

## Knowledge of Norovirus and Attitudes toward a Potential Norovirus Vaccine in Rural Guatemala: A Cross-Sectional Exploratory Survey

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**Abstract.** Given limited data on norovirus vaccine acceptance, we performed an exploratory survey in a rural Guatemalan community on knowledge, interest, and willingness to pay (WTP) for a norovirus vaccine. Cluster-randomized households with children aged 6 weeks to 17 years were enrolled into one of two norovirus surveillance studies: 1) a prospective cohort ( $N = 207$  households) and 2) two separate, community-based, cross-sectional surveys ( $N = 420$  households). After completion of the surveillance study, vaccine surveys were completed by 564 (90%) of 627 households. Most households correctly answered questions regarding norovirus symptoms and transmission; 97% indicated interest in a hypothetical norovirus vaccine. Households with higher education had greater WTP for a vaccine (prevalence ratios = 2.2, 95% confidence interval: 1.2–3.1) and households with lower WTP were more likely to use pharmacies, the Ministry of Health, and radios for health care and information. These results suggest that a future norovirus vaccination program could be acceptable and feasible even in rural areas.

Noroviruses cause an estimated 18% of acute gastroenteritis (AGE) globally and more than 200,000 deaths each year, with children under 5 years bearing the greatest disease burden.<sup>1,2</sup> An effective norovirus vaccine has the potential to greatly reduce AGE-associated morbidity and mortality. Currently, there are several norovirus vaccines in development, with the most advanced demonstrating safety, immunogenicity, and efficacy against severe diseases in Phase 1 trials.<sup>3,4</sup> As the scientific community advances toward an effective norovirus vaccine, it is essential to characterize acceptability and willingness to pay (WTP) for such a vaccine, especially in low- and middle-income countries (LMICs), where it is most needed.

Vaccine hesitancy appears to be an increasing problem in LMICs and can be categorized into contextual (i.e., political and cultural barriers) individual/group (i.e., risk/benefit and knowledge), and vaccine-specific (i.e., schedule and cost) influences.<sup>5–7</sup> Although several studies have identified risk factors for vaccine hesitancy in general, data on vaccines against norovirus and other diarrheal diseases are limited.<sup>6,8–11</sup> Like many LMICs, Guatemala has a high burden of enteric diseases, including norovirus.<sup>12,13</sup> In anticipation of forthcoming vaccines, we characterized norovirus vaccine attitudes in this population and explored associations between socio-demographic factors, vaccine hesitancy, and WTP.

A cross-sectional vaccine knowledge and attitude survey was administered to 627 households who had recently participated in a norovirus surveillance study, which was performed among 13 communities within a 200-km<sup>2</sup> catchment area along the coastal lowlands of southwest Guatemala. The people living in this region suffer from high levels of food insecurity, poverty, low access to health care, and high levels of diarrheal and respiratory disease.<sup>12,14</sup>

Households with children aged 6 weeks to 17 years were randomly selected and enrolled in one of two surveillance programs: 1) a prospective participatory surveillance system (PSS) conducted from April 2015 to September 2016 in

which, after enrollment and baseline sampling, children were monitored for AGE using a weekly smartphone-based symptom diary, with diagnostic testing performed for self-reported AGE (norovirus); or 2) two separate rapid active cross-sectional sampling (RAS) surveys conducted in October–November 2015 and January–February 2016 in which children in randomly selected households were screened for AGE symptoms in the previous week and tested for AGE regardless of a symptom report.<sup>12</sup> Randomization and enrollment of the households were conducted using a two-stage cluster sampling strategy in which 30 clusters of seven households each were enrolled in the PSS cohort and each of the two RAS cycles separately, as previously described.<sup>12</sup> Households in both arms received an information brochure about norovirus at the time of enrollment. The vaccine knowledge and attitude survey was administered at the conclusion of this study, in September 2016.

A 66-question vaccine knowledge and attitude survey (“Survey”) was administered to the heads of households via in-person interview by local study nurses. The survey was adapted, in part, from a previously validated World Health Organization Strategic Advisory Group of Experts on Vaccine Hesitancy Report and a survey assessing knowledge and attitudes about dengue virus and vaccine hesitancy.<sup>5,15</sup> The survey collected household demographic information and asked about vaccine hesitancy, knowledge of norovirus, acceptability of a norovirus vaccine, and participant WTP for a hypothetical norovirus vaccine.

