Country-level correlates of cervical cancer mortality in Latin America and the Caribbean

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Abstract

Objective. To identify country-level correlates of geographical variations in cervical cancer (CC) mortality in Latin America and the Caribbean (LAC). **Materials and methods.** CC mortality rates for LAC countries (n=26) were examined in relation to country-specific socio-economic indicators (n=58) and Human Papilloma Virus (HPV) prevalence using linear regression models. **Results.** High mortality at ages <5 years, low per capita total expenditure on health, and low proportion of the population with access to sanitation were identified as the best independent predictors of CC mortality (R^2=77%). In the subset of countries (n=10) with HPV prevalence estimates, these socio-economic indicators together with high-risk HPV prevalence explained almost all the between-country variability in CC mortality (R^2=98%). **Conclusion.** The findings suggest that continuing socio-economic improvements in LAC countries will be associated with further reductions in CC mortality even in the absence of organised population-based screening and vaccination programmes.

Keywords: uterine cervical neoplasms; papillomaviridae; mass screening; Latin America

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Resumen

Objetivo. Identificar variables a nivel de país que expliquen las variaciones geográficas en la mortalidad por cáncer cervicouterino (CaCu) en América Latina y el Caribe (AL). **Materiales y métodos.** Se examinaron las tasas de mortalidad por CaCu de cada país (n=26) mediante modelos de regresión lineal en relación con indicadores socioeconómicos (n=58) y prevalencia del virus del papiloma humano (VPH). **Resultados.** Alta mortalidad en menores de cinco años, bajo gasto total en salud per-cápita y baja proporción de población con acceso a saneamiento básico son los mejores predictores de mortalidad por CaCu (R^2=77%). En los países (n=10) con estimaciones de prevalencia de VPH, estos indicadores socioeconómicos y la prevalencia de VPH de alto riesgo explicaron el 98% de la variabilidad de CaCu en AL. **Conclusión.** Las mejoras en el nivel socioeconómico en AL están asociadas con reducciones en la mortalidad por CaCu, a pesar de la ausencia de programas organizados de tamizaje e inmunización contra VPH.

Palabras clave: neoplasias del cuello uterino; papillomaviridae humano; tamizaje masivo; América Latina

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Cervical cancer (CC) is the second most common female non-skin cancer in the world. According to Globocan 2008,[1] 13% of all CC cases and 11% of all CC deaths worldwide occur in Latin America and the Caribbean (LAC), with rates being higher than in more developed countries. There is, however, marked between-country variability in CC rates in LAC with a four to five-fold difference in rates between high (e.g. Nicaragua and Guyana) and low risk countries (e.g. Uruguay and Chile).[1,2] Persistent infection with high-risk Human Papillomavirus (HPV) is a necessary cause for CC development,[3] but geographical variations in the prevalence of HPV do not seem to fully explain the variability in CC rates worldwide.[4] Organised cervical screening programmes based on cytology can reduce CC incidence and mortality rates[5] by as much as 80-90%.[6] Both ecological and individual-based studies have shown that markers of socio-economic (SE) status, such as educational level, are related to CC incidence and mortality, with women with low SE status being at higher risk of developing, or dying from, this cancer.[7,8]
We conducted an ecological study to assess the extent to which between-country differences in CC mortality in LAC are accounted by level of SE development, HPV prevalence and screening activity.

Materials and methods

CC mortality rates

Country-specific CC mortality rates (age-adjusted to the World standard population) for 2008 were extracted from GLOBOCAN 2008.[1] These rates were estimated from death certification data provided by each country to the World Health Organization (WHO) except for Bolivia, Guyana, Honduras, Jamaica and Haiti. For these countries, CC mortality estimates were corrected for under-reporting (Guyana), or derived using data on CC incidence rates and survival (Bolivia) or CC mortality from neighbouring countries (Honduras, Jamaica).[1] Haiti was excluded from the analysis because its GLOBOCAN estimates were markedly different for 2002 and 2008 (i.e. age-adjusted rates of 48 and 10 per 100 000 women, respectively).[1,9]

