Sexual Behavior, Condom Use, and Human Papillomavirus: Pooled Analysis of the IARC Human Papillomavirus Prevalence Surveys

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Abstract

Human papillomavirus (HPV) is a sexually transmitted infection but it is unclear whether differences in transmission efficacy exist between individual HPV types. Information on sexual behavior was collected from 11 areas in four continents among population-based, age-stratified random samples of women of ages ≥15 years. HPV testing was done using PCR-based enzyme immunoassay. Unconditional logistic regression was used to estimate odds ratios (OR) of being HPV positive and corresponding 95% confidence intervals (95% CI). Variables were analyzed categorically. When more than two groups were compared, floating confidence intervals were estimated by treating ORs as floating absolute risks. A total of 11,337 women (mean age, 41.9 years) were available. We confirmed that lifetime number of sexual partners is associated with HPV positivity (OR for ≥2 versus 1, 1.86; 95% CI, 1.63-2.11) but the association was not a linear one for HPV18, 31, and 33 (i.e., no clear increase for ≥3 versus 2 sexual partners). Women who had multiple-type infection and high-risk HPV type infection reported a statistically nonsignificant higher number of sexual partners than women who had single-type and low-risk type infections, respectively. Early age at sexual debut was not significantly related to HPV positivity. Husband's extramarital sexual relationships were associated with an OR of 1.45 (95% CI, 1.24-1.70) for HPV positivity in their wives after adjustment for age and lifetime number of women's sexual partners. We did not observe a significant association with condom use. Our study showed an effect of both women's and their husbands' sexual behavior on HPV positivity. Furthermore, it suggests some differences in the pattern of the association between sexual behavior and different HPV types. (Cancer Epidemiol Biomarkers Prev 2006;15(2):326–33)

Introduction

Human papillomavirus (HPV), the necessary cause of invasive cervical cancer and its precursor lesions (1), is sexually transmitted (2). Many studies (3-5) found a direct association of HPV infection with number of sexual partners, most notably with recent sexual partners (6-8). A few studies (8-10) suggested different risk profiles for high-risk and low-risk HPV types, but no study thus far has included a sufficient number of HPV-positive women to assess whether the strength of the association with sexual behavior varies between individual HPV types.

Furthermore, a woman's risk of contracting an HPV infection depends strongly on the sexual behavior of her male partners, and relatively little information is available on this issue (11). Finally, it is not clear whether age at sexual debut has any influence on the risk of being HPV positive later in life (3) and to what extent condom use might prevent HPV transmission (12).

To further explore these issues, we present here an analysis of the sexual behavioral determinants of prevalent HPV infection from the International Agency for Research on Cancer (IARC) HPV Prevalence Surveys.

Materials and Methods

Contributing Studies and Data Collection. Similar protocols were developed for each of 11 areas in nine different countries and studies were carried out between 1993 and 2003. Population sampling methods have previously been described for the individual areas: Vietnam (13), Thailand (14), Korea (15), Mexico (16), Argentina (17), Chile (18), Colombia (19), Nigeria (20), and Spain (21). Vietnam and Thailand participated with two studies each in different areas (Hanoi and Ho Chi Minh, Vietnam; Lampang and Songkla, Thailand). In Colombia, the study population was selected from women attending screening centers and family planning clinics.

In summary, each area attempted to obtain an age-stratified sample of the population that included ~100 women in each 5-year age group, from 15-19 to ≥65. Participation ranged from 48% in Songkla, Thailand (where most nonparticipants were not found at the address given by the population list) to 94% in Hanoi, Vietnam. IARC HPV Prevalence Surveys exclusion criteria were pregnancy at time of recruitment, previous hysterectomy or cervical conization, and physical or mental incompetence. The number of individuals can differ from that reported in the original findings due to missing values for sexual variables.

Trained interviewers questioned study participants face-to-face using a questionnaire that included information on sociodemographic characteristics, smoking habits, reproductive history, Papanicolaou smear screening history, and use of contraceptive methods. Information on sexual behavior was also collected and included lifetime number of sexual partners and age at sexual debut. Women were also asked whether they thought their stable male sexual partners (referred to as ''husbands'') had had extramarital sexual relationships with other women and, specifically, with female sex workers.

All participants signed informed consent forms according to the recommendations of the IARC and the local ethical review committees that approved the study.

Gynecologic Examination, Specimen Collection, and Cytology. Study participants underwent a pelvic examination done by a gynecologist or specially trained personnel. Samples of exfoliated cells from the ectocervix were collected with two wooden Ayre spatulas and from the endocervix with a cytobrush (Cervibrush, CellPath, Herte, United Kingdom). After the preparation of a Papanicolaou smear, the remaining exfoliated cervical cells were placed in tubes with PBS and stored on ice. Cells were centrifuged at $3,000 \times g$ and the resulting pellet was resuspended in PBS and shipped to IARC for storage. Cytologic findings were read locally and classified according to the Bethesda System. Atypical squamous cells of undetermined significance or worse were found in 4% of study women (between 1% in Hanoi, Vietnam, to 9% in Nigeria). Seventy-four women (0.7%) had a diagnosis of high-grade squamous intraepithelial lesion or worse.

HPV DNA Detection Techniques. HPV testing was done on exfoliated cervical cells in the pathology laboratory of the VU University Medical Center (Amsterdam, the Netherlands) with the exception of the Mexican study. Only women who tested positive for β-globin were included in this analysis.

