efficacy in high SES group (SDE = 0.818) was significantly higher than that in other SES groups (CR = 2.676 and 3.169 > 1.960); and the effect Self-Efficacy exerted on Vaccine Habitancy was the highest in high SES group (SDE = -0.685), while that in other SES groups (SDE = -0.560 and -0.263) were significantly lower (CR = > -2.582 , -3.658 , and $-2.173 < -1.960$).

Discussion

As a behavioral outcome of a complex decision-making process, vaccination acceptance can be potentially influenced by a wide range of factors. In “3Cs Model,” confidence is defined as trust in the effectiveness and safety of vaccines, in the system that delivers them (the reliability and competency of the health services and health professionals), and in the motivations of policy-makers who decide on the needed vaccines; complacency exists where perceived risks of vaccine-preventable diseases are low and vaccination is not deemed a necessary preventive action; and convenience is a significant factor when physical availability, affordability and willingness-to-pay, geographical accessibility, ability to understand, appeal of immunization services and so on affect uptake.¹⁹ Apart from “3Cs” mentioned above, two more “Cs” of determinants on vaccine hesitancy (i.e., communications and context) were proposed by Razai and Mills, which refer to sources of information and socio-demographic characteristics, respectively.²⁹ The “5Cs” of determinants underpinned the constructs which constituted the framework in the research.

Socio-demographic characteristics, including gender, age, city, education, occupation, income, and socio-economic status, which the “context” refers to were involved in the survey. Socio-economic status was defined by Mueller and Parcel in 1981 as the relative position of a family or individual on a hierarchical social structure, based on their access to or control over wealth, prestige and power.³⁰ More recently, SES has been defined as a broad concept that refers to a number of more measurable factors, including education, occupation, and family income by sociologists, economists, and other scientists, which can have either a positive or negative impact on a person’s life and health. In our research, the population was categorized into low, middle, and high SES based on statistically significant factors of education, occupation, and family income. We found that parents who were at low SES had the

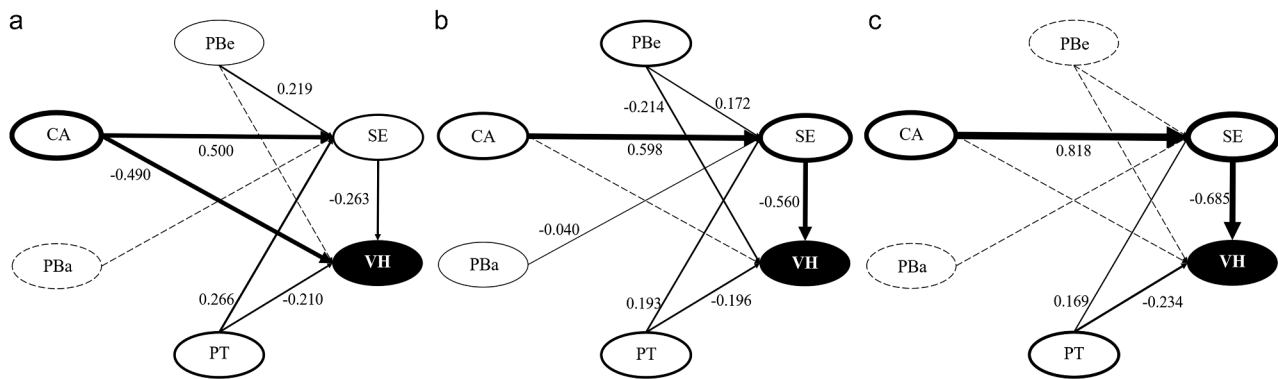


Figure 3. Comparisons between structural models of multi-group structural equation model across SES groups. Figure a for low SES group, figure b for middle SES group, figure c for high SES group; The width of the ellipse and arrow indicated the effect of latent variables, one-way straight arrows indicated the effect path of each factor with standardized regression weights; correlations between CS, PBa, PBe, and PT were statistically significant, but didn't show in the figures; path coefficients with solid line were statistically significant ($p < .05$)

Table 7. Parameters comparisons between structural models of multi-group structural equation model across SES groups.

Path		CA to SE	CA to VH	PT to SE	PT to VH	PBe to SE	PBe to VH	PBa to SE	SE to VH	VH
M ₁	B	0.467***	-0.436***	0.260***	-0.196***	0.220*			-0.250**	
	β	0.500***	-0.490***	0.266***	-0.210***	0.219*			-0.263**	
	STE	-0.621		-0.280		-0.058			-0.263	
	R ²								0.875	0.850
M ₂	B	0.561***		0.182***	-0.166***	0.174***	-0.194***	-0.030**	-0.504***	
	β	0.598***		0.193***	-0.196***	0.172***	-0.214***	-0.040**	-0.560***	
	STE	-0.335		-0.304		-0.310		0.023	-0.560	
	R ²								0.845	0.825
M ₃	B	0.770***		0.153***	-0.204***				-0.658***	
	β	0.818***		0.169***	-0.234***				-0.685***	
	STE	-0.560		-0.349					-0.685	
	R ²								0.908	0.778
M ₁ vs. M ₂	CR	0.891		-1.385	0.550	-0.489			-2.582*	
M ₁ vs. M ₃	CR	2.676*		-1.536	-0.107				-3.658*	
M ₂ vs. M ₃	CR	3.169*		-0.567	-0.673				-2.173*	

