

RESEARCH PAPER



## Low willingness to vaccinate against herpes zoster in a Chinese metropolis

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### ABSTRACT

**Background:** Herpes zoster vaccine (HZV) has been available in China's mainland since June 2020. This study estimated willingness to receive HZV to characterize factors that may influence vaccination willingness.

**Methods:** We conducted a face-to-face questionnaire survey in adults aged 50–69 years in 13 communities in Shanghai in late 2020. We explored the relationship between vaccination willingness and independent factors including demographic factors, medical history, knowledge of herpes zoster and HZV, and vaccine hesitancy. Outcomes included participants' willingness to vaccinate themselves, their partners, and their parents, under both the current payment scenario (self-payment) and a hypothetical scenario (payment by basic medical insurance).

**Results:** A total of 1672 respondents aged 50–69 years were included in this study. The proportion of respondents willing to get vaccinated was 16.57% for themselves, 13.88% for their partners, and 8.49% for their parents. If the vaccine was covered under insurance, these numbers increased to 72.25%, 62.50%, and 29.96%, respectively. Younger age, female gender, higher income, higher educational level, local residents, and lower vaccine hesitancy were associated with increased willingness to vaccinate. Knowledge of herpes zoster and HZV positively influenced the willingness in the hypothetical payment scenario.

**Conclusion:** We determined a very low willingness to vaccinate HZV in adults aged 50–69 years in a Chinese metropolis. Decreasing costs is important to increase coverage. Additionally, strengthening advocacy and health promotion for the vaccine will be particularly important, especially for groups with certain underlying diseases.

### ARTICLE HISTORY

Received 25 May 2021

Revised 7 July 2021

Accepted 20 July 2021

### KEYWORDS

Herpes zoster; varicella-zoster virus; herpes zoster vaccine; vaccination willingness; vaccine hesitancy; influencing factor

## Introduction

Herpes zoster, or shingles, is an infectious disease caused by reactivation of varicella-zoster virus (VZV) that has been latent in the dorsal root ganglia or intracranial ganglia of the spinal cord for a long time, characterized by the appearance of herpes in clusters along the peripheral nerves on one side of the body.<sup>1–3</sup>

Herpes zoster is more common among elderly and people with immunodeficiency, in which approximately 22% of the cases may progress to postherpetic neuralgia (PHN). The pain can last for months and even years, and seriously affects the quality of life.<sup>4</sup> Data from Canada, Israel, Japan, China and the USA estimated the age-adjusted incidence of herpes zoster to be 3.4/1000 person-years – 5.0/1000 person-years.<sup>5</sup> A study in 27 European countries showed that the incidence rate for people over 50 years old was 9.92/1000 person-years, and increased with age.<sup>6</sup> Compared to healthy people, incidence of herpes zoster may be higher in people with immunodeficiency and certain underlying diseases. Studies found that bone marrow or stem cell transplant recipients (43.03/1000 person-years) had a higher incidence than solid organ transplant recipients (17.04/1000 person-years).<sup>7</sup> In addition, people with diabetes were more susceptible to herpes zoster, as previously documented in Japan and Israel.<sup>8,9</sup>

Two kinds of herpes zoster vaccines (HZV) have been available globally. One is the live attenuated herpes zoster

vaccine Zostavax (ZVL, Merck), which is one-dose schedule and applicable for people aged 60 and above.<sup>10</sup> Another one is the recombinant zoster vaccine Shingrix (RZV, GlaxoSmithKline), which is two-dose schedule and applicable for people aged 50 and above.<sup>11</sup> Vaccination coverage of HZV has remained low, e.g., 6.1% in Canada (2009–2013) and 25.8% in the USA (2007–2013).<sup>12,13</sup> There are multiple factors that could influence vaccination uptake of HZV, including age, educational level, history of herpes zoster infection, and awareness of herpes zoster and HZV.<sup>14</sup> RZV came on to the Chinese market in June 2020. Initial investigations have shown that the Chinese population ≥50 years has relatively low willingness to receive this vaccine due to its high price (one dose is CNY 1600, or approximately USD 250). With the goal of providing scientific evidence for increasing vaccination uptake in the future, this study estimated willingness to receive HZV to characterize factors that may influence vaccination willingness.

## Methods

### Study design

We designed a survey in adults aged 50–69 years in Shanghai, China, in late 2020. A convenience sampling strategy was

employed to recruit respondents in a total of 13 urban and rural communities.

### Questionnaire design

This study investigated the answers to the questions on herpes zoster and HZV, using a questionnaire which was completed by professionally trained investigators in a face-to-face manner. The content of the questionnaire included:

- (1) Demographics such as age, gender, household registration, educational level, and monthly income;
- (2) Past medical history, including herpes zoster and varicella, systemic lupus erythematosus, cardiovascular and cerebrovascular diseases, rheumatoid arthritis, diabetes, chronic respiratory diseases, malignant tumors, and other immunodeficiency diseases;
- (3) Knowledge of herpes zoster and HZV, and willingness to vaccinate themselves, their partners and parents against herpes zoster;
- (4) Vaccine hesitancy.

