



Socioeconomic and Attitudinal Variables Associated with Acceptance and Willingness to Pay Towards Dengue Vaccine: A Systematic Review

Jonny Karunia Fajar,¹ and Harapan Harapan^{1,2,3,*}

¹Medical Research Unit, School of Medicine, Syiah Kuala University, Banda Aceh, Indonesia

²Tropical Disease Centre, School of Medicine, Syiah Kuala University, Banda Aceh, Indonesia

³Department of Microbiology, School of Medicine, Syiah Kuala University, Banda Aceh, Indonesia

*Corresponding author: Harapan Harapan, Medical Research Unit, School of Medicine, Syiah Kuala University. Tel: +62-6517551843, E-mail: harapan@unsyiah.ac.id

Received 2017 May 23; Accepted 2017 June 22.

Abstract

Background: Currently, a dengue vaccine has been approved in some countries. The problem with this new vaccine is whether the public could accept and be willing to purchase.

Objectives: This study aimed to provide solid data regarding factors associated with acceptance and willingness to pay for dengue vaccine.

Methods: A systematic review with a meta-analysis was conducted on September-October 2016 for previous studies. Literatures from PubMed and Embase were searched for eligible publications (cut-off date for updates: September 10, 2016). The combined odds ratios (ORs) and 95% confidence intervals (95% CIs) were assessed using random or fixed effect model. Narrative review was used to analyze the data when they were not qualified for meta-analysis.

Results: There were several factors associated with acceptance of dengue vaccine including attitude toward vaccination, preventive measures against dengue, attitude towards dengue, knowledge on dengue, socioeconomic level, and dengue experience. However, our meta-analysis revealed that only attitude towards vaccination (OR95%CI = 0.313 [0.137 - 0.713], P = 0.006) and socioeconomic level (OR95%CI = 0.576 [0.385 - 0.862], P = 0.007) had significant associations with dengue vaccine acceptance. Studies also revealed that preventive measures against dengue, attitude towards dengue, knowledge on dengue fever, knowledge on dengue viruses, socioeconomic levels, dengue experience, and vaccine price were associated with willingness to pay. However, none of those data was qualified for meta-analysis.

Conclusions: Meta-analysis reveals that good attitude towards vaccination and higher socioeconomic levels are associated with better acceptance of dengue vaccine.

Keywords: Dengue, Dengue Fever, Dengue Vaccine, Dengue Vaccine Acceptance, Willingness to Pay

1. Background

Dengue fever (DF) is primarily an urban disease of the tropics (1), but currently it has become a global problem (2). A study estimated that the incidence of dengue is 390 million per year (3). The incidence of dengue infection has an increase trend every year. World health organization reported that the incidence of dengue infection increased from 2.2 million in 2010 to 3.2 million in 2015 (4). A report using 1,636 country-years of case reports of dengue from 76 countries found a substantial increase in the incidence of dengue between 1990 and 2013, with the number of apparent cases more than doubling every decade, from 8.3 million (3.3 - 17.2 million) in 1990 to 58.4 million (23.6 - 121.9 million) in 2013 (5). The highest dengue incidence rates occurred in Southeast Asia, with an annual average of 34.3 cases per 1000 people (5).

Fluid therapy is the only treatment for the management of dengue infection to date and there is no specific treatment (6, 7). Vaccination is an effective method to prevent certain infectious diseases (8) and it is the most important achievement of public health (9). Effective dengue vaccine is difficult to develop because it has to protect against all four serotypes of dengue virus (10). Nevertheless, several dengue vaccine candidates (CYD, DENVax, TV003/TV005, TDENV PIV, V180, and DiME100) have been tested in clinical trials (10) and one of them, CYD, has been approved in some countries. In vaccination programs, a new vaccine has the potential to bring a variety of problems. The problem of dengue vaccine that is categorized as a new vaccine is whether the public will accept and be willing to purchase the vaccine (11). If so, what attitudinal factors are associated with public hesitancy or acceptance

and willingness to pay (WTP).

