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Measuring Vaccine Confidence in a Pilot Introduction of Human Papillomavirus (HPV) in Cambodia

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2016

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An abstract of
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Abstract

Measuring Vaccine Confidence in a Pilot Introduction of Human Papillomavirus (HPV) Vaccine in Cambodia
By Chandni Jaggi

Introduction: Vaccine confidence is becoming increasingly important to study, as vaccine refusal has been increasing in high-income countries. While vaccine confidence has been assessed in high-income countries, there have been few studies on measuring vaccine confidence in low and middle-income countries. As vaccination rates continue to increase in low and middle-income countries, monitoring vaccine confidence is import for ensuring high vaccine uptake. An HPV vaccine demonstration program in Cambodia done by the CDC allowed for us to measure vaccine confidence in this context.
Methods: Respondent demographics and vaccine confidence data were collected during an HPV vaccine demonstration program coverage survey in Cambodia. Four constructs were used to measure vaccine confidence: "I believe vaccines are important," "I believe vaccines are safe," "I believe vaccines are effective," and "I believe vaccines are compatible with my religious beliefs." Respondents were asked to respond on whether they agreed or disagreed with each statement or didn't know, and those responses were coded as 1-no, 2-I don't know, and 3-yes. A Vaccine Confidence Summary Score (VCSS) was created as the sum of each respondents' answers to the four questions. Associations between vaccine uptake and vaccine confidence were measured.
Results: There were a total of 316 respondents in the survey, of which 312 respondents answered all four vaccine confidence questions and were included in this analysis. Ninety percent of respondents agreed with all four of the vaccine confidence questions. There were no statistically significant associations found between vaccine uptake and vaccine confidence, both overall and for the individual statements.
Discussion: Overall, vaccine confidence was found to be very high in this sample in two provinces in Cambodia. There was an almost unanimous agreement among respondents that vaccines are important. There was some hesitancy documented among the other three measures, however people still overwhelmingly confident. Issues with vaccine confidence, specifically vaccine safety, have been seen in high-income countries regarding the HPV vaccine and have caused low rates of vaccine uptake. Therefore, future monitoring of vaccine confidence should continue to ensure confidence stays high and subsequently uptake remains high. Factors affecting vaccine confidence in low and middle-income countries should also be analyzed in future studies.

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Table of Contents

1. Introduction

Vaccines are one of the greatest discoveries of the 20th century. The use of vaccines has contributed to the eradication of smallpox and global polio eradication is within reach thanks to accessible and effective vaccines. Vaccines save millions of lives each year and prevent countless cases of illness and disability. However, without community trust in immunization programs and high uptake of life saving shots, vaccines themselves are worthless. Low vaccine hesitance, and by extension, high vaccine confidence, are key to high vaccine uptake. Vaccine hesitance continues to be a concern globally even in an environment rich with evidence showing the benefits of vaccines in reducing morbidity and mortality (1). Vaccine hesitance, which can range from a lack of confidence in vaccines or immunization programs to complete refusal to vaccinate, is increasingly important to study, as low vaccination coverage and vaccine-preventable disease outbreaks continue to occur (2,3). As immunization coverage continue to increase in low and middle-income countries through widespread vaccination efforts, vaccine confidence should also be monitored to ensure vaccine uptake remains high.

Human papillomavirus (HPV) is the most common sexually- transmitted infection and can lead to the development of cervical cancer, along with anogenital tract cancers, oropharyngeal cancers, and genital warts. Cervical cancer is the fourth most frequent type of cancer among women in the world and the second leading cancer among women in developing regions due to a lack of prevention and treatment resources; globally there are over 500,000 new cases and 266,000 deaths annually (4). Cervical cancer is the leading cause of cancer among women in Cambodia, where the age-standardized incidence of cervical cancer in 2012 was 23.8 cases per 100,000 women and the age-standardized

