Effect of interventions to control sexually transmitted disease on the incidence of HIV infection in female sex workers

Peter D. Ghys[a,b], Mamadou O. Diallo[a], Virginie Ettiègne-Traoré[a], Glen A. Satten[c], Camille K. Anoma[a], Chantal Maurice[a], Jean-Claude Kadjo[a], Issa-Malik Coulibaly[d], Stefan Z. Wiktor[a,c], Alan E. Greenberg[a,c] and Marie Laga[b]

Objective: To compare the seroincidence of HIV infection among female sex workers in Abidjan, Côte d'Ivoire before and during an intervention study to control sexually transmitted diseases (STD) and to study the effect of two STD diagnosis and treatment strategies on the prevalence of STD and on the seroincidence of HIV infection.

Method: A screening facility for STD and HIV had been available since October 1992 for female sex workers. From June 1994, women who were HIV seronegative or HIV-2 positive during the screening could enroll in the intervention study in which participants reported once a month to a confidential clinic where they received health education, condoms and STD treatment if indicated. Women in the study were randomized either to a basic STD diagnosis and treatment strategy, which included a gynecologic examination when symptomatic, or to an intensive strategy that included a gynecologic examination regardless of symptoms. An outcome assessment every 6 months included a gynecologic examination, HIV serology and laboratory tests for STD.

Results: Of 542 women enrolled in the study, 225 (42%) had at least one outcome assessment. The HIV-1 seroincidence rate during the intervention study was significantly lower than before the study (6.5 versus 16.3 per 100 person-years; $P = 0.02$). During the study, the HIV-1 seroincidence rate was slightly lower in the intensive than in the basic strategy (5.3 versus 7.6 per 100 person-years; $P = 0.5$).

Conclusion: National AIDS control programs should consider adopting as policy the type of integrated approach used in this intervention study for HIV prevention in female sex workers.

AIDS 2001, **15**:1421–1431

Keywords: HIV-2, sexually transmitted disease, sex worker

Introduction

Female sex workers play an important role in the HIV epidemic in Abidjan. Recent studies show that they have a high prevalence rate of HIV infection: 40% in 1987, 68% in 1990 [1] and 80% in 1992–1994 [2]. Many men in Abidjan use the services of female sex workers [3] and contact with sex workers has been a strong risk factor for HIV infection in men [4]. Prevention of HIV transmission to and from female sex workers is, therefore, essential to try to slow the HIV epidemic.

From the [a]Projet RETRO-CI Abidjan, Côte d'Ivoire, the [b]Institute of Tropical Medicine, Antwerp, Belgium, the [c]Centers for Disease Control and Prevention, Atlanta, Georgia, USA and the [d]National AIDS/STD/TB Control Program, Abidjan, Côte d'Ivoire.

Correspondence to Dr P. D. Ghys, UNAIDS, 20 Avenue Appia, CH-1211 Geneva 27 Switzerland.

Date of receipt: 28 July 2000; revised: 12 January 2001; accepted: 21 February 2001.

Condom use can prevent sexual transmission of HIV, and a condom promotion program in Nairobi targeted to female sex workers was effective in reducing HIV incidence in sex workers [5]. Several studies have shown that other sexually transmitted diseases (STD) facilitate the transmission of HIV [6–10]. In a program for female sex workers in Kinshasa that combined condom promotion with treatment for STD, women who received very regular check ups and treatment were less likely to acquire HIV than those who received irregular check ups, even when controlled for level of condom use [8]. However, some of the treatment decisions were based on sophisticated laboratory support, which is not available in many developing countries. The World Health Organization has proposed diagnostic algorithms [11] that are independent of such support. Sensitive algorithms have been designed for screening for cervicitis among Abidjan sex workers using a combination of signs: cervical mucopus and friability, and simple microscopy for vaginal and cervical white blood cells [12]. In a 1992–1994 cross-sectional study among female sex workers, many women were not aware of the presence of an STD, even when prompted [2]. Since a considerable proportion of STD in female sex workers would not cause symptoms and the female sex worker would, therefore, not seek clinical services while carrying an infection, it is important to evaluate the possible benefit of regular screening for STD for female sex workers. Regular screening is done in some African countries where sex workers are registered, for example in Senegal [13].

