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Original Studies

Assessment of Knowledge and Attitudes of Young Uninsured Women toward Human Papillomavirus Vaccination and Clinical Trials

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Abstract. *Study Objective:* To assess knowledge and attitudes of young uninsured women toward human papillomavirus (HPV) vaccination and clinical trials.

Design: Cross-sectional study.

Setting: Clinic-based sample in Brazil.

Participants: A consecutive sample of 204 women aged 16 to 23 years, attending a public outpatient gynecological clinic.

Interventions: A questionnaire administered by in-person interview.

Main Outcome Measures: Data on knowledge and attitudes towards HPV vaccination.

Results: Overall, 72% of the respondents would enroll in a HPV vaccine trial, despite the fact that 69% of women were ignorant of what HPV may cause, and only 10% acknowledged that HPV might lead to cervical cancer. The need of a placebo arm (31%) and three vaccinations injections (26%) were the trial design characteristics most cited for deterring participation. Factors promoting participation were ''careful/detailed consultations by the same physician'' (92%), ''access to more information on women's health'' (84%), and ''office visits on time'' (79%); whereas ''clinic too far from home'' (36%), ''fear of adverse events'' (29%), and ''gynecologic examination discomfort'' (25%) were the most commonly reported reasons for not enrolling in a trial. Being sexually active, more than three lifetime sexual partners and perception of high risk for cervical cancer were predictors of participation in a HPV vaccine trial.

Conclusions: Knowledge of HPV infection and cervical cancer is low in this urban, young population. Thus, when planning HPV vaccine trials, it is important to consider implementing educational programs to provide knowledge of the benefits of a preventive vaccine and information on the etiology of and risk factors for cervical cancer.

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Introduction

Human papillomavirus (HPV) is estimated to be one of the most prevalent sexually transmitted viral diseases.[1–4] Among other reasons, the papillomaviruses are of great importance because of the role of certain genotypes (types 16, 18, 31, 33, 45) as a major cause world-wide for cervical cancer in women.[5,6] Most research indicates that at least 50% of sexually active women have been infected with genital HPV and that many of these infections (up to 50% or more) are with high-risk subtypes.[1,7,8] Progression to cervical cancer appears to be associated with persistent infection with the high-risk subtypes.[9,10]

Vaccines designed to prevent low-risk and high-risk subtypes of HPV are currently being developed and tested.[11–13] Justification for a prophylactic vaccine against HPV infection is based on studies in animal models showing that Papillomavirus vaccines can protect against infection and prevent the cancers associated with this virus.[14,15] Phase I-III clinical trials have demonstrated that HPV vaccines are safe and effective.[11,13,16–18]

The target population for prophylactic HPV vaccines will probably be girls who have not initiated sexual activity. Studies of attitudes about hepatitis B immunization and other sexually transmitted disease (STD) vaccines in development suggest that high rates of acceptability cannot be presumed and that characteristics of the vaccine itself, patients' health

beliefs, and physician recommendation may strongly influence vaccine acceptability.[19–22] This study was conducted to assess knowledge and attitudes of young uninsured women toward HPV vaccination and clinical trials in an urban center in Brazil.

Methods

Study Population and Site

A consecutive sample of women age 16 to 23 years old was recruited at the waiting room of the gynecological clinic at the Santo Antônio Hospital in Salvador city, in northeastern Brazil. This free, non-governmental clinic delivers health care to uninsured women of lower socioeconomic status. Patients were approached by interviewers and invited to participate in the study. Out of 237 eligible women, 33 refused to participate, and 204 (86.1% response rate) were surveyed from May to July 2002. The protocol was approved by the Hospital Ethical Committee. All respondents who agreed to participate, or if a minor, the respective legal representative, signed an informed consent form and were given assurance of confidentiality.

Data Collection

Interviews were conducted by three individuals (two males and one female) who were given an orientation on the protocol and specific details concerning participation in the study. Prior to study commencement, they carried out practice sessions with authentic respondents. These preliminary interviews were observed and critiqued by the investigators. The interview guides were developed from a review of the literature and contained sections of questions that addressed the major areas to be explored by the study.[19,23]

The 150-item questionnaire was divided into sections that sought information about the following: (1) demographic data and social background; (2) a series of questions to assess knowledge, awareness and understanding of HPV, genital warts and cervical cancer; (3) sexual behavior and self-perceived risk of acquiring a STD; and in the end, (4) attitudes toward being vaccinated against HPV and willingness to participate in a clinical trial of a HPV vaccine. The questionnaire was piloted on a sample of 20 female volunteer patients attending the clinic to refine the wording of items and ensure clarity of the text. All items were assessed for face validity by health survey experts. The individual interviews lasted an average 20–25 minutes, and the sessions occurred in a private room.

