

# Social differences in sexual behaviour and cervical cancer

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In this chapter we first describe the variation of cervical cancer in relation to social class. Thereafter we examine the causes for the occurrence of socioeconomic differences in invasive cervical cancer, using data from two case-control studies carried out in Colombia and Spain. Cervical cancer is the most common cancer in developing countries and the sixth most common in developed countries. In all areas, it is more frequent among women of low socioeconomic status, it is associated with multiple sexual partners and early age at first sexual intercourse, and both incidence and mortality are reduced by screening. According to population-based surveys in industrialized countries, men of low socioeconomic status report fewer sexual partners than men of high socioeconomic status but there is no clear indication that the same is true of women of low socioeconomic status. In the case-control studies in Spain and Colombia, the human papillomavirus and all other sexually transmitted diseases were more prevalent among women in low socioeconomic strata. Number of sexual partners and particularly contacts with prostitutes were higher among husbands of women of low socioeconomic status. Other potential risk factors for the disease, such as smoking and oral contraceptive use, and also cervical cancer screening (Pap smears), were more common in women of high social strata. Women with no schooling had a threefold higher risk in Spain and a fivefold higher risk in Colombia of having cervical cancer compared with women who had achieved a higher educational level. After adjustment for sexual behaviour, HPV DNA status, history of Pap smears and husband's contact with prostitutes, this association was considerably reduced. These results are indicative that socioeconomic differences in the incidence of cervical cancer can be partly explained by differences in the prevalence of HPV DNA. Men's sexual behaviour and particularly contacts with prostitutes might be a major contributor to the higher prevalence of HPV DNA among the poor.

Cervical cancer has been consistently associated with low socioeconomic status (Hakama *et al.*, 1982; Baquet *et al.*, 1991; Kogevinas, 1990; Tomatis, 1992). Differences in sexual and reproductive behaviour across socioeconomic groups have been advanced as explanations for the variation in the incidence rates of cervical cancer with socioeconomic status (Brown, 1984; Brinton, 1992). For many cancer sites, the involvement of multiple factors and/or a limited knowledge of the mechanisms of carcinogenesis are hampering the evaluation of the role of socioeconomic status in cancer etiology. Cervical cancer is one of the few exceptions. The identification of human papillomavirus (HPV) as a cause specific to the majority of cervical cancer cases permits a re-evaluation of previously established risk factors and provides new insights into the causes of the higher incidence of cervical cancer among the poor. The high worldwide incidence

of cervical cancer (it is the second most common cancer in women and the most common in countries of the developing world) and the significant geographical differences in incidence rates add further importance to understanding the link between cervical cancer and poverty.

In this chapter, we first review the most recent surveys on sexual behaviour that provide information on its relationship with social class. We then assess the association between characteristics commonly associated with cervical cancer, including HPV infection as a basis for explaining social class differences in cervical cancer. For this purpose we use data generated by two case-control studies carried out simultaneously in Colombia and Spain in which HPV DNA was detected by a method based on amplification by the polymerase chain reaction (PCR). These countries have contrasting wealth (gross national product per capita in 1986 was US\$ 1204

Table 1. Sexual partnership as reported in population-based studies

Author (country)	Sex and age	Indicator of partnership	Socioeconomic level		P value
			Low No. (%)	High No. (%)	
Leigh <i>et al.</i> , 1993 (USA)	Men & women: 42.8	≥5 sexual partners in last 5 years	234 (5.5)	731 (12.2)	0.016
Seidman <i>et al.</i> , 1992 (USA)	Women: 15–44	≥ 2 sexual partners 3 months before interview	1954 (6.5)	5057 (2.6)	0.000
Laumann <i>et al.</i> , 1994 (USA)	Men & women: 18–59	>10 sexual partners in adult lifetime	431 (14.6)	1776 (22.2)	0.0004
Johnson & Wadsworth, 1994 (UK)	Men:	≥2 sexual partners			
	35–44	1 year before interview	254 (6.8)	932 (10.1)	0.0003
	45–59		291 (2.8)	845 (7.3)	0.0049
	Women:	>1 sexual partner			
	35–44	1 year before interview	403 (4.4)	1190 (4.1)	0.89
	45–59		518 (2.4)	1033 (2.2)	0.91
Spira <i>et al.</i> , 1993 (France)	Men: 18–69	>1 sexual partner 1 year before interview	375 (7.4)	699 (15.9)	0.000
	Women: 18–69	>1 sexual partner 1 year before interview	359 (3.0)	565 (7.6)	0.004
Melbye & Beggar, 1992 (Denmark)	Men: 18–59	>1 partner 1 year before interview	483 (5.4)	796 (25.7)	0.0000

P value refers to the comparison between high and low socioeconomic status.

in Colombia and US\$ 7640 in Spain) and contrasting incidence rates of cervical cancer (the age-standardized incidence rate was 42.2 per 100 000 in Colombia and 7.7 per 100 000 in Spain) (Parkin *et al.*, 1992).

