Correlates of National HIV Seroprevalence

An Ecologic Analysis of 122 Developing Countries

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Background: Ecologic analyses of social and developmental correlates of country-level HIV seroprevalence may suggest strategies for combating the HIV/AIDS epidemic.

Methods: Regression analyses were performed for 81 variables obtained primarily from United Nation agencies for 122 developing countries. Variable measures were compared between highest and lowest tertiles of HIV seroprevalence.

Results: Geography, religion, and income inequality were independently associated with HIV seroprevalence. Countries with earlier ages at first sex, higher teenage birth rates, and higher fertility rates had higher HIV seroprevalence. Countries with high HIV seroprevalence had fewer women using contraceptives, more persons with casual sex partners, and higher herpes simplex virus 2 seroprevalence. Male circumcision and Muslim religion were colinearly associated with lower HIV seroprevalence. Countries with high HIV seroprevalence had fewer doctors, more midwives, and less access to essential medications, but health spending differences were minor.

Conclusions: Ecologic analyses support population-level behavioral approaches, such as delaying sexual debut and discouraging casual sex partners, and reinforce biologic measures, such as controlling sexually transmitted infections and promoting male circumcision, for HIV prevention. Fewer births attended by skilled personnel, but more midwives, in countries with the highest HIV seroprevalence suggest potential strategies for reducing mother-to-child transmission. Correlations with selected health indicators suggest additional obstacles for implementing HIV treatment programs.

Key Words: HIV seroprevalence, sexually transmitted infections, epidemiology, developing countries, sexual behavior, ecologic analysis

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In 2000, HIV infection/AIDS caused >5% of all deaths worldwide, as the world's fourth leading cause of mortality, and became the leading cause of lost disability-adjusted life years for females.[1] Although HIV infection/AIDS was the leading cause of mortality in sub-Saharan Africa, in some other world regions, HIV infection /AIDS failed to appear within the top 15 causes of mortality.[1] In many developed countries, rates of HIV infection have decreased in association with programs that target reduction in risky sexual behaviors and sexually transmitted infection morbidity and provide widespread access to voluntary counseling and testing, prophylaxis for and treatment of HIV-related opportunistic infections, and, recently, multidrug antiretroviral therapy.[2,3] However, in most developing countries, access to HIV prevention and treatment programs has been extremely limited, contributing to disparities between developed and developing countries in seroprevalence and mortality rates of HIV infection.[4–7] Analyses of socioeconomic and developmental correlates of country-specific HIV seroprevalence might increase our understanding of the influence of societal characteristics on HIV transmission, reinforce individual-level studies, and suggest potential population-level interventions.

METHODS

We used country-specific age-standardized HIV seroprevalences per 100 adults 15–49 years old and number of children (younger than 15 years of age) living with HIV infection for the beginning of the year 2000 from the Joint United Nations Programme on HIV/AIDS.[8] Countries with <0.1% of adults infected with HIV were assumed to have an adult seroprevalence of 0.05%. Child seroprevalences were calculated by dividing a country's estimated number of children living with HIV infection in the year 2000[8] by its child population in the year 2000.[9] Country-specific data were collected for the 167 countries listed in the Joint United Nations Programme on HIV/AIDS report.

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The United Nations Development Programme[10] provided the Human Development Index data, which measure a country's development status on the basis of life expectancy, educational attainment, and adjusted real income. After summarizing the global distribution of population and HIV infection/AIDS cases among adults and children for 167 countries (Fig. 1), the 45 countries classified as high human development ("developed countries") were excluded, restricting subsequent analyses to the 122 countries classified as low and medium human development ("developing countries") (Table 1).

Data Collection

Country-level statistics were compiled from various sources for 81 variables, including age of the HIV epidemic (estimated as the number of years before the year 2000 that the first case of HIV or AIDS was reported by each country), development (7 indicators), sexual behavior (12), reproductive health (12), infectious diseases (5), health services (15), economic (11), education (4), population (11), religion (2), and percent of males circumcised (Appendix 1). Major data sources included the United Nations Development Programme,[10,11] the World Health Organization,[12] the United Nations Children's Fund,[13] United Nations Statistics Division data for 2000 and 2001,[14] the Joint United Nations Programme on HIV/AIDS,[8] the World Bank,[15,16] Save the Children,[17] Macro International,[18] and others.[19–24] All population statistics were estimated for the year 2000 and obtained from the United Nations Population Division.[9] Countries were categorized in geographic regions based on an International Agency for Research on Cancer classification system.[24] The US Central Intelligence Agency provided each country's predominant religion and percentage of the population predominantly Christian or Muslim.[25] Data on herpes simplex virus 2 seroprevalence, generally representing the overall prevalence among reproductive-age, non–high-risk women, were obtained from a recent review of published literature.[26] Cleland and Ferry[19] provided observations for female age at first sexual intercourse and first marriage and polygamy to supplement Macro DHS data; however, data were not attainable for all countries for most variables.

Male circumcision prevalence was the only variable not obtained from a published source. Halperin and Bailey[27] supplied male circumcision data by using the same method and expanding on their previous study. To minimize potential misclassification, countries were classified as having low (<20%), medium (20–80%), or high (>80%) male circumcision rates.

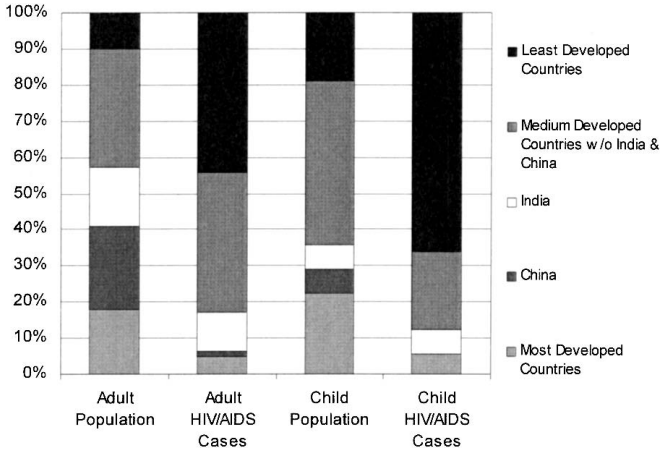

FIGURE 1. Global distribution of adult and child populations[9] with the number of adult and child HIV infection/AIDS cases[8] by human development category.