Demographic variables and survey responses were compared between the PSS and RAS cohorts using  $\chi^2$  tests. Logistic regression was used to explore associations between socio-demographic factors (independent variables), comparing those who indicated WTP > 25 Quetzales (~\$3.40 US) for a potential norovirus vaccine versus WTP < 25 Quetzales. Logistic regression was also used to explore associations between independent variables and interest in a norovirus vaccine. A survival analysis was performed that examined WTP for a vaccine as the price level increased.<sup>16,17</sup> No variables met the criteria to be considered a confounder. All analyses were conducted using SAS version 9.4 (Cary, NC). The study was approved by the Colorado Multiple Institutional Review Board and the Universidad del Valle de Guatemala Institutional Review Board.

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The surveys were completed by 564 (90%) of 627 households. Sociodemographic variables were similar between the PSS and RAS households, and most households demonstrated an appropriate understanding of norovirus

transmission and symptoms regardless of their exposure to study personnel (Table 1). Most respondents (84%) reported receiving health information from the Ministry of Health (MOH), 65 (12%) stated a household member had been recently

TABLE 1  
Norovirus and vaccine hesitancy survey participant characteristics and responses in southwest Guatemala, September 2016

Survey question	Response	PSS, n (%)	RAS, n (%)	Total, n (%)	P Value
		179 (32)	385 (69)	564	
<b>Demographics</b>					
Mother's education	None	33 (18)	60 (16)	93 (17)	0.66
	Primary	114 (64)	252 (66)	366 (65)	
	Secondary/university	32 (18)	73 (19)	105 (19)	
# Children per HH	1	56 (31)	87 (23)	143 (25)	0.26
	2	46 (26)	130 (34)	176 (31)	
	3	38 (21)	78 (20)	116 (21)	
	≥ 4	39 (22)	90 (23)	129 (23)	
# Adults per HH	1	15 (8)	23 (6)	38 (7)	0.35
	2	93 (52)	178 (46)	271 (48)	
	3	35 (20)	74 (19)	109 (19)	
	≥ 4	36 (20)	110 (29)	146 (26)	
Father's employment	Self-used	82 (46)	173 (45)	255 (45)	0.16
	Used	74 (41)	142 (37)	216 (38)	
	Unemployed	9 (5)	15 (4)	24 (4)	
	Other	14 (8)	55 (14)	69 (12)	
<b>Health attitude</b>					
Where do you seek medical care?*	Public health post	120 (67)	249 (68)	369 (65)	0.92
	Pharmacy	59 (32)	126 (33)	185 (33)	
	Private	49 (27)	102 (27)	151 (27)	
Where do your children get vaccinated?	Public health post	176 (98)	381 (98)	557 (99)	0.89
	Private	1 (1)	2 (1)	3 (1)	
	Pharmacy	1 (1)	1 (0)	2 (0)	
Where do you obtain information about diarrhea?*	MOH	151 (84)	324 (84)	475 (84)	0.95
	Neighbors	37 (21)	134 (35)	171 (30)	< 0.001
	Radio	27 (15)	115 (30)	142 (25)	< 0.001
	Television	28 (16)	111 (29)	139 (25)	< 0.001
	Doctor	5 (3)	22 (6)	27 (5)	0.13
	Newspaper	3 (2)	5 (1)	8 (1)	0.72
	Internet	0	1 (0)	1 (0)	0.51
	What are trustworthy information sources regarding diarrhea?*	MOH	155 (87)	328 (85)	483 (86)
Radio	23 (13)	74 (19)	97 (17)	0.06	
Television	15 (8)	70 (18)	85 (15)	0.003	
Neighbors	14 (8)	28 (7)	42 (8)	0.82	
Doctor	5 (3)	16 (4)	21 (4)	0.43	
Newspaper	1 (1)	6 (2)	7 (1)	0.32	
Internet	0	1 (0)	1 (0)	0.50	
<b>Norovirus knowledge and Vaccine acceptance</b>					
How is norovirus transmitted?	Correct response†	142 (79)	327 (85)	469 (83)	0.07
Who usually gets norovirus?	Correct response‡	176 (98)	369 (96)	545 (97)	0.13
How severe is norovirus?	Serious	159 (88)	325 (84)	484 (86)	0.16
	Not serious	20 (11)	60 (16)	80 (14)	
What are the most common symptoms of norovirus? (> 1 response possible)	Vomiting	173 (97)	382 (99)	555 (98)	0.03
	Diarrhea	179 (100)	381 (99)	560 (99)	
	Fever	101 (56)	175 (46)	276 (49)	
	Cough/Cold	0	1 (< 1)	1 (< 1)	
What is the most common cause of diarrhea in children?	Parasites	88 (49)	200 (52)	288 (51)	0.54
	Bacteria	53 (30)	94 (24)	147 (26)	
	Virus	32 (18)	78 (20)	110 (20)	
	Evil eye	2 (1)	8 (2)	10 (2)	
	Other	0	0	0	
Has any HH member been hospitalized from diarrhea?	Yes	17 (10)	48 (13)	65 (12)	0.30
If a norovirus vaccine was available, would you want it for your child?	Yes	168 (94)	376 (98)	544 (97)	0.02
	No or don't know	11 (6)	9 (2)	20 (4)	
If the vaccine was not free, how much would you be willing to pay for it for your child?§	\$0-\$3.40	77 (46)	219 (58)	296 (54)	0.005
	\$3.40-\$6.80	52 (31)	110 (29)	162 (30)	
	\$6.80-\$10.20	13 (8)	14 (4)	27 (5)	
	\$10.20-\$13.60	12 (7)	22 (6)	34 (6)	
	> \$13.60	14 (8)	11 (3)	25 (5)	