### Sexual behaviour and social class

There are now extensive surveys that illustrate variations in sexual behaviour across socioeconomic strata. The results of several studies referring to sexual partnership are summarized in Table 1 (Leigh *et al.*, 1993; Johnson & Wadsworth, 1994; Spira *et al.*, 1993; Seidman *et al.*, 1992; Melbye & Biggar, 1992). These are population-based studies, from industrialized countries, that characterized sexual behaviour of populations to allow better predictions for the control of the AIDS epidemic. We could not find similar data for developing countries.

Within 48 states of the United States of America, Leigh *et al.* (1993) interviewed 2058 randomly

selected men and women. Data were obtained using a self-administered questionnaire. In this study individuals with a high level of education (some college education) were almost three times more likely to have had more than five sexual partners the year preceding the interview than individuals who had not completed high school.

Data from the National Survey Growth conducted in 1988 in the United States were used to investigate the sexual behaviour of 7011 women (Seidman *et al.*, 1992). Having two or more recent sexual partners was associated with marital status, race, family income/poverty status, age at first sexual intercourse and religious affiliation. Women with a low family income were 2.5 times more likely to report two or more recent sexual partners than women with a higher income level. Among single Black women, formal education was inversely associated with having multiple recent partners.

Among divorced/separated White women, educational level was positively associated with having multiple partners. After controlling for the effects of age, education, residence in a metropolitan area, age at first sexual intercourse, religious affiliation and religiosity on the number of sexual partners, educational level (college education) remained an independent risk factor among divorced/separated White women of having multiple recent partners. This was not observed among Black women.

In another study in the United States, 3432 men and women were randomly selected from the national sampling frame and personally interviewed about sexual experiences (Laumann *et al.*, 1994). Men and women who had graduated from college (or reached a higher educational level) were more likely to report 11 or more sexual partners during their adult life (since age 18) than men and women who had only high school or some college education [the adjusted predicted probabilities were 24.4 versus 19.0 ( $P < 0.05$ ), respectively]. Men and women with less than a high-school educational level reported fewer sexual partners in their lifetimes as compared with those with high-school grades [adjusted predicted probabilities were 12.9 versus 19.0 ( $P < 0.05$ ), respectively]. These differences were statistically significant after controlling for the effect of age, gender, marital status, ethnic group, sexual activity in early life, religious guidance, a period in jail, and having been touched before puberty. In Table 1 crude percentages are provided for comparison with other studies.

Concurrently, two large studies on sexual behaviour were carried out in the United Kingdom (Johnson & Wadworth, 1994) and in France (Spira *et al.*, 1993). The studies aimed to provide information on sexual attitudes that could be related to transmission of HIV and other sexually transmitted infections. In the United Kingdom, marital status and age were strong predictors of sexual behaviour. Among married men and women, those in social classes I and II were more likely to report a greater number of sexual partners than those in social classes IV and V. In men, this observation was more evident among those over the age of 45. The trend with social class remained after controlling for age, marital status and age at first sexual intercourse. In France, men and women of all ages with higher education were more likely to have had more than one sexual partner in the last year than those with

a lower educational level. Multiple partnership increased with decreasing age, and was higher among single people and those living in Paris compared with those living in other geographical areas of the country.

Melbye & Beggar (1992) investigated 'at risk' sexual behaviour with relation to acquiring AIDS among 3178 subjects in Denmark using a self-administered questionnaire. Sexual promiscuity increased with educational level. Also, higher educational level was a risk factor for 'sexual risk exposures' (sexual contacts with homosexual/bisexual men, intravenous drug users, sub-Saharan residents or prostitutes).

Overall, in the United Kingdom, France, Denmark and probably the United States, men in high socioeconomic strata reported higher promiscuity than men in the low socioeconomic strata. Women appeared to have a much less consistent pattern across socioeconomic strata; for example, French women in high socioeconomic strata reported a higher number of sexual partners than those in low socioeconomic strata; in the United Kingdom no difference across strata was observed; and in the United States women in low socioeconomic strata reported a higher number of recent sexual partners.