Statistical Analyses

Statistical analyses concentrated on the 122 developing countries and were weighted by each country's adult or child populations to adjust for the precision of sampling methods. All regression analyses used a robust variance to account for unmeasured ecologic and population differences.[28] Subanalyses were also conducted without India, China, or Bangladesh, because of their large populations and often outlying indicator values, to determine their impact on the results. Stata Version 6 was used for conducting all statistical analyses.[29]

Differences in mean HIV seroprevalences by geographic region and predominant religion were analyzed using a 1-way analysis of variance, and subsequent pairwise comparisons used Bonferroni multiple-comparison tests. Both adult and child HIV seroprevalences were natural log (ln)–transformed to create more normal distributions for regression analyses. Univariate linear regression statistics examined each independent variable with ln HIV seroprevalences as the dependent variable. Variables are presented in the tables by order of the R^2 value, signifying the strength of correlations between independent variables and HIV seroprevalence obtained from univariate regression analyses. Reproductive health measures were regressed with child HIV seroprevalences as dependent variables. Variables measured on a continuous scale were explored for linear fit, abnormal patterns, and residual distribution. All variables with <30 observations, such as herpes simplex virus seroprevalence, were examined for asymmetric distribution of observations.

Countries were categorized into approximate tertiles as having low (≤100), medium (101–1500), and high (>1500) HIV seroprevalences per 10^5 adults.[8] The mean and SD for each independent variable were separately summarized among the low and high HIV seroprevalence groups. Low versus high mean values for each variable were analyzed for statistical significance using 2-sample *t* tests for independent samples with unequal variances.

A multivariate analysis of covariance model for ln adult HIV seroprevalences included the major geographic and reli-

TABLE 1. One Hundred Sixty-Seven Countries Listed by HDI Category (High, Medium, or Low) and Major Geographic Region

High HDI	Medium HDI	Medium HDI	Low HDI
Americas and the Caribbean	Africa	Asia and Pacific Islands	Africa
Argentina	Algeria	Ameniz	Angola
Bahamas	Botswana	Azerbaijan	Benin
Barbados	Cameroon	Cambodia	Burkina Faso
Canada	Comoros	China	Burundi
Chile	Congo (Brazzaville)	Fiji	Central African Republic
United States	Egypt	Georgia	Chad
Uruguay	Equatorial Guinea	India	Cote d'Ivoire
Asia and Pacific Islands	Gabon	Indonesia	Democratic Republic of the Congo
Australia	Ghana	Kazakhstan	Djibouti
Brunei Darussalam	Kenya	North Korea	Eritrea
Hong Kong SAR	Lesotho	Kyrgyzstan	Ethiopia
Japan	Libyan Arab Jamahiriya	Malaysia	Gambia
South Korea	Mauritius	Maldives	Guinea
New Zealand	Morocco	Mongolia	Guinea-Bissau
Singapore	Namibia	Myanmar	Liberia
Europe	South Africa	Pakistan	Madagascar
Austria	Swaziland	Papua New Guinea	Malawi
Belgium	Tunisia	Philippines	Mali
Czech Republic	Zimbabwe	Sri Lanka	Mauritania
Denmark	Americas and the Caribbean	Tajikistan	Mozambique
Estonia	Belize	Thailand	Niger
Finland	Bolivia	Turkmenistan	Nigeria
France	Brazil	Uzbekistan	Rwanda
Germany	Colombia	Viet Nam	Senegal
Greece	Costa Rica	Middle East	Sierra Leone
Hungary	Cuba	Iran, Islamic Republic of	Sudan
Iceland	Dominican Republic	Iraq	Tanzania, United Republic of
Ireland	Ecuador	Jordan	Togo
Italy	El Salvador	Lebanon	Uganda
Luxembourg	Guatemala	Oman	Zambia
Malta	Guyana	Saudi Arabia	Americas and the Caribbean
Netherlands	Honduras	Syrian Arab Republic	Haiti
Norway	Jamaica	Turkey	Asia and Pacific Islands
Poland	Mexico	Europe	Afghanistan
Portugal	Nicaragua	Albania	Bangladesh
Slovakia	Panama	Belarus	Bhutan
Slovenia	Paraguay	Bosnia and Herzegovina	Lao, People's Democratic Republic
Spain	Peru	Bulgaria	Nepal
Sweden	Suriname	Croatia	Middle East
Switzerland	Trinidad and Tobago	Latvia	Yemen
United Kingdom	Venezuela	Lithuania	
Middle East		Macedonia, The FYR of	
Bahrain		Moldova, Republic of	
Cyprus		Romania	
Israel		Russian Federation	
Kuwait		Ukraine	
Qatar		Yugoslavia	
United Arab Emirates			

Data are from the HDI indicates Human Development Index. United Nations Development Programme.[10]

gious categories and continuous variables with >90 observations and significant univariate associations ($P < 0.10$) with HIV seroprevalence either initially or upon exploration. China was excluded from the multivariate analysis because of its large population weight, previously reported low rates of sexually transmitted infections,[30,31] and uncertainty about reported rates of HIV infection.[32] Indicators influenced by the HIV epidemic, such as life expectancies, population growth rates, and tuberculosis cases, were excluded from the model. From each group of highly correlated variables, only 1, which appeared to best capture the common factor, was included. For example, the 4 measures of immunization rates were highly correlated; therefore, only diphtheria and tetanus toxoids and pertussis immunization was included. In addition, because the percent of males circumcised was colinearly correlated with the proportion of Muslim populations, these 2 variables were independently examined in the model. Nonsignificant variables ($P > 0.05$) were removed 1 at a time from the full model in a backward fashion and reexamined in the final model. Several other variables, with a significant univariate association and between 50 and 90 observations, such as age at first sexual intercourse for females, teenage birth rate, and Gini index (a measure of increasing income inequality), were individually examined in the full model. Countries included in the final model were explored for any selection biases or differences from countries excluded by the model.

