



Community acceptance and willingness-to-pay for a hypothetical Zika vaccine: A cross-sectional study in Indonesia



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ABSTRACT

Background: Understanding people's perceptions of the economic benefits of a potential Zika vaccine (ZV) is critical to accelerating its introduction into either public sector programs or private market. The aim of this study was to assess the acceptance and willingness-to-pay (WTP) for a hypothetical ZV and the associated explanatory variables in Indonesia.

Methods: We conducted a health facility-based cross-sectional study in Aceh and West Sumatra province from 1 February to 13 June 2018. Patients who visited outpatient departments, have had children or were expecting their first child, were approached and interviewed to collect information on acceptance, WTP, demographic and socio-economic variables and attitudes towards childhood vaccines. Associations of explanatory variables influencing acceptance and WTP were assessed using logistic regression and linear regression analysis, respectively.

Results: In total, 956 respondents were included in the final analysis of acceptance, of whom 338 (35.3%) expressed their WTP. We found that 757 (79.1%) of the respondents were likely to be vaccinated and to recommend their partner to be vaccinated. Higher educational attainment, having a job, having heard about Zika and a good attitude towards childhood vaccination were associated with ZV acceptance in the univariate analyses. In the multivariate analysis, attitude towards childhood vaccination was the

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strongest predictor for ZV vaccination. We found the geometric mean and median of WTP was US\$ 13.1 (95% CI: 11.37–15.09) and US\$ 7.0 (95% CI: 4.47–10.98), respectively. In the final model, having heard about Zika, having a job, and higher income were associated with a higher WTP.

Conclusion: Although the acceptance rate of the ZV is relatively high in Indonesia, less than 40% of respondents are willing to pay, underscoring the need for a low-cost, high-quality vaccine and public sector subsidies for Zika vaccinations in the country.

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1. Introduction

Zika virus (ZIKV), a member of the Flaviviridae family, was first isolated from rhesus monkeys in the Zika forest of Uganda in 1947 [1] and was isolated for the first time from a human in 1954 [2]. Since its identification, rare and sporadic cases in humans were reported in Africa and Asia, without drawing concerns or interest for investigation due to the mild clinical presentation and limited number of recorded cases [3]. In 2007, the first recognized outbreak of ZIKV occurred on Yap island (Federated States of Micronesia) in the Western Pacific [4]. A series of outbreaks with cases having neurological and autoimmune complications followed in 2014 in other Pacific islands [5]. Outbreaks and reports of ZIKV infection then appeared in Americas, Africa and other regions [6], and to date, Zika has been reported in 86 countries around the globe [7]. The scale of the recent outbreaks and the consequential findings on associated complications and transmission modalities have increased awareness of the disease globally [6]. The World Health Organization (WHO) declared ZIKV infection as a Public Health Emergency of International Concern (PHEIC) in February 2016 with the implication that Zika is as an ongoing challenge requiring intense action through sustained research focusing on vaccines and treatments [8].

The Asian region is susceptible to epidemic ZIKV transmission when taking into consideration the widespread distribution of relevant mosquito vectors (*Aedes aegypti* and *Ae. albopictus*), the large amount of travel to and from Zika-affected areas, local conditions conducive to transmission, and limited health resources [9–11]. Soon after the WHO declared Zika as a PHEIC, an outbreak of ZIKV was detected in Singapore in August 2016 and continued until November 2016 with 455 confirmed cases [12].

In Indonesia, seroprevalence studies in Central Java and Lombok identified anti-ZIKV antibodies 1978 and 1983 using haemagglutination inhibition test [13,14], although these antibodies might be cross-reactive with Dengue virus. More recently, recent ZIKV infection among children aged 1–4 years, sampled in 2014, was detected in much of western and central Indonesia using ZIKV microneutralization test. [15]. Around the same time, two Australian travelers were reported to have acquired ZIKV infection after visiting Indonesia in 2013 and 2014 [16,17]. In 2015, ZIKV was isolated for the first time in Indonesia, from a patient in Jambi province of Sumatra Island [18]. The patient had no history of travelling abroad, indicating that the virus was circulating in Indonesia [18]. Although no other cases have been reported since, the potential misclassification of Zika and Dengue diagnoses due to similar clinical presentations and the lack of a widely available Zika diagnostic test, could lead to underestimation of Zika cases [19]. A recent modeling study ranked Indonesia as the third country most at risk for Zika virus exposure, after India and China, due to the monthly volume of airline travelers [10]. In aggregate, this evidence suggests that Indonesia is at risk for a Zika epidemic.

