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INTERNATIONAL TRENDS IN INCIDENCE OF CERVICAL CANCER: II. SQUAMOUS-CELL CARCINOMA

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Time trends in the incidence of squamous-cell carcinomas of the cervix during the period 1973–1991 were examined using data provided by 60 population-based cancer registries from 32 defined populations in 25 countries. Three components of the incidence trend were studied: age, calendar period of diagnosis and birth cohort. Cumulative incidence rates per 1,000 person-years for 2 groups, age ranges 25–49 and 50–74 years, were calculated from the model that best described the incidence data. A significant decline in incidence was noted in the American populations (except for US Hispanic), Australia, the non-Maori women of New Zealand, northern and western Europe (except Italy and Spain, where the rates remain stable) and Asian populations (except Malay women of Singapore, who have stable rates). These trends were of similar magnitude for the whole age range studied (25–74 years). An increasing trend, mainly restricted to younger women, was found for Slovakia, Jewish women born in Israel and the United Kingdom. In Slovenia, the increasing trend was observed for all age groups. The predominant pattern shown by cancer registries in developed countries is of a reduction in the incidence of squamous cervical cancer. This could be, at least partially, attributed to the widespread practice of screening for cervical lesions. The major exception to the pattern is observed in the United Kingdom, though the increasing incidence in young women has changed to a decrease in recent years. There are only a few series covering a long period of time in developing countries, but there is little evidence for a major impact of screening. *Int. J. Cancer* 86:429–435, 2000.

Cancer of the uterine cervix is the 3rd most common cancer in women, accounting for 9.8% of all new cancer cases worldwide. The geographical distribution is uneven; in developing countries, it ranks 2nd, with a relative frequency of 15% of all cancers in women, whereas it is 5th in developed countries, with a relative frequency of 4.4% (Parkin *et al.,* 1999). A marked reduction in the incidence of this tumor has been documented over the past 2 decades in some countries in Europe and North America, which has been largely attributed to widespread screening and early treatment of pre-invasive lesions (Devesa *et al.,* 1989; Eide, 1987; Nieminen *et al.,* 1995). Similar decreases have not been reported in other developed countries (Coleman *et al.,* 1993; Beral *et al.,* 1994).

Squamous-cell carcinoma is the predominant histological type among all cervical cancers and the principal component of the trend. Previously, we reported an increasing secular trend in cervical adenocarcinomas among women under 50 years of age in some countries (Vizcaino *et al.,* 1998). In this report, we present a detailed analysis of the time trends in incidence of squamous-cell carcinoma of the cervix for a wide range of countries in the period between 1962 and 1991.

MATERIAL AND METHODS

Details of data collection have been described elsewhere (Vizcaino *et al.,* 1998). In brief, data were collected from 60 cancer registries for which incidence data of comparable quality were available for a minimum of 15 years within the period 1962–1991. Each participating registry coded cervical cancers by histological type according to the 4 digits of the International Classification of Diseases for Oncology (ICD-O) (Percy *et al.,* 1990). For analysis, cases were grouped as follows: squamous-cell carcinoma (ICD-O codes 8050–8082), adenocarcinoma (ICD-O codes 8140–8550, 8560, 8570), other (ICD-O codes 8800–8932, 8990, 8991, 9040–9044, 9120–9134, 9540–9581) and unspecified (ICD-O codes 8000–8004, 8010–8034, 9990).

Cases were stratified by 5-year intervals and 5-year age groups, between the ages of 25 and 74 years. Age-specific rates were calculated using mid-period population denominators for each age group, and summary age-adjusted incidence rates were estimated using direct standardization with the world standard population. Time trends were explored using Poisson regression models with age, period and cohort terms fitted in sequence as described in Clayton and Schifflers (1987). Comparison of models with the likelihood ratio statistic allowed ranking the relative contribution of the cohort and period effects. For those countries in which the fit of the age-period-cohort model was poor, models with random effects based on the negative binomial distribution were considered to account for the over-dispersion of the data (Breslow, 1984). Each term was smoothed with polynomials in a stepwise procedure to minimize the effects of existing extreme values. The effects of age, period and cohort expressed with polynomials enabled separation of the linear trend, called net drift, which estimates the sum of the cohort and period effects, from higher-order terms that describe the curvature or deviation from linearity of each effect (Holford, 1983; Clayton and Schifflers, 1987; Coleman *et al.,* 1993; Estève, 1990).

For simplicity in summarizing the results, we have calculated the annual percentage change over the interval from the coefficient of the linear component for the cohort and period effect (net drift), adjusted for age, and the cumulative rate per 1,000 for the age ranges 25–49 years and 50–74 years. The latter may be interpreted as the probability that a woman develops a squamous-cell cervical cancer in these age intervals. Age-specific incidence rates for age groups not observed but needed for these calculations were derived from the expected values of the best-fitting polynomial smoothed model (Estève *et al.,* 1994).

