Human papillomavirus and cervical cancer risk perception and vaccine acceptability among adolescent girls and young women in Durban, South Africa

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Background. The relationship between HIV and cervical cancer is well established. Interventions that focus on creating human papillomavirus (HPV) vaccine and cervical cancer prevention messaging for adolescents, caregivers and educators will increase uptake of HPV vaccinations, HPV testing and cervical cancer screening for high-risk adolescent girls and young women (AGYW). In order to effectively develop appropriate interventions, it is important to examine AGYW's perceptions regarding their personal risk of acquiring HPV, as well as vaccine acceptability.
Objectives. To measure the level of perceived personal risk of acquiring HPV and developing cervical cancer; examine the sociodemographic and behavioural factors associated with perceived risk; and assess HPV vaccine acceptability.
Methods. AGYW aged 16 - 24 years participating in the AYAZAZI study in Durban, South Africa (SA), were invited to participate in the AYA-HPV Prevention Project (AHPP), and were administered a questionnaire that assessed HPV, cervical cancer and vaccine awareness and knowledge, self-perceived HPV and cervical cancer risk, HPV vaccine uptake and acceptability, and participation in cervical cancer screening. The questionnaire measured self-perceived risk of acquiring HPV and developing cervical cancer for the respondent and other young women, as well as vaccine acceptability. Data from the main AYAZAZI study (12-month) visit were linked to AHPP substudy data. Descriptive statistics were used to analyse sociodemographic variables at the 12-month time point. Self-perceived HIV, HPV and cervical cancer risk was measured using an ordinal scale. Chi-square analyses were used to examine differences in sociodemographic and behavioural factors according to self-perceived risk of HPV and cervical cancer.
Results. Only a small portion of participants (14.3%) had heard of HPV. Overall, 43.0% (n=49) perceived themselves as at low HPV risk. There were significant differences in self-perceived risk of cervical cancer by age group, income and pregnancy status. The highest proportion of AGYW who perceived themselves as at high risk of cervical cancer reported being sexually active (p=0.002). Although many participants reported not knowing about HPV prior to the study, after learning about it during the study, most said that they would be willing to receive the vaccine (97.5%).
Conclusions. Most young women in SA do not have access to the national HPV vaccine programme, as only girls in grade 4 in some public schools qualify. Almost all participants indicated that if the vaccine was free and recommended by a healthcare professional, they would accept it. Availability of the HPV vaccine and timely treatment of HPV infections are key issues to address in efforts to decrease cervical cancer worldwide.

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Cervical cancer is largely preventable, yet remains one of South African (SA) women's most significant health issues. Cervical cancer is the second leading cancer among women in SA, with 12 983 new cases diagnosed in 2018. It is one of the top contributors to cancer mortality, with an estimated 5 595 deaths. Specifically, it is the leading cause of cancer deaths in women aged 15 - 44 years, many

of whom are living with HIV.[1-3] Many young women suffer from an array of sexual and reproductive health (SRH) challenges that can be attributed to limited access to prevention, early diagnosis and treatment, competing health and economic needs, low levels of awareness and perceived risk and endemic HIV rates, as well as important socio-structural inequities including gender-based violence.[4-9] A disconnect can also occur for women in SRH services, such as lack of trust in healthcare professionals, feeling judged, experiencing discrimination, and/or unequal power dynamics between patient and service providers.[4,10,11]

The relationship between HIV and cervical cancer is well established. Women living with HIV (WHIV) have higher human papillomavirus (HPV) infection rates than HIV-negative women, as they have a lower likelihood of clearing infections, and therefore develop cervical cancer sooner.[3,12,13] These outcomes are further compounded for WHIV in low- and middle-income countries. For example, HIV-infected women in Africa are six times more likely than uninfected women to develop cervical cancer as a result of HIV-mediated immune dysfunction.[14,15] It is therefore a priority to focus on HPV prevention among young women in SA, with a particular focus on KwaZulu-Natal Province, which has the highest rates of HIV among young people in the country.