mortality rate in Cambodia was 13.4 per 100,000 women (5,6). Cambodia's cervical cancer incidence rate was 1.7x higher than the global incidence rate. In April 2014, the World Health Organization's (WHO) Strategic Advisory Group on Immunizations (SAGE) recommended a 2-dose HPV vaccine schedule for girls ages 9 to 14 years (1). As of January 2018, 79 countries have introduced HPV vaccine into national immunization programs (7). However, these programs are mainly in high-income or upper-middle income countries including most of North and South America, Western Europe and Australia (8). While low and middle-income countries are just beginning to introduce HPV vaccine, many industrialized countries have administered HPV vaccine for 10 years or more. Some high-income countries have encountered vaccine hesitancy issues related to the HPV vaccine, which can be a barrier to achieving high vaccination coverage (9,10).

In 2016, the Cambodia Ministry of the Health (MOH) received Gavi support to conduct a 2-year HPV demonstration project in two provinces. The demonstration project targeted 9-year-old girls in and out of school in six operational districts (ODs) within two provinces of Cambodia. Two doses of the bivalent HPV vaccine were administered during January and July of 2017 through a primarily school-based vaccination program; girls not enrolled in school were invited to come to the nearby school be vaccinated. The HPV vaccine was also available at health facilities.

A community-based household-level vaccination coverage survey was done by the Cambodia National Institutes of Public Health (NIPH), with support from the U.S. Centers for Disease Control (CDC) in September 2017, to assess vaccine uptake, acceptability and knowledge/attitudes around the HPV vaccination campaign. This

survey also included four questions assessing vaccine confidence, modeled after previous research done by Dr. Heidi Larson's team at the London School of Hygiene and Tropical Medicine (2). These vaccine confidence questions had been previously used to assess perceptions around vaccination importance, safety, effectiveness and religious compatibility, to the residents of 67 countries around the world (2). This study found that the WHO Western Pacific Region (WPR) reported the highest proportion of people who believe vaccines are not compatible with their religious beliefs compared to all other WHO regions (2). While this study did not include Cambodia specifically, it surveyed 10 countries in the region including Vietnam, which borders Cambodia (2). To date, these vaccine confidence questions have only been used broadly including all vaccines and has not been validated for use in analyzing vaccine confidence among specific vaccines. It has also not been used to assess how vaccine confidence is associated with vaccine uptake (2). This report details a secondary analysis of data obtained during the HPV demonstration project coverage survey in Cambodia, to assess vaccine confidence in the population targeted for HPV vaccination in 2017.

2. Methods

2.1. Data collection

Respondent demographics and vaccine confidence data were collected during an HPV vaccine demonstration program coverage survey in Cambodia, conducted by the NIPH with support from CDC. The survey was conducted in September 2017 using a standard questionnaire administered during house-to-house visits by trained interviewers. The sampling frame included households in the four ODs in Svay Rieng Province and two ODs in Siem Reap Province targeted during the demonstration project. Eligible girls

were residents of the selected OD in Svay Rieng or Siem Reap Province during January 2017 (1st dose vaccination date) and 9 years old in January 2017. Respondents of the survey were parents or caregivers of the eligible girl; if a parent or caregiver was not available, girls could respond to the survey themselves. A limited subset of the survey data was provided by CDC for secondary analysis of vaccine confidence measures. Respondents were not stratified in the analysis by province due to low numbers. Thus, the operational district information was not requested in the limited subset of the data.

2.2. Measures

During the coverage survey, each respondent was asked whether or not they agreed with the following four statements: "vaccines are important for children to have;" "overall I think vaccines are safe;" "overall I think vaccines are effective;" and "vaccines are compatible with my religious beliefs." Answer choices were "yes," "no," or "I don't know." In addition, demographic data on respondents' relationship to girls receiving vaccine (including girls who responded for themselves), sex, highest level of education, along with information about the girl receiving the vaccine, including her grade, school enrollment status, HPV vaccination status, and reasons for receiving or not receiving the vaccine were requested.