HH = household; MOH = Ministry of Health; PSS = participatory syndromic surveillance cohort; RAS = rapid active sampling group.

\* > 1 possible answer.

† Correct response: diarrhea or vomiting.

‡ Correct response: age < 5 years.

§ Corresponds to the following in Quetzales (Q): 0-\$3.40 = Q0-25, \$3.40-\$6.80 = Q26-50, \$6.80-\$10.20 = Q51-75, \$10.20-\$13.60 = Q76-100, > \$13.60 = > Q100.

hospitalized with diarrhea, and 544 (97%) indicated interest in a norovirus vaccine. Of those interested in a vaccine, more than half (54%) were willing to pay \$0–\$3.40 for the vaccine and nearly 30% were willing to pay \$3.40–\$6.80 (Table 1, Figure 1).

Higher level of parental education was associated with increasing WTP for a potential vaccine. Compared with mothers with no formal education, mothers with a primary, secondary, and university education were increasingly likely to be in the higher WTP group (> \$3.40), with prevalence ratios (PR) of 1.5 (95% confidence interval [CI] 1.0–2.0), 2.2 (95% CI 1.2–3.1), and 2.4 (95% CI 1.5–3.9), respectively. Similar but weaker findings were seen with the father's education level, with a PR of 1.3 (95% CI 1.0–1.8), 1.7 (95% CI 1.3–2.2), and 1.8 (95% CI 1.1–3.0), respectively. Respondents with WTP > \$3.40 for a potential vaccine were 1.5 (95% CI 1.1–2.1) times as likely to have purchased a vaccine in the past.

The 4% ( $N = 20$ ) of respondents who were uninterested in a norovirus vaccine were 9.8 (95% CI 1.9–51.6) times as likely to believe that vaccines in general do not prevent serious disease and 4.3 (95% CI 1.4–13.7) times as likely to have refused a vaccine in the past. These households receive their information about diarrhea primarily from the MOH (80%), neighbors (40%), and television (25%). The MOH was also the most trusted source for information about diarrhea in this group (85%). Households with low WTP were more likely to be crowded, receive their medical care from a pharmacy, and obtain their health information from the radio and MOH (Table 2).

This is the first study to evaluate population-level acceptability of a future norovirus vaccine in an LMIC. Our randomized sample of households from a rural Guatemalan community with recent participation in a norovirus surveillance study demonstrated a high level of knowledge of norovirus disease, recognition of local disease burden, and positive attitudes and acceptability of a potential norovirus vaccine, with 97% of participants expressing interest in such a vaccine. Households reported obtaining their health information from a variety of sources, most commonly the MOH and radio. Most respondents reported trust in the local MOH for health information and nearly all participants relied on local public health posts for routine immunizations.

