Determinants of the Geographic Variation of Invasive Cervical Cancer in Costa Rica[1]

ROLANDO HERRERO,[2,3] LOUISE A. BRINTON,[3] PATRICIA HARTGE,[3] WILLIAM C. REEVES,[4] MARÍA M BREÑES,[5] RODRIGO URCUYO,[2] MARIO PACHECO,[6] FRANCISCO FUSTER,[7] & RAFAËLA SIERRA[8]

♦♦♦

The incidence of cervical cancer in Costa Rica is about twice as high in the coastal regions as in the interior. To study these regional variations, we used data from a 1986–1987 case-control study of 192 Costa Rican women with invasive cervical cancer and 372 controls.

Risk factors identified included the following: The study participant's (1) number of sexual partners, (2) age at first sexual intercourse, (3) number of live births, (4) presence of type 16/18 human papillomavirus (HPV) DNA, (5) venereal disease (VD) history, (6) Pap smear history, and (7) socioeconomic status. The adjusted relative risks (RR) and 95% confidence intervals (CI) for each of these risk factors were as follows: (1) ≥4 vs. 1 sexual partner: RR = 2.0, 95% CI = 1.1–3.5; (2) age of initiation ≤15 vs. ≥18 years: RR = 1.5, 95% CI = 0.9–2.5; (3) ≥6 vs. ≤1 live birth: RR = 1.7, 95% CI = 0.7–3.9; (4) HPV 16/18 DNA in cervix: RR = 2.8, 95% CI = 1.9–4.2; (5) VD history: RR = 2.2, 95% CI = 1.2–4.0; (6) no Pap smear: RR = 2.4, 95% CI = 1.5–3.8; and (7) low socioeconomic status: RR = 2.0, 95% CI = 1.2–3.2. The population-attributable risks related to HPV detection, four or more sexual partners, six or more live births, no prior Pap smear, and low socioeconomic status were 39%, 38%, 29%, 23%, and 22%, respectively.

Several of the sexual and reproductive risk factors were relatively more prevalent in the high-risk region, but Pap screening and detection of HPV were equally prevalent in the high-risk and low-risk regions. Though differences in screening quality (laboratory and follow-up) may have been involved, we conclude that the observed regional differences reflect behavioral more than screening differences. This suggests that screening programs should be more aggressive in the high-risk area, given the more frequent occurrence of the disease there. Failure to detect a higher prevalence of HPV in the high-risk region could reflect weaknesses in the in situ *hybridization test employed. Alternatively, cofactors may have to be present in order for HPV to exert its role in cervical carcinogenesis.*

Costa Rica is a small country that despite limited economic resources has a highly developed health system delivering care to a majority of its inhabitants. Health indicators show that conditions in

[1]This article was also published in Spanish in the *Boletín de la Oficina Sanitaria Panamericana*, vol. 114, no. 1, 1993. A working group that met in Panama in 1983 under the auspices of PAHO provided the initial impetus for this study. The actual study was supported in part by contract N01-CP-41026 and grant R01-CA-42042 from the National Cancer Institute, U.S. National Institutes of Health, and by a grant from the National Cancer Institutes of Canada. Reprint requests should be addressed to Dr. Rolando Herrero, Unidad Nacional de Cáncer, Apartado 1287-1250, San José, Costa Rica.

[2]Unidad Nacional de Cáncer, Hospital San Juan de Dios, Caja Costarricense de Seguro Social, San José, Costa Rica.

[3]Environmental Epidemiology Branch, National Cancer Institute, Bethesda, Maryland, USA.

[4]Viral Exanthems and Herpesvirus Branch, Centers for Disease Control, Atlanta, Georgia, USA.

[5]Gorgas Memorial Laboratory, Panama City, Panama.

[6]Hospital México, Caja Costarricense de Seguro Social, San José, Costa Rica.

[7]Hospital Calderón Guardia, Caja Costarricense de Seguro Social, San José, Costa Rica.

[8]Instituto de Investigaciones en Salud, Universidad de Costa Rica, San José, Costa Rica.