2. Objectives

The present study aimed to provide data regarding socioeconomic and attitudinal factors associated with acceptance and WTP towards dengue vaccine. This study sought to provide solid data that could be used to generate recommendations for vaccination program policy-makers.

3. Methods

3.1. Study Setting

A systematic review with a meta-analysis was conducted to assess the associated factors regarding acceptance and WTP towards dengue vaccine. Interested data from previous studies were collected for calculating combined odds ratios (ORs) and 95% confidence intervals (95% CIs) using fixed or random effect model. If the data were not qualified for meta-analysis, the data were described narratively. Articles were searched in PubMed and Embase (updated: September 10, 2016). The study was conducted on September-October 2016.

3.2. Study Procedures

The procedures of this study were: (1) identifying the potentially relevant studies through PubMed and Embase; (2) determining eligibility of the study; (3) collecting the abstract and full text data from the studies; (4) collecting the data for calculating OR95%CI; and (4) analyzing data statistically.

3.3. Eligibility Criteria and Data Extraction

Eligibility criteria consisted of predefined inclusion criteria. Studies were included in the analysis if they met the following inclusion criteria: (1) evaluating the factors associated with dengue vaccine acceptance or WTP towards dengue vaccine and (2) providing sufficient data for calculation of OR and 95%CI. If the data did not meet the inclusion criteria, the data were only described narratively.

3.4. Search Strategy and Literature

Potential studies, restricted to English, were searched using specified key words. The search strategy involved the use of combination of the following key words: dengue vaccine", "vaccine acceptance" and "willingness to pay". The reference lists of the retrieved articles were hand-searched. If more than one article was published using the same study data, only the study with the largest sample size was included.

3.5. Statistical Analysis

The association of explanatory factor with dengue vaccine acceptance and WTP was estimated by calculating pooled OR95%CI. The pooled ORs was determined by Z tests ($P < 0.05$ was considered statistically significant). A Q test was employed to evaluate whether the heterogeneity existed. Random effect model was used to calculate OR95%CI if heterogeneity existed ($P < 0.10$). Fixed effect model was used to calculate OR and 95%CI if no heterogeneity existed. These tests were performed if the data were qualified with inclusion and exclusion criteria. A comprehensive meta-analysis (CMA) 2.0 was used to analyze the data.

4. Results

4.1. Characteristics of the Studies

A total of 196 potentially relevant papers regarding vaccine acceptance and 107 papers regarding WTP were identified. Of these, 189 and 99 papers regarding vaccine acceptance and WTP were excluded, respectively, due to obvious irrelevance by reading their titles and abstracts. After reading the full texts, five additional papers regarding vaccine acceptance were excluded because they did not provide sufficient data for calculation of OR95%CI. Therefore, two studies regarding dengue vaccine acceptance were included in the meta-analysis (12, 13). While, all papers (eight papers) regarding WTP for dengue vaccine were excluded because they were not qualified to calculate OR95%CI. Nevertheless, four papers regarding WTP for dengue vaccine were included for narrative review (12, 14-16).

4.2. Quantitative Data Synthesis and Source of Heterogeneity Regarding Vaccine Acceptance

In total, 1151 participants from two studies regarding dengue vaccine acceptance were identified (12, 13). The results showed that attitude toward vaccination (OR95%CI = 0.313 [0.137 - 0.713], $P = 0.006$) and socioeconomic level (OR95%CI = 0.576 [0.385 - 0.862], $P = 0.007$) had significant associations with dengue vaccine acceptance. While, other variables including preventive measures against dengue (OR95%CI = 1.281 [0.820 - 2.001], $P = 0.276$), attitude towards dengue (OR95%CI = 0.340 [0.102 - 1.134], $P = 0.079$), knowledge on dengue (OR95%CI = 0.769 [0.495 - 1.194], $P = 0.242$), and dengue experience (OR95%CI = 0.648 [0.371 - 1.132], $P = 0.127$) had no association with dengue vaccine acceptance. See Table 1 and Figure 1 for details.