### Scoring of answers to the questions

In order to measure the knowledge of survey respondents, we scored their answers as follows. Generally, in the questions transformed into categorical variables, 3 points were given for correct answers, 0 point for false answers, and 1 point for those answered “not sure” (Table 1). In addition, several questions were transformed into continuous variables, including principal symptoms of herpes zoster, principal incentives to herpes zoster, and transmission routes of herpes zoster, in which 1 point was given for each correct answer and overall points were counted.

Vaccine hesitancy was measured with a 10-item scale, with each question using a 5-point Likert scale, as described elsewhere.<sup>15</sup> Negative attitude questions toward vaccine hesitancy were scored directly; for positive attitude questions, six points were subtracted from the questions' scores so that all items had scores in the same direction. Then, scores of vaccine hesitancy were added together to get the total score, which could range between 10 and 50.

### Statistical analysis

Descriptive statistics compared the demographic characteristics of survey respondents. The proportion of respondents being willing to be vaccinated with HZV was calculated, and then was standardized according to the population demographics (age/sex distribution) in Shanghai in the 2010 census. Moreover, multivariable logistic regression analysis was employed to separately determine the factors associated with the willingness to be vaccinated with HZV for themselves, their partners, and their parents, in the current payment scenario (self-payment) and a hypothetical scenario (payment by basic medical insurance). Demographics, medical history, knowledge of herpes zoster and HZV, and vaccine hesitancy were included as independent variables. Statistical analysis was performed

using the IBM SPSS 23.0 (Armonk, NY, USA). A *P* value <.05 was considered statistically significant.

### Ethical approval

This study was approved by the Institutional Review Board (IRB) of the Fudan University School of Public Health (IRB 00002408 and FWA 00002399) under IRB #2021-04-0895 and the IRB of Minhang District Center for Disease Control and Prevention under EC-P-2020-010.

### Results

#### Willingness to vaccinate against herpes zoster

A total of 1672 respondents aged 50–69 years were included in this study. A majority were local residents (80.74%), had an educational level of below college and university (86.72%), and moderate monthly income (67.52%) (Table 1). In the answers to the questions, respondents were relatively likely to know about higher susceptibility to herpes zoster among the elderly (61.48%) and to believe in the vaccine's effectiveness (72.61%); in contrast, they were less likely to know about the risk of re-contracting VZV (36.06%), or to know whether or not there was enhanced susceptibility of having VZV if in contact with those had herpes zoster (29.78%). A majority were “not sure” about the target population of HZV vaccination (82.81%) or about the HZV vaccination schedule (83.97%). In addition, their average ( $\pm$ standard deviation) score for vaccine hesitancy was determined to be  $21.67 \pm 3.63$ , which differed significantly by monthly income ( $F = 5.99, P = .003$ ).

The unstandardized proportion of respondents willing to get vaccinated was 16.57% for themselves and the proportion standardized to Shanghai's age/sex distribution was 17.69%. In the actual payment scenario, 318 respondents were willing to vaccinate, including for themselves ( $n = 277$ ; 16.57%), their partners ( $n = 232$ ; 13.88%), or their parents ( $n = 142$ ; 8.49%), whereas 1354 (80.98%) were unwilling to vaccinate. If the HZV would be included in basic medical insurance, the respondents willing to receive a vaccine increased greatly: for themselves ( $n = 1208$ ; 72.25%), for their partners ( $n = 1045$ ; 62.50%), and for their parents ( $n = 501$ ; 29.96%), while 434 (25.96%) remained unwilling to vaccinate.

#### Factors associated with willingness to vaccinate

We performed six logistic regression models to separately determine the factors associated with the willingness to be vaccinated with HZV for themselves, their partners, and their parents, in the actual payment scenario (self-payment) and assumed scenario (payment by basic medical insurance) (Table 2).

In the actual scenario of self-payment, respondents aged 50–59 years, with a higher educational level, higher monthly income, and lower vaccine hesitancy were more willing to vaccinate (Table 3). In addition, those reported being “not sure” toward the schedule of HZV doses were less willing to vaccinate. However, those had lower knowledge of herpes zoster and HZV, through questions such as susceptibility of

**Table 1.** Willingness to vaccinate herpes zoster vaccines (HZV) for themselves across the demographics and answers to questions.

