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RESEARCH

Frequency and risk factors for prevalent, incident, and persistent genital carcinogenic human papillomavirus infection in sexually active women: community based cohort study


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Abstract

Objective To investigate frequency and risk factors for prevalent, incident, and persistent carcinogenic human papillomavirus (HPV) in young women before the introduction of immunisation against HPV types 16 and 18 for schoolgirls.

Design Cohort study

Setting 20 London universities and further education colleges.

Participants 2185 sexually active female students, mean age 21 years (range 16-27), 38% from ethnic minorities, who took part in the POPI (prevention of pelvic infection) chlamydia screening trial in 2004-08 and who provided duplicate, self taken vaginal swabs and completed questionnaires at baseline. At follow-up, a median of 16 months later, 821 women (38%) returned repeat vaginal swabs by post. In 2009-10, stored samples were tested for HPV.

Results Samples from 404/2185 (18.5% (95% CI 16.9% to 20.2%)) of the cohort were positive for carcinogenic HPV at baseline, including 15.0% (327) positive for non-vaccine carcinogenic genotypes. Reporting two or more sexual partners in the previous year and concurrent *Chlamydia trachomatis* or bacterial vaginosis were independent risk factors for prevalent vaginal HPV infection. Infection with one or more new HPV types was found in 17.7% (145/821) of follow-up samples, giving an estimated annual incidence of carcinogenic HPV infection of 12.9% (95% CI 11.0% to 15.0%). Incident infection was more common in women reporting two or more partners in the previous year, aged<20, of black ethnicity, or with *C trachomatis* vaginosis at baseline. Multiple partners was the only independent risk factor for incident infection (adjusted relative risk 1.99 (95% CI 1.46 to 2.72)). Of 143 women with baseline carcinogenic HPV infection, 20 (14% (8.3% to 19.7%) had infection with the same carcinogenic HPV type(s) detected after 12-28 months. Of these women, 13 (65%) had redetected infection with HPV 16 or 18, and nine (45%) with non-vaccine carcinogenic HPV genotypes.

Conclusion In the first UK cohort study of carcinogenic HPV in young women in the community, multiple sexual partners was an independent predictor of both prevalent and incident infection. Infection with non-vaccine carcinogenic genotypes was common. Although current HPV vaccines offer partial cross protection against some non-vaccine carcinogenic HPV types, immunised women will still need cervical screening.

Introduction

Each year around 500 000 women are diagnosed with invasive cervical cancer worldwide and 250 000 women die from it, mainly in developing countries.[1] Persistent infection with a carcinogenic human papillomavirus (HPV) is a prerequisite for cervical cancer,[2] and around 20% of women with one year persistence of HPV infection in the cervix will develop cervical intraepithelial neoplasia or cervical cancer in the next five years.[3] HPV genotypes 16 and 18 are responsible for around 70% of cervical cancers, with the remaining 30% caused by other

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Extra material supplied by the author. Table 1: participants' baseline characteristics by whether they provided follow-up samples. Table 2: Risk factors for persistent or redetected HPV infection of specific type (see http://www.bmj.com/content/344/bmj.e4168?tab=related#webextra)

carcinogenic HPV types. HPV16 is the most carcinogenic type in terms of numbers of cases of cervical intraepithelial neoplasia or cervical cancer.[4 5] Low risk genotypes 6 and 11 cause most cases of genital warts. Although HPV infections are the most common viral sexually transmitted infection, most infections are transient and asymptomatic, with about 70% of new infections resolving within a year.[2 6 7]

Immunisation against HPV types 16 and 18 protects against cervical intraepithelial neoplasia.[8 9] Since 2008, the UK-wide HPV immunisation programme has been vaccinating adolescent schoolgirls against carcinogenic HPV16 and HPV18, but there is a dearth of UK baseline data on HPV infection in women from non-healthcare settings, especially those in some ethnic minorities who may have a higher risk of cervical cancer but lower uptake of immunisation and cervical screening.[10 11] These data are essential to monitor the impact of the vaccination programme and to guide the ongoing introduction of HPV testing.

We used stored vaginal samples from women who took part in the POPI (prevention of pelvic infection) chlamydia screening trial,[12] which was before the introduction of the immunisation programme, to investigate the frequency and risk factors for prevalent, incident, and persistent carcinogenic HPV infection in young women in the community.

