

The acceptability of and willingness to pay for a herpes zoster vaccine: A systematic review

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Abstract Patients, predominantly the elderly, with Herpes Zoster (HZ) not only suffer symptoms of the disease but also bear considerable expenses. This study systematically reviewed the acceptability of and willingness to pay for the HZ vaccine. This review was registered in PROSPERO 2023 (CRD42023403062). We used “acceptance”, “willing to pay”, and “HZ vaccine” (and variations thereof) as keywords in a systematic search for original English research articles published up to April 7, 2023. The search was conducted over Scopus, PubMed, ScienceDirect, Cochrane, and Google Scholar in accordance with PRISMA 2020 guidelines. The inclusion criteria were as follows: studies (1) that mentioned HZ vaccination, (2) related to acceptability or willingness to pay, and (3) with full texts available and peer-reviewed prior to final publication. Grey literature, letters to editors, commentaries, case reports or series, systematic reviews, meta-analyses, articles of poor quality, and articles with ambiguously defined and measured outcome variables were excluded. The Joanna Briggs Institute (JBI) critical appraisal checklist was used to evaluate the methodological quality of the studies. Finally, the search yielded 24 studies, of which 9 were conducted in Asia, 8 in Europe, and 7 in America. General adults or patients aged 50 or older were often the target populations, for whom treatments were accompanied by healthcare providers’ recommendations. The willingness to pay and willingness to accept the vaccine ranged from \$8 to \$150 and 16.6% to 85.8%, respectively. Compared to the US, Asia and Europe had higher acceptance rates for HZ immunization. The most frequent excuses given for not being vaccinated are side effects, cost, lack of recommendations, anti-vaccination views, ignorance about the HZ vaccine, and the belief that one is not at risk for the disease. National campaigns should be developed to increase public awareness of HZ, and more international research should be conducted to understand the WTA and WTP for HZ immunizations.

Keywords: Acceptability, herpes zoster, systematic review, willingness to pay, vaccination.

1 Introduction

Herpes zoster (HZ), also known as zona or shingles, is caused by the varicella zoster virus (VZV) or human herpesvirus 3. VZV belongs to the *Herpesviridae* family, and its target tissue is the human nervous system. It is not completely eliminated but exists in latent, inactive form in a host’s body, especially in the entire nervous system. This persistence can be explained by the similarity of the VZV genome to that of a human (double-stranded DNA). Accordingly, VZV may be reactivated and cause HZ, damaging skin cells, at any time under favorable conditions. Although there is no clear explanation of the reactivation of the virus, scientists have found that

cellular-mediated immunity (CMI) is related to the pathogenesis of HZ [1]. More specifically, CMI maintains the latency of VZV in the human body, thereby diminishing CMI function and leading to virus reactivation. Because CMI decreases with age [1], HZ predominantly affects the elderly [2], among whom one of the most common complications is post-herpetic neuralgia (PHN). PHN is a long-lasting pain that can become a chronic condition that ultimately exerts negative effects on the quality of life and daily activities of patients [1] [2]. PHN is a complication of HZ, occurring with a frequency of 5% to 30%, and each year, the global HZ incidence ranges from 3.0 to 5.0 for every 1000 individuals [1].

A study in Thailand showed that the HZ morbidity rate increases gradually with age and the disease spreads

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across many countries, such as the UK, France, Germany, the US, Canada, Taiwan, and Australia) [3]. The median age of HZ onset is 59.4 years, and 68% of cases are individuals older than 50 years [3]. HZ imposes considerable health care, economic, and societal burdens on countries. HZ patients not only suffer the symptoms of the disease but also bear significant expenses, including the costs of treatments, medical examinations, diagnostic tests, hospitalization, and emergencies [1]. In developed countries, the direct annual costs (e.g., healthcare utilization and medicine costs) of HZ and its complications range from US\$2.7 million to US\$2.6 billion, while their indirect yearly costs (e.g., loss of productivity and absenteeism) range from US\$1.7 to US\$241.5 million [4]. To prevent HZ, adults are prescribed and administered a zoster vaccine, which is regarded as effective when it functions as a therapeutic vaccine and induces a more potent immune response to prevent reactivation in an already infected individual with pre-existing immunity to VZV [5]. There are two types of vaccines: a live attenuated vaccine (Zostavax[®]) and a recombinant subunit vaccine (HZ/su) (Shingrix[®]) [6].

