Increased risk of HPV infection, but not increased risk of cervical dysplasia: HIV-negative commercial sex workers in Senegal

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Abstract

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Human papillomavirus (HPV) is a causative agent in cervical cancer development and commercial sex workers (CSW) are at high risk for exposure to STDs, including HPV. From October 1994-January 1998, CSW and non-CSW were interviewed, cervical swabs were taken for HPV DNA testing, and cervical cytology was conducted. We found that CSW have a higher prevalence of current HPV infection with high-risk HPV-16 (OR: 2.56, 95% CI: 1.46-4.46) and HPV-18 (OR:2.08, 95% CI:1.03-4.20) compared to non-CSW. Likewise, CSW had a higher rate of incident HPV-16 DNA detection (HR: 3.01, 95% CI: 1.20-7.54). However, prevalence of low and high grade squamous intraepithelial lesions (LSIL) and (HSIL) were not significantly higher in CSW compared to non-CSW (OR: 0.61, 95% CI: 0.32-1.16 and OR: 0.21, 95% CI: 0.07-0.65, respectively) and neither were incident cases of LSIL or HSIL (HR: 0.95, 95% CI: 0.0.51-1.77 and OR: 0.76, 95% CI: 0.30-1.91, respectively). We hypothesize that unmeasured immune responses in repeatedly exposed women may be responsible for the lack of association between commercial sex work and cervical dysplasia despite the increased risk of infection with high-risk types of HPV.

Introduction

Worldwide, cervical cancer is the third most frequent cancer in women and is disproportionately high in low-resource countries where access to routine screening is limited (1, 2). Human papillomavirus (HPV), the most common sexually transmitted disease (STD), has been recognized as a necessary cause of cervical cancer and HPV DNA has been found in 99.7% of cervical cancers (3-6). HPV types 16 and 18 account for a disproportionate number of cervical cancer cases—approximately 70% of invasive cervical cancer (ICC) can be attributed to HPV-16 or HPV-18 (7, 8). Development of cervical cancer typically spans a period of 5-20 years and involves a number of steps: infection of the cervix with HPV, persistence of HPV infection, progression to precancerous squamous intraepithelial lesions (SIL), and development of invasive cancer (9). Factors associated with cervical cancer are much the same as factors shown to be associated with acquiring HPV infection, some because they increase the risk for HPV infection and others because they promote HPV related carcinogenesis. These include a high number of sexual partners, early age at first sexual intercourse, increased frequency of intercourse, prostitution, the sexual behavior of the women's sexual partners, tobacco smoking, high parity, inconsistent condom use, other STDs, and long-term use of oral contraceptives (3, 10-17).

Although persistent infection with high-risk types of human papillomavirus (HPV) is causally associated with development of disease in the genital tract (18-22), mounting evidence suggests that most HPV infections are self-limiting and only a minority progress to invasive cervical cancer (2, 23). Most genital HPV infections are benign, subclinical,

and self-limited and a high proportion of HPV associated with low grade SIL (LSIL) regress spontaneously (9, 23). It remains unclear why some untreated cases of HPV progress to cervical cancer while others do not (24). One hypothesis is that an immune response may mediate the progression to cervical cancer: a number of studies have investigated the role of the immune system in development of high grade SIL (HSIL) and ICC by looking at immunocompromised individuals (HIV-positive) and the effect of persistence of HPV on the development of HSIL/ICC (25, 26).

Because risk for HPV infection has been associated with an increased number of sex partners and increased frequency of sex, (10, 15, 27-32) female commercial sex workers (CSW) are considered a high-risk group for HPV infection, but there is mixed evidence of the true risk sex workers are at for acquiring infection or developing HPV-related cervical abnormalities. In a study from Eastern India, the prevalence of HPV of any type in female sex workers was high (73.3%)(33). In a study in Spain of commercial sex workers and controls from a family planning clinic, commercial sex work was associated with a higher incidence and persistence of high-risk HPV infection (34). However, in a cross sectional study conducted of female sex workers in Madagascar, the prevalence of HPV infection (36.7%) was lower than that observed in the United States' National Health and Nutrition Examination Survey (NHANES) (42.5%) (50). Regardless of their high-risk status, there were no cases of HSIL detected in sex workers in the Madagascar study (15). In a study of commercial sex workers and controls in Sydney, HPV-related cytological abnormalities were more common in CSW, but there was no significant difference in the rates of cervical HPV infection between CSW and controls (35).