2.3.*Statistical Analysis*

A vaccine confidence summary score (VCSS) was created for each respondent. The VCSS was the sum of the answers to the four vaccine confidence questions, coded as no=1, I don't know=2, and yes=3. A similar scoring system was used by the Parent Attitudes to Childhood Vaccines (PACV) survey (11). Responses were summarized into a single VSCC per respondent. The minimum possible score was a 4 (answered "no" to

all four questions) and the maximum score, indicating high vaccine confidence, was a 12 (answered "yes" to all four questions). The VCSS was analyzed as both a continuous and categorical variable. The initial choice of categorization cut-points was 4-9 (low confidence), 10-11 (medium confidence), and 12 (high confidence). Due to a high level of skewing with the majority of respondents scoring 12, an additional analysis was conducted comparing respondents who scored 12 (high confidence) to all respondents scoring less than 12 (lower confidence). We conducted a bivariate analysis to look at associations between sociodemographic factors and confidence. Risk ratios with 95% confidence intervals were used to assess these associations.

High uptake was defined as receiving at least one dose of the HPV vaccine and low uptake was defined as receiving 0 doses of the vaccine. Vaccine uptake was compared to the VCSS, along with the four vaccine confidence measurements independently, using contingency tables. For the individual confidence variables, vaccine importance, safety, effectiveness and religious compatibility, people who responded yes were considered high confidence and those who responded "no" or "I don't know" were considered low confidence. Fisher's exact p-values were obtained to evaluate at the associations between vaccine confidence and vaccine uptake. The Fisher's exact test was used because some cell counts were less than 5, making chi square tests unreliable.

2.4. IRB

Original coverage survey data collection and vaccine hesitancy sub-analyses were approved by CDC IRB and determined to be non-human research/program evaluation. Emory IRB determined the secondary analysis of previously collected data to be non-

human research. The data was de-identified and there were no risks to participants or ethical concerns with the study.

3. Results

There were a total of 316 respondents in the survey, of which 312 respondents answered all four vaccine confidence questions and were included in this analysis (Table 1). Out of the 312 respondents included in the analysis, 227 (73%) were parents of the girl who received the vaccine, and only 3 (1%) of respondents were girls who answered the survey for themselves. Half (50%) of the respondents' highest level of education was primary school and over a quarter (27%) never attended school. Of 312 respondents enrolled in the survey, 310 (99%) indicated that the girl was enrolled in school during the demonstration program. Of 312 girls, 268 (86%), received at least one dose of HPV vaccine. The most common reason listed for not receiving vaccine among the 44 not vaccinated was lack of awareness of the HPV vaccine campaign (n=15, 35%); other reasons included not normally attending school (n=2, 5%) and not being in the village during the campaign period (n=2, 5%). Of those who received vaccine, over 60% of caregivers listed "protection from cervical cancer" as their main reason for the girl receiving vaccine. Other frequently listed reasons for vaccine receipt included vaccines are thought to be good for health (13%), vaccines provide protection from cancer (10%) and vaccines prevent girls from getting sick (6%) (Table 1). Bivariate associations between sociodemographic factors and vaccine confidence were analyzed using risk ratios (Table 2). Due to the distribution of the data, there was a lack of precision in most estimates, as evidenced by wide confidence intervals (Table 2). There were only five statistically significant associations, which also had similarly wide confidence intervals.

Ninety percent of respondents had a VCSS of 12, and no respondents had a summary score of 4. First, we categorized the VCSS into three categories. There were 9 people who initially scored in the low confidence range (VCSS=4-9), with the lowest score being 6. There were 22 respondents who had moderate confidence (VCSS=10-11), while 90% of people had a high confidence score (VCSS=12). After a secondary analysis categorizing lower confidence as anyone with a VCSS less than 12, 31 (10%) respondents had a lower confidence score. High confidence included all respondents who scored a 12 (281 respondents, 90%).

In an effort to understand how confidence may influence vaccine uptake, Fisher's exact tests were used to examine any association between the two (Table 3). There were 268 (86%) respondents classified as high uptake (receiving at least one vaccine dose) and 44 respondents classified as low uptake (receiving no vaccine doses). The Fisher's exact test showed no association between vaccine uptake and overall vaccine confidence (p value = 0.1722) (Table 3). There was also no statistically significant association between vaccine uptake and respondent perceptions that vaccines are important (p = 0.2626), safe (p = 0.0944), effective (p = 0.1516), and compatible with their religious beliefs (p = 0.2422) (Table 3).