Level of SE development

Data on demographic, SE and public health indicators for the years 2000-2005 were extracted, for each LAC country, from official web pages or reports published by non-governmental organisations, including the WHO,[10] the Pan-American Health Organisation (PAHO),[11-13] the United Nations Statistics Division[14] and Human Development Report.[15] These indicators were categorised into nine strata (table I): demographic (eight indicators), mortality (eight), morbidity (two), immunisation coverage (five), tobacco use (two), sexual and reproductive behaviour (six), health services (ten), economic (eleven) and development (six) indicators. Linear univariate regression models, weighted by size of the female population in each country, were fitted to examine the association between each one of these 58 indicators and CC mortality at a country level. For each one of the nine strata described above, the indicator with the highest R^2, a p-value<0.05 and available data for all LAC countries examined was chosen to be included in a multiple regression model. The tobacco use stratum was excluded because none of its indicators had information for all the countries examined (table I). The correlation between the remaining eight selected stratum-specific indicators was then evaluated and whenever two of these were strongly correlated (r>0.80), the one with the larger p-value and/or smaller R^2 was replaced by the next indicator in the same stratum that most closely fulfilled the above criteria. This process was repeated until none of the eight stratum-specific indicators were strongly correlated with each other (r<0.80). A multiple linear regression model was then fitted to the final selection of stratum-specific indicators, and the log-likelihood ratio test used to identify the best independent predictors of CC mortality.

A composite risk score was generated on the basis of the identified predictors. Firstly, the 26 LAC countries were ranked separately according to the values of each one of the identified predictors and a predictor-specific risk score assigned to each country to reflect this ranking (e.g. for a predictor positively associated with CC mortality a score of 1 was assigned to the country with the lowest predictor value and a score of 26 to the country with the highest; for a predictor inversely associated with CC mortality a score of 1 was assigned to the country with the highest predictor value and a score of 26 to the country with the lowest). A composite risk score for each country was then calculated as the sum of its predictor-specific risk scores (i.e. for 3 predictors, country-specific composite scores could range from 3 to 78 depending on the direction of their association with CC mortality).

HPV prevalence

Data on country-specific HPV prevalence estimates, any genotype and high-risk genotypes (HPV16 and HPV18), and the women's ages at the time of HPV assessment, were extracted from the WHO/ICO Information Centre on HPV and CC.[16] Its website presents worldwide data

Table I

COUNTRY-LEVEL DEMOGRAPHIC, SOCIOECONOMIC AND PUBLIC HEALTH CORRELATES, IN 2000-2005, OF CERVICAL CANCER MORTALITY IN LATIN AMERICA AND THE CARIBBEAN ISLANDS (LAC)

Type of Indicator *Indicator (no. of countries for which data were available) / [reference]*	*50%*	*Percentil* *Interquantil Range* *25%-75%*	*ß*	R^2	*P*
Demographical characteristics					
Urban population (%) (26)/[11]	63.60	57.80- 77.40	-0.18	0.4	0.001
Proportion of population aged less than 15 years (%) (26)/[11]	28.94	25.90- 31.61	0.57	0.47	<0.001
Proportion of population aged 60 years and over (%) (26)/[11]	8.04	6.71- 10.20	-0.83	0.37	0.001
Dependency ratio [Dependent population per 100 productive population] (26)/[11]	57.55	52.70- 64.80	0.22	0.34	0.002
Annual rate of population growth (%) (26)/[11]	1.40	0.70- 1.70	5.41	0.41	<0.001
Crude birth rate (per 1 000 population) (26)/[11]	20.75	18.30- 23.90	0.64	0.54	<0.001
% of the population of Native origin (26)/[10]	4.00	2.00- 14.00	0.08	0.22	0.015
% of the population of Afro American origin (15)(a)/[10]	9.00	2.00- 21.00	-0.02	0.03	0.53
Public health indicators					
Mortality					
Female life expectancy at birth (in years) (26)/[10]	74.00	71.00- 78.00	-0.75	0.48	<0.001
Female healthy life expectancy at birth (in years) (26)/[10]	64.20	62.20- 68.00	-0.6	0.38	0.001
Infant mortality rate (per 1 000) (26)/[10]	22.00	16.00- 31.00	0.14	0.16	0.046
Neonatal mortality rate (per 1 000) (26)/[10]	15.00	10.00- 18.00	0.52	0.35	0.001
Maternal mortality ratio (per 100 000) (26)/[10]	120	78.00-170.00	0.01	0.23	0.013
Age-standardized cancer (all sites combined)mortality rate (per 100 000) (26)/[10]	130.30	112.20- 141.80	0.03	0.06	0.217
Percentage of years of life lost to non-communicable diseases (%) (26)/[10]	44.55	36.50-56.80	-0.2	0.43	<0.001
Estimated mortality under 5 years of age (per 1 000) (26)/[10]	28.80	16.70-43.60	0.2	0.57	<0.001
Morbidity					
Crude annual incidence of tuberculosis (100 000 population) (26)/[10]	66.85	32.80- 106.80	0.04	0.38	<0.001
Prevalence of low birth weight [%] (26)/[10]	9.50	7.00- 12.00	0.81	0.32	0.003
Immunization Coverage					
Proportion of one-year-olds immunized with one dose of measles (%) (26)/[10]	92.00	86.00- 95.00	-0.23	0.31	0.003
Proportion of one-year-olds immunized with three doses of diphtheria tetanus toxoid and pertussis (DTP3) (%) (26)/[10]	90.00	85.00- 94.00	-0.29	0.31	0.003
Proportion of one-year-olds immunized with three doses of Hepatitis B (HepB3) (%) (23)(b)/[10]	89.00	83.00- 94.00	-0.29	0.32	0.003
Proportion of under-one-year population immunized against poliomyelitis (%) (26)/[11]	91.50	88.00- 95.00	-0.27	0.3	0.004
Proportion of under-one-year population immunized against tuberculosis (%) (22)(c) /[11]	96.00	92.00- 99.00	-0.49	0.31	0.007
Tobacco Use					
Prevalence of current tobacco smoking among adult women (%) (9)(d)/[10]	13.20	7.00- 17.50	-0.28	0.61	0.012
Prevalence of tobacco smoking among adolescents aged 12-18 years (%) (25)(e)/[11]	20.50	18.30- 25.40	-0.31	0.25	0.01
Sexual and reproductive behaviour					
Total fertility rate (26)/[11]	2.50	2.20- 2.80	4.69	0.49	<0.001
Specific fertility rate in women aged 15-19 years (per 1 000 population) (26)/[11]	74.60	58.50- 85.20	0.08	0.14	0.055
Percentage of women who gave birth between 15-19 years (26)/13	7.00	5.00- 9.00	0.58	0.09	0.094
Prevalence of use of any contraceptive methods among women (%) (26)/[11]	59.40	46.30- 69.00	-0.04	0.04	0.315
Use of oral contraceptives among women (21)(f) /[12]	11.80	7.10- 20.70	-0.47	0.37	0.003
Age of first intercourse among women (11)(g)/[12]	19.00	18.55- 19.20	-1.04	0.17	0.186