Costa Rica are among the best in Latin America, with the epidemiologic patterns of most of the common diseases generally resembling those found in developed countries (*1*).

Within this context, invasive cervical cancer constitutes a noteworthy exception. For although the incidence of invasive cervical cancer has declined markedly in the developed countries over the last 30 years (*2*), it has remained a leading cause of morbidity and mortality in most Latin American countries, including Costa Rica (*3*).

Inside Costa Rica, it has been observed that the incidence of invasive cervical cancer is higher in the country's three coastal provinces, which are relatively rural and less developed (*4*). Until now, it has been unclear whether or not this regional difference has reflected a greater prevalence of known risk factors (including early sexual activity, multiple sex partners, and high parity—*5*), inadequate screening, or the presence of specific infectious agents such as human papillomavirus (HPV).

As part of a multi-center investigation reported elsewhere (*6–8*), we conducted a case-control study in Costa Rica. This was directed at obtaining detailed information on various risk factors, including the prevalence of HPV cervical infections, and calculation of attributable risks (by exposure and region) in order to weigh the merits of possible explanations for the regional differences observed.

MATERIALS AND METHODS

Within this context (*9*), we determined who were the patients with histologically confirmed cases of incident invasive cervical cancer at the three major cancer referral hospitals in Costa Rica: San Juan de Dios, México, and Calderón Guardia. These hospitals are responsible for treating at least 80% of all invasive cervical cancers diagnosed in the country (*10*).

All women less than 70 years old who had lived in the country for at least six months were eligible for inclusion in the study. Initially, gynecologic oncologists diagnosed the patients and assessed the stage of their disease. Patients with positive diagnoses were then referred, before treatment, to study personnel. To ensure inclusion of all cases, study personnel regularly visited all wards likely to admit patients with this diagnosis and reviewed admission lists and pathology department reports several times a week.

One hospital control and one community control were selected for each case. Both controls were matched to the case by age, all three being within the same five-year age group. Hospital controls were selected randomly from hospital admission lists at nine regional hospitals where the cases would have been admitted for nonspecialized treatment. For this purpose periodic visits were made to these hospitals, during which lists of eligible patients were compiled. The study participants were then selected using tables of random numbers. No woman known to have had a hysterectomy or a diagnosed neoplastic, endocrine, nutritional, selected circulatory, smoking-related, or psychiatric disorder was eligible for selection as a hospital control. Community controls were randomly selected from census listings of a randomly chosen segment of the district where the corresponding case resided. As with the hospital controls, lists of eligible women were compiled and each control was selected from the appropriate list using a table of random numbers.

After informed consent was obtained, a personal interview lasting an average of one hour was conducted with each study participant in order to procure detailed information about the person's demographic, sexual, reproductive, med-

ical, contraceptive, and dietary history. The information collection process was carried out in a standardized manner under strict quality control, as has been described in another publication (*11*). A cervical scrape was obtained from the lesions of cases and from the cervical os of controls to test for the presence of specific types of human papillomavirus (HPV) by filter *in situ* hybridization, as described elsewhere (*6*). Each control was also given a Papanicolaou test in order to rule out the presence of cervical disease.

During the 18-month study period, 194 patients with eligible cases were identified and 192 (99%) were interviewed. Also, 388 controls were selected and 384 (99%) were interviewed. The reasons for no response in six instances were death (one case), refusal (one control), loss to follow-up (two controls), and mental incompetence (one case and one control).

Because the community controls and hospital controls showed a similar distribution of risk factors (*11*), they were combined into one pooled control group. However, virgins were eliminated from the analysis for the purpose of calculating relative risks, so as to permit simultaneous adjustment for the effects of the number of sexual partners and of age at first intercourse. Estimated relative risks were derived from unconditional logistic regression that included terms for all confounding and matching factors. Tests for trend were performed by categorizing the exposure variable and treating the scored variable as continuous. A Mantel-Haentzel chi-square was performed to test for statistical significance of the regional differences in age-adjusted risk factor prevalences. Population-attributable risks (*12*) were calculated for various risk factors, both overall and within high-risk and low-risk regions, using the pooled estimates of relative risks. The method employed assumes that risk estimates are unbiased and that the case series is representative of the cases in the whole population under 70 years old. The population-attributable proportion is calculated as the product of the attributable proportion among the exposed ([RR-1]/RR) and the fraction of cases exposed.