Table 1. Sample Characteristics (n=312)

	n	%
Respondent's relationship to girl		
Girl (self)	3	1
Parent	227	73
Grandparent	54	17
Sibling	13	4
Other	15	5
Respondent's sex		

Male	37	12
Female	272	88
Respondent's education attainment		
Never attended school	87	28
Nursery/Kindergarten	6	2
Primary	156	50
Secondary	50	16
Higher Education	11	4
Other	1	0
Respondents age		
Under 18	8	3
18 - 24	12	4
25 - 34	72	23
35 - 44	119	38
45 - 54	57	18
55 - 64	30	10
65+	14	4
Girl's grade		
Grade 2	13	4
Grade 3	71	23
Grade 4	154	50
Grade 5	64	21
Other	8	3
Respondent reported girl's school enrollment		
Enrolled	310	99
Not enrolled	2	1
Number of HPV Doses Received		
0	44	14
1	11	4
2	257	82
Main Reason Received the Vaccine (n=264)		
Protection from cancer	26	10
Protection from cervical cancer	159	60
Vaccines thought good for health	35	13

Prevents girl from getting sick	14	5
Vaccine is free	4	2
Followed advice of someone	3	1
Followed advice of media	1	0
School was providing it	15	6
Other	7	3
Main Reason Did Not Receive the Vaccine (n=36)		
Girl does not normally attend school	2	6
Girl not in school that day	1	3
Girl refused vaccine	1	3
Girl not aware of HPV campaign	15	42
Concerns about vaccine safety	2	6
Parent/girl did not believe vaccine is good for health	1	3
Girl followed advice of someone	1	3
Girl followed advice of media channels	1	3
Girl not in village during campaign period	2	6
Other	10	28

Table 2. Bivariate Analysis of sample characteristics and confidence (n=312)

	Low Confidence n	Total n	RR	95% CI	
Respondent's relationship to girl					
Girl (self)	2	3	7.2063	2.936	17.6872
Parent	21	227	1.00		
Grandparent	5	54	1.0009	0.3953	2.5344
Sibling	0	13	0.00		
Other	3	15	2.16	0.7261	6.4369
Respondent's sex					
Male	4	37	1.09	0.4037	2.9378
Female	27	272	1.00		
Respondent's education attainment					
Never attended school	8	87	1.02	0.4476	2.3454
Nursery/Kindergarten	0	6	0.00		
Primary	14	156	1.00		
Secondary	8	50	1.78	0.7946	4.0003
Higher Education	1	11	1.01	0.1464	7.0099
Respondents age					
Under 18	2	8	2.70	0.7184	10.1822
18 – 24	0	12	0.00		
25 – 34	8	72	1.20	0.5074	2.8475
35 – 44	11	119	1.00		
45 – 54	8	57	1.52	0.6462	3.5675
55 – 64	1	30	0.36	0.0484	2.6848
65+	1	14	0.77	0.1077	5.5454
Girl's grade					
Grade 2	2	13	1.48	0.3813	5.7498
Grade 3	6	71	0.81	0.3323	1.9909
Grade 4	16	154	1.00		