Although non-vaccine control measures for ZIKV transmission are available, such as vector control and safe sex practices [20], development of a vaccine remains a priority public health prevention strategy for ZIKV considering the multiple routes of

non-vector transmission [21]. The WHO has listed the prophylactic vaccination strategy as a priority to prevent severe ZIKV complications such as microcephaly and brain abnormalities [22]. Although a Zika vaccine (ZV) is currently not available, multiple vaccine candidates are being developed and some of them have entered clinical trials. There are some key considerations that will affect ZV uptake and future distribution in an immunization program; two of the most important issues are public acceptance and willingness-to-pay (WTP) for the vaccine.

Studies have been conducted to assess the acceptance of ZV in the United States including among travelers [23], community members [24], and university students [25]. However, information on ZV acceptance in Asia is limited to a single study among pregnant women in Malaysia [26]. No findings related to WTP for a ZV are available currently. One cost-effectiveness study of a hypothetical ZV has been published [27], although this study used a predictive WTP per disability-adjusted-life-years in relation to the national gross domestic product.

The present study sought to assess the community acceptance and WTP for a hypothetical ZV and associated modifiable determinants in Aceh and West Sumatra provinces of Indonesia. The findings are expected to inform policies and strategies for the prevention and control of ZIKV if a vaccine is made available in the near future.

2. Methods

2.1. Ethics approval

The study protocol was approved by the Institutional Review Board of the School of Medicine, Syiah Kuala University. All participants signed written informed consent forms prior to enrolment. Participation in this study was voluntary and no financial incentive was given.

2.2. Study design, setting and location

A health facility-based cross-sectional study was conducted in Aceh and West Sumatra province from 1 February to 13 June 2018. Both provinces are located in Sumatra Island which is situated in the westernmost region of the Indonesian archipelago. Sumatra Island has a surface area of 473,481 km² with a total population of 50.37 million in 2010. Aceh was selected because this province has previously been the location for other population studies related to ZIKV infection [28,29]. West Sumatra was selected because this province is in close proximity to Jambi where ZIKV has been isolated [18].

The study was conducted in seven regencies or municipalities of Aceh (Banda Aceh, Bireun, Aceh Utara, Aceh Selatan, Lhokseumawe, Aceh Jaya, Aceh Besar) and three regencies of West Sumatra (Padang Panjang, Tanah Datar and Solok). The design, setting, analyses and reporting within this study adhered to the STROBE guidelines for cross-sectional studies in epidemiology (see Additional file 1 for the detailed checklist of STROBE criteria [30]).

2.3. Sampling and sample size

Study participants were patients who visited the infection and non-infection outpatient departments either in hospitals or community health centres (*Puskesmas*) in Aceh and West Sumatra. Based on the population of both provinces in 2017 (10.51 million) the minimum sample size required was 385, based on the assumption that the acceptability rate was conservatively estimated to be 50% with a 5% margin of error and a confidence interval of 95%. To recruit the samples, eleven out of 42 regencies or municipalities in both provinces were purposefully selected to include both urban and suburban areas, such that the minimum sample size, the number of participants required from each study site was 35. To avoid repetitive field visits, to minimize the study design effect and to obtain a more robust estimate, the number of sampled participants was increased for each study site. The number of additional participants was adjusted based on the population of each study site (i.e. the percentage of additional participants was allocated higher to regencies with high population density). Participants who were married, have had children or were expecting their first child during the study, had resided in the specified regency or municipality for more than 3 months, and were able to communicate in Bahasa Indonesia (the national language) were considered to be eligible for inclusion. Participants were approached and recruited via a convenience sampling method.

2.4. Study instrument and testing

To facilitate the interviews, a set of a structured questionnaires consisting of five sections was used. The first section collected sociodemographic information. The second section assessed participants' attitude towards childhood vaccination using an established Parent Attitudes about Childhood Vaccines (PACV) questionnaire [31]. The third section provided brief information on ZIKV infection including the cause of the disease, epidemiology, the pregnancy-related complications and transmission. This section also provided a description of the hypothetical ZV, including efficacy, safety, and the administration procedure. The fourth and fifth section determined the acceptance and WTP for a ZV, respectively.

The English version of PACV questionnaire was translated to Bahasa Indonesia. A panel consisting of a medical doctor, a family medicine doctor and a microbiologist were appointed to evaluate the content validity of the questionnaire. Prior to use in the actual study, the questionnaire was tested for accuracy among 10 patients, who visited an outpatient department of a community health centre in Banda Aceh, the capital of Aceh. Corrections were made accordingly based on findings during the pilot study.

2.5. Study variables

2.5.1. Explanatory variables

Sociodemographic data such as age, sex, educational attainment, employment status, monthly income, and numbers of children were collected. The explanatory variables in this study were grouped or divided as proposed previously [32]. The date of birth was recorded, converted into actual age and then grouped into four groups (20–29, 30–39, 40–49 and more than 50-year old). Educational attainment was defined as the highest level of formal education completed and grouped into primary school (year 6), junior high school (year 9), senior high school (year 12), diploma certificate and university graduate. Employment status was divided into employed and unemployed. Monthly income was defined as the average amount of money earned by participants each month in Indonesian Rupiah (IDR) and grouped into three groups (less than IDR 3 million, 3–5 million and more than 5 million, equivalent to US\$ 210.2, US\$ 210.2–US\$ 350.3 and US\$ 350.3, using a July

2018 exchange rate). The participants were also asked whether they had heard about Zika infection prior to the interview.

