# Ecological and individual level analysis of risk factors for HIV infection in four urban populations in sub-Saharan Africa with different levels of HIV infection

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**Objective:** To identify factors that could explain differences in rate of spread of HIV between different regions in sub-Saharan Africa.

**Design:** Cross-sectional study.

**Methods:** The study took place in two cities with a relatively low HIV prevalence (Cotonou, Benin and Yaoundé, Cameroon), and two cities with a high HIV prevalence (Kisumu, Kenya and Ndola, Zambia). In each of these cities, a representative sample was taken of about 1000 men and 1000 women aged 15–49 years. Consenting men and women were interviewed about their socio-demographic background and sexual behaviour; and were tested for HIV, herpes simplex virus type 2 (HSV-2), syphilis, *Chlamydia trachomatis* and *Neisseria gonorrhoea* infection, and (women only) *Trichomonas vaginalis*. Analysis of risk factors for HIV infection was carried out for each city and each sex separately. Adjusted odds ratios (aOR) were obtained by multivariate logistic regression.

**Results:** The prevalence of HIV infection in sexually active men was 3.9% in Cotonou, 4.4% in Yaoundé, 21.1% in Kisumu, and 25.4% in Ndola. For women, the corresponding figures were 4.0, 8.4, 31.6 and 35.1%. High-risk sexual behaviour was not more common in the high HIV prevalence cities than in the low HIV prevalence cities, but HSV-2 infection and lack of circumcision were consistently more prevalent in the high HIV prevalence cities than in the low HIV prevalence cities. In multivariate analysis, the association between HIV infection and sexual behavioural factors was variable across the four cities. Syphilis was associated with HIV infection in Ndola in men [aOR = 2.7, 95% confidence interval (CI) = 1.5–4.9] and in women (aOR = 1.7, 95% CI = 1.1–2.6). HSV-2 infection was strongly associated with HIV infection in all four cities and in both sexes (aOR ranging between 4.4 and 8.0). Circumcision had a strong protective effect against the acquisition of HIV by men in Kisumu (aOR = 0.25, 95% CI = 0.12–0.52). In Ndola, no association was found between circumcision and HIV infection but sample sizes were too small to fully adjust for confounding.

**Conclusion:** The strong association between HIV and HSV-2 and male circumcision, and the distribution of the risk factors, led us to conclude that differences in efficiency of HIV transmission as mediated by biological factors outweigh differences in sexual behaviour in explaining the variation in rate of spread of HIV between the four cities.



AIDS 2001, **15** (suppl 4):S15–S30

**Keywords: HIV, sub-Saharan Africa, cross-sectional study, male circumcision, herpes simplex virus type 2, risk factors, HIV spread, ecological study, sexually transmitted infections, sexual behaviour**

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## Introduction

By the end of the year 2000, an estimated 36.1 million people were living with HIV worldwide [1]. Of these, 70% were living in sub-Saharan Africa, which houses about 10% of the world's population. It has been estimated that 8.8% of adults in sub-Saharan Africa are infected with HIV and that 90% of these infections are acquired through sexual intercourse between men and women. However, the burden of the HIV/AIDS epidemic is not equally distributed over the continent: the prevalence of HIV infection is generally higher in East and South Africa than in West and Central Africa [2]. The general objective of the multicentre study on factors determining the differential spread of HIV in four African cities was to identify factors that could explain differences in prevalence of HIV infection between different regions in sub-Saharan Africa. The study was conducted in two cities with a high HIV prevalence (Kisumu, Kenya and Ndola, Zambia) and two cities with a relatively low HIV prevalence (Cotonou, Benin and Yaoundé, Cameroon). There is evidence that the differences in prevalence between these four cities are due to differences in rate of spread of HIV, rather than to differences in time since the start of the HIV epidemics [3].

Numerous studies have been conducted in sub-Saharan Africa on risk factors for HIV infection. These risk factors can be grouped into two categories, including sexual behavioural risk factors [4–9] and factors that influence the transmission of HIV during sexual intercourse [10]. The latter factors include, among others, classical sexually transmitted infections (STIs) [11], male circumcision [12], condom use and certain sexual practices, such as anal intercourse and possibly also 'dry sex' [10].

This paper first presents a comparison between the four cities of the distribution of factors that have been found in other studies to be risk factors for HIV infection, or that are believed to be associated with an increased risk of HIV. Following this, the association between these risk factors and HIV infection is explored at the individual level in men and women in the four cities. Factors found to be associated with an increased risk of HIV infection at the individual level and more prevalent in the two high HIV prevalence cities than in the two low HIV prevalence cities are likely to play a major role in explaining the differences in HIV prevalence between the four cities.

## Methods

The methods of the data collection and laboratory procedures are described in detail elsewhere and only a summary is given here [3]. In each of the four cities, a survey was conducted in the general population and among a random sample of sex workers. The surveys took place between June 1997 and March 1998. The aim was to collect data on a representative sample of 1000 men and 1000 women aged 15–49 years from the general population in each city. Households were selected by two-stage random sampling, and all eligible men and women in the selected households were asked to participate in the study. After giving their informed verbal consent, study participants were interviewed about their socio-demographic characteristics and sexual behaviour, using a standardized questionnaire [13]. The questionnaire on sexual behaviour included a section on characteristics of the spouse and of the non-spousal partnerships of the past 12 months (to a maximum of eight). Men were also interviewed about past and present symptoms suggestive of a STI and about their health-seeking behaviour. After the interview, study participants were asked to give a blood sample, which was tested for HIV, syphilis and herpes simplex virus type 2 (HSV-2), and a urine sample, which was tested for *Neisseria gonorrhoea* and *Chlamydia trachomatis* infection. Women were asked to insert a swab into the vagina, which was immediately inoculated into a culture medium for *Trichomonas vaginalis*.

### Statistical analysis

All data were double-entered and validated in EPI-INFO version 6.04a (CDC, Atlanta, Georgia, USA). Further data cleaning and data analysis was carried out with SPSS version 8.0 for Windows (SPSS, Inc., Chicago, Illinois, USA) and SAS (version 6.12; Cary, North Carolina, USA).

The analyses presented in this paper were restricted to men and women who reported that they had ever had sexual intercourse. In each of the four cities. almost all HIV infections were in respondents who reported sexual activity [14].

#### *Variables*

The socio-demographic variables examined included: age; educational attainment; having a job, as opposed to not having a job; having made more than one trip out of the city in the past 12 months; religion (Catholic, Protestant, Muslim or other); ethnic group; and alcohol consumption in the past month. In men, circumcision was also explored as a potential risk factor for HIV infection. Men were categorized as being circumcised on the basis of the clinical examination, but if no clinical examination was performed they were categorized as circumcised if they reported this in the interview.

The sexual behaviour characteristics that were explored as potential risk factors for HIV infection included: marital status, age at first sexual intercourse, residence in the city at age of first sex, lifetime number of sex partners, number of non-spousal partners in the past 12 months, one or more short-term partnerships (of less than 1 months duration) in the past 12 months, and sex in exchange for money. In men, contact with a female sex

worker in the past 12 months was also explored as a potential risk factor for HIV infection. The following partnerships were considered as contacts with sex workers: a relationship where money was always or often exchanged and the female partner was reported to exchange sex for money with others, or the female partner was reported to have 12 or more partners in the past 12 months. Risk factors that were specific for women included dry sex (always or often using something to dry or tighten the vagina before having sexual intercourse), sex during menstruation and taking hormonal contraception (the pill or injectable hormonal contraception).

The following STI-related risk factors were explored: HSV-2 infection, syphilis seroreactivity, *N. gonorrhoea* infection, chlamydial infection, trichomoniasis in women, abnormal genital examination in men (swollen inguinal lymph glands, or a genital ulceration or genital discharge, or swollen and tender scrotum), genital ulceration in men, an episode of genital ulceration in men in the past 12 months, and an episode of symptoms suggestive of urethritis in men in the past 12 months. If a man reported an episode of symptoms suggestive of a STI, he was asked where he had sought care for his problem and the distinction was made between the formal health sector (clinic, hospital or allopathic health worker) and the informal sector.

Two additional sets of variables were defined: one for married individuals, and one for men and women who reported non-spousal partnerships in the past 12 months. The additional variables for the married individuals included: age difference between spouses (in case of a polygamous marriage, the maximum value was taken for men), number of sex partners before marriage, interval between first sexual intercourse and first stable union, age at first marriage, polygamy, and HIV status of the spouse (if a man had more than one spouse, this variable was positive if at least one spouse was HIV-positive). For respondents who reported at least one non-spousal partnership in the past 12 months, the following additional variables were explored: age difference between non-spousal partners (if there was more than one non-spousal partner, the maximum value was taken), consistent condom use ('always' or 'most of the time') with all non-spousal partners in the past 12 months, having had a relationship with a partner who had at least two other partners in the past 12 months, and monthly number of episodes of sexual intercourse with non-spousal partners (more than four per month or less).