The present study is an intervention study among female sex workers to determine the impact of an integrated prevention approach on the incidence of HIV infection, and to assess whether an intensive STD diagnosis and treatment strategy can further reduce HIV incidence.

Methods

Since 1991, a Côte d'Ivoire Ministry of Health HIV/STD prevention campaign, called the 'Programme de Prévention et de Prise en charge des MST/SIDA chez les femmes libres et leurs Partenaires' (PPP), has used peer education to promote the consistent use of condoms by sex workers. Since October 1992, female sex workers in Abidjan have been invited through a network of peer educators to participate in a cross-sectional study of STD and HIV conducted at Clinique de Confiance, a confidential HIV/STD clinic accessible only for female sex workers and their stable sex partners. Consenting participants were interviewed, clinically examined, screened and treated for STD and counselled and tested for HIV infection. From June 1994 to November 1997, female sex workers who were HIV negative or HIV-2 seropositive when tested in the cross-sectional study were invited at the time of the post-test counselling session (1 week after the initial visit in the cross-sectional study) to participate in the intervention study. Women who had failed to attend 1 week after the initial visit in the cross-sectional study were invited to enroll in the intervention study at the first visit following participation in the cross-sectional study, regardless of the time elapsed between these two visits. Women who were HIV seronegative or HIV-2 seropositive when tested in the cross-sectional study between October 1992 and May 1994 (before the start of the intervention study) and who came back to Clinique de Confiance after May 1994 were also invited to enroll in the intervention study. Following informed consent, women were randomized to either an intensive or a basic STD screening and treatment strategy. If 2 weeks or less had elapsed between participation in the cross-sectional study and enrollment in the intervention study, the results of the interview, the clinical examination, the screening for STD and HIV performed in the cross-sectional study were used for the enrollment assessment. If more than 2 weeks had elapsed between participation in the cross-sectional study and enrollment in the intervention study, an interview, a clinical examination including an STD diagnostic evaluation and a blood draw for HIV and syphilis serology were performed prior to enrollment. Women were asked to keep a sexual activity log in which they recorded the number of sexual acts with and without condoms per day. The study was approved by the Ethical Committee of the Côte d'Ivoire Ministry of Health, Abidjan, Côte d'Ivoire; the Ethical Committee of the Institute for Tropical Medicine, Antwerp, Belgium; and the Institutional Review Board of the Centers for Disease Control and Prevention, Atlanta, Georgia, USA.

Study follow-up

Women participating in the intervention study were invited to come to the clinic on a monthly basis. Every month they received health education talks, 96 condoms and a new sexual activity log booklet. During an individual interview the information in the sexual activity log was verified and summarized. Women were screened and treated for STD depending on their randomization group. Women randomized to the basic STD screening and treatment strategy were examined only if they reported vaginal discharge, lower abdominal pain or a genital ulcer. Symptomatic women were treated using treatment algorithms based on the results of the examination. All women in whom a vaginal discharge was confirmed following a bimanual and external examination were treated for cervical infections. In addition, based on the appearance of the vaginal discharge, they were also treated for either candidiasis or for trichomoniasis and bacterial vaginosis. Women randomized to the intensive STD screening

and treatment strategy were examined every month, regardless of the presence of symptoms. This examination included a bimanual and external examination, the use of a speculum with direct visualization of the vagina and cervix, and direct microscopy for white blood cells, trichomonas and yeasts. Women in the intensive group were treated using treatment algorithms based on these examinations. Women received treatment for cervical infections when either cervical mucopus or cervical friability were detected during the clinical examination, or when more than 10 white blood cells per microscopic field were present. Women received treatment for vaginal infections based on the appearance of the vaginal discharge and on the results of wet mount microscopy. All STD treatment was dispensed free of charge at the clinic.

Outcome assessment

Every 6 months, an outcome assessment was scheduled. This assessment included an interview and a clinical examination during which gynecologic samples were taken for STD diagnosis and blood for HIV and syphilis serology. The sexual activity data and the number of treatments recorded during the monthly visits were summarized and recorded for the period since enrollment for the first outcome assessment or since the previous outcome assessment for the other outcome assessments. Treatment for STD was given free of charge based on applying the clinical and microscopical findings to treatment algorithms for vaginitis, cervicitis, genital ulcer and pelvic inflammatory disease.