RESULTS

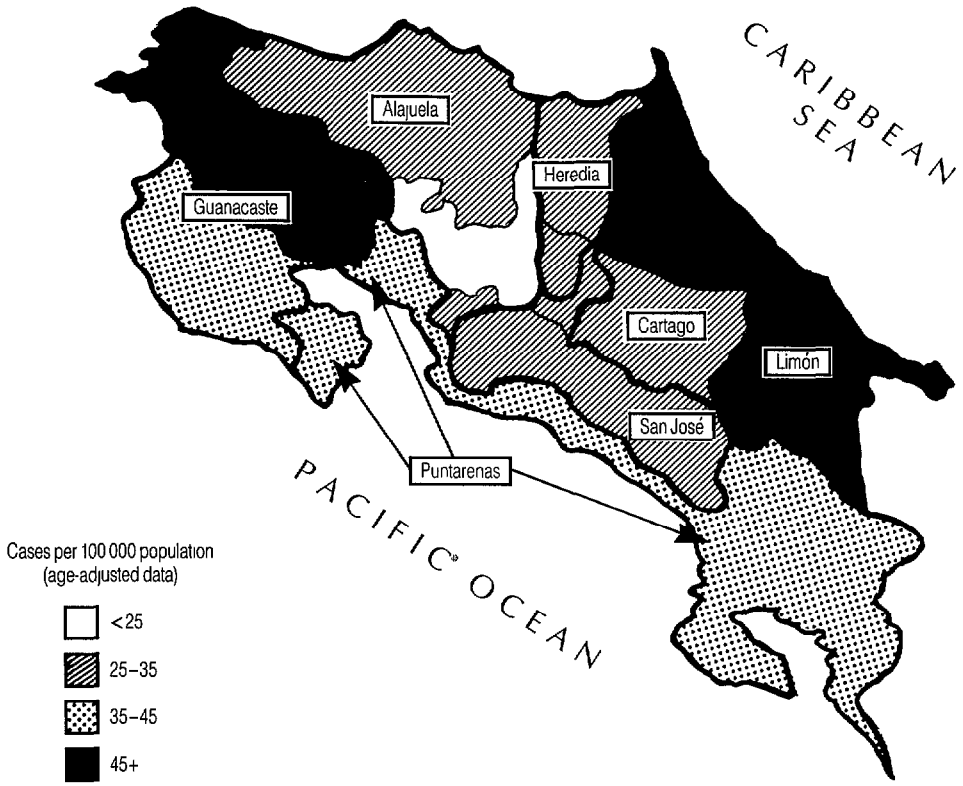
Figure 1 shows the geographic location of the high-risk and low-risk areas in Costa Rica according to incidence figures derived from National Tumor Registry data for the period 1979–1983 (*4*). Preliminary National Tumor Registry data for the 1985–1989 period indicate a similar regional pattern (Sierra, personal communication). For purposes of the analyses presented here, it was considered that the high-risk area consisted of the provinces with an incidence of 35 cases or more per 100 000 women (the provinces of Guanacaste, Puntarenas, and Limón, all located in the coastal regions), while the low-risk area consisted of the inland provinces with lower incidence rates (the provinces of San José, Heredia, Alajuela, and Cartago). The place of residence of each study subject was taken to be that subject's current residence.

Table 1 shows some demographic characteristics of cases and controls in the two regions. Cases tended to be slightly younger at diagnosis in the high-risk area, the mean age of cases in the high-risk area being 44.5 years, as compared to 45.9 years in the low-risk area. Also, both cases and controls were less likely to be white, to be Catholic, or to be relatively well-educated in the high-risk than in the low-risk area. Cases were diagnosed at similar stages of the disease in both areas (data not shown).