### *Ecological level analysis*

The distribution of the presented variables was compared between the four cities. If the difference between cities was statistically significant, then any differences between the two high HIV prevalence cities and the two low HIV prevalence cities were examined by comparing each high HIV prevalence city with each of the two low HIV prevalence cities. Of the four $P$ values thus obtained, only the highest value is presented. If that value was 0.05 or less, the difference between the two high HIV prevalence cities and the two low HIV prevalence cities was considered statistically significant. Differences in categorical variables were tested using the chi-square test, or Fisher's exact test if numbers were small. Differences in continuous variables were tested using the Kruskal–Wallis test. All reported $P$ values are two-tailed.

### *Individual level analysis*

Univariate and multivariate logistic regression was used to explore the associations between the variables and HIV infection, for each city and for men and women separately. The likelihood ratio test was used to assess the statistical significance of the associations, and odds ratios (ORs) and adjusted ORs (aORs) with their 95% confidence interval (CI) were calculated. Variables that were found to be associated with HIV infection after adjusting for age ($P \leq 0.1$) were included in the multivariate analyses. The final models were obtained using forward stepwise regression. The models were fitted in two stages as STI-related variables may be on the causal path between the socio-demographic and behavioural variables and HIV infection. First, the model was fitted with only the socio-demographic and behavioural variables, then the STI-related variables were added.

Separate models were constructed for various subgroups, including married men and women, men and women who reported non-spousal partnerships in the past year, men who had a STI in the past year, and men who underwent clinical examination. Because of the high HIV prevalence rates in young people and because HIV infections in the younger age groups are likely to have been acquired more recently than HIV infections in the older age groups, separate analyses were carried out on women aged 15–24 years and men aged 15–29 years.

### *Identification of key variables*

Factors were identified as key variables if they were found to be independent risk factors for HIV infection in at least one city, and if they were distributed differently between the two high HIV prevalence cities and the two low HIV prevalence cities. These factors are assumed to play an important role in explaining the differences in HIV prevalence between the four cities.

### *Attributable fractions*

To assess the relative importance of the risk factors associated with HIV infection in each city, the proportion of HIV cases attributable to the risk factor (population attributable fraction) was computed using the formula given by Bruzzi *et al.* [15]. This formula gives the estimated proportion of cases in a population attributable to a given risk factor. The relative risk was estimated using the adjusted prevalence ratio given by the log-binomial model [16,17].

### Ethical approval

Ethical approval for the study was obtained from the national ethical committee in each of the countries where the study took place, as well as from the ethical committees of the Institute of Tropical Medicine, Antwerp, the London School of Hygiene and Tropical Medicine, and The Population Council.

## Results

In Cotonou, 88% of men (896/1023) reported that they had ever had penetrative sexual intercourse; in Yaoundé, this percentage was 91% (889/980), in Kisumu it was 92% (765/828) and in it was Ndola 89% (642/720). The corresponding figures for women were 87% (953/1094), 91% (1020/1120), 91% (962/1060) and 88% (889/1010). The HIV prevalence among sexually active men was 3.9% in Cotonou, 4.4% in Yaoundé, 21.1% in Kisumu and 25.4% in Ndola (Table 1). The corresponding prevalence rates in women were 4.0, 8.4, 31.6 and 35.1% (Table 2). Among men aged 15–29 years, the prevalence was 3.8% ($n = 471$) in Cotonou, 1.9% ($n = 479$) in Yaoundé, 14.3% ($n = 342$) in Kisumu and 17.3% ($n = 301$) in Ndola. The HIV prevalence among women aged 15–24 years in the four cities was 4.5% ($n = 291$), 7.3% ($n = 384$), 33.7% ($n = 362$) and 34.9% ($n = 341$), respectively.

### Ecological level analysis

Tables 1 and 2 compare the characteristics of the study populations in the four cities. Men and women in the low HIV prevalence cities were more often Catholic or Muslim than men and women in the high HIV prevalence cities. Almost all men in Cotonou and Yaoundé were circumcised, whereas in Kisumu and Ndola only 30 and 9% of men, respectively, were circumcised. Women in the low HIV prevalence cities reported alcohol consumption in the past month more often than women in the high HIV prevalence cities.

Men and women in the high HIV prevalence cities tended to marry at an earlier age, and so the proportion ever married was higher in these cities than in Cotonou and Yaoundé. Women in the high HIV prevalence cities were more likely to have their sexual debut before age 15. The other sexual behavioural variables did not differ in a systematic way between the high HIV prevalence cities and the low HIV prevalence cities. Men and women in Yaoundé reported more lifetime sex partners and more non-spousal partners in the past 12 months than men and women in the other cities. Men in Yaoundé also reported one or more contacts with a sex worker in the past 12 months more often than men in the other cities.

Women in the high HIV prevalence cities were more likely to use hormonal contraception at the time of the interview than women in Cotonou and Yaoundé. The prevalence of HSV-2 infection, in both men and women, was higher in the high HIV prevalence cities than in the low HIV prevalence cities, as was the prevalence of trichomoniasis in women. The prevalence of the other STIs was not higher in the two high HIV prevalence cities than in the two low HIV prevalence cities.

When restricting these comparisons to the younger age range, the results were similar (data not shown).

### Individual level analysis

Tables 3 and 4 present the risk factors that were associated with HIV infection ($P \leq 0.1$) after adjusting for age in at least one city, and those that were distributed differently between the two high HIV prevalence and the two low HIV prevalence cities. Among men, the following factors were associated with an increased prevalence of HIV infection in all four cities (although the associations were not always statistically significant): older age, having a job, higher lifetime number of sex partners, HSV-2 infection, syphilis, abnormal genital examination or genital ulceration, and history of symptoms suggestive of a STI in the past 12 months. Being married or having been married was associated with an increased risk of HIV infection in all cities except Yaoundé. Being circumcised was associated with a statistically significant protective effect in Kisumu only.

Women in all four cities were more likely to be HIV infected if they reported one or more non-spousal partners in the past 12 months. Risk of HIV infection also increased with increasing number of lifetime sex partners and was higher in women with HSV-2 infection, syphilis or gonorrhoea. Trichomoniasis was associated with HIV infection in all cities except Ndola.

Married men and women were at greatly increased risk of HIV infection if the spouse was HIV-positive

Tables 5–8 present the multivariate models for HIV infection. Model 1 excludes STI-related factors that may be on the causal pathway for the effect of behavioural factors on HIV infection; model 2 includes these factors. The final models differ from one city to another but reveal a common pattern with regards to sexual behaviour and STIs. Being married or having been married was a risk factor for HIV infection among men in Kisumu (aOR = 2.0, 95% CI = 1.1–3.9) and Ndola (aOR = 2.3, 95% CI = 1.1–4.5), and in women in Kisumu (aOR = 2.5, 95% CI = 1.4–4.5) and Ndola (aOR = 2.3, 95% CI = 1.4–3.9), for the model excluding STIs. Rate of partner change (as measured by lifetime number of sex partners and number of non-spousal partners in the past 12 months) was a risk factor in most models for both men and women in Kisumu and Ndola, and also for women in Cotonou and Yaoundé. In Yaoundé, sex in exchange for money was a risk factor for women, while having a job was a risk factor for men.