It has been hypothesized that sex workers may have differential immunological responses to infection with HPV due to more consistent and repetitive exposure to HPV compared to the general population (27, 36). A number of studies of CSW suggest that older women, who remain sexually active with multiple partners, have significantly lower risk of HPV detection (12, 37-39) which may be indicative of immune protection. Likewise, in a study from Mexico City, CSW involved in prostitution for less than a year were at higher risk of HPV acquisition than more experienced sex workers (40). In addition, Hernandez, et al. found that infection with any type of HPV was less prevalent among sex workers that had the highest number of clients (27). To expand the immunological hypothesis, it has been suggested that the use of oral contraceptives compared to condoms is associated with decreased risk for HPV infection, possibly because of the influence of estrogens and progestins on the local immune response (20). Laurence postulates that local cellular immunity to HPV can be elicited in women with multiple sex partners and that male-to-female transmission of HPV can be blocked by local mucosal-based responses that require repetitive, uninterrupted exposure to a pathogen (36).

In this study, we investigated the prevalence and incidence of HPV infection and cervical dysplasia in a group of HIV-negative CSW, women presumably continuously exposed to HPV, compared to HIV-negative low-risk non-CSW. The purpose of this paper is 1) to compare the prevalence of HPV-16, HPV-18, and cytologic abnormalities related to HPV infection in a cross sectional study between CSW and non-CSW, 2) to compare the

incidence of HPV-16, HPV-18, and cytology in a longitudinal study between CSW and non-CSW and 3) to see if the association between HPV and cervical dysplasia differs between CSW and non-CSW.

Methods

Study Population

The study population, collection of specimens, and study procedures have been described in detail elsewhere (25, 26). In brief, from October 1994-January 1998, women over 15 years of age who presented at the University of Dakar outpatient infectious disease clinic (n=4349) and commercial sex workers attending an STD clinic in either Dakar (n=773) or M'Bour (n=270) were offered HIV testing as well as cytolological screening with cervical swabs for detection of abnormal cervical cells and type-specific HPV DNA. Only individuals who were HIV-negative at baseline are included in the current analysis (893 CSW and 3907 non-CSW); HIV-positive individuals (150 CSW and 442 non-CSW) were excluded.

In the parent study, HPV and HIV positive women were oversampled for enrollment into follow-up for high grade dysplasia, with and 939 women were prospectively. As with the cross-sectional study, only HIV-negative individuals are included in this analysis (160 CSW and 236 non-CSW). Women were followed up every 4 months for a maximum of 5.4 years to assess the risk of developing cervical lesions. At each visit, women completed a detailed interview with questions about sexual behavior and medical history. Cervical HPV DNA detection was done with polymerase chain

reaction with HPV L1 consensus primers, HPV type-specific oligonucleotide probes (high-risk types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56 and a generic probe). Initially, screening for the presence of high-risk HPV was done with a 10-probe mixture, testing for HPV DNA by PCR that used the consensus primers MY09 and MY11, which are specific for a highly conserved region in the L1 open reading frame. Positive samples were then reamplified to assess presence of 12 HPV types in primer groups for low-risk HPV types (i.e., combined HPV 6 and 11) and for high-risk HPV types (i.e., HPV 16; HPV 18; combined HPV 31, 33, 35, and 39; combined HPV 45 and 56; and combined HPV 51 and 52).When new probes were available in April, 1998, HPV detection and typing with probes for high and low-risk types was completed (high-risk types 16, 18, 26, 31, 33, 35, 39, 45, 51, 52, 55, 56, 58, 59, 68, 73, 82, and 83 and low-risk types 6, 11, 40, 42, 53, 54, 57, 66, 84). Details of PCR detection have been detailed elsewhere (41). Only women who were negative for the specific outcome of interest (HPV-16, HPV-18, LSIL, HSIL) at baseline were included in the follow-up analysis.