Evidence for heterogeneity between studies was found in the attitude towards dengue variable ($P = 0.051$); therefore, the data were assessed using random effect model. Evidence for heterogeneity was not found regarding other variables including attitude towards vaccination ($P =$

Table 1. Factors Associated with Dengue Vaccine Acceptance (Willingness vs. Not-Willingness)

Factor	Location (Reference)	Sample Size (n)		Poor (n)		Good (n)		OR (95%CI)	P	ph
		Poor	Good	Willing	Not	Willing	Not			
Socioeconomic level	Aceh (13)	261	391	222	39	352	39	0.576 (0.385 - 0.862)	0.007	0.480
	Bandung (12)	198	292	181	17	280	12			
Attitude towards vaccination	Aceh (13)	555	97	479	76	95	2	0.313 (0.137 - 0.713)	0.006	0.147
	Bandung (12)	48	451	43	5	427	24			
Preventive measures against dengue	Aceh (13)	497	155	442	55	131	24	1.281 (0.820 - 2.001)	0.276	0.299
	Bandung (12)	108	392	101	7	370	22			
Dengue attitude	Aceh (13)	489	163	416	73	158	5	0.340 (0.102 - 1.134)	0.079	0.051
	Bandung (12)	110	384	101	9	364	20			
Dengue knowledge										
Dengue experience	Aceh (13)	595	57	524	71	50	7	0.648 (0.371 - 1.132)	0.127	0.135
	Bandung (12)	151	349	137	14	334	15			

Abbreviations: 95%CI: 95% confidence interval, n: number of sample, OR: odds ratio, ph: P value of heterogeneity.

Attitude Toward Vaccination

Model	Study Name	Statistics for Each Study					Odds Ratio and 95% CI					Weight (Fixed) Relative Weight	
		Odds Ratio	Lower Limit	Upper Limit	Z-Value	p-Value	0,01	0,10	1,00	10,00	100,00		
Fixed	Harapan et al 2016	0,133	0,032	0,550	-2,785	0,005							33,70
	Hadisoemarto & Castro 2013	0,483	0,175	1,331	-1,406	0,160		66,30					
	0,313	0,137	0,713	-2,762	0,006	0,006							

Preventive Against Dengue

Model	Study Name	Statistics for Each Study					Odds Ratio and 95% CI					Weight (Fixed) Relative Weight	
		Odds Ratio	Lower Limit	Upper Limit	Z-Value	p-Value	0,01	0,10	1,00	10,00	100,00		
Fixed	Harapan et al 2016	1,472	0,877	2,471	1,465	0,143							74,23
	Hadisoemarto & Castro 2013	0,858	0,356	2,065	-0,342	0,732		25,77					
	1,281	0,820	2,001	4,088	0,276	0,276							

Dengue Attitude

Model	Study Name	Statistics for Each Study					Odds Ratio and 95% CI					Weight (Fixed) Relative Weight	
		Odds Ratio	Lower Limit	Upper Limit	Z-Value	p-Value	0,01	0,10	1,00	10,00	100,00		
Random	Harapan et al 2016	0,180	0,072	0,454	-3,632	0,000							48,39
	Hadisoemarto & Castro 2013	0,617	0,272	1,396	-1,160	0,246		51,61					
	0,340	0,102	1,134	-1,755	0,079	0,079							

Dengue Knowledge

Model	Study Name	Statistics for Each Study					Odds Ratio and 95% CI					Weight (Fixed) Relative Weight	
		Odds Ratio	Lower Limit	Upper Limit	Z-Value	p-Value	0,01	0,10	1,00	10,00	100,00		
Fixed	Harapan et al 2016	0,700	0,412	1,188	-1,323	0,186							69,06
	Hadisoemarto & Castro 2013	0,950	0,431	2,094	-0,127	0,899		30,94					
	0,769	0,495	1,194	-1,170	0,242	0,242							

Socioeconomic Level

Model	Study Name	Statistics for Each Study					Odds Ratio and 95% CI					Weight (Fixed) Relative Weight	
		Odds Ratio	Lower Limit	Upper Limit	Z-Value	p-Value	0,01	0,10	1,00	10,00	100,00		
Fixed	Harapan et al 2016	0,631	0,392	1,014	-1,904	0,057							72,07
	Hadisoemarto & Castro 2013	0,456	0,213	0,978	-2,017	0,044		27,93					
	0,576	0,385	0,862	-2,682	0,007	0,007							