A first screening was done to determine the overall presence of HPV DNA using a general GP5+/6+ primer−mediated PCR

(22). PCR products were assessed by enzyme immunoassay using oligoprobe cocktails to detect the following 36 HPV types: HPV6, 11, 16, 18, 26, 31, 33-35, 39, 40, 42-45, 51, 52-59, 61, 66, 68, 70, 71 (equivalent to CP8061), HPV72 and 73 (equivalent to MM9), HPV81 (equivalent to CP8304), HPV82 (IS39 and MM4 subtypes), HPV83 (equivalent to MM7), HPV84 (equivalent to MM8), and CP6108 (22). In addition, PCR products were tested using a low-stringency Southern blot analysis of PCR products with a cocktail probe of HPV-specific DNA fragments. Subsequently, typing of samples positive for HPV was done by enzyme immunoassay or reverse line blot analysis of GP5+/6+ PCR product using HPV type-specific oligoprobes for the HPV types described above (22, 23). Samples that were GP5+/6+ positive by low-stringent Southern blot analyses, but were not identified by the above-mentioned typing protocols, were considered as *HPV*X (i.e., uncharacterized HPV types).

The determination of HPV types in the Mexican study has previously been described (16) and was carried out on specimens from women with normal cytology at the Department of Molecular Microbiology and Immunology, Johns Hopkins University School of Public Health (Baltimore, MD) and at the National Institute of Public Health (Cuernavaca, Morelos, Mexico) using biotinylated MY09/11 consensus primers and genotyping (27 HPV types: 6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51-59, 66, 68, 73, 82-84) by a single-hybridization, reverse line blot detection method (24).

HPV types considered as high-risk for this report included HPV16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, 68, 73, and 82 (25). All other HPV types, including HPV 26, 53, and 66, which were considered as probably carcinogenic (25), were classified as low-risk types.
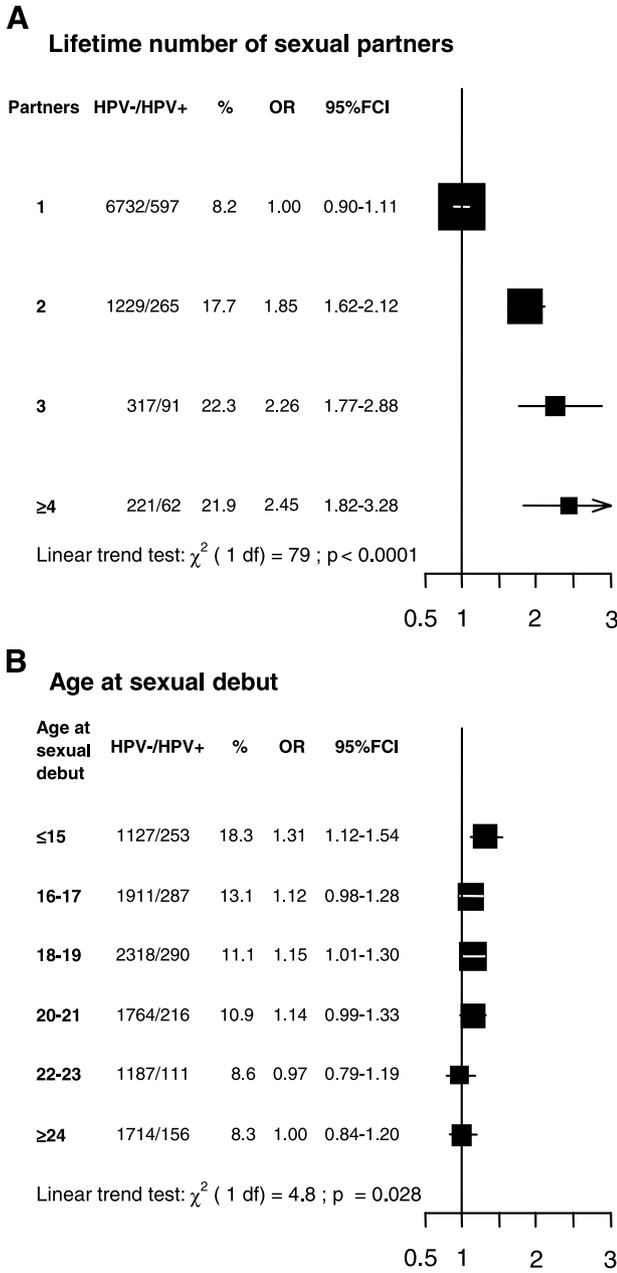
Herpes Simplex Virus Type 2 Serum Antibodies. The presence of type-specific plasma immunoglobulin G antibodies against herpes simplex virus type 2 (HSV-2) was tested for in sera obtained in Vietnam, Thailand, Korea, Mexico, Argentina, Nigeria, and Spain. Serologic testing was conducted blindly in a central laboratory in Seattle, Washington, using a HSV-2 ELISA assay developed by Focus Technology (formerly MRL, Cypress, CA; ref. 26). All HSV-2-positive sera were retested to confirm results.