Grade 5	7	64	1.05	0.4549	2.4361
Other	0	8	0.00		
Respondent reported girl's school enrollment					
Enrolled	310	312	1.00		
Not enrolled	0	2	0.00		
Number of HPV Doses Received					
0	7	44	1.78	0.8122	3.8907
1	1	11	1.02	0.1506	6.853
2	23	257	1.00		
Main Reason Received the Vaccine					
Protection from cancer	1	26	0.53	0.0713	3.8747
Protection from cervical cancer	12	164	1.00		
Vaccines thought good for health	7	35	2.73	1.1593	6.4447
Prevents girl from getting sick	1	15	0.91	0.127	6.5352
Vaccine is free	0	4	0.00		
Followed advice of someone	1	3	4.56	0.8402	24.7002
Followed advice of media	0	1	0.00		
School was providing it	0	16	0.00		
Other	2	7	3.90	1.073	14.2102
Main Reason Did Not Receive the Vaccine					
Girl does not normally attend school	0	2	0.00		
Girl not in school that day	0	1	0.00		
Girl refused vaccine	0	1	0.00		
Girl not aware of HPV campaign	3	15	1.00		
Concerns about vaccine safety	2	2	5.00	1.8172	13.7572
Parent/girl did not believe vaccine is good for health	1	1	5.00	1.8172	13.7572

Girl followed advice of someone	0	1	0.00		
Girl followed advice of media channels	0	1	0.00		
Girl not in village during campaign period	1	2	2.50	0.4494	13.9075
Other	0	14	0.00		

[a]Low confidence is defined as a vaccine confidence summary score less than 12.

Table 3. Comparison of HPV vaccine uptake by vaccine confidence measures, Cambodia, 2017

	High Uptake (1 or 2 doses) n=268		Low Uptake (0 doses) n=44		Fisher's Exact Test P-value
	n	%	n	%	
Overall[a]					
High Confidence	244	91.04	37	84.09	0.1722
Low Confidence	24	8.96	7	15.91	
Vaccines are Important[b]					
High Confidence	267	99.63	43	97.73	0.2626
Low Confidence	1	0.37	1	2.27	
Vaccines are Safe[b]					
High Confidence	259	96.64	40	90.91	0.0944
Low Confidence	9	3.36	4	9.09	
Vaccines are Effective[b]					
High Confidence	255	95.15	39	88.64	0.1516
Low Confidence	13	4.85	5	11.36	
Vaccines are Compatible with Religious Beliefs[b]					
High Confidence	257	95.9	40	90.91	0.2422
Low Confidence	11	4.1	4	9.09	

[a]High confidence is defined as a vaccine confidence summary score equal to 12. Low confidence is defined as a vaccine confidence summary score less than 12.
[b]High confidence is defined as a response of "yes", or agreed with the statement. Low confidence is defined as a response of"no" or "I don't know."

4. Discussion

We performed a secondary analysis of data collected during an HPV demonstration project vaccination coverage survey in Cambodia to assess vaccine confidence and its association with vaccine uptake, using a vaccine confidence scale previously utilized in a multi-country study (2). In this analysis, there were no significant associations between vaccine confidence and vaccine uptake. While vaccine safety had the lowest Fisher's exact p-value, 0.09, there was still no association. Most girls enrolled in this study were vaccinated and had high vaccine confidence.

The bivariate analysis done showed that there is no significant association between low confidence and sociodemographic features within the two ODs surveyed. The table shows a statistically significant association (RR=7.2063) between girls who answered the survey and low confidence. However, only six girls answered the survey for themselves and among those only three answered all four vaccine confidence questions, therefore creating a sample too small to be representative of all girls their age. The confidence interval is also very wide, showing that the RR is very imprecise. Further research should be done to analyze vaccine confidence among young girls themselves. This will be important to know as they transition into adolescents and begin to make vaccine decisions for themselves.

While some respondents had lower vaccine confidence scores, they almost unanimously agreed that vaccines are important. Interestingly, there was no single measure of the four vaccine confidence questions that appeared to be a predominant driver of lower vaccine confidence scores. This is reassuring in that we did not identify any specific reasons for vaccine hesitance (importance, safety, effectiveness or religious compatibility) among respondents in this survey.