In the development of a country's vaccination policy, an important index is vaccine acceptance (willingness to accept, WTA), and a high WTA is more likely to result in successful immunization programs [7]. Therefore, studies on WTA are necessary because such investigations reveal patients' assessments of vaccine suitability and vaccination readiness [7]. The belief in and acceptance of a vaccine depends not only on the safety and effectiveness of these preparations but also on health care delivery systems as well as policymakers who develop vaccination requirements [8]. This reality means that a partnership between academic researchers and governments is needed to integrate evidence-informed strategies into vaccination policies and programs, thereby enhancing vaccine WTA [9]. Another important index in this process is willingness to pay (WTP), which reflects how a product is valued by customers. The WTP for vaccines is a monetary indicator that reveals the amount of money that a person is willing to spend to derive the benefits of vaccines [10]. Early scientific investigations of WTP inform policy decisions on sustainable financing mechanisms for vaccination campaigns, particularly in resource-limited countries [11].

Currently, there are relatively few studies on the WTA and WTP for HZ vaccines, and these constructs are mainly treated separately in these studies. For example, Binshan Jiang et al. explored the WTA of HZ vaccines in China and reported that 43.02% of the participants intend to get vaccinated against HZ [12]. Another representative work is that of Eilers et al., who estimated the potential HZ vaccination rate among older adults to be 58.1% [13]. A 2016 study in Italy involving 1001 participants whose mean age was 67 years found that 58% of surveyed individuals support HZ vaccination campaigns and that 73% of them are willing to pay for a vaccine at an ideal cost of €50 [14]. Finally, research in Thailand which was conducted from December 2013 to December 2014 and recruited 118 zoster patients older than 18 years from the Dermatologic Clinic of the Outpatient Department at Siriraj Hospital, showed that HZ vaccines have yet to be

included in vaccination policy and that knowledge about HZ among Thai patients remains limited. Although the authors found no data on the WTP for HZ vaccines, they found that the WTP for HZ treatment was THB500 (range: THB50-10,000) or only 4.2% of people's median income per month [15].

As can be seen, some studies have been devoted to the WTA and WTP for HZ vaccination, but only a brief systematic review of these works has been made [7]. A complete and comprehensive systematic review of research on the issues of interest is necessary to determine the intention to acquire vaccination against HZ and promote vaccination among the public. The results of such reviews cannot only contribute to other research and practices but also serve as reference for helping national health systems develop vaccination policies for high-risk groups.

2 Materials and methods

2.1 Research questions

The research questions that guided this work are as follows:

- What is the global level of acceptance of an HZ vaccine?
- What is the WTP for such a vaccine globally?

2.2 Study setting

This systematic review was directed toward studies that administered global surveys.

2.3 Data source and search strategy

Articles were searched from academic thematic databases, including PubMed, ScienceDirect, Scopus, the Cochrane Library, and Google Scholar. The keywords used in the search were "acceptability," "herpes zoster," "willingness to pay," "vaccination," and variations thereof. The search strategies are detailed in [Supplementary File 1](#).

2.4 Ethical approval

Ethical approval for this systematic review was not necessary because data were collected from previous studies that were granted such approval. However, the review protocol was registered at the International Prospective Register of Systematic Reviews (registration number: PROSPERO 2023 CRD42023403062).

2.5 Inclusion and exclusion criteria

Studies were included in the analysis if they met the following criteria:

- (1) Studies based on PICO elements (population: participants worldwide;

intervention: HZ vaccine; comparison: none; outcome: acceptance and/or WTP; study type: cross-sectional surveys);

- (2) Studies on attitudes, reluctance, and/or barriers to HZ vaccine acceptability among a given population;
- (3) Papers with the full texts available;
- (4) Original research involving cross-sectional surveys and including quantitative, qualitative, or mixed-methods analyses and peer-reviewed research;
- (5) Studies published in English.

Studies that were excluded were as follows:

- (1) Gray literature, including presented abstracts, letters to editors, commentaries, case reports or series, systematic reviews, and meta-analyses;
- (2) Studies focusing on other types of intervention (e.g., surgery, drug administration, radiotherapy);
- (3) Poor-quality articles and articles in which the outcome variables were ambiguously defined and measured;
- (4) Research with insufficient or no information about the acceptability of or WTP for HZ vaccination.

2.6 Main outcomes

In this systematic review, the primary outcomes of interest were the WTA and WTP for HZ vaccines.