Cytology Screening

Pap smears were interpreted and classified according to the Bethesda System as unsatisfactory, negative, atypical squamous cells of uncertain significance (ASCUS), low grade squamous intraepithelial lesions (LSIL), high grade squamous intraepithelial lesions (HSIL), or invasive cervical cancer (ICC). More detail can be found elsewhere (25).

Variables

Outcomes of interest in this analysis are HPV-16, HPV-18, LSIL (mild dysplasia, koilocytic or condylomatous atypia), and HSIL (moderate to severe dysplasia). The variables for HPV-16 and HPV-18 are binary indicators of whether or not an individual has type-specific DNA positivity for HPV. A woman was considered to have dysplasia if cytology revealed LSIL or greater.

Potential confounders of interest included age, smoking status, alcohol use, contraceptive method, number of children, and previous Pap exam were obtained from the questionnaire. A categorical variable for age was created for individuals less than 35 years and 35 years and older in order to capture the risk of both younger and older individuals. Binary indicators for alcohol use (current use of alcohol) and smoking status (current smoker or non-smoker) were used in the modeling. A categorical variable was used to adjust for current contraceptive method—categories included were none, hormonal contraceptive, condoms, or other. The variable used for exposure to a previous Pap exam was a binary indicator of self-report of having received a Pap test prior to enrollment (ever or never).

Analysis

All statistical analyses were performed using Stata 11. Unadjusted logistic regression models were first fit to compare CSW to non-CSW for the outcomes of HPV-16 DNA detection, HPV-18 DNA detection, low grade squamous intraepithelial lesions or greater, or high grade squamous intraepithelial lesions or greater. Age, as a categorical variable

(<25 years, 25-34 years, 35+ years), was evaluated as an effect modifier due to an *a priori* hypothesis that highest rates of HPV infection would be seen in the youngest and oldest age groups, due to evidence that prevalence peaks in the early twenties, is followed by an age-related decline, and in developing countries a second prevalence peak is observed in older women (42). However, no effect modification was observed in these age groups. Younger vs. older age (<35 years, 35+ years) was then considered as an effect modifier due to *a priori* information that younger individuals may be at a different risk than older individuals and the potential for a differential immune response to HPV infection by age. Age, as a continuous variable was also considered a potential confounder to more precisely adjust for age. Smoking status, alcohol use, contraceptive method, previous Pap test, and number of children were also considered potential confounders. Confounders were adjusted for in the model if they changed the point estimate of the odds ratio by 10% or more in a bivariate analysis. 95% confidence intervals were calculated for the odds ratio and associations were considered statistically significant at an alpha level of 0.05.

Using the subset of individuals with follow-up data, Cox proportional hazards models were fit to compare incidence of DNA detection of any HPV types between CSW and non-CSW. Age, smoking status, alcohol use, contraceptive method, and number of children were considered *a priori* as potential confounders in the model. Confounders were adjusted for in the model if they changed the point estimate of the hazard ratio by 10% or more. 95% confidence intervals were calculated for the hazard ratio and associations were considered statistically significant at an alpha level of 0.05.

Incidence of LSIL or greater and incidence of HSIL or greater were compared between CSW and non-CSW using Cox proportional hazards models. Separate risk estimates were calculated for strata defined by high-risk HPV status (detection of HPV-16 DNA and/or HPV-18 DNA).

Results

Socio-demographic characteristics

A complete list of socio-demographic characteristics by sex-worker status can be found in Table 1. The age distribution in CSW and non-CSW was fairly similar, with approximately 20% less than 25 years of age. Non-CSWs had, on average, slightly more children than CSW (4.0 vs 2.6, respectively). CSW were less likely to be currently married and more likely to be single or previously married than non-CSW. CSW were also more likely to have had a previous Pap, use condoms as a form of contraception, be a current smoker, and use alcohol.

Prevalence of HPV detection and cervical dysplasia

Prevalence of HPV infection and results of cytology comparing commercial sex workers to non-commercial sex workers can be seen in Table 2. Effect modification by age was assessed for all outcomes, but the point estimate of the odds ratio did not differ significantly between age groups for HPV-16, HPV-18, LSIL or greater, or HSIL or greater. The odds of being infected with any type of HPV differed between younger (<35 years) and older (35+ years) age groups and separate odds ratios were reported for these

two groups. Age was considered a residual confounding variable and was adjusted for as a continuous variable in all analyses.