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Health services indicators					
Number of physicians (per 1 000 population) (25)(h)/[10]	1.21	1.05- 1.50	-1.37	0.17	0.04
Number of nurses (per 1 000 population)(25) (i)/[10]	1.57	0.90- 2.87	0.1	0	0.797
Number of outpatient care facilities (26)/[11]	1818.0	367.00- 5835.0	-0.001	0.11	0.106
Hospital beds ratio (per 1 000 population) (26)/[111]	1.60	1.00- 2.90	-1.31	0.22	0.016
Outpatient health care visits ratio (per 1 000 population) (25)(j)/[11]	1774.3	1070.70- 2502.3	-0.001	0.07	0.188
Hospital discharges ratio (per 1 000 population) (26)/[11]	63.45	54.20- 80.00	-0.03	0.07	0.202
Proportion of pregnant women followed by trained personnel during pregnancy (%) (26)/[11]	88.10	79.00- 94.00	-0.02	0.02	0.443
Proportion of deliveries attended by trained personnel (%) (26)/[11]	94.25	83.70- 99.10	-0.16	0.41	<0.001
Coverage of death registrations (%) (22)(k) /[10]	87.05	73.80- 97.00	-0.13	0.43	0.001
Proportion of certified deaths due to ill-defined and unknown conditions (%)(25)(h)/[11]	6.40	2.40- 12.50	0.15	0.14	0.06
Economic statistics					
Total expenditure on health as percentage of GDP (26)/[10]	6.95	5.30- 7.60	-1.1	0.2	0.022
General government expenditure on health as a percentage of total expenditure on health (26)/[10]	48.35	44.30- 64.00	-0.04	0.02	0.449
Per capita total expenditure on health at USD (international dollar rate) (26)/[10]	322.00	233.00- 597.00	-0.01	0.64	<0.001
Per capita government expenditure on health at USD (international dollar rate)	187.50	109.00- 345.00	-0.02	0.61	<0.001
GDP per capita, PPP (24)(l) /[10]	6779.2	4018.7- 9109.5	-0.001	0.76	<0.001
Annual GDP growth rate (%) (25)(m) /[11]	2.50	1.30- 3.90	-0.25	0.09	0.157
Increase of GDP per capita PPP in the last 10 years(24)(l) /[11]	11.48	6.61- 22.79	-0.12	0.14	0.075
Highest 20%/Lowest 20% income ratio (22)(n) /[11]	18.00	11.00- 21.50	-0.11	0.03	0.439
Proportion of the population living below the poverty line (living with less than $1 a day) (21)(o)/[11]	8.20	3.00- 16.40	0.39	0.62	<0.001
Proportion of the population below the national poverty line (%) (23)(p)/[11]	35.00	21.80- 49.00	0.09	0.21	0.058
Proportion of the labour force who are currently unemployed (%) (26)/[11]	9.85	6.40- 14.00	-0.05	0.01	0.665
Development					
Proportion of the population with sustainable access to an improved water source (%) (26)/[11]	91.00	85.00- 94.00	-0.59	0.54	<0.001
Proportion of the population with access to improved sanitation (%) (26)/[11]	76.00	66.00- 92.00	-0.25	0.57	<0.001
Female literacy rate (%) (26)/[13]	92.50	87.20- 96.60	-0.32	0.42	<0.001
Average number of years of formal education for the total population (25)(q)/[14]	13.00	12.00- 14.00	-1.03	0.16	0.048
Average number of years of formal education for the female population (22)(r) /[14]	13.00	12.00 14.00	-1.16	0.27	0.014
Human Development Index*, 2004 (26)/[15]	0.78	0.73- 0.83	-64.38	0.77	<0.001