2.7 Data extraction

A quality assurance process was implemented in stages during the critical appraisal of studies. All the articles identified during the database search were downloaded to EndNote version 8 (<http://endnote.com/>), and duplicate articles were removed from the list. The remaining articles were screened at the title/abstract level, after which a full-text review was conducted by one reviewer. Double screening and record validation was performed by another reviewer. The data extracted included the titles, authors, years of publication, journals, study designs, durations of time search, number of participants, demographic characteristics of participants, WTA (in percentage), and WTP mean \pm SD or median.

Two reviewers independently evaluated the full texts and checked for relevance, and discrepancies were resolved by discussion or with reference to a third reviewer if consensus could not be reached. The search method was presented in a PRISMA flow chart showing the included and excluded studies. In the case of missing data and/or additional details, an investigation was carried out by reaching out to the corresponding authors of the reviewed studies. The data was entered into a Microsoft Excel spreadsheet.

2.8 Quality assessment

The risk of bias (quality of research articles) was assessed independently by two researchers, with a third consulted upon a lack of consensus. Two independent reviewers also assessed the quality with which the findings of the articles were reported, and disagreements were resolved through discussion. The assessment tool used in the quality assessment was the Joanna Briggs Institute's (JBI) critical appraisal checklist for analytical cross-sectional studies. The results of the evaluation are presented in **Table 3**.

The above-mentioned checklist was also used to analyze the risk of reporting bias [16]. Eight questions related to the following points were used for this purpose: (1) a clear definition of criteria for inclusion in the sample, (2) detailed descriptions of study subjects and settings, (3) validity and reliability of exposure measurements, (4) objective and standard criteria for measuring the condition, (5) the definition of confounding factors, (6) strategies for dealing with confounding factors, (7) the validity and reliability of outcome measurement, and (8) appropriateness of statistical analyses. The satisfaction of each criterion was denoted by "yes," "no," "unclear," or "not applicable." The risk of bias was considered low, moderate, and high when more than 70%, 50% to 69%, and 0% to 49% of the criteria received a response of "yes" [17].

2.9 Data reporting

The overall process and results of this systematic review were documented according to the flowchart of the Preferred Reporting Items for Systematic Review and Meta-Analysis (PRISMA) [18]. The PRISMA checklist is shown in **Figure 1**.

2.10 Data synthesis

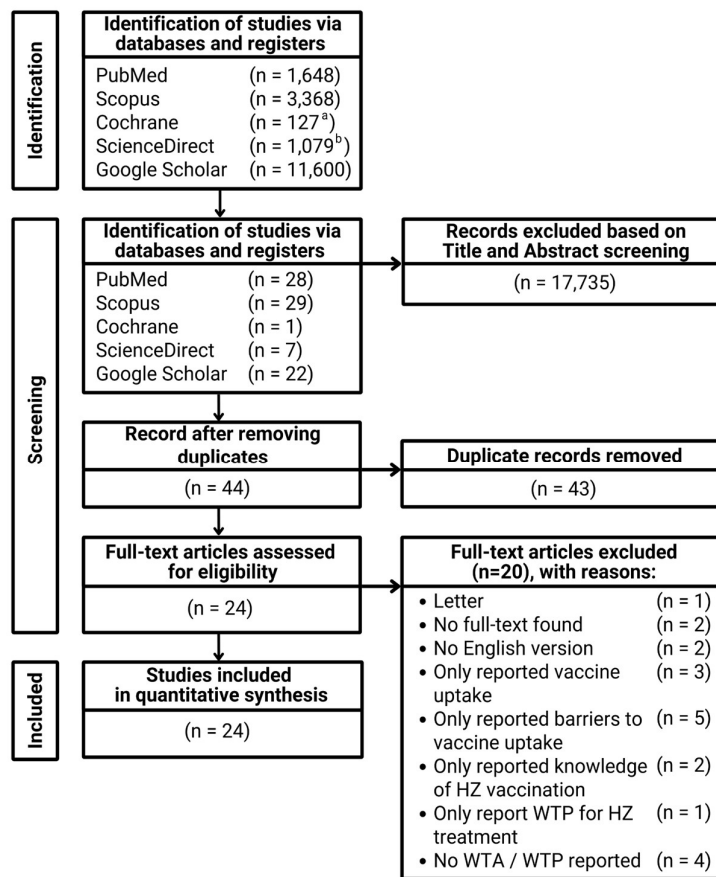
We did not synthesize the results of the data analyses to address the heterogeneity of the cross-sectional survey methods and outcome measures used in the examined studies. Instead, the results were presented using a qualitative synthesis approach that was aimed at identifying methodological and population differences. This systematic review used percentage (%) and US dollars as units of measurement for WTA and WTP, respectively. In cases where countries' currency values reported in studies were not US dollars, units of this parameter were converted on the basis of the exchange rate during the year at which a given study was carried out. The conversion was done on a free online website.