The prevalence of any HPV infection was significantly greater in CSW than non-CSW in the younger age group after adjusting for contraceptive method, number of children and smoking status (OR=1.54, 95% CI: 1.07-2.20), but there was not a significant difference in prevalence of infection with any HPV between CSW and non-CSW of the older age group (OR=0.97, 95% CI: 0.43-2.16).

HPV-16 was more prevalent than HPV-18 in both CSW and non-CSW (5.1% vs 2.2% and 2.7% vs 1.6%, respectively). HPV-16 and HPV-18 infection were both significantly higher among CSW than among non-CSW. Controlling for age, contraceptive method, number of children and smoking status, CSW had 2.56 times the odds of HPV-16 DNA detection compared to non-CSW (95% CI: 1.46-4.46). Likewise, CSW had 2.08 times the odds of HPV-18 DNA detection compared to non-CSW (95% CI: 1.03-4.20).

Despite the higher HPV infection rate, the prevalence of LSIL or greater was somewhat higher in non-CSW compared to CSW (3.9% vs 3.3%, respectively), though not statistically significant. After adjustment for age, contraceptive method, number of children, and smoking status, the odds of LSIL or greater in CSW was 0.61 times the odds of development of LSIL or greater in non-CSW (95% CI: 0.32-1.16).

Prevalence of HSIL or greater was low in both CSW and non-CSW and the power to detect an association was low: there were only 8 cases on HSIL or greater in CSW. However, the odds of having prevalent HSIL or greater was significantly lower in CSW compared to non-CSW after adjusting for age, contraceptive method, number of children, and smoking status(OR=0.21, 95% CI: 0.07-0.65).

Incidence of HPV detection and cervical dysplasia

The number of individuals included in each of the follow-up analyses are shown in the risk tables in Figures 1 and 2. The cumulative incidences of HPV-16 (15 cases in CSW vs. 12 cases in non-CSW over 48 months) and HPV-18 (6 cases in CSW vs. 9 cases in non-CSW over 48 months) were higher among CSW than non-CSW (Table 3). After adjusting for age, smoking status, and contraceptive method, CSW were detected with HPV-16 DNA at 3 times the rate of non-CSW (95% CI: 1.20-7.54). The incidence of HPV-18 DNA detection was lower in CSW compared to non-CSW, though the difference was not significant (HR=0.64, 95% CI: 0.16-2.64).

The cumulative incidence of LSIL was higher in non-CSW compared to CSW (25 cases in CSW vs. 43 cases in non-CSW over 48 months) and the incidence of LSIL was higher among the group with current HPV DNA detection. After adjustment for age, smoking status, and contraceptive method, HPV-negative and HPV-positive CSW were less likely than non-CSW to develop LSIL (HR=0.34, 95% CI: 0.11-1.08 and HR=0.87, 95% CI: 0.39-1.97, respectively), though the difference was not significant. The cumulative incidence of HSIL was lower in CSW compared to non-CSW (12 cases in CSW vs. 21

cases in non-CSW over 48 months). Similar to LSIL, currently HPV-positive individuals were more likely to develop HSIL. After adjustment for age, smoking status, and contraceptive method, HPV-negative and HPV-positive CSW were less likely than non-CSW to develop LSIL (HR=0.30, 95% CI: 0.04-2.00 and HR=0.79, 95% CI: 0.25-2.47 respectively), though the difference was not significant.

Discussion

HPV DNA of any type was detected in 19.0% of CSW and 11.3% of non-CSW less than 35 years of age, while HPV of any type was detected in similar proportions in both CSW and non-CSW (7.6% and 7.4%, respectively) greater than 35 years of age. Not surprisingly, as HPV-16 is the most prevalent type of HPV worldwide, (18) HPV-16 was more prevalent than HPV-18 in this population, with 5.1% of CSW and 2.2% of non-CSW testing positive for HPV-16 DNA and 2.7% of CSW and 1.6% of non-CSW testing positive for HPV-18 DNA.