#### **Case-control studies on invasive cervical cancer in Spain and Colombia**

Two case-control studies on invasive cervical cancer have been carried out in two countries with contrasting incidence rates of cervical cancer: a low rate in Spain and a high rate in Colombia. The study methods have been described in detail (Muñoz *et al.*, 1992). The field work was conducted in Spain from June 1985 to December 1987 and in Colombia from June 1985 to December 1988. The studies included all incident, histologically confirmed, invasive squamous cell carcinomas of the cervix identified among residents in the city of Cali, Colombia, in eight provinces of Spain (Alava, Gerona, Guipuzcoa, Murcia, Navarra, Salamanca, Seville and Vizcaya) and in the city of Zaragoza, Spain. Controls, one per case, were a five-year age-stratified random sample selected from the general population that generated the cases. Study subjects and their husbands were interviewed using a structured questionnaire that covered sociodemographic characteristics, reproduction, sexual behaviour, smoking habit, oral contraceptive use, practice of

Table 2. Odds ratios (ORs) of invasive cervical cancer and schooling attainment

	Spain				Colombia			
	Cases/controls	OR <sup>a</sup>	OR <sup>b</sup>	OR <sup>c</sup> (95% CI)	Cases/controls	OR <sup>a</sup>	OR <sup>b</sup>	OR <sup>c</sup> (95% CI)
<b>Education</b>								
Secondary and higher	11/23	1	1	1	13/26	1	1	1
Primary schooling	85/81	2.0	1.7	1.5 (0.5–4.5)	59/65	2.1	1.9	0.8 (0.3–2.3)
No schooling	46/26	3.3 <sup>e</sup>	2.8 <sup>e</sup>	2.9 (0.9–9.4)	15/7	5.3 <sup>e</sup>	5.7 <sup>e</sup>	2.8 (0.6–12.6)
<b>No. of women<sup>d</sup></b>	<b>142/130</b>				<b>87/98</b>			

<sup>a</sup>OR adjusted for age.

<sup>b</sup>OR adjusted for age, number of sexual partners, age at first sexual intercourse, history of Pap smears, area of recruitment (only in Spain) and husband's contacts with prostitute.

<sup>c</sup>OR adjusted in addition for HPV DNA.

<sup>d</sup>Only those with known HPV DNA status included.

<sup>e</sup>95% CI does not include 1.

Papanicolaou (Pap) smears and history of common sexually transmitted diseases. Among different indicators of socioeconomic status, women's schooling and educational attainment are used in this report as the socioeconomic indicator with which to evaluate behavioural differences. Household income level, parental and husband's educational attainment and household amenities were also explored. None of these showed a statistically significant association with cervical cancer risk after controlling for HPV status (de Sanjosé *et al.*, 1996).

HPV DNA sequences were sought in cytological specimens obtained by cervical scraping, and in males by scraping the distal urethra and the coronal sulcus of the glans. PCR amplification using HPV L1 consensus primers was carried out for 60% of the study subjects (Guerrero *et al.*, 1992). Antibodies to *Chlamydia trachomatis*, *Neisseria gonorrhoea*, *Treponema pallidum* or Herpes virus type 2 (HSV-2) were tested in 87% of the subjects (de Sanjosé *et al.*, 1994).

The prevalence of exposure to each cervical cancer risk factor was calculated for control women of different educational categories as percentages of women exposed. When appropriate, tests for linear trends across socioeconomic strata or the  $\chi^2$  test for heterogeneity were applied. Logistic regression techniques were used to estimate odds ratios (ORs) and 95% confidence intervals (95% CIs), adjusting for potential confounding factors (Breslow & Day, 1980).

A total of 760 women (373 cases and 387 controls) and 425 husbands were included, which represented 80% of the incident cases, 74% of the eligible controls and 55% of the eligible husbands.

### Results

Of control women, 22.7% in Spain and 6% in Colombia had not attended school. Cases in both countries were less educated than their age-stratified controls. Cervical cancer was strongly associated in Spain and in Colombia with no schooling (Table 2). After adjustment for sexual and reproductive behaviour and history of Pap smears, the association between women's education and cervical cancer was reduced. Adjustment for history of Pap smears reduced the OR for low education from 5.2 to 4.6 in Colombia and from 3.3 to 3.0 in Spain. The adjustment for HPV DNA presence reduced the OR for those with no schooling from 5.7 to 2.8 in Colombia and increased the OR from 2.8 to 2.9 in Spain.