Statistical Analysis. The lifetime number of sexual partners was calculated using the information on both regular and casual sexual partners. On account of differences in the questionnaire, Colombia could contribute to the analysis on lifetime number of sexual partners only when the variable was considered on two levels: one partner and two partners or more. Women's answers about their husbands' sexual

Table 1. Prevalence of HPV and selected characteristics among 11,337 women by study area (IARC HPV Prevalence Surveys)

	Subjects tested for HPV	HPV positivity,* %	Mean age, y (SD)	Mean no. sexual partners, *n* (SD)	Mean age at sexual debut, y (SD)	HSV-2 positivity, %	Husband's extramarital sexual relationships, %	Condom use, % of years of sexually active life
Study area								
Hanoi, Vietnam	990	1.6	45.2 (16.0)	1.1 (0.3)	20 (3.1)	9	26	9
Ho Chi Minh, Vietnam	913	11.2	42.1 (15.3)	1.1 (0.5)	22 (4.5)	35	40	47
Lampang, Thailand	1,020	9.3	46.2 (16.6)	1.2 (0.5)	20 (4.1)	33	59	6
Songkla, Thailand	704	4.0	47.8 (16.5)	1.1 (0.5)	20 (4.1)	28	61	10
Korea	854	15.6	45.4 (10.8)	1.2 (0.5)	23 (3.2)	42	56	4
Spain	908	2.9	42.8 (16.0)	1.5 (1.3)	21 (4.0)	9	69	60
Mexico	1,340	12.7	41.6 (17.2)	1.4 (1.7)	18 (3.8)	32	—	9
Argentina	907	17.5	40.4 (14.3)	1.8 (1.5)	19 (4.1)	37	91	40
Chile	947	14.2	43.2 (15.7)	1.6 (1.1)	19 (4.3)	—	100	15
Colombia	1,823	15.4	32.7 (11.0)	—	18 (3.9)	—	72	35
Nigeria	931	27.0	44.1 (16.3)	1.7 (1.0)	19 (3.1)	61	84	9
All areas	11,337	12.5	41.9 (15.7)	1.4 (1.1)	20 (4.2)	32	63	23

*Age standardized to the world population.

A

Lifetime number of sexual partners

Partners	HPV-/HPV+	%	OR	95%FCI
1	6732/597	8.2	1.00	0.90-1.11
2	1229/265	17.7	1.85	1.62-2.12
3	317/91	22.3	2.26	1.77-2.88
≥4	221/62	21.9	2.45	1.82-3.28

Linear trend test: χ^2 (1 df) = 79 ; p < 0.0001

B

Age at sexual debut

Age at sexual debut	HPV-/HPV+	%	OR	95%FCI
≤15	1127/253	18.3	1.31	1.12-1.54
16-17	1911/287	13.1	1.12	0.98-1.28
18-19	2318/290	11.1	1.15	1.01-1.30
20-21	1764/216	10.9	1.14	0.99-1.33
22-23	1187/111	8.6	0.97	0.79-1.19
≥24	1714/156	8.3	1.00	0.84-1.20

Linear trend test: χ^2 (1 df) = 4.8 ; p = 0.028

Figure 1. ORs and corresponding 95% FCIs of HPV positivity by lifetime number of sexual partners and age at the sexual debut. IARC HPV Prevalence Surveys. ORs were adjusted for age, study area and, in (*B*) only, for lifetime number of sexual partners.

relationships with other women, including sex workers, before or after marriage (in the present report we referred to it as extramarital sexual relationships) were classified as ''no'' and ''uncertain/yes,'' on account of the similarity of HPV findings among women who answered ''uncertain'' and ''yes.'' Information on husband's extramarital sexual relationships was not available for Colombia and Mexico. The variable ''condom use'' was evaluated as ''ever'' versus ''never'' use, and as percent of years (i.e., never, <70%, ≥70%; ref. 27) when condom was used out of years of sexual activity (i.e., between age at sexual debut and age at interview). In the comparison of differences in risk factors between infections with high-risk and low-risk types, women who were positive for both types were excluded.

Unconditional logistic regression was used to estimate odds ratios (OR) of being HPV positive and the corres-

ponding 95% confidence intervals (CI) according to several characteristics. All ORs were adjusted for age group (<25, 25-34, 35-44, 45-54, ≥55 years) and, when appropriate, for study area.

The variables were analyzed categorically, and when more than two groups were compared, floating CIs (FCI) were estimated by treating ORs as floating absolute risks (28, 29). This method assigns a variance to the reference category and reduces unwanted correlation between coefficients, thus reducing the variance of ORs not defined as 1.0. No change is made, however, to the point estimate of the ORs. Floating methods enable valid comparison between any two exposure groups even if neither is the baseline group. Tests for linear trend of ORs were done, giving an increasing score for each level of the categorized variable and fitting them into the model as continuous variables.

Most results are presented graphically, plotting the summary ORs as black squares, the size of which is inversely proportional to the variance of the estimate. A horizontal line represents the 95% CI. Diamonds are used to plot the summary OR for all studies together. The diamonds represent the pooled OR and the extremes show the limits of the 95% CI.

Heterogeneity of the OR between areas was tested by calculating the difference between the log likelihood of the model that considered the interaction term between the areas and exposure of interest and the log likelihood of the model that included the exposure only, and comparing it to the χ^2 distribution with degrees of freedom equal to the number of areas minus one.

