

Multicentre study on factors determining differences in rate of spread of HIV in sub-Saharan Africa: methods and prevalence of HIV infection

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Objective: The objective of this study was to explore whether the differences in rate of spread of HIV in different regions in sub-Saharan Africa could be explained by differences in sexual behaviour and/or factors influencing the probability of HIV transmission during sexual intercourse.

Methods: A cross-sectional, population-based study was conducted in two cities with a high HIV prevalence (Kisumu in Kenya and Ndola in Zambia) and two cities with a relatively low HIV prevalence (Cotonou in Benin and Yaoundé in Cameroon). In each of these cities, approximately 1000 men and 1000 women, aged 15–49 years, were randomly selected from the general population. Consenting men and women were interviewed and were tested for HIV, syphilis, herpes simplex virus type 2 (HSV-2), gonorrhoea, chlamydial infection and trichomoniasis (the latter for women only). In addition, a survey was conducted on a random sample of 300 sex workers in each city. The research instruments, including the questionnaires and the laboratory procedures, were standardized to permit comparison of results.

Results: The numbers of men interviewed were 1021 in Cotonou, 973 in Yaoundé, 829 in Kisumu, and 720 in Ndola. The corresponding figures for women were 1095, 1116, 1060 and 1130. In Yaoundé, Kisumu and Ndola, the response rates for men were lower than for women due to failure to make contact with eligible men. The proportion of eligible women who were interviewed was 86% in Yaoundé, and 89% in Kisumu and Ndola. In Yaoundé, 76% of eligible men were interviewed, along with 82% in Kisumu and 75% in Ndola.

The prevalence of HIV infection in men was 3.3% in Cotonou, 4.1% in Yaoundé, 19.8% in Kisumu and 23.2% in Ndola. For women, the respective figures were 3.4, 7.8, 30.1 and 31.9%. The prevalence of HIV infection among women aged 15–19 years was 23.0% in Kisumu and 15.4% in Ndola. Among women in Kisumu who had their sexual debut 5 years before the interview, the prevalence of HIV infection was 46%; in Ndola, it was 59%. Among sex workers, the prevalence of HIV infection was 57.5% in Cotonou, 34.4% in Yaoundé, 74.7% in Kisumu and 68.7% in Ndola.

Conclusions: The HIV prevalence rates in the general population confirmed our preliminary assessment of the level of HIV infection in the four cities, which was based on estimates of HIV prevalence from sentinel surveillance among pregnant women.

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The very high prevalence of HIV infection among young women in Kisumu and Ndola calls for urgent intervention.

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Introduction

Of all new HIV infections that occurred in 1999, over 70% were in sub-Saharan Africa [1]. Over 90% of HIV-infected adults on the African continent have acquired their infection through heterosexual intercourse. However, there are large variations in the prevalence of HIV infection within Africa. In many large cities in Eastern and Southern Africa, the HIV prevalence among pregnant women currently exceeds 20%, whereas it is less than 5% in urban pregnant women in most of West Africa, with the exception of Ivory Coast and Nigeria [1,2]. In 1998, the prevalence of HIV infection among pregnant women in cities in Ivory Coast ranged between 8 and 14%. In Nigeria, the HIV prevalence among pregnant women in some cities was as high as 8% in 1996 [2]. Differences in HIV prevalence between different regions in Africa cannot always be explained by the differences in time since introduction of the virus into the population [3]. One of the most striking examples of variation in rate of spread of HIV is provided by a comparison of the epidemiology of HIV infection in the Democratic Republic of Congo (formerly Zaire) and South Africa. There is evidence that HIV was circulating in Kinshasa, the capital of the Democratic Republic of Congo, well before 1980 [4]. Between 1985, when the first survey among pregnant women took place, and 1999, the prevalence of HIV infection in pregnant women remained relatively stable at around 5% [2]. This is in contrast to the situation in South Africa where the HIV prevalence among pregnant women increased from 1% in 1991 to 23% in 1998 [2].

In many instances, variations in HIV prevalence between different regions of Africa reflect differences in rate of spread of HIV. Elucidation of the factors that determine these differences in rate and extent of spread of HIV would considerably add to our knowledge about the dynamics of HIV in populations where the main mode of transmission is heterosexual intercourse. It would also aid the development of more targeted interventions to slow the spread of the virus.

Factors that determine the rate of spread of HIV in the population include sexual behaviour patterns, which determine the probability of exposure to an infected partner, and factors that determine the probability of transmission of the virus during sexual intercourse [3]. It is now established that other sexually transmitted infections (STIs) enhance the transmission of HIV during sex-

ual intercourse [5]. Other factors for which there is evidence that they facilitate HIV transmission include lack of male circumcision [6], high viral load of the infecting partner [7-10] and anal intercourse [11-13]. Sex during menstruation has been found to be associated with an increased risk of HIV infection in some studies, but not in others [3]. It is biologically plausible that 'dry sex' (sex with a dry and tight vagina) enhances the transmission of HIV but, to date, no study has convincingly demonstrated that dry sex is associated with an increased risk of acquisition of HIV infection by women [3,14].

Previous comparisons of the prevalence of factors that determine the rate of spread of HIV in different regions of sub-Saharan Africa have been hampered by a lack of comparable data. We undertook a study in four African cities with markedly different levels of HIV infection, including a survey on large and representative samples of the general population and a study among sex workers. We explored sexual behaviour patterns, other STIs, circumcision status of men, condom use and distribution of circulating HIV-1 subtypes as factors that could potentially explain the observed differences in HIV prevalence in the four cities. The research instruments, including the interviews and the laboratory procedures, were standardized across the study sites. This paper presents the methods of the study and the HIV prevalence results.