Relative Risks

The patterns of relative risk found in Costa Rica (Table 2) were similar to those

Figure 1. Invasive cervical cancer incidence in Costa Rica by region, 1979–1983, age-standardized per 100 000 population (based on a map published in Sierra et al.—4).



found in the aforementioned multi-center study, with the exception of dietary practices (*13*) and the male factor (*14*), which were predictors of risk when the analysis took in the combined multi-center population but not when it was restricted to Costa Rica.

As Table 2 indicates, the informant's number of lifetime sexual partners was significantly associated with increasing risk, those women reporting four or more partners experiencing an average risk twice as great as that experienced by monogamous women. The level of risk also tended to increase with decreasing age at first coitus, and although this relationship was confounded by the other sexual variables, an adjusted RR of 1.5 persisted for women initiating sexual activity at or before age 15 as compared to those becoming active at age 18 or older. The informant's number of live births was also associated with increasing risk, those women reporting six or more live births having an adjusted RR of 1.7 compared to those with zero to one.

Sixty-one percent of the cases tested for HPV 16/18 yielded positive results, as compared to 37% of the controls. Detection of HPV 16/18 was associated with a 2.8-fold excess risk (95% CI = 1.9–4.2), but HPV detection was not found to be related to sexual behavior. A reported history of one or more venereal diseases (including syphilis, gonorrhea, genital herpes, warts, and crab lice) was associated with an RR of 2.2 (95% CI = 1.2–4.0), even after adjustment for HPV and

Table 1. Demographic characteristics of cases and controls residing in the low-risk and high-risk areas.

Characteristic	Low-risk area[a]		High-risk area[b]	
	Cases (%) (n = 126)[c]	Controls (%) (n = 278)[c]	Cases (%) (n = 64)[c]	Controls (%) (n = 104)[c]
Age group (years):				
<30	9	10	6	10
30–39	23	24	39	41
40–49	28	27	19	15
50–59	26	23	17	15
≥60	14	16	19	19
Race:				
White	97	95	78	67
Indian or mestizo	1	4	17	23
Black or mulatto	2	1	4	8
Other	0	0	1	2
Religion:				
Catholic	85	77	62	66
Other	13	19	35	28
None	2	4	3	6
Years of education:				
≥9 years	11	21	9	6
3–8 years	64	68	50	58
<3 years	25	11	41	36

[a]The provinces of San José, Heredia, Alajuela, and Cartago.
[b]The provinces of Guanacaste, Puntarenas, and Limón.
[c]Cases and controls with unknown residence excluded.

the sexual variables. Previous use of oral contraceptives for at least six months was associated with a nonsignificant adjusted relative risk of 1.2; no trend was observed for increasing duration of usage, but few women were long-term users.

Unadjusted estimates for cigarette smoking showed increasing risk with increased intensity of smoking, but this association disappeared for heavy smokers after adjustment for other risk factors.

Women who reported never having had a Pap smear were at an adjusted RR of 2.4 compared to those who had received one, regardless of the interval since the last smear.

The socioeconomic estimator most strongly related to risk in this population was the number of certain household utilities—these being a radio, a TV set, a stove, a refrigerator, electricity, and a toilet inside the house. Lower numbers of utilities were associated with an increasing risk that persisted after adjustment for the other factors (p for trend = 0.013). Limited education was significantly associated with risk, but the effect of this variable disappeared after adjustment for the other risk factors, mainly the number of household utilities (data not shown).

Relative risk estimates for the numerous risk factors were generally similar in the high-risk and low-risk regions, except that oral contraceptive use and previous venereal disease had somewhat stronger effects in the low-risk regions. (The p-values of the test for regional difference

Table 2. Relative risks of invasive cervical cancer associated with specific risk factors in Costa Rica.