Separate models were fitted for each cancer registry. However, for some countries, the data from several cancer registries were pooled, provided that they presented patterns similar to those from individual registries, to provide larger numbers for analysis. Cancer cases were combined for the registries of the SEER program in the United States (10 registries in Connecticut, Iowa, New Mexico, Utah, Hawaii, Alameda County, San Francisco–Oakland, metropolitan Detroit, metropolitan Atlanta and Seattle), Canada (12

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registries in Alberta, Newfoundland, Northwest Territories, Yukon, Nova Scotia, Prince Edward Island, Saskatchewan, Manitoba, British Columbia, New Brunswick, Quebec and Ontario), Australia (2 registries in South Australia and New South Wales), England (5 registries in Oxford, Mersey, northwestern region, southwestern region and Thames), Scotland (5 registries in east, north, northeast, southeast and west), Switzerland (2 registries in Geneva and Basel), Spain (3 registries in Navarra, Zaragoza and Tarragona), France (4 registries in Bas-Rhin, Doubs, Calvados and Isere) and Italy (2 registries in Varese and Ragusa). When needed, these combined analyses were stratified by registry.

RESULTS

A total of 175,110 cases of cervical cancer were assembled from 60 registries belonging to 32 populations defined by either nationality or ethnic group. Overall, 75.9% of cases were squamous-cell carcinomas. Table I shows, for each population, the number of cases and the age-standardized incidence rates (ASRs) of squamous-cell carcinomas. These populations were grouped by somewhat arbitrary geographical and socio-political considerations. Great variability in incidence is observed for this histological type, with an 8-fold difference between Colombia (ASR = 23.6) and Finland (ASR = 2.7). Within the United States, the rate among Hispanic women is almost 3 times that for white women. A similar range of incidence rates is observed between Denmark and Finland and between the non-Maori and Maori populations of New Zealand. The proportion of cases diagnosed as "other carcinomas" or of non-specified histology was 12.7% overall and ranged from 0.6% in Sweden to 20.7% for the non-Maori population of New Zealand.

Table II shows the results of fitting Poisson models to the data. For 7 populations, no trend was observed and the age effect was enough to explain the variability of the data (US Hispanic, New Zealand Maori, Jews born in Europe or America, Singapore Malay, Poland, Italy and Spain). For half of the populations studied, the best-fitting model contained only age and cohort effects. Only for the black populations of the United States was the age-period model adequate. For the remaining registries, age, period and cohort effects were statistically significant, and among these, a poor fit was obtained in 2 populations in Canada and Japan.

Table III shows the secular trends of squamous-cell carcinoma expressed as the average yearly percent change over the interval,

TABLE I – OBSERVATION PERIOD, NUMBER OF CASES AND ASR FOR SQUAMOUS-CELL CARCINOMAS (SQCC) BY COUNTRY

Country/population	Period	SQCC N (%)	ASR world (95% CI)	Other/NOS N (%)	Total[1] N (100%)
Americas					
United States, SEER (10 registries)					
White	1973–1991	14,926 (74.6)	5.5 (5.3–5.4)	1,974 (9.9)	19,993
Black	1973–1991	3,504 (79.6)	9.8 (9.1–10.5)	460 (10.5)	4,404
Hispanic	1978–1987	1,267 (85.0)	15.4 (14.1–16.6)	57 (3.8)	1,491
Canada (12 registries)	1969–1991	18,706 (73.1)	8.6 (8.3–8.9)	3,555 (13.9)	25,592
Puerto Rico	1973–1991	3,645 (82.9)	7.8 (7.3–8.4)	306 (6.9)	4,395
Colombia, Cali	1973–1991	2,563 (72.8)	23.6 (21.8–25.4)	712 (20.2)	3,520
Oceania					
Australia (2 registries)	1973–1991	6,109 (78.3)	7.1 (6.8–7.5)	532 (6.8)	7,806
New Zealand	1978–1991				
Maori		301 (69.8)	20.8 (16.9–24.7)	93 (21.5)	431
Non-Maori		1,983 (68.3)	7.1 (6.6–7.7)	600 (20.7)	2,902
United Kingdom					
England (5 registries)	1972–1991	15,444 (68.9)	8.5 (8.3–8.8)	4,184 (18.6)	22,426
Scotland (5 registries)	1977–1991	4,684 (72.1)	9.5 (9.0–9.9)	1,063 (16.3)	6,500
North Europe					
Denmark	1978–1990	5,949 (78.4)	12.7 (12.1–13.3)	625 (8.2)	7,590
Finland	1968–1991	3,884 (75.7)	2.7 (2.4–2.9)	513 (9.9)	5,134
Sweden	1973–1991	9,063 (85.7)	6.3 (6.0–6.6)	69 (0.6)	10,576
Central Europe					
Estonia	1968–1987	2,774 (79.5)	11.9 (10.9–12.8)	511 (14.6)	3,489
Slovakia	1971–1990	6,924 (78.1)	13.8 (13.2–14.4)	1,263 (14.3)	8,863
Slovenia	1971–1990	1,745 (75.7)	9.0 (8.2–9.7)	314 (13.6)	2,304
Poland, Cracow City	1978–1990	984 (77.4)	16.3 (14.5–18.1)	215 (17.0)	1,271
Western Europe					
Netherlands, Eindhoven	1973–1991	361 (77.0)	4.5 (3.7–5.3)	36 (7.7)	469
Germany, Saarland	1972–1990	2,275 (81.0)	9.0 (8.0–9.8)	327 (11.6)	2,807
Switzerland (2 registries)	1973–1991	653 (82.9)	4.6 (3.9–5.4)	24 (3.0)	788
France (4 registries)	1978–1991	2,443 (81.1)	7.6 (6.8–8.4)	263 (8.7)	3,014
Italy (2 registries)	1976–1987	551 (70.7)	6.1 (5.1–7.0)	121 (15.5)	779
Spain (3 registries)	1978–1991	662 (70.4)	4.8 (3.9–5.7)	148 (12.7)	941
Asia					
Israel, Jews	1962–1991	1,686 (78.9)	3.9 (3.5–4.3)	210 (9.8)	2,136
Jews born in Asia or Africa		647 (83.3)	4.6 (3.7–5.4)	67 (8.6)	777
Jews born in Europe or America		760 (76.4)	2.8 (2.2–3.5)	101 (10.1)	995
Jews born in Israel		270 (76.5)	4.2 (3.3–5.2)	41 (1.6)	353
Unknown origin		9 (0.8)		1 (0.09)	11
Non-Jews[2]		118 (77.1)		24 (15.7)	153
India (Bombay)	1973–1991	6,667 (75.2)	13.4 (12.8–14.0)	1,785 (20.1)	8,865
Japan (Osaka)	1973–1991	10,553 (78.7)	8.1 (7.7–8.4)	2,010 (15.0)	13,407
Singapore	1973–1991				
Chinese		2,232 (82.5)	14.1 (13.0–15.2)	202 (7.5)	2,704
Indian		124 (81.0)	9.5 (5.2–13.6)	12 (7.8)	153
Malay		148 (71.5)	7.5 (5.3–9.7)	14 (6.8)	207
Total		132,928 (75.9)		22,222 (12.7)	175,110