Attitude for childhood vaccination was assessed using PACV questionnaire. This questionnaire consisted of 15 questions and in which 2, 4 and 9 questions assessed the sub-domain of vaccination behavior, belief in vaccine safety and efficacy, and general attitude towards childhood vaccination, respectively [33]. The scoring system of PACV questionnaire followed previous studies [31,33]. Briefly, for questions with a “yes”/“no”/“do not know” responses, the responses were categorized as hesitant or non-hesitant, as appropriate. For questions with a 5-point Likert-scale responses (“strongly agree” to “strongly disagree”), “strongly agree”/“agree”, and “strongly disagree”/“disagree” were considered as hesitant or non-hesitant as appropriate to the valence of the question stem. Questions with a 5-point Likert-scale (“not at all concerned” to “very concerned”), “somewhat”/“very concerned” and “not at all”/“not too concerned” were categorized as hesitant or non-hesitant as appropriate where the reverse was true. Items with a 10-point Likert-scale were grouped into hesitant (0–5), not sure (6–7), and non-hesitant (8–10). All responses of “do not know”, and “neither agree nor disagree” were categorized as a not sure response. Lastly, all responses were scored hesitant (scored as 2), not sure (scored as 1) or non-hesitant response (scored as 0). The sum of the response scores giving the additive scale scores ranged from 0 to 30. However, for those who were currently expecting their first child during the interview, two questions (behavior domain) were not applicable therefore their maximum total score was 26.

2.5.2. Response variables

The response variables in this study were the acceptance and WTP for a ZV. Prior to data collection, participants were provided with the following information: (a) Zika is caused by ZIKV; (b) the disease is mostly present in the Americas; (c) there has been no Zika patient reported in Aceh or West Sumatra but there is potential that this disease will become present in the country; (d) infection during pregnancy could cause neurological defects in newborns and cause impairment for their entire life; and (f) the virus is transmitted by mosquitos but could be transmitted through sexual contact. Because there was no licensed ZV available during the study; it was hypothesized that a safe and 90% protective vaccine against ZIKV was available. The participants were informed that the vaccine need to be injected into the body through the deltoid muscle.

To assess the acceptance for ZV, participants were asked to respond two questions: “How likely would it be for you to get yourself vaccinated against Zika virus infection?” and “How likely would it be for you to recommend your partner to get himself/herself vaccinated against Zika virus infection?”. The possible responses were scored on a five-point Likert-type scale, ranging from “very unlikely”, to “very likely.” Responses for “very unlikely” and “unlikely” scored as 0, “undecided” scored as 1 and score of 2 was given to “likely” and “very likely”.

To assess the amount of money that participants would be willing to pay for a ZV, the participants were asked whether they would be willing to pay according to a randomly chosen bid amount from the following bids: IDR 50,000; 100,000; 250,000; 500,000; 750,000; 1 million; 2 million; and 3 million (equivalent to US\$ 3.50, 7.01, 17.52, 35.04, 52.55, 70.07, 140.14, and 210.21). The possible responses were “yes” or “no”. The WTP was defined as the highest accepted bid, i.e., the highest price the participants said they were willing to pay.

2.6. Interview and data collection

Structured interviews assisted by a validated questionnaire were conducted in Bahasa Indonesia to collect the information of

interest from respondents. In some occasions, sentence(s) or word (s) were translated into local languages (Acehnese or Bahasa Minang, in Aceh and West Sumatra, respectively) to give a clearer explanation. Prior to the interview, a potential participant was informed of the study aims, risks and benefits. Participants were also informed that they could withdraw from the study any time during the interview. Once the participants agreed to participate, they were asked to sign an informed consent form. Each informed consent form and its matching questionnaire was assigned an identifier code and this was used in all analyses.

2.7. Statistical analysis

For statistical analysis, the total raw score for the attitude towards childhood vaccination was converted to a 0–100 scale and the then dichotomized into two categories: good attitude (score < 50) and poor attitude (score \geq 50), following previous literature [33–35]. The score of acceptance to ZV were computed as the sum of the response scores from two questions giving the additive scale scores ranged from 0 to 4. The acceptance was then categorized into “willing” and “not willing” based on a 75% cut-off point (i.e. score 3 or more classified as “willing”). Studies have frequently used a similar cut-off point of either 75% or 80% to dichotomize attitudinal variables [28,29,36–39]. To assess the explanatory variables influencing participants’ ZV acceptance, a logistic regression was employed. The estimated odds ratio (OR) was interpreted in relation to one of the categories, which was designated as the reference category (R).