CSW had over a two-fold increase in risk of being currently infected with high risk HPV (HPV-16 and HPV-18). Commercial sex work is associated with many of the well-documented risk factors for HPV-infection: higher number of sex partners, smoking, oral contraceptive use, inconsistent condom use, and infection with other STDs (10-15); even after adjustment for current smoking and contraceptive use, the risk was higher among CSW. This supports the hypothesis that CSW have more consistent and repetitive exposure to STDs, including high-risk HPV types (27).

The higher prevalence of high-risk types observed in CSW compared to non-CSW is confirmed in the increased incidence of high-risk types observed in the follow-up study; CSW who were HPV-16 negative at baseline were more likely than non-CSW who were HPV-16 negative at baseline to develop detectable HPV-16 in follow-up. Again, this is consistent with the literature that CSW are at increased risk for development of HPV infection (10, 15, 27, 34, 43-45). There was not a statistically significant increase in risk of detection of HPV-18 in CSW in the follow-up study, potentially due to small numbers.

Commercial sex work can serve as a proxy for measurement of both recent and lifetime sex partners and it makes intuitive sense that the greater the number of partners, the greater risk of infection. Previous work has shown that a high number of sex partners increases the risk of high-risk HPV infection, but that there may be a threshold for increasing risk (46). Future studies of this population should include the number of lifetime sex partners in order to determine if a similar threshold for HPV risk is observed among commercial sex workers.

Age did modify the association between CSW and detection of any type of HPV DNA. Detection of any type of HPV was significantly greater in CSW compared to non-CSW in women less than age 35. These findings are consistent with previous studies that have suggested older women who remain sexually active, even with multiple partners, have significantly lower risk of HPV infection compared to sexually active younger women (12, 37-39). CSW greater than age 35 were at no increased risk of detection of HPV of any type compared to non-CSW. This supports the hypothesis that consistent and

repetitive exposure to HPV could elicit a protective immune response to the virus (36). Another reason why there may be no difference between CSW and non-CSW in the older age group is because it is likely that type-specific infection elicits immune protection against subsequent reinfection (47) and may provide cross protection (48). It is likely that CSW were exposed to many types of HPV as young women, cleared the infection, and developed immunity.

It is possible that immune protection may play a role in our observation that age did not modify the association between CSW and detection of the high-risk types (HPV-16 and HPV-18). This finding may suggest that infection with high-risk types is more likely to persist than infection with low-risk types, however this study used cross-sectional data, making it difficult to assert anything about persistence in this population. Another explanation for the lack of effect modification by age for HPV-16 and HPV-18 is that prevalence may not have been high enough in this population for us to observe any effect modification by age.

In the absence of differential immunity to repeated HPV exposure, one might expect that CSW would have a higher risk of LSIL and HSIL due to the increased risk of infection with high-risk HPV and other STDs among CSW (3-6). However, there was not an increased prevalence of LSIL or HSIL among CSW compared to non-CSW and, in fact, there was a statistically significant decrease in the prevalence of HSIL in commercial sex workers. This may provide further evidence that sustained high levels of exposure to HPV could generate an immune response strong enough to decrease the risk of

developing cervical dysplasia (36). One limiting factor of this finding is that this was cross-sectional data and that there was a relatively small number of individuals with HSIL, resulting in limited study power.

CSW in the follow-up study were at a decreased risk for development of LSIL and HSIL compared to non-CSW. As expected, the hazard ratio for development of LSIL or HSIL comparing CSW to non-CSW was higher among those who had detectable high-risk HPV and those who did not. Again, this may suggest that sustained high levels of exposure to high-risk HPV confer natural immunity that is protective against development of cervical lesions and cervical cancer (27, 36, 40). However, it is important to note that low-risk types cause LSIL, so it is not surprising that high-risk types are not associated with LSIL development (49).

The incidence and prevalence of HPV detection in both CSW are lower than the estimates of HPV infection from CSW in other populations (15, 33), and lower than the rates seen recently in general populations (50). This may be because the PCR assays that were available when this study was conducted, and used in this analysis, were less sensitive than PCR assays used in more recent studies. However, we do not suspect any differential misclassification of HPV status between CSW and non-CSW, leading us to believe that the associations we observe are real, and not due to measurement error.