3 Results

The initial database search yielded 17,822 papers, after which title and abstract screening resulted in the exclusion of 17,735 of these. With the removal of duplicates, 44 studies remained. The final sample comprised 24 (0.13%) articles [12-14, 19-39], letters, articles with no full-text version or English version, articles with no data on WTA

or WTP for HZ vaccines were excluded from the study (**Figure 1, Table 1**). Among 24 included studies, 21 studies reported the rate of vaccine acceptance, 15 studies were concerned with the refusal or reluctance to receive HZ vaccines, and 4 studies reported the WTP for HZ vaccination. Most of the studies were published between 2021 and 2023, and they were conducted across three continents: Asia, America, and Europe. The target groups were primarily members of the general population aged ≥ 50 years, and the analysis software mainly used was the Statistical Package for the Social Sciences. Acceptability rates among the general population ranged from 16.6% to 85.8%, whereas those among patients ranged from 25.4%

to 32%. The willingness to accept HZ vaccines ranged from 55% to 86.9% and was 74.2% among the general population and patients, respectively, upon recommendation by a healthcare provider. The WTA values for HZ vaccines are presented in **Figure 2**. The factors affecting WTA identified in all the studies were divided into four groups: socio-demographic factors, the perception of risk, concerns about vaccines, and others (**Figure 3**) [40]. As previously stated, the JBI critical appraisal checklist was used to evaluate the methodological quality of the studies (**Table 3**). The risk of bias in the 24 studies ranged from moderate to high.



Note: ^a: Only Cochrane reviews; ^b: Only Review articles and Research articles

Fig. 1. PRISMA flowchart (2023).

Table 1. Descriptive summary of the characteristics of the 24 studies in the sample (2023).

Characteristics	WTA		WTP		Refuse/ Hesitancy	
	n	%	n	%	n	%
Publication year	21	100.0	4	100.0	15	100.0
Until 2010	3	14.0	-	-	2	13.0
2011 - 2015	3	14.0	-	-	1	7.0
2016 - 2020	6	29.0	3	75.0	4	27.0
2021 - 2023	9	43.0	1	25.0	8	53.0
Age groups	21	100.0	4	100.0	15	100.0
≥ 50	10	48.0	4	100.0	6	40.0
≥ 60	2	10.0	-	-	2	13.0
≥ 65	2	10.0	-	-	2	13.0
Others	7	32.0	-	-	5	34.0
Target population	21	100.0	4	100.0	15	100.0
General population	12	57.0	2	50.0	7	47.0
Patients	8	38.0	2	50.0	7	47.0
Healthcare provider and General population	1	5.0	-	-	1	6.0
Region	21	100.0	4	100.0	15	100.0
Asia	8	38.1	-	-	7	46.7
Europe	8	38.1	1	25.0	5	33.3
America	5	23.8	3	75.0	3	20.0
Data analysis software	21	100.0	4	100.0	15	100.0
SPSS	9	43	1	25	7	47
R	2	10	-	-	2	13
STATA	2	10	1	25	1	7
SAS	3	14	2	50	1	7
Others	5	23	-	-	4*	26