Methods

Study population

The design of the POPI trial has been described elsewhere.[12] Briefly, during 2004-06, 2529 female students were recruited from 20 London universities and further education colleges. Students were eligible to take part if they were aged ≤27 years, female, sexually experienced, not pregnant, and had not been tested for *Chlamydia trachomatis* infection in the previous three months. They were asked to complete a questionnaire and to provide two self-taken vaginal swabs.[13] One swab was used for the chlamydia screening trial. The other was rolled over a glass slide for bacterial vaginosis analysis, placed in Aptima transport medium (Gen Probe) and stored at –80°C. Twelve months after recruitment, 94% of participants were followed up by questionnaire or medical record search.[12] Those who agreed to repeat vaginal swabs were sent two swabs for return by post. One swab was tested for *C trachomatis* immediately and the result fed back to the participant, the other was stored. For the current study we analysed stored baseline samples (including a subset previously described[14]) and the follow-up samples, enabling repeat testing for HPV.

Laboratory testing for HPV

In 2009-10 the stored specimens from the baseline and follow-up vaginal swabs were tested for HPV by the Health Protection Agency. HPV testing was conducted anonymously; results were not fed back to participants. Samples were initially screened for HPV infection with the Digene Hybrid Capture 2 assay, which includes probes for high risk and low carcinogenic risk. The specimens that tested positive were subsequently genotyped using the Roche Linear Array HPV Genotyping assay.[14 15] This test can detect 37 HPV types (6, 11, 16, 18, 26, 31, 33, 35, 39, 40, 42, 45, 51, 52, 53, 54, 55, 56, 58, 59, 61, 62, 64, 66, 67, 68, 69, 70, 71, 72, 73 (MM9), 81, 82 (MM4), 83 (MM7), 84 (MM8), IS39, and CP6108) and includes a β-globin probe to check for sample integrity to reduce the risk of false negatives. Of 323 samples that tested positive with the Hybrid Capture 2 assay but negative with the Linear Array assay, β-globin was not detected in two baseline samples and these were excluded. In line with the 2009 classification by the International Agency Research on Cancer,[16] we defined 13 "probably carcinogenic" genotypes as high risk carcinogenic HPV types (16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68).

We defined incident HPV infection as a positive swab at follow-up in women who were negative for the same carcinogenic HPV genotype at baseline. Infection with the same carcinogenic HPV genotype in both baseline and follow-up samples was classified as persistence or redetection of HPV infection, recognising that some of these cases could have been due to clearance and subsequent re-infection with the same HPV genotype.[8]

Sample size

The sample size for the study was constrained by the 2529 women recruited to the POPI trial.[12] We assumed the prevalence of HPV16 was 5%.[4] Given that 28% of the cohort was of black ethnicity,[12] this sample size would allow detection of a difference in the prevalence of HPV16 of 7% in black women compared with 4% in the remainder with 80% power and 5% significance.

Statistical analysis

We investigated demographic and behavioural risk factors often associated with sexually transmitted infections: young age, black ethnicity, smoking, multiple sexual partners, sexual debut at age <16 years, and use of oral contraception or condoms.[6 13 17 18] As sexually transmitted infections often coexist, we also looked at concurrent *Chlamydia trachomatis*, *Mycoplasma genitalium*, *Neisseria gonorrhoeae*, or bacterial vaginosis.

We used data on the baseline samples for analysis of predictors of prevalent carcinogenic HPV infection and used data for women who returned follow-up samples to analyse predictors of incident infection and persistent or redetected infection. We examined the relation between possible risk factors and prevalent carcinogenic HPV infection at baseline, and incident or persistent or redetected HPV at follow-up, using binomial regression with a log link in Stata, version 10. Results are presented as relative risks. For prevalent and incident infections, multivariate analyses were conducted which included all variables found to be statistically significant in the univariate analyses, plus variables that were non-significant but have previously been shown to be related to HPV infection (age <20, age <16 at sexual debut, and smoking[6 17 18]). As the number of persistent or redetected infections was small, we performed only univariate analyses for the eight risk factors found to be associated with prevalent or incident infection.