The high rate of cervical cancer among young women, particularly WHIV or those at risk of HIV, highlights the critical need to expand HPV vaccination efforts to target girls and women across each stage of their life course. Much more work is needed to better understand awareness and acceptability of the HPV vaccine, particularly among females at the highest risk of HIV (16 - 25 years of age). Challenges to vaccine uptake for adolescents in Africa, particularly the HPV vaccine, include cost of the vaccine for those not eligible in national roll-out efforts, and lack of awareness and knowledge among adolescents, caregivers and educators.[16] Even with reported low levels of knowledge, the HPV vaccine remains highly acceptable. Interventions that focus on creating HPV vaccine and cervical cancer prevention messaging for adolescents, caregivers and educators will increase the uptake of HPV vaccinations, HPV testing and cervical cancer screening for high-risk adolescent girls and young women (AGYW) internationally.[17]

Research demonstrates the bivalent, quadrivalent and nonavalent HPV vaccines to be safe and immunogenic in WHIV, being most effective for those with a CD4+ count >200 cells/μL.[18,19] However, there are as yet no efficacy data on WHIV in sub-saharan Africa. The HPV vaccine is a critical and effective primary prevention measure against HPV-related cancers, particularly for young women in low-resource settings with limited screening resources and high HIV and HPV prevalences.[20,21] In SA, bivalent (Cervarix) and quadrivalent (Gardasil) vaccines were approved and made available in 2008.[22]

Objectives

There is a gap in knowledge about perceived risk and HPV vaccine acceptability among AGYW. In order to effectively develop appropriate interventions for cervical cancer in this population, it is important to examine young women's perceptions regarding their personal risk of acquiring HPV and developing cervical cancer, as well as vaccine acceptability. We studied a cohort of female adolescents and young adults (aged 17 - 24 years) in Durban, KwaZulu-Natal, to: (*i*) measure the level of perceived personal risk of acquiring HPV and developing cervical cancer; (*ii*) examine the sociodemographic and behavioural factors associated with perceived risk; and (*iii*) assess HPV vaccine acceptability.

Methods

Study design and participants

Female adolescents and young adults enrolled in the AYAZAZI study, a youth-centered, community-based, prospective cohort study focused on understanding linked patterns of sociobehavioural and biomedical HIV risk among youth in SA,[23] were invited to participate in the present study. AYAZAZI study inclusion criteria included being 16 - 24 years of age, residing in Soweto (Gauteng Province) or Durban, self-reporting HIV-negative or unknown HIV status, and being willing and able to provide voluntary written informed consent. Exclusion criteria included current participation in another clinical or observational HIV prevention study. The Soweto cohort was based at the Perinatal HIV Research Unit (PHRU) located at Chris Hani Baragwanath Academic Hospital. The Durban cohort was based at the Commercial City research site led by the MatCH Research Unit (MRU, a division of the Wits Health Consortium in the Department of Obstetrics and Gynaecology, Faculty of Health Sciences, University of the Witwatersrand).

Posters, pamphlets and word-of-mouth and in-person community outreach were used to recruit 425 participants (253 female, 172 male) across both sites. In Soweto, participants were also recruited through the PHRU's HIV testing and counselling clinic, while in Durban, participants were also recruited through a public sector reproductive health clinic at Commercial City. Enrolment occurred between November 2014 and April 2015 in Soweto and between September 2015 and April 2016 in Durban. Additional information about AYAZAZI has been reported by Kaida *et al.*[23]

In September 2016, as part of the 12-month AYAZAZI follow-up visit, the substudy of female AYAZAZI participants enrolled at the Commercial City Centre MRU site in Durban, called the AYA-HPV Prevention Project (AHPP), were administered a questionnaire. Only female participants from the Durban cohort were included in the substudy.

The AYAZAZI study was centered on a youth engagement approach, which recognises young people's right to participate in decisions that affect them and values the knowledge, skills and perceptions young individuals contribute. In a research setting, youth engagement involves leadership that is able to see the potential and impact of adults and young people working together. Young people are therefore included as partners in the design and implementation of projects involving key issues that affect their lives, generating relevant and relatable knowledge to inform interventions and community mobilisation.[24] Recognising the pivotal role that young people play in developing interventions and community mobilisation, the AYAZAZI team spent a significant amount of time engaging with youth and young adults, and provided a youth-friendly space and access to SRH services with warm, trusting team members, including adolescent and young adult staff.

