Stated preferences for human papillomavirus vaccination for adolescents in selected communities in Ibadan, Southwest Nigeria: A discrete choice experiment

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ABSTRACT
Administration of the human papillomavirus (HPV) vaccine in early adolescence is effective in preventing cervical cancer, a common cancer in sub-Saharan Africa. Nigeria is in the pre-introduction era of the HPV vaccine. Understanding the preferences of the population for the vaccine can help design the HPV immunization program to ensure high uptake of the vaccine. This study explored the preferences for the HPV vaccine among stakeholders in selected communities in Ibadan, Nigeria. A discrete choice experiment survey based on six attributes of the HPV vaccine (which were the number of doses, the efficacy of the vaccine, cost of the vaccine, location of the service point, other benefits of the vaccine apart from prevention of cervical cancer and the odds of a side effect from the vaccine) was carried out in five communities. Data were analyzed using conditional and mixed logit models. Seven hundred community members were recruited, 144 (20.7%) were adolescents and 248 (35.4%) were males. In line with expectations, respondents preferred vaccines with higher efficacy, less severe side effects and lower costs. Preference heterogeneity was identified for adolescents that were less price-sensitive and other community members who were less likely to prefer using services as the school service point. The high socio-economic class preferred a vaccine that also prevents genital warts. There were variabilities in the preferences for the attributes of the HPV vaccine in the study communities. These variabilities need to be considered in the introduction of the HPV vaccine to ensure high uptake of the vaccine.

KEYWORDS
Human papillomavirus vaccine; adolescent immunization; discrete choice experiment; stated preferences; Ibadan

Introduction
The human papillomavirus (HPV) vaccine has become a game-changer in the prevention of cervical cancer in the last decade. The vaccine circumvents the limitations of cervical screening, whose implementation in many developing countries has not been impressive due to many factors, including limited trained personnel and poor organization of the services. The HPV vaccine protects against subtypes 16 and 18 of the HPV, which are responsible for about seventy percent of all cases of cervical cancer. In addition, Gardasil-9 (a nanovalent vaccine) also protects against five other subtypes (31, 33, 45, 52 and 58) conferring extra twenty percent protection compared with the earlier vaccines. The vaccine also protects from other cancers linked with HPV (mostly cancers of the head and necks, and anogenital cancers) as well as genital warts. The effectiveness of the vaccine is highest when it is given in early adolescence, before the onset of sexual activities, because it is mostly transmitted through such activities. Most developed countries now have HPV vaccine as a routine vaccine for adolescents. It is gradually being introduced in developing countries, including sub-Saharan African countries, where the burden of cervical cancer is very high.

An infection rate of 25.6% has been reported for HPV among Nigerian women with normal cytology and the HPV serotypes 16 and 18 have been found in 66.8% of invasive cervical cancer in sub-Saharan Africa. The same region had the highest incidence of cervical cancer and the highest rate of mortality associated with the cancer in 2018. In Nigeria, the incidence of invasive cervical cancer is 25 per 100,000 women, with approximately 8,000 new cases diagnosed each year. However, only 1.2% of girls aged 10–20 years got a full course of HPV vaccines in 2014, compared to 31.1% and 35.6% of their counterparts in Europe and North America, respectively. Sundstrom et al. suggested that to reduce the inequality in HPV vaccine coverage there is a need for the vaccine to be acceptable to the underserved global regions. This acceptability is tied to the importance of the HPV vaccine and this can be deduced from the preferences of the people for the vaccine.

The HPV vaccine was introduced in Nigeria in 2008, but it is yet to be included in the routine vaccination program. However, it can be procured from selected health-care facilities. Nigeria is eligible for GAVI, the vaccine Alliance’s subsidized HPV vaccines, but the decision to roll out the program in the country is still pending. There have been studies about the acceptability of the HPV vaccine for Nigerian adolescents, but these are often carried out among mothers and usually in hospital settings. These studies do not represent the typical settings where vaccination decisions will be made since such decisions often include the input of fathers and other community stakeholders. The participants in hospital settings are not representative of the typical community dwellers as they represent just a class of community members.
Several stakeholders can influence families’ decision-making regarding adolescents’ uptake of the HPV vaccine, and this is often a complex web in many African communities where individuals rarely make health-care decisions alone, but there is a heavy influence of the people in the social circle in the decision-making processes. The decision-making usually have influences from extended family members, friends, and religious and traditional leaders. Therefore, studying how decisions are made concerning the uptake of HPV vaccine by adolescents among only the parents or adolescents could yield misleading results.