Results

Overall, 11,337 women were available for the present analysis (Table 1) and the majority (79%) were married at the time of interview (data not shown). The mean age was 41.9 years (range, 15-86 years), varying between 32.7 years in Colombia and 47.8 years in Songkla, Thailand (Table 1). Very low HPV prevalence was found in Hanoi, Vietnam (1.6%) and in Spain (2.9%) whereas the highest HPV prevalence was found in Nigeria (27.0%). The range of lifetime number of sexual partners was broad (1-50) with a mean number of 1.4. The highest mean numbers in individual study areas were found in Nigeria (1.7) and Argentina (1.8; Table 1). The OR for HPV positivity increased significantly from one sexual partner (OR, 1.00; 95% FCI, 0.90-1.11) to two sexual partners (OR, 1.85; 95% FCI, 1.62-2.12), but then it increased little (OR for 3 sexual partners versus 1, 2.26; OR for ≥4 sexual partners versus 1, 2.45; Fig. 1A). ORs were not substantially modified after additional adjustment for husband's extramarital relationships (OR for 1 sexual partner, 1.00; 95% FCI, 0.89-1.12; OR for 2 sexual partners, 1.65; 95% FCI, 1.42-1.92; OR for 3 sexual partners = 2.01; 95% FCI, 1.54-2.62; OR for ≥4 sexual partners = 2.25; 95% FCI, 1.64-3.09; data not shown).

There was a significant trend of decreasing HPV positivity with the increase of age at sexual debut after adjustment for age, study area, and lifetime number of sexual partners (Fig. 1B). Nevertheless, even for women who reported sexual debut at age 15 or younger, the OR (1.31; 95% FCI, 1.12-1.54) for being HPV positive compared with women who reported sexual debut at age 24 or older (OR, 1.00; 95% FCI, 0.84-1.20) was not significantly increased.

Women who reported two sexual partners or more (i.e., between 6% in Hanoi, Vietnam and 47% in Nigeria) showed an OR of 1.86 (95% CI, 1.63-2.11) as compared with women who reported only one sexual partner (Fig. 2A). However, significant heterogeneity was found between study areas. The strongest association between having more than one sexual partner and HPV positivity was found in Spain (OR, 3.62; 95% CI, 1.49-8.75) and the weakest in Nigeria (OR, 1.35;
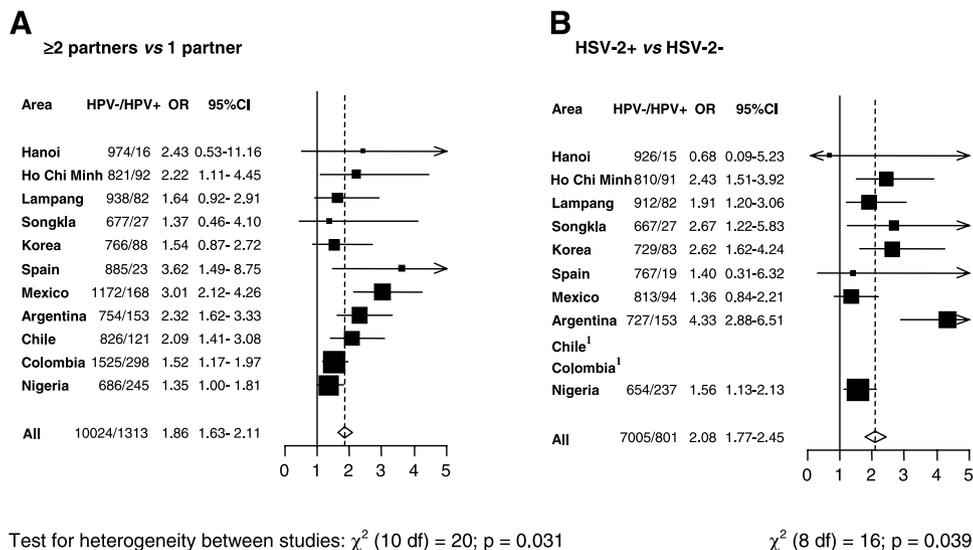
Figure 2. ORs and corresponding 95% CIs of HPV positivity by number of sexual partners, HSV-2 seropositivity, and study area. IARC HPV Prevalence Surveys. ORs were adjusted for age and, for the pooled estimates, for study area. [1], information not available.

95% CI, 1.00-1.81). The OR for two or more sexual partners was more elevated among women of ages <25 years (OR, 2.41; 95% CI, 1.84-3.16) than among women of ages ≥25 years (OR, 1.70; 95% CI, 1.47-1.97), but the difference between the two ORs was not significant. The effect of multiple sexual partners was similar across age groups between 35-44 and ≥55 (data not shown).

Among 7,806 participants with a valid HSV-2 result, the proportion of HSV-2 seropositivity was 54% among HPV-positive women and 29% among those who were HPV negative. An increased risk of being HPV positive was observed among HSV-2-positive women (OR, 2.08; 95% CI, 1.77-2.45), but again, significant heterogeneity was found between study areas (Fig. 2B).

Information on husband's extramarital sexual relationships was available in all study areas except Mexico (Fig. 3A). Women who reported that their husbands had, or might have had, extramarital sexual relationships with women who were not sex workers showed a significantly increased OR (1.45; 95% CI, 1.24-1.70) of HPV positivity as compared with women who excluded this possibility. Similar results were found for extramarital sexual relationships with sex workers (OR, 1.54; 95% CI, 1.29-1.84; Fig. 3B). There was no evidence of heterogeneity between study areas in either case.