**Table 1.** Characteristics of sexually active men

| | Low HIV prevalence sites | | High HIV prevalence sites | | |
|---|---|---|---|---|---|
| | Cotonou | Yaoundé | Kisumu | Ndola | Comparison[a] |
| **General population** | | | | | |
| *Background* | | | | | |
| Mean age (years) | 29.1 (892) | 28.8 (883) | 28.2 (765) | 30.0 (642) | Ov |
| Education | | | | | |
| Illiterate | 16.1% (886) | 3.1% (882) | 4.3% (764) | 5.1% (641) | Ov |
| Secondary level | 18.9% (891) | 34.0% (883) | 36.9% (765) | 41.9% (642) | Hi ($P = 0.24$) |
| Alcohol consumption in past month | 56.6% (892) | 59.5% (883) | 34.7% (764) | 67.0% (642) | Ov |
| Has a job | 74.5% (834) | 62.7% (860) | 77.0% (717) | 72.2% (604) | Ov |
| Made > 1 trip in the past 12 months | 46.3% (862) | 57.8 %(787) | 61.8% (685) | 24.2% (594) | Ov |
| Religion | | | | | |
| Protestant | 4.9% (892) | 22.8% (883) | 54.5% (765) | 58.7% (642) | Hi ($P = 0.000$) |
| Catholic | 61.1% (892) | 56.2% (883) | 29.4% (765) | 28.5% (642) | Lo ($P = 0.000$) |
| Muslim | 14.0% (892) | 12.9% (883) | 3.7% (765) | 1.1% (642) | Lo ($P = 0.000$) |
| *Circumcised* | 99.0% (890) | 99.2% (882) | 29.8% (763) | 9.0% (636) | Lo ($P = 0.000$) |
| *Sexual behaviour* | | | | | |
| Now married/has been married in the past | 49.2% (889) | 41.5% (880) | 60.6% (763) | 62.4% (639) | Hi ($P = 0.000$) |
| Age at first sex < 15 years | 10.5% (885) | 17.5% (878) | 28.4% (758) | 18.8% (624) | Hi ($P = 0.59$) |
| Resident in town at age of first sex | 65.2% (884) | 46.9% (878) | 46.2% (758) | 54.7% (623) | Ov |
| Contact with a commercial sex worker | 1.8% (892) | 9.4% (883) | 1.4% (765) | 3.0% (642) | Ov |
| At least one non-spousal partner in the past 12 months | 50.1% (892) | 73.2% (883) | 48% (765) | 35.8% (642) | Lo ($P = 0.40$) |
| Sex in exchange for money in the past 12 months | 7.5% (892) | 17.0% (888) | 9.4% (765) | 15.7% (642) | Ov |
| Short-term relationship in the past 12 months | 9.4% (892) | 15.5% (883) | 6.1% (765) | 7.6% (642) | Lo ($P = 0.23$) |
| Median number of lifetime sex partners | 5 (886) | 10 (852) | 5 (762) | 5 (620) | Ov |
| *Sexually transmitted diseases and health* | | | | | |
| HIV | 3.9% (803) | 4.4% (811) | 21.1% (578) | 25.4% (558) | Hi ($P = 0.000$) |
| Herpes simplex virus type 2 | 13.9% (742) | 29.1% (807) | 36.9% (540) | 39.7% (544) | Hi ($P = 0.004$) |
| Positive syphilis serology | 2.1% (780) | 6.7% (810) | 3.2% (538) | 12.7% (544) | Ov |
| *Neisseria gonorrhoea* infection | 1.3% (776) | 1.7% (803) | 0.0% (577) | 0.7% (561) | Hi ($P = 0.41$) |
| *Chlamydia trachomatis* infection | 2.6% (776) | 6.5% (803) | 2.6% (578) | 2.0% (562) | Ov |
| Abnormal genital examination | 7.2% (735) | 10.2% (756) | 15.4% (547) | 7.2% (500) | Ov |
| Genital ulceration | 4.4% (745) | 5.5% (785) | 7.4% (566) | 5.1% (507) | Ov |
| History of ulceration in the past 12 months | 6.2% (884) | 12.3% (879) | 9.2% (763) | 8.9% (638) | Ov |
| History of symptoms of urethritis in the past 12 months | 7.9% (889) | 19.7% (878) | 11.0% (763) | 11.6% (637) | Ov |

*Continued overleaf*

**Table 1.** Continued

| | Low HIV prevalence sites | | High HIV prevalence sites | | |
|---|---|---|---|---|---|
| | Cotonou | Yaoundé | Kisumu | Ndola | Comparison[a] |
| **Married men** | | | | | |
| HIV | 5.5% (380) | 6.2% (321) | 30.5% (338) | 34.6% (347) | Hi ($P \approx 0.000$) |
| Age difference between spouses > 11 years | 7.5% (429) | 10.6% (341) | 8.1% (405) | 8.0% (364) | Ov |
| Had > 5 partners before first marriage | 31.9% (436) | 57.5% (365) | 36.2% (461) | 25.3% (399) | Ov |
| Interval between first sex and first marriage > 9 years | 33.4% (434) | 35.2% (364) | 27.6% (206) | 25.3% (388) | Lo ($P \approx 0.068$) |
| Age at first marriage > 27 years | 31.7% (436) | 33.7% (365) | 15.4% (462) | 16.5% (399) | Lo ($P \approx 0.000$) |
| Polygamous union | 15.3% (437) | 6.6% (365) | 11.7% (462) | 5.3% (399) | Ov |
| HIV-positive spouse | 4.6% (259) | 6.4% (172) | 28.5% (256) | 31.7% (268) | Hi ($P \approx 0.000$) |
| ***Men with casual partnerships in the past 12 months*** | | | | | |
| HIV | 4.1% (412) | 4.0% (606) | 14.7% (299) | 24.9% (205) | Hi ($P \approx 0.000$) |
| Age difference with non-spousal partners > 11 years | 16.9% (443) | 21.3% (640) | 13.9% (352) | 9.8% (193) | Lo ($P = 0.28$) |
| Frequent condom use with all non-spousal partners | 20.4% (411) | 23.6% (619) | 23.6% (343) | 24.1% (212) | Ov |
| Partner had > 2 partners in past 12 months | 29.0% (221) | 57.6% (479) | 30.9% (311) | 30.9% (165) | Ov |
| Intercourse > 4 times per month | 9.4% (447) | 20.9% (646) | 13.6% (367) | 17.8% (230) | Ov |
| **Men reporting at least one STD episode in the past 12 months** | | | | | |
| HIV | 6.5% (107) | 6.5% (231) | 33.6% (107) | 45.8% (83) | Hi ($P = 0.000$) |
| Sought care from modern facilities | 42.1% (114) | 64.9% (239) | 56.9% (123) | 53.3% (92) | Ov |

[a] The result is given as 'Lower' (Lo), 'Higher' (Hi) or 'Overlap' (Ov). It is 'Higher' when the highest prevalence in Cotonou and Yaoundé is lower than the lowest prevalence in Kisumu and Ndola. It is 'Lower' when the lowest prevalence in Cotonou and Yaoundé is higher than the highest prevalence in Kisumu and Ndola. It is 'Overlap' when the prevalence in Cotonou or/and Yaoundé is between the prevalences in Kisumu and Ndola, or when the prevalence in Kisumu or/and Ndola is between the prevalences in Cotonou and Yaoundé. When the result is 'Higher' or 'Lower', the $P$ value is the maximum value obtained in the site-by-site comparisons between the 'low' HIV prevalence sites and the high HIV prevalence sites. STD, sexually transmitted disease.

**Table 2.** Characteristics of sexually active women

| | Low HIV prevalence sites | | High HIV prevalence sites | | |
|---|---|---|---|---|---|
| | Cotonou | Yaoundé | Kisumu | Ndola | Comparison[a] |
| **General population** | | | | | |
| *Background* | | | | | |
| Mean age (years) | 29.8 (950) | 28.3 (1013) | 27.5 (962) | 27.8 (889) | Lo ($P = 0.24$) |
| Education | | | | | |
| Illiterate | 46.7% (929) | 6.1% (1012) | 16.6% (958) | 17.1% (885) | Ov |
| Secondary level | 4.3% (948) | 15.8% (1013) | 19.2% (962) | 17.3% (888) | Hi ($P = 0.39$) |
| Alcohol consumption in past month | 36.9% (950) | 45.5% (1013) | 8.7% (962) | 23.3% (889) | Lo ($P = 0.000$) |
| Has a job | 73.8% (931) | 37.3% (989) | 53.4% (921) | 32.5% (877) | Ov |
| Made > 1 trip in the past 12 months | 35.4% (901) | 47.2% (897) | 46.5% (805) | 20.1% (791) | Ov |
| Religion | | | | | |
| Protestant | 5.3% (950) | 22.6% (1013) | 52.5% (962) | 65.0% (889) | Hi ($P = 0.000$) |
| Catholic | 62.0% (950) | 64.2% (1013) | 28.3% (962) | 27.8% (889) | Lo ($P = 0.000$) |
| Muslim | 12.8% (950) | 7.6% (1013) | 4.1% (962) | 0.4% (889) | Lo ($P = 0.001$) |
| *Sexual behaviour* | | | | | |
| Now married/has been married | 72.9% (938) | 59.0% (999) | 81.0% (959) | 81.7% (873) | Hi ($P = 0.000$) |
| Age at first sex < 15 years | 6.1% (947) | 11.4% (1005) | 30.2% (953) | 19.4% (878) | Hi ($P = 0.000$) |
| Resident in town at age of first sex | 63.3% (945) | 52.0% (1004) | 29.1% (951) | 59.2% (876) | Ov |
| At least one non-spousal partner in the past 12 months | 19.7% (950) | 48.7% (1013) | 21.1% (962) | 15.1% (889) | Ov |
| Sex in exchange for money in the past 12 months | 1.2% (950) | 6.6% (1013) | 8.5% (962) | 6.4% (889) | Ov |
| Short-term relationship in the past 12 months | 0.8% (950) | 1.3% (1013) | 1.1% (962) | 0.8% (889) | Ov |
| Median number of lifetime sex partners | 2 (946) | 3 (992) | 2 (960) | 2 (883) | Ov |
| Dry sex | 3.2% (946) | 4.5% (1011) | 2.2% (960) | 14.7% (885) | Ov |
| Sex during menstruation in the past 12 months | 9.7% (945) | 17.9% (1011) | 11.8% (961) | 6.1% (886) | Ov |
| Hormonal contraception | 5.0% (944) | 7.1% (1011) | 10.3% (961) | 13.7% (884) | Hi ($P = 0.013$) |
| *Sexually transmitted diseases and health* | | | | | |
| HIV | 4.0% (880) | 8.4% (942) | 31.6% (826) | 35.1% (803) | Hi ($P = 0.000$) |
| Herpes simplex virus type 2 | 33.4% (806) | 55.4% (911) | 72.4% (762) | 60.9% (781) | Hi ($P = 0.023$) |
| Positive syphilis serology | 1.4% (831) | 6.0% (921) | 4.2% (763) | 15.4% (787) | Ov |
| *Neisseria gonorrhoea* infection | 0.9% (845) | 3.0 % (913) | 1.0% (808) | 2.6% (803) | Ov |
| *Chlamydia trachomatis* infection | 1.3% (845) | 9.7 % (913) | 4.6% (808) | 2.7% (805) | Ov |
| *Trichomonas vaginalis* infection | 3.2% (836) | 18.4% (658) | 29.9% (441) | 33.4% (494) | Hi ($P = 0.000$) |
| **Married women** | | | | | |
| HIV | 4.1% (631) | 9.5% (525) | 32.2% (671) | 36.9% (643) | Hi ($P = 0.000$) |
| Age difference between spouses > 11 years | 23.8% (656) | 25.0% (553) | 27.7% (674) | 15.6% (591) | Ov |
| Had > 1 partner before first marriage | 30.0% (681) | 47.6% (586) | 54.6% (777) | 24.3% (713) | Ov |
| Interval between first sex and first marriage > 3 years | 28.5% (663) | 39.9% (571) | 26.5% (758) | 16.4% (697) | Lo ($P = 0.41$) |
| Age at marriage > 20 years | 41.1% (682) | 40.5% (588) | 20.2% (777) | 20.8% (713) | Lo ($P = 0.000$) |
| Polygamous union | 27.5% (684) | 11.2% (589) | 19.9% (777) | 2.9% (713) | Ov |
| HIV-positive spouse | 6.2% (259) | 6.9% (174) | 32.2% (225) | 36.0% (253) | Hi ($P = 0.000$) |
| **Women with casual partnerships in the past 12 months** | | | | | |
| HIV | 5.6% (179) | 9.4% (457) | 43.7% (174) | 50.8% (120) | Hi ($P = 0.000$) |
| Age difference with non-spousal partners > 11 years | 14.0% (179) | 18.5% (486) | 12.5% (176) | 13.0% (115) | Lo ($P = 0.86$) |
| Frequent condom use with all non-spousal partners | 11.0% (181) | 16.3% (486) | 19.8% (197) | 24.2% (132) | Hi ($P = 0.27$) |
| Partner had > 2 partners in the past 12 months | 21.1% (95) | 46.4% (358) | 25.0% (180) | 28.2% (85) | Ov |
| Intercourse > 4 times per month | 13.9% (187) | 19.3% (493) | 10.8% (203) | 12.7% (134) | Lo ($P = 0.87$) |