Earlier studies have shown that stakeholders consistently expressed concerns (about timing, necessity, side effects, importance, possible repercussions, etc.) regarding the HPV vaccine in countries where it is routine, and this may be responsible for its low uptake by adolescents compared with other vaccines which are traditionally administered in adolescence. It is therefore important to explore the preferences of stakeholders about the HPV vaccine for adolescents in Nigeria (the country with the highest number of adolescents in Africa), because of the vast benefits the country stands to gain from the elimination of HPV infection and the associated diseases. This study, therefore, set out to determine the preferences of stakeholders in selected communities in Ibadan, southwest Nigeria about the HPV vaccine for adolescents using a discrete choice experiment. The findings from this study can guide policy decisions about the rollout of the HPV vaccination program in Nigeria and reduce vaccine hesitancy associated with the rollout of HPV vaccination as seen in some countries.

Methods

Discrete choice experiment

The study used a Discrete Choice Experiment (DCE), which is a stated preference method where respondents choose between different combinations of attributes of a service or product (or status quo), with different levels experimentally assigned to each attribute. The data from the DCE is analyzed based on the Random Utility Theory (RUT) framework, which assumes that individuals rationally make decisions and aim at maximizing utility with each choice made. The utility associated with each attribute is thus inferred from the choices made by respondents, and will depend on how each respondent values each attribute.

Study area

The DCE survey was carried out in five communities in Ibadan, a cosmopolitan city in southwest Nigeria. All the communities were located in Ibadan North Local Government Area (LGA), which is the most densely populated LGA in Oyo State. Different socioeconomic classes were represented in these communities, and the predominant ethnicity was Yoruba. The HPV vaccine was not a routine vaccine at the time of the study in Nigeria, but it was already introduced and could be obtained (after payment) at a government-owned tertiary health center and some private hospitals providing health-care services for these communities.

Study population

The DCE was carried out among a sample of stakeholders who were either involved in, or could influence the decision-making process regarding adolescents’ uptake of the HPV vaccine. They were parents/guardians of adolescents, adolescents, traditional healers, and religious leaders who must have been residing in the study communities for at least a year.

Sample size calculation and sampling

Participants were recruited using a four staged sampling technique to select streets, houses/compounds, families with adolescents and participants. The sample size was determined using the Kish and Leslie formula assuming that 70% of mothers allow their adolescents to get the HPV vaccine. The minimum sample size from the formula was multiplied by a design effect factor of 2 due to the clustering nature of the communities. The final sample size was rounded (upwards) to the nearest hundred and indicated a need to sample 700 respondents. Of this number, 20% (144) was allocated to adolescents to represent their actual population in the communities in line with the last national census data.

Design of the discrete choice experiment

The attributes of the HPV vaccine and their levels were determined using findings from existing literature and results of Focus Group Discussions (FGD) among parents of adolescents (4 FGD), in and out of school adolescents (10 FGD), religious leaders (3 FGD), and Key Informant Interviews (KII) with traditional healers (4 KII) in the study communities. The selected attributes and their levels are shown in Table 1. The levels for other added benefits of HPV vaccine, location of vaccination services, the number of required shots and the effectiveness of the vaccine in the prevention of cervical cancer were obtained from the literature. Although severe side effects of the HPV vaccine are rare, it was included among the attributes because it was important to the community members, as seen from the interviews. Hypothetical levels were then created for the likely chance of severe side effects. The levels for the out-of-pocket payments for the vaccine were based on the

| Attributes of HPV vaccine | Level 1 | Level 2 | Level 3 |
|---------------------------|---------|---------|---------|
| Other added benefits      | Prevention of cancer of the head and neck | Prevention of genital warts | Prevention of anal cancer |
| Frequency of severe side effects | 1/10,000 | 1/10,000 | 1/100,000 |
| Out of pocket payment (N) | N14,000* | N21,000# | Government pays |
| Location of the vaccination services | School based services | Health facility-based services | Community based services |
| Number of doses required | 2 doses | 3 doses | |
| Effectiveness in the prevention of cancer of the cervix | 70% | 90% | |

*Equal to $38.89 for the two-dose course.
#Equal to $56.91 for the three-dose course.
prevailing cost of the HPV vaccine at the time of the study for two and three shots of the vaccine, which was recommended for adolescents aged 14 years and below, and 15 years and older, respectively. The third level for this attribute was for the government to pay for the vaccine.