[1] Number of cases of cervical cancer (all histologies) registered in the interval.–[2]Population not available.

TABLE II – RESULTS OF FITTING POISSON MODELS TO THE ASR OF CERVICAL SQUAMOUS-CELL CARCINOMA BY COUNTRY

Country	Best model[1]	Deviance[2]	df[3]	*p* value
Americas				
United States, SEER (10 registries)				
White	A4C3P2	35.4	31	0.27
Black	A4P2	28.0	33	0.71
Hispanic	A4	8.21	6	0.22
Canada[4] (12 registries)	A8C6P3	50.5	32	0.02
Puerto Rico	A3C2	28.0	34	0.29
Colombia, Cali	A3C1	36.0	35	0.42
Oceania				
Australia	A8C8	21.1	22	0.51
New Zealand				
Maori	A2	26.0	26	0.46
Non-Maori	A4C1	18.3	24	0.79
United Kingdom				
England (5 registries)	A8C10P3	26.1	18	0.09
Scotland (5 registries)	A7C6P2	25.3	15	0.05
North Europe				
Denmark	A4C4P2	20.6	20	0.41
Finland	A3C5	47.4	41	0.22
Sweden	A4C5	34.5	30	0.26
Central Europe				
Estonia	A5C6	35.7	28	0.15
Slovakia	A4C7P2	26.5	27	0.54
Slovenia	A6C3P3	36.7	28	0.14
Poland, Cracow City	A4	35.1	25	0.09
Western Europe				
Netherlands, Eindhoven	A2C5P3	36.8	30	0.18
Germany, Saarland	A7C5	31.9	27	0.23
Switzerland (2 registries)	A4C10	32.9	25	0.13
France (4 registries)	A8C12	11.2	9	0.27
Italy (2 registries)	A4	33.6	25	0.12
Spain (3 registries)	A2	88.7	75	0.13
Asia				
Israel, Jews	A3C3	55.8	53	0.37
Jews born in Asia or Africa	A3C3P2	55.4	52	0.35
Jews born in Europe or America	A3	62.4	56	0.26
Jews born in Israel	A2C2	49.5	45	0.30
Non-Jews[5]				
India, Bombay	A6C7	32.6	25	0.14
Japan, Osaka[4]	A4C3P3	63.3	30	<0.01
Singapore				
Chinese	A3C1	38.0	35	0.33
Indian	A2C2	33.4	35	0.54
Malay	A2	44.5	37	0.19

[1] Degree of polynomial for factors age (A), period (P) or cohort (C) in the model.–[2]Deviance from the saturated Poisson model.–[3]Degrees of freedom.–[4]Cumulative rate estimated with random effects.–[5]Population not available.

with a 95% confidence interval. A negative sign indicates a decreasing trend. For the entire age range studied (25–74 years), a significant decline in incidence was noted in the American populations (except US Hispanic), Australia, the non-Maori women of New Zealand, northern and western Europe (except Italy and Spain) and Asian populations (except Malay women of Singapore). An increase was evident for the United Kingdom, Slovakia, Slovenia and Jewish women born in Israel.