GDP: Growth Domestic Product, PPP: Purchasing power parity

* Human Development Index: is a composite statistic used to rank countries by level of "human development" which takes into account life expectancy, literacy, level of education and standards of living

(a) excluded: Argentina, Bahamas, Barbados, Belize, Chile, El Salvador, Guatemala, Guyana, Jamaica, Suriname, Trinidad and Tobago
(b) excluded: Chile, Guatemala, Suriname
(c) excluded: Bahamas, Barbados, Suriname & Trinidad & Tobago
(d) included: Brazil, Chile, Dominican Republic, Ecuador, Guatemala, Honduras, Mexico, Paraguay, Uruguay,
(e) excluded: Dominican Republic
(f) excluded: Argentina, Chile, Panama, Uruguay, Venezuela
(g) excluded: Argentina, Barbados, Belize, Bolivia, Brazil, Chile, Colombia, Cuba, Guayana, Mexico, Panama, Suriname, Trinidad and Tobago, Uruguay, Venezuela
(h) excluded: Honduras
(i) excluded: Venezuela
(j) excluded: Colombia
(k) excluded: Bolivia, Honduras, Jamaica, Suriname
(l) excluded: Cuba, Suriname
(m) excluded: Cuba
(n) excluded: Barbados, Belize, Cuba, Suriname
(o) excluded: Barbados,Belize, Bolivia, Cuba, Suriname
(p) excluded: Mexico, Uruguay, Venezuela, Barbados, Belize, Bolivia, Cuba, Suriname
(q) excluded: Ecuador
(r) excluded: Bolivia, Costa Rica, Ecuador, Guyana

on HPV prevalence[4,17] compiled through systematic reviews of the literature published between 1995 and 2009; publications were eligible if HPV assessment was based on polymerase chain reaction (PCR) or Hybrid Capture2 (HC2), and the sample included >90 women with normal cytological findings. Age-specific HPV prevalence estimates were available from the WHO/ICO website for 10 LAC countries (Argentina, Brazil, Chile, Colombia, Costa Rica, Guatemala, Honduras, Mexico, Paraguay and Peru). Regression models, restricted to these 10 countries, were fitted to examine the association between HPV prevalence (any and high-risk HPV) and CC mortality, adjusting for age at HPV ascertainment and also additionally for the SE predictors identified by the analysis described above.

Cervical screening

Information on screening policies and their level of implementation, including Pap smear coverage estimates from nationally representative surveys and other sources, were extracted from a previously published source[18] and updated using the same methodology as previously. Information was also gathered on the use of HPV detection methods and on HPV vaccination policies.

Analyses were conducted in Stata v.10. The study was carried out at the London School of Hygiene and Tropical Medicine. Ethical approval was not required because only publicly-available secondary data were analysed.

Results

There were marked between-country differences for most demographic, SE and public health indicators (table I). For instance, there was a 9.5-fold difference between the countries with the highest (Bolivia) and the lowest (Chile) mortality rate among children aged under 5 years, and a 7-fold difference between the countries with the highest (Bahamas) and the lowest (Bolivia) per-capita expenditure on health.