Study sites

The study was conducted in two cities with a relatively low and stable HIV prevalence, and two cities with a high HIV prevalence. The cities were selected according to the following criteria: data available on HIV prevalence in pregnant women; local research teams interested in collaborating on this study; the national AIDS control programme endorsing the research; and a stable political situation. The cities with 'low' and relatively stable HIV prevalence were Cotonou in Benin and Yaoundé in Cameroon; the high HIV prevalence cities were Kisumu in Kenya and Ndola in Zambia (Figs. 1 and 2).

Cotonou is the business capital of Benin, in West Africa, and a major port city. Its population was estimated at 625 000 in 1992. The first case of AIDS in Benin was reported in 1985 and the first HIV survey among pregnant women was conducted in 1986-1987. This first survey found no case of HIV infection among 878 pregnant women. In 1994, the prevalence of HIV infection among pregnant women was 0.6%. Among sex workers,



Fig. 1. Map of Africa indicating study sites.

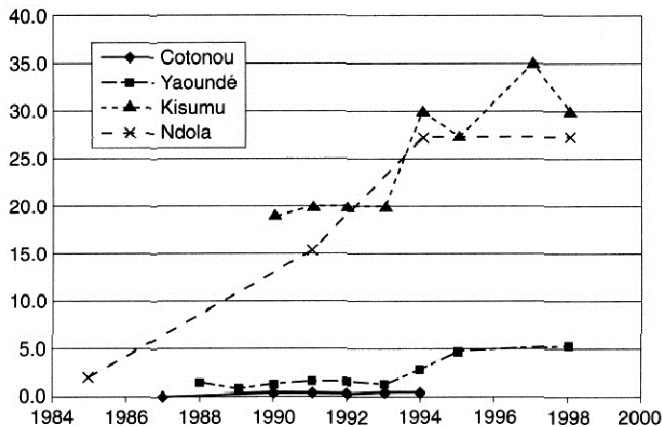


Fig. 2. Trends in HIV prevalence (%) in pregnant women. Source: Sentinel surveillance data quoted in the HIV/AIDS Surveillance Data Base of the US Bureau of the Census, Population Division, International Programs Center (June 2000).

the prevalence of HIV infection was 3.7% in 1987 and 40.0% in 1991 [2].

Yaoundé, the administrative capital of Cameroon, is situated in Central Cameroon and has a population of over 1 000 000. In 1986, 21 AIDS cases were reported in Cameroon. The first HIV survey among pregnant women took place in 1988 and found an HIV prevalence of 1.5%. Ten years later, in 1998, it was 5.5%. In sex workers, a prevalence of 6.9% was recorded in 1987–1988 and 34.0% in 1997 [2]. A striking feature of the HIV/AIDS epidemic in Cameroon is the large variety of HIV strains that are circulating in the population. All known HIV types and subtypes have been isolated

from Cameroonian patients [15,16]. The large variety of HIV strains in Cameroon and recent evidence of zoonotic transmission of SIVcpz suggests that the HIV epidemic in this part of Africa is among the oldest in Africa [15–17].

Kisumu is the third largest city in Kenya, with a population of around 200 000. It is situated in Western Kenya, on the shores of Lake Victoria, near the border with Uganda. It is the capital of Nyanza Province, which is the province in Kenya most badly affected by the HIV/AIDS epidemic. The first survey among pregnant women in Kisumu took place in 1990 and found an HIV prevalence of 19.2% that increased to 30.1% by 1998. This pattern is similar to that found in Kampala (Uganda), about 5 years earlier.

Ndola is the capital of the Copperbelt Province in the north of Zambia and is the second largest city in Zambia, with more than 300 000 inhabitants. The first AIDS cases in Zambia were detected in 1983 [18]. The first survey among pregnant women in Ndola was conducted in 1985 and found an HIV prevalence of 2.0%. By 1994, the HIV prevalence among pregnant women was 27.5%.

It is impossible to ascertain when exactly the HIV epidemics started in the four cities, and it could be argued that the HIV epidemics in Cotonou and Yaoundé are at an earlier stage than the HIV epidemics in Kisumu and Ndola. However, if this were true and if the HIV epidemics in Cotonou and Yaoundé were to follow the same pattern as in Kisumu and Ndola, one would have to assume that HIV was introduced in the populations of Cotonou and Yaoundé more than 10 years later than in the populations of Kisumu and Ndola (see Fig. 2). This seems highly unlikely, especially in the case of Yaoundé as mentioned previously.

Methods

The study in the four cities took place in 1997 and 1998. The first phase consisted of a rapid ethnographic assessment in each of the sites. Using qualitative methods, including interviews with key informants, observations and focus-group discussions, data were collected on social, economic and cultural factors that could help in understanding sexual behaviour patterns. In addition, a census of self-acknowledged sex workers was carried out in each of the study sites. All places where sex workers could be found were listed and mapped, and the number of sex workers present in each place at the time of the study team visit was recorded. Finally, data collection instruments for the main survey were developed and pre-tested. Questionnaires for men and women in the general population and for sex workers were developed, translated into the most commonly spoken local languages and extensively piloted in each of the cities.

The acceptability of blood and urine collection was assessed, and standardized methods for the collection and processing of these specimens were pre-tested.