Figures 1 to 4 show the cumulative rate (per 1,000) for women aged 25–49 years and women aged 50–74 years in selected populations. For most countries analyzed, the pattern of the trend in incidence of squamous-cell carcinomas was similar in younger and older women. A remarkable exception is the United Kingdom, where an increase in incidence was observed for younger women and a decrease for the older age groups in both England and Scotland. The cumulative rate for ages 25–49 increased from about 0.3 per 1,000 for women born in 1935 to 0.6 per 1,000 for those born in 1955. The average annual increase in this age group was about 3% (Table III), almost doubling in 20 years. However, for these populations, a change in the pattern was observed for the most recent period, when a general decline in incidence appears to have started for both younger and older women.

In populations where an increase in squamous-cell carcinoma incidence has been observed (United Kingdom, Slovakia, Slovenia and Jews born in Israel), the trend is restricted mainly to younger women, with the exception of Slovenia.

DISCUSSION

Main findings

Our results show an overall decrease in the age-adjusted incidence rates of invasive squamous-cell carcinoma. This pattern was observed in 60 cancer registries in 24 countries between 1962 and 1991. However, there were some exceptions. In the United Kingdom, increases in ASR of 3% per year were found among women below the age of 50 years and increases between 3% and 4% per year were reported in Slovakia, Slovenia and the Jewish population born in Israel.

Quality of data

All of the data used for this analysis had appeared in the series *Cancer incidence in five continents* (Waterhouse *et al.*, 1982; Muir *et al.*, 1987; Parkin *et al.*, 1992, 1997). This constitutes the most reliable source of international cancer incidence statistics available, and peer-reviewed procedures are applied to decide on the inclusion or otherwise of the results in each volume. In this analysis, close to 175,000 cases were considered, of which 133,000 were squamous-cell carcinomas. For the study period, histological verification of diagnosis was high (>90%) and the fraction of cases included based on death certificate information was low (<5%). Squamous-cell carcinomas represented approximately 80% of all tumors of the cervix, while cases without histological diagnosis and those with ill-defined histology (grouped as “other and unspecified cancers”) generally comprised <10%. There were no significant trends in incidence of this latter group (*e.g.*, reflecting improved diagnostic methods) that would have influenced the observed trends in squamous-cell carcinomas. The statistical methods used in the analysis of the secular trends are standards in cancer epidemiology and were developed to separate the effects of age from the effects of calendar period and the effects linked to generation as reflected by the year of birth.

Limitations of the data: impact of screening activities

Despite the size of the study and the generally high quality of the data, the interpretation of trends has some intrinsic limitations. Some have been described for other cancers as well and refer to the progress over time of the methods and techniques of diagnosis and to the access of the population to medical services. Cervical cancer has the unique feature that widespread screening for pre-invasive disease, either organized or spontaneous, effectively reduces the incidence of invasive disease. As a consequence, comparisons across countries or across social groups in a given country may be a poor reflection of underlying risk if the effectiveness and the coverage of the screening activities are not taken into account. Unfortunately, this information is not available for most populations, so the respective roles of reduction in underlying risk of disease and the effects of screening are not easy to distinguish.

Geographic variation in incidence rates of squamous-cell carcinoma of the cervix

The average annual incidence of cervical cancer in each country varies greatly, from the high rates in Latin America and Hispanic