RESULTS

All Countries

Adults

Country-specific adult HIV seroprevalence (cases per 10^5 adults) ranged from 50 to 35,800 for the 167 countries (data not shown), averaging 1229 for the 122 developing countries and 314 for the 45 developed countries. The mean adult HIV seroprevalence for the 37 least-developed countries (4525) was nearly 15 times higher than that for the 45 most-developed countries. The adult HIV seroprevalence for the 85 medium-developed countries was 759 (1082 without China).

The global distribution of adult population and adult HIV infection/AIDS cases by human development category (least, medium [with separate results for India and China], and most developed) is shown in Figure 1. The 37 least-developed countries, with 10% of the world's adult population, had 44% of the total adult cases. The 83 medium-developed countries, excluding India and China, had 32% of the adult population and 39% of the world's adult HIV infection/AIDS cases. India, with 16% of the population, had 11% of the cases. China, with 23% of the global adult population, reported only 2% of adult cases. The 45 most-developed countries had 18% of the adult population and only 5% of adult HIV infection/AIDS cases.

Children

Country-specific child HIV seroprevalence (cases per 10^5 children) ranged from 0.19 to 1540 for 159 countries with available data (data not shown). The mean child HIV seroprevalence was 80 for 116 developing countries and 11 for 43 developed countries. The mean prevalence for the 35 least-developed countries (237) was >22 times higher than that for the 43 most-developed countries. The child HIV seroprevalence for the 81 medium-developed countries was 43 and 61 without India and China.

The global distribution of children and children living with HIV infection/AIDS was also related to human development and had even more disparity than the adult distribution (Fig. 1). The 35 least-developed countries, with 19% of the world's child population, had 66% of the total child cases. The 79 medium-developed countries, excluding India and China, had 45% of the child population and 22% of children living with HIV infection/AIDS. India, with 7% of the child population, had 6.6% of cases. China, with nearly 7% of the child population, reported only 0.2% of cases. The 43 most-developed countries had 22% of the child population and only 5.5% of child cases.

Developing Countries

Geography and Religion

For developing countries, both geographic region and predominant religion were independently associated with adult HIV seroprevalence ($P < 0.001$). Although HIV seroprevalences differ significantly across the region, Africa had the highest adult HIV seroprevalence with an average of 6700 (Table 2). Latin America and the Caribbean and Asia had the next highest adult seroprevalences with 593 and 346, respectively. The mean adult HIV seroprevalence for developing countries in Europe (292) was slightly less than the mean seroprevalence for all developed countries. The mean adult HIV seroprevalence for the Middle Eastern region (10) was nearly 700 times lower than the average for the African region.

The distribution of the mean adult HIV seroprevalence differed significantly between predominant religions (Table 3). Countries whose predominant religion was classified as indigenous African, all of which are located in sub-Saharan Africa, had a mean adult seroprevalence of 5893. Predominantly Christian countries, with an average of 3074, had the second highest average seroprevalence. Predominantly Muslim and Hindu countries had mean adult seroprevalences of 1086 and 691, respectively. Predominantly Buddhist countries had the lowest mean seroprevalence (247), although this increased to 1197 without inclusion of China.

Univariate Analyses

Associations between HIV seroprevalence and other variables are presented in Table 4 together with comparisons

TABLE 2. Mean Adult HIV Seroprevalence Weighted by Adult Population for Developing Countries by Geographic Region

Geographic Region	No. Countries	Mean HIV Seroprevalence*	Minimum, Maximum
Africa	49	6700	20, 35,800
Southern Africa	8	19724	13,220, 35,800
Eastern Africa	12	9688	80, 15,960
Central Africa	8	5474	510, 13,840
Western Africa	15	4620	520, 10,760
Northern Africa	6	195	20, 990
Latin America and the Caribbean	22	593	30, 5170
Caribbean	5	2041	30, 5170
Central America	8	489	200, 2010
South America	9	484	100, 3010
Asia and Pacific Islands	29	346	5, 4040
Southeast Asia	8	637	50, 4040
Southcentral Asia	6	605	5, 700
Without India	5	58	5, 290
India	1	700	—
Pacific	2	197	70, 220
East Asia	3	69	5, 70
Without China	2	5	5, 5
China	1	70	—
West Asia	10	63	5, 100
Europe	13	292	5, 960
Eastern Europe	8	315	10, 960
Southern Europe	5	55	5, 100
Middle East	9	10	5, 110

Seroprevalences per 100,000 adults aged 15–49 years were obtained from 2000 estimates of the Joint United Nations Programme on HIV/AIDS.

*$P < 0.0001$ by 1-way analysis of variance for major geographic regions.

between developing countries with the lowest (≤100) versus the highest (>1500) HIV seroprevalence. Countries with more years since the beginning of the HIV/AIDS epidemic had higher HIV seroprevalences.

Less-developed countries, as measured by the Human Development Index rank, had significantly higher HIV seroprevalences. Of the 3 variables used to calculate "human development," longer life expectancy was significantly associated with lower HIV seroprevalences; high educational attainment and gross national product per capita were both higher in the low HIV seroprevalence countries and showed trends toward significance. However, associations between HIV and life expectancy are partially explained by recalculations of life expectancies to reflect increasing HIV seroprevalence in many developing countries. Of other development indicators, more human development, such as access to safe water, was generally associated with lower HIV seroprevalences.