A full factorial design would yield 324 alternatives (3x3x3x3x2x2) which will be combined as 324 x 323/4, with each respondent having to complete 26163 choice sets. This is not feasible for anyone to complete. Therefore, the DCE was designed using a D-optimal design program developed by Hole A.R. The D-optimal design was used to minimize the size of the variance-covariance matrix and reduce the associated error. In total, 16 choice sets were created, which were then split into four blocks, giving four choice sets for each participant. Each choice set had two alternatives describing hypothetical HPV vaccines with a third alternative to opt-out. The opt-out option simulates real-life scenarios in which the participants may not be interested in either of the other two alternatives.

**Data collection procedure**

Trained research assistants collected the data. The study was explained to each recruited participant and written informed consent/assent was obtained. The HPV vaccine was introduced to the participants, and the meaning of each attribute of the vaccine and their levels were explained, as well as the process of completing the choice sets. An interviewer-administered questionnaire was used to obtain the sociodemographic data and each participant completed four choice sets, each with an option to opt-out. Both the English and Yoruba versions of the questionnaire and choice sets were used depending on each participant’s preference.

**Statistical analysis**

The data were analyzed using Stata version 13. The characteristics of the study participants were described using descriptive statistics. Socioeconomic classes were determined using a method described earlier in Nigeria, where the classes were determined by parental or adult’s highest educational attainment and job types. The responses to the choice sets were analyzed based on random utility theory, and the utility (Uijt) that a respondent i derives from choosing an alternative j in choice set t, is given by:

\[ U_{ijt} = \beta_1 \text{Benefit}_i + \beta_2 \text{Freq SE}_j + \beta_3 \text{OPP}_i + \beta_4 \text{Location}_i + \beta_5 \text{Doses}_j + \beta_6 \text{Effectiveness}_i + \epsilon_{ij} \]

Where \( \epsilon_{ij} \) is the alternative-specific constant for the status-quo (opt-out) alternative, \( \beta_1 \) to \( \beta_6 \) are coefficients to be estimated, and \( \epsilon_{ij} \) is the random error term. Dummy binary variables were generated for each attribute and level for dose, location of service, and extra benefits of HPV vaccine since these were categorical variables. The level used as reference category for each attribute is seen in Table 2. The frequency of severe side effects, out-of-pocket payment and effectiveness were modeled as continuous variables. The estimated coefficients indicate the relative importance of each attribute, and the sign of the coefficient shows if the attribute has a negative or positive effect on the utility when compared with the reference category.

Preference heterogeneity was assessed by creating interaction variables between sociodemographic characteristics of the participants (age-group, religion, and socioeconomic class) and the different attributes of the HPV vaccine. The interaction terms are used in analyses to assess if the importance of the different attributes and levels vary across different sociodemographic characteristics. Conditional logit and mixed logit models were used to determine the preferences of the community.

**Table 2.** Sociodemographic characteristics of participants in the discrete choice experiment to determine societal preference of HPV vaccine.

| Characteristics       | Frequency | Percentage |
|-----------------------|-----------|------------|
| **Gender**            |           |            |
| Male                  | 248       | 35.4       |
| Female                | 452       | 64.5       |
| **Age-group (years)** |           |            |
| 10-19                 | 144       | 20.7       |
| 20-44                 | 393       | 56.6       |
| ≥45                   | 157       | 22.6       |
| **Religion**          |           |            |
| Christianity          | 256       | 36.6       |
| Islam                 | 431       | 61.6       |
| Traditionalist        | 9         | 1.2        |
| **Socioeconomic class** |         |            |
| High                  | 365       | 52.1       |
| Middle                | 192       | 27.5       |
| Low                   | 142       | 20.3       |
| **Ethnicity**         |           |            |
| Yoruba                | 676       | 96.6       |
| Igbo                  | 18        | 2.6        |
| Hausa                 | 4         | 0.6        |
| Others                | 2         | 0.2        |

*There were some non-responses.
members for the different attributes of the HPV vaccine. The conditional logit model is often used as a baseline model with DCE data, but it carries an assumption often seen as unrealistic in that it assumes that respondents have the same preferences for changes in the attributes. To relax this assumption, we also estimated the coefficients using a mixed logit model. The level of statistical significance was $p < .05$ for all analyses.