Survey of the general population

The calculation of sample sizes was based on the results of a World Health Organization survey on sexual behaviour, as well as published data on the prevalence of STIs in men in the general population [19–21]. Taking account of a design effect of 1.5 reflecting the use of two-stage sampling, it was estimated that, for most outcomes, a random sample of 1000 men and 1000 women aged 15–49 years in each city would be adequate in terms of precision of estimates. To allow for non-response, about 1200 men and 1200 women were selected from the general population in each city.

Households were selected by two-stage sampling, and all men and women aged 15–49 years, who slept in the house the night before the first visit by the study team, were eligible for inclusion in the study. Clusters were selected from the lists of census enumeration areas that were obtained from the census office in each country. Cotonou is divided into 429 census areas and the last census had taken place in 1992. Of the 429 areas, 38 were sampled with probability proportional to size. After enumeration of all households in the selected clusters, 25 households were randomly selected from each cluster. The city of Yaoundé was divided into 660 census areas that had not been updated since the last census in 1987. Forty-five clusters were sampled with probability proportional to the size of the population in 1987. An additional five clusters were randomly selected from the new urban zones recently incorporated in the city. After enumeration of all households in the selected census areas, the number of households to be selected in each cluster was calculated, taking into account changes in population size since 1987. Data were analysed both with and without a weighting factor for the total population in each cluster. The results were similar and thus, for simplicity, the results of the unweighted analyses are presented. In Kisumu, 23 clusters were used that are sentinel clusters representative of the city population and that are regularly updated by the census office. They were supplemented with 17 census areas that were selected by systematic sampling so that all areas of the city were represented in the sample. After enumerating the households in these census areas, the required number of households was selected by systematic sampling. In Ndola, 30 standard enumeration areas were randomly selected from the 370 that divide up the city. After enumeration of the households, the required number of households was selected by systematic sampling.

The study teams in each city consisted of interviewers and doctors or nurses. They received 5 days of training in interview techniques, on how to maintain confidentiality and how to respond to questions from study participants.

Each household was visited by a study team. If eligible participants were not home, the team made two repeat visits. After giving their verbal informed consent, study participants were interviewed face to face on their socio-demographic characteristics and sexual behaviour [22]. Data were collected on background variables including age, educational attainment, occupation, ethnic group, religion, length of residence at present address and previous addresses, travel in the past 12 months, marital status and age at first marriage. The section on sexual behaviour included questions on age at first sexual intercourse, lifetime number of sex partners, number of partners before first marriage, and number of non-spousal partners in the past 12 months. Married individuals were asked a number of questions concerning their spouse (age, whether or not the spouse lived with the respondent) and frequency of sexual intercourse and condom use. Respondents who reported at least one non-spousal partner in the past 12 months were asked more detailed questions concerning each of these partnerships (up to a maximum of eight), including socio-demographic characteristics of the partners and whether they had other partners, duration of the relationship, frequency of sexual intercourse, condom use and whether money was exchanged for sex. Women were also asked whether they had sex during menses and whether they used anything to dry the vagina before sexual intercourse. Men were asked about symptoms of a STI in the past 12 months and whether they were circumcised.

After the interview, study participants were requested to give a blood sample, which was tested for HIV, syphilis and herpes simplex virus type 2 (HSV-2) antibodies, and a urine sample, which was tested for gonorrhoea and chlamydial infection. Women were also asked to insert a swab into the vagina, which was immediately inoculated into a culture medium for *Trichomonas vaginalis*. Men underwent a genital examination to check for the presence of genital ulcerations and to ascertain their circumcision status. A randomly selected subsample of HIV-positive samples was used for HIV-1 subtyping.

The interviews and specimen collections were carried out in the homes of the study participants or in a field station near their homes. HIV testing was performed anonymously, but linked to the interview data and the results of the other laboratory tests. Study participants who wished to know their HIV serostatus were referred for pre- and post-test counselling and re-testing, free of charge. Study participants with symptoms and/or signs suggestive of a STI were treated immediately by the study team. Any participants with serological evidence of syphilis or with *T. vaginalis* infection were traced back and treated. It was not possible to treat study participants after they were found to have gonorrhoea or chlamydial infection as the urine samples were tested for these infections many months later in Antwerp, Belgium (see 'Laboratory procedures').

Survey among commercial sex workers

The maps and lists of sex workers served as sampling frames for the selection of a random sample of about 300 sex workers in each city. This sample size was considered feasible and was comparable with the sample size in several other studies of commercial sex workers [23–25]. Consenting sex workers were interviewed at their place of work, concerning their socio-demographic characteristics, the number of years they practised sex work, the number of clients they had and the price asked, condom use and sexual practices with clients. After the interview, they were invited to attend a clinic where they underwent a full genital examination, and where blood and urine, and vaginal swab specimens were taken. The specimens were tested in the same way as those from the general population.

Laboratory procedures

In Cotonou, Kisumu and Ndola, serum samples were first tested for HIV by enzyme-linked immunosorbent assay (ELISA) (ICE HIV-1.0.2; Murex Diagnostics, Dartford, UK; or HIV-1/HIV-2 3rd Generation Plus; Abbott Laboratories, Abbott Park, Illinois, USA). Confirmation was carried out with a rapid test (Capillus HIV-1/HIV-2; Cambridge Diagnostics, Galway, Ireland; or HIV Multispot; Sanofi Diagnostics Pasteur S.A., Marne La Coquette, France). Samples giving discrepant results were tested with HIV 2.2 Blot (Genelabs, Singapore) or using an algorithm with Vironostika HIV Uniform II Plus O (Organon Teknika, Boxtel, The Netherlands) followed by Enzygnost Anti-HIV 1/2 Plus (Behring Diagnostics, Marburg, Germany) and INNO-LIA HIV Confirmation (Innogenetics, Zwijnaarde, Belgium) if necessary. Because of the presence of HIV-1 group O in Cameroon, a different testing strategy was applied in Yaoundé. Samples were first tested with Behring 1 + 2 + O (Behring Diagnostics), then confirmed with ICE HIV-1.0.2. Samples with optical density < 5 on ICE HIV-1.0.2 were tested with HIV Multispot for the detection of HIV-2, a V3 loop EIA for the detection of HIV-1 group O, and HIV 2.2 Blot for the detection of HIV-1 group M in seroconversion phase.