Of sexual behavior variables, more polygamy and higher divorce rates appeared strongly related to higher HIV seroprevalence, with limited observations. Countries with earlier ages at female sexual debut, more births to women younger than 20 years of age, higher total fertility, and more females having nonregular sexual partners had significantly higher

TABLE 3. Mean Adult HIV Seroprevalance Weighted by Adult Population for Developing Countries by Predominant Religion

Predominant Religion	No. Countries	Mean HIV Seroprevalence*	Minimum, Maximum
Indigenous African	10	5893	150, 35,800
Christian	55	3074	5, 25,250
Muslim	43	1086	5, 11,750
Hinduism	4	691	80, 1260
Buddhism	10	247	5, 4040

Seroprevalences per 100,000 adults aged 15–49 years were obtained from 2000 estimates of the Joint United Nations Programme on HIV/AIDS.

*$P < 0.001$ by 1-way analysis of variance for major predominant religions.

TABLE 4. Univariate Regression Analyses of the Relationship Between Independent Variables and Natural Log of Adult HIV Seroprevalence (Cases per 10^5 Adults) (or Child HIV Seroprevalence [Cases per 10^5 Children]) for Relationships to Reproductive Health Variables Only) for All Developing Countries and Comparison of Mean Values for Independent Variables Between Developing Countries with Low (≤100 Cases Versus High (>1500) Seroprevalence

	All Developing Countries			Developing Countries With Low Seroprevalence		Developing Countries With High Seroprevalence	
Variable	**No.**	**Coefficient**	**R^2***	**No.**	**Mean†**	**No.**	**Mean†**
Age of the HIV/AIDS epidemic by country (y)	99	0.27	**0.077**	37	14.2	38	14.9
Development							
Human development index rank‡	117	0.028	**0.17**	41	**103**	45	**138**
Urban population with access to safe water (%)	115	−0.063	*0.090*	38	**93**	46	**82**
Rural population with access to safe water (%)	113	−0.025	0.065	38	**71**	45	**48**
Rural population with access to adequate sanitation (%)	111	−0.012	0.024	41	*39*	43	*50*
Male unemployment rate (%)	55	0.043	0.022	28	4.6	8	4.6
Female unemployment rate (%)	55	0.030	0.020	28	5.9	8	6.1
Urban population with access to adequate sanitation (%)	113	−0.011	0.0051	41	77	43	80
Sexual behavior							
Divorces (% of marriages)	21	0.063	**0.84**	16	16.0	0	—
Polygamy (% of marriages)	34	0.083	**0.42**	4	**4**	25	**28**
Female age at first sexual intercourse (y)	51	−0.57	**0.29**	9	**20.3**	28	**17.8**
Births to mother younger than 20 years (%)	56	0.16	**0.22**	29	**9.4**	7	**12.4**
Total fertility rate (births/woman)	122	0.58	**0.20**	45	**2.5**	46	**5.1**
Females with nonregular sex partners (%)	35	0.15	**0.20**	5	**2.6**	22	**8.4**
Females using condoms with nonregular sex partners (%)	20	0.032	0.14	1	33.4	11	31.3
Female age at first birth (y)	59	−0.27	0.052	15	20.8	28	20.0
Female age at first without Bangladesh (y)	58	−0.62	**0.23**	14	**21.5**	28	**20.0**
Males using condom with nonregular sex partners (%)	31	−0.012	0.021	5	**55**	17	**31**
Female age at first marriage (y)	62	−0.095	0.011	16	18.6	29	18.3
Female age at first marriage without Bangladesh (y)	61	−0.33	**0.12**	15	**19.5**	29	**18.3**
Male age at first sexual intercourse (y)	18	−0.052	0.0071	3	*26.0*	10	*17.5*
Males with nonregular sex partners (%)	38	−0.0028	0.0007	6	19.3	23	20.5
Reproductive health							
Married women using any contraception (%)	103	−0.054	**0.35**	38	**64**	39	**23**
Married women using modern contraception (%)	96	−0.049	**0.31**	33	**59**	38	**18**
Infant mortality rate (deaths/1000)	116	0.041	**0.31**	45	**49**	46	**97**
Babies exclusively breast-fed during first 4 months (%)	96	−0.050	**0.20**	37	**51**	41	**28**
Infants with low birth weight (%)	96	0.078	**0.14**	36	**10.9**	38	**14.7**
Babies breast-fed in the first hour of life (%)	60	0.049	*0.13*	19	**20**	24	**41**
Duration of only breast-feeding or providing water (mo)	59	0.27	**0.11**	15	*5.1*	28	*6.9*
Births attended by skilled personnel (%)	111	−0.027	0.089	44	**59**	44	**42**
Married women using oral contraception (%)	94	−0.077	0.072	30	7.7	39	5.5
Married women using oral contraception without China (%)	93	−0.12	**0.19**	29	**12.3**	39	**5.5**
Pregnant women with ≥2 tetanus toxoid immunizations (%)	86	0.017	0.043	27	38	42	48

TABLE 4. *(continued)* Univariate Regression Analyses of the Relationship Between Independent Variables and Natural Log of Adult HIV Seroprevalence (Cases per 10^5 Adults) (or Child HIV Seroprevalence [Cases per 10^5 Children]) for Relationships to Reproductive Health Variables Only) for All Developing Countries and Comparison of Mean Values for Independent Variables Between Developing Countries with Low (≤100 Cases Versus High (>1500) Seroprevalence