The sexual behaviors of study women and their husbands were positively correlated but each variable seemed to have an independent effect on HPV positivity (Fig. 4). Among women who had one lifetime sexual partner, those who reported that their husbands had had extramarital sexual relationships were more often HPV positive (OR, 1.35; 95% FCI, 1.20-1. 52) than those whose husbands were believed not to have had other sexual relationships with other women (OR, 1.00; 95% FCI, 0.84-1.19). The OR among women with three sexual partners or more and whose partners had had extramarital sexual relationships was 2.65 (95% FCI, 2.11-3.31). No departure from multiplicativity of the ORs was detected ($\chi_2^2 = 3.64$; $P = 0.16$).

In the analyses restricted to HPV-positive women, women who had multiple-type infection (Fig. 5A) and high-risk HPV type infection (Fig. 5B) reported a slightly higher number of sexual partners than women who had single-type and low-risk type infections, respectively. These differences did not, however, reach statistical significance.

Figure 6 represents ORs for HPV positivity by lifetime number of sexual partners separately for the five high-risk HPV types most frequently detected in the IARC HPV Prevalence Surveys and for HPV6 or 11. The OR for HPV16 for three sexual partners or more was 3.26 (95% FCI, 2.23-4.76) as compared
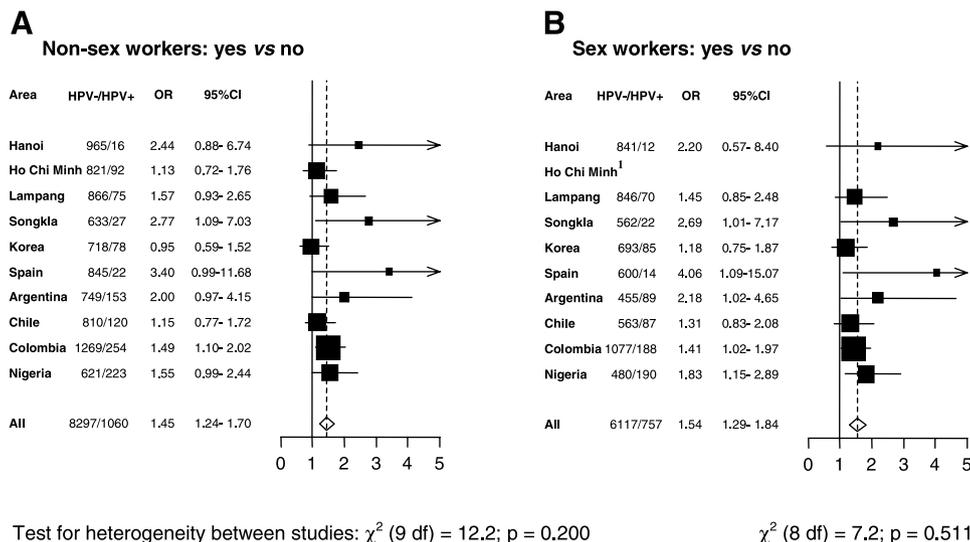
Figure 3. ORs and corresponding 95% CIs of HPV positivity by husbands' extramarital sexual relationships with different types of partners and study area. IARC HPV Prevalence Surveys. ORs were adjusted for age and, for the pooled estimates, for study area. [1], information not available.
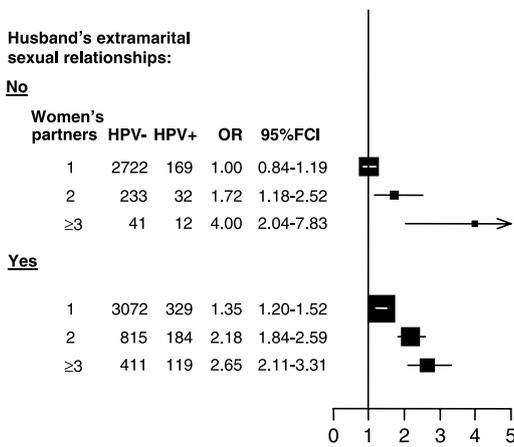
Test for departure from multiplicativity of the ORs: χ^2 (2 df) = 3.64; p = 0.162

Figure 4. ORs and corresponding 95% FCIs of HPV positivity by the combination of women's lifetime number of sexual partners and report of husbands' extramarital sexual relationships. IARC HPV Prevalence Surveys. ORS were adjusted for age and study area.

with one partner (OR, 1.00; 95% FCI, 0.78-1.27). The OR for HPV58 positivity for three partners or more compared with one was similar to the corresponding OR for HPV16 positivity. The findings on HPV18, 31, and 33 suggested no further increase in HPV positivity among women with three partners or more compared with two partners (Fig. 6). Women positive for HPV6 and 11 were combined on account of the relative rarity of the two types and the OR for three sexual partners or more compared with one was 2.62.

Condom use was not related to HPV positivity either before (OR for ever- versus never-use, 0.94, CI, 0.81-1.10; data not shown) or after adjustment for lifetime number of sexual partners (OR for ever- versus never-use, 0.94; 95% CI, 0.80-1.09; Fig. 7A). ORs did not vary significantly by study area and the only area where the association between condom use and HPV positivity was significantly different from the pooled OR was Songkla, Thailand, where a significant positive association (OR, 3.18; 95% CI, 1.12-9.04) was found. The ORs for HPV positivity were not different among women who had used condom for <70% (OR, 0.88; 95% FCI, 0.72-1.07) or ≥70% (OR, 1.33; 95% FCI, 0.91-1.95) of their sexually active life compared with those who never used condom (OR, 1.00; 95% FCI, 0.88-1.14).