Subtyping was carried out at the Institute of Tropical Medicine in Antwerp. The method used was the heteroduplex mobility assay as described by Delwart *et al.* [26], supplemented by sequencing if needed. Subtyping of HIV-1 was performed on all HIV-positive samples from the general population from Cotonou and Yaoundé, and on a random selection of 100 samples from Kisumu and Ndola. In addition, a random selection of 50 HIV-positive serum samples from sex workers from each site was subtyped.

Screening for syphilis was carried out with the rapid plasma region (RPR) Card Antigen Suspension (Becton Dickinson and Company, Cockeysville, Maryland, USA). Positive samples were tested with the Serodia®-

Treponema pallidum particle agglutination (TPPA; Fujirebio Inc., Tokyo, Japan). A positive RPR (at any titre) and TPPA was considered as evidence of recently acquired and/or untreated syphilis. Testing for HSV-2 was carried out with an HSV-2 Type Specific IgG ELISA (Gull Laboratories, Bad Homburg, Germany).

The urine samples were frozen and shipped on dry ice to Antwerp, where they were tested for gonorrhoea and chlamydial infection using DNA amplification methods. The samples were first tested with the Amplicor *Chlamydia trachomatis*/*Neisseria gonorrhoeae* Test (Roche Diagnostics, Branchburg, New Jersey, USA) and the positive samples were confirmed with the LCx™ *Neisseria gonorrhoeae* Assay or LCx™ *Chlamydia trachomatis* Assay (Abbott Laboratories).

The culture medium used for the diagnosis of *T. vaginalis* infection was the InPouch™ TV (Biomed Diagnostics, San José, California, USA), which was read 3 and 5 days after inoculation.

Data management and analysis

All data were double-entered and validated in a specially designed EPI-INFO (CDC, Atlanta, Georgia, USA) database. Further data cleaning was performed using SPSS 8.0 for Windows (SPSS Inc. 1997, Chicago, Illinois, USA). Data analysis was performed using SPSS or STATA 6.0 (StataCorp. 1999, College Station, Texas, USA). Data were analysed without adjustment for clustering.

Validation of data on sexual behaviour

To assess the reliability of the data on sexual behaviour, a random selection of about 25 male and 25 female respondents under age 30 were re-interviewed within 3 months of the survey. These in-depth interviews covered a selection of topics only, including age at first sex, lifetime number of partners and number of non-spousal partners in the past 12 months. The results of the in-depth interviews were compared with the individual survey results. Due to time constraints, this part of the study was not conducted in Yaoundé.

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

Study population: general population

Information was collected on 98% of the selected households in Cotonou, 75% in Yaoundé, 89% in Kisumu and 88% in Ndola. Table 1 presents the numbers of eligible men and women in those households and the response

rates for the interview and for the blood tests. In all four cities, the response rate for women was higher than for men. In Yaoundé and Kisumu, the response rate among men decreased with age. The main reason for non-response was failure to contact potential study participants despite repeated visits to the home. There were relatively few outright refusals for interview: 33 in Cotonou, 62 in Yaoundé, 69 in Kisumu and 121 in Ndola.

In Kisumu and Ndola, the initial response rates of men were unacceptably low (67 and 56% for the interview, respectively), and a second round was organized in an attempt to enrol eligible men who were missed previously. Due to logistical constraints, it was not possible in Kisumu to collect blood and urine specimens at this second round and, consequently, the proportion of eligible men who provided a blood sample was lower in Kisumu (62%) than in Cotonou (86%), Yaoundé (70%) and Ndola (65%). The proportions of eligible women who provided blood were higher than for men, and ranged between 75% in Kisumu and 89% in Cotonou (Table 1).

Men and women who were not tested for HIV were compared with those tested with respect to socio-demographic characteristics and sexual behaviour. In Cotonou, men who were not tested had more lifetime sex partners than men who were tested. Among women, there were no differences in sexual behaviour between those tested and those who were not. In Yaoundé, men who were not tested reported fewer non-spousal partners in the past 12 months than men who were tested, and were less likely to report an episode of STI in the past 12 months. Women in Yaoundé who were not tested did not differ significantly from those tested. In Kisumu, men who were not tested were more likely, compared with those who were HIV tested, to have been married, to have had fewer lifetime sex partners, to have had fewer non-spousal partners in the past 12 months, and were less likely to have reported an episode of STI in the past 12 months. Among women in Kisumu, the proportion not sexually active was significantly higher in the group of women who were not tested. When restricting the analysis to women who were sexually active, women who were not tested reported fewer lifetime sex partners but an equal number of non-spousal partners, than women who were tested. In Ndola, there were no significant differences between men and women who were tested and those who were not.

The participation rates for submission of a urine sample were very similar to those for blood. In Cotonou, 83% of eligible men gave a urine sample, 69% in Yaoundé, 62% in Kisumu and 66% in Ndola. The corresponding figures for women were 86, 77, 73 and 81%. The proportions of eligible women who were tested for trichomoniasis were lower: 83% in Cotonou, 55% in Yaoundé, 38% in Kisumu and 50% in Ndola.