	All Developing Countries			Developing Countries With Low Seroprevalence		Developing Countries With High Seroprevalence	
Variable	**No.**	**Coefficient**	**R^2***	**No.**	**Mean†**	**No.**	**Mean†**
Duration of breast-feeding (mo)	59	0.029	0.0043	15	20.7	28	20.2
Pregnant women with ≥1 antenatal visit (%)	105	−0.0048	0.0016	39	69.3	45	70.1
Infectious disease							
Herpes simplex virus 2 seroprevalence (/100 adult females)	25	0.12	**0.64**	5	**26**	14	**48**
Cervical cancer incidence (/10^5 women)	121	0.090	**0.41**	44	**10**	46	**31**
Tuberculosis (cases/10^5)	117	0.016	**0.25**	41	**46**	45	**109**
Malaria (cases/10^5)	67	0.00021	**0.091**	22	**94**	25	**3207**
Hepatitis C prevalence (/100 adults)	81	−0.10	0.022	23	3.6	30	3.9
Health service							
Male disability-adjusted life expectancy (y)	122	−0.17	**0.49**	45	**59.4**	46	**41.1**
Male life expectancy (y)	122	−0.17	**0.47**	45	**66.4**	46	**49.4**
Female disability-adjusted life expectancy (y)	122	−0.13	**0.39**	45	**61.2**	46	**42.2**
Female life expectancy (y)	122	−0.14	**0.39**	45	**69.3**	46	**51.3**
Cigarette consumption no./year/adult)	87	−0.0014	**0.36**	32	**1531**	30	**517**
Population with access to essential medications (%)	114	−0.044	**0.32**	39	**81**	44	**56**
Younger than age 5 mortality rate (deaths/1000)	122	0.021	**0.29**	45	**57**	46	**143**
Children fully immunized for polio (%)	122	−0.048	**0.23**	45	**89**	46	**59**
Children fully immunized for measles (%)	121	−0.042	**0.20**	45	**87**	46	**58**
Children fully immunized for diphthoria and tetanus toxoids and pertussis (%)	122	−0.042	**0.19**	45	**88**	46	**59**
No. doctors (/10^5)	119	−0.0077	**0.16**	44	**135**	44	**21**
Children fully immunized for tuberculosis (%)	118	−0.046	**0.14**	43	**91**	46	**71**
Overall health system performance rank	122	0.015	0.079	45	**120**	46	**154**
No. nurses (/10^5)	118	−0.0019	0.039	44	*141*	43	*84*
No. midwives (/10^5)	61	0.00048	0.0001	23	19	25	30
Economic							
Gini index‖	79	0.082	**0.11**	24	**38.5**	29	**45.3**
External debt (US $ × 10^6)	121	−0.0000057	0.043	45	**113**	45	**22**
Gross national product measured at purchasing parity power (US $/capita)	106	−0.00020	0.036	37	**3211**	41	**2257**
Public spending of total health expenditures (%)	122	−0.020	0.035	45	41.3	46	46.5
Gross domestic product spent on health (%)	122	0.27	0.033	45	4.3	46	4.2
Total public expenditures spent on health (%)	122	−0.075	0.024	45	10.1	46	9.4
Public expenditures on health (international $/capita)	122	−0.0034	0.019	45	64	46	48
Gross domestic product (US $/capita)	122	−0.00016	0.014	45	1055	46	868
Total (private and public) spending on health (international $/capita)	122	−0.0014	0.0078	45	*143*	46	*98*
Public spending on health at official exchange rate (US $/capita)	122	−0.0017	0.0015	45	21.4	46	22.3
Total spending on health at official exchange rate (US $/capita)	122	0.00059	0.0006	45	44.3	46	49.9

TABLE 4. *(continued)* Univariate Regression Analyses of the Relationship Between Independent Variables and Natural Log of Adult HIV Seroprevalence (Cases per 10^5 Adults) (or Child HIV Seroprevalence [Cases per 10^5 Children]) for Relationships to Reproductive Health Variables Only) for All Developing Countries and Comparison of Mean Values for Independent Variables Between Developing Countries with Low (≤100 Cases Versus High (>1500) Seroprevalence

	All Developing Countries			Developing Countries With Low Seroprevalence		Developing Countries With High Seroprevalence	
Variable	**No.**	**Coefficient**	**R^2***	**No.**	**Mean†**	**No.**	**Mean†**
Education							
Male adult illiteracy rate (%)	118	0.041	*0.10*	43	**14**	44	**25**
Female adult illiteracy rate (%)	118	0.020	0.051	43	**29**	44	**39**
Total schooling for females (y)	51	0.083	0.011	20	8.9	18	7.8
Total schooling for males (y)	51	−0.068	0.0056	20	10.0	18	8.3
Population							
Crude birth rate (/1000 population)	122	0.093	**0.21**	45	**22**	46	**37**
Females between 15 and 49 years of age (%)	122	−0.22	**0.20**	45	**51.5**	46	**47.3**
Population between 15 and 59 years of age (%)	122	−0.17	**0.20**	45	**62.0**	46	**53.4**
Population younger than age 25 (%)	122	0.08	**0.16**	45	**46.6**	46	**61.3**
Median age of population (y)	122	−0.13	**0.13**	45	**25.4**	46	**18.7**
Males older than age 60 (%)	122	−0.22	**0.086**	45	**8.0**	46	**5.0**
Population annual growth rate (%)	122	0.64	**0.083**	45	**1.3**	46	**2.2**
Population sex ratio (males/100 females)	122	−0.087	0.051	45	**100.6**	46	**98.3**
Females older than age 60 (%)	122	−0.10	0.049	45	**9.5**	46	**5.9**
Population urban (%)	122	−0.016	0.026	45	**39.0**	46	**33.4**
Population density (population/km^2)	122	−0.00085	0.0055	45	**131**	46	**62**
Religion							
Population predominantly Muslin (%)	108	−0.018	*0.13*	41	36	41	28
Population predominantly Muslin without China (%)	107	−0.032	**0.36**	40	**77**	41	**28**
Population predominantly Christian (%)	108	0.020	**0.11**	41	**6**	41	**38**
Population predominantly Christian without India (%)	107	0.028	**0.23**	41	**6**	41	**38**
Male circumcision¶							
Categorical males circumcised (%)	119	−0.45	0.043	43	1.8	46	2.0
Categorical males circumcised without China (%)	118	−0.91	**0.17**	42	**2.8**	46	**2.0**

All 122 developing countries are included, but the observations were limited for most variables. The column heading "No." in the first numerical column refers to the number of countries included in linear regression analyses. The column heading "No." in the fourth and sixth numerical columns refer to the number of countries included in comparisons between low and high HIV seroprevalence, respectively.