Discussion

The IARC HPV Prevalence Surveys allowed a reevaluation of the association between HPV positivity and different indicators of sexual behavior in a broad spectrum of female populations from four continents. The large study size and the availability of high-quality information on many individual HPV types made it possible to assess the association with the number of sexual partners of the most common HPV types, including the four types (HPV6, 11, 16, and 18) included in the HPV vaccines currently under evaluation (30, 31).

Lifetime number of sexual partners was confirmed to be an important risk factor for HPV infection. Women tend to underreport their lifetime number of sexual partners (32) and this problem is probably more severe in traditional Asian societies (14, 15) than in Europe (21), Africa (20), or Latin America (16-19).

Between-area heterogeneity in the ORs for HPV positivity associated with multiple sexual partners was, however, also seen in the analyses of an objective marker of sexual behavior (HSV-2 serology). This suggests a real variation between populations in the effect of sexual behavior on HPV positivity [e.g., the relatively small importance of differences in sexual behavior of the women or their husbands in areas where HPV prevalence is very high (33) as in Colombia or Nigeria]. Areas where the OR for two sexual partners or more was lower than the pooled OR but the OR for HSV-2 positivity was not (e.g., Songkla, Thailand, and Korea) probably suffer from greater problems of inaccuracy in the report of sexual behavior than areas where ORs for number of sexual partners and HSV-2 positivity were consistent. In Hanoi, Vietnam, and Spain, the number of sexual partners seemed to be a better predictor of HPV positivity than HSV-2 probably on account of the rarity (<10%) of the HSV-2 infection in those populations.

There was a tendency for multiple-type and high-risk type infections to be more strongly related to the lifetime number of sexual partners than single-type or low-risk type infections, respectively, but neither difference attained statistical significance. The association with lifetime number of sexual partners was confirmed for all of the most commonly detected individual HPV types, especially in the comparison of women with two partners or more versus one only. The similarity of HPV16 and 58 is of interest as the two types use the same endocytosis pathway to enter the cells (34). Cervical infection with HPV6 and 11, the low-risk types responsible for genital warts (2), seemed to be as strongly associated with the number of lifetime sexual partners as HPV16. No further increase in the prevalence of HPV18, 31, and 33 was seen for three partners or more versus two, but this possible difference between
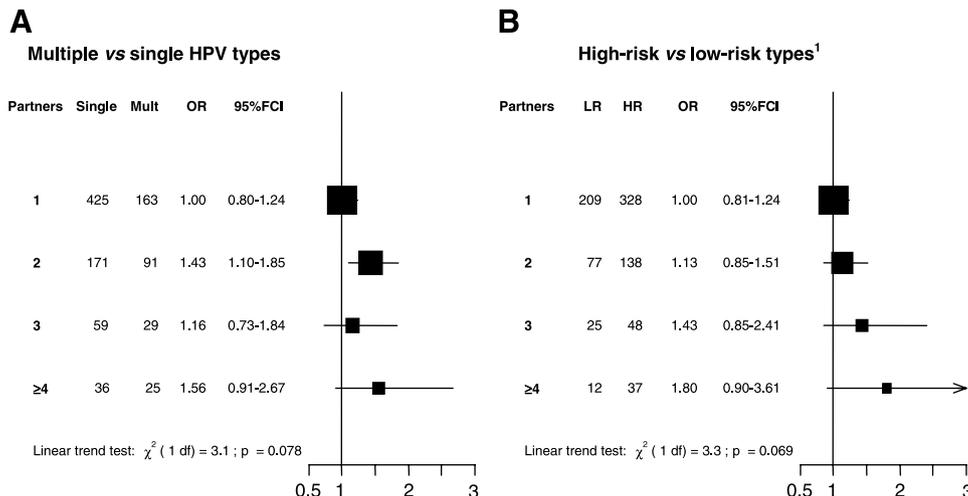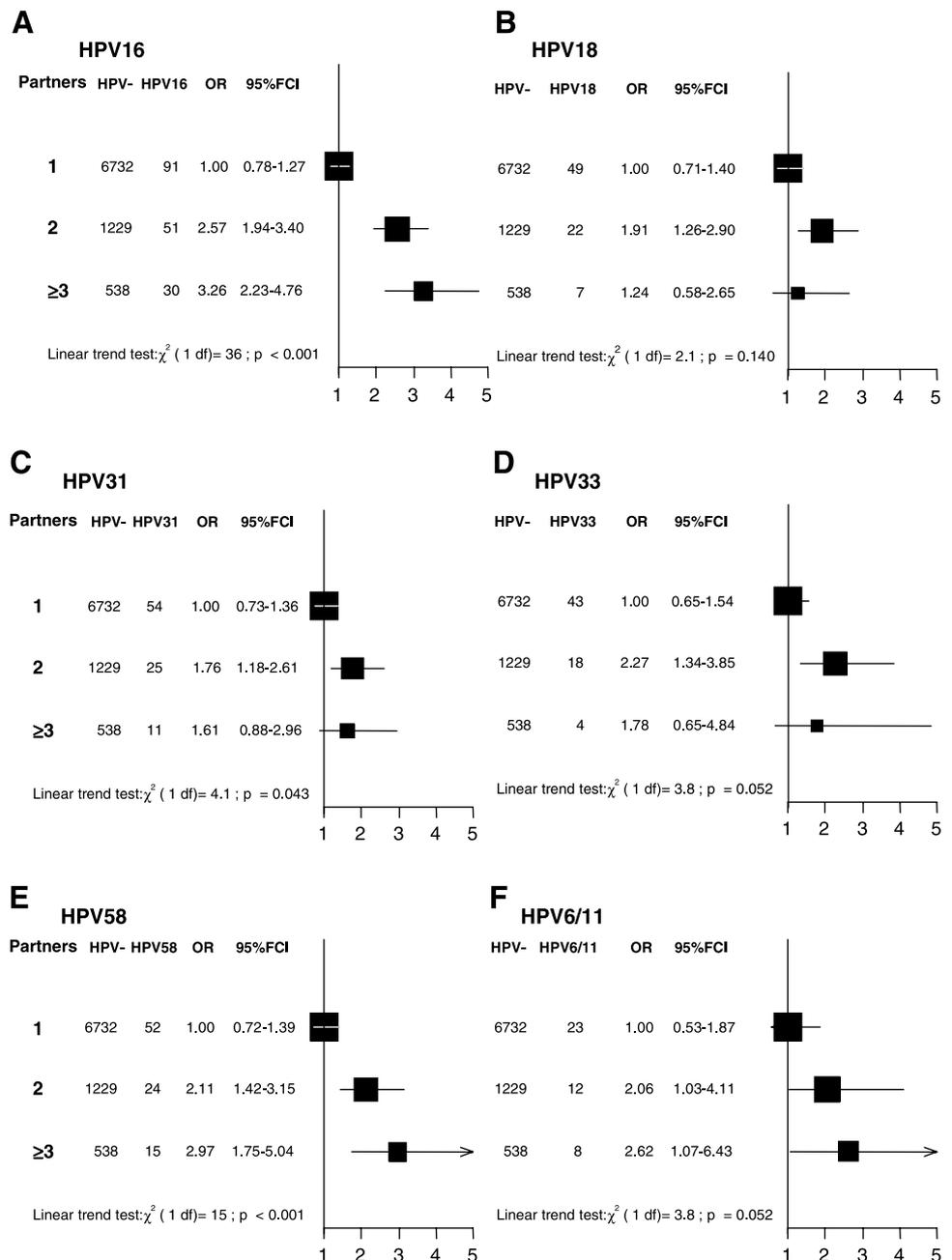