Study procedures

Following informed consent and/or assent (if minors), participants completed a structured questionnaire (supported by DataFAX (USA) software) at enrolment, administered in person by youth interviewers. The AGYW AHPP questionnaire was administered following the main questionnaire and assessed HPV, cervical cancer and vaccine awareness and knowledge, self-perceived HPV and cervical cancer risk, HPV vaccine uptake and acceptability, and participation in cervical cancer screening. Following the section of the questionnaire about awareness and knowledge, participants were read a standardised paragraph providing information about

HPV, cervical cancer and vaccines. Questionnaires were conducted in English, isiZulu or Sesotho, according to participant preference. Participants received reimbursement of ZAR250 (~USD18, exchange rate ZAR1 = USD0.063 as at 30 May 2016) (ZAR150 for the main study and ZAR100 for the AHPP) to compensate for transportation costs and time. Data collection took place between 30 September 2016 and 3 May 2017.

Measures

The AHPP substudy questionnaire measured self-perceived risk of acquiring HPV and developing cervical cancer for the respondent and other young women, as well as vaccine acceptability. Sociodemographic details, information about sexual health behaviours, and self-perceived risk for acquiring HIV were measured on the AYAZAZI main study questionnaire. Age, relationship status, income, type of housing and student status were also captured from the main study questionnaire, as were behaviours including sexual activity, number of sexual partners, and condom use/frequency of use. HIV status of participants was reported from the main questionnaire, as was perceived risk of acquiring HIV.

Statistical analysis

Data from the main AYAZAZI study (12-month) visit were linked to AHPP substudy data. Descriptive statistics were used to analyse sociodemographic variables at the 12-month time point. Frequencies and proportions were used to describe categorical variables and medians and interquartile ranges for continuous variables. Sociodemographic variables included the age of the participant, with dichotomised age categories of adolescents (16 - 19 years) and young adults (20 - 25); relationship status (in a relationship/living together v. in a relationship/not living together v. single); student status (current student v. not a student); type of housing (formal v. informal housing); and monthly income (<ZAR400 v. ZAR401 - 1 600 v. ≥ZAR1 601). The current clinical HIV status of participants was also reported (HIV-positive v. HIV-negative). Sexual health behaviour descriptors were chosen based on factors associated with risk of HIV and HPV acquisition, self-perceived risk and acceptance of the HPV vaccine, including sexual experience ('yes' or 'no'); number of sexual partners in the past 6 months (1 sexual partner v. ≥2 sexual partners); male condom use in the past 6 months ('yes' or 'no'); and frequency of male condom use in the past 6 months ('never' v. 'sometimes' v. 'always').

Self-perceived HIV, HPV and cervical cancer risk was measured using an ordinal scale ranging from 1 to 5 (1 = 'not at all at risk', 2 = 'low risk', 3 = 'medium risk', 4 = 'high risk'). Self-perceptions of risk scores for self in all categories were dichotomised into low- and high-risk groups (1 and 2 = low, 3 and 4 = high). With regard to vaccine acceptability, participants were asked 'Would you be willing to receive a vaccine to help prevent HPV infections and cervical cancer?' ('yes' v. 'no' v. 'I don't know'). Willingness to vaccinate a child against HPV included 'yes' v. 'no' v. 'I don't know' responses. Two questions about the importance of cost in acceptance of the HPV vaccine were 'Would you consider getting the HPV vaccine if it cost you ZAR2 300 to purchase?' and '... if it was free?', and were measured on a 5-point scale ranging from 'definitely would not' to 'definitely would'. The role of cost in acceptability questions was recorded into three categories: 'definitely/probably would not' be vaccine acceptant, 'neutral', and 'probably/definitely would'.

Chi-square analyses were used to examine differences in sociodemographic and behavioural factors according to self-perceived risk of HPV and cervical cancer. When the number of observations in a cell was <5, Fisher's exact test was used instead. Fisher's exact test was also used to determine whether a significant difference existed between participants' perceived risk level for themselves compared with other women in their community; participants who indicated that they 'don't know' or 'prefer not to answer' were removed from the analysis.

Ethics and informed consent

Ethical approval for the substudy was obtained from the research ethics boards of the participating institutions prior to its commencement. The institutions for the main study (AYAZAZI) were Simon Fraser University (ref. no. 2014s0413) and the University of the Witwatersrand (ref. no. #140707). Additional harmonised ethics proposals for the substudy were also approved by the University of British Columbia (ref. no. UBC-H16-02132). All procedures followed were in accordance with the ethical standards of the responsible committee on human experimentation (institutional and national) and with the Helsinki Declaration of 1975, as revised in 2008. Direct participant consent was obtained from participants aged ≥18 years; for those aged <18 years, assent forms were signed by the participant and a consent form was signed by her parents or guardians prior to data collection.