Dengue Experience

Model	Study Name	Statistics for Each Study					Odds Ratio and 95% CI					Weight (Fixed) Relative Weight	
		Odds Ratio	Lower Limit	Upper Limit	Z-Value	p-Value	0,01	0,10	1,00	10,00	100,00		
Fixed	Harapan et al 2016	1,033	0,451	2,367	0,077	0,938							45,35
	Hadisoemarto & Castro 2013	0,439	0,207	0,935	-2,134	0,033		54,65					
	0,648	0,371	1,132	-1,526	0,127	0,127							

Figure 1. Forest Plot Regarding Factors Associated with Dengue Vaccine Acceptance (Willingness vs. Not-Willingness)

0.147), socioeconomic level ($P = 0.480$), preventive measures against dengue ($P = 0.299$), knowledge on dengue ($P = 0.528$), and dengue experience ($P = 0.135$). Therefore, fixed effect model was used to calculate OR95%CI.

4.3. Narrative Review Regarding Willingness to Pay Towards Dengue Vaccine

Narrative review was used to analyze WTP towards dengue vaccine because the data were not qualified for meta-analysis. In four studies (12, 14-16), there were 12 factors that were assessed related to WTP towards dengue vaccine. They were attitude towards vaccination, preventive measures against dengue, attitude towards dengue, knowledge on dengue fever, knowledge on dengue viruses, socioeconomic levels, dengue experience, knowing someone who had dengue, vaccine price, having family member(s) suffering from dengue, and previous vaccine purchase. Of those, preventive measures against dengue ($P = 0.029$; $P < 0.05$; $P = 0.036$) (14-16), attitude towards dengue ($P = 0.005$) (14), knowledge on dengue fever ($P = 0.050$; $P = 0.024$) (12, 16), knowledge on dengue viruses ($P = 0.028$) (14), socioeconomic levels ($P < 0.01$) (12, 15), dengue experience ($P = 0.041$), and vaccine price ($P < 0.01$) (15) were associated with WTP. Other factors had no significant association with WTP towards dengue vaccine (Table 2).

5. Discussion

5.1. Factors Associated with Dengue Vaccine Acceptance

Vaccine acceptance is an important predictor to determine the acceptance of the society of the vaccine. Vaccine acceptance is a problem that may arise to new vaccines including dengue vaccine. Data regarding dengue vaccine acceptance is very limited. However, several studies had reported vaccine acceptance in the context of other diseases (17-20) and they were very helpful for immunization programs. We reviewed several factors associated with dengue vaccine acceptance. Until now (updated-January 2, 2017), only two studies (11, 12) evaluated factors associated with dengue vaccine acceptance. Although there were several factors associated with vaccine acceptance from individual study (attitude towards vaccination, preventive measures against dengue, attitude towards dengue, knowledge on dengue fever, socioeconomic level, and dengue experience), our meta-analysis revealed that only attitude towards vaccination and socioeconomic level had significant associations with dengue vaccine acceptance.

Attitude towards vaccination is an individual perspective toward the vaccination program and it was revealed to be correlated with vaccination coverage rates (21). Attitude

towards vaccination was shown to be associated with acceptance towards vaccine against infectious diseases such as H1N1 (22), measles (23), rubella (23), and human papillomavirus (24). These results indicate that a society with a good attitude towards vaccination has a tendency to be able to receive a new vaccine. Therefore, to improve dengue vaccine acceptance and increase community attitude, the socialization of dengue vaccine might be essential.

Our meta-analysis data also showed that dengue vaccine acceptance was associated with socioeconomic level. Other studies also revealed consistent findings in the context of other infectious diseases including human papillomavirus (25, 26), influenza (27), and cholera (28). These results suggest that high socioeconomic level is closely associated with better dengue vaccine acceptance. Therefore, to improve the dengue vaccine acceptance, socialization programs should intensively target populations with low socioeconomic level.