Laboratory methods

A wet mount preparation of vaginal secretions collected from the posterior vaginal fornix was examined for the presence of *Trichomonas vaginalis* and yeasts. *Chlamydia trachomatis* was detected by enzyme immunoassay (EIA Microtrak, Syva Co, Palo Alto, CA, USA) in an endocervical swab. Material from a second endocervical swab was cultured on modified Thayer–Martin medium for the diagnosis of *Neisseria gonorrhoeae* [14].

Venous blood samples for HIV and syphilis serology were obtained from consenting counselled participants. From October 1992 to June 1996, sera were tested either by a virus-specific (HIV-1, HIV-2) enzyme-linked immunosorbent assay (ELISA) (Genetic Systems, Seattle, Washington, USA) or by a mixed antigen ELISA (Genelavia-mixt, Diagnostics Pasteur, Marnes-la-Coquette, France). From July 1996, sera were tested by two ELISA methods: Enzygnost Anti-HIV 1/2 Plus (Behring Diagnostic, Marburg, Germany) and ICE* 1.0.2 (Murex, Dartford, UK), with an additional test for discordant samples by Vironostika HIV Uni-Form II plus O (Organon-Technika, Boxtel, the Netherlands). From July 1996 to July 1997, repeatedly ELISA-reactive sera were confirmed and typed by a virus-specific synthetic peptide-based test (Pepti-LAV, Diagnostics Pasteur) and ELISA-reactive, synthetic peptide negative sera were further tested by HIV-1- and HIV-2-specific Western blot (New-LAV Blot (Diagnostics Pasteur) and HIV Blot 2.2 (Diagnostic Biotechnology, Geneva, Switzerland), respectively) [15]. From July 1997 onwards, ELISA-reactive sera were typed by two monospecific additional ELISA methods: Wellcozyme HIV Recombinant (Murex) for HIV-1 and ICE*2; (Murex) for HIV-2 [16].

Specific antitreponemal antibodies were detected by *Treponema pallidum* haemaglutination assay (Fujirebio, Tokyo, Japan), while a rapid plasma reagin test was also performed (Macro-Vue, Becton-Dickinson, Cokeysville, Maryland, USA). A woman was considered to have syphilis when both tests were positive, regardless of the rapid plasma reagin titer and treatment history.

Statistical analysis

For the univariate analysis of socio-demographic and behavioral characteristics and STD prevalence rates in the cross-sectional study, significance tests ($P < 0.05$) were performed by a 2×2 table chi square test with Yates' correction or by Fisher's exact test for proportions, and by the Wilcoxon rank sum test for continuous variables. Consistent condom use in the cross-sectional study was defined as condom use with all clients during the last working day. Anal sex, sex during menses and vaginal use of herbs were assessed in the cross-sectional study for the past month. Information on anal sex, sex during menses, vaginal use of herbs and cervical ectopy was collected after April 1994 only.

HIV-1 seroconversion was assessed in women who had at least one outcome assessment in the intervention study and in women who were re-screened prior to enrollment. A seroconversion was defined as a change in serologic result occurring during follow-up from HIV negative to HIV-1 seropositive, or from HIV-2 seropositive to seroreactive to both HIV-2 and HIV-1. A seroconversion would also have been defined as a change in serologic result from HIV negative to HIV-2 seropositive, but no such change occurred. A parametric model for interval-censored failure-time data assuming a constant hazard (SAS LIFEREG procedure; SAS Institute, Cary, North Carolina, USA) was used to estimate the HIV-1 seroconversion rate. Covariates measured during the cross-sectional study were used to determine risk factors for seroconversion, including the initial HIV status (HIV seronegative or HIV-2 seropositive), socio-demographic and behavioral characteristics and STD. The randomization group was also used as a covariate to study its effect on seroconversion. For the estimation of the HIV-1 seroconversion rate, the parametric model is equivalent to considering that seroconversion occurred halfway between the last negative and the first positive HIV-1 serology test

result. Time-dependent covariates were used for comparison of the incidence before the intervention and during the intervention. Multivariate models of the same type were used to estimate the effect of the intervention controlling for other factors. Results from the bivariate and multivariate models are presented as estimates of the incidence rate per 100 person-years by subgroup and the incidence rate ratio with its 95% confidence interval (CI). Condom use at the first outcome assessment of the intervention study was measured for the period since enrollment. The proportion of women who used condoms for $> 90\%$ of sexual acts during this period was compared with the proportion of the same women who used condoms for $> 90\%$ of sexual acts during their last working day as assessed in the cross-sectional study. McNemar's chi square test was used for this comparison and for the comparison of STD prevalence rates in the same individuals during the cross-sectional study and at the first outcome assessment. For the comparison of STD prevalence rates between women in the basic and the intensive STD diagnosis and treatment strategies a 2×2 table chi square test with Yates' correction was used.