Results

Participant characteristics

Of the 132 females in the AYAZAZI study at the Durban site, 122 (92.4%) completed the AHPP questionnaire at the 12-month visit. At the 12-month data collection stage, participants ranged from 17 to 25 years of age (mean (standard deviation, SD) 20.16 (2.05)). Of the 122 AGYW included in this analysis, most reported being in a relationship (84.4%) but not living with their partner (82.0%), with a personal monthly income of ZAR401 - 1 600 (45.1%). A considerable proportion (25.4%) reported a monthly income <ZAR400, 63.9% were currently in school, and most reported living in formal housing (72.1%). Eight young women who were either HIV-negative or undiagnosed at time of enrolment in the AYAZAZI main study were living with HIV 12 months later. Of the 122 participants, 80.3% or 98 reported being sexually experienced. Most participants reported having had consensual sex with ≥2 partners within the past 6 months (68.4%), with the number ranging considerably from 1 to 25 partners (mean (SD) 3.3 (3.69)). Just over half of the participants (54.5%) said that they used condoms for contraception (Table 1).

Self-perceived risk of acquiring HPV and developing cervical cancer

Prior to involvement in the study, only a small portion of participants (14.3%) had heard of HPV. Overall, 43.0% (n=49) perceived themselves as at low HPV risk and 57.0% (n=65) as at high HPV risk. By age group, 61.2% of participants with low HPV self-perceived risk were young adults aged 20 - 25 years, compared with 52.3% of those with high self-perceived risk. There was no significant difference in self-perceived risk of acquiring HPV between adolescents and young adults (p=0.342) (Table 2).

Significant differences in self-perceived HPV risk were observed for participants who stated they had never heard (v. had heard) of HPV, for those who had (v. had not had) consensual sex, and for those with high v. low perceived HIV risk. Not having (v. having) heard of HPV, having (v. not having) consensual sex, and low (v. high) perceived HIV risk were associated with significantly lower

Table 1. Characteristics and sexual history variables of participants (age 17 - 25 years) (*N*=122)*

	n (%)
Sociodemographics	
Age category (years)	
17 - 19	55 (45.1)
20 - 25	67 (54.9)
Monthly personal income (ZAR†)	
<400	31 (25.4)
401 - 1 600	55 (45.1)
≥1 601	36 (29.5)
Currently in school	
Yes	78 (63.9)
No	44 (36.1)
Housing	
Formal	88 (72.1)
Informal‡	34 (27.9)
Relationship status	
Has partner, do not live together	100 (82.0)
Has partner, live together	3 (2.5)
Does not have partner	19 (15.6)
HIV status	
HIV-positive	8 (6.6)
HIV-negative	114 (93.4)
Sexual history	
Sexually experienced	
Yes	98 (80.3)
No	24 (19.7)
≥2 sexual partners in past 6 months§ (*N*=98)	
Yes	67 (68.4)
No	31 (31.6)
Condom use in past 6 months	
Yes	67 (54.5)
No	55 (44.7)

*Participants were given the option of skipping questions or not answering questions that made them feel uncomfortable. Not all participants therefore answered all the questions.
†ZAR400 = USD25 and ZAR1 601 = USD100, using the exchange rate of ZAR1 = USD0.063, as at 30 May 2016.
‡Informal housing includes RDP (government-subsidised) housing, shacks or hostels.
§The 6 months prior to the interview.

self-perceived HPV risk. There was no significant difference in self-perceived HPV risk by income distribution and pregnancy status. None of the AGYW who self-perceived themselves as at high risk for HPV had heard of it before receiving the explanation of what it is. Of participants who perceived themselves as at high risk of HPV, the highest proportion had engaged in consensual sex ($p<0.001$). The majority (38.8%) of participants who perceived themselves as at low HPV risk also perceived themselves as at low HIV risk, whereas 37.9% of participants who perceived themselves as at high HPV risk also perceived themselves as at high HIV risk ($p=0.004$). Overall, 39.6% ($n=49$) perceived themselves as at low risk and 60.4% ($n=65$) as at high risk.