5.2. Factors Associated with Willingness to Pay Towards Dengue Vaccine

We evaluated several factors that had the possibility to be correlated with WTP towards dengue vaccine and tried to conduct meta-analysis, but the data were not suitable for meta-analysis. Therefore, we analyzed the data narratively. There were four studies identified with different results (Table 2).

First, a study by our group found that preventive measures against dengue, attitude towards dengue, and knowledge on dengue viruses were associated with WTP (14). Second, another study in Bandung showed that only knowledge on dengue fever and socioeconomic levels were associated with WTP (12). Third, a study in Metro Manila (Philippines) found that vaccine price, socioeconomic levels, and preventive measures against dengue were associated with WTP. The last study was conducted in Vietnam, Thailand, and Colombia (16). In Vietnam, knowledge on dengue fever, dengue experience, and preventive measures against dengue had significant associations with WTP, while among Thai only dengue experience was associated with WTP. Interestingly, none of the variables was associated with WTP towards dengue vaccine in Colombia.

One of interesting finding is no constant association between socioeconomic status and WTP. Our study (14) revealed no association but another study in Indonesia (12) showed a strong association. It might indicate that the socioeconomic variable behaves differently across regions in Indonesia due to the diverse contexts of local specific situations.

There are some limitations in this study. First, false positive findings regarding dengue vaccine acceptance could

Table 2. Factors Associated with Willingness to Pay Towards Dengue Vaccine

Country (n)	Variables	OR (95%CI) or Correlation Coefficient	P	Reference
Indonesia (476)	Attitude towards vaccination	0.249 (-0.028 - 0.526)	0.078	(14)
	Preventive measures against dengue	0.232 (0.024 - 0.440)	0.029	
	Dengue attitude	0.340 (0.105 - 0.576)	0.005	
	Dengue fever knowledge	-0.114 (-0.318 - 0.089)	0.271	
	Dengue viruses knowledge	0.231 (0.025 - 0.437)	0.028	
	Socioeconomic levels	-0.086 (-0.351 - 0.178)	0.522	
	Dengue experience	0.202 (-0.143 - 0.548)	0.251	
Indonesia (438)	Socioeconomic levels	0.563 (0.280 - 0.847)	< 0.01	(12)
	Preventive measures against dengue	-0.038 (-0.247 - 0.171)	0.72	
	Dengue fever knowledge	0.227 (0.01 - 0.44)	0.05	
	Knowing someone who had dengue	0.129 (-0.04 - 0.30)	0.15	
Philippines (205)	Dengue viruses knowledge	-0.017	> 0.05	(15)
	Dengue fever knowledge	-0.138	> 0.05	
	Preventive measures against dengue	0.367	< 0.05	
	Have family member(s) who suffered from dengue	0.081	> 0.05	
Vietnam (386)	Dengue fever knowledge	NA	0.024	(16)
	Dengue experience	NA	0.041	
	Preventive measures against dengue	NA	0.036	
	Previous vaccine purchase	NA	0.08	
Thailand (379)	Dengue fever knowledge	NA	0.061	(16)
	Dengue experience	NA	0.043	
	Preventive measures against dengue	NA	0.173	
Colombia (392)	Dengue fever knowledge	NA	0.084	(16)
	Dengue experience	NA	0.084	
	Preventive measures against dengue	NA	0.059	
	Previous vaccine purchase	NA	0.114	

Abbreviations: 95%CI, 95% confidence interval; OR, odds ratio.

occur due to small sample size even when combined. Second, data regarding WTP towards dengue vaccine could not be analysed statistically and therefore, they were analyzed using narrative review. Third, studies regarding dengue vaccine acceptance and WTP towards dengue vaccine were very limited and therefore, they could not be explored specifically.

5.3. Conclusion

The meta-analysis reveals that attitude towards vaccination and socioeconomic status are associated with dengue vaccine acceptance while other variables (preventive measures against dengue, attitude towards dengue,

knowledge on dengue, and dengue experience) have no association. Limited data suggest that some factors are associated with WTP towards dengue vaccine including socioeconomic level and attitudinal factors such as knowledge on dengue fever and dengue viruses, attitude towards dengue, preventive measures against dengue, and dengue experience.

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