Commercial sex work in Senegal is unique because CSW are screened monthly for STDs and if they test positive, are treated for their STD (51). Infection with HPV has been

shown to be significantly associated with other STDs(20) and there is some evidence that other sexually transmitted diseases, including *Trichomonas vaginalis* (TV), *Chlamydia trachomatis* (CT), and *Herpes simplex virus* type 2 (HSV2) may increase risk of development of HPV-related cervical cancers (52-54). In addition, CT is associated with the persistence of HPV (55), a known risk factor for the development of cervical cancer and CT and GC infections were associated with the development of HSIL(56, 57). If CSW in this population are being tested and treated for other STDs, perhaps there is a protective effect resulting in less development of cervical cancer.

One limitation the limited study power, particularly for HSIL, in this population. Future studies should seek to utilize a similar longitudinal study design, powered to detect the risk associated with commercial sex work and development of LSIL and HSIL.

Future studies of similar populations should determine if CSW have a decreased likelihood of persistent HPV infection and seek to quantify the effect of continuous exposure to high-risk HPV. Serologic studies comparing CSW to non-CSW could determine if antibody responses are associated with HPV clearance, and if level of continuous HPV exposure is associated with the strength of the antibody response. Future work should also further investigate the role of type-specific antibodies to HPV in the development of LSIL and HSIL. Finally, more work is needed to understand the biological role of repetitive and continuous exposure to high-risk types of HPV in the potential protection against LSIL, HSIL and invasive cervical cancers. A better

understanding of the natural immune response to HPV will help better prevent progression to invasive cervical cancer after infection with high-risk strains of HPV.

Tables and Figures

Table 1. Demographic characteristics of HIV-negative commercial sex workers and non-commercial sex workers in Senegal.

	CSW (N=893)	non-CSW (N=3907)
	N (%)	N (%)
Age Category		
<25 years	180 (20.2)	731 (18.7)
25-34 years	456 (51.1)	1782 (45.6)
35+ years	257 (28.8)	1394 (35.7)
Number of Children (mean, SD)	2.6 (2.3)	4.0 (3.2)
Marital Status		
Single	304 (34.5)	416 (10.8)
Married	31 (3.5)	3070 (79.5)
Previously Married	547 (62.0)	374 (9.7)
Place of Birth		
Senegal	612 (69.4)	3659 (94.5)
Other	270 (30.6)	215 (5.6)
Ethnic Group		
Wolof	132 (28.1)	1042 (45.0)
Pulaar	81 (17.3)	476 (20.6)
Serere	57 (12.2)	271 (11.7)
Sarakhole	5 (1.1)	38 (1.6)
Mandjack	5 (1.1)	31 (1.3)
Diola	10 (2.1)	172 (7.4)
Other	179 (38.2)	285 (12.3)
Religion		
Muslim	336 (72.0)	2110 (91.2)
Christian	126 (27.0)	192 (8.3)
Other	5 (1.1)	12 (0.5)
Any School	296 (64.1)	1472 (63.7)
Contraceptive Method		
None	170 (19.2)	2152 (55.5)
Condoms	521 (58.8)	105 (2.7)
Hormone (pill, injection)	143(16.1)	712(18.4)
Other	52(5.9)	912 (23.5)
Previous Pap	221 (25.2)	620 (16.0)
Current Smoker	477 (53.7)	161 (4.1)
Any Alcohol Use	279 (31.6)	73 (1.9)

Table 2. Type-specific HPV infection and cytology outcomes by age category and commercial sex worker status.

	CSW		non-CSW		Odds Ratio[a]		
	n	%	n	%	OR	95% CI	p-value
Any HPV							
<35 years (N=3031)	119	19.0	279	11.3	1.54	(1.07, 2.20)	0.02
35+ years (N=1598)	19	7.6	102	7.4	0.97	(0.43, 2.16)	0.94
HPV-16 (N=4629)	45	5.1	85	2.2	2.56	(1.46, 4.46)	0.001
HPV-18 (N=4629)	24	2.7	60	1.6	2.08	(1.03, 4.20)	0.04
LSIL or greater (N=4498)	28	3.3	146	3.9	0.61	(0.32, 1.16)	0.13
HSIL or greater (N=4498)	8	0.9	57	1.5	0.21	(0.07, 0.65)	0.007

[a]Adjusted for age, contraceptive method, number of children, and smoking status.