The distribution of perceived cervical cancer risk and associated factors is presented in Table 3. There were significant differences in self-perceived risk for cervical cancer by age group, income and pregnancy status. The highest proportion of participants who perceived themselves as at high risk of cervical cancer reported being sexually active ($p=0.002$). With regard to HIV, 36.8% of those who perceived themselves as at high cervical cancer risk also perceived themselves as at high HIV risk ($p=0.009$).

Self-perceived risk of acquiring HPV and developing cervical cancer: Risk for self v. other young women

In general, participants reported feeling that they were at lower risk of acquiring HPV and developing cervical cancer compared with other young women in their community. While 39.6% of participants perceived themselves as being at no or low risk of developing cervical cancer, only 10.8% felt that other young women in the community were at this risk level. Of the participants, 57.0% and 89.2% perceived themselves as being at medium to high risk of HPV and cervical cancer, respectively (Table 4).

While there was no significant difference between participants' perception of the risk of acquiring HPV themselves compared with other young women (p=0.80), with regard to perceived risk of developing cervical cancer compared with other young women, participants stated that they felt that other young women were at significantly higher risk ($p<0.001$).

HPV vaccine acceptability

Prior to the study, few of the 122 participants had heard about the HPV vaccine (16.4%) and even fewer had heard about HPV infection (6.6%). Although many participants reported not knowing about HPV prior to the study, after learning about it during the study, most (97.5%) said that they would be willing to receive the vaccine. Two participants said that they had received HPV vaccine prior to the study. HPV vaccine acceptability for self and children (or future children) was similarly high at 95.1%. A cross-tabulation was run to explore whether current mothers and participants who were pregnant would accept the HPV vaccine for their children. All mothers in the cohort ($n=34$) and women who were currently pregnant ($n=6$) reported that they would want the HPV vaccine for their children. Participants were asked how likely they would be to accept the HPV vaccine if it was recommended by a healthcare professional v. friends/family members. Most stated that they would definitely accept if the vaccine was recommended by a healthcare professional (77.9%).

Discussion

Cervical cancer, although preventable, is a significant global health concern. SA, and in particular the province of KwaZulu-Natal with its dense population and extremely high rate of HIV, is the epicentre of both the HIV and cervical cancer epidemics. Young women specifically are at a significant risk of acquiring HIV and HPV infections and also tend to access SRH services less than older women, resulting in disproportionately high rates of cervical cancer nationally. All but 3 women in our cohort indicated that they would like access to the HPV vaccine, with fiscal constraints cited most often as a barrier. Many of the women reported not knowing about HPV or that a vaccine existed prior to involvement with this study, but most reported that they would accept the HPV vaccine for their children and/or future children as well as for themselves. Notably, all participants who currently had children wanted to have them vaccinated against HPV.

The AGYW who participated in this study were representative of a population at the highest risk of HPV, HIV and cervical cancer in SA. The sexual behaviours reported by study participants were representative of national reports. For example, many reported having multiple sexual partners (mean 3.3). These findings are also consistent with national data showing that 39% of women aged 15 - 24 years reported not having used a condom the last time they had intercourse. National data also show that 4.6% of young women had had ≥2 sexual partners over the past year, with a mean of 2.9 lifetime partners.[25] The sexual practices of the young women in the present study may place them at a considerably increased risk of acquiring

Table 2. Distribution of HPV perceived risk and associated factors using the χ^2 test or Fisher's exact test*

	Perceived HPV risk, *n* (%)		*p*-value	
	Low	High	χ^2	Fisher's exact
Age group (years)				
17 - 19	19 (38.8)	31 (47.7)	0.342	-
20 - 25	30 (61.2)	34 (52.3)		
Heard of HPV				
Yes	7 (14.3)	0	-	0.002
No	42 (85.7)	65 (100)		
Income (ZAR)				
<800	29 (59.2)	28 (43.1)	0.089	-
≥801	20 (40.8)	37 (56.9)		
Currently pregnant				
Yes	3 (6.3)	3 (4.6)	-	0.698
No	45 (93.8)	62 (95.4)		
Ever had consensual sex				
Yes	30 (61.2)	60 (92.3)	<0.001	-
No	19 (38.8)	5 (7.7)		
Perceived HIV risk				
Low	41 (87.2)	36 (62.1)	0.004	-
High	6 (12.8)	22 (37.9)		

HPV = human papillomavirus.
*Participants were given the option of skipping questions or not answering questions that made them feel uncomfortable. Not all participants therefore answered all the questions.