The univariate analyses showed that countries with the highest CC mortality rates tended to be those with the youngest age-structure, lowest degree of urbanisation, lowest SE development and poorest health indicators (table I). Crude birth rate, mortality rate under five years, incidence of tuberculosis, proportion of one-year-olds immunized with one dose of measles, total fertility rate, proportion of deliveries attended by trained personnel, per capita total expenditure on health, and proportion of the population with access to improved sanitation were the variables selected to represent each one of the eight strata of indicators in the multiple regression analysis. Mortality rate under 5 years of age, per capita total expenditure on health and proportion of the population with access to improved sanitation were identified as the best independent predictors of CC mortality in LAC (table II), accounting for 77% of the between-country variability in rates. There was a positive linear association between the composite risk score and CC mortality at a country level (figure 1).

Stratifying LAC countries according to their CC mortality (table III) showed, as expected, that the highest CC mortality-stratum had, on average, the highest mortality rate at age under-5-years, the lowest mean per capita total expenditure on health, and the lowest proportion of the population with access to improved sanitation.

In analyses restricted to the subset of 10 countries with available HPV data, the three independent SE predictors identified above explained 90% of the between-country variability in CC mortality (table II) whereas age-adjusted prevalence of any HPV genotype, or of high-risk HPV genotypes, alone explained only 8-9% (table II). The correlation between HPV and SE predictors was low ($r<0.30$). Nevertheless, the R^2 increased to 98% when both SE predictors and high-risk HPV prevalence (to 97% if the latter was replaced by prevalence of any HPV genotype) were included in the same model (table II).

Cytology-based screening programmes were first introduced in LAC in the early 1960s (table IV). Most programmes are opportunistic. Only the Chilean national programme recommends a national call-recall system,[19] but there is no evidence that such recommendation has been implemented. A few local organised screening programmes have been set up (e.g. certain regions of Brazil),[20-22] but none has established a call-recall system. Different methodologies and age-groups were used to estimate Pap smear coverage, thus making between-country comparisons difficult. Estimates for Pap-smear coverage within 2-3 years prior to the survey (available for nine countries) ranged from 31 to 69%.[20,23-31] Estimates of the proportion of women ever screened (available for seven countries) ranged from 35 to 85%,[25,29,32-35] being greater than 80% (at ages 15-49) only in El Salvador.[33] Those that report annual screening ranged from 22.7% to 44.8%.[35-38] Screening relied mainly on cytology (Papanicolaou test), but in recent years visual inspection after the application of acetic acid (VIA) and HPV testing have also been incorporated into national screening policies (e.g. the latter is currently being used in primary screening in Mexico and in demonstration projects in Argentina, Colombia, and Peru). National HPV vaccination programmes, targeting girls aged 9-11 years, were initiated in 2008 in Mexico, Panama, Argentina and Peru.[39-43]

Table II
Multiple regression analyses to identify the best demographic, socioeconomic and public health correlates, in 2000-2005, of between-country differences in cervical cancer mortality, in 2008, in Latin America and the Caribbean Islands

Correlates	*ß**	*95% CI*	*P*	R^2
All LAC countries examined (n=26)				
Model with SE variables only				77%
Estimated mortality under 5 years old (per 1 000)[10]	0.05	(-0.04, 0.15)	0.26	
Per capita total expenditure on health ‡[10]	-0.01	(-0.10; -0.003)	0.04	
Proportion of population with access to improved sanitation (%)[11]	-2.42	(-0.22, 0.01)	0.07	
Subset of LAC countries with available HPV prevalence data (n=10)				
Model with any HPV prevalence only§				8%
Prevalence of any HPV genotype[16]	0.17	(-0.38, 0.72)	0.49	
Model with high-risk HPV prevalence only §,#				9%
Prevalence of high-risk HPV genotypes[16]	0.50	(-0.93, 1.93)	0.44	
Model with SE variables only				90%
Estimated mortality under 5 years old (per 1 000)[10]	0.14	(-0.005, 0.28)	0.06	
Per capita total expenditure on health‡[10]	-0.004	(-0.01, 0.001)	0.10	
Proportion of population with access to improved sanitation (%)[11]	-0.07	(-0.22, 0.08)	0.31	
Model with SE variables and prevalence of any HPV genotype§				97%
Estimated mortality under 5 years old (per 1 000)[10]	0.21	(0.04, 0.38)	0.03	
Per capita total expenditure on health‡[10]	0.002	(-0.01, 0.003)	0.24	
Proportion of population with access to improved sanitation (%)[11]	-0.01	(-0.18, 0.17)	0.93	
Prevalence of any HPV genotype[16]	0.16	(0.01, 0.32)	0.04	
Model with SE variables and prevalence of high-risk HPV genotypes§,#				98%
Estimated mortality under 5 years old (per 1 000)[10]	0.15	(0.07, 0.82)	0.03	
Per capita total expenditure on health ‡[10]	-0.005	(-0.01, 0.004)	0.07	
Proportion of population with access to improved sanitation (%)[11]	-0.04	(-0.19, 0.11)	0.52	
Prevalence of high-risk HPV genotypes[16]	0.45	(0.07, 0.82)	0.03	