Table 1. Response rates by age group, sex and city

Age (years)	Cotonou			Yaoundé			Kisumu			Ndola		
	Eligible	Interview (% eligible)	Blood taken (% eligible)	Eligible	Interview (% eligible)	Blood taken (% eligible)	Eligible	Interview (% eligible)	Blood taken (% eligible)	Eligible	Interview (% eligible)	Blood taken (% eligible)
Men												
15-19	208	194 (93%)	181 (87%)	253	205 (81%)	189 (75%)	239	194 (81%)	146 (61%)	165	125 (76%)	110 (67%)
20-29	470	447 (95%)	413 (88%)	506	395 (78%)	371 (73%)	376	319 (85%)	242 (64%)	392	293 (75%)	257 (66%)
30-39	273	259 (95%)	229 (84%)	333	239 (72%)	213 (64%)	259	211 (81%)	154 (59%)	247	191 (74%)	169 (68%)
40-49	129	121 (94%)	105 (81%)	190	134 (71%)	122 (64%)	140	105 (75%)	84 (60%)	151	111 (74%)	89 (59%)
All	1080	1021 (95%)	928 (86%)	1282	973 (76%)	896 (70%)	1014	829 (82%)	626 (62%)	955	720 (75%)	625 (65%)
Women												
15-19	242	226 (93%)	212 (88%)	296	254 (86%)	238 (80%)	323	281 (87%)	226 (70%)	275	251 (91%)	227 (83%)
20-29	471	452 (96%)	419 (89%)	540	468 (87%)	424 (78%)	469	427 (91%)	368 (78%)	491	435 (89%)	390 (79%)
30-39	254	250 (98%)	228 (90%)	292	251 (86%)	224 (77%)	266	234 (88%)	196 (74%)	240	218 (91%)	201 (84%)
40-49	172	167 (97%)	156 (91%)	175	143 (86%)	131 (75%)	133	118 (89%)	103 (77%)	124	106 (85%)	93 (75%)
All	1139	1095 (96%)	1015 (89%)	1303	1116 (86%)	1017 (78%)	1191	1060 (89%)	893 (75%)	1130	1010 (89%)	911 (81%)

Table 2. Prevalence (%) of HIV infection by age group, sex and city*

Age (years)	Cotonou	Yaoundé	Kisumu	Ndola
Men	(n = 928)	(n = 896)	(n = 622)	(n = 624)
15–19	0	0	3.5	3.7
20–24	2.3	1.4	12.3	13.2
25–29	6.7	3.1	28.7	27.3
30–39	3.9	9.9	33.1	39.6
40–49	3.8	5.7	27.7	25.8
All (95% CI)	3.3 (2.3–4.8)	4.1 (3.0–5.7)	19.8 (16.8–23.2)	23.2 (20.0–26.8)
Women	(n = 1015)	(n = 1017)	(n = 893)	(n = 910)
15–19	2.4	3.4	23.0	15.4
20–24	3.8	9.3	38.3	41.8
25–29	4.8	11.2	37.1	43.8
30–39	3.5	8.9	30.1	34.8
40–49	2.6	6.1	18.5	20.4
All (95% CI)	3.4 (2.4–4.8)	7.8 (6.2–9.6)	30.1 (27.2–33.3)	31.9 (28.9–35.0)
Female sex workers	(n = 275)	(n = 320)	(n = 296)	(n = 319)
All (95% CI)	57.5% (51.4–63.3)	34.4% (29.2–39.9)	74.7% (69.2–79.4)	68.7% (63.2–73.6)

* Fifteen indeterminate results have been excluded: four from Yaoundé, four from Kisumu and seven from Ndola. CI, confidence interval.

Study population: female sex workers

The estimated number of sex workers was 1900 in Cotonou, 5600 in Yaoundé, 1400 in Kisumu and 2300 in Ndola. Relating this to the size of the adult male population in the four cities, it was estimated that there were 10 sex workers per 1000 men in Cotonou, 14 in Yaoundé, 19 in Kisumu and 21 per 1000 men in Ndola. Completed questionnaires were obtained for 433 women in Cotonou, 328 in Yaoundé, 300 in Kisumu and 332 in Ndola. HIV test results were available for 324 (98.8%) of these women in Yaoundé, 296 (98.6%) in Kisumu and 324 (97.6%) in Ndola. In Cotonou, the proportion of sex workers who were tested for HIV was much lower (63.5%; 275 out of 433) because of an initial reluctance to go to the health centre after the interview was completed.

Prevalence of HIV infection in the general population

The overall general population prevalence of HIV infection in men was 3.3% in Cotonou, 4.1% in Yaoundé, 19.8% in Kisumu and 23.2% in Ndola. For women, the corresponding figures were 3.4, 7.8, 30.1 and 31.9% (Table 2). In all cities except Cotonou, the HIV prevalence in men peaked in the age group 30–39. In women in all four cities, it peaked in the age group 20–29. The HIV prevalence was higher in women than in men, except in Cotonou: the ratio of the HIV prevalence in women to the HIV prevalence in men was 1.03 for Cotonou, 1.9 for Yaoundé, 1.5 for Kisumu and 1.38 for Ndola. The difference in HIV prevalence between men and women was most accentuated in Kisumu and Ndola

in the age group 15–19 years. In this age group in Kisumu, the HIV prevalence in women was more than six times higher than in men, and in Ndola it was more than four times higher (Table 2).