Results

Numbers of participants

From October 1992 to 1 June 1994, 1370 women participated in the cross-sectional study of whom 1292 were screened for HIV (Fig. 1). Of the 268 (21%) HIV-seronegative women and the 32 (2%) HIV-2-seropositive women identified during this period, 31 (10%) women were re-screened prior to enrollment in the intervention study. From 2 June 1994 to November 1997, 2917 women were enrolled in the cross-sectional study of whom 2620 were screened for HIV. Of the 1172 (45%) eligible HIV-seronegative women and the 40 (2%) eligible HIV-2-seropositive women identified during this period, 521 (43%) women returned for enrollment in the intervention study. Of these 521 women, 448 enrolled within 2 weeks of participation in the cross-sectional study and 73 were re-screened prior to enrollment because they returned more than 2 weeks after initial screening. Of the 104 women who were re-screened prior to enrollment (32 first screened before June 1994 and 73 first screened between June 1994 and November 1997), 10 had seroconverted at re-screening, leaving 94 HIV-seronegative or HIV-2-seropositive women. The total of 542 women who were effectively enrolled in the intervention study comprised these 94 women and the 448 women who enrolled within 2 weeks of initial screening. Of the 542 women enrolled in the intervention study, 269 (50%) and 273 (50%) women were randomized to the basic and intensive strategies, respectively. During the intervention study, 225 women (42%) out of the 542 enrolled women were followed up through the first outcome assessment at 6 months to May 1998, when the study ended. In addition to the 225 women who had at least one outcome assessment in the intervention study, 59 women who did not have an outcome assessment during the intervention study had an enrollment assessment when they enrolled late in the intervention study. HIV incidence could, therefore, be studied in 284 of 552 women (51%). Of the 225 women with at least one outcome assessment in the intervention study, 111 (49%), 59 (26%), 30 (13%), 7 (3%), 11 (5%), 3 (1%) and 4 (2%) women had their last outcome assessment at 6, 12, 18, 24, 30, 36 and 42 months, respectively. Before their last outcome assessment, the large majority of these women (179 out of 220; 81%) attended at least four out of the five scheduled visits since their previous assessment, while only six (3%) did not attend any of these five scheduled visits.

Baseline characteristics of participants

Women from the cross-sectional study who were enrolled in the intervention study and those not enrolled were comparable for most characteristics except that enrolled women were less likely to be immigrants and to have sex during menses (Table 1). Enrolled women also had a lower prevalence of *C. trachomatis* infection but the prevalence rates of other STD were similar between the two groups.

Enrolled women who were followed up through the first outcome assessment at 6 months were comparable for most characteristics to enrolled women who were not followed up (Table 1), except that women with follow-up were slightly older and reported consistent condom use less frequently.

There were no differences in baseline characteristics and STD rates at enrollment between women randomized to either the basic or the intensive STD diagnosis and treatment strategy.

Among women with at least one outcome assessment, the 12 HIV-2-seropositive women were significantly older than the 272 HIV-seronegative women (median 30 versus 26 years; $P = 0.04$) and more likely to have syphilis (33% versus 10%; $P = 0.03$). Compared with HIV-seronegative women, HIV-2-seropositive women had also been in sex work for longer (median of 42 versus 24 months; $P = 0.3$), charged less for intercourse [median of 500 versus 1500 francs CFA (1 US$ is approximately 600 frances CFA); $P = 0.1$], were less likely to have had any schooling (42% versus 71%; $P = 0.05$) and were more likely to have gonorrhea (27% versus 12%; $P = 0.2$) and trichomoniasis (42% versus 23%; $P = 0.2$), although these differences were not statistically significant.