We estimated the annual incidence of HPV infection by dividing the number of incident cases by the total person years of follow-up from date of recruitment to date of providing the repeat vaginal sample (range 11-32 months). We then expressed the rate per 100 person years as the percentage annual incidence. Calculation of the true incidence for new infections would have required information on the date of infection, which was not available. We calculated rates of persistence or redetection for each carcinogenic genotype for HPV positive women at baseline who returned repeat samples by dividing the number of women with the same HPV genotype at both baseline and follow-up by the number with that genotype at baseline.

Results

Follow-up

Of the 2529 women recruited to the trial, 2185 (86%) provided duplicate vaginal samples at baseline that were suitable for HPV

analysis (see figure⇓). Of these women, 821 (38%) returned repeat postal samples after 11-32 months (median 16 months). Compared with non-responders, the women who returned repeat samples were slightly older and less likely to be of black ethnicity, or to smoke, use condoms, or have bacterial vaginosis at baseline (see appendix table 1 on bmj.com).

Prevalence of carcinogenic HPV infection at baseline

Of the 2185 women, 404 (18.5% (95% CI 16.9% to 20.2%)) were positive for carcinogenic HPV at baseline (table 1⇓). HPV16 was the most common carcinogenic HPV infection (prevalence 5.4% (4.5% to 6.4%)). However, 327 women (15%) had infection with at least one non-vaccine carcinogenic HPV type and 144 (7%) had multiple carcinogenic HPV infections. Of the 51 women infected with HPV6 and nine women infected with HPV11, only two (3.3%) gave a history of genital warts.

Predictors of prevalent carcinogenic HPV infection

Carcinogenic HPV infection was more common among women of black ethnicity, those who smoked, those reporting two or more sexual partners in the previous 12 months, those who reported using condoms (no data available on frequency of use), and those with concurrent *C trachomatis*, *M genitalium*, *N gonorrhoeae*, or bacterial vaginosis (table 2⇓). Multivariate analysis showed that having multiple partners in the previous 12 months and co-infection with *C trachomatis* or concurrent bacterial vaginosis were independent predictors of carcinogenic HPV infection.

Incidence of carcinogenic HPV infection

Of the 821 women who provided follow-up samples, 145 (17.7% (15.1% to 20.4%)) were infected with one or more new HPV genotypes (table 1⇓ and figure⇓). Taking into account the timing of the follow-up sample (median 16 months after recruitment), the estimated annual incidence was 12.9% (11.0% to 15.0%) for any carcinogenic HPV infection and 9.8% (8.1% to 11.7%) for non-vaccine genotypes. Predictors of incident infection were age <20 years, black ethnicity, reporting two or more sexual partners in the previous 12 months, reported condom use, and *C trachomatis* infection at baseline (table 3⇓). Having two or more partners was the only independent predictor of incident carcinogenic HPV infection.

Persistence or redetection of carcinogenic HPV infection of specific type

Of the 821 women returning follow-up samples, 143 (17.4%) had one or more carcinogenic HPV infections at baseline, and 20/821 (2.4% (1.4% to 3.5%)) had infection with at least one of the same genotypes redetected after 12-28 months. Thus one in seven women (20/143, 14.0% (8.3% to 19.7%)) with baseline infection had either not cleared their infection or been reinfected with the same genotype (table 1⇓). Of these 20 women, 13 (65%) had persistent or redetected HPV16 or HPV18 infection and nine (45%) had a non-vaccine HPV type. Persistence or redetection of specific carcinogenic HPV types was not significantly associated with sexual behaviour, demography, smoking, or co-infection but the numbers were small (appendix table 2 on bmj.com).

Vaccine HPV types (HPV16 and HPV18)

Rates of prevalent, incident, and persistent or redetected infection with HPV16 or HPV18, or both, are shown in table 4⇓. Around one in five women with HPV16 or HPV18 at baseline had persistent or redetected infection after a median of 16 months follow-up. Infections with vaccine HPV types were more likely to persist or be redetected than infections with non-vaccine HPV types: 21% (13/63) versus 9% (9/104).