Note: *: One study does not state its data analysis software

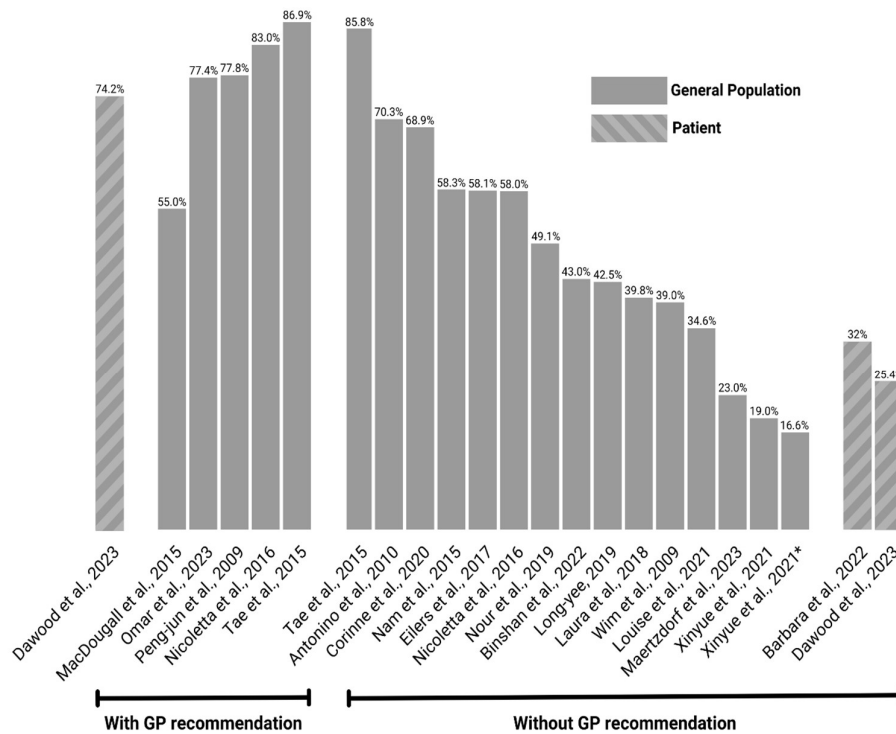


Fig. 2. WTA values for HZ vaccines.

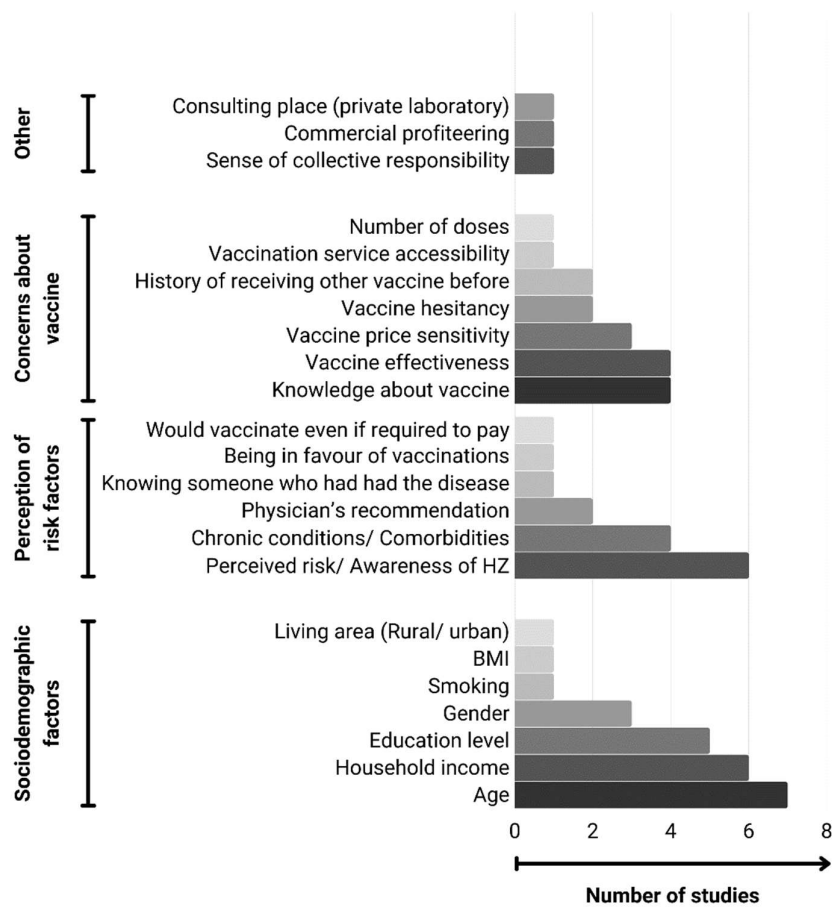


Fig. 3. Factors associated with WTA, as determined using multivariate logistic regression.