HPV=Human Papillomavirus; SE=socioeconomic
* This coefficient represents the slope of the linear regression, which means the rate of change of CC mortality associated with a unit increase in the exposure variable
‡ At international dollar rate
§ Adjusting for age at time of HPV ascertainment
# HPV16 and HPV 18

Discussion

This ecological study found that markers of level of SE development were inversely associated with CC mortality. Using data from 127 developing countries, Drain *et al.*[44] found that country-specific CC incidence rates were negatively associated with health indicators but, in contrast to our study, CC incidence was not inversely associated with most SE indicators; in fact, there was a positive relationship between health expenditure and CC incidence, which was attributed to China having both low health spending and low CC incidence.

Individual-based studies carried out in LAC have shown that CC mortality and incidence are associated with SE status.[45] Women with a low SE status may have a more risky sexual behaviour, thus increasing their likelihood of acquiring a HPV infection, and an increased risk of HPV persistence and progression to pre-invasive lesions due, for instance, to higher smoking prevalence[46] and higher parity.[47] They are also more likely to have poor access to health services including early detection, diagnostic and treatment facilities.[7,48]

Improvements in the SE level of a country, even in the absence of a well-established screening programme,

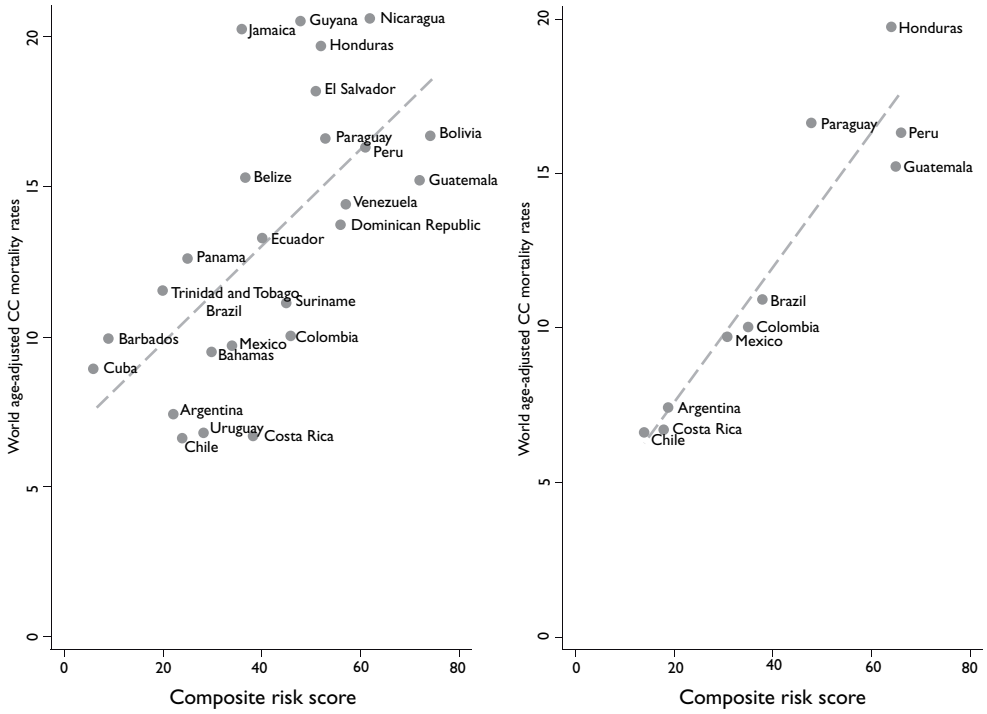

Figure 1. Correlation between the composite risk score (see Methods and Results sections), 2000-2005, and age-adjusted CC mortality rates, in 2008, in Latin America and the Caribbean Islands (LAC): (a) all 26 LAC countries examined (b) restricted to 10 LAC countries with available HPV prevalence data. (The dots correspond to the observed CC rates and the line to those predicted by the linear regression model)

may decrease CC mortality rates,[49] perhaps to declines in HPV prevalence and increased access to early detection and treatment.[50,51] Data from three population-based cancer registries in LAC (Cali in Colombia, Costa Rica and Ecuador) show a decline in CC incidence from 1970 to 1995, a period when Pap smear coverage remained low but SE level improved.[2]

In the subset of 10 countries for which HPV prevalence estimates were available, high-risk HPV prevalence alone explained only 9% of the between-country variability in CC mortality whereas SE correlates explained 90%. However, when both SE correlates and high-risk HPV prevalence were included in the same model, these variables explained practically all between-country variability in CC mortality (R^2=98%). These findings suggest that SE indicators may be a better correlate of between-country differences in CC mortality than HPV prevalence; however, they may simply reflect the much better quality of the SE data.