TABLE III – PERCENT CHANGE PER YEAR OF INCIDENCE RATE OF CERVICAL SQUAMOUS-CELL CARCINOMAS BY AGE GROUP AND COUNTRY

Country	Age 25–74		Age 25–49		Age 50–74
	Number	% I (95% CI)[1]	Number	% I (95% CI)[1]	% I (95% CI)[1]
Americas					
United States, SEER (10 registries)					
White	13,051	−2.3 (−2.6 to −2.0)	6,768	−1.4 (−1.8 to −1.0)	−3.2 (−3.6 to −2.8)
Black	3,080	−4.1 (−4.8 to −3.3)	1,575	−4.1 (−4.8 to −3.3)	−4.1 (−4.9 to −3.3)
Hispanic	1,170	−0.5 (−2.1 to 1.3)	723	−1.3 (−3.3 to 0.9)	0.9 (−1.9 to 4.1)
Canada (12 registries)	16,635	−1.8 (−2.0 to −1.6)	8,978	−1.1 (−1.4 to −0.7)	−2.6 (−3.0 to −2.3)
Puerto Rico	3,157	−4.4 (−4.9 to −3.9)	1,360	−3.4 (−4.2 to −2.6)	−5.2 (−5.8 to −4.5)
Colombia, Cali	2,393	−3.2 (−3.8 to −2.6)	1,213	−3.3 (−4.2 to −2.4)	−3.0 (−3.9 to −2.1)
Oceania					
Australia (2 registries)	5,500	−2.1 (−2.5 to −1.6)	2,821	−1.2 (−1.8 to −0.5)	−3.0 (−3.6 to −2.3)
New Zealand					
Maori	291	0.1 (−2.6 to 3.2)	195	−1.3 (−4.3 to 2.3)	3.3 (−2.0 to 10.3)
Non-Maori	1,804	−2.5 (−3.5 to −1.5)	1,006	−2.5 (−3.8 to −1.1)	−2.6 (−4.0 to −1.0)
United Kingdom					
England (5 registries)	13,889	0.4 (0.1 to 0.7)	6,256	2.7 (2.1 to 3.3)	−1.1 (−1.5 to −0.7)
Scotland (5 registries)	4,227	1.0 (0.3 to 1.8)	1,916	3.3 (2.0 to 4.6)	−0.7 (−1.6 to 0.3)
Northern Europe					
Denmark	5,238	−1.5 (−2.1 to −0.8)	2,294	−0.5 (−1.5 to 0.5)	−2.2 (−3.0 to −1.4)
Finland	5,360	−5.4 (−5.8 to −5.0)	1,730	−5.3 (−6.0 to −4.6)	−5.4 (−5.9 to −5.0)
Sweden	7,708	−3.2 (−3.6 to −2.9)	3,496	−2.2 (−2.7 to −1.6)	−4.1 (−4.5 to −3.6)
Central Europe					
Estonia	2,570	−1.5 (−2.1 to −0.8)	817	−2.8 (−3.8 to −1.7)	−0.8 (−1.6 to −0.0)
Slovakia	7,290	2.2 (1.7 to 2.7)	3,723	4.0 (3.3 to 4.8)	0.5 (−0.2 to 1.1)
Slovenia	1,594	2.6 (1.6 to 3.7)	690	4.1 (2.4 to 5.8)	1.6 (0.4 to 3.0)
Poland, Cracow	924	0.5 (−1.1 to 2.2)	420	1.0 (−1.4 to 3.8)	0.0 (−2.1 to 2.4)
Western Europe					
Netherlands, Eindhoven	320	−6.3 (−7.6 to −4.8)	134	1.7 (−4.4 to 1.4)	9.0 (−10.4 to −7.3)
Germany, Saarland	2,088	−5.4 (−5.9 to −4.8)	755	−4.3 (−5.3 to −3.3)	−5.9 (−6.6 to −5.2)
Switzerland (2 registries)	543	−4.8 (−5.9 to −3.6)	233	−5.2 (−6.8 to −3.4)	−4.5 (−6.0 to −2.9)
France (4 registries)	2,134	−4.9 (−5.9 to −4.0)	828	−3.4 (−4.9 to −1.8)	−5.9 (−7.0 to −4.8)
Italy (2 registries)	491	−1.2 (−3.2 to 1.1)	188	0.8 (−2.7 to 5.0)	−2.4 (−4.8 to 0.5)
Spain (3 registries)[3]	506	0.2 (−2.3 to 3.0)	165	2.0 (−2.4 to 7.4)	−0.7 (−3.6 to 2.7)
Asia					
Israel, Jews	1,455	−0.2 (−0.8 to 0.4)	721	0.8 (−0.1 to 1.7)	−1.5 (−1.8 to −0.3)
Jews born in Asia or Africa	568	−1.2 (−2.1 to −0.3)	283	−0.5 (−1.8 to 0.9)	−1.8 (−2.9 to −0.5)
Jews born in Europe or America	627	−0.7 (−1.6 to 0.2)	189	−0.0 (−1.5 to 1.7)	−1.0 (−2.1 to 0.0)
Jews born in Israel	206	3.1 (0.8 to 5.6)	162	3.7 (1.1 to 6.7)	1.0 (−3.0 to 5.9)
Non-Jews[2]					
India, Bombay	6,517	−1.4 (−1.8 to −1.0)	3,530	−1.8 (−2.3 to −1.2)	−1.0 (−1.6 to −0.3)
Japan, Osaka	9,776	−4.2 (−4.5 to −3.9)	4,016	−3.8 (−4.3 to −3.3)	−4.5 (−4.9 to −4.1)
Singapore					
Chinese	2,099	−0.9 (−1.7 to −0.2)	910	−0.7 (−1.8 to 0.5)	−1.1 (−2.1 to −0.1)
Indian	120	−6.4 (−8.4 to −4.0)	60	−3.0 (−6.5 to 1.3)	−9.2 (−11.5 to −6.3)
Malay	145	−0.1 (−2.9 to 3.2)	65	−2.7 (−6.1 to 1.6)	2.6 (−1.7 to 7.9)

[1] Percent change and 95% confidence intervals (CI) per year derived from the linear term of the Poisson model. A negative sign denotes a decreasing trend.–[2]Population not available.

populations in the United States to the low rates in Israel. In Europe, low rates are observed in the Nordic countries, where organized screening was effectively introduced as early as 1960 and coverage has been consistently high. Denmark, however, has retained relatively high rates of squamous-cell cervical carcinoma. Screening programs have evolved differently in the individual Nordic countries. In Finland and Sweden, there are nationwide cervical cancer screening programs, and the overall attendance rate in Finland is 70% to 80% of the female population, whereas only a few counties in Denmark, including the most populous ones, have organized screening programs and the attendance rate is low (Hakama, 1997; Sigurdsson, 1999).