[a] See footnote to Table 1.

**Table 3.** Age-adjusted risk factors for HIV infection: sexually active men

| | Low HIV prevalence sites | | High HIV prevalence sites | |
|---|---|---|---|---|
| | Cotonou | Yaoundé | Kisumu | Ndola |
| **General population** | | | | |
| *Background* | | | | |
| Age | | | | $P = 0.0000$ |
| 15–24 years | 1, $P = 0.093$ | 1, $P = 0.0009$ | 1, $P = 0.0000$ | 1 |
| 25–34 years | 3.0 (1.1–8.3) | 3.9 (1.3–12) | 4.5 (2.7–7.6) | 4.7 (2.7–8.1) |
| 35–49 years | 2.7 (0.9–8.1) | 7.7 (2.6–23) | 3.8 (2.2–6.7) | 3.4 (1.9–6.2) |
| Education | | | | |
| Illiterate | 2.6 (1.1–5.8), $P = 0.022$ | 0.74 (0.09–5.8, $P = 0.78$ | 0.64 (0.21–2.0), $P = 0.43$ | 1.1 (0.46–2.8), $P = 0.78$ |
| Secondary level | 0.24 (0.0.6–1.0), $P = 0.057$ | 0.44 (0.19–0.99), $P = 0.047$ | 0.73 (0.47–1.1), $P = 0.17$ | 0.98 (0.66–1.5), $P = 0.93$ |
| Alcohol consumption in past month | 0.69 (0.33–1.4), $P = 0.32$ | 0.95 (0.46–2.0, $P = 0.89$ | 1.8 (1.2–2.8), $P = 0.0059$ | 1.2 (0.77–1.9), $P = 0.42$ |
| Has a job | 3.5 (0.7–17), $P = 0.12$ | 3.8 (1.1–13), $P = 0.036$ | 2.0 (0.94–4.4), $P = 0.07$ | 2.1 (1.2–3.8), $P = 0.015$ |
| Religion | nev | | | |
| Protestant | | 1, $P = 0.77$ | 1, $P = 0.87$ | 1, $P = 0.46$ |
| Catholic | | 1.1 (0.19–2.5) | 1.0 (0.6–1.6) | 1.4 (0.9–2.1) |
| Muslim | | 1.0 (0.32–3.2) | 0.54 (0.12–2.5) | nev |
| Other | | 0.36 (0.04–3.0) | 1.1 (0.57–2.0) | 0.95 (0.88–1.8) |
| Ethnic group[a] | | | | |
| Group 1 | 1, $P = 0.87$ | 1, $P = 0.77$ | 1, $P = 0.0002$ | 1, $P = 0.38$ |
| Group 2 | 2.0 (0.26–16) | 1.3 (0.52–3.2) | 0.23 (0.0.93–0.55) | 1.1 (0.68–1.7) |
| Group 3 | 1.4 (0.14–14) | 1.8 (0.57–5.9) | 0.29 (0.12–0.70) | 0.70 (0.36–1.4) |
| Group 4 | 1.9 (0.25–15) | 1.2 (0.50–2.7) | – | – |
| Circumcised | nev | 0.21 (0.02–2.0), $P = 0.17$ | 0.25 (0.14–0.46), $P = 0.0000$ | 0.79 (0.40–1.6), $P = 0.51$ |
| *Sexual behaviour* | | | | |
| Now married/has been married | 1.9 (0.73–4.9), $P = 0.18$ | 0.64 (0.27–1.5), $P = 0.31$ | 3.3 (1.6–6.7), $P = 0.0011$ | 3.7 (2.0–6.9), $P = 0.0000$ |
| Age at first sex < 15 years | 0.65 (0.15–2.8), $P = 0.57$ | 1.2 (0.45–3.4), $P = 0.69$ | 1.3 (0.83–2.1), $P = 0.23$ | 0.81 (0.47–1.4), $P = 0.43$ |
| Resident in town at age of first sex | 1.2 (0.56–2.7), $P = 0.61$ | 0.91 (0.44–1.9), $P = 0.80$ | 1.1 (0.72–1.7), $P = 0.66$ | 1.4 (0.95–2.2), $P = 0.10$ |
| Short-term relationship in the past 12 months | 1.2 (0.34–4.0), $P = 0.81$ | 2.4 (1.1–5.2), $P = 0.027$ | 0.49 (0.17–1.5), $P = 0.20$ | 1.1 (0.56–2.4), $P = 0.71$ |
| Number of lifetime sex partners | 1.1 (0.96–1.2), $P = 0.20$ | 1.1 (0.93–1.2), $P = 0.45$ | 1.1 (1.0–1.2), $P = 0.0068$ | 1.2 (1.1–1.3), $P = 0.0000$ |
| *Sexually transmitted diseases and health* | | | | |
| Herpes simplex virus type 2 | 5.4 (2.2–13), $P = 0.0003$ | 5.6 (2.3–14), $P = 0.0002$ | 9.0 (5.1–16), $P = 0.0000$ | 6.6 (4.2–11), $P = 0.0000$ |
| Positive syphilis serology | 3.3 (0.71–16), $P = 0.13$ | 1.2 (0.39–3.5), $P = 0.77$ | 1.9 (0.65–5.6), $P = 0.24$ | 3.4 (2.0–5.9), $P = 0.0000$ |
| *Neisseria gonorrhoea* infection | 2.6 (0.31–22), $P = 0.37$ | 3.7 (0.75–18), $P = 0.11$ | nev | 9.2 (0.84–101), $P = 0.069$ |
| Abnormal genital examination | 2.6 (0.85–8.0), $P = 0.09$ | 1.4 (0.47–4.2), $P = 0.54$ | 2.9 (1.7–5.0), $P = 0.0002$ | 4.4 (2.1–9.4), $P = 0.0001$ |
| Genital ulceration | 4.5 (1.4–14), $P = 0.01$ | 2.5 (0.69–8.9), $P = 0.16$ | 2.2 (1.1–4.6), $P = 0.036$ | 5.8 (2.3–14), $P = 0.0001$ |
| Ulceration in the past 12 months | 1.1 (0.25–5), $P = 0.92$ | 2.7 (1.2–6.1), $P = 0.016$ | 2.6 (1.4–4.8), $P = 0.0024$ | 3.5 (1.9–6.5), $P = 0.0001$ |
| History of symptoms of urethritis in the past 12 months | 3.17 (1.2–8.1), $P = 0.017$ | 2.6 (1.2–5.3), $P = 0.012$ | 2.7 (1.5–4.8), $P = 0.0011$ | 2.6 (1.5–4.6), $P = 0.007$ |
| **Married men** | | | | |
| Had > 5 partners before first marriage | 1.4 (0.56–3.5), $P = 0.48$ | 2.1 (0.75–6.0), $P = 0.16$ | 1.1 (0.67–1.8), $P = 0.73$ | 2.3 (1.4–3.8), $P = 0.0013$ |
| Age at first marriage >27 years | 0.89 (0.33–2.4), $P = 0.82$ | 1.4 (0.56–3.8), $P = 0.46$ | 0.64 (0.32–1.3), $P = 0.22$ | 1.5 (0.8–2.7), $P = 0.19$ |
| HIV-positive spouse | 129 (21 to >500), $P = 0.0000$ | 36 (7–192), $P = 0.0000$ | 8.6 (4.3–17), $P = 0.0000$ | 19 (9.5–38), $P = 0.0000$ |
| **Men with casual partnerships in the past 12 months** | | | | |
| Partner had > 2 partners in past 12 months | 1.5 (0.33–6.4), $P = 0.62$ | 1.7 (0.60–5.0), $P = 0.31$ | 0.72 (0.34–1.5), $P = 0.40$ | 2.5 (1.1–5.1), $P = 0.0033$ |
| **Men reporting at least one STD episode in the past 12 months** | | | | |
| Sought care from modern facilities | 0.43 (0.08–2.4), $P = 0.34$ | 0.32 (0.11–0.95), $P = 0.04$ | 1.1 (0.46–2.7), $P = 0.80$ | 1.9 (0.77–4.8), $P = 0.16$ |