	No. answered	Respondents willing to vaccinate (%)	Respondents unwilling to vaccinate (%)
<b>Age (years)</b>			
50–59	727	139 (19.12)	588 (80.88)
60–69	945	138 (14.60)	807 (85.40)
<b>Gender</b>			
Male	777	127 (16.34)	650 (83.66)
Female	895	150 (16.76)	745 (83.24)
<b>Location of household registration</b>			
Local	1350	229 (16.96)	1121 (83.04)
Non-local	322	48 (14.91)	274 (85.09)
<b>Educational level</b>			
Middle school or below	831	129 (15.52)	702 (84.48)
High school	619	101 (16.32)	518 (83.68)
College and university	222	47 (21.17)	175 (78.83)
<b>Monthly income (CNY)</b>			
≤ 2000	336	43 (12.80)	293 (87.20)
2001–5000	1129	179 (15.85)	950 (84.15)
≥ 5001	207	55 (26.57)	152 (73.43)
<b>Are people in contact with those who have herpes zoster susceptible to contracting varicella-zoster virus?</b>			
Not susceptible	747	131 (17.54)	616 (82.46)
Not sure	427	115 (26.93)	383 (73.07)
Susceptible	498	31 (6.22)	396 (93.78)
<b>Are the elderly susceptible to contracting varicella-zoster virus?</b>			
Not susceptible	273	57 (20.88)	216 (79.12)
Not sure	371	32 (8.63)	339 (91.37)
Susceptible	1028	188 (18.29)	840 (81.71)
<b>Can people who had had herpes zoster contract varicella-zoster virus again?</b>			
Cannot contract again	526	103 (19.58)	423 (80.42)
Not sure	543	59 (10.87)	484 (89.13)
Can contract again	603	115 (19.07)	488 (80.93)
<b>Did you have herpes zoster?</b>			
No	1401	224 (15.99)	1177 (84.01)
Yes	271	53 (19.56)	218 (80.44)
<b>Did you have varicella?</b>			
No	1455	228 (15.67)	1227 (84.33)
Yes	217	49 (22.58)	168 (77.42)
<b>Can herpes zoster be prevented?</b>			
Cannot be prevented	192	25 (13.02)	167 (86.98)
Not sure	542	65 (11.99)	477 (88.01)
Can be prevented	938	187 (19.94)	751 (80.06)
<b>Can vaccination prevent herpes zoster?</b>			
Cannot prevent	47	4 (8.51)	43 (91.49)
Not sure	396	35 (8.84)	361 (91.16)
Can only relieve the symptoms	15	5 (33.33)	10 (66.67)
Can prevent herpes zoster	1214	233 (19.19)	981 (80.81)
<b>What are the recipients of the HZV vaccination in China?</b>			
Children	159	44 (27.67)	115 (72.33)
Not sure	883	108 (12.23)	775 (87.77)
Adult	91	26 (28.57)	65 (71.43)
Adult ≥50 years	539	99 (18.37)	440 (81.63)
<b>What is the HZV vaccination schedule in China?</b>			
One dose or three doses	110	33 (30.00)	77 (70.00)
Not sure	1404	196 (13.96)	1208 (86.04)
Two doses	158	48 (30.38)	110 (69.62)
<b>What are the principal symptoms of herpes zoster? (multi-choice)</b>			
≥ one correct answer	1380	242 (17.54)	1138 (82.46)
No correct answer	292	35 (11.99)	257 (88.01)
<b>What are the principal incentives to herpes zoster? (multi-choice)</b>			
≥ one correct answer	1136	212 (18.66)	924 (81.34)
No correct answer	536	65 (12.13)	471 (87.87)
<b>What are the transmission routes of herpes zoster? (multi-choice)</b>			
≥ one correct answer	712	133 (18.68)	579 (81.32)
No correct answer	960	144 (15.00)	816 (85.00)

contracting VZV in contact with those who have herpes zoster, susceptibility of contacting VZV among elderly, and targeted population of HZV vaccination in China, were more likely to have higher willingness.

In the hypothetical scenario that HZV would be included in basic medical insurance, age, educational level, and vaccine

hesitancy had a similar impact on the willingness as they did for self-payment (Table 4). In contrast to the actual payment scenario, respondents with higher knowledge of herpes zoster and HZV were more likely to vaccinate. In addition, those with more underlying diseases were more willing to get vaccinated for themselves.

**Table 2.** Factors that influence the respondents' willingness to vaccinate herpes zoster vaccine (HZV) under two payment scenarios.