The geographical variation in the incidence of cervical cancer observed between countries can also be observed between populations within them. For example, in France, there is an almost 2-fold variation between the rates in the Herault region (14.1) and the Tarn (7.7). Similar variations are observed in Spain and Italy. The populations within countries should theoretically benefit from similar quality of screening and medical-care programs, but inequalities or cultural differences could modify the impact of the programs in some areas. Alternatively, the observed differences could be related to differences in exposure to the key risk factors (namely, sexual behavior patterns and prevalence of human papillomavirus infection).

Singularities in trends

In the majority of countries, there has been a progressive decline in the incidence of invasive squamous-cell carcinoma, while in 8 countries studied, rates were essentially stable. The United Kingdom recorded an upward trend in the incidence and mortality due to cervical cancer among women below the age of 50, but this trend was not paralleled among older women. In fact, there are marked birth cohort–specific differences in the risk of cervical cancer in the United Kingdom, which, in its early years, the screening program was unable to hide (Parkin *et al.*, 1985). However, after 1988, the program was substantially improved, mostly by reinforcement of the centralized (and computerized) services of call and recall of women, resulting in a substantial increase in coverage (from 42% in 1988 to 85% in 1995) and a new reversal of the secular trend, with a consistent decrease in the incidence and mortality rates in the young age groups from 1994 onward (Patnick, 1997; Gibson *et al.*, 1997; Quinn *et al.*, 1999). Accelerated declines in cervical cancer incidence and mortality have been also observed in Scotland (Walker *et al.*, 1998).

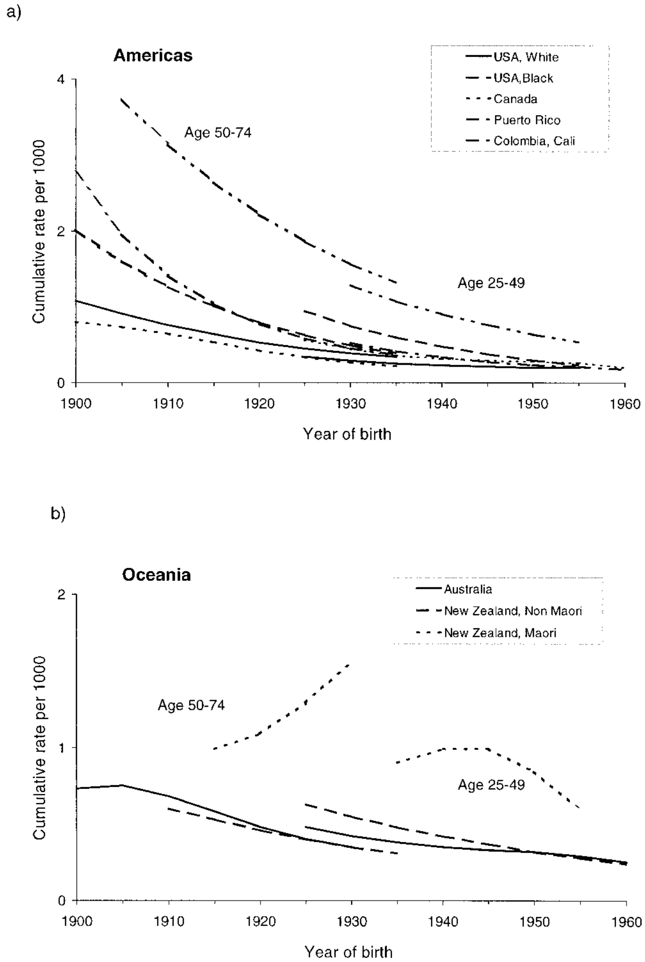

FIGURE 1 – Cumulative rates of squamous-cell cervical cancer for women aged 25–49 and 50–74 years in the Americas *(a)* and Oceania *(b)*.