Risk factor	Cases	Controls[a]	RR[b]	RR[c]	95% CI
Number of sexual partners:					
1	73	215	1.0	1.0	
2–3	77	107	2.1	1.7	(1.1–2.7)
≥4	42	50	2.5	2.0	(1.1–3.5)
p for trend			<0.0001	0.012	
Age at first sexual intercourse:					
≥18	73	204	1.0	1.0	
16–17	55	91	1.7	1.2	(0.7–2.0)
≤15	64	77	2.4	1.5	(0.9–2.5)
p for trend			<0.0001	0.16	
Number of live births:					
0–1	10	37	1.0	1.0	
2–3	36	97	1.4	1.1	(0.4–2.6)
4–5	42	84	2.0	1.3	(0.6–3.1)
≥6	104	154	3.0	1.7	(0.7–3.9)
p for trend			0.0002	0.09	
Detection of HPV 16/18 DNA:					
Negative	71	218	1.0	1.0	
Positive	111	128	2.7	2.8	(1.9–4.2)
Unknown	10	26			
History of any venereal disease:					
Negative	161	342	1.0	1.0	
Positive	31	30	2.2	2.2	(1.2–4.0)
Ever used oral contraceptives for ≥6 months:					
No	132	255	1.0	1.0	
Yes	60	117	1.0	1.2	(0.8–2.0)
Number of cigarettes smoked per day:					
0	134	283	1.0	1.0	
<20	40	63	1.3	1.4	(0.9–2.3)
≥20	18	26	1.5	1.0	(0.5–2.2)
p for trend			0.12	0.42	
Ever had a Papanicolaou smear:					
Yes	107	285	1.0	1.0	
No	73	84	2.6	2.4	(1.5–3.8)
Unknown	12	3			
Number of utilities in the home:[d]					
6	65	186	1.0	1.0	
4–5	52	113	1.3	1.1	(0.7–1.8)
≥3	75	73	2.9	2.0	(1.2–3.2)
p for trend			<0.0001	0.013	

[a]Virgins excluded from the analysis.
[b]Adjusted for age.
[c]Adjusted for age and all other risk factors shown.
[d]Includes stove, refrigerator, TV set, radio, electricity, and toilet inside the home.

in these estimates were 0.25 and 0.39.) Therefore, we used the overall estimate of relative risk from all regions to compute population-attributable proportions associated with the different risk factors.

Exposure Patterns

Figure 2 shows the age-adjusted prevalences of the controls' exposure to the different risk factors, according to whether they lived in the high-risk or low-risk region. The major difference between the two regions was in socioeconomic status, measured by the number of household utilities. Seventy-one percent of the control women residing in the high-risk area lacked one or more of the six listed utilities, as compared to 41% of those in the low-risk area ($p < 0.0001$).

In general, control women residing in the high-risk area reported earlier first sexual intercourse, more partners, and more live births than did their counterparts in the low-risk area. Surprisingly, a slightly higher percentage of control women in the low-risk area were positive for HPV 16/18. Venereal diseases and oral contraceptive use were more common in the high-risk area. The likelihood that a control subject had ever smoked was fairly similar in the two areas (17% in the high-risk area vs. 21% in the low-risk area). In the high-risk area, 27% of the controls said they had never had a Pap smear, as compared to 22% in the low-risk area ($p = 0.48$).

Population-attributable Proportions

Table 3 shows the estimated proportions of disease cases that would not have occurred if all women had been in the lowest risk category for that factor. The

Figure 2. Prevalences of invasive cervical cancer risk factors among controls, adjusted for age, in Costa Rica's high-risk and low-risk regions.