Figure 3 presents the prevalence of HIV infection in women by number of years since initiation of sexual activity. In Kisumu and Ndola, the prevalence of HIV infection among women who were sexually active for less than 1 year was 14 and 17%, respectively. The HIV prevalence increased with time since sexual debut and was 46 and 59% in women in Kisumu and Ndola, respectively, who started sexual activity 5 years before the interview. The test for trend was statistically significant in these two cities ($P < 0.001$). Such a trend of increasing HIV prevalence with number of years since sexual debut was not seen in Cotonou and Yaoundé.

Prevalence of HIV infection among sex workers

As expected, the prevalence of HIV infection among sex workers was higher in the high HIV prevalence cities than in the low prevalence cities: 75% in Kisumu and 69% in Ndola, versus 58% in Cotonou and 34% in Yaoundé (Table 2). However, in Cotonou, there was a striking contrast between the high HIV prevalence among sex workers and the relatively low prevalence in the general population.

Conclusions

There are large differences in HIV prevalence between Eastern/Southern Africa and West/Central Africa, and

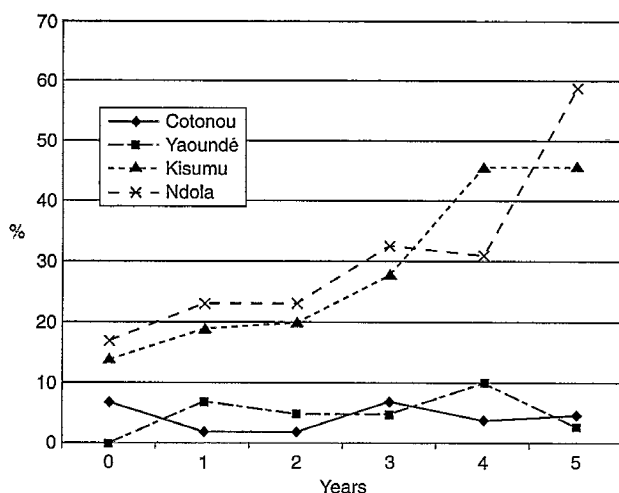


Fig. 3. HIV prevalence (%) in women by years since sexual debut.

there is evidence that these differences are largely due to differences in the rate of spread of HIV. The objective of the multicentre study on factors determining the differential spread of HIV in four African cities was to identify behavioural and biological factors that could explain why HIV has spread much more rapidly in the populations of Kisumu (Kenya) and Ndola (Zambia) than in Cotonou (Benin) and Yaoundé (Cameroon). In each of the four cities, a cross-sectional survey was conducted in the general population and among a random sample of self-acknowledged sex workers. The research instruments, including the questionnaires and the laboratory procedures, were standardized to permit comparison of results.

The response rates achieved were very good in women, but were less than optimal in men, with the exception of Cotonou. The low response rates in Yaoundé, Kisumu and Ndola were due to failure to make contact with eligible men. Once contact was made, very few men and women refused to be interviewed. The overall response rates that were achieved in the multicentre study compare well with surveys on sexual behaviour in Europe, where participation rates varied between 60 and 75% once contact was made with potential study participants [27]. Not surprisingly, participation rates for blood and urine sampling were lower. However, comparison of sexual behaviour characteristics of men and women who were tested with those who were not revealed very few differences, and non-response seems unlikely to have induced substantial bias in our estimates of general population HIV prevalence rates. The proportions of women tested for trichomoniasis were rather low. Women were requested to insert a swab in the vagina and to submit it to the nurse who inoculated the swab immediately in a culture medium for *T. vaginalis*. Self-administration of the vaginal swab was well accepted and the low participation rates for testing for trichomoniasis

were due mainly to delays in the delivery of culture medium to the research sites. A more detailed discussion of the implications of non-response is given in another paper in this supplement [28].

The HIV prevalence rates in the general population confirmed our preliminary assessment of the level of HIV infection in the general population in the four cities, which was based on estimates of HIV prevalence from sentinel surveillance among pregnant women. Although not entirely unexpected, the high HIV rates in women aged 15–19 years in Kisumu and Ndola are alarming. Once sexually active, adolescent girls in Kisumu and Ndola very quickly become HIV infected. Similar observations have been made in young women in the general population in Carltonville, South Africa [29,30]. The high HIV rates among young women in Kisumu and Ndola can only be explained if the male-to-female HIV transmission is very high in these two cities [31].

In Yaoundé, Kisumu and Ndola, the prevalence of HIV infection was substantially higher in women than in men. Studies conducted in the general population elsewhere in Africa have made similar observations [32–35]. In the multicentre study, the difference in HIV prevalence between men and women was especially marked in the younger age groups in Kisumu and Ndola. Possible explanations for this were explored and the results of the analyses are presented in a separate paper in this supplement [31].

As expected, HIV prevalence among sex workers was higher than in the general population, and higher in the high HIV prevalence cities than in the low HIV prevalence cities. The difference between Ndola and Cotonou, however, was modest. The most likely explanation for the strong contrast in prevalence in Cotonou between sex workers (57.5%) and men in the general population (3.3%) is a reduced probability of transmission of HIV from sex workers to men, due to high rates of condom use by sex workers and their clients, and due to the fact that almost all men in Cotonou are circumcised. This is explored in more detail in the paper on the role of commercial sex in the HIV epidemics in the four cities [36].