	Willing to vaccinate themselves (95% CI)	Willing to vaccinate partners (95% CI)	Willing to vaccinate parents (95% CI)
<b>Actual payment scenario (self-payment)</b>			
<b>Age (years)</b>			
50–59	1.455 (1.081–1.959)	1.586 (1.155–2.177)	4.947 (3.149–7.771)
60–69	1.0	1.0	1.0
<b>Educational level</b>			
Middle school or below			0.368 (0.218–0.621)
High school			1.0
College and university	1.0	1.0	1.0
<b>Monthly income (CNY)</b>			
≤ 2000	0.458 (0.269–0.781)	0.445 (0.255–0.775)	
2001–5000	0.570 (0.378–0.860)	0.500 (0.327–0.765)	
≥ 5001	1.0	1.0	1.0
<b>Are people in contact with those who have herpes zoster susceptible to contracting varicella-zoster virus?</b>			
Not susceptible	1.889 (1.181–3.022)	1.777 (1.078–2.930)	
Not sure	2.748 (1.705–4.428)	2.299 (1.379–3.832)	
Susceptible	1.0	1.0	1.0
<b>Are the elderly susceptible to contracting varicella-zoster virus?</b>			
Not susceptible	1.459 (1.007–2.114)		
Not sure			
Susceptible	1.0	1.0	1.0
<b>What are the recipients of the HZV vaccination in China?</b>			
Children	2.035 (1.297–3.192)	2.167 (1.347–3.486)	
Not sure			
Adult			2.137 (1.090–4.189)
Adult ≥50 years	1.0	1.0	1.0
<b>What is the HZV vaccination schedule in China?</b>			
One dose or three doses			
Not sure	0.434 (0.282–0.666)	0.436 (0.277–0.685)	
Two doses	1.0	1.0	1.0
<b>Vaccine hesitancy (score)</b>			
	0.866 (0.829–0.905)	0.860 (0.821–0.901)	0.859 (0.808–0.912)
<b>Hypothetical payment scenario (payment by basic medical insurance)</b>			
<b>Age (years)</b>			
50–59		1.423 (1.133–1.788)	4.255 (3.308–5.475)
60–69	1.0	1.0	1.0
<b>Gender</b>			
Male			0.694 (0.541–0.890)
Female	1.0	1.0	1.0
<b>Location of household registration</b>			
Local	1.671 (1.240–2.253)		
Non-local	1.0	1.0	1.0
<b>Educational level</b>			
Middle school or below	0.578 (0.374–0.894)	0.688 (0.475–0.998)	
High school	0.514 (0.335–0.788)	0.619 (0.429–0.892)	
College and university	1.0	1.0	1.0
<b>Are people in contact with those who have herpes zoster susceptible to contracting varicella-zoster virus?</b>			
Not susceptible			1.508 (1.053–2.160)
Not sure			1.493 (1.025–2.173)
Susceptible	1.0	1.0	1.0
<b>Are the elderly susceptible to contracting varicella-zoster virus?</b>			
Not susceptible			
Not sure	0.680 (0.488–0.947)		
Susceptible	1.0	1.0	1.0
<b>Can people who had had herpes zoster contract varicella-zoster virus again?</b>			
Cannot contract again	0.703 (0.519–0.952)	0.761 (0.583–0.993)	
Not sure			
Can contract again	1.0	1.0	1.0
<b>Can vaccination prevent herpes zoster?</b>			
Cannot prevent	0.477 (0.247–0.921)		
Not sure	0.613 (0.464–0.810)	0.667 (0.514–0.865)	
Can only relieve the symptoms			
Can prevent herpes zoster	1.0	1.0	1.0
<b>What are the recipients of the HZV vaccination in China?</b>			
Children			
Not sure	0.632 (0.465–0.860)	0.609 (0.464–0.799)	0.537 (0.399–0.722)
Adult			
Adult ≥50 years	1.0	1.0	1.0
<b>Vaccine hesitancy (score)</b>			
	0.864 (0.835–0.894)	0.915 (0.888–0.943)	0.945 (0.913–0.979)
<b>Underlying diseases (number)</b>			
	1.539 (1.229–1.926)	–	–

**Table 3.** Factors that influence willingness to receive herpes zoster vaccine (HZV) for themselves or give HZV to their partners and parents under actual payment scenario (self-payment).