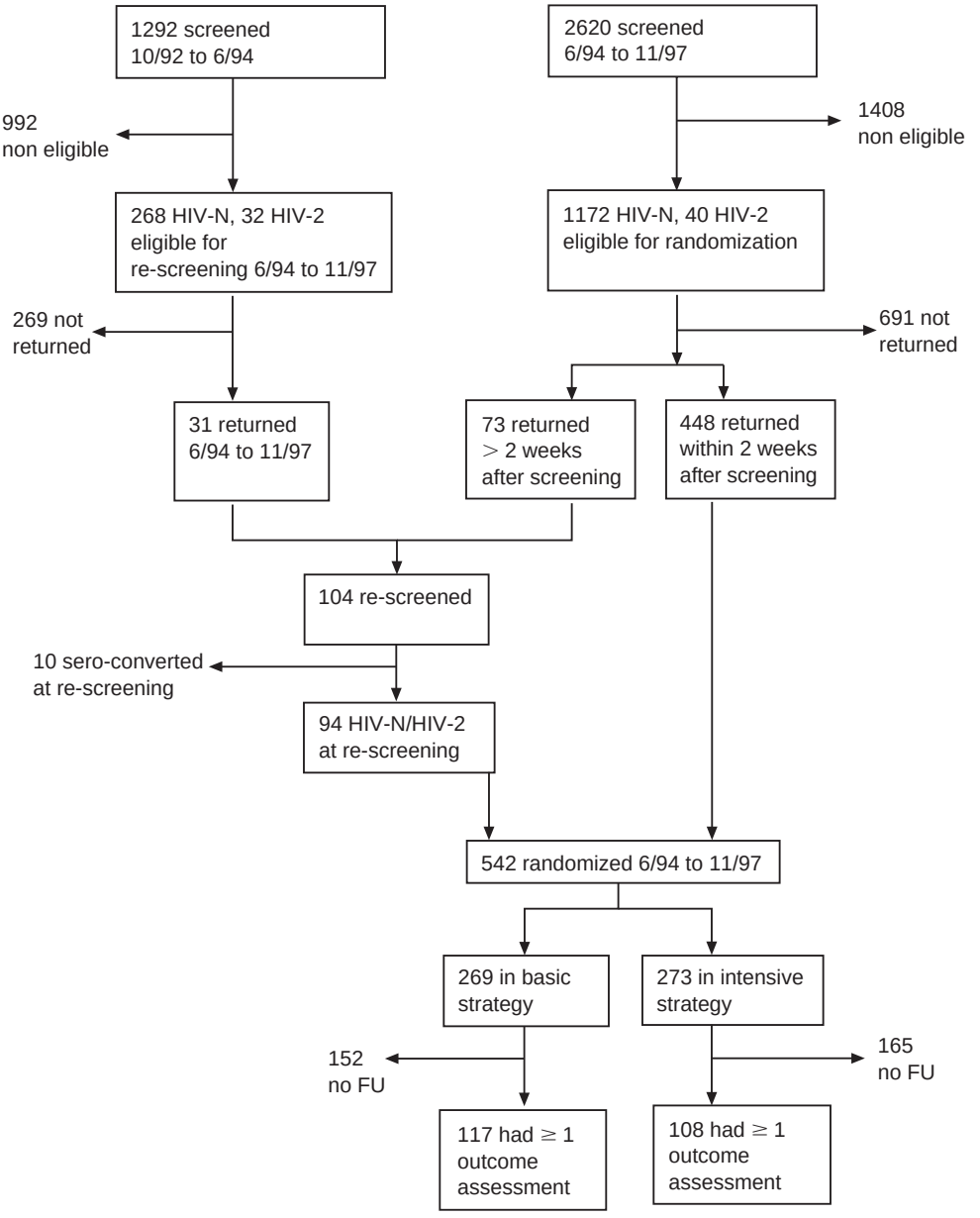

Fig. 1. Study profile.

HIV-1 seroincidence

Overall, 26 of 284 women seroconverted for HIV-1 during 318 person-years of observation for an overall seroconversion rate of 8.5/100 person-years (95% CI, 5.8–12.4). No seroconversions for HIV-2 were observed among HIV-seronegative women.