*Bold values were statistically significant ($P < 0.05$). Italic values had P values between 0.05 and 0.10.

†Mean values in bold were statistically significantly different ($P < 0.05$). Mean values in italics differed, with P values between 0.05 and 0.10.

‡Measures a country's level of human development on the basis of life expectancy, educational attainment, and adjusted real income. Lower rank numbers signify more human development.

§Reproductive health variables were analyzed with child HIV seroprevalence as the dependent variable.

‖A measure of income inequality, where higher coefficients signify greater income inequality.

¶Categories of male circumcision were as follows: 1, ≤20%; 2, 20–80%; 3, ≥80%.

HIV seroprevalences. Initial analyses suggested that HIV seroprevalence was not significantly higher in countries with younger female age at first marriage or first delivery. However, the associations between rates of HIV infection and younger female ages at first marriage and at first delivery became significant in subanalyses that excluded Bangladesh, which has a low HIV prevalence and extremely young women entering marriage and motherhood. Countries with the highest HIV seroprevalence also had a 3-fold higher percentage of females with nonregular sex partners than did countries with lowest HIV seroprevalences and had a smaller percentage of males using condoms with nonregular sex partners.

For reproductive health measures (Table 4), analyses were conducted with child HIV seroprevalence as the dependent variable. Contraception was associated with lower HIV seroprevalences both for children (Table 4) and for adults (women using any contraception: coefficient = −0.041, R^2 = 0.26, $P \leq 0.001$; women using modern contraception: coefficient = −0.034, $R^2 = 0.21$, $P \leq 0.001$). Countries with low HIV seroprevalence generally had lower infant mortality rates and fewer infants with low birth weights. Countries with more frequent reports of exclusive breast-feeding during a child's first 4 months had lower HIV seroprevalences among children, while countries with more breast-feeding in the first hour after birth and longer duration of breast-feeding had higher child HIV seroprevalences.

Of infectious disease variables, herpes simplex virus 2 seroprevalence, cervical cancer incidence, and tuberculosis prevalence were associated with HIV seroprevalence; this association was significantly higher for countries with the highest HIV seroprevalences. Few countries had type-specific herpes simplex virus 2 serologic data, but they were evenly distributed and not geographically limited. Countries with the highest HIV seroprevalence had higher prevalences of malaria, which was itself highly correlated with geographic region.

Almost all indicators of better health services in Table 4 were significantly associated with lower HIV seroprevalence. Countries with more access to essential medications, lower child mortality rates, and better delivery of health services had lower HIV seroprevalences.

For economic variables, countries with more income inequality, as measured by the Gini index, had significantly higher HIV seroprevalences. Countries with the highest HIV seroprevalences had lower gross national products and tended to spend less on health per capita.

Although none of the education indicators were significantly associated with HIV seroprevalence, countries with the highest HIV seroprevalence had more illiterate adult males and females than countries with high seroprevalence and tended to have less total schooling.

Of population indicators, higher HIV seroprevalences were associated with higher birth rates, population growth rate, younger population median age, and larger percentages of population younger than 25 years of age.

All religious variables had strong associations with HIV prevalence in subanalyses, when excluding India and China, which are neither predominantly Muslim nor predominantly Christian. Countries with large Muslim populations had substantially lower HIV seroprevalences, whereas those with large Christian populations had generally higher HIV seroprevalences.

Male circumcision was not significantly associated with HIV seroprevalence when including China, which had low male circumcision practice and low HIV seroprevalence. However, subanalyses excluding China showed that countries with >80% of males circumcised had significantly lower HIV seroprevalence than countries with <20% of males circumcised. This association was not independent of religion, sexual practices, or other confounders and was not established as causal.

Multivariate Model

In the multivariate model, higher HIV seroprevalences were associated with a lower percent of males circumcised, older HIV epidemics, geographic region, and younger populations, (percent of population younger than 25 years of age) (Table 5). The relationship between HIV and female adult illiteracy changed from a positive to a negative correlation coefficient in the multivariate model. HIV seroprevalence was negatively associated with the number of doctors and the percentage of children fully immunized for diphtheria and tetanus toxoids and pertussis, suggesting better health services in general are associated with lower seroprevalences and lower HIV

TABLE 5. Analysis of Covariance Model of the Relationship Between Independent Variables and the Natural Log of HIV Seroprevalence for All Developing Countries

	All Developing Countries	
Variable*	**Coefficient**	***P***
Categorical males circumcised† (%)	−1.5	<0.001
Age of the HIV/AIDS epidemic by country (y)	0.32	<0.001
Geographic region		<0.001
Eastern/Southern Europe	1.5	0.17
Africa	1.1	0.019
Asia	Reference	
Middle East	−1.7	<0.001
Latin America	−1.8	<0.001
Population younger than age 25 (%)	0.11	<0.001
Female adult illiteracy rate (%)	−0.020	<0.001
Children fully immunized for diphtheria, tetanus, and pertussis (%)	−0.023	<0.001
No. of doctors (/10^5	−0.0039	0.021

Variables ranked by analysis of variance R^2. Number of observations, 89; $P < 0.0001$; $R^2 = 0.84$.

*Variables eliminated from the model because of nonsignificance were the following: total fertility rate, married women using any contraception, births attended by skilled personnel, percent of population younger than age 15, percent of population between 15 and 24 years of age, urban population with access to safe water, gross national product measured at purchasing parity power, population with access to essential medications, and predominant religion.