Households with higher levels of education had greater WTP for a potential vaccine. Because the survey did not obtain household income, we cannot state whether this was due to better understanding of norovirus risk among more educated households or if education is acting as a proxy for income,

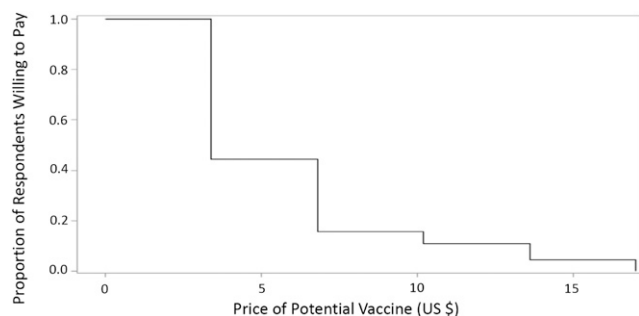


FIGURE 1. Willingness to pay (WTP) for a hypothetical norovirus vaccine among a rural population in southwest Guatemala, 2016. Legend: Survival analysis of price of norovirus vaccine (in U.S. dollars) and proportion of respondents willing to pay that price out-of-pocket.

TABLE 2

Characteristics of households with low willingness to pay (< \$3.40 US) for a norovirus vaccine in southwest Guatemala, September 2016 ( $N = 296$ )

Survey question	PR	95% CI	P Value
Where do you obtain medical care?			
Pharmacy	1.22	1.05–1.42	0.01
Private	0.74	0.60–0.90	0.003
Where do you learn about diarrhea?			
Radio	1.21	1.03–1.41	0.02
MOH	1.30	1.00–1.67	0.046
Number of adults in house	1.08	1.03–1.14	0.002
Number of children in house	1.07	1.04–1.10	< 0.001
Father's employment:			
Used	Ref	Ref	Ref
Self-used	1.22	1.03–1.46	0.02
Unemployed	1.27	0.89–1.81	0.20
Other	1.16	0.90–1.50	0.25

CI = confidence interval; MOH = Ministry of Health; PR = prevalence ratio; Ref = reference variable.

which enables them to pay more and has been found to be associated with greater WTP for other vaccines.<sup>16</sup> Other studies have shown that affordability and parental educational level were the strongest predictors of anticipated vaccine acceptance.<sup>10,11,17</sup> Most households in our sample were willing to pay \$0–\$3.40 for a norovirus vaccine, with very few willing to pay greater than \$6.80. A potential price point in the \$3.00–\$4.00 range is consistent with prices of rotavirus vaccines.<sup>18</sup>

One small group within the population demonstrated vaccine hesitancy. There were strong associations between having refused a vaccine for a child in the past and not being interested in the norovirus vaccine. This group was also less likely to believe that vaccines can prevent serious disease. Other studies have found that low socioeconomic status is associated with poor vaccine acceptance.<sup>14</sup> Fear of adverse effects, exposure to rumors regarding a vaccine, and lack of awareness have also been associated with decreased vaccine acceptance.<sup>19</sup> A physician's recommendation for a vaccine and known protection against severe diseases have previously been shown to improve vaccine acceptability.<sup>20</sup> Although more data are needed, MOH and community-level education may offer an approach to overcome hesitancy in this community.<sup>21</sup>

Strength of this study includes the high rate of survey completion in this randomized sample. The community also represents an ideal target population for a potential norovirus vaccine, given the high vaccine interest and burden of disease.<sup>12</sup> Limitations include possible response bias due to the population's recent participation in a norovirus surveillance study, which provided some education about norovirus. The majority (69%) of survey respondents, however, had only a single study visit up to a year before the survey was conducted, so any educational benefit was likely minimal. Also, the survey did not include questions regarding a possible vaccine schedule or differing levels of vaccine efficacy, which have been shown to be associated with WTP in other studies.<sup>17</sup> Finally, other confounders, such as household income, were not fully explored and should be included in future studies.

In summary, this study provides insight into a rural Guatemalan population's norovirus knowledge, interest, and WTP for a vaccine. Although a small group (4%) demonstrated

vaccine hesitancy, a large majority of survey respondents expressed interest in a norovirus vaccine, with more highly educated individuals demonstrating WTP. As norovirus and other enteric vaccines advance in their preclinical development, future studies should explore vaccine acceptability in relation to the estimated efficacy, the number of doses, additional variables (household income and ethnicity), and the behaviors and determinants of the small group expressing some vaccine hesitancy.

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