The paucity of comparable data on Pap smear coverage precluded examination of the extent to which between-country differences in CC mortality reflected differences in screening activity. The available estimates indicate that coverage is likely to have been low in most countries. Previous studies revealed low cytology quality, poor follow-up and poor treatment compliance.[52] A study carried out by RedPac, an initiative set up to monitor and improve Pap smear quality in LAC, showed that cytology quality was poor in many countries (e.g. percentage of false-negatives in 2000 was 27% in Peru, 23% in Venezuela, and <5% in Chile and Costa Rica).[18,35] The effectiveness of screening was also affected by poor turnaround time,[53] mainly in rural areas,[54] with only 34% abnormal smears being appropriately followed-up in Peru, 59% in Bolivia, and >90% in Chile and Cuba.[18] New screening methods (e.g. visual inspection after acetic acid [VIA] and HPV testing) are being adopted in certain LAC countries (table IV) but their introduction is far too recent to have had any major impact on the mortality rates examined here.

Our study is not exempt of limitations. Firstly, the analyses relied on mortality data, which reflects both

Table III

The best identified demographic, socioeconomic and public health correlates (and corresponding composite scores*), in 2000-2005, of between-country differences in cervical cancer mortality, in 2008, in Latin America and the Caribbean Islands

Country (composite risk score)	*Adjusted CC Mortality rate*	*Estimated mortality under 5 years old (per 1 000)*[10]	*Per capita total expenditure on health at international dollar rate*[10]	*Proportion of population with access to improved sanitation (%)*[11]
CC mortality less than 10 per 100 000 women year				
Chile (15)	6.6	9.3	707	92
Costa Rica (17)	6.7	11.9	616	92
Uruguay (14)	6.8	14.8	824	94
Argentina (19)	7.4	16.7	1 067	82
Cuba (23)	8.9	7.1	251	98
Bahamas (8)	9.5	15.3	1 220	100
Mexico (31)	9.7	22.9	582	77
Barbados (9)	9.9	11.6	1 050	99
Mean (SD)	**8.2 (1.5)**	**13.7 (4.9)**	**789.6 (316.5)**	**91.8 (8.3)**
CC mortality 10 to 16 per 100 000 women year				
Colombia (35)	10.0	30.9	522	86
Brazil (38)	10.9	33.3	597	75
Suriname (34)	11.1	29.4	309	93
Trinidad and Tobago (19)	11.5	18.6	532	100
Panama (35)	12.6	25.7	555	72
Ecuador (51)	13.3	28.2	220	72
Dominican Republic (59)	13.7	47.7	335	57
Venezuela (51)	14.4	28.0	231	68
Guatemala (65)	15.2	48.1	235	61
Belize (59)	15.3	40.2	309	47
Mean (SD)	**12.8 (1.9)**	**33.0 (9.6)**	**384.5 (149.7)**	**73.1 (10.9)**
CC mortality more than 16 per 100 000 women year				
Peru (66)	16.3	49.5	233	62
Paraguay (48)	16.6	43.6	301	78
Bolivia (78)	16.7	67.6	176	45
El Salvador (49)	18.2	32.5	378	63
Honduras (65)	19.7	46.3	184	68
Jamaica (43)	20.3	20.3	216	80
Guyana (59)	20.5	64.6	283	70
Nicaragua (62)	20.6	38.0	208	66
Mean (SD)	**18.6 (1.9)**	**45.3 (15.7)**	**247.4 (68.7)**	**66.5 (10.9)**

* country-specific score estimated as the sum of the ranking of the three predictors identified by the multiple regression analysis with a possible range from 3 to 78 (see Methods and Results sections)

incidence of, and survival from, CC. There are few population-based cancer registries in LAC and most are local. The quality of the mortality data was also far from ideal. The estimates produced by GLOBOCAN (IARC/WHO) took into account under-registration of death and percentage of registered deaths coded as "ill-defined" conditions, but different methods were used to estimate rates for each country depending on data availability. Secondly, the SE data came from different sources although for every single variable the same source was