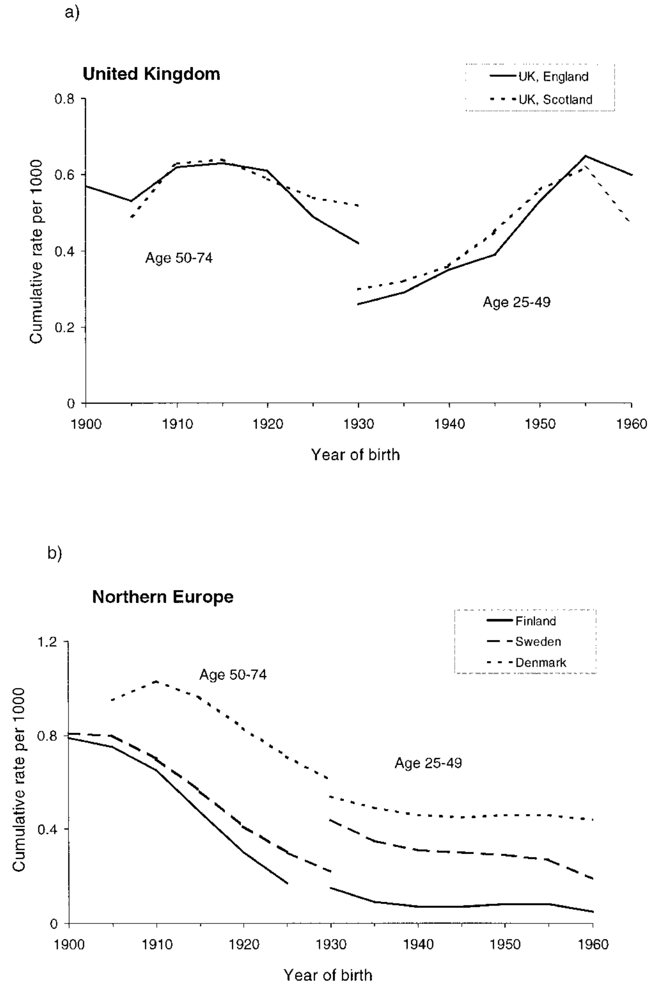

FIGURE 2 – Cumulative rates of squamous-cell cervical cancer for women aged 25–49 and 50–74 years in the United Kingdom *(a)* and northern Europe *(b)*.

An increase in incidence and mortality of cervical carcinomas among young women was noted in previous studies in other European countries (Beral *et al.,* 1994). Slovakia and Slovenia, for example, show increases in the incidence rates of squamous-cell cervical cancer among young women. It is likely that deficiencies of screening programs in these countries can explain such changes (Vlasák *et al.,* 1991; Pompe Kirn *et al.,* 1992).

Our study included mostly developed countries with either established screening programs or high levels of opportunistic screening. In an earlier report (Vizcaino *et al.,* 1998), we found that in many countries [*e.g.,* the white population of the United States, Australia, New Zealand (non-Maori), Japan (Osaka), the Chinese population of Singapore, Denmark and Sweden] there has been an increase in the incidence of adenocarcinoma among younger women, despite a concomitant decrease in squamous-cell carcinoma. This is coherent with an underlying increase in risk of both histological types of cervical cancer but less efficient prevention of adenocarcinoma by conventional screening. In an evaluation of the screening program in Iceland, it was calculated that the sensitivity of the standard cytology for identifying pre-invasive squamous-cell carcinoma following a 3-year interval was 81% but only 42% for pre-invasive adenocarcinoma (Sigurdsson, 1995). In a case-control study in Australia, Mitchell *et al.* (1995) observed that the risk of adenocarcinoma was not reduced by screening.

We conclude that the likely explanation of the pattern reported here is that squamous carcinoma of the cervix is being largely prevented by screening programs in developed countries. As a result, incidence is actually declining, or relatively stable, when perhaps an increase in risk might have been anticipated due to a change in sexual life-style favoring transmission of HPV. In general, it is accepted that organized programs, with regular screening of a defined population (such as in the Nordic countries and the United Kingdom), are more efficient than spontaneous or opportunistic screening (Hakama *et al.,* 1985; Sigurdsson, 1999). However, even "opportunistic" screening, although wasteful of resources, can clearly achieve a beneficial result if it is sufficiently intensive, as the results for several countries, including the United States, demonstrate.

The situation in developing countries is, however, far from satisfactory. Although some cytological screening is done, there are no organized programs and the testing is often distributed inefficiently among the population and of poor quality (Lazcano Ponce *et al.,* 1998). As a result, in several Latin American countries, for example, there has been a very limited impact on the incidence of cervical cancer, despite relatively large numbers of cytological examinations, as in Cuba (Fernandez *et al.,* 1996) and Costa Rica (Herrero *et al.,* 1997).

In developing countries with no resources for screening, there are few long time series available to monitor cancer incidence, but data from Uganda (Wabinga *et al.,* 1999) indicate that, at least in