The prevalence of exposure to established risk factors for cervical cancer among control women by educational level is summarized in Table 3 (Spain) and Table 4 (Colombia). In Spain, the prevalence of ever having had a Pap test, having more than one sexual partner, ever use of oral contraceptives and smoking habit increased with educational level. Husbands of women who did not attend school or reached only primary-school level reported use of prostitutes twice as often as husbands of women

**Table 3. Characteristics of Spanish control women and their husbands by women's education**

	No schooling	Primary schooling	Further schooling	P value for trend
<b>No. of women (mean age)</b>	<b>54 (59)</b>	<b>142 (53)</b>	<b>40 (42)</b>	
	%	%	%	
History of Pap smear	20.4	26.1	45.2	0.009
Sexual partners >1	3.7	6.3	22.5	0.002
First intercourse <18 years old	5.6	6.3	5.0	0.942
Ever use oral contraceptives	7.4	25.3	52.5	0.000
No. of children >4	25.9	21.8	10.0	0.150
Ever smoking	3.7	2.7	35.0	0.000
Antibodies to STDs <sup>a</sup>	25.9	19.7	16.7	0.250
HPV-DNA-positive <sup>b</sup>	7.6	3.8	4.0	0.450
<b>No. of husbands</b>	<b>26</b>	<b>89</b>	<b>24</b>	
	%	%	%	
Sexual partners >5	46.2	46.1	39.1	0.636
Use of prostitutes	61.5	64.0	29.2	0.025
HPV-DNA-positive <sup>c</sup>	0	5.3	0	0.941

STD, sexually transmitted disease.

<sup>a</sup>Antibodies to any of four STDs: *N. gonorrhoea*, *C. trachomatis*, *T. pallidum* and Herpes virus type II.

<sup>b</sup>Due to untested samples, denominators for the three columns are 26, 79 and 25, respectively.

<sup>c</sup>Due to untested samples, denominators for the three columns are 17, 27 and 18, respectively.

with higher education. Although women with a lower educational level had fewer sexual partners, they were 1.9 times more likely to harbour HPV DNA than women with a higher educational level. However, differences between strata were not statistically significant.

In Colombia, the percentages of ever having had a Pap test and ever use of oral contraceptives were higher among the more educated women. Women who did not attend school or reached only primary-school level were significantly more likely to have higher parity than better-educated women. Husbands of less-educated women reported a higher use of prostitute services than husbands of more highly educated women. Women with a low educational level had a prevalence of HPV DNA 4.4 times as high as women with a higher educational level, although differences did not reach statistical significance ( $P = 0.09$ ); their husbands were also more likely to harbour HPV DNA.

The characteristics associated with low educational attainment (no schooling or only primary schooling) in Colombia and Spain are shown in Figure 1. Results are presented as ORs where the risk

among women with a low educational level (no schooling or primary school) for each potential risk factor for cervical cancer is compared with that of women with a higher educational level (secondary schooling or higher). ORs are adjusted for age and history of Pap smears. However, the control for age and history of Pap smears did not modify the association between sexual behaviour, oral contraceptive use and smoking habit shown in Tables 3 and 4.

### Discussion

The association between HPV and cervical cancer offers us an etiological model similar to that of smoking habit and lung cancer. For both cancer sites, a major cause of the disease with an uneven social distribution has been identified. Prior to the advent of highly sensitive techniques to identify HPV, high number of sexual partners, early age at first sexual intercourse and low socioeconomic status were found to have independent effects in cervical cancer causation (Brinton, 1992). The results presented here add evidence that socioeconomic status in Spain and Colombia is associated

**Table 4. Characteristics of Colombian control women and their husbands by women's education**

	No schooling and primary schooling	Further schooling	<i>P</i> value for heterogeneity test
<b>No. of women (mean age)</b>	<b>110 (50)</b>	<b>39 (41)</b>	
	%	%	
History of Pap smear	63.6	92.3	0.001
First intercourse <18 years old	46.4	35.9	0.257
Sexual partners >1	43.6	35.9	0.400
Ever use oral contraceptives	28.2	58.9	0.001
No. of children >4	61.8	30.8	0.001
Ever smoking	32.7	25.6	0.410
Antibodies to STDs <sup>a</sup>	69.1	64.1	0.566
HPV-DNA-positive <sup>b</sup>	16.7	3.8	0.098
<b>No. of husbands</b>	<b>53</b>	<b>19</b>	
	%	%	
Sexual partners >5	95.8	88.9	0.29
Use of prostitutes	92.4	73.7	0.03
HPV-DNA-positive <sup>c</sup>	31.0	10.0	0.188

STD, sexually transmitted disease.