B = unstandardized regression weight, β = standardized regression weight, CR = Critical Ratio; M₁ = model for low SES group, M₂ = model for middle SES group, M₃ = model for high SES group; * $p < .05$, ** $p < .01$, *** $p < .001$.

highest vaccine hesitancy, in other words, parents who had high school or below education, worked as non-healthcare professional, and earned less than 100 thousand yuan per year in their family as a whole were less likely to vaccinate their children with Hib-combined vaccine, which might result from that they were not confident in the safety and effectiveness of the vaccine, were not fully aware of susceptibility of Hib and severity of Hib disease, were lack of strong suggestions and recommendations from doctors and relatives, and/or had low self-efficacy of vaccinating their children with combined vaccine.

Cues to Action, factors (e.g., salient individuals or groups) which trigger action, was strongly and negatively associated with vaccine hesitancy. We found that this determinant strongly and negatively affected vaccine hesitancy especially in parents at low SES. For parents at low SES with weak education background and family condition, they are more eager for someone reliable to help with making decision on whether it is better to vaccinate their children with combined vaccine. Therefore, the cues from intimate relatives or professionals, even social media would greatly accelerate the process of decision making, and directly or indirectly (through self-efficacy) reduce vaccine hesitancy.

Self-Efficacy was the most crucial determinant of decreasing vaccine hesitancy particularly for parents at middle SES and above. Self-efficacy is defined by Bandura³¹ as the degree of one's feelings about one's ability to accomplish goals. For these groups of parents with strong material condition and health awareness, internal momentum became the biggest driver of decreasing vaccine hesitancy instead of external cues. Self-efficacy in the study is vaccinating children with initiative and internal momentum based on a preliminary tendency toward the combined vaccine and basic knowledge in terms of the risk and severity of Hib. As a result, considering low vaccine hesitancy in parents at high SES, effective intervention measures regarding improvement of self-efficacy, e.g., health education and public dissemination related to susceptibility and severity of Hib diseases, and benefits of combined vaccine, should mainly aim at parents at middle SES.

Fundamentally, introducing Hib vaccine into the NIP is the most vital approach, which was researched to prevent approximately 2700 deaths and 235,700 cases of Hib disease, and save 2.487 billion yuan in surgery for the 2017 birth cohort at the Chinese national level.³² If so, it could free parents from payment and from hesitancy of choosing either single or combined vaccine, could tremendously tackle the vaccine hesitancy and

improve the vaccine coverage, and could fundamentally prevent Hib diseases from Chinese children. Consequently, we call on China to introduce Hib vaccine into the NIP as soon as possible, so as to make contribution to build a community of shared health for mankind and Chinese children.

The study has some limitations. First, the research was a cross-sectional study, which could not address the causal effects between determinants and vaccine hesitancy. Determinants could affect conversely or reciprocally. Second, the parents were recruited by accidental sampling, and may not be representative, and it's relatively hard to generalize the findings to other kind of vaccine. Third, the determinant of "communication" was not included in the research framework, which may account for greatly or may affect the associations between other determinants and vaccine hesitancy. As a matter of fact, social media platforms in terms of Hib-combined vaccine barely offered to the public, which could be a reason why we didn't include the factor into the research framework. Fourth, the scales in the survey were not completely express the core meaning of each construct or "3Cs/5Cs," future studies should promote the scales in quantity and integrity. Fifth, the scales were self-reported, hence, the subjective intention might exaggerate or conceal the fact situation.

Conclusions

Hib-combined vaccine hesitancy in Chinese parents was low, the lower the socio-economic status, the higher the vaccine hesitancy, or rather, it was low in groups of parents at high socio-economic status, however, it was relatively high in the group at low socio-economic status. Overall, latent variables of Perceived Benefits, Perceived Barriers, Perceived Threats, Self-Efficacy, Cues to Action all imposed effect on vaccine hesitancy to varying degrees, amongst which Self-Efficacy, Cues to Action, and Perceived Threats played primary role in declining vaccine hesitancy and increasing vaccine coverage, yet Perceived Barriers got the least impact.

Hence, significant effect would be attained after considering and taking highly recommended comprehensive vaccinating intervention measures and approaches for parents with focused socio-demographic characteristics, including providing external cues of strong suggestions and recommendations regarding vaccine administration from relatives and professionals, even social media, mainly for parents who were at low socio-economic status; and promoting internal self-efficacy of vaccine administration through health education and public dissemination related to susceptibility and severity of Hib diseases, and benefits of combined vaccine mainly targeting at parents at middle and high socio-economic status.

Abbreviation

Hib	<i>Haemophilus influenzae</i> type b
DTaP	Diphtheria, tetanus, acellular pertussis
MMR	Measles, mumps and rubella
IPV	Inactivated poliovirus
MCV-AC	Meningococcal group AC

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Ethical statement

The manuscript does not contain clinical studies or patient data. The study procedure was carried out in accordance with the rules of ethics. Ethics approval was obtained from the Ethics Committee, Zhejiang Provincial Center for Disease Control and Prevention.

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