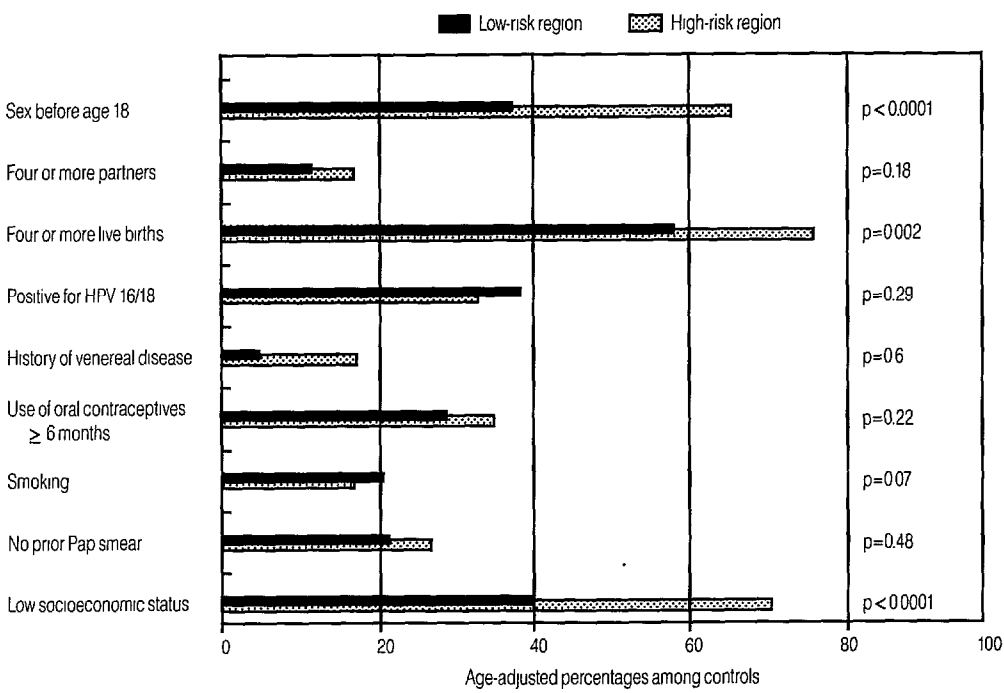


Table 3. Proportions (percentages) of invasive cervical cancer cases attributable to specific risk factors, by region. The proportions shown are the products of the attributable proportion among the exposed ([RR-1]/RR) and the fraction of cases exposed.

Risk factor	Region		Whole country
	High-risk	Low-risk	
Number of sexual partners:			
2–3	21	14	16
≥4	22	22	22
Age at first intercourse:			
16–17	14	11	12
≤15	7	5	6
Number of live births:			
2–3	2	2	2
4–5	5	5	5
≥6	25	20	22
Detection of HPV 16/18 DNA:			
Yes	39	38	39
History of venereal disease:			
Yes	7	10	9
Use (ever) of oral contraceptives for ≥6 months:			
Yes	6	5	5
Cigarette smoking (ever):			
Yes	6	6	6
Ever had a Papanicolaou smear:			
No	24	23	23
Number of household utilities:			
4–5	2	4	3
≤3	32	13	19

single factor found to contribute the highest apparent proportion of cases was the presence of HPV 16/18 (39% overall). This proportion hardly differed in the high-risk and low-risk regions. Among the other factors contributing substantially to cervical cancer in the country as a whole were multiple sex partners, early age at first intercourse, multiple live births, and low socioeconomic status. These particular factors also contributed more to the total disease burden in the high-risk area than to that in the low-risk area, explaining much of the regional risk variation.

Of course, many women at increased risk because of high parity were also at risk because of multiple sexual partners or early age at first intercourse. Although the adjusted relative risks indicate that each of these factors independently influences risk, the attributable proportions necessarily overlap. For example, it appears that some of the cases could have been avoided by changing either parity or age at first intercourse. However, very

few women in this study reported late first intercourse, only one partner, and low parity, so it was not possible to estimate the relative risk or attributable proportion in relation to a single low-risk baseline group. Nor do these behavior characteristics have a "natural" unexposed level, in the manner of cigarette smoking and oral contraceptive use.

Lack of screening accounted for approximately 23% of the overall disease burden but did not account for the regional risk difference. Smoking, oral contraceptive use, and venereal diseases made lesser contributions to the overall disease burden in both regions.

DISCUSSION AND CONCLUSIONS

The risk factors identified for Costa Rica, as reported here, were similar to those indicated by the combined data from the other centers (Mexico City, Bogotá, Colombia, and Panama) participating in the larger multi-center study (*9*). Multiple sexual partners, early sexual activity, and high parity were identified as important risk predictors, as were a history of venereal disease, detection of HPV 16/18 in the cervix, nonparticipation in screening programs, and low socioeconomic status. While HPV detection was associated with increased risk, it did not explain the increased risk associated with sexual and reproductive factors. This could reflect the low sensitivity and specificity of the hybridization assay used (*15*). It seems likely that a more valid determination of HPV's presence would explain more of the relationship between sexual and reproductive behaviors and cervical cancer risk (*16*).