Explanatory variables influencing participants’ stated WTP were determined using a multivariate linear regression model as described elsewhere [37]. A series of diagnostic assessments was conducted to check how well the data met the model assumptions used in the multivariate model. To assess multicollinearity, heteroscedasticity and residual normality, the Variance Inflation Factor (VIF) [40], Glejser test [41] and Kolmogorov-Smirnov test [42] were employed, respectively. A VIF value of lower than 10 and a tolerance value (1/VIF) of greater than 0.1 was used to define no multicollinearity between variables. A cut-off point of P-value greater than 0.05 in the Glejser test, and Kolmogorov-Smirnov test was used applied to indicate no heteroscedasticity, and normal distribution of residuals, respectively [37].

This initial diagnostic step indicated that the data violated two assumptions: heteroscedasticity, and normality of residuals. After transforming the WTP values using a natural logarithm function (ln), the model showed better adherence to the aforementioned assumptions. Therefore, the transformed WTP value was used in multivariate linear regression model. All explanatory variables that were not significant at $P < 0.25$ in the initial model were excluded and to achieve the final model, backward elimination approach was employed. All associations between an explanatory and WTP was also interpreted in relation to reference category (R).

The mean estimated WTP in US\$ and its 95% CI were calculated as $\text{Exp}(\widehat{X\beta} + \widehat{\sigma}^2/2)$ where $\widehat{\beta}$ was the estimated regression coefficients (B) and $\widehat{\sigma}^2$ was the mean squared error (MSE) of the multivariate model [37,43,44]. All analyses were performed using Statistical Package for the Social Sciences software (SPSS for Windows, Version 15, Chicago, USA).

3. Results

3.1. Study population characteristics

We approached and interviewed 1102 respondents in eleven regencies and 145 (13.2%) refused to participate or had incomplete interviews. Most participants discontinued the interview when

they were called by a nurse to meet a doctor. A total of 956 (86.8%) participants were analyzed for ZV acceptance. The characteristics of the participants are depicted in Table 1. A majority of the respondents (73.1%) was between 20 and 39 years old. No participants were illiterate and approximately 85% of the respondents had finished their senior high school (year 12). More than half of the participants earned less than IDR 3 million (US\$ 210.2) each month. Approximately 60% of the participants had 1 or 2 children and less than 5% of participants were pregnant. Approximately a quarter of the participants had heard about Zika.

According to the PACV questionnaire, 152 (15.9%) of the respondents had a poor attitude towards childhood vaccination. With each subdomain analyzed separately, poor attitudes were held by 61.6% for vaccine safety and efficacy, 39.8% for vaccination behavior, and 7.2% for general attitudes.

3.2. Acceptance of Zika vaccine and associated explanatory variables

A total of 757 (79.1%) participants expressed their acceptance of ZV. The univariate analysis demonstrated that having a diploma certificate, having a job, having heard about Zika and having a good attitude towards childhood vaccination predicted ZV acceptance (Table 1). Although participants who had a diploma certificate had an increased odds of having a good ZV acceptance compared to the participants who only completed primary school, there was no significant difference between the highest educational category and the reference category of primary school. Having a job was associated with better support for ZV, with an OR of 1.43 (95% CI: 1.04–1.95). In addition, having heard information on Zika also predicted vaccine acceptance with an OR: 2.98 (95% CI: 1.91–4.66), $P < 0.001$.

As predicted, those with good attitude towards childhood vaccination were more supportive of ZV (OR: 7.68; 95% CI: 5.27–11.19, $P < 0.001$). When divided by subdomain, each subdomain was also strongly associated with ZV acceptance. Compared to participants with poor attitude towards vaccination behavior and safety-efficacy, those with good attitude were approximately three times more likely to have a better acceptance for ZV, with OR: 2.92 (95% CI: 2.10–4.06) and 3.38 (95% CI: 2.30–4.97), respectively. Those with a good general attitude towards childhood vaccination were 14 times more likely to have a better support for ZV (95% CI: 8.04–24.91).

In the multivariate analysis, those who heard about Zika (OR: 2.37, 95% CI: 1.44–3.88) and who had a good attitude towards childhood vaccination (OR: 3.41, 95% CI: 2.01–5.79) were significantly associated with acceptance of ZV (Table 1). This positive association was also true for the subdomains within childhood vaccination attitude that were included in the multivariate analysis (i.e., general attitude and the vaccine safety-efficacy subdomain).

3.3. Willingness-to-pay for a Zika vaccine

Out of 956 respondents who provided completed information, a very small number of them ($n = 34$, 3.6%) stated that they would not be vaccinated even if ZV was provided for free, while a majority of respondents ($n = 584$, 61.1%) stated they would be vaccinated only if ZV was provided for free. Only 338 respondents (35.3% of those with complete data) were willing to pay for a ZV and these were included in the final data analysis. The mean and median of WTP was US\$ 13.1 (95% CI: 11.37–15.09) and US\$ 7.0 (95% CI: 4.47–10.98), respectively.