Table 3. Hazard ratios comparing the incidence of type-specific HPV infection, LSIL, and HSIL in CSW to non-CSW.

	Hazard Ratio[a]	95% CI	p-value
HPV-16	3.01	(1.20, 7.54)	0.02
HPV-18	0.64	(0.16, 2.64)	0.55
LSIL[b]	0.95	(0.51, 1.77)	0.87
HPV-	0.34	(0.11, 1.08)	0.07
HPV+	0.87	(0.39, 1.97)	0.75
HSIL[b]	0.76	(0.30, 1.91)	0.55
HPV-	0.30	(0.04, 2.00)	0.21
HPV+	0.79	(0.25, 2.47)	0.87

[a]Adjusted for smoking status, age, and contraceptive method.
bDetection of any HPV types.

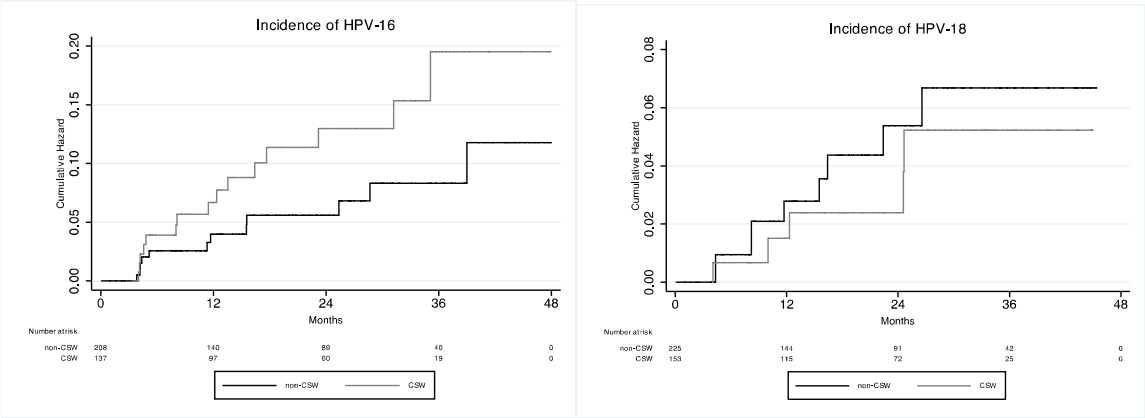

Figure 1. Incidence of HPV-16 and HPV-18 by CSW and non-CSW status.

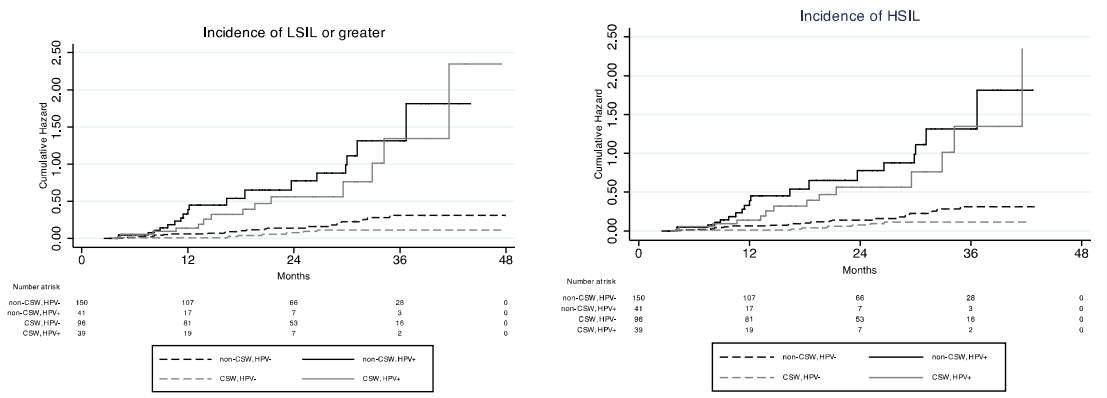

Figure 2. Incidence of LSIL and HSIL by CSW and non-CSW, stratified by presence or absence of HPV.

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