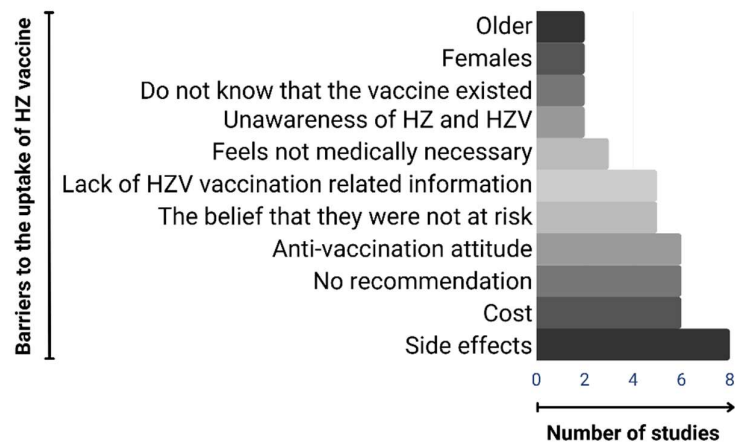


Fig. 4. Barriers to vaccine uptake.

The studies also identified barriers to the uptake of HZ vaccines (Figure 4), of which the most popular was side effects ($n = 8$), followed by cost, the absence of a recommendation, and anti-vaccination attitudes ($n = 6$). Among the sample, only four mentioned WTP. We found

that this parameter oscillates over a wide range of 8 to 150 USD. The participants' preferences for each range of WTP and some of the factors affecting this parameter are presented in Table 2.

Table 2. WTP for HZ vaccines and associated factors.

Author, Year	WTP threshold (\$USD)	Participant preference (%)	Factors associated with WTP
Brandon J. Patterson et al., 2021	8 - 13 USD*	75%	- Out-of-pocket price - Flu-like symptoms - Injection-site reactions
	140 - 150 USD*	51.20%	
Nour A. Baalbaki et al., 2019	0 USD	31.4%	N/a
	24.99 USD	36%	
	25 - 50 USD	18.7%	
Nicoletta Valente et al., 2016	55.34 USD**	73%	- Higher education - Being in favour of vaccinations in general - General practitioner advice
Osayi E. Akinbosoye et al., 2016	44.06 - 95 USD	N/a	N/a

Note: *: For the second dose; **: Equivalent to €50; N/a: Not available.
 €1 = 1.1068 USD (Source: Exchange Rates UK: Euro to US Dollar Spot Exchange Rates for 2016)

Table 3. Risk of bias analysis using the JBI checklist.

Source	Questions								Quality level
	Q1	Q2	Q3	Q4	Q5	Q6	Q7	Q8	
Dawood et al., 2023	1	1	4	4	4	4	1	1	Moderate
Omar et al., 2023	1	1	4	4	4	4	1	1	Moderate
Maertzdorf et al., 2023	1	1	4	4	4	4	4	1	High
Aygin et al., 2022	1	1	4	4	4	4	4	1	High
Nikhita et al., 2022	1	4	4	4	4	4	1	4	High
Barbara et al., 2022	1	1	4	4	4	4	1	4	High
Binshan et al., 2022	1	1	4	4	4	4	1	1	Moderate
Xinyue et al., 2021	1	4	4	4	4	4	1	1	High
Xinyue et al., 2021*	1	4	4	4	4	4	1	1	High
Louise et al., 2021	1	1	4	4	4	4	3	1	High
Brandon et al., 2021	1	1	4	4	4	4	1	1	Moderate
Corinne et al., 2020	1	1	4	4	4	4	1	1	Moderate
Nour et al., 2019	1	1	4	4	4	4	1	1	Moderate
Long-yee et al., 2019	1	1	4	4	4	4	1	1	Moderate
Laura et al., 2018	1	1	4	4	4	4	4	1	High
Eilers et., 2017	1	1	4	4	4	4	1	1	Moderate
Nicoletta et al., 2016	1	1	4	4	4	4	1	1	Moderate
Osayi et al., 2016	1	1	4	4	4	4	4	1	High
Nam et al., 2015	4	1	4	4	4	4	1	1	High
MacDougall et al., 2015	4	1	4	4	4	4	1	4	High
Tae et al., 2015	4	1	4	4	4	4	4	4	High
Antonino et al., 2010	1	1	4	4	4	4	1	4	High
Wim et al., 2009	1	1	4	4	4	4	1	1	Moderate
Peng - jun et al., 2009	4	1	4	4	4	4	4	1	High

Notes: Q: Question; 1: Yes; 2: No; 3: Unclear; 4: Not applicable

Score: The quality assessment score ranged from 0 to 8 based on each question of the Joanna Briggs Institute checklist.