The HIV rates recorded in the general population and in sex workers in these four cities illustrate once again the large variations in HIV spread that exist between different regions of sub-Saharan Africa. Several explanatory hypotheses have been tested in the multicentre study on factors determining the differential spread of HIV in four African cities. Risk factors for HIV infection have been examined in each of the four cities and prevalences of relevant risk factors compared between the cities [37]. Differences in sexual behaviour patterns including concurrent partnerships, and the role of sex workers in the spread of HIV are explored in separate papers [36,38,39]. Other STIs have been shown to enhance the transmis-

sion of HIV. The epidemiology of gonorrhoea, chlamydial infection, syphilis, HSV-2 infection and trichomoniasis has been compared between the four cities, and the role of these STIs in the spread of HIV examined [40–42]. It has been suggested that differences in the prevalence of male circumcision may explain differences in the rate of HIV spread between different African regions. The role of male circumcision in the HIV epidemics in the four cities is explored in more detail in a separate paper in this supplement [43]. Large-scale promotion of condom use in sub-Saharan Africa has only started fairly recently, and it is unlikely that differences in condom use play a major role in explaining the differences in HIV prevalence between the East African and the West African cities. To confirm this, condom use in the four cities was compared and the protective effect of condom use assessed [44]. The cross-sectional design of the multicentre study does not allow comparison of the transmission efficiency of different HIV strains. However, to investigate whether differences in the epidemics might be explained by differences in prevailing subtypes, the distribution of HIV subtypes in the general population and in sex workers in the four cities was compared [45]. The final paper in this supplement summarizes the findings of all the analyses.

References

1. Joint United Nations Programme on HIV/AIDS (UNAIDS). *Report on the Global HIV/AIDS Epidemic*. Geneva: UNAIDS; June 2000.
2. US Bureau of the Census. *HIV/AIDS Surveillance Data Base*. Washington DC: Population Division, International Programs Center; June 2000.
3. Buvé A, Caraël M, Hayes R, Robinson NJ. *Variations in HIV prevalence between urban areas in sub-Saharan Africa: do we understand them?* *AIDS* 1995, 9 (suppl A):S103–S109.
4. Clumeck N, Mascart-Lemone F, De Maubeuge J, Brenez D, Marcelis L. *Acquired immune deficiency syndrome in black Africans [letter]*. *Lancet* 1983, i:642.
5. Fleming DT, Wasserheit JN. *From epidemiological synergy to public health policy and practice: the contribution of other sexually transmitted diseases to sexual transmission of HIV infection*. *Sex Transm Infect* 1999, 75:3–17.
6. Weiss HA, Quigley M, Hayes R. *Male circumcision and risk of HIV infection in sub-Saharan Africa: a systematic review and meta-analysis*. *AIDS* 2000, 14:2361–2370.
7. Operskalski EA, Stram DO, Busch MP, *et al.* *Role of viral load in heterosexual transmission of human immunodeficiency virus type 1 by blood transfusion recipients*. *Am J Epidemiol* 1997, 146:655–661.
8. Ragni MV, Faruki H, Kingsley LA. *Heterosexual HIV-1 transmission and viral load in hemophilic patients*. *J Acquir Immune Defic Syndr* 1998, 17:42–45.
9. Pedraza MA, del Romero J, Roldan F, Garcia S, Ayerbe MC, Noriega AR, Alcamí J. *Heterosexual transmission of HIV-1 is associated with high plasma viral load levels and a positive viral isolation in the infected partner*. *J Acquir Immune Defic Syndr* 1999, 21:120–125.
10. Quinn TC, Wawer MJ, Sewankambo N, *et al.* *Viral load and heterosexual transmission of human immunodeficiency virus type 1*. *N Engl J Med* 2000, 342:921–929.
11. European Study Group on Heterosexual Transmission of HIV. *Comparison of female to male and male to female transmission of HIV in 563 stable couples*. *BMJ* 1992, 304:809–813.
12. Seidlin M, Vogler M, Lee E, Lee YS, Dubin N. *Heterosexual transmission of HIV in a cohort of couples in New York City*. *AIDS* 1993, 7:1247–1254.
13. Padian NS, Shiboski SC, Jewell NP. *The effect of number of exposures on the risk of heterosexual HIV transmission*. *J Infect Dis* 1990, 161:883–887.
14. Sandala L, Lurie P, Sunkutu MR, Chaim EM, Hudes ES, Hearst N. *'Dry sex' and HIV infection among women attending a sexually transmitted diseases clinic in Lusaka, Zambia*. *AIDS* 1995, 9 (suppl 1):S61–S68.
15. Nkengasong JN, Janssens W, Heyndrickx L, *et al.* *Genotypic subtypes of HIV-1 in Cameroon*. *AIDS* 1994, 8:1405–1412.
16. Takehisa J, Zekeng L, Ido I, *et al.* *Various types of HIV mixed infections in Cameroon*. *Virology* 1998, 245:1–10.
17. Gao F, Bailes E, Robertson DL, *et al.* *Origin of HIV-1 in the chimpanzee *Pan troglodytes troglodytes**. *Nature* 1999, 397:436–441.
18. Bayley AC, Cheinsong-Popov R, Dalgleish AG, *et al.* *HTLV-III serology distinguishes atypical and endemic Kaposi's sarcoma in Africa*. *Lancet* 1985, i:359–361.
19. Caraël M, Cleland J, Adekun L. *Overview and selected findings of sexual behaviour surveys*. *AIDS* 1991, 5 (suppl):S65–S74.
20. Arya OP, Nsanzumuhire H, Taber SR. *Clinical, cultural, and demographic aspects of gonorrhoea in a rural community in Uganda*. *Bull World Health Org* 1973, 49:587–595.
21. Grosskurth H, Mayaud P, Mosha F, *et al.* *Asymptomatic gonorrhoea and chlamydial infection in rural Tanzanian men*. *BMJ* 1996, 312:277–280.
22. UNAIDS. *Looking Deeper Into the HIV Epidemic: A Questionnaire for Tracing Sexual Networks*. Best Practice Collection. UNAIDS/98.27. Geneva: UNAIDS; 1998.
23. Mann JM, Nzilambi N, Piot P, *et al.* *HIV infection and associated risk factors in female prostitutes in Kinshasa, Zaire*. *AIDS* 1988, 2:249–254.
24. Kaptue L, Zekeng L, Djoumessi S, Monny-Lobe M, Nichols D, Debuysscher R. *HIV and chlamydia infections among prostitutes in Yaoundé, Cameroon*. *Genitourin Med* 1991, 67:143–145.
25. Lankoandé S, Meda N, Sangaré L, *et al.* *Prevalence and risk of HIV infection among female sex workers in Burkina Faso*. *Int J STD AIDS* 1998, 9:146–150.
26. Delwart EL, Shpaer EG, Louwagie J, *et al.* *Genetic relationships determined by a DNA heteroduplex mobility assay: analysis of HIV-1 env genes*. *Science* 1993, 262:1257–1261.
27. Hubert M. *Studying and comparing sexual behaviour and HIV/AIDS in Europe*. In *Sexual Behaviour and HIV/AIDS in Europe*. Edited by Michel Hurbert, Nathalie Bajos and Theo Sandfort. London: UCL Press; 1998.
28. Buvé A, Lagarde E, Caraël M, *et al.* *Interpreting sexual behaviour data: validity issues in the multicentre study on factors determining the differential spread of HIV in four African cities*. *AIDS* 2001, 15 (suppl 4):S117–S126.
29. Williams B, Campbell C, Gilgen D, *et al.* *Assessing the risk of HIV/AIDS in the Carletonville gold mining area [abstract MoPpC1026]*. Paper presented at the XIIIth International AIDS Conference. Durban, South Africa, 9–14 July 2000.
30. Auvert B, Taljaard D, Williams BG, *et al.* *Dramatic epidemic of HIV infection among young women in Carletonville (South Africa) [abstract TuPeC3454]*. Paper presented at the XIIIth International AIDS Conference. Durban, South Africa, 9–14 July 2000.
31. Glynn JR, Caraël M, Auvert B, *et al.* *Why do young women have a much higher prevalence of HIV than young men? A study in Kisumu, Kenya and Ndola, Zambia*. *AIDS* 2001, 15 (suppl 4):S51–S60.
32. Berkley S, Naamara W, Okware S, *et al.* *AIDS and HIV infection in Uganda — are more women infected than men?* *AIDS* 1990, 4:1237–1242.
33. Barongo LR, Borgdorff MW, Mosha F, *et al.* *The epidemiology of HIV-1 infection in urban areas, roadside settlements and rural villages in Mwanza Region, Tanzania*. *AIDS* 1992, 6:1521–1528.
34. Wilkins A, Ricard D, Todd J, Whittle H, Dias F, Da Silva AP. *The epidemiology of HIV infection in a rural area of Guinea-Bissau*. *AIDS* 1993, 7:1119–1122.
35. Fylkesnes K, Ndhlovu Z, Kasumba K, Musonda RM, Sichone M. *Studying dynamics of the HIV epidemic: population-based data compared with sentinel surveillance in Zambia*. *AIDS* 1998, 12:1227–1234.
36. Morison L, Weiss HA, Buvé A, *et al.* *Commercial sex and the spread of HIV in four cities in sub-Saharan Africa*. *AIDS* 2001, 15 (suppl 4):S61–S69.