	Willing (%)	Unwilling (%)	OR value	95%CI
<b>For themselves</b>				
<b>Age (years)</b>				
50–59	139 (19.12)	588 (80.88)	1.455	1.081–1.959
60–69	138 (14.60)	807 (85.40)	1.0	
<b>Monthly income (CNY)</b>				
≤ 2000	43 (12.80)	293 (87.20)	0.458	0.269–0.781
2001–5000	179 (15.85)	950 (84.15)	0.570	0.378–0.860
≥ 5001	55 (26.57)	152 (73.43)	1.0	
<b>Are people in contact with those who have herpes zoster susceptible to contracting varicella-zoster virus?</b>				
Not susceptible	131 (17.54)	616 (82.46)	1.889	1.181–3.022
Not sure	115 (23.09)	383 (76.91)	2.748	1.705–4.428
Susceptible	31 (7.26)	396 (92.74)	1.0	
<b>Are the elderly susceptible to contracting varicella-zoster virus?</b>				
Not susceptible	57 (20.88)	216 (79.12)	1.459	1.007–2.114
Not sure	32 (8.63)	339 (91.37)		
Susceptible	188 (18.29)	840 (81.71)	1.0	
<b>What are the recipients of the HZV vaccination in China?</b>				
Children	44 (27.67)	115 (72.33)	2.035	1.297–3.192
Not sure	108 (12.23)	775 (87.77)		
Adult	26 (28.57)	65 (71.43)		
Adult ≥50 years	99 (18.37)	440 (81.63)	1.0	
<b>What is the HZV vaccination schedule in China?</b>				
One dose or three doses	33 (30.00)	77 (70.00)		
Not sure	196 (13.96)	1208 (86.04)	0.434	0.282–0.666
Two doses	48 (30.38)	110 (69.62)	1.0	
<b>Vaccine hesitancy</b>	20.27 ± 3.33	21.94 ± 3.63	0.866	0.829–0.905
<b>For partners</b>				
<b>Age (years)</b>				
50–59	124 (17.06)	603 (82.94)	1.586	1.155–2.177
60–69	108 (11.43)	837 (88.57)	1.0	
<b>Monthly income (CNY)</b>				
≤ 2000	37 (11.01)	299 (88.99)	0.445	0.255–0.775
2001–5000	144 (12.75)	985 (87.25)	0.500	0.327–0.765
≥ 5001	51 (24.64)	156 (75.36)	1.0	
<b>Are people in contact with those who have herpes zoster susceptible to contracting varicella-zoster virus?</b>				
Not susceptible	113 (15.13)	634 (84.87)	1.777	1.078–2.930
Not sure	92 (18.47)	406 (81.53)	2.299	1.379–3.832
Susceptible	27 (6.32)	400 (93.68)	1.0	
<b>What are the recipients of the HZV vaccination in China?</b>				
Children	38 (23.90)	121 (76.10)	2.167	1.347–3.486
Not sure	92 (10.42)	791 (89.58)		
Adult	23 (25.27)	68 (74.73)		
Adult ≥50 years	79 (14.66)	460 (85.34)	1.0	
<b>What is the HZV vaccination schedule in China?</b>				
One dose or three doses	24 (21.82)	86 (78.18)		
Not sure	167 (11.89)	1237 (88.11)	0.436	0.277–0.685
Two doses	41 (25.95)	117 (74.05)	1.0	
<b>Vaccine hesitancy</b>	20.18 ± 3.30	21.90 ± 3.63	0.860	0.821–0.901
<b>For parents</b>				
<b>Age (years)</b>				
50–59	109 (14.99)	618 (85.01)	4.947	3.149–7.771
60–69	33 (3.49)	912 (96.51)		
<b>Educational level</b>				
Middle school or below	59 (7.10)	772 (92.10)		
High school	42 (6.79)	577 (93.21)	0.367	0.218–0.621
College and university	41 (18.49)	181 (81.51)	1.0	
<b>What are the recipients of the HZV vaccination in China?</b>				
Children	24 (15.09)	135 (84.91)		
Not sure	46 (5.21)	837 (94.79)		
Adult	18 (19.78)	73 (80.22)	2.137	1.090–4.189
Adult ≥50 years	54 (10.02)	485 (89.98)	1.0	
<b>Vaccine hesitancy</b>	20.15 ± 3.17	21.81 ± 3.64	0.859	0.808–0.912

## Discussion

This study found that the willingness to receive HZV for themselves was only 16.57% in adults aged 50–69 years in Shanghai. Recently, a survey reported that the willingness to

receive HZV was as high as 49.64% in Shanghai. This study shared similar context and settings with our study; the difference might be attributable to the measurement by questionnaires, sample size, and date of survey.<sup>16</sup> The burden of disease

**Table 4.** Factors that influence willingness to receive herpes zoster vaccine (HZV) for themselves or give HZV to their partners and parents under the hypothetical scenario (payment by basic medical insurance).