†Because of close colinearity between male circumcision and Muslim religion, only male circumcision, which fit better with other variables, was selected for the model.

seroprevalences. These 7 variables accounted for 84% of variations in adult HIV seroprevalence for the 89 countries included in the multivariate model. These 89 countries did not appear systematically different from the 33 countries excluded because of missing information. Variables with fewer observations showed no trend toward significance when included in the full model.

DISCUSSION

Both geography and religion were independently associated with adult HIV seroprevalence for 122 developing countries. In Africa, HIV seroprevalence was 10–20 times higher than those in Latin America, Asia, and Europe and 67 times higher than that in the Middle East. Middle Eastern and predominantly Buddhist countries tended to have the lowest seroprevalences, while African and predominantly indigenous African and Christian countries generally had the highest seroprevalences. After excluding China, male circumcision prevalence and higher percentages of Muslim populations had colinearity; both were associated with lower HIV seroprevalences. Countries with the highest HIV seroprevalence tended to have older HIV epidemics, younger female ages at sexual debut and first delivery, higher total fertility, and more women with nonregular sex partners. The associations of lower child HIV seroprevalence with more exclusive breast-feeding in the first 4 months and with shorter total duration of breast-feeding are consistent with observational studies,[33,34] but these relationships may have residual confounding and should not be interpreted as causal. Contraception use by married women was associated with lower HIV seroprevalences among children. Countries with high HIV seroprevalences had 2-fold higher herpes simplex virus 2 seroprevalence and 3-fold higher cervical cancer incidence among women. Almost all health service measures were positively associated with lower HIV seroprevalences, and countries with low HIV seroprevalence generally had longer life expectancies, less child mortality, more immunization coverage, and better access to essential medications and health care personnel. Of economic spending measures, greater income inequality but not less health spending was associated with higher HIV seroprevalences. Countries with high HIV seroprevalence tended to have younger more illiterate populations with less access to safe water. The multivariate model indicated that countries with more male circumcision, younger HIV/AIDS epidemics, and a lower percentage of the population younger than 25 years of age had lower HIV seroprevalences.

A previous ecologic analysis by Over[35] of HIV seroprevalence among urban high-risk and low-risk groups using data from the US Census Bureau examined 13 variables for 72 developing countries. This study found that age of the epidemic, gross national product per capita, and Gini index were most strongly correlated with HIV seroprevalence after adjusting for other variables, while male circumcision, condom availability, and public health expenditures as a percent of the gross national product had no significant relation to HIV seroprevalence. Because this study found a significant relationship of HIV seroprevalence with educational disparity between sexes, we also examined the sex gap in illiteracy and years of schooling but found no association with adult HIV seroprevalence (data not presented). Our study differed from the study by Over by using more recent Joint United Nations Programme on HIV/AIDS data (1997 vs. 2000), including 70% more countries, utilizing country-level HIV seroprevalence estimates from the Joint United Nations Programme on HIV/AIDS instead of estimated rates for urban high- and low-risk populations that were published by the US Census Bureau, and analyzing additional variables.

Ecologic studies have several limitations. First, although ecologic analyses can describe population-level rates of disease occurrence in relation to population-level socioeconomic and developmental patterns, they cannot estimate individual risk or causal associations, because variables are not measured at the individual level and the temporal sequence of events is unknown.[36] Second, HIV seroprevalences reflect exposures that may have occurred several years earlier, and those analyses do not reflect how behavioral, economic, and demographic measures may have changed during this time. Third, validity of country-level data varies, and some data, such as those describing sexual behaviors, were not recorded for many countries, particularly countries in the Middle East. Where reliable data on male circumcision were lacking, prevalence of circumcision for some countries was estimated by examining the percentage of a country's population that was Muslim; the percentage of Muslims and circumcision rates were not independent. Finally, our analysis could not include measures of several key potential influences on the HIV/AIDS epidemic, such as characteristics of sexual networks, injection drug use, unsafe injections, and male homosexual behaviors. Nonetheless, findings from this ecologic analysis can help to inform decisions concerning needs for additional data, allocation of health care resources, and design of prevention programs.

This study highlights potential contributions of several behavioral and biologic factors that help determine differences in HIV seroprevalence between developing countries. Our ecologic analyses support observations from a systematic comparison of population-level data from 4 African cities,[37–39] which suggested that differences in the rate of genital herpes and male circumcision explain much of the differences in HIV seroprevalence between the cities. A recent reanalysis of the 4-city data found that the reported number of lifetime partners and male circumcision were the main independent predictors of regional variations in the prevalence of HIV infection.[40] In addition, our analysis suggests the potential independent importance of several other behavioral, economic, and development factors. Our findings that countries with high HIV seroprevalence have higher proportions of women with nonregular

sex partners and fewer proportions of men using condoms with nonregular partners are consistent with the examples of countries such as Thailand, Uganda, and Zambia, which have had reductions in the incidence of HIV infection concurrently with apparent reductions in such sexual behavior risks.[41–44]

In conclusion, ecologic analyses of existing data portray a complex set of sociobehavioral, economic, developmental, and biologic factors as potential determinants of HIV seroprevalence in developing countries. Although these findings may not provide many new insights into risk factors for HIV infection, global ecologic analyses reinforce previous observations based on individual-level analyses of HIV risk determinants. These analyses also illustrate the wealth of ecologic data available that could be used in conjunction with more detailed studies of individuals of high-risk, low-risk, and bridge populations using multilevel analyses of risk determinants for HIV infection. In addition, the finding of fewer births attended by skilled personnel, but more midwives, in countries with high HIV seroprevalence suggests both challenges and feasible channels for reducing mother-to-child transmission of HIV. Finally, the fact that countries with the highest HIV seroprevalences tended to have lower total health expenditure, had fewer nurses and doctors, and provided more limited access to essential medications highlights the challenges in providing antiretroviral therapy to HIV-infected patients in developing countries.