Table 3. Distribution of cervical cancer perceived risk and associated factors

	Perceived cervical cancer risk, %		*p*-value	
	Low	High	χ^2 test	Fisher's exact test
Age group (years)				
17 - 19	45.2	43.	0.88	-
20 - 25	54.8	56.3		
Heard of cervical cancer				
Yes	57.1	57.8	0.946	-
Income (ZAR)				
<800	57.1	42.2	0.132	-
≥801	42.9	57.8		
Currently pregnant				
Yes	7.3	4.7	-	0.676
Ever had consensual sex				
Yes	64.3	89.1	0.002	-
Perceived HIV risk				
Low	87.2	63.2	0.009	-
High	12.8	36.8		

sexually transmitted infections (STIs). Sexual behaviours linked to a high prevalence of STIs increase both HIV and HPV transmission and acquisition for AGYW. Overall, rates of infections for this cohort at baseline were high, with 70.2% of females diagnosed with ≥1 STI.[23]

Approximately 60% of the respondents perceived themselves as being at high risk of acquiring HPV and developing cervical cancer. However, they consistently rated other females their age in their community as being at higher risk than themselves for both acquisition of HPV (96%) and developing cervical cancer (89%). Our findings of AGYW having low self-perceived risk of acquiring STIs are consistent with the literature on females in similar settings.[26,27] Self-perceived risk of acquiring sexually transmitted and blood-borne infections is regarded as an important determinant in protection motivation, particularly in the early stages of behaviour change.[28] Risk perception may contribute to and influence healthy sexual behaviours when the risk is perceived to be acute and serious, when personal vulnerability is perceived as high, and when people feel confident that they can indeed do something to avoid the risk. However, despite participants' perceptions of risk generally being low, most still reported wanting to receive the HPV vaccine. Perceptions of self-risk did not appear to play a role in health behaviour preferences for the cohort of AGYW in this study. Of important note is the pivotal role that healthcare professionals play in education and promotion of the HPV vaccine for AGYW in SA.

Study limitations

Limitations of this study include the small sample size and the fact that participants had already been enrolled in a youth-

Table 4. Participants' (females aged 17 - 25 years) self-perceived risk for acquiring HPV and developing cervical cancer v. perceived risk levels for other young women in their community (*N*=122)*

	Overall, *n* (%)	*p*-value
Perceptions of HPV risk for self and other young women in their community		0.80
Risk for self (*N*=114)		
None/low	49 (43.0)	
Medium/high	65 (57.0)	
Risk for other young women in community (*N*=113)		
None/low	5 (4.4)	
Medium/high	108 (95.6)	
Perceptions of cervical cancer risk for self and other young women in their community		<0.001
Risk for self (*N*=106)		
None/low	42 (39.6)	
Medium/high	64 (60.4)	
Risk for other young women in community (*N*=111)		
None/low	12 (10.8)	
Medium/high	99 (89.2)	

HPV = human papillomavirus.
*Participants were given the option of skipping questions or not answering questions that made them feel uncomfortable. Not all participants therefore answered all the questions.

centered study (AYAZAZI) for a year before participating in the AHPP substudy. In the course of this youth engagement project, the AGYW had built trusting relationships with study team members and healthcare providers, so social desirability bias may have influenced responses, leading to an overestimation of HPV vaccine acceptability. Meetings with research assistants revealed that participants wanted to talk more about these topics (e.g. stories about family members with cervical cancer). Findings from this study would have been more robust using a mixed-methods approach, i.e. conducting focus group sessions and interviews in addition to using a questionnaire.

Conclusions

Most AGYW in SA do not have access to the national HPV vaccine programme, as only girls in grade 4 in some public schools qualify.[29] Even most health insurance programmes do not cover the HPV vaccine,[30] which costs ~ZAR2 300 to purchase. As demonstrated in the present study, most participants would not be prepared (or able) to pay such a large amount, but almost all indicated that if the vaccine was free they would accept it. Availability of the HPV vaccine and timely treatment of HPV infections are key issues to address in efforts to decrease cervical cancer worldwide.

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