Data Analysis

The data were analyzed using the Statistical Package for the Social Sciences (SPSS, Inc., Chicago, IL, USA). Basic descriptive statistics and frequency calculations were performed on all variables, a chi-square test was used to assess differences in answers by categories of stratifying variables, with statistical significance at 5%. In the multivariate analysis, full models were fitted, and the nonsignificant ($P > 0.1$) variables were eliminated in a stepwise, backward elimination algorithm, least significant first, to determine the final model (exceptions were made for age and some sociodemographic variables, which were forced into the model as being of primary concern as potential confounders). P values less than 0.05 were considered statistically significant.

Results

The socio-demographic characteristics of the study population are shown in Table 1. The sample was ethnically diverse and 61% of women had some high school or more. The majority was single, even though 41% of women had at least one child. More than half of the participants were Catholic, and 40% were full-time students. Selected information on sexual behavior of the study participants is also depicted in Table 1. Ninety-two percent of women reported current or previous sexual activity and were classified as sexually experienced. Forty-two percent of the respondents perceived themselves at a high risk of acquiring STDs; notwithstanding, 55% never or rarely used condoms. The majority of women were first-time users of the clinic, and had come for a Pap smear test.

In general, women in our study demonstrated a vague and poor knowledge on how HPV is diagnosed or treated. Overall, more than two thirds of the respondents (68.6%) were ignorant of what HPV causes, and less than 10% of the women acknowledged that HPV might lead to cervical cancer. In contrast, most women knew that HPV is sexually transmitted (66.7%). Knowledge of cervical cancer was also unsatisfactory. The majority of women (60.8%) did not realize what might cause cervical cancer, and only 3.9% reported STDs, non-specifically, as a possible reason for this cancer. Nevertheless, most women in our study (73%) reported they were moderately/extremely worried about having/developing cervical cancer. Understanding about Pap smear test among subjects in our survey was also low. Regardless of educational attainment, the vast majority of women in our study (78%) had limited knowledge about the purpose of this screening test. They either reported that it serves to prevent ‘‘diseases,’’ non-specifically, or were not sure why they should have a smear test done. Approximately 19% of the women had not undergone a Pap smear test before. The most common reason reported for not having a screening test performed was embarrassment (63.2%), followed closely

Table 1. Participant Characteristics, Salvador, Brazil, 2002 (n = 204)

	n	(%)
Age (in years)		
16 to 17	30	(14.7)
18 to 19	55	(27.0)
20 to 21	59	(28.9)
22 to 23	60	(29.4)
Race/Ethnicity		
White	4	(2.0)
Mixed	148	(72.5)
Black	52	(25.5)
Education		
Less than Middle school	47	(23.0)
Middle school	32	(15.7)
High school incomplete	59	(28.9)
High school or more	66	(32.4)
Employment Status		
Student	82	(40.2)
Working part time/full time	43	(21.1)
Unemployed	52	(25.5)
Housewife	27	(13.2)
Marital Status		
Single	151	(74.0)
Married/living with partner	52	(25.5)
Divorced	1	(0.5)
Religion Affiliation		
None	53	(26.0)
Catholic	111	(54.4)
Protestant	38	(18.6)
Espiritist	2	(1.0)
Number of lifetime sexual partners		
None	16	(7.8)
1 partner	78	(38.2)
2 partners	44	(21.6)
3 partners	30	(14.7)
4 partners	18	(8.8)
≥5 partners	18	(8.8)
Number of live births		
0	120	(58.8)
1	56	(27.5)
2	26	(12.7)
≥3	2	(1.0)
How often do you use condom?[a]		
Never	45	(23.9)
Rarely	58	(30.9)
Often	34	(18.1)
Always	51	(27.1)
Self-perceived risk of acquiring a sexually transmitted disease[a]		
None	34	(18.1)
Low	68	(36.2)
Moderate	7	(3.7)
High	79	(42.0)
Use of Clinic		
First time at the clinic	121	(59.3)
Main reason for the consultation		
Pap smear screening test	103	(50.5)
Birth control	30	(14.7)
Other gynecological consultation	71	(34.8)

[a]Only for sexually active women (n = 188).

by fear of pain (60.5%). All these results did not vary significantly by respondent's age.