	Willing (%)	Unwilling (%)	OR value	95%CI
<b>For themselves</b>				
<b>Location of household registration</b>				
Local	1016 (75.26)	334 (24.74)	0.598	0.444–0.807
Non-local	192 (59.63)	130 (40.37)	1.0	
<b>Educational level</b>				
Middle school or below	584 (70.28)	247 (29.72)	0.578	0.374–0.894
High school	441 (71.24)	178 (28.76)	0.514	0.335–0.788
College and university	183 (82.43)	39 (17.57)	1.0	
<b>Are the elderly susceptible to contracting varicella-zoster virus?</b>				
Not susceptible	195 (71.43)	78 (28.57)		
Not sure	213 (57.41)	158 (42.59)	0.680	0.488–0.947
Susceptible	800 (77.82)	228 (22.18)	1.0	
<b>Can people who had had herpes zoster contract varicella-zoster virus again?</b>				
Cannot contract again	377 (71.67)	149 (28.33)	0.703	0.519–0.952
Not sure	352 (64.83)	191 (35.17)		
Can contract again	479 (79.44)	124 (20.56)	1.0	
<b>Can vaccination prevent herpes zoster?</b>				
Cannot prevent	28 (59.57)	19 (40.43)	0.477	0.247–0.921
Not sure	230 (58.08)	166 (41.92)	0.613	0.464–0.810
Can only relieve the symptoms	10 (66.67)	5 (33.33)		
Can prevent herpes zoster	940 (77.43)	274 (22.57)	1.0	
<b>What are the recipients of the HZV vaccination in China?</b>				
Children	123 (77.36)	36 (22.64)		
Not sure	573 (64.89)	310 (35.11)	0.632	0.465–0.860
Adult	75 (82.42)	16 (17.58)		
Adult ≥50 years	437 (81.08)	102 (18.92)	1.0	
<b>Vaccine hesitancy</b>				
Number of underlying diseases	21.13 ± 3.24	23.05 ± 4.19	0.864	0.835–0.894
	0.40 ± 0.68	0.21 ± 0.48	1.539	1.229–1.926
<b>For partners</b>				
<b>Age (years)</b>				
50–59	484 (66.57)	243 (33.43)	1.423	1.133–1.788
60–69	561 (59.37)	384 (40.63)	1.0	
<b>Educational level</b>				
Middle school or below	502 (60.41)	329 (39.59)	0.688	0.475–0.998
High school	380 (61.39)	239 (38.61)	0.619	0.429–0.892
College and university	163 (73.42)	59 (26.58)	1.0	
<b>Can people who had had herpes zoster contract varicella-zoster virus again?</b>				
Cannot contract again	325 (61.79)	201 (38.21)	0.761	0.583–0.993
Not sure	297 (54.70)	246 (45.30)		
Can contract again	423 (70.15)	180 (29.85)	1.0	
<b>Can vaccination prevent herpes zoster?</b>				
Cannot prevent	29 (61.70)	18 (38.30)		
Not sure	190 (47.98)	206 (52.02)	0.667	0.514–0.865
Can only relieve the symptoms	9 (60.00)	6 (40.00)		
Can prevent herpes zoster	817 (67.30)	397 (32.70)	1.0	
<b>What are the recipients of the HZV vaccination in China?</b>				
Children	110 (69.18)	49 (30.82)		
Not sure	481 (54.47)	402 (45.53)	0.609	0.464–0.799
Adult	67 (73.63)	24 (26.37)		
Adult ≥50 years	387 (71.80)	152 (28.20)	1.0	
<b>Vaccine hesitancy</b>				
	21.20 ± 3.22	22.44 ± 4.12	0.915	0.888–0.943
<b>For parents</b>				
<b>Age (years)</b>				
50–59	340 (46.77)	387 (53.23)	4.255	3.308–5.475
60–69	161 (17.04)	784 (82.96)	1.0	
<b>Gender</b>				
Male	200 (25.74)	577 (74.26)	0.694	0.541–0.890
Female	301 (33.63)	594 (66.37)	1.0	
<b>Educational level</b>				
Middle school or below	208 (25.03)	623 (74.97)	0.408	0.282–0.591
High school	181 (29.24)	438 (70.76)	0.391	0.272–0.562
College and university	112 (50.45)	110 (49.55)	1.0	
<b>Are people in contact with those who have herpes zoster susceptible to contracting varicella-zoster virus?</b>				
Not susceptible	240 (32.13)	507 (67.87)	1.508	1.053–2.160
Not sure	175 (35.14)	323 (64.86)	1.493	1.025–2.173
Susceptible	86 (20.14)	341 (79.86)	1.0	
<b>What are the recipients of the HZV vaccination in China?</b>				
Children	63 (39.62)	96 (60.38)		
Not sure	198 (22.42)	685 (77.58)	0.537	0.399–0.722
Adult	34 (37.36)	57 (62.64)		
Adult ≥50 years	206 (38.22)	333 (61.78)	1.0	
<b>Vaccine hesitancy</b>				
	21.20 ± 3.33	21.87 ± 3.74	0.945	0.913–0.979

of herpes zoster is relatively high. The annual economic burden caused by herpes zoster and postherpetic neuralgia in China has been estimated to be as high as CNY 9.2 billion (approximately USD 1.3 billion), and this estimate includes only in-hospital medical expenses and excludes direct non-medical expenses and indirect expenses.<sup>17</sup> Thus, increasing willingness to receive HZV may improve middle-aged and elderly adults' health, and further provides scientific evidence for subsequent formulation of immunization strategies for other adult vaccines, like influenza, pneumococcal, or COVID-19 vaccinations. However, vaccination coverage of HZV has remained low even in high-income countries, such as 20.0% and 25.8% in Greece and the USA, respectively.<sup>18,19</sup> Increasing HZV uptake among the elderly has therefore become a public health concern. Under a scenario where the costs would be covered by insurance, we saw a great increase in vaccination coverage: up to 72.2% for themselves and 74.0% for themselves, a partner, or parent, suggesting that cost of vaccination is an important barrier to vaccination.