Discussion

Principal findings

In this community based cohort of multiethnic female students, the prevalence and annual incidence of carcinogenic HPV were 18% and 13%, and reporting multiple sexual partners in the previous 12 months was an independent predictor of both prevalent and incident infection. Among women who returned follow-up samples after a median of 16 months, 14% of those with baseline infection (that is, 2% overall) had persistent or redetected HPV infection with the same carcinogenic genotype. Nearly half of these women had persistent or redetected infection with non-vaccine HPV genotypes.

Strengths and weaknesses

This is the first UK cohort study of carcinogenic HPV infection in women recruited at educational institutions rather than from healthcare facilities. It provides useful baseline data on HPV infection in England before the introduction of HPV immunisation. It enabled some investigation of the association of carcinogenic HPV infection with concurrent *C trachomatis*, *M genitalium*, *N gonorrhoeae*, or bacterial vaginosis. More than a third of the women returning follow-up samples were teenagers, many from ethnic minorities. Although black ethnicity was associated with prevalent and incident carcinogenic HPV infection in univariate analysis, it was not a significant independent risk factor for infection. Finally the study provides new information on demographics, smoking, and sexual behaviour related to carcinogenic HPV infection in England.

The main weakness is the study was not population based. This limits generalisability of our findings. However, these data may be the best currently available from a community based cohort of young women in the UK. A recent Scottish population based survey requesting 5500 unscreened young women aged over 21 to take vaginal swabs and return them by post for HPV testing had a 13% response rate.[19]

We may have underestimated the annual incidence of carcinogenic HPV infection for three reasons. Only 38% of the cohort returned follow-up postal samples so data on incidence (and on redetection or persistence) are based on a self selected, probably lower risk group as they were older and less likely to smoke or to be from an ethnic minority. Secondly, we used length of follow-up as a proxy for time to infection, which will have overestimated the time at risk and underestimated the incidence. Thirdly, as median duration of HPV infection is around eight months,[6] we probably missed some women who acquired and cleared a new HPV infection in the median 16 month interval between testing at baseline and at follow-up swab. Also we cannot be sure that some cases of apparent HPV persistence were not clearance and reinfection with the same genotype.

The sample size was restricted to 2185 women who took part in the POPI trial and 821 who participated in follow-up, limiting the power to identify and adjust for risk factors. Small numbers of women with persistent or redetected infection meant that risk

factors for this could not be robustly evaluated. However, other cohort studies were of similar size.[4 6 17] Although self collected vaginal swabs are reliable for detection of HPV,[20] HPV types in the vagina may differ from those in the cervix. In the samples that screened positive for HPV infection but were negative in the HPV genotyping assay there were some indications of reduced sensitivity (notwithstanding the high rate of β-globin positivity indicating sample integrity), probably due to the long storage time.[14] Finally, findings may not be applicable to different populations such as those in developing countries or women attending genitourinary, family planning, or hospital clinics.

Comparison with other studies

The most common carcinogenic HPV genotypes we found were 16, 18, 51, 52, and 59, which is similar to findings from other UK studies[4 14 15 21] and multinational incidence studies in men.[22] As in reports from clinic based studies, risk factors for prevalent and incident carcinogenic HPV infection were similar to those for other sexually transmitted infections: multiple sexual partners,[6 17 18] young age,[6] ethnic minority background,[6] and co-infection.[17] The unexpected association of prevalent HPV with reported condom use may be because condoms are more likely to be used, but not consistently, by those at higher risk. Others have also found reported condom use was not protective against HPV infection,[18] although consistent condom use may be.[23]

However it is persistent carcinogenic HPV infection which explains virtually all cases of cervical cancer.[1] Ho and colleagues' finding that 28% (7/25) of women with HPV16 at baseline had persistent HPV16 infection for 24 months[6] is similar to our redetection rate of HPV16 of 24% (11/46); and, as in our study, persistent infection for six months was not associated with smoking, but numbers were small.[6] Another report from a selected population of women with equivocal or mildly abnormal cytology also suggested that six month persistence of HPV infection was not associated with smoking except possibly in women smoking more than 20 cigarettes daily.[24]