**Ethical considerations**

The study protocol was approved by the University of Ibadan/University College Hospital Ethics Committee with approval number UI/EC/16/0014. All the study participants who were older than 18 years gave written informed consent before recruitment into the study. For the adolescents who were younger than 18 years, both parental consent and adolescents’ assent were obtained. The participants were assured of the anonymity of their responses and only codes were used to identify each questionnaire.

**Results**

The sociodemographic characteristics of the community members who participated in the study are shown in Table 2. About a third (35.4%) were males and more than half (56.6%) were from the age group 20–44 years.

The overall preferences for the attributes of the HPV vaccine are as shown in Table 3, with results from conditional logit and mixed logit models. In line with expectations, respondents preferred a vaccine with lower out-of-pocket payments, lower frequency of side-effects, and a higher vaccine effectiveness. Although the latter finding was not statistically significant in the mixed logit model, both models provide qualitatively similar interpretations. The results for the location of vaccination indicated negative preferences for a community-based service

| Attribute | Conditional logit | Mixed logit |
|-----------|------------------|-------------|
|           | Coeff. [95% CI]  | Coeff. [95% CI] |
| Opt-out constant | −1.31 [−1.96, −0.67] | −2.88 [−3.81, −1.96] |
| Out-of-pocket payment (N) | −0.14 [−0.15, −0.13] | −0.21 [−0.23, −0.19] |
| Frequency of severe side effects | −155.67 [−300.60, −10.73] | −270.59 [−479.15, −62.02] |
| Effectiveness | 0.85 [0.12, 1.58] | 0.66 [−0.40, 1.73] |
| Location of service | reference | reference |
| Health facility | | |
| School | 0.11 [−0.05, 0.3] | 0.03 [−0.21, 0.27] |
| Community | −0.17 [−0.35, 0.002] | −0.34 [−0.59, −0.09] |
| Number of required doses | reference | reference |
| 2 doses | | |
| 3 doses | 0.05 [−0.07, 0.17] | 0.04 [−0.15, 0.22] |
| Added benefits prevention | reference | reference |
| Head and neck cancers | 0.05 [−0.14, 0.25] | 0.03 [−0.27, 0.34] |
| Genital warts | 0.09 [−0.06, 0.25] | 0.15 [−0.08, 0.38] |

Attributes in bold were included as continuous variables in the regression model, whereas the non-bold variables were included as binary dummy variables (with the reference categories included for ease of interpretation).

| Attribute | Age 20–44 (vs Age 10–19) | Age 45+ (vs Age 10–19) | Christian (vs Non-Christian) | Mid SES (vs Low SES) | High SES (vs Low SES) |
|-----------|---------------------------|------------------------|----------------------------|---------------------|-----------------------|
| Model 1: Cost interactions | −0.05 (p < .01) | −0.07 (p < .01) | −0.02 (p < .01) | 0.03 (p < .01) | 0.03 (p < .01) |
| Model 2: Effectiveness interactions | 0.28 (p = .08) | 0.14 (p = .43) | −0.10 (p < .01) | 0.63 (p < .01) | 0.71 (p < .01) |
| Model 3: Side-effect interactions | 339.90 (p = .06) | 34.06 (p = .87) | −27.78 (p < .01) | 294.22 (p = .16) | 240.11 (p = .18) |
| Model 4: Location of service interactions | −0.14 (p < .01) | −0.78 (p < .01) | −0.06 (p < .01) | 0.49 (p < .01) | 0.24 (p < .01) |
| School-facility (vs health-facility) | 0.52 (p < .01) | 0.52 (p < .01) | −0.08 (p < .01) | 0.69 (p < .01) | 0.43 (p < .01) |
| Community-facility (vs health-facility) | 0.04 (p < .01) | −0.15 (p < .01) | −0.09 (p < .01) | 0.46 (p < .01) | 0.22 (p < .01) |
| Model 5: Dose (3 vs 2) interactions | −0.04 (p = .77) | −0.15 (p = .37) | −0.09 (p = .41) | 0.46 (p < .01) | 0.14 (p < .01) |
| Anal cancer (vs head & neck cancer) | −0.39 (p = .07) | −0.73 (p < .01) | −0.06 (p < .01) | 0.99 (p < .01) | 0.66 (p < .01) |
| Genital warts (vs head & neck cancer) | 0.28 (p = .12) | 0.08 (p < .01) | −0.24 (p < .01) | 0.38 (p < .01) | 0.53 (p < .01) |