HPV 16/18 as detected by filter *in situ* hybridization accounted for a higher proportion of cervical cancer cases than any of the other risk factors identified, and we believe that this proportion would be even higher with a more accurate viral test. Alternatively, other unidentified sexual factors may play an important role in the etiology of invasive cervical cancer. Furthermore, for public health purposes the large proportions attributable to sexual and reproductive behaviors remain critical even if the biologic explanation of their effect shifts with improved tests for detecting HPV infection.

Regarding the study participants' screening history, we found that risk did not increase with the time elapsed since the last cytologic examination, but that a twofold excess risk existed for women who said they had never had a Pap smear. This observation underlines the importance of the first Pap smear and the need to direct programs at testing as many women as possible at least once.

As previously noted, the incidence of cervical cancer in Costa Rica varies by region, with lower incidences generally occurring in the inland areas and the capital city. Overall, women in the high-risk area were less likely to be white, Catholic, and educated than women in the low-risk area. We also found that the population in the high-risk area had a higher prevalence of the sexual and reproductive risk factors for cervical cancer than the population in the low-risk area, and that much of the regional risk variation was accounted for by differences in these factors.

More specifically, women in the high-risk region tended to have had more sexual partners and live births and to have started sexual activity earlier. Among other things, this earlier sexual activity could explain the slightly younger age at which cervical cancer cases tended to be diagnosed in the high-risk area. Also, a recent study of socioeconomic differences in cervical cancer risk factors that was conducted in England found that women with low socioeconomic status were relatively likely to start sexual activity earlier, suggesting that this latter factor contributes

to important risk differences arising from social class (*17*).

Hardly any regional difference was detected in the prevalence of HPV 16/18. This agrees with recent findings in other populations indicating that the prevalence of HPV in the normal female population does not correlate with cervical cancer incidence (*18, 19*). However, as discussed earlier, this could be related to erroneous classification arising from sensitivity and specificity problems, or it could be that cofactors need to be present in order for HPV to exert its role in cervical carcinogenesis.

In an earlier study (*20*), Pap smear screening histories accounted for some of the regional differences. However, information on other risk factors was lacking. In the present study, screening histories appeared to differ surprisingly little between women in high-risk and low-risk areas, while the socioeconomic and behavioral risk factors were substantially more prevalent in the high-risk area.

One might hypothesize that the quality of follow-up or treatment could be inadequate in the high-risk area, allowing precursor lesions to progress for longer periods. However, we found that the distribution of cases by stage of disease was similar in the high-risk and low-risk regions, arguing against screening as an explanation for the regional differences. In sum, while regional differences in the quality of the screening process are possible or even probable, it appears that the main factors producing marked regional risk variation in Costa Rica are differences in sexual and reproductive behavior combined with socioeconomic differences.