Implications of study

Many women diagnosed with carcinogenic HPV infection of the cervix are worried about the risk of developing cervical cancer. Although they can be reassured that most new infections clear spontaneously, we found that one in seven women with carcinogenic HPV infection at baseline had persistent or redetected infection for up to 28 months, nearly half of them with carcinogenic genotypes not covered by current HPV vaccines. In September 2012 the UK-wide HPV vaccination programme will be switching from the bivalent vaccine targeting HPV types 16 and 18 to the quadrivalent vaccine, which also targets HPV types 6 and 11.[25] Both vaccines provide some cross protection against cervical intraepithelial neoplasia associated with carcinogenic HPV types 31, 33, 45, 52, and 58,[9 26 27] though cross protection seems stronger with the bivalent vaccine.[9] However, since around 20-30% of cervical cancers in the UK and many persistent infections are due to non-vaccine genotypes, choice of vaccine may need to be re-evaluated when a second generation broad spectrum HPV vaccine including these additional five carcinogenic genotypes becomes available. Meanwhile, both vaccinated and unvaccinated women should be informed of the importance of continued cervical cytology and/or HPV testing.[1 26] New English guidelines recommend that cervical samples from women with borderline or mild dyskaryosis are analysed for carcinogenic HPV infection. Women who test positive will be referred for colposcopy. Those who are negative will be returned to routine recall. But policy makers need more evidence on which women are most at risk of carcinogenic HPV, which HPV genotypes should be included in assays used for cervical screening, and appropriate intervals between tests. Our findings may be used to inform modelling of the possible impact of HPV vaccination in the UK, including changes in the epidemiology of non-vaccine carcinogenic HPV types, and the development of cervical screening strategies.[28 5]

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Contributors: PO, AA, PEH, and FR designed the study. SB was responsible for the HPV testing, AA led the analysis with input from FR, RHJ, KS, and PO. PO wrote the first draft of the manuscript, and all authors contributed to and approved the final version.

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What is already known on this topic

Among women not immunised against HPV, around 20% of those with persistent carcinogenic HPV infection of the cervix for a year develop cervical intraepithelial neoplasia or cancer over the next five years

Immunisation against HPV types 16 and 18 can prevent cervical intraepithelial neoplasia due to these genotypes and gives partial protection against some other carcinogenic HPV genotypes

There are no UK data on risk factors for incident or persistent carcinogenic HPV in young women in the community

What this study adds

Women reporting multiple sexual partners in the previous year were at highest risk of incident carcinogenic HPV infection

Fourteen per cent of women with a baseline carcinogenic HPV infection had genital infection with the same carcinogenic HPV genotype redetected after 12-28 months, nearly half of them with genotypes not targeted by current HPV vaccines

Findings highlight the importance of continued cervical cytology and/or HPV testing for both vaccinated and unvaccinated women

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Tables

Table 1| Prevalence, incidence, and persistence or redetection of genital infection with carcinogenic HPV genotypes in 2185 female students, of whom 821 (38%) returned follow-up samples after a median of 16 months

	Prevalence (infected at baseline)		Incidence (new infection at follow-up)		Persistence or redetection (same HPV type at follow-up)*	
Carcinogenic HPV genotype	No (%) infected of 2185 women tested	% of 404 women infected with each genotype	No (%) of women tested†	% of 145 women infected with each genotype	No (%) of women with specific HPV type at baseline	% of 20 women infected with each genotype
Any	404 (18.5)	100	145/821 (17.7)	100	20/143 (14)‡	100
16	118 (5.4)	29.2	45/775 (5.8)	31.0	11/46 (24)	55
18	50 (2.3)	12.4	12/801 (1.5)	8.3	2/20 (10)	10
31	40 (1.8)	9.9	16/810 (2.0)	11.0	2/11 (18)	10
33	21 (1.0)	5.2	3/813 (0.4)	2.1	0/8	0
35	20 (0.9)	5.0	5/816 (0.6)	3.4	0/5	0
39	30 (1.4)	7.4	7/809 (0.9)	4.8	0/12	0
45	29 (1.3)	7.2	9/815 (1.1)	6.2	3/6 (50)	15
51	97 (4.4)	24.0	29/787 (3.7)	20.0	0/34	0
52	52 (2.4)	12.9	22/805 (2.7)	15.2	1/16 (6)	5
56	28 (1.3)	6.9	11/811 (1.4)	7.6	0/10	0
58	41 (1.9)	10.1	12/812 (1.5)	8.3	0/9	0
59	53 (2.4)	13.1	23/805 (2.9)	15.9	2/16 (13)	10
68	16 (0.7)	4.0	5/817 (0.6)	3.4	1/4 (25)	5
16,18, or both	159 (7.3)	39.4	50/758 (6.6)	34.5	13/63 (21)‡	65
≥2 genotypes	144 (6.6)	35.6	43/821 (5.2)	29.7	4/40 (10)‡	20
Non-vaccine genotypes§	327 (15.0)	80.9	110/821 (13.4)	75.9	9/104 (9)‡	45

Percentages for individual genotypes sum to >100% because women could be infected with >1 genotype.