<sup>a</sup>Antibodies to any of four STDs: *N. gonorrhoea*, *C. trachomatis*, *T. pallidum* and Herpes virus type II.

<sup>b</sup>Due to untested samples, denominators for the two columns are 72 and 26, respectively.

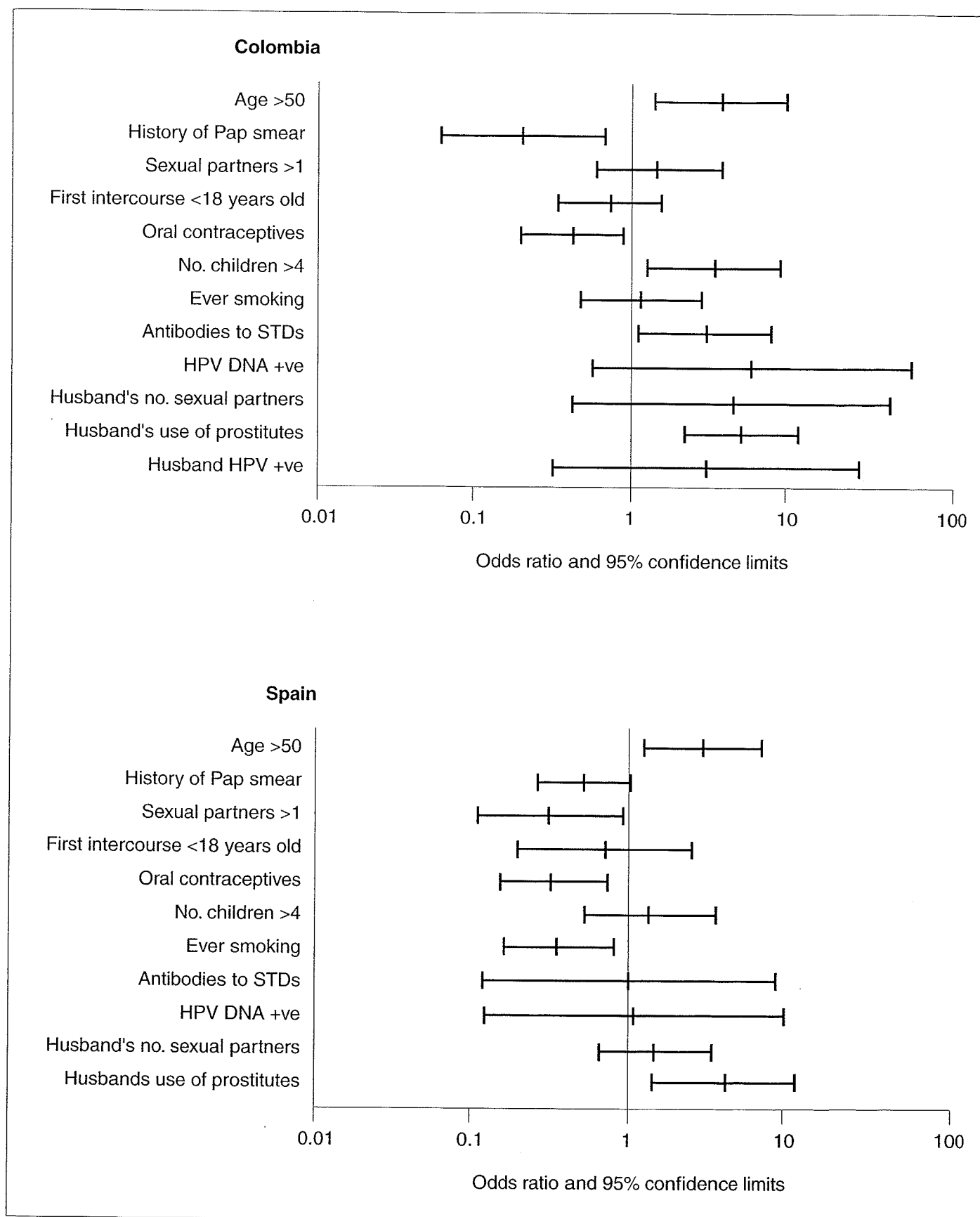
<sup>c</sup>Due to untested samples, denominators for the two columns are 29 and 10, respectively.

with aspects of sexual behaviour favouring the acquisition of HPV infections.