Among those who were willing to pay for ZV, 11.4% of participants expressed their WTP at US\$ 3.5, and decreased constantly to 7.7%, 6.5%, and 2.3% as the price for ZV went up to US\$ 7.0, US\$ 17.5, and US\$ 35.0, respectively (Fig. 1). Only 3.2% (30/956) of

Table 1
Univariate and multivariate logistic regression analysis showing predictors of acceptance for a Zika vaccine (*Willing vs. Not willing*) ($n = 956$).

Variable	n (%)	Willing n (%)	Univariate		Multivariate	
			OR (95% CI)	P-value	aOR (95% CI)	P-value
Age group (years)						
20–29 (R)	230 (24.0)	184 (80.0)	1		–	
30–39	469 (49.1)	365 (77.8)	0.88 (0.59–1.30)	0.511		
40–49	189 (19.8)	152 (80.4)	1.03 (0.63–1.67)	0.914		
More than 50	68 (7.1)	56 (82.4)	1.17 (0.58–2.36)	0.667		
Gender						
Male (R)	129 (13.5)	97 (75.2)	1		1	
Female	827 (86.5)	660 (79.8)	1.30 (0.85–2.01)	0.231	1.39 (0.82–2.35)	0.223
Educational attainment						
Primary school (R)	42 (4.4)	30 (71.4)	1		1	
Junior high school	106 (11.1)	86 (81.1)	1.72 (0.75–3.94)	0.199	1.34 (0.51–3.50)	0.555
Senior high school	361 (37.8)	269 (74.5)	1.17 (0.58–2.38)	0.665	0.65 (0.28–1.50)	0.310
Diploma certificate	223 (23.3)	194 (87.0)	2.68 (1.23–5.81)	0.013	1.05 (0.40–2.76)	0.919
University graduate	224 (23.4)	178 (79.5)	1.55 (0.74–3.26)	0.250	0.74 (0.29–1.92)	0.537
Employment status						
Unemployment (R)	471 (49.3)	359 (76.2)	1		1	
Employee	485 (50.7)	398 (82.1)	1.43 (1.04–1.95)	0.027	1.27 (0.81–2.00)	0.301
Monthly income (IDR)						
Less than 3 million (R)	523 (54.7)	402 (76.9)	1		1	
3–5 million	328 (34.3)	270 (82.3)	1.40 (0.99–1.99)	0.058	1.12 (0.74–1.69)	0.607
More than 5 million	105 (11.0)	85 (80.9)	1.25 (0.73–2.15)	0.416	0.99 (0.52–1.89)	0.982
Number of children						
The first pregnancy (R)	31 (3.2)	22 (71.0)	1		1	
1–2	564 (59.0)	444 (78.7)	1.51 (0.68–3.37)	0.311	1.56 (0.63–3.88)	0.340
3–5	337 (35.3)	274 (81.3)	1.78 (0.78–4.05)	0.170	2.01 (0.78–5.18)	0.147
More than 5	24 (2.5)	17 (70.8)	0.99 (0.31–3.21)	0.991	1.23 (0.32–4.77)	0.762
Have heard about Zika						
No (R)	704 (73.6)	530 (75.3)	1		1	
Yes	252 (26.4)	227 (90.1)	2.98 (1.91–4.66)	<0.001	2.37 (1.44–3.88)	0.001
Attitude towards childhood vaccination						
Poor (R)	152 (15.9)	67 (44.1)	1		1	
Good	804 (84.1)	690 (85.8)	7.68 (5.27–11.19)	<0.001	3.41 (2.01–5.79)	<0.001
Vaccination behavior subdomain						
Poor (R)	368 (39.8)	253 (68.8)	1		–	
Good	557 (60.2)	482 (86.5)	2.92 (2.10–4.06)	<0.001		
General attitude subdomain						
Poor (R)	69 (7.2)	18 (26.1)	1		1	
Good	887 (92.8)	739 (83.3)	14.15 (8.04–24.91)	<0.001	3.71 (1.80–7.63)	<0.001
Vaccine safety and efficacy subdomain						
Poor (R)	589 (61.6)	427 (72.5)	1		1	
Good	367 (38.4)	330 (89.9)	3.38 (2.30–4.97)	<0.001	1.91 (1.23–2.94)	0.004

aOR: adjusted odds ratio.

CI: confidence interval.

OR: odds ratio.

R: reference group.

the respondents were still willing to pay for the vaccine at the highest price provided (US\$ 210.2).

3.4. Factors associated with the willingness to pay for a Zika vaccine

The initial model of multivariate linear regression indicated that having a monthly income more than IDR 5 million (US\$ 350.3) and having heard about Zika were the only variables associated with WTP for a ZV ($P < 0.05$) (Table 2).