Women in the intensive STD diagnosis and treatment strategy group were less likely to seroconvert (6 of 108; 5.3/100 person-years) than those in the basic strategy group (10 of 117; 7.6/100 person-years), although this difference was not statistically significant (Table 2). The seroconversion rate during the intervention study was significantly lower than before the intervention study (6.5 versus 16.3/100 person-years; rate ratio 0.40; $P = 0.02$). The HIV-1 seroconversion rate among initially HIV-2-seropositive women was significantly higher (5 of 12; 36.4/100 person-years) than among HIV-seronegative women (21 of 272; 7.2/100 person-years; rate ratio 5.1; $P = 0.001$). Women who had a gonococcal infection at baseline were significantly more likely to seroconvert (9 of 36; 27.2/100 person-years) than women without (16 of 240; 6.0/100 person-years; rate ratio 4.5; $P = 0.0003$). Women with trichomoniasis at baseline were significantly more likely to seroconvert (11 of 68; 15.1/100 person-years) than women without (15 of 216; 6.4/100 person-years; rate ratio 2.4; $P = 0.03$).

Table 1. Socio-demographic and behavioral characteristics and STD prevalence rates in female sex workers in the cross-sectional study by enrollment status and follow-up status in the intervention study.

	Enrolled[a]	Not enrolled[a]	*P* value	Followed up	Not followed up	*P* value
Number	521	691		284	268	
Median age [years (IQR)]	24 (20–31)	25 (20–30)	0.9	27 (22–32)	24 (19–30)	0.001
Median duration of sex work [months (IQR)]	24 (10–36)	18 (5–36)	0.07	24 (12–36)	22 (11–36)	0.1
Median No. clients [per day (IQR)]	2 (2–4)	3 (2–4)	0.1	2 (2–4)	2 (2–4)	0.6
Price for intercourse [francs CFA[b] (IQR)]	1500 (1000–3000)	1500 (1000–3000)	0.8	1500 (750–3000)	1500 (1000–3000)	0.2
Worker characteristics						
Immigrant (%)	49.9	60.1	0.001	54.6	48.5	0.2
Any schooling (%)	66.8	70.0	0.3	69.7	63.0	0.1
Consistent condom use (%)	46.8	50.6	0.2	40.1	50.8	0.02
HIV-2 seropositive (%)	3.1	3.5	0.8	4.2	2.6	0.4
Anal sex (%)	7.9	5.2	0.08	6.2	9.3	0.2
Sex during menses (%)	25.3	32.4	0.01	22.6	28.0	0.2
Current hormonal contraceptive use (%)				7.8	9.3	0.5
Vaginal use of herbs (%)				9.3	11.2	0.6
Cervical ectopy (%)				8.6	7.9	0.9
C. trachomatis (%)	3.7	8.0	0.004	3.3	3.8	0.9
N. gonorrhoeae (%)	11.2	10.5	0.8	13.0	9.9	0.3
T. vaginalis (%)	23.2	26.2	0.3	23.9	21.6	0.6
Genital ulcer (%)	1.9	2.5	0.7	2.8	1.5	0.4
Syphilis (%)	8.1	8.4	0.9	10.6	6.4	0.1

IQR, interquartile range.
[a]For sex workers screened since June 1994 in the cross-sectional study and enrolled/not enrolled in the intervention study.
[b]1 $ (US) is approximately 600 francs CFA.

Table 2. Factors associated with HIV-1 seroconversion among 284 HIV-seronegative or HIV-2-seropositive female sex workers.