It is well accepted that the major etiological cause of cervical cancer is persistence of certain types of HPV infections (Muñoz *et al.*, 1992). In trying to explain socioeconomic differences in the disease rates, a higher HPV DNA prevalence, a higher number of sexual partners or an earlier age at first sexual intercourse were expected among the socially less privileged. In our data for both countries, HPV prevalence decreased with increasing education. In Spain, women with a lower educational level reported fewer sexual partners, but their partners were more likely to have used prostitute services. In Colombia, the prevalence of sexually related risk factors for cervical cancer was higher than in Spain, and higher for less-educated women; also husbands of less-educated women reported use of prostitute services more often. Taken together these results indicate that social differences in cervical cancer are at least partially due to differences in HPV prevalence and that sexual contacts

by the husband with prostitutes may be a more important source of HPV infection than the woman's lifetime number of sexual partners. This is in agreement with our previous observation of a higher rate of preneoplastic lesions among prostitutes relative to nonprostitutes (de Sanjosé *et al.*, 1993). Prostitutes may be an important reservoir of HPV infection.

In addition to HPV infection, no regular practice of Pap smears probably also contributes to the higher rates of cervical cancer among women in low socioeconomic strata. In both countries, women in the low socioeconomic strata had a lower record of ever having a Pap smear than better-educated women. In Colombia, history of Pap smears was high in all social strata and almost all women of a high educational level reported having had a Pap smear at least once. The higher rate of practice of Pap smears reported in Colombia, even among less-educated women (63.6%), compared with a much lower rate of screening practice in Spain (20.4% among less-educated women; 45.2%



**Figure 1.** Odds ratios and 95% confidence intervals for potential risk factors for cervical cancer in Colombia and Spain of women with low educational attainment, relative to risks among women of high educational attainment (secondary-school level and higher). ORs are adjusted for age and history of Pap smear.

among the best-educated women) is not surprising. In Spain, cervical cancer is perceived as a minor public health problem and Pap smears are usually taken as an opportunistic adjuvant to gynaecological care. Colombia has one of the highest incidence rates of cervical cancer in the world; in Cali, there is an organized cervical cancer screening programme and in 1984 about 30% of women reported having an annual screening (Aristizabal *et al.*, 1984).

Smoking and oral contraceptive use have been advanced as possible risk factors for cervical cancer. We had previously shown no association with smoking habit and cervical cancer but there was an association between ever use of oral contraceptives and cervical cancer among HPV-DNA-positive women (Bosch *et al.*, 1992). Better-educated women in both countries were more likely to have used oral contraceptives and in Spain also to be smokers. This inverse relationship of smoking and oral contraceptives with socioeconomic status may well be limited to the age cohort under study, particularly for smoking. In some societies, smoking has been accepted first by those in the higher social groups, but later these are the first to give up the habit in response to public health actions (Marmot *et al.*, 1987). Data available for one Spanish region show that the smoking habit among women is increasing and is higher among the better educated. Social differences in smoking are diminishing, however (Enquesta de Salut de Barcelona, 1994).

Probably the major potential source of classification error in these studies is under-detection of HPV infection. Even using a highly sensitive PCR technique to detect HPV DNA, we have reported that HPV DNA among cases was under-detected when using cervical scrapes rather than tissue samples (Bosch *et al.*, 1994). The exclusion of those subjects with unknown HPV status reduced considerably the association between cervical cancer and socioeconomic indicators, even though it implied an important reduction of the sample size.

Hildesheim *et al.* (1993) reported a negative correlation between years of education and HPV DNA prevalence among young Hispanic women. Our study assessed older women, so it is likely that their sexual and reproductive history and that of their partners reflect almost all their lifetime experiences. Although the women investigated were cytologically normal, those who are HPV-positive are likely to be HPV carriers rather than recently

infected, as is probably the case for other studies (Wheeler *et al.*, 1993; Bauer *et al.*, 1993; Hildesheim *et al.*, 1993).

In conclusion, socioeconomic differences in the incidence of invasive cervical cancer could partly be explained by differences in the prevalence of HPV DNA and in the use of preventive medical care. Male behaviour may contribute to the link between socioeconomic status and cervical cancer through higher use of prostitute services by men in lower socioeconomic strata.

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