The final multivariate model indicated that having a job, a higher income (more than IDR 5 million) and preexisting knowledge related to Zika disease were all significantly associated with WTP (Table 3). Compared to unemployed respondents, those who had a job were willing to pay US\$ 21.51 more, and those with a highest income were willing to pay US\$ 33.80 more than those with a monthly income less than IDR 3 million (US\$ 210.2). Compared to respondents who never heard about Zika prior the study, those who had preexisting information about Zika were willing to

pay US\$ 26.64 more. These data indicate that the monthly income is the strongest predictor for WTP for a ZV (see Table 3).

4. Discussion

This study was conducted to assess the acceptance and WTP for a ZV in Indonesia and to determine their associated explanatory variables. Although some studies have been conducted to assess the acceptance for a ZV in the US [23–25], data from Asian countries are limited [26] and no study is available for WTP. This will be the first published report of WTP for a hypothetical ZV in Asia.

We found that 79.1% of the participants expressed their acceptance for a hypothetical ZV. As predicted, having preexisting knowledge related to Zika disease was associated with higher ZV acceptance. Previous studies have also found that a good knowledge about ZIKV is associated with acceptance for a ZV [23,25]. In the present study, we confirmed that preexisting knowledge about Zika is also associated with an increase in WTP. Therefore,

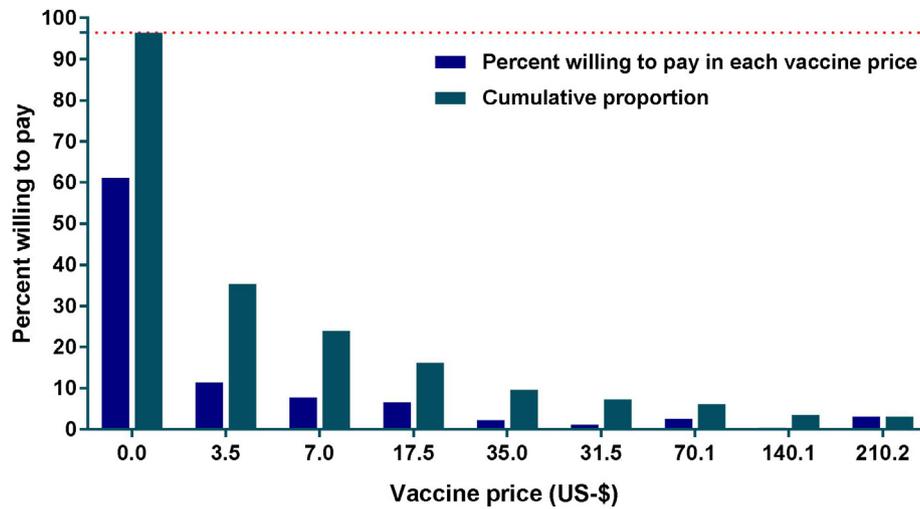


Fig. 1. Relationship between the presented price and proportion of participants who are willing to pay a Zika vaccine in Aceh and West Sumatra, Indonesia. Red dotted line indicates the percentage of participants who are willing to be vaccinated if the vaccine was provided for free. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

Table 2

Initial model of multivariate linear regression analysis showing factors associated with the willingness to pay for a Zika vaccine (n = 338).

Variable	Unstandardized coefficients				US\$ estimate			P-value
	B	95% CI of B		SE	Mean	95% CI		
		Lower	Upper			Lower	Upper	
Intercept	1.809	0.731	2.887	0.550	12.64	10.27	15.00	0.001
Age group (20–29 years)								
30–39	–0.023	–0.384	0.338	0.184	12.35	9.99	14.71	0.920
40–49	0.102	–0.370	0.574	0.241	13.99	11.63	16.36	0.671
More than 50	0.575	–0.262	1.412	0.427	22.46	20.10	24.83	0.179
Gender (Male)								
Female	0.191	–0.232	0.614	0.216	15.30	12.93	17.66	0.376
Education (Primary school)								
Junior high school	0.286	–0.469	1.041	0.385	16.82	14.46	19.19	0.459
Senior high school	0.406	–0.300	1.112	0.360	18.97	16.60	21.33	0.261
Diploma certificate	0.721	–0.065	1.507	0.401	25.99	23.63	28.36	0.073
University graduate	0.431	–0.373	1.235	0.410	19.45	17.08	21.81	0.293
Employment status (Unemployment)								
Employee	0.353	–0.012	0.718	0.186	17.99	15.62	20.35	0.059
Monthly income (IDR) (Less than 3 million)								
3–5 million	0.019	–0.330	0.368	0.178	12.88	10.51	15.24	0.914
More than 5 million	0.785	0.354	1.216	0.220	27.71	25.35	30.08	<0.001
Number of children (The first pregnancy)								
1–2	–0.073	–0.863	0.717	0.403	9.22	6.83	11.60	0.857
3–5	–0.191	–0.512	0.130	0.164	10.44	8.07	12.80	0.245
More than 5	–0.578	–1.407	0.251	0.423	7.09	4.72	9.45	0.172
Have heard about Zika (No)								
Yes	0.579	0.242	0.916	0.172	22.55	20.19	24.92	0.001
Attitude towards childhood vaccination (Poor)								
Good	0.158	–0.412	0.728	0.291	14.80	12.44	17.17	0.587
Vaccination behavior subdomain (Poor)								
Good	0.083	–0.262	0.428	0.176	13.73	11.37	16.10	0.636
General attitude subdomain (Poor)								
Good	–0.476	–1.260	0.308	0.400	7.85	5.48	10.21	0.235
Vaccine safety and efficacy subdomain (Poor)								
Good	–0.184	–0.494	0.126	0.158	10.51	8.15	12.88	0.248
Mean squared error (MSE)	1.456							
F value	4.416 (P < 0.001)							
R ²	0.215							