Table 2 summarizes the acceptability and attitudes toward HPV vaccination among study participants. Overall, 72% of the respondents would enroll in a HPV vaccine trial, and 89% reported that recommendation by a physician would positively influence their enrollment. Most women in our study would participate in a HPV vaccine trial despite disapproval by parents, boyfriends, or friends (Table 2). In a hypothetical HPV vaccination trial, the need of a placebo control arm (31%) and three vaccination injections (26%) were the most common reasons cited for deterring participation. The most frequently reported factors that would strongly influence enrollment in a HPV clinical trial were "to have careful/detailed consultations by the same physician" (92%), "access to more information on women's health" (84%), and "office visits on time" (79%); whereas "clinic too far from home" (36%), "fear of adverse events" (29%), and "gynecologic examination discomfort" (25%) were the most commonly reported reasons for not enrolling in such a trial (Table 2).

As shown in Fig. 1, among three hypothetical HPV vaccines, the majority of respondents (87%) preferred the vaccine A (protecting against 70% of cervical cancer and 100% of genital warts), 82% of the women were willing to enroll in a trial to test this hypothetical vaccine. The vaccine B (protecting against 85% of cervical cancer exclusively) and the vaccine C (protecting against 100% of genital warts exclusively) were rated as first choice by only 10% and 3% of the study participants, respectively; yet, most participants would enroll in a trial to test vaccine B (61%) or vaccine C (54%). Moreover, women in our study believed their partners would be more likely to accept vaccination against HPV if the vaccine protected against both cervical cancer and genital warts than if the vaccine protected against cervical cancer only, 81% vs. 31%, respectively (Fig. 2).

Sociodemographic factors, attitudes and behaviors evaluated for their association with willingness to participate in a HPV vaccine trial are summarized in Table 3. Age, education, marital status, religion and ethnicity were not associated with intention to enroll in a HPV vaccine trial. Being sexually active, having had more than three lifetime sexual partners, and perception of high risk for cervical cancer (vs. medium and low), however, were positively associated with willingness to participate in a HPV vaccine trial as hypothesized.

Discussion

This is the first comprehensive survey on knowledge and attitudes toward HPV vaccination and clinical

Table 2. Acceptability and Attitudes towards Human Papillomavirus (HPV) Vaccination and Enrollment in a Clinical Trial among 204 Women in Salvador, Brazil, 2002

	%
Would participant enroll in a HPV vaccine trial?	
Yes	71.6
No	28.4
Would enrollment in a HPV vaccine trial be influenced if the vaccine was recommended by a physician?	
Yes, strongly	55.9
Yes, somewhat	23.0
No	21.1
Participant would enroll in a clinical trial for a HPV vaccine, even if:	
Parents disapproved	83.5
Boyfriend/significant disapproved	83.7
Friends disapproved	94.5
Participant would not enroll in a HPV vaccine trial that required:	
A placebo control arm	30.9
Three vaccination shots (intramuscular injections)	26.0
More than one office visit per year	12.3
More than one pelvic examinations per year	8.8
Attributes and beliefs that would strongly influence participants to enroll in a HPV vaccine trial[a]*:*	
To have careful/detailed consultations by the same physician	92.2
Access to more information on women's health	83.8
Office visits on time (without having to wait long)	79.4
Potential for their own benefit	78.4
Access to consultation with other medical specialties	77.5
Potential for other women benefit	73.0
Monetary reimbursement	66.7
Gender of gynecologist (female)	57.8
Attributes and beliefs that would strongly influence participants not to enroll in a HPV vaccine trial[a]*:*	
Clinic is too far from home	35.8
Fear of adverse events	28.9
Discomfort of gynecologic examination	24.5
Need to get three intramuscular injections	19.6
Long duration of the trial (more than 3 years)	18.6
More than one visit per year	17.2

[a]In a scale with the following three categories: ''no influence,'' ''some influence,'' ''strong influence.''

trials among young uninsured women in northeastern Brazil. Our results show that very little is known about HPV in the study population. Overall, more than two thirds of the women in our sample did not know what HPV causes, and less than 10% acknowledged that it might lead to cervical cancer. Similar findings have been reported among women attending college in the USA.[24–26] Thus, indicating that HPV-related knowledge deficits also occur among subjects with higher educational attainment, and suggesting that HPV educational programs may be needed in both developing and developed countries. Most women in our study (73%) reported they were moderately/extremely worried about having or developing cervical cancer. In this scenario, where poor HPV-related knowledge coexists with high perceived susceptibility to cervical cancer, one may argue that HPV educational programs are not only needed, but also very likely to be welcomed.