Only variables with $P \leq 0.10$ after adjusting for age and variables significantly different between the low and high HIV prevalence sites (see Table 1) are shown. nev, Not evaluable because of a low sample size. [a] For Cotonou: group 1, Ninas; group 2, Fons; group 3, Gouns; group 4, others. For Yaoundé: group 1, Pahouins; group 2, Bamileke; group 3, Bassa & Bokoko; group 4, others. For Kisumu: group 1, Luos; group 2, Luyas; group 3, others. For Ndola: group 1, Nyanjas; group 2, Bembas; group 3, others. STD, sexually transmitted disease.

**Table 4.** Age-adjusted risk factors for HIV infection: sexually active women

| | Low HIV prevalence sites | | High HIV prevalence sites | |
|---|---|---|---|---|
| | Cotonou | Yaoundé | Kisumu | Ndola |
| **General population** | | | | |
| *Background variables* | | | | |
| Age | | | | |
| 15–24 years | 1, $P = 0.69$ | 1, $P = 0.17$ | 1, $P = 0.050$ | 1, $P = 0.0071$ |
| 25–34 years | 0.94 (0.44–2.0) | 1.5 (0.90–2.6) | 1.0 (0.72–1.4) | 1.3 (0.93–1.8) |
| 35–49 years | 0.68 (0.28–1.7) | 0.93 (0.48–1.8) | 0.62 (0.41–0.93) | 0.67 (0.45–1.0) |
| Illiterate | 1.8 (0.91–3.6), $P = 0.09$ | 1.4 (0.58–3.6), $P = 0.44$ | 0.77 (0.50–1.2), $P = 0.25$ | 0.72 (0.48–1.1), $P = 0.11$ |
| Alcohol consumption in past month | 1.1 (0.56–2.2), $P = 0.76$ | 1.4 (0.85–2.3), $P = 0.19$ | 1.3 (0.78–2.2), $P = 0.31$ | 1.9 (1.4–2.7), $P = 0.003$ |
| Religion | | | | |
| Protestant | 1, $P = 0.76$ | 1, $P = 0.75$ | 1, $P = 0.16$ | 1, $P = 0.56$ |
| Catholic | 1.1 (0.25–4.7) | 0.81 (0.47–1.4) | 1.4 (1.0–2.0) | 1.2 (0.9–1.6) |
| Muslim | 1.0 (0.32–3.2) | 0.83 (0.32–2.1) | 0.94 (0.44–2.0) | 3.6 (0.33–41) |
| Other | 0.36 (0.04–3.0) | 0.54 (0.15–1.9) | 1.1 (0.66–1.6) | 1.0 (0.56–1.9) |
| Ethnic group[a] | | | | |
| Group 1 | 1, $P = 0.98$ | 1, $P = 0.10$ | 1, $P = 0.072$ | 1, $P = 0.35$ |
| Group 2 | 0.87 (0.27–2.8) | 0.41 (0.19–0.89) | 0.71 (0.46–1.1) | 0.79 (0.55–1.1) |
| Group 3 | 0.74 (0.18–3.0) | 0.49 (0.17–1.4) | 0.51 (0.25–1.0) | 0.72 (0.44–1.2) |
| Group 4 | 0.87 (0.28–2.7) | 0.86 (0.48–1.5) | – | – |
| *Sexual behaviour* | | | | |
| Now married/has been married | 1.8 (0.68–4.7), $P = 0.24$ | 1.4 (0.80–2.5), $P = 0.23$ | 1.4 (0.92–2.2), $P = 0.11$ | 1.7 (1.1–2.7), $P = 0.014$ |
| Age at first sex < 15 years | 1.5 (0.44–5.0), $P = 0.53$ | 1.3 (0.6–1.5), $P = 0.50$ | 1.1 (0.84–1.6), $P = 0.40$ | 1.0 (0.69–1.4), $P = 0.99$ |
| At least one non-spousal partner in the past 12 months | 1.6 (0.68–3.6), $P = 0.30$ | 1.4 (0.87–2.3), $P = 0.16$ | 2.0 (1.4–2.8), $P = 0.0002$ | 2.1 (1.4–3.2), $P = 0.0002$ |
| Sex in exchange for money in the past 12 months | 0.017 (0–>500), $P = 0.71$ | 4.4 (2.3–8.1), $P = 0.0000$ | 1.6 (0.94–2.6), $P = 0.086$ | 2.0 (1.1–3.5), $P = 0.019$ |
| Short-term relationship in the past 12 months | nev | 3.8 (1.0–15), $P = 0.049$ | 4.3 (1.0–19), $P = 0.050$ | 0.97 (0.17–5.4), $P = 0.97$ |
| Number of lifetime sex partners | 1.4 (1.0–1.9), $P = 0.048$ | 2.1 (1.5–2.8), $P = 0.0000$ | 1.5 (1.3–1.8), $P = 0.0000$ | 1.6 (1.4–1.8), $P = 0.0000$ |
| Dry sex | 3.0 (0.87–11), $P = 0.08$ | 1.1 (0.37–3.1), $P = 0.91$ | 0.90 (0.34–2.4), $P = 0.83$ | 1.3 (0.86–1.9), $P = 0.23$ |
| Sex during menstruation in the past 12 months | 2.3 (0.98–5.6), $P = 0.056$ | 1.2 (0.65–2.1), $P = 0.63$ | 1.1 (0.70–1.7), $P = 0.70$ | 2.0 (1.1–3.5), $P = 0.019$ |
| Hormonal contraception | 0.51 (0.069–3.8), $P = 0.52$ | 0.96 (0.37–2.5), $P = 0.93$ | 0.58 (0.34–0.99), $P = 0.047$ | 0.68 (0.43–1.1), $P = 0.081$ |
| *Sexually transmitted diseases and health* | | | | |
| Herpes simplex virus type 2 | 7.0 (2.9–17), $P = 0.000$ | 11 (4.7–28), $P = 0.0000$ | 4.7 (3.0–7.5), $P = 0.0000$ | 7.1 (4.8–10), $P = 0.0000$ |
| Positive syphilis serology | 5.4 (1.1–27), $P = 0.036$ | 4.3 (2.2–8.3), $P = 0.0000$ | 2.5 (1.2–5.0), $P = 0.014$ | 2.6 (1.8–3.9), $P = 0.0000$ |
| *Neisseria gonorrhoea* infection | 3.5 (0.41–30), $P = 0.25$ | 2.2 (0.72–6.5), $P = 0.17$ | 2.9 (0.63–13), $P = 0.18$ | 4.8 (1.8–13), $P = 0.0015$ |
| *Chlamydia trachomatis* infection | nev | 1.3 (0.62–2.8), $P = 0.47$ | 0.9 (0.43–1.9), $P = 0.77$ | 2.1 (0.86–5.2), $P = 0.10$ |
| *Trichomonas vaginalis* infection | 2.0 (0.44–8.8), $P = 0.38$ | 2.6 (1.4–5.0), $P = 0.0028$ | 1.9 (1.2–2.8), $P = 0.0084$ | 1.0 (0.68–1.6), $P = 0.89$ |
| **Married women** | | | | |
| Age difference between spouses > 11 years | 1.8 (0.82–4.0), $P = 0.14$ | 1.8 (0.94–3.3), $P = 0.076$ | 1.2 (0.83–1.8), $P = 0.31$ | 0.88 (0.54–1.5)$P = 0.63$ |
| Had > 1 partner before first marriage | 1.8 (0.79–3.9), $P = 0.17$ | 1.5 (0.83–2.8), $P = 0.17$ | 1.3 (0.95–1.9), $P = 0.092$ | 1.6 (1.1–2.3), $P = 0.010$ |
| Interval between first sex and first marriage > 3 years | 1.9 (0.81–4.3), $P = 0.15$ | 0.72 (0.38–1.4), $P = 0.30$ | 1.5 (1.0–2.2), $P = 0.034$ | 1.6 (1.0–2.5), $P = 0.033$ |
| Age at first marriage > 20 years | 1.8 (0.78–4.1), $P = 0.18$ | 1.3 (0.68–2.3), $P = 0.47$ | 1.3 (0.8–1.9), $P = 0.30$ | 1.2 (0.8–1.9), $P = 0.29$ |
| HIV-positive spouse | 82 (17–388), $P = 0.000$ | 40 (8.2–200), $P = 0.0000$ | 9.3 (4.7–19), $P = 0.0000$ | 20 (10–41), $P = 0.0000$ |
| **Women with casual partnerships in the past 12 months** | | | | |
| Age difference with non-spousal partners > 11 years | 0.62 (0.07–5), $P = 0.68$ | 2.3 (1.1–4.6), $P = 0.021$ | 1.4 (0.48–3.9), $P = 0.56$ | 1.97 (0.29–3.3), $P = 0.96$ |
| Partner has > 2 partners | 3.0 (0.43–21), $P = 0.27$ | 3.2 (1.4–7.1), $P = 0.0049$ | 0.88 (0.41–1.9), $P = 0.74$ | 2.0 (0.65–5.8), $P = 0.23$ |
| Intercourse > 4 per month | 0.72 (0.086–6.0), $P = 0.76$ | 2.3 (1.1–4.5), $P = 0.0020$ | 1.8 (0.65–5.2), $P = 0.25$ | 1.6 (0.49–5.4), $P = 0.42$ |