REFERENCES

1. Mata L, Rosero L. *National health and social development in Costa Rica: a case study of intersectoral action.* Washington, DC: Pan American Health Organization; 1988.
2. Devesa SS. Descriptive epidemiology of cancer of the uterine cervix. *Cancer.* 1989; 64:2184–2190.
3. Restrepo HE, González J, Roberts E, Litvak J. Epidemiología y control del cáncer del cuello uterino en América Latina y el Caribe. *Bol Of Sanit Panam.* 1987;102: 578–593.
4. Sierra R, Maxwell Parkin D, Muñoz Leiva G. Cancer in Costa Rica. *Cancer Res.* 1989; 49:717–724.
5. Brinton LA, Fraumeni J. Epidemiology of uterine cervical cancer. *J Chron Dis.* 1986; 39:1051–1065.
6. Reeves WC, Brinton LA, García M, et al. Human papillomavirus infection and cervical cancer in Latin America. *N Engl J Med.* 1989;320:1437–1441.
7. Brinton LA, Reeves WC, Breñes MM, et al. Parity as a risk factor for cervical cancer. *Am J Epidemiol.* 1989;130:486–496.
8. Herrero R, Brinton LA, Reeves WC, et al. Invasive cervical cancer and smoking in Latin America. *J Natl Cancer Inst.* 1989; 81:205–211.
9. Herrero R, Brinton LA, Reeves WC, et al. Risk factors for invasive carcinoma of the uterine cervix in Latin America. *Bull Pan Am Health Organ.* 1990;24(3):263–283.
10. Sierra R, Barrantes R, Múñoz G, Parkin DM, Bieber CA, Múñoz N. *Cancer in Costa Rica.* Lyon: International Agency for Research on Cancer; 1988. (IARC technical report 1).
11. Brinton LA, Herrero R, Breñes MM, et al. Considerations for conducting epidemiologic case-control studies of cancer in developing countries. *Bull Pan Am Health Organ.* 1991;25:1–26.
12. Bruzzi P, Green SB, Byar DP, Brinton LA, Schairer C. Estimating the population attributable risk for multiple risk factors using case-control data. *Am J Epidemiol.* 1985;122:904–914.
13. Herrero R, Potischman N, Brinton LA. A case-control study of nutrient status and invasive cervical cancer: I. dietary indicators. *Am J Epidemiol.* 1991;134:1335–1346.
14. Brinton LA, Reeves WC, Brenes MM. The male factor in the etiology of cervical cancer among sexually monogamous women. *Int J Cancer.* 1989;44:199–203.
15. Brandsma J, Burk RD, Lancaster WD, Pfister H, Schiffman MH. Inter-laboratory variation as an explanation for varying prevalence estimates of human

papillomavirus infection. *Int J Cancer.* 1989;43:260–262.

16. Ley C, Bauer HM, Reingold A, Schiffman MH, Chambers JC, Tashiro CJ, Manos MM. Determinants of genital human papillomavirus infection in young women. *J Natl Cancer Inst.* 1991;83:997–1003.
17. Mant D, Vessey M, Loudon N. Social class differences in sexual behaviour and cervical cancer. *Community Med.* 1988;10: 52–56.
18. Kjaer SK, De Villiers EM, Haugaard BJ, et al. Human papillomavirus, herpes simplex virus and cervical cancer incidence in Greenland and Denmark: a population-based cross-sectional study. *Int J Cancer.* 1988;41:518–524.
19. Villa LL, Franco EL. Epidemiologic correlates of cervical neoplasia and risk of human papillomavirus infection in asymptomatic women in Brazil. *J Natl Cancer Inst.* 1989;81:332–340.
20. Sierra R, Barrantes R. Epidemiología del cáncer de cuello uterino en Costa Rica, 1980–1983. *Bol Of Sanit Panam.* 1988;105:345–351.

♦♦♦

International Leprosy Congress

The number of leprosy patients has fallen dramatically in recent years, and in 1991 the World Health Organization (WHO) resolved to eliminate leprosy as a public health problem by the year 2000. The 14th International Leprosy Congress, which will meet in Orlando, Florida (USA), from 29 August through 4 September 1993, will explore the technical, social, and economic challenges that must be met to achieve that goal and will formulate plans of action.

Presentations at the Congress will cover all aspects of leprosy and its control, including experimental and laboratory science, clinical science, program planning and management, training, education, and the psychosocial sciences. Each day a "state-of-the-art" lecture will be presented on a key Congress issue. Special emphasis will be given to poster presentations in order to maximize discussion of the participants' research and work. Teaching and training sessions will also be held daily. Summaries of pre-Congress workshops attended by invited experts will be available to all delegates at the close of the meeting.

The Congress is cosponsored by the International Leprosy Association (ILA), the International Federation of Anti-Leprosy Associations (ILEP), and WHO. For more information, contact Secretary for Administration, ILA Congress, c/o ALM International, 1 ALM Way, Greenville, South Carolina 29601, USA; telephone (803) 271-7040; fax (803) 271-7062.