The success of HPV immunization programs will depend on both effectiveness of the vaccine and on coverage attained, which strongly depends on the public's acceptance of the vaccine. Similarly, HPV vaccine trials will be effective only if sufficient numbers of individuals accept the vaccine. In general, women in our study were favorably disposed toward enrolling in a HPV vaccine trial. Furthermore, recommendation by a physician contributed positively to vaccine acceptability, a finding similar to those reported in previous studies of acceptance of HPV immunization[20] and hepatitis B vaccine.[27] However, neither parental, boyfriend, nor friend disapproval would prevent respondents from participating in a HPV vaccine trial. These results emphasize the importance of informing and training healthcare providers about the vaccines and about the contribution of provider recommendations to decision making about health.

The requirement of a placebo arm and the need of three intramuscular injections were the trial design characteristics most commonly reported to discourage enrollment. The negative impact of the need of a placebo arm may reflect the expectation to receive the vaccine (a common misconception among lay people is that joining a clinical trial means receiving the experimental medicine). Fear of injections is a possible explanation for the negative effect of the three vaccination shots requirement on trial participation; another plausible reason is the time commitment required for three vaccination visits, although few women reported more than one office visit or pelvic examination per year as a significant limitation for trial enrollment.

Among the factors promoting participation in a HPV vaccine trial in our survey, careful/detailed consultation by the same physician, access to more information on women's health and office visits at scheduled time were the strongest inducements for this group of young women to participate. This may reflect the lack of access of these uninsured women to good quality health care. The potential for a vaccine to help women was also a strong incentive for this group to participate, a finding similar to one reported in a study of HPV vaccine acceptance;[28] emphasis on this issue may be a useful message for recruiting women into a HPV vaccine trial. Surprisingly, monetary reimbursement ranked only seventh among the factors positively influencing trial enrollment in this sample of women of low socioeconomic status.

Clinic too far from home, fear of adverse events, and discomfort of gynecologic examination were the

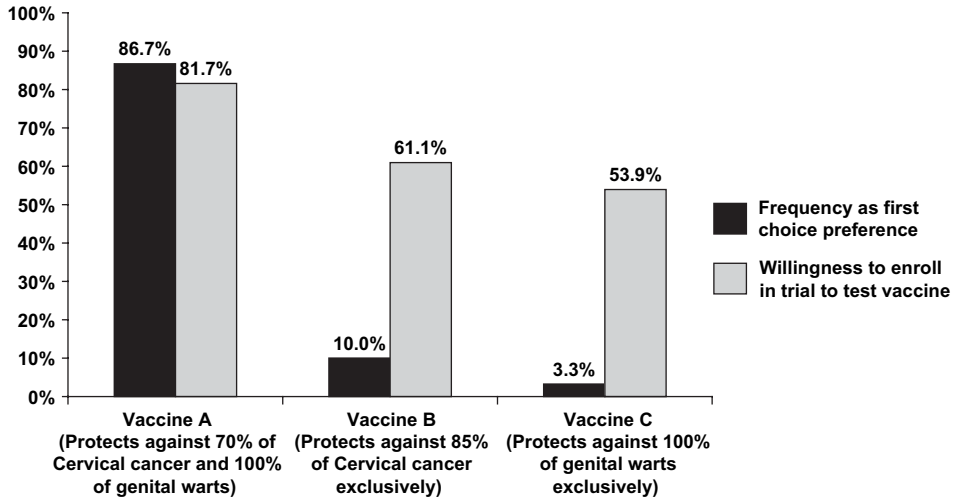

Fig. 1. Frequency as a first choice preference of three hypothetical types of human papillomavirus vaccine and willingness to enroll in a trial for each of these vaccines among 204 young women in Salvador, Brazil, 2002.

most commonly reported factors deterring women in our survey from participation in a HPV trial. Although these issues may lie beyond the control of the staff conducting a clinical trial, detailed information on vaccine safety and protocol requirements should always be given to all potential participants in order to make sure that study entrants have fully considered these issues before enrolling.

The findings of this survey suggest that sexually active women and those with a history of three or more sexual partners are more likely to enroll in a HPV immunization trial, regardless of other factors. Perception of risk was also a strong predictor of vaccine acceptance. This result is consistent with previous studies on the acceptability of vaccines against hepatitis B virus[22] and type II herpes virus,[19] where perceiving the benefits of the vaccine and being aware of the risk of the disease were the main factors associated with vaccine acceptability. Thus, when planning HPV vaccine clinical trials, it is important to consider implementing educational programs to provide knowledge of the benefits of a preventive vaccine and information on the etiology of and risk factors for cervical cancer. This is necessary because some women may not be aware of the risk and severity of diseases that can be prevented with vaccines. In addition, women may avoid being immunized due to concerns of the safety and effectiveness of specific vaccines.