There are multiple factors influencing the willingness and uptake of HZV vaccination. In terms of willingness to vaccinate, awareness of diseases and vaccines can have an impact. In a systematic review and meta-analysis, 67.1% of the respondents in 17 countries reported that they knew little or nothing about HZV.<sup>20</sup> In a survey in Hong Kong, China, 47.1% of the respondents who had not been vaccinated with HZV did not know about HZV, and 32.4% reported insufficient information from doctors and public education campaigns.<sup>14</sup> Similarly, in our study, the respondents also had limited knowledge of herpes zoster and HZV, which may be attributable to insufficient information from vaccination clinics or other health care providers. However, we noted that some answers on the knowledge of herpes zoster and HZV, such as susceptibility of contracting VZV in contact with those who have herpes zoster, susceptibility of contacting VZV among elderly, targeted population of HZV vaccination in China, and effect of vaccination against herpes zoster, demonstrate both positive and negative impact on the willingness to vaccinate HZV under different scenarios. Prior to this study, we hypothesized that greater knowledge and awareness in the respondents would contribute to higher willingness, but our findings did not support the hypothesis. This discrepancy be explained in that knowledge and awareness of herpes zoster and HZV may play a minor role in the decision to take the vaccination, compared to the significant role of the high price of HZV; in a hypothetical scenario where insurance covered the vaccine, vaccination willingness remarkably increased and then knowledge and awareness influenced the willingness as we had hypothesized.

In addition, we characterized how demographic factors influenced willingness to receive a vaccine. A Canadian study found that the vaccination rates of HZV for men and women were 4.8% and 7.3%, respectively; people living in urban centers (6.2%) had a higher vaccination rate than those living in rural areas (5.3%), suggesting that demographics also affected vaccination behavior.<sup>13</sup> Our study identified similar demographic factors, including younger age, female, higher income, higher educational level, and local residents, which were associated with increased willingness to vaccinate HZV. We also

found that vaccine hesitancy affected the willingness to vaccinate. Interestingly, vaccine hesitancy differed significantly in the respondents with diverse income in this study, further suggesting the impact of high price of HZV.

This study has several limitations. First, this study recruited the respondents in only 13 communities, which may have limited representation. Second, this study used a face-to-face survey to fill out the questionnaire, so the respondents may tend to choose a more positive answer due to the Hawthorne effect.

In conclusion, we determined a very low willingness to vaccinate HZV in adults aged 50–69 years in a Chinese metropolitan population under the current scenario of self-payment. To increase vaccination coverage, identifying ways to decrease the price or to cover it under public funding or insurance programs will be very important. The lack of knowledge and awareness of the vaccine and the disease was also problematic. Increasing this knowledge will be particularly important among populations with certain underlying diseases.

## Acknowledgments

We appreciate the respondents completed the questionnaire.

## Authors' contribution

YL and JL conceived of this study. XL, YL, FZ and ALW drafted initial manuscript, and analyzed data. JL, XL, LZ, and KM collected the data. ALW and BG revised the manuscript and helped interpret data. All authors reviewed the final manuscript.


## Disclosure of potential conflicts of interest

The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

## Funding

This work was supported by the Key Discipline (2020-2022) of Public Health in Minhang District (MGWXX04) and 2019 Cooperation Programme of Fudan University – Minhang District Joint Health Center (2019FM03).

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## References

1. Adams EN, Parnapy S, Bautista P. Herpes zoster and vaccination: a clinical review. *Am J Health Syst Pharm.* 2010;67:724–27. doi:10.2146/ajhp090118.
2. Koshy E, Mengting L, Kumar H, Jianbo W. Epidemiology, treatment and prevention of herpes zoster: a comprehensive review. *Indian J Dermatol Venereol Leprol.* 2018;84:251–62. doi:10.4103/ijdv.IJDVL\_1021\_16.
3. Saguil A, Kane S, Mercado M, Lauters R. Herpes Zoster and Postherpetic Neuralgia: prevention and Management. *Am Fam Physician.* 2017;96:656–63.