This table shows results from six conditional logit models with each row representing the results from separate conditional logit model (as in Table 3) with interaction variables – i.e., the first row is a conditional logit model where the cost attribute was interacted with the individual characteristics seen in each column.
DISCUSSION

This study explored the preferences of the studied community members regarding HPV vaccination of adolescents, and it was shown that, in line with expectations, they preferred an HPV vaccine with higher effectiveness, lower cost, and less side effects.

The effectiveness of the HPV vaccine was very influential for the choices of the community members, which is in line with findings from earlier studies, and is not surprising as the primary aim of the vaccination in the first instance is to prevent cervical cancer. A Canadian study reported that almost half of parents interviewed allowed their adolescents to take the HPV vaccine because of its effectiveness. The effectiveness of the HPV vaccine has been demonstrated in longitudinal studies around the globe regarding protection from HPV infection as well as from genital warts and other HPV-related cancers. The preferences for a vaccine with a high effectiveness were more pronounced among respondents with a higher socioeconomic status. Although it is not possible to conclude on the reason for this finding in this study, it could be that the higher educational attainment is related to a better comprehension of what higher effectiveness entails.

The number of doses (two or three) did not seem to make a significant impact in the overall choice among respondents but the middle socioeconomic class preferred three dose regimen. Despite the earlier recommendation of three HPV vaccine shots for older adolescents, there is evidence that a two dose regimen provides good immune response with comparable level of antibodies seen with three dose regimen at 18 months. The effectiveness in the prevention of HPV infection was also similar. A single dose HPV vaccine has also been shown to offer significant degree of protection from HPV infection and cervical cancer and there are now proposals that a single dose of the vaccine may be what is required to prevent cervical cancer. However, the results from this study showed that the number of doses was not likely to have a substantial impact on the acceptability or likelihood of vaccine uptake, except for those in the middle socioeconomic class. Further research is required to understand the reasons for these choices.

The high cost of HPV vaccine has repeatedly been a major concern of stakeholders in earlier studies and the results in this study also highlighted the strong preferences for a vaccine with lower cost. This could be as a result of other competing needs, a high poverty rate, and combined with the stress of out-of-pocket health expenditures that is common in the study environment. However, the higher socioeconomic class understandably were less bothered about the cost of the vaccine as they will more likely be able to afford it. The results also showed that adolescents were less concerned with the cost of the vaccine compared to the older age groups. This is in contrast to reports from other countries where female adolescents and young women have been shown to be especially concerned that the high cost of a HPV vaccine would be a barrier to vaccination. The reason why adolescents in the current study were not as bothered about the cost may be because they still depend on their parents and guardians for their needs and did not comprehend the financial implication of paying for the vaccine. Preference heterogeneity with respect to the cost of the vaccine was also seen among different religious groups, where Christians showed more concern for the high cost of the vaccine. The reason for this is not clear, but it could be a result of their exposure with health focused outreach programs that churches organize at intervals, where they access highly subsidized health-care services. The high cost has been a major factor that has hindered the introduction of the HPV vaccine as a routine vaccine in many low- and middle-income countries. This has led to selective vaccination of girls in a bid to prevent cervical cancer, despite the evidences that the vaccination of both genders was cost effective when other cancers and diseases associated with HPV were considered. There has also been concern about the high cost of the vaccine even in developed countries, especially among older women who fall outside the catchment age for the government sponsored HPV vaccine for adolescents. The GAVI Vaccine alliance has stepped in to help developing countries who meet a set of criteria to have access to subsidized HPV vaccine. The criteria include a national DPT3 coverage of at least 70% and being able to demonstrate the ability to deliver multi-dose vaccine to at least 50% of the target age group. This is the support that has helped many sub-Saharan African countries to start the
HPV vaccination program for adolescents. Nigeria qualifies for GAVI’s assistance but the decision to support the country is still pending, as the roll-out is being done in phases.