When given a choice among three hypothetical vaccines, women in our study preferred a vaccine that offers less protection against cervical cancer, but also protects against genital warts, to vaccines that protect only against either cervical cancer or genital warts. It

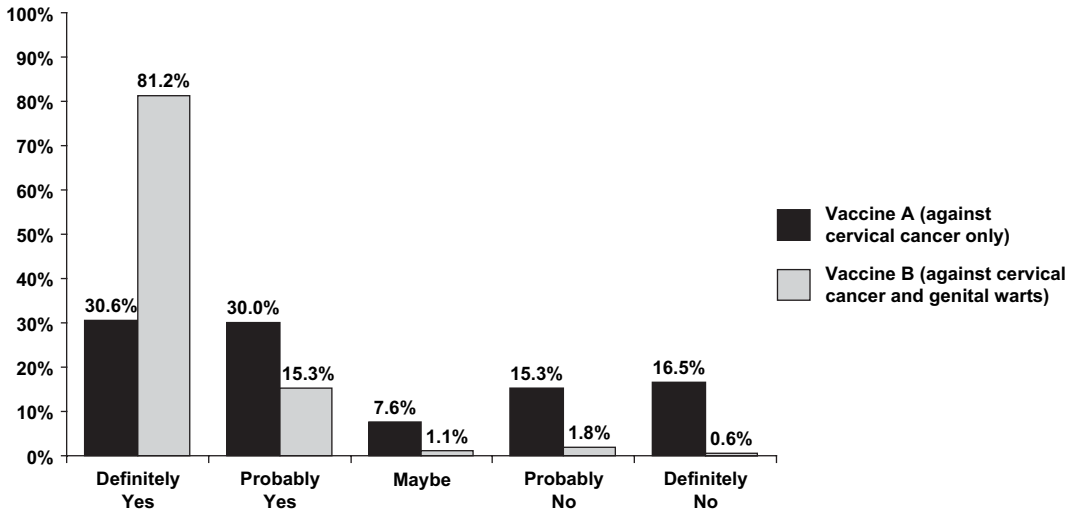

Fig. 2. Perceptions of young women in regard to their partners' willingness to get vaccinated against human papillomavirus according to the type of vaccine, Salvador, Brazil, 2002 (n = 188).

Table 3. Results of Multivariate Analysis of Selected Study Variables and Their Association with Willingness to Participate in a Human Papillomavirus Vaccine Trial, Salvador, Brazil, 2002 (n = 204)

Characteristics	OR (95% C.I.)[a]
Age (1 year increment)	1.0 (0.8–1.2)
High school education or more (vs. less than High school)	0.7 (0.3–1.3)
Married or living with partner	0.9 (0.4–2.0)
Catholic affiliation	1.4 (0.7–2.8)
Black ethnicity (vs. other)	0.8 (0.4–1.7)
Being sexually active	3.7 (1.3–12.3)[b]
More than three lifetime sexual partners	2.0 (1.0–4.1)[b]
Perception of high risk for cervical cancer (vs. medium and low)	3.4 (1.1–15.7)[b]

[a]Odds Ratio (95% Confidence Interval).
[b]$P < 0.05$.

may be better for a four-valent HPV vaccine to include both types of HPV that cause genital warts and the two oncogenic types causing most cases of cervical cancer rather than including only leading types of oncogenic HPV. Interestingly, most respondents in our survey would still accept enrolling in trials to test the least preferred HPV vaccines. In addition, nearly all women in our study felt that their partners would be more willing to receive a vaccine that protects against not only cervical cancer but also against genital warts. Although research on men's attitudes toward HPV immunization is needed to answer this question, inclusion of protection against genital warts may make a HPV vaccine more acceptable to men thus increasing its use by both genders.

The availability in the near future of effective HPV vaccines will possibly be the best strategy for controlling cervical cancer in developing countries where screening programs have failed. Nevertheless, it is important to consider that successful vaccination programs require public education. In order for specific populations to accept the use of vaccines, these persons must understand their necessity and be informed of their benefits and risks. Further research on HPV knowledge and acceptability of vaccines is needed among mothers and their teenaged daughters, women in different age groups and socioeconomic status, and all risk groups, including men.

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