B: estimated regression coefficients.
 CI: confidence interval.
 SE: standard error.
 US\$: United States dollar.

Table 3
Final model of multivariate linear regression analysis showing factors associated with the willingness to pay for a Zika vaccine ($n = 338$).

Variable	Unstandardized coefficients				US\$ estimate			P-value
	B	95% CI of B		SE	Mean	95% CI		
		Lower	Upper			Lower	Upper	
Intercept	1.954	1.748	2.160	0.105	14.592	12.229	16.955	<0.001
Age group (20–29 years)								
More than 50	0.462	-0.300	1.224	0.389	23.162	20.799	25.525	0.236
Education (Primary school)								
Diploma certificate	0.272	-0.051	0.595	0.165	19.154	16.791	21.517	0.100
Employment status (Unemployment)								
Employee	0.388	0.102	0.674	0.146	21.510	19.147	23.873	0.008
Monthly income (IDR) (Less than 3 million)								
More than 5 million	0.840	0.497	1.183	0.175	33.801	31.438	36.164	<0.001
Have heard about Zika (No)								
Yes	0.602	0.306	0.898	0.151	26.642	24.279	29.005	<0.001
Mean squared error (MSE)	1.453							
F value	14.825	$(P < 0.001)$						
R ²	0.183							

B: estimated regression coefficients.

CI: confidence interval.

SE: standard error.

US\$: United States dollar.

to increase support for a Zika vaccination, a program should also be designed to increase knowledge of Zika itself.

Notably, we found that more positive attitudes towards childhood vaccination was strongly associated with a higher acceptance for ZV. More specifically, better immunization behavior, good beliefs about vaccine safety and efficacy, and a better general attitude towards vaccination (including trust for vaccination) were associated with greater acceptance, and participants' general attitude towards vaccination was the strongest predictor. A previous study similarly found that misbelief about complications from childhood vaccinations (that MMR vaccination causes autism in children) reduced intentions to vaccinate against ZIKV and was the strongest predictor [24]. Thus preexisting attitudes and beliefs about childhood vaccination are critical factors for accepting a new vaccine, especially when the public members show lack of understanding of the threat of the disease. Altogether, these results indicate that to achieve increased ZV acceptance, it is critical not only to increase the knowledge about Zika itself but also to minimize vaccine hesitancy. This approach would increase positive beliefs related to vaccine safety and efficacy, and improve attitudes and trust forwards vaccination. In the Indonesian context, a mixed religion-health-based approach might be the most suitable strategy to disseminate ZV information. In this strategy, as explained previously [45–47], trusted individuals (health professionals such as nurses and doctors, and religious leaders) are involved together with a recommendation from trusted authorities such as the Ministry of Health and Provincial Health Office. The involvement of trusted parties is critical because trust is one of the most important factors for a successful vaccination program [48]. This strategy minimizes barriers to vaccination such as fear of side effects, improves beliefs regarding the efficacy and usefulness of vaccines, and also minimizes distrust and religious barriers. In our perspective, distrust and religious barriers are the most important factors that should be mitigated. In Indonesia, with 87.18% of population Muslim in 2010, one of the crucial issues is related to *halal* certification (does not contain any haram materials). It is critical that a ZV can be distributed after receiving certification from the Indonesian Ulema Council, Indonesia's top Muslim clerical body. Unsorted *halal* certification issues not only increases the potential for rejecting a new vaccine, but it also increases the refusal and hesitancy

related to compulsory childhood vaccinations. This issue is one of the important contributing factors related to the increase of vaccine-preventable diseases cases in Muslim-majority countries [49]. Therefore, information addressing religious concerns of *halal* issue must be given priority before a new vaccine being introduced in Muslim-majority countries, including Indonesia.