*Detection of same carcinogenic HPV genotype in baseline and follow-up samples.

†Denominators exclude women with the same HPV genotype at baseline.

‡Infected with any of the same genotypes at follow-up.

§Defined as not HPV types 16 or 18.

Table 2| Risk factors for prevalent carcinogenic HPV infection (n=404) in 2185 women at baseline

Characteristic	No (%) of women with characteristic	No (%) of women with HPV infection by presence of characteristic		Relative risk (95% CI) of HPV infection	
		With characteristic	Without characteristic	Crude	Adjusted*
Age <20 years	939/2185 (43)	185/939 (19.7)	219/1246 (17.6)	1.12 (0.94 to 1.34)	0.97 (0.81 to1.17)
Black ethnicity	579/2172 (27)	127/579 (21.9)	273/1593 (17.1)	1.28 (1.06 to 1.54)	1.20 (0.98 to1.47)
Smoker	682/2175 (31)	149/682 (21.8)	254/1493 (17.0)	1.28 (1.07 to 1.54)	1.07 (0.88 to1.30)
≥2 sexual partners in previous year	932/2172 (43)	245/932 (26.3)	156/1240 (12.6)	2.09 (1.74 to 2.51)	1.87 (1.54 to 2.26)
Age <16 years at first sex	612/2148 (28)	117/612 (19.1)	281/1536 (18.3)	1.05 (0.86 to1.27)	0.97 (0.79 to1.18)
Use of oral contraception	1046/2163 (48)	197/1046 (18.8)	203/1117 (18.2)	1.04 (0.87 to 1.24)	-
Use of condoms†	1160/2164 (54)	239/1160 (20.6)	162/1004 (16.1)	1.28 (1.07 to1.53)	1.11 (0.93 to1.34)
Chlamydia trachomatis infection	126/2182 (5.8)	45/126 (35.7)	359/2056 (17.5)	2.05 (1.59 to 2.63)	1.57 (1.21 to 2.04)
Mycoplasma genitalium infection	71/2153 (3.3)	20/71 (28.2)	381/2082 (18.3)	1.54 (1.05 to 2.26)	1.07 (0.71 to1.63)
Bacterial vaginosis	515/2075 (25)	133/515 (25.8)	258/1560 (16.5)	1.56 (1.30 to1.88)	1.34 (1.11 to 1.63)
Neisseria gonorrhoeae infection	6/2160 (0.3)	3/6 (50)	398/2154 (18.5)	2.71 (1.21 to 6.01)	1.11 (0.46 to 2.66)

*Controlled for all significant variables from the unadjusted analysis and for age <20 and age <16 at first sex.

†No data on frequency of condom use.

Table 3| Risk factors for incident carcinogenic HPV infection (n=145) in 821 women who provided follow-up samples after a median of 16 months