Only variables with $P \leq 0.10$ after adjusting for age and variables significantly different between the low and high HIV prevalence sites (see Table 2) are shown. [a]See footnote to Table 3.

**Table 5.** Multivariate risk factor analysis for HIV infection of sexually active men in Cotonou and Yaoundé

| | Adjusted odds ratio (95% confidence interval) | | | |
|---|---|---|---|---|
| | Cotonou | | Yaoundé | |
| | Model 1[a] | Model 2 | Model 1[a] | Model 2 |
| **General population** | | | | |
| Sample size (HIV-positive) | 749 (26) | 740 (24) | 790 (35) | 786 (32) |
| Age | | | | |
| 15–24 years | ne | 1, $P = 0.097$ | 1, $P = 0.024$ | 1, $P = 0.11$ |
| 25–34 years | | 2.8 (0.9–9.0) | 3.6 (0.99–13) | 4.2 (0.9–20) |
| 35–49 years | | 1.2 (0.31–4.9) | 5.8 (1.7–21) | 5.4 (1.1–26) |
| Has a job | 4.4 (1.0–19), $P = 0.047$ | ne | 3.8 (1.09–13), $P = 0.036$ | ne |
| Herpes simplex virus type 2 | – | 5.4 (2.1–14), $P = 0.0004$ | – | 6.2 (2.7–14), $P = 0.0000$ |
| History of symptoms of urethritis in the past 12 months | – | 3.4 (1.2–9.9), $P = 0.023$ | – | ne |
| **Married men[b]** | | | | |
| Sample size (HIV-positive) | 347 (16) | 221 (11) | 313 (20) | 162 (7) |
| *HIV-positive spouse* | – | 144 (12 to > 500), $P = 0.0001$ | – | 42 (13–293), $P = 0.0000$ |

Variables were selected from Table 3 by a forward stepwise procedure. All models were adjusted for age except model 1 for Cotonou, where no factor was selected when adjusted for age. –, Not applicable; ne, not entered in the model by the stepwise procedure.
[a] In this model, the variables related to sexually transmitted infections and health were not considered. [b] Effect of variables is adjusted on variables of Model 1 and Model 2 related to general population.

HSV-2 infection was strongly associated with HIV infection in all four cities and in both sexes, with the aOR ranging from 4.4 to 8.0. Positive syphilis serology was associated with HIV risk in men and women in Ndola; in women in Kisumu, syphilis seroreactivity was also an independent risk factor for HIV infection but the association was not statistically significant (aOR = 1.8, 95% CI = 0.87–3.8). A history of symptoms suggestive of urethritis in the past 12 months was a risk factor for men in Cotonou and Kisumu. In Kisumu, circumcised men had a significantly lower risk of HIV infection than uncircumcised men (aOR = 0.25, 95% CI = 0.12–0.52). Further analyses of the association between male circumcision and HIV infection are presented elsewhere [18].

The comparison between the two models for men in Kisumu shows that the estimated effect of circumcision remained unchanged after adding STIs to the logistic regression model. In contrast, the association between HIV infection and marital status and number of lifetime sex partners became weaker after introducing STIs in the model.

Analysis of risk factors for men aged 15–29 years showed that HSV-2 was an independent risk factor in all four cities. High lifetime number of sex partners was a risk factor in Kisumu and Ndola; being married or having been married, and syphilis were risk factors in Ndola. Among women aged 15–24 years, HSV-2 infection was an independent risk factor in all four cities, trichomoniasis in Kisumu, and syphilis seroreactivity a risk factor in Ndola.

## Key factors in explaining the differences in prevalence between the four cities

Three factors were identified that are more prevalent in the two high HIV prevalence cities than in the two low HIV prevalence cities and that are independent risk factors for HIV infection in at least one city: being married or having been married, HSV-2 infection, and not being circumcised (men only). There were no paradoxical variables (variables that were significantly more prevalent in the low HIV prevalence cities and that were associated with an increased risk of HIV infection in at least one city). Male circumcision was a protective risk factor in Kisumu (aOR = 0.23 in model 1 and aOR = 0.25 in model 2; see Table 6), indicating a strong and independent protective effect. In Ndola, there was no difference in HIV prevalence between circumcised men and uncircumcised men (univariate analysis OR = 1.0, 95% CI = 0.5–1.9) but, due to small sample sizes, no allowance could be made for confounding [18].

Analyses restricted to men aged 15–29, and to women aged 15–24 gave similar results as the analyses of the general populations, despite the reduced power. Among these young men and women, HSV-2 was a risk factor in all four cities and was significantly more prevalent in Kisumu and Ndola than in Cotonou and Yaoundé. In Kisumu and Ndola, more men were married or had been married than in the low HIV prevalence cities, but marital status was significantly associated with HIV risk in Ndola only. In Kisumu, the association between HIV and circumcision was not statistically significant.

**Table 6.** Multivariate risk factor analysis for HIV infection of sexually active men in Kisumu and Ndola

| | Adjusted odds ratio (95% confidence interval) | | | |
|---|---|---|---|---|
| | Kisumu | | Ndola | |
| | Model 1[a] | Model 2 | Model 1[a] | Model 2 |
| **General population** | | | | |
| Sample size (% HIV-positive) | 577 (122) | 535 (101) | 537 (137) | 519 (134) |
| Age | | | | |
| 15–24 years | 1, $P = 0.060$ | 1, $P = 0.027$ | 1, $P = 0.015$ | 1, $P = 0.076$ |
| 25–34 years | 2.1 (1.0–4.2) | 2.4 (1.3–4.7) | 1.9 (1.0–3.8) | 1.5 (0.8–3.2) |
| 35–49 years | 1.3 (0.60–1.8) | 1.6 (0.8–3.2) | 1.1 (0.50–2.3) | 0.9 (0.4–2.0) |
| Lifetime partners | 1.1 (1.0–1.2), $P = 0.018$ | ne | 1.2 (1.1–1.3), $P = 0.0000$ | 1.1 (1.0–1.2), $P = 0.029$ |
| Now married/has been married | 3.0 (1.5–6.2), $P = 0.0026$ | 2.0 (1.1–3.9), $P = 0.031$ | 3.9 (2.0–7.3), $P = 0.0000$ | 2.3 (1.1–4.5), $P = 0.019$ |
| Circumcised | 0.23 (0.15–0.42), $P = 0.0000$ | 0.25 (0.12–0.52), $P = 0.0002$ | ne | ne |
| Alcohol consumption in past month | 1.7 (1.1–2.7), $P = 0.021$ | 1.9 (1.2–3.2), $P = 0.012$ | ne | ne |
| Herpes simplex virus type 2 | – | 7.7 (4.3–14), $P = 0.0000$ | – | 4.9 (3.0–8.2), $P = 0.0000$ |
| Positive syphilis serology | – | ne | – | 2.7 (1.5–4.9), $P = 0.0015$ |
| History of symptoms of urethritis in the past 12 months | – | 2.3 (1.2–4.7), $P = 0.016$ | – | ne |
| **Married men[b]** | | | | |
| Sample size (% HIV-positive) | 297 (85) | 155 (41) | 292 (104) | 214 (82) |
| HIV-positive spouse | – | 12 (5–30), $P = 0.0000$ | – | 18 (8.0–39), $P = 0.0000$ |
| **Men having had a clinical examination[b]** | | | | |
| Sample size (% HIV-positive) | 484 (105) | 451 (86) | 463 (121) | 452 (119) |
| Abnormal genital examination | – | ne | | 2.5 (1.1–5.7), $P = 0.033$ |

Variables were selected from Table 3 by a forward stepwise procedure. All models were adjusted for age. –, Not applicable; ne, not entered in the model by the stepwise procedure. [a] In this model, the variables related to sexually transmitted infections and health were not considered. [b] Effect of variables is adjusted on variables of Model 1 and Model 2 related to general population.