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Appendix 1. List of Primary Data Sources With Web Site and Defined Variables

Organization	Source; Web Site	Variables
Joint United Nations Programme on HIV/AIDS	Report on the Global HIV/AIDS Epidemic June 2000; www.unaids.org/epidemic%5Fupdate/report/index.html#full	Males and females with nonregular sex partners (percent of adult men/women with at least 1 nonregular partner in last 12 months); males and females using condom with nonregular sex partner (percent of adult men/women who reported condom usage with a nonregular sex partner); HIV seropravalence (per 100,000 adults) at end of 1999.
	Report on the Global HIV/AIDS Epidemic June 1998	Age of the HIV/AIDS epidemic for each country (year that the first case of HIV infection or AIDS was reported by the country).
	Sexual Behaviour and AIDS in the Developing World	Male and female age at first sexual intercourse (among men/women aged 20–49); female age at first marriage (among women aged 25–49); males and females with nonregular sex partners (percent of adult men/women with at least 1 nonregular partner in last 12 months); polygamy (percent of married women aged 20–49 in a marriage with at least 1 other wife).
United Nations Development Programme	Human Development Report 2000; www.undp.org/hdro/	Total births to women younger than age 20 (percent) 1993–1998; human development index rank; divorces (as percent of marriages) 1996.
	Human Development Report 2001; www.undp.org/hdro/	Percent of population with access to essential drugs 1999; tuberculosis and malaria (cases per 100,000 estimated for 1997 and 1998); cigarette consumption (average annual number of cigarettes consumed per adult between 1992 and 1998); percent of infants with low birth weight 1995–1999.
United Nations Statistics Division	United Nations Statistics Division 2001; www.un.org/Depts/unsd/	Females using any contraception (percent of married women aged 15–49 using any method of contraception); females using modern contraception (percent of married women aged 15–49 using modern method of contraception); gross domestic product (per capita in US $ for

		1998); male/female unemployment rate (percentage of males and females who are unemployed): population younger than age 15 (percent); male/female population older than age 60 (percent) 2000; male and female adult illiteracy rate (percent of adult males/females aged 15 or older who are illiterate) 2000; male and female expected number of years of formal schooling; urban/rural population with access to safe water (percent): urban/rural population with access to adequate sanitation (percent) 2000; percent of population urban.
United Nations Children's Fund	The State of the World's Children 2000; www.unicef.org/sowc00/	Children immunized for tuberculosis, dipththeria and tetanus toxoids and pertussis, polio, and measles (percent of 1-year-old children fully immunized between 1995 and 1998); infant mortality rate (per 1000 births estimated for 1998); child mortality rate (younger than age 5 mortality rate per 1000 births estimated for 1998).
World Health Organization	World Health Report 2000; www.who.int/whr/	Male and female life expectancy (years of life expectancy at birth estimates for 1999); overall health system performance rank.
	World Health Report 2001; www.who.int/whr/	Percent of gross domestic product spent on health (expenditures on health as a percent of gross domestic product); percent of total expenditures on health (public expenditure as percent of total expenditure on health); percent of total public expenditure on health (public expenditure on health as percent of total public expenditure); total and public spending on health at official exchange rate (US $); total and public spending on health (expenditures on health per capita in international $).
	World Health Organization Statistical Information Systems, 2001; www3.who.int/whosis	Rates of physicians, nurses, and midwives per 100,000 population.
	World Health Organization	Hepatitis C virus infection rates (percent of population) as of June 1999.
	Health Life Expectancy Rankings, WHO Press Release 2000	Male and female disability-adjusted life years (years of disability-adjusted life expectancy at birth).
United Nations Population Division	World Population Prospects The 2000 Revision; www.un.org/esa/population/publications/wpp2000	Percent of population younger than age 15; percent of population between ages 15 and 24; percent of population between ages 15 and 59; percent of population older than age 60; total, male, and female population; population sex ratio (males per 100 females); percent of women between ages 15 and 49; median age for total population; total fertility rate 1995–2000; population density (per km^2); population growth rate (%); crude birth rate (per 1000 population).

Macro International	Demographic and Health Surveys; www.measuredhs.com/data/indicators	Female age at first sexual intercourse (among women aged 20–49); female age at first marriage (among women aged 25–49); female age at birth of first child (among women aged 25–49); polygamy (percent of married women aged 20–49 in a marriage with at least 1 other wife); mean duration of breast-feeding in months; mean duration of only breast-feeding or providing water.
World Bank	World Development Indicators 2000; www.worldbank.org/poverty/wdrpoverty/index.htm	Gini index
	World Development Report 2000/2001; www.worldbank.org/poverty/wdrpoverty/index.htm	Gross national product measured at purchasing parity power per capita 1999.
International Agency for Research on Cancer	GLOBOCAN 2000 database; www-dep.iarc.fr/globocan/globocan.html	Annual cervical cancer incidence and mortality rates (per 100,000 females) and prevalence estimates for the year 2000; classification of countries by geographic region.
Save the Children	State of the World's Newborns 2001.	Percent of pregnant women with at least 1 antenatal visit 1995–1999; percent of pregnant women with at least 2 tetanus toxoid immunizations 1997–1999; percent of births attended by skilled personnel 1995–2000; percent of babies breast-fed in the first hour of life 1995–1999; percent of babies aged 0–4 months exclusively breast-fed (24-hour recall) 1995–1999.
US Central Intelligence Agency	World FActbook 2001; www.cia.gov/cia/publications/factbook/index.html	Predominant religion; percentages of people predominantly Christian and Muslim; external debt.
Johns Hopkins University	Population Report 2000; www.jhuccp.org/pr/a9edsum.stm	Females using oral contraceptives (percent of married women aged 15–49 using oral contraception).
Other publication	Smith and Robinson[26]	Herpes simplex virus 2 seroprevalence among females.
Unpublished data	Halperin and Bailey	Categorized percent of males circumcised (low [<20%], medium [20–80%], or high [>80%]).