4. Thompson RR, Kong CL, Porco TC, Kim E, Ebert CD, Acharya NR. Herpes Zoster and post-herpetic Neuralgia: changing incidence rates from 1994 to 2018 in the United States. *Clin Infect Dis*. 2020;ciaa1185. doi:10.1093/cid/ciaa1185.
5. Pentikis HS, Matson M, Atiee G, Boehlecke B, Hutchins JT, Patti JM, Henson GW, Morris A. Pharmacokinetics and safety of FV-100, a novel oral anti-herpes zoster nucleoside analogue, administered in single and multiple doses to healthy young adult and elderly adult volunteers. *Antimicrob Agents Chemother*. 2011;55:2847–54. doi:10.1128/AAC.01446-10.
6. Kawai K, Gebremeskel BG, Acosta CJ. Systematic review of incidence and complications of herpes zoster: towards a global perspective. *BMJ Open*. 2014;4:e004833. doi:10.1136/bmjopen-2014-004833.
7. Hata A, Kuniyoshi M, Ohkusa Y. Risk of Herpes zoster in patients with underlying diseases: a retrospective hospital-based cohort study. *Infection*. 2011;39:537–44. doi:10.1007/s15010-011-0162-0.
8. Heymann AD, Chodick G, Karpati T, Kamer L, Kremer E, Green MS, Kokia E, Shalev V. Diabetes as a risk factor for herpes zoster infection: results of a population-based study in Israel. *Infection*. 2008;36:226–30. doi:10.1007/s15010-007-6347-x.
9. Imafuku S, Matsuki T, Mizukami A, Goto Y, de Souza S, Jégou C, Bianco V, Rosillon D, Ito C, Curran D, et al. Burden of Herpes Zoster in the Japanese population with immunocompromised/chronic disease conditions: results from a cohort study claims database from 2005-2014. *Dermatol Ther (Heidelb)*. 2019;9:117–33. doi:10.1007/s13555-018-0268-8.
10. Willis ED, Woodward M, Brown E, Popmihajlov Z, Saddier P, Annunziato PW, Halsey NA, Gershon AA. Herpes zoster vaccine live: a 10 year review of post-marketing safety experience. *Vaccine*. 2017;35:7231–39. doi:10.1016/j.vaccine.2017.11.013.
11. Syed YY. Recombinant Zoster Vaccine (Shingrix®): a review in Herpes Zoster. *Drugs Aging*. 2018;35:1031–40. doi:10.1007/s40266-018-0603-x.
12. Zhang D, Johnson K, Newransky C, Acosta CJ. Herpes zoster vaccine coverage in older adults in the U.S., 2007-2013. *Am J Prev Med*. 2017 Jan;52(1):e17–e23. Epub 2016 Oct 26. doi:10.1016/j.amepre.2016.08.029.
13. Liu XC, Simmonds KA, Russell ML, Svenson LW. Herpes zoster vaccine (HZV): utilization and coverage 2009-2013, Alberta, Canada. *BMC Public Health*. 2014;14:1098. doi:10.1186/1471-2458-14-1098.
14. Lam AC, Chan MY, Chou HY, Ho SY, Li HL, Lo CY, Shek KF, To SY, Yam KK, Yeung I. A cross-sectional study of the knowledge, attitude, and practice of patients aged 50 years or above towards herpes zoster in an out-patient setting. *Hong Kong Med J*. 2017;23:365–73. doi:10.12809/hkmj165043.
15. Akel KB, Masters NB, Shih SF, Lu Y, Wagner AL. Modification of a vaccine hesitancy scale for use in adult vaccinations in the United States and China. *Hum Vaccin Immunother*. 2021;1–8. doi:10.1080/21645515.2021.1884476.
16. Qiu J, Sun X, Hu J, Huang Z, Guo X, Liang X. Willingness to receive herpes zoster vaccine and factors influencing willingness among ≥50-year-old adults of Shanghai in May-June 2020. *Chin J Vaccines Immunization*. 2020;27:307–310, 327.
17. Yin D, Van Oorschot D, Jiang N, Marijam A, Saha D, Wu Z, Tang H, Diaz-Decaro J, Watson P, Xie X, et al. A systematic literature review to assess the burden of herpes zoster disease in China. *Expert Rev Anti Infect Ther*. 2021;19:165–79. doi:10.1080/14787210.2020.1792290.
18. Papagiannis D, Rachiotis G, Mariolis A, Zafiriou E, Gourgoulianis KI. Vaccination coverage of the elderly in Greece: a cross-sectional nationwide study. *Can J Infect Dis Med Microbiol*. 2020;2020:5459793. doi:10.1155/2020/5459793.
19. Williams WW, Lu PJ, O'Halloran A, Kim DK, Grohskopf LA, Pilishvili T, Skoff TH, Nelson NP, Harpaz R, Markowitz LE, et al. Surveillance of vaccination coverage among adult populations - United States, 2015. *MMWR Surveill Summ*. 2017;66:1–28. doi:10.15585/mmwr.ss6611a1.
20. Tricco AC, Zarin W, Cardoso R, Veroniki AA, Khan PA, Nincic V, Ghassemi M, Warren R, Sharpe JP, Page AV, et al. Efficacy, effectiveness, and safety of herpes zoster vaccines in adults aged 50 and older: systematic review and network meta-analysis. *BMJ*. 2018;363:k4029. doi:10.1136/bmj.k4029.