Table IV
CERVICAL SCREENING AND HPV VACCINATION POLICIES IN LATIN AMERICA AND THE CARIBBEAN ISLANDS (LAC), 2011*

Country	*Start year*‡	*Screening centres*	*Screening age (years)*	*Screening scheme (years)*§	*Screening test*	*Coverage Estimates*				*HPV vaccination policies*
						No. of women studied (year)	*Age*	*Interval*	*% of women screened (reference)*	
Argentina	1997	Health care centres	35-64	1-1-3	Pap, HPV test (pilot study)	41 392 (2005)	>18	2/Ever	51.6/74.4[24]	All girls from 11 years from 2011[42]
Bolivia	1988 and 1998	Reproductive health service	25-49	1-1-3	Pap	--	--	--	--	--
Brazil	1968/1996-98	Health facilities	25-59	1-1-3	Pap	NS (2003)	> 24	3	68.7[20]	Not universal, study assessing cost-effectiveness in Brasil[40]
Chile	1987 and 1994	Health primary clinics	25-64	Every 3	Pap	270 000 (2003)	> 15	3	51.4[31]	Not universal
Colombia#	1991 and 2000	NS	25-69	1-1-3	Pap	41 012 (2005)	18-69	2	67[27]	--
Costa Rica	1995	Health public and private centres	> 20	Every 2	Pap	1612 (1999-2000)	18-44	2/Ever	44.8/78.8[25]	--
Cuba#	1968	Health primary clinics	25-59	Every 3	Pap	NS (1993-1994)	<20	2	54.2[26]	--
Dominican Republic#	1993	Family planning services	25-59	6-6-12 (months)		4 996 (1996)	NS	1	44.8[35]	--
Ecuador&	1996	Health primary service	35-64	Every 5	Pap	10 813 (2004)	15-49	2	3128	--
El Salvador	2002	Family planning services	30-59	Every 2	Pap	10 689 (2002-2003)	15-49	Ever	84.7[33]	--
Guatemala	2004	Familyplanningservices	25-49	1-1-1-3 or 5	Pap	12 119 (2002)	15-49	1	41.2[36]	--
Honduras	NS	Maternal health	25-59	Annually	Pap	9 362 (2001)	15-49	Ever	60.9[33]	--
Mexico	1974/1994-98	Public health sector	25 -64	1-1-3	PAP, VIA and HPV test	4 594 672 (2000)	>25	3	57.8(f)[30]	About to start national vaccination programme of 9-11 years old (2009)[39]
Nicaragua	2003	Women's health clinics	25-59	1-1-1-3	Pap	14 671 (2001)	14-49	1	23.3[38]	--
Panama	NS	NS	25-years	Every 3	Pap	--	--	--	--	Originally >10 years, entire country since 2008, program under evaluation[43]
Paraguay	2002r	Health care centres and hospitals	25-69	1-1-1-3	Pap	7 321 (2004)	15-44	2/Ever	50.9/69.6[29]	--
Peru	2000 and 2004	Primary care health service	30-49	Every 3	PAP, VIA and HPV test	NS(1998)	15-49	1	22.7[37]	260 thousands girls 11 years to be vaccinated since 2011[41]
Trinidad & Tobago#	Development	NS	20-59	1-1-3	Pap	903 (1987)	NS	Ever	35.4[35]	--
Uruguay	Have not issued any cervical cancer screening guidelines. Opportunistic screening is offered by some clinics since 1994				Pap	-	(NS)	20-59	Ever70[34]	--
Venezuela	1996	NS	25-64	Every 3	Pap	--	--	--	--	--

NS: Not specified
* Updated (to the end of 2011) and modified from Murillo *et al* 2008[18]
‡ Second date is the year of re-launch of the programme
§ Screening schemes in the format "1-1-3" mean annual screening until 2 consecutive negative smears and every 3 years afterwards
# Source: unpublished data, based on personal reports
& Started in Quito and the Manabi province and was used as a reference for the whole country
r Start of programme implementation
∞ Estimated by data from the Screening Programm

used for all 26 countries examined; reassuringly, the SE correlations with CC mortality were rather consistent despite the different quality of the data on the various SE indicators. Thirdly, HPV prevalence estimates, available for only 10 countries, were derived from local surveys using HCII or PCR methodology. The extent to which such surveys were nationally representative is unknown. Fourthly, data on screening activity and quality were scarce; national estimates of Pap-smear coverage were available only for a few countries based on different (non-comparable) methodologies. Finally, the findings relate to countries and cannot be extrapolated to an individual level.

In summary, CC mortality remains high in LAC. Our findings imply that improvements in the level of SE development of a country may reduce CC mortality even in the absence of organised screening programmes and HPV vaccination programmes.

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