In summary, three factors (HSV-2 infection, male circumcision and marital status) differentiate the cities with high HIV prevalence from the cities with low HIV prevalence, and are likely to play an important role in explaining the differences in HIV prevalence.

### Attributable fractions

In Kisumu, it was estimated that 46.3% of HIV cases in men were attributable to lack of circumcision. The proportion of HIV cases attributable to HSV-2 infection ranged between 32.3% in Cotonou and 62.3% in Yaoundé for men, and between 56.6% in Kisumu and 75.4% in Yaoundé for women. The proportion of HIV cases in men in Kisumu and Ndola that could be attributed to being married or having been married was 31.5 and 34.1%, respectively.

## Discussion

We explored risk factors for HIV infection in sexually active men and women in the general population of four cities in sub-Saharan Africa with contrasting levels of HIV infection and compared the distribution of these risk factors between the four populations. We examined those factors that have been shown in other studies to increase the risk of HIV infection or that are believed to be associated with an increased risk.

Risk of HIV infection was higher in men and women who reported high lifetime numbers of sex partners, although this association was not always statistically significant after adding the STI variables to the model. This finding is consistent with the results from other studies

**Table 7.** Multivariate risk factor analysis for HIV infection of sexually active women in Cotonōu and Yaoundé

| | Adjusted odds ratio (95% confidence interval) | | | |
|---|---|---|---|---|
| | Cotonou | | Yaoundé | |
| | Model 1[a] | Model 2 | Model 1[a] | Model 2 |
| **General population** | | | | |
| Sample size (% HIV-positive) | 877 (35) | 806 (26) | 906 (76) | 894 (66) |
| Age | | | | |
| 15–24 years | 1, $P = 0.67$ | 1, $P = 0.0026$ | 1, $P = 0.0009$ | 1, $P = 0.0003$ |
| 25–34 years | 0.89 (0.41–1.9) | 0.81 (0.55–1.2) | 0.99 (0.69–1.4) | 0.98 (0.67–1.5) |
| 35–49 years | 0.66 (0.27–1.6) | 0.45 (0.28–0.71) | 0.46(0.29–0.72) | 0.42 (0.27–0.67) |
| Number of lifetime sex partners | 1.4 (1.0–1.9), $P = 0.048$ | ne | 1.9 (1.4–2.6), $P = 0.0000$ | 1.5 (1.1–2.0), $P = 0.015$ |
| Sex in exchange for money in the past 12 months | ne | ne | 3.1 (1.6–5.9), $P = 0.0006$ | 3.8 (1.5–7.0), $P = 0.0003$ |
| Sex during menstruation in the past 12 months | ne | ne | ne | ne |
| Herpes simplex virus type 2 | – | 7.0 (2.9–17), $P = 0.0000$ | – | 8.0 (3.2–20), $P = 0.0000$ |
| **Married women[b]** | | | | |
| Sample size (% HIV-positive) | 612 (25) | 227 (7) | 478 (47) | 155 (11) |
| Age difference between spouses > 11 years | ne | ne | 2.2 (1.1–4.2), $P = 0.020$ | ne |
| HIV-positive spouse | – | 217 (18 to > 500), $P = 0.0000$ | – | 211 (7–6188), $P = 0.0019$ |
| **Women with casual partnerships in the past 12 months[b]** | | | | |
| Sample size (% HIV-positive) | 177 (10) | 164 (10) | 444 (42) | 436 (36) |
| Intercourse > 4 per month | ne | ne | 2.1 (1.1–4.3), $P = 0.037$ | 2.2 (1.04–4.8), $P = 0.04$ |

Variables were selected from Table 4 by a forward stepwise procedure. All models were adjusted for age. –, Not applicable; ne, not entered in the model by the stepwise procedure. [a] In this model, the variables related to sexually transmitted infections and health were not considered. [b] Effect of variables is adjusted on variables of Model 1 and Model 2 related to general population.

[4,5,9,19,20] and is in accordance with a crude representation of the spread of HIV, in which the probability of intercourse with an HIV-infected person and the risk of becoming HIV infected increases with the number of sex partners.

In men, no association was found between HIV risk and contacts with sex workers, as has been found in other studies [19,21,22]. However, there is evidence that men in all four cities have been under-reporting their contacts with sex workers, so that any association between HIV risk in men and contacts with sex workers may have been missed [23]. Another possible explanation for this lack of association is that the epidemics in the four cities are mature and that core groups no longer play such a major role in the spread of HIV as in the earlier stages. This is consistent with patterns seen using simulation models [24]. Other parameters of sexual mixing that were explored at the individual level included partnerships with high-activity partners and large age differences with partners. Neither sex with a highly active partner nor sex with a partner who was at least 11 years older or younger was associated with an increased risk of HIV infection. More detailed analysis of the association between large age differences with partners and HIV risk in young women in Kisumu and Ndola are presented in another paper in this supplement [25]. The findings of our study are in contrast with the results from a study in Zimbabwe, where a large age difference between sexual partners was indeed found to increase the risk of HIV infection in women [26]. However, in our study, sample sizes were small and young women may have under-reported their sexual activity [14]. Concurrent partnerships as a risk factor for HIV infection have been explored in a separate paper [27]. No association was found between concurrent partnerships and HIV risk at the individual level, and neither were concurrent partnerships more prevalent in the two high HIV prevalence cities than in the two low HIV prevalence cities.

Women in Kisumu and Ndola were more likely to have their sexual debut before age 15 compared with women in Cotonou and Yaoundé. However, in multivariate

**Table 8.** Multivariate risk factor analysis for HIV infection of sexually active women in Kisumu and Ndola

| | Adjusted odds ratio (95% confidence interval) | | | |
|---|---|---|---|---|
| | Kisumu | | Ndola | |
| | Model 1[a] | Model 2 | Model 1[a] | Model 2 |
| **General population** | | | | |
| Sample size (% HIV-positive) | 696 (219) | 761 (233) | 784 (274) | 772 (273) |
| Age | | | | |
| 15–24 years | 1, $P = 0.0027$ | 1, $P = 0.0051$ | 1, $P = 0.0009$ | 1, $P = 0.0003$ |
| 25–34 years | 0.80 (0.55–1.2) | 0.83 (0.56–1.2) | 0.99 (0.69–1.4) | 0.98 (0.67–1.5) |
| 35–49 years | 0.45 (0.29–0.71) | 0.46 (0.29–0.74) | 0.46 (0.29–0.72) | 0.42 (0.27–0.67) |
| Number of lifetime sex partners | 1.4 (1.2–1.6), $P = 0.0000$ | 1.4 (1.2–1.6), $P = 0.0001$ | 1.4 (1.2–1.7), $P = 0.0000$ | 1.2 (1.1–1.4), $P = 0.012$ |
| Now married/has been married | 2.5 (1.4–4.5), $P = 0.0014$ | ne | 2.3 (1.4 3.9), $P = 0.0010$ | ne |
| At least one non-spousal partner in the past 12 months | 2.9 (1.8–4.7), $P = 0.0000$ | 2.0 (1.3–3.0), $P = 0.0006$ | 2.3 (1.5–3.8), $P = 0.0004$ | 1.9 (1.2–3.0), $P = 0.0064$ |
| Herpes simplex virus type 2 | | 4.4 (2.7–7.1), $P = 0.0000$ | – | 5.8 (3.9–8.47), $P = 0.0000$ |
| Positive syphilis serology | – | ne | – | 1.7 (1.1–2.6), $P = 0.016$ |
| **Married women[b]** | | | | |
| Sample size (% HIV-positive) | 569 (180) | 193 (56) | 292 (104) | 231 (75) |
| HIV-positive spouse | – | 8.3 (3.9–18), $P = 0.0000$ | – | 14 (6.5–28), $P = 0.0000$ |

Variables were selected from Table 4 by a forward stepwise procedure. All models were adjusted for age. –, Not applicable; ne, not entered in the model by the stepwise procedure. [a] In this model, the variables related to sexually transmitted infections and health were not considered. [b] Effect of variables is adjusted on variables of Model 1 and Model 2 related to general population.

analysis, sexual debut before age 15 was not an independent risk factor for HIV infection. It thus seems unlikely that differences in age at first sex are a major factor explaining the differences in HIV spread between the four cities. This does not mean that a change in age at first sexual intercourse would not have an impact on the HIV epidemics in the four cities. Several studies have documented an association between high-risk sexual behaviour and young age at first sexual intercourse. A change towards later age at sexual debut may thus be accompanied by a change towards safer sexual behaviour (e.g., lower rates of partner change) and reduced transmission of HIV.