4 Discussion

Evidence from this systematic review indicates that the majority of populations have positive attitudes toward HZ vaccines and would accept their use for prevention. Worldwide, HZ vaccines were regarded as acceptable by 44.9% of the population on average, but 59.6% of individuals expressed a reluctance to get vaccinated. Respondents' attitudes and knowledge about HZ vaccines and the HZ virus were also assessed in all the examined studies. The assessments revealed that the core factors associated with the willingness of individuals over 50

years of age to accept HZ vaccines included age, household income, awareness of HZ and HZ vaccines, vaccine effectiveness, and education level. The side effects of vaccines cause hesitation among people to acquire vaccination, and the high costs of vaccines, the lack of such preparations, and the wave of anti-vaccine sentiments remain a considerable concern in national vaccination programs.

Recommendations from healthcare providers significantly affected vaccination behaviors. A higher vaccine acceptance was observed with the intervention of medical staff, with acceptance rates increasing from

44.9% to 75.7%. However, the number of studies on the influence of caregivers is limited. Therefore, more research should be conducted to determine the willingness of health care staff to introduce HZ vaccines. The systematic review uncovered that the WTP for HZ vaccines worldwide was 56.86 USD, with the cost that people are willing to shoulder peaking at 150 USD. The factors associated with WTP included out-of-pocket expenses, flu-like symptoms, injection site reactions, higher education, being in favor of vaccinations in general, and advice from general practitioners. Respondents' WTP for HZ vaccines was mentioned in only four of the evaluated surveys, and only two of these analyzed related factors. More studies should be carried out to derive additional data for future systematic reviews.

The implications of the review for HZ vaccination policy and practice encompass several aspects:

- (1) Vaccine effectiveness: Policy and practice with respect to HZ vaccination may be influenced by the ongoing monitoring of its effectiveness. Research and real-world data analysis can determine how strategies can be adjusted (e.g., providing booster shots or changing vaccine doses).
- (2) Immunization programs: The effectiveness, safety, and cost-effectiveness of HZ vaccines can affect national immunization programs. Governments and public health organizations should consider including the vaccine in routine immunization schedules or recommending it for specific high-risk groups, such as immunocompromised individuals or healthcare workers.
- (3) Accessibility and coverage: Policy decisions should prioritize ensuring the accessibility and affordability of HZ vaccines. Governments and healthcare systems can explore strategies for increasing vaccine coverage, including providing financial assistance, having vaccination covered by insurance, and integrating it into existing vaccination campaigns.
- (4) Education and awareness: Policies and practices should prioritize educating healthcare providers and the general public about HZ vaccines. This can include disseminating accurate information about the benefits, risks, and timing of vaccination, addressing common misconceptions, and promoting vaccine acceptance among eligible individuals.
- (5) Research and development: Such efforts can lead to the introduction of new HZ vaccines or improvements to existing ones. Therefore, policy and practice need to remain adaptable to incorporate advancements in vaccine technology, potential changes in dosing schedules, and the development of more effective and durable vaccines.

4.1 Limitations

Several limitations of this systematic review were discovered. The representativeness of the samples in the study was not reliable, only 6 out of 24 studies use a random sampling method. The sample size of most of the studies were limited and there were large differences between studies. The number of studies on willingness to pay for HZ vaccine were extremely meager. Restricting the search to limited databases and English-only peer-reviewed articles is another limitation, as some important articles could have been excluded from the review. This study was purely descriptive statistics, without further research, so its reliability is limited.

5 Conclusion

Our study indicated that the HZ vaccine acceptance rate was higher in Asia and Europe than in the US. Popular reasons for the reluctance to get vaccinated included side effects, cost, the absence of recommendations, anti-vaccination attitudes, the lack of HZ vaccination-related information, and the belief of individuals that they are not at risk of developing the disease. The WTA increased dramatically because of the influence of general practitioners' recommendations, but few studies in the sample mentioned WTP. More explorations should be conducted in different countries to achieve a better overview of WTA and WTP for HZ vaccines, and national programs should be developed to enhance HZ awareness among citizens.

ABBREVIATIONS

HZ: Herpes zoster; VZV: Varicella-Zoster Virus; GP: General practitioner; WTA: Willingness to accept; WTP: Willingness to pay.

CONFLICT OF INTEREST

The authors declare that the research was carried out without potential conflicts of interest.

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