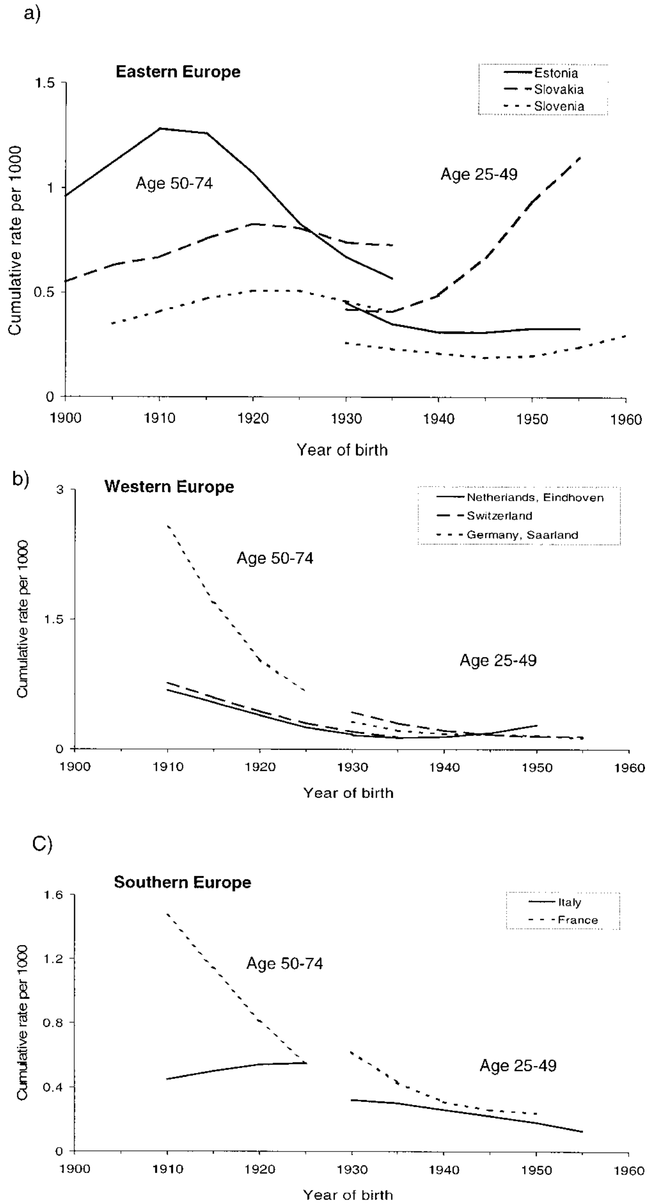

FIGURE 3 – Cumulative rates of squamous-cell cervical cancer for women aged 25–49 and 50–74 in eastern Europe *(a)*, western Europe *(b)* and southern Europe *(c)*.

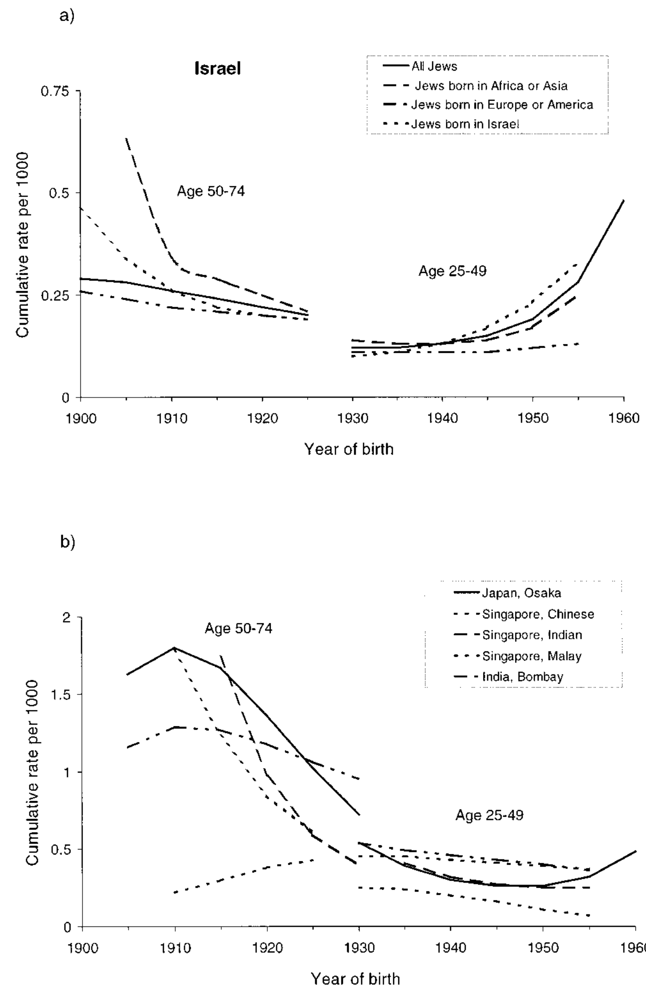

FIGURE 4 – Cumulative rates of squamous-cell cervical cancer for women aged 25–49 and 50–74 in Israel *(a)* and India, Japan and Singapore *(b)*.

some areas, substantial increases in the incidence of cervical cancer may have occurred.

In conclusion, developed countries should continuously monitor the coverage and the quality of cytology-based screening programs. Particular attention should be given to the evaluation of alternatives to reduce false-negative results in detecting cervical adenocarcinoma. In most developing countries, an effort is required to validate and introduce simple and more effective screening techniques. In the long run, primary prevention with an HPV vaccine might be a more effective solution to the control of this disease.

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