In Kisumu and Ndola, men who were married or who had been married were more likely to be HIV infected than single men. In a population-based study in Uganda, being married, as opposed to being single, was associated with an increased risk of HIV infection in the younger age groups, but was protective in the older age groups [8]. In studies in Mwanza Region, Tanzania, and Guinee-Bissau, HIV risk was found to be increased in men and women who had been married in the past [9,28]. The increased risk of HIV infection associated with being married can be explained by the fact men and women acquire an additional sex partner at the time of marriage, who is more likely to be HIV-infected than casual partners before marriage as he/she is older. This is suggested by the fact that being married remained an independent risk factor for HIV infection after adjusting for lifetime number of sex partners. In addition, the higher frequency of unprotected sexual intercourse within a marriage results in a higher probability of HIV transmission, compared with casual partnerships where sexual intercourse is less frequent.

In all four cities and in both sexes there was a strong and statistically significant association between HIV infection and positive HSV-2 serology. This association appeared not to be confounded by behavioural factors, although some residual confounding cannot be excluded. However, the large adjusted odds ratios (between 4.4 and 7.3) suggest that not all the association can be explained by residual confounding. There are two possible explanations for this association: (1) HSV-2 infection increases the susceptibility to HIV infection; and (2) HIV infection increases the susceptibility to HSV-2 infection. Several prospective studies have found that HSV-2 infection increases the susceptibility to HIV infection during heterosexual intercourse [29–31], and we believe that the strong associations between HIV and HSV-2 that we found in the four cities is probably, in large part, due to an increased susceptibility to HIV infection in HSV-2-infected individuals. This is discussed more fully in a separate paper in this supplement [32].

Positive syphilis serology was also associated with an increased risk of HIV infection, although the association was only statistically significant in men and women in Ndola. Current infection with *N. gonorrhoeae* or with *C. trachomatis* was not associated with HIV infection. In Yaoundé and Kisumu, but not in Ndola, women with trichomoniasis were more likely to be HIV infected. The association was weak to moderately strong and did not remain statistically significant in multivariate analysis. The role of trichomonas infection in the transmission of HIV remains unclear. So far, only one prospective study has found trichomoniasis to increase the risk of HIV acquisition [33]. The association between HIV infection and trichomoniasis is described in more detail in another paper in this supplement [34].

In Kisumu, circumcision had a strong protective effect against the acquisition of HIV infection by men. This is in line with the results from a recent meta-analysis of studies from sub-Saharan Africa that produced convincing evidence for a protective effect of male circumcision against HIV infection [12]. In Ndola no such protective effect was seen, and in Cotonou and Yaoundé the effect of circumcision on HIV could not be assessed because almost all men in these two cities are circumcised. More detailed analyses of the association between HIV infection and male circumcision are presented in another paper in this supplement [18].

When comparing the distribution of the risk factors between the four cities, sexual behaviour does not appear to be the key factor explaining the differences in HIV prevalence. Rate of partner change, which was found to be associated with an increased risk of HIV infection, was higher in Yaoundé than in any of the other cities, including the two high HIV prevalence cities. Also, concurrent partnerships and contacts with a sex worker were no more common in the two high HIV prevalence cities than in Cotonou and Yaoundé. However, we found three factors that were independent risk factors for HIV infection in at least one city and that were more prevalent in Kisumu and Ndola than in Cotonou and Yaoundé: (1) being married or having been married; (2) lack of male circumcision; and (3) HSV-2 infection. It is difficult to imagine that young age at first marriage was an important driving force in the rapid spread of HIV in Kisumu and Ndola. It seems more likely that, as HIV prevalence increased, the probability of marrying an HIV-infected partner increased and thus the likelihood of acquiring HIV from a spouse. We believe that lack of male circumcision and HSV-2 infection are the two key factors explaining the differences in HIV prevalence between the four cities.

The population attributable fractions (PAFs) were estimated for lack of male circumcision in men in Kisumu and for HSV-2 in men and women in each of the four cities. The PAFs for HSV-2 infection ranged between 32 and 75%, and were higher for women than for men. The PAF for lack of circumcision in men in Kisumu was estimated at 46%. This suggests that substantial reductions in HIV incidence and prevalence may be achieved by reducing the prevalence of HSV-2 infection, and by circumcising all men in the high HIV prevalence cities. However, PAFs for a study such as this must be interpreted with caution. Population attributable fractions assume a simple and causal link between the exposure and the outcome [35]. Obviously, the situation is more complex in this study.

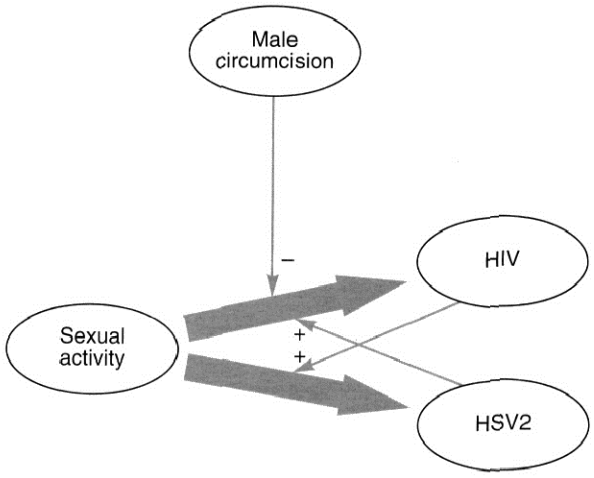


**Fig. 1.** Simplified theory of HIV spread in sub-Saharan Africa. In this theory, the HIV and herpes simplex virus type 2 (HSV-2) infection mutually activates and male circumcision reduces HIV transmission.

In the case of male circumcision, a causal relationship between circumcision and HIV infection is very likely, as the majority of men were circumcised before their sexual debut and, thus, before they could have become exposed to HIV. The protective effect of 0.23–0.25 that we found in men in Kisumu was adjusted for confounding by sexual behaviour. However, we cannot exclude that there is still some residual confounding; neither can we be certain that the HIV prevalence among partners of circumcised men was not lower than among partners of uncircumcised men [18]. On the contrary, the introduction of generalized circumcision of men in Kisumu may lead to a greater than 46% reduction in HIV cases, as the HIV prevalence in women eventually also decreases and thus the exposure of men to HIV decreases.

With regards to HSV-2 infection, the interpretation of the PAF is even more complex. As pointed out previously, part of the strong association between HIV and HSV-2 is probably due to residual confounding by sexual behaviour and increased susceptibility of HIV-infected individuals to HSV-2 infection. This would tend to overestimate the PAF for HSV-2. On the contrary, the

PAF has been estimated for the acquisition of HIV and does not take into account increased transmission of HIV by dually HIV/HSV-2-infected individuals.

Figure 1 shows a tentative qualitative synthesis of the driving forces behind the HIV epidemics in men. In this simplified model, sexual activity leads to the spread of HIV and HSV-2. Male circumcision reduces the transmission efficiency of HIV and possibly also HSV-2. HSV-2 increases the transmission efficiency of HIV, and HIV increases the transmission efficiency of HSV-2. In this 'male circumcision–HSV-2' model of HIV spread, HSV-2 and HIV have a mutually positive feedback, and male circumcision has a negative feedback on HIV transmission and possibly HSV-2 transmission. This simplified model suggests that: (i) without a high prevalence of male circumcision, the mutual activation of HIV and HSV-2 leads to a rapid spread of both infections even if sexual activity is not particularly high; (ii) with a high prevalence of male circumcision, HIV and HSV-2 spread remains relatively limited; and (iii) with a high prevalence of male circumcision, HIV could only spread relatively widely if HSV-2 reaches high levels as a result, for example, of high levels of sexual activity. This could explain the relatively low HIV prevalence in Yaoundé. The high prevalence of HIV in Kisumu and Ndola is mainly due to HSV-2 infection in a non-circumcising population.

It is not within the scope of this paper to discuss in detail the implications of our findings for prevention strategies. However, some general and preliminary conclusions can be drawn. Male circumcision should be considered a prevention strategy in non-circumcising populations that are heavily affected by the HIV epidemic, as has been suggested previously [36]. Because HIV is likely to be transmitted between spouses, voluntary HIV testing and counselling, particularly before marriage, should be encouraged — provided it remains truly 'voluntary'. So far, there are no specific tools for the prevention of HSV-2 infection. Suppressive therapy as a prevention strategy for HSV-2 infection is not feasible in sub-Saharan Africa, considering the high prevalence of HSV-2. The development of a vaccine against the infection or a therapeutic vaccine is needed and trials with it should include HIV infection as an endpoint. In the meantime, prevention of HSV-2 infection has to rely on the promotion of safe sex; in particular, condom use.

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