Characteristic	No (%) of women with characteristic	No (%) of women with incident HPV infection by presence of characteristic		Relative risk (95% CI) of HPV infection	
		With characteristic	Without characteristic	Crude	Adjusted*
Age <20 years†	292/821 (36)	66/292 (22.6)	79/529 (14.9)	1.51 (1.13 to 2.03)	1.20 (0.89 to 1.63)
Black ethnicity	148/820 (18)	35/148 (23.6)	110/672 (16.4)	1.44 (1.03 to 2.02)	1.37 (0.96 to1.94)
Smoker†	216/819 (26)	43/216 (19.9)	102/603 (16.9)	1.18 (0.85 to1.62)	0.98 (0.70 to1.37)
≥2 sexual partners in previous year‡	297/819 (36)	79/297 (26.6)	66/522 (12.6)	2.10 (1.57 to 2.82)	1.99 (1.46 to 2.72)
Age <16 years at first sex	228/812 (28)	47/228 (20.6)	97/584 (16.6)	1.24 (0.91 to1.70)	1.20 (0.86 to1.65)
Use of oral contraception‡	448/819 (55)	82/448 (18.3)	62/371 (16.7)	1.10 (0.81 to1.48)	—
Use of condoms‡	439/800 (55)	93/439 (21.2)	49/361 (13.6)	1.56 (1.34 to 2.14)	1.25 (0.91 to1.72)
Chlamydia trachomatis infection	40/820 (4.9)	12/40 (30.0)	133/780 (17.1)	1.76 (1.07 to 2.90)	1.06 (0.60 to1.87)
Bacterial vaginosis	163/790 (21)	36/163 (22.1)	105/627 (16.7)	1.32 (0.94 to1.85)	—
Mycoplasma genitalium infection	23/807 (2.9)	6/23 (26.1)	138/784 (17.6)	1.49 (0.73 to 3.00)	—
Neisseria gonorrhoeae infection	2/808 (0.25)	0/2	143/806 (17.7)	—	—

*Controlled for all significant variables from the unadjusted analysis and for age <20 and age <16 at first sex.

†Reported at baseline.

‡Reported at follow-up. No data on frequency of condom use.

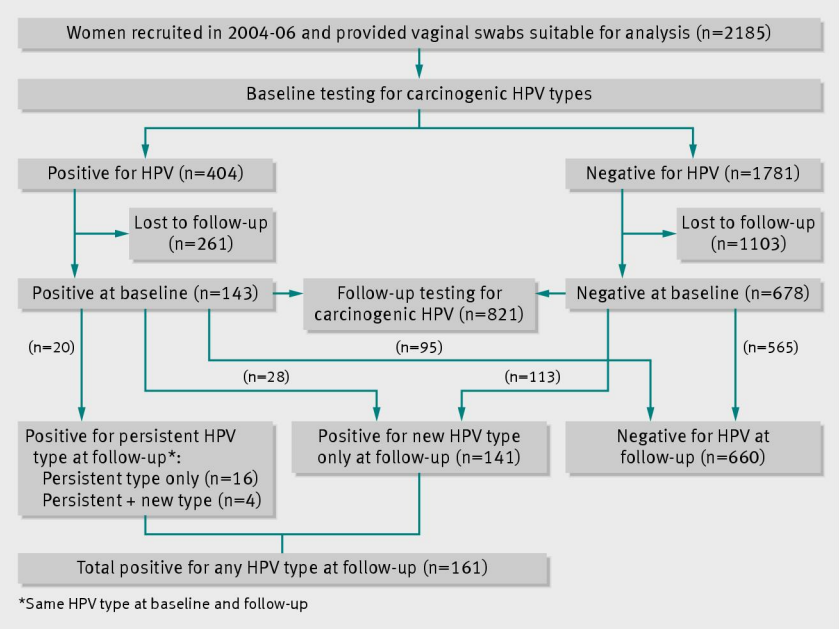
Table 4| **Prevalence, incidence, annual incidence, and persistence or redetection of infection with HPV types 16 or 18, or both, in 2185 female students, of whom 821 (38%) returned follow-up samples after a median of 16 months. Values are numbers and percentages (95% confidence intervals)**

				Persistence or redetection (same HPV type at follow-up)	
HPV genotype	Prevalence (infected at baseline)	Incidence (new infection at follow-up)*	Estimated annual incidence	In women with same HPV type at baseline†	In all women with follow-up samples*
16	118/2185	45/775	4.2% (3.1% to 5.6%)	11/46	11/821
	5.4% (4.5% to 6.4%)	5.8% (4.3% to 7.7%)		24% (12.6% to 38.8%)	1.3% (0.7% to 2.4%)
16, 18, or both	159/2185	50/758	5.3% (4.0% to 6.9%)	13/63	13/821
	7.3% (6.2% to 8.4%)	6.6% (4.9% to 8.6%)		21% (11.5% to 32.7%)	1.6% (0.8% to 2.7%)

*Follow-up 11–32 months (median 16 months) from recruitment.

†Follow-up 12–23 months (median 16 months) from recruitment for HPV16 alone and for HPV16, 18, or both.

Figure



Flow of participants through the study