37. Auvert B, Buvé A, Ferry B, *et al.* 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. *AIDS* 2001, 15 (suppl 4):S15-S30.
38. Ferry B, Caraël M, Buvé A, *et al.* Comparison of key parameters of sexual behaviour in four African urban populations with different levels of HIV infection. *AIDS* 2001, 15 (suppl 4): S41-S50.
39. Lagarde E, Auvert B, Caraël M, *et al.* Concurrent sexual partnerships and HIV prevalence in five urban communities of sub-Saharan Africa. *AIDS* 2001, 15:877-884.
40. Buvé A, Weiss HA, Laga M, *et al.* The epidemiology of gonorrhoea, chlamydial infection and syphilis in four African cities. *AIDS* 2001, 15 (suppl 4):S79-S88.
41. Weiss HA, Buvé A, Robinson NJ, *et al.* The epidemiology of HSV-2 infection and its association with HIV infection in four urban African populations. *AIDS* 2001, 15 (suppl 4):S97-S108.
42. Buvé A, Weiss HA, Laga M, *et al.* The epidemiology of trichomoniasis in women in four African cities. *AIDS* 2001, 15 (suppl 4):S89-S96.
43. Auvert B, Buvé A, Lagarde E, *et al.* Male circumcision and HIV infection in four cities in sub-Saharan Africa. *AIDS* 2001, 15 (suppl 4):S31-S40.
44. Lagarde E, Auvert B, Chege J, *et al.* Condom use and its association with HIV/sexually transmitted diseases in four urban communities of sub-Saharan Africa. *AIDS* 2001, 15 (suppl 4): S71-S78.
45. Morison L, Buvé A, Zekeng L, *et al.* HIV-1 subtypes and the HIV epidemics in four cities in sub-Saharan Africa. *AIDS* 2001, 15 (suppl 4):S109-116.