Although almost 80% participants expressed their acceptance of ZV, our study found that only 35.3% of respondents were willing to pay for ZV. This underscores that the provision of partially or fully subsidized vaccines will be necessary to achieve high vaccine coverage and this should be taken into account for ZV vaccine policy. There are at least three predictors identified for WTP: having heard about Zika disease, having a permanent job, and earning a high monthly income (more than IDR five million). Understandably, wealthy respondents with a permanent job and higher income are willing to pay more money for ZV. In the context of other vaccines, previous studies also constantly found that income per capita or economic status is one of the robust predictors for WTP [50–55]. This indicates that individuals with a higher income can afford a more expensive ZV.

Our data also indicated that having heard about Zika prior to our study is associated with a higher WTP for a ZV. So far there is no study that has confirmed the association of preexisting information with WTP. Although the attitude towards childhood vaccination is the strongest factor for acceptance, this variable is not associated with WTP. We found that, WTP is more influenced by socioeconomic-related variables such as having a job and a high monthly income. This indicates that the provision of partially or fully subsidized ZV will be necessary in Indonesia.

Our study also indicated that prior knowledge on Zika is an independent predictor for an increased WTP for ZV. On the other hand, attitude towards childhood vaccination, which is a significant predictor for acceptance, is not associated with an increase in WTP. Plausible explanation for this is that acceptance and WTP are two distinct behavioral constructs, and hence are explained by different sets of predictors. Hence, although attitude is a predictor of behavior, including for WTP [56], acceptance and WTP are likely to be preceded by different kind of attitudes. This may also explains why most of our subject refused to pay for the proposed vaccine, in spite of their acceptance. Further, it has been

demonstrated that awareness of consequences of a certain action is a determinant of attitude that supports WTP for that action [57] that is likely to be influenced by knowledge. That is, we postulate that knowledge of Zika increases WTP for ZV, insofar as that knowledge contributes to the awareness of consequences of Zika infection.

There are some limitations of this study. Firstly, although there is evidence of recent widespread ZIKV infection throughout Indonesia [15], Zika cases have been reported among travelers after visiting Indonesia [16,17] and ZIKV has recently been isolated from a local inhabitant [18], no symptomatic Zika cases or Zika-related microcephaly has been reported in the country. Therefore, the respondents were provided with brief information related to ZIKV infection prior to interview. This might have diluted the OR and therefore reduced the association power between the variable of “having heard about Zika” and both acceptance and WTP, compared to those who never heard about Zika prior to our study. Secondly, a convenience sampling method was used and therefore a selection bias might exist in this study. Thirdly, most of our continuous variables were converted into dichotomous scores. Although it helps in interpreting the results, this potentially leads to a considerable loss of explanatory power. Fourthly, social desirability bias was inevitable in which participants might tend to give perceived favorable answers about acceptance and WTP. Finally, this study was conducted when no ZV had been approved and licensed and therefore a hypothetical bias might exist in which respondents misstate their actual preferences on acceptance or WTP.

5. Conclusions

Acceptance of the ZV among inhabitants of Aceh and West Sumatra of Indonesia was relatively high, approximately 80%. Some significant modifiable determinants for ZV acceptance were identified such as having heard information about Zika and good attitude towards childhood vaccination including good belief about vaccine safety and efficacy and better attitude and trust towards vaccination. Notably, less than 40% of the respondent were willing to pay for ZV with the mean WTP of US\$ 13.1. Economic-related variables such as having a job and a high monthly income predicted a higher WTP. Our data indicate that an introduction program which is related to Zika and its vaccine and which uses trusted parties is critical not only to educate the community about Zika but also to increase their attitude towards general vaccination. In addition, our findings suggest at least two potential strategies to achieve a high coverage of ZV, should it be made a policy. First, it seems that a vaccine that is provided free of charge or very heavily subsidized will be necessary. Secondly, the private market still can cover a significant proportion of the population, provided that information on ZV is to be made widely available, especially focusing on the potential consequences of Zika infection.

Competing interest

The authors declare that they have no competing interests.

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Authors' contributions

Conceptualization: HH; Methodology: HH, AY, YN; Software: SA, AI; Validation: HH, MM, SA, FY, NH, NPW, RR, DF, NFM, MS, II, TPF, MS, FWA, PFH; Formal analysis: HH, SA; Investigation: HH, AY, NW, FY, NH, NPW, RR, DF, NFM, MS, II, TPF, MS, FWA; Resources: HH, DAG, RM, RTS, AI; Data curation: HH, MM, AA, KFJ, YR, PFH, ALW, RM; Writing – original draft preparation: HH, AA; Writing – review & editing: MM, KFJ, YR, PFH, ALW, DAG, UK, RM, AI, RTS, AI; Supervision: RTS, AI; Funding acquisition, DAG, RM, AI.

Appendix A. Supplementary material

Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) checklist of the study. Supplementary data to this article can be found online at <https://doi.org/10.1016/j.vaccine.2019.01.062>.

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