The literature has consistently reported the concern of stakeholders about potential side effects of the HPV vaccine, despite the evidence of no or minor side effects. This could be attributed to earlier unpleasant experiences with vaccination and rumors that fuel distrust in vaccine programs. The results in our study also showed that the risk of side effects had significant impact on the preferences for the vaccine. Thus, this highlights the need for well-informed and effective communication about the safety of the vaccine for a successful take-up. Good health education can prevent fears and stop rumors from spreading widely, and health education is fundamental to avoid the rejection of the HPV vaccine like the previous polio vaccine boycott in Nigeria. The health-care workers have been identified as being influential in the uptake of HPV vaccine by adolescents as parents trust their judgments. Therefore, health-care workers can be useful in health education of stakeholders and actively recommending the vaccine for optimal uptake.

Generally, there were no clear results in terms of the favored location of the service. However, the analyses for preference heterogeneity showed that respondents with a lower socioeconomic status put less weight in the location of service in their community. This could be related to privacy issues due to crowded neighborhoods. Lack of privacy was reported to be a barrier for the uptake of HPV vaccine in a study carried out in the United States among women with lower socioeconomic status. Parents of adolescents have also expressed this concern in an earlier research. The results also indicated that adolescents preferred a program located in school premises compared with the other community members. This is an important finding given that the rate of completion of HPV vaccination series have been shown to be lower in services located out of schools and such arrangement also has socioeconomic inequalities compared to school-based programs. While the preference of these adolescents cannot be downplayed because their involvement in decision-making process for vaccine uptake has been shown to reduce vaccine hesitancy, consideration needs to be given for the significant proportion of Nigerian adolescents who are out of school. Diversification of HPV vaccination location has been advocated to cater for the diverse preferences of different classes of adolescents and their parents. This calls for concerted and meticulous research to identify the best location for this service where majority of the adolescents can both initiate and complete their vaccination schedule without the program losing its appeal to adolescents.

As with the location of services, the overall results did not point in any clear directions in terms of the most valuable added prevention benefits. The HPV vaccine has been shown to prevent up to 90% of genital warts, and an earlier study has reported the preference of parents for an HPV vaccine that could prevent genital warts. Since all choices in our study included some type of added prevention benefits, the results could also be interpreted such that they were deemed equally valuable. In the specific sociodemographic groups, there were indications that younger respondents and respondents with higher socioeconomic status were positive to vaccines with stated added benefits of reducing anal cancer.

In conclusion, the community members preferred an HPV vaccine which is highly effective, not costly and with less severe side effect. There were some variations in the preferences among the different age groups, and among respondents with different socioeconomic status and religion. The findings in this study can help in the design of an acceptable HPV vaccination program that will be sensitive to the needs and preferences of the different community members.

This study has a number of strengths. First, the study used a DCE to determine the stated preference of the study population, and the relevant attributes and their levels were meticulously selected based on reports from previous studies and interviews of community members. This made room for the selection of the important and relevant attributes in the study population. Also, the procedure of choice selection and the option to opt out simulated real-life scenarios. The inclusion of stakeholders in the community, apart from parents, represented the real-world situation in which the final family decision about adolescents’ uptake of HPV vaccine will depend on the direct and indirect input of the important others in the families’ social circle. Finally, this is one of the few studies that included fathers in adolescent HPV vaccine decision-making.

There are some limitations in the study as well. This study showed the stated preference of the community members for the HPV vaccine and not the revealed preference. However, the validity threat was reduced by providing an option to opt out of the selection of alternatives in each choice set. This study was also limited to only one geopolitical zone out of six that exist in Nigeria, which may limit the generalization of the findings. However, the shared cultures and national policies that are in operation in the country are likely to have similar influences on the preferences of the citizens from other geopolitical zones.

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