Notably, the vaccine confidence construct with the lowest score was vaccine effectiveness, although not significantly lower than the others. However, this is different from what has previously been seen in the WPR, where religious incompatibility was more commonly cited as the construct with the lowest vaccine confidence (2). The previous study using these questions did not include Cambodia (2). Our research agreed with the previous study that found people in the WPR overwhelmingly believe that vaccines are important (2). Overall, our analysis found vaccine confidence to be very

high in Cambodia. That compliments the success of routine immunization in Cambodia, where vaccination coverage has reached 99% for DPT3 in 2016 (12). The routine immunization program in Cambodia has been very successful, showing that people have trust in the government vaccination program in Cambodia. Other studies in the region have shown a perception of high importance of vaccines and a high willingness to receive vaccines (2). Future studies should continue monitoring vaccine confidence to gather more data on the subject.

Continual monitoring of vaccine confidence among communities, specifically for HPV vaccine, is important. In high-income countries that have introduced HPV vaccine decreases in HPV vaccine uptake have been seen due to concerns about vaccine safety (10). Japan completely halted their HPV vaccination program because of a lack of confidence in the safety of the vaccine (10). Denmark has suffered from low HPV vaccine uptake also due to safety concerns, mainly circulated through the media (14). High-income countries have faced vaccine confidence issues that have directly impacted vaccine uptake, illustrating the importance of understanding and monitoring vaccine confidence as more and more countries introduce the HPV vaccine nationally. Media, especially social media, have been large factors in creating low confidence in vaccines, as seen in Denmark with the HPV vaccine (14). Monitoring media and how media portrays vaccines in country is critical as low and middle-income countries continue to introduce new vaccine introductions. Building vaccine confidence in these countries as they introduce vaccines is important for current and future vaccine uptake. Further research is needed to explore what factors may impact vaccine confidence in Cambodia specifically,

along with other low and middle-income countries, and how that might differ from high income countries.

Some strengths of this study include use of vaccine confidence questions that have previously been used in a multi-country setting, including 10 countries from WPR. Questions used in this study to assess vaccine confidence have been used in over 67 countries to evaluate vaccine confidence. The scoring system was done on a yes/no scale because similar studies using a Likert scale in other developing countries resulted in problems with question comprehension leading to poor data quality (13). Therefore, a simplified yes/no/don't know system was used to generate a vaccine confidence score. Although previous research used a Likert scale, the results ended up being dichotomized into positive or negative views on vaccines for analysis, similar to our analysis using yes/no (2). Therefore, these findings are not likely to differ from studies that did utilize a Likert scale (15).

However, this study had some limitations. First, the analysis was done on a sample and within that sample there were too few people reporting low confidence to conduct more detailed analysis on the associations of vaccine confidence constructs on uptake. Collapsing everyone who responded "I don't know" and "no" into one group might have impacted the data. People who respond "I don't know", or seem neutral, have been seen to be swayed to either the "yes" or "no" group depending on what the media is saying around vaccines, specifically vaccine safety (16). Therefore, representing people who say "I don't know" as "no" is not necessarily predictive of vaccine confidence, and especially vaccine uptake. Also, this study was a demonstration project that took place in two provinces. This is a limitation as the data retrieved from the two provinces may not be

representative of the country as a whole or other countries. As Cambodia considers national introduction of the HPV vaccine and other new vaccines, it will be important to understand community-level influencers for vaccine uptake. Future studies should look at vaccine confidence across the entire country to see if there is a variation in confidence among different communities.

This study is one of the first studies to assess vaccine confidence in low-income countries. While vaccine confidence has been evaluated in detail in high-income countries, there is a lack of data around vaccine hesitance in low and middle-income countries and this analysis provides an introductory step to assessing confidence in these countries. As more and more new vaccines are introduced, it is important to better understand community factors that impact confidence. It would be interesting to study vaccine confidence going forward in Cambodia using qualitative methods such as focus groups and interviews to try to get richer data on these complex concepts. Through this was a single cross-sectional study, this information provides a baseline for future evaluations. Given that vaccine acceptance can change over time in countries (9,10), this study may provide a starting point for future assessments of vaccine confidence in Cambodia. These questions should be used in future routine monitoring of vaccine coverage to see how vaccine confidence changes over time. Monitoring vaccine confidence can identify target populations and help guide interventions to increase uptake of vaccines and prevent future vaccine preventable disease outbreaks.

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