Figure 5. ORs and corresponding 95% FCIs of multiple- versus single-type (A) and high-risk versus low-risk type HPV infection (B) by lifetime number of sexual partners. 1,015 HPV-positive women. IARC HPV Prevalence Surveys. ORs were adjusted for age, study area and, in (B), for multiplicity of infection. [1], excluded were 181 women positive for both high- and low-risk types.

individual types should be confirmed in other studies. When we compared the alpha-9 species, which includes HPV16 (35), with the alpha-7 species, which includes HPV18 (35), we did not detect a difference in the ORs for number of sexual partners.
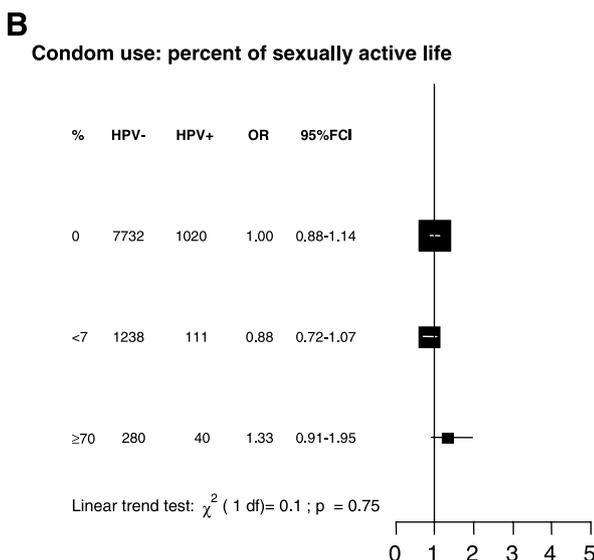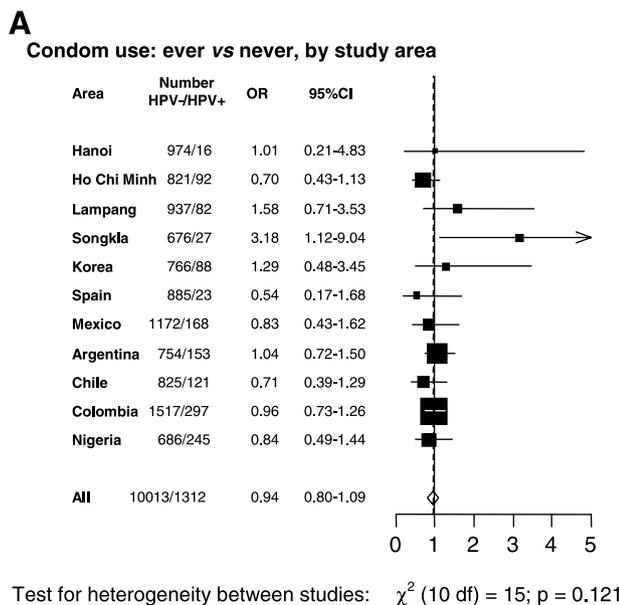
By and large, positivity for all HPV and the most common HPV types tended to at least double from one to two sexual partners, but to increase little, if at all, for three or four partners or more. HPV infection is relatively common in many populations and HPV prevalence, as in our present cross-sectional study, depends on both incidence and duration of the infection. The latter is likely to be influenced not only by viral but also by host factors (2). Therefore, it is not surprising that the relationship between the number of lifetime sexual partners and HPV positivity is not a linear one. Under-reporting of lifetime number of sexual partners, particularly among the most sexually active women, could contribute to the "plateau effect" that has also been observed for HPV positivity in other populations (36) and in the relationship between sexual partners and cervical cancer risk (37, 38).

Unfortunately, we did not have information on recent sexual partners, which are the strongest determinant of prevalent (6) and incident (7, 8) HPV infection. The only indirect support to the strong role of recent number of sexual partners on a woman's risk to be HPV positive came, in our study, from the tendency of the OR for two sexual partners or more to be more elevated in women below the age of 25 years, for whom some partners were probably recent ones, than among older women.

Studies on the association between age at sexual debut on HPV positivity have been relatively few (36, 39). We have been able to assess this issue over an especially broad range of age and found only a weak, nonsignificant excess of HPV positivity in women who started having intercourse before age 15 after adjustment for the number of sexual partners in addition to age and study area. The weakness of the association between age at sexual debut and HPV positivity contrast with the strength of the one between age at sexual debut and cervical cancer risk (40). The relationship between early sexual debut and cervical cancer risk is likely to be due to

Figure 6. ORs and corresponding 95% FCIs of the positivity for selected HPV types by lifetime number of sexual partners. IARC HPV Prevalence Surveys. ORs were adjusted for age and study area.

A

Condom use: ever *vs* never, by study area

Area	Number HPV-/HPV+	OR	95%CI
Hanoi	974/16	1.01	0.21-4.83
Ho Chi Minh	821/92	0.70	0.43-1.13
Lampang	937/82	1.58	0.71-3.53
Songkla	676/27	3.18	1.12-9.04
Korea	766/88	1.29	0.48-3.45
Spain	885/23	0.54	0.17-1.68
Mexico	1172/168	0.83	0.43-1.62
Argentina	754/153	1.04	0.72-1.50
Chile	825/121	0.71	0.39-1.29
Colombia	1517/297	0.96	0.73-1.26
Nigeria	686/245	0.84	0.49-1.44
All	10013/1312	0.94	0.80-1.09

Test for heterogeneity between studies: χ^2 (10 df) = 15; p = 0.121

B

Condom use: percent of sexually active life

%	HPV-	HPV+	OR	95%FCI
0	7732	1020	1.00	0.88-1.14
<7	1238	111	0.88	0.72-1.07
≥70	280	40	1.33	0.91-1.95

Linear trend test: χ^2 (1 df)= 0.1 ; p = 0.75

Figure 7. ORs and corresponding 95% CIs of HPV positivity by condom use. IARC HPV Prevalence Surveys. ORs were adjusted for age, lifetime number of sexual partners, and, when appropriate, for study area.

the duration of the infection among the infections that persist. Most HPV infections clear in a year or two (41); therefore, HPV point prevalence years later would not be expected to be substantially influenced by age at first sexual intercourse.

We confirmed the influence of husband's sexual behavior on HPV positivity among both women who had only one lifetime sexual partner and those who had two or more. Notably, only a minority of women in the IARC HPV Prevalence Surveys excluded the possibility that their husbands had extramarital sexual relationships. Husband's extramarital sexual relationships with sex workers were associated with a similar risk increase as compared with women who were not sex workers.

The protective effect of condom use against HPV infection in women (12) or men (42) is not well established and does not seem to be as strong as for other sexually transmitted infections (43). Our findings, which reflect associations with prevalent rather than newly acquired infections, showed substantial heterogeneity in the effect of condom use,

including some nonsignificant negative associations. In Thailand, the positive association observed between condom use and HPV positivity may be attributable to indication bias (i.e., condom being a proxy for relatively high-risk sexual behavior). An underestimate of the potential protective effect of condom is possible as very few women used it consistently throughout their life. We did not, however, observe a negative association with HPV positivity even among women who reported to have used condom for >70% of their sexually active life.

Appendix A

In addition to the aforementioned, collaborators of the IARC HPV Prevalence Surveys Study Group include, in alphabetical order by country: **Argentina** (L. Herrera, D. Loria, M.A. Prince); **Chile** (A. Luzoro, J.M. Ojeda, R. Prado); **Colombia** (H. Posso, M. Ronderos); **France** (A. Arslan, M. Plummer); **India** (R. Rajkumar); **Italy** (V. Ghisetti, A. Gillio-Tos, G. Ronco, N. Segnan); **Korea** (D-H. Lee); **Mexico** (M. Hernández); **Nigeria** (A. Omigbodun, K. Ojemakinde); **Spain** (F.X. Bosch, R. Font); **Thailand** (V. Kesararat, S. Kongchuchuy, S. Tunsakul); **the Netherlands** (M. Jacobs); **Vietnam** (N.T. Hieu).

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