	No.[a]	Total No.	Patient-years	Incidence/100 patient years	Rate ratio (95% CI)	*P* value	Adjusted rate ratio (95% CI)	*P* value
Intervention								
Before	10	104	68	16.3	1		1	
During	16	225	247	6.5	0.40 (0.18–0.88)	0.02	0.42 (0.18–0.96)	0.04
STD strategy								
Basic	10	117	135	7.6	1			
Intensive	6	108	112	5.3	0.70 (0.25–1.9)	0.5		
HIV status								
Negative	21	272	302	7.2	1		1	
HIV-2-positive	5	12	16	36	5.1 (1.9–13.5)	0.001	3.8 (2.1–11.4)	0.02
N. gonorrhoeae								
No	16	240	273	6.0	1		1	
Yes	9	36	37	27.2	4.5 (2.0–10.3)	0.0003	4.8 (2.1–10.9)	0.0002
T. vaginalis								
No	15	216	240	6.4	1		1	
Yes	11	68	78	15.1	2.4 (1.1–5.2)	0.03	2.8 (1.3–6.2)	0.01
Syphilis								
No	22	254	274	8.3	1			
Yes	4	30	44	9.4	1.13 (0.39–3.3)	0.8		
Genital ulcer								
No	25	275	310	8.3	1			
Yes	1	8	7	14.7	1.77 (0.24–13.1)	0.6		
Age (years)								
⩾ 30	10	107	140	7.3	1			
< 30	15	174	172	9.1	1.23 (0.55–2.75)	0.6		
Sex work duration (months)								
⩾ 12	20	216	216	8.3	1			
< 12	6	68	68	9.1	1.10 (0.44–2.73)	0.8		
Number of clients								
< 4	18	207	231	8.0	1			
⩾ 4	8	77	77	9.7	1.21 (0.53–2.79)	0.7		
Price for sex (francs CFA)[b]								
⩾ 1000	16	210	233	7.1	1			
< 1000	10	73	86	12.4	1.76 (0.80–3.88)	0.2		
Immigrant								
No	11	129	133	8.5	1			
Yes	15	155	185	8.4	0.99 (0.46–2.16)	1.0		
Schooling								
Yes	16	198	226	7.3	1			
No	10	86	92	11.5	1.58 (0.72–3.48)	0.3		
Consistent condom use								
Yes	9	114	127	7.4	1			
No	17	170	191	9.2	1.25 (0.56–2.80)	0.6		
Hormonal contraceptive use								
No	24	262	285	8.7	1			
Yes	2	22	33	6.3	0.72 (0.17–3.04)	0.6		
Anal sex								
No	15	241	252	6.1	1			
Yes	3	16	15	21.2	3.50 (1.01–12.1)	0.05		
Sex during menses								
No	13	199	199	6.7	1			
Yes	5	58	69	7.5	1.12 (0.66–3.14)	0.8		
Vaginal use of herbs								
No	16	233	241	6.8	1			
Yes	2	24	26	7.9	1.16 (0.27–5.06)	0.8		
Cervical ectopy								
No	17	234	249	7.0	1			
Yes	1	22	18	5.8	0.83 (0.11–6.23)	0.9		

CI, confidence interval.

[a]Missing data: age missing for three women, of whom one seroconverted; *N. gonorrhoeae* data missing for eight women of whom one seroconverted; genital ulcer status missing for one woman; price for sex missing for one woman; hormonal contraceptive use missing for four women; anal sex, sex during menses and vaginal use of herbs missing for 27 women of whom eight seroconverted; ectopy missing for 28 women of whom eight seroconverted.

[b]1 $ (US) is approximately 600 francs CFA.

Independent associations were assessed with a multivariate model incorporating the intervention (both the basic and intensive arms), the initial HIV status, trichomoniasis and gonococcal infection. In this model, the magnitude of the effect of the intervention remained practically unchanged with an adjusted rate ratio of 0.42, while gonococcal infection at baseline remained the strongest risk factor, with an adjusted rate ratio of 4.8 ($P = 0.0002$) (Table 2). Women who attended at least four out of the five programmed visits before their last outcome assessment were less likely to seroconvert than women who attended three or less visits (4.6 versus 13/100 person-years; $P = 0.04$).

Effect of the intervention on sexually transmitted disease prevalence and condom use

Among the 225 women who had at least one outcome assessment in the intervention study, Fig. 2 compares condom use and the prevalence of selected STD between the cross-sectional study and the first outcome assessment. The increase in reported consistent condom use (from 40 to 82%) was statistically significant ($P < 0.001$). There were statistically significant decreases in the prevalence of *N. gonorrhoeae* infection (from 14 to 5%; $P < 0.005$) and *T. vaginalis* infection (from 24 to 11%; $P < 0.001$). The prevalence of *C. trachomatis* and of genital ulcers also decreased, but not significantly.

Women who attended at least four out of the five programmed visits before their first outcome assessment had lower prevalence rates than women who attended three or less visits for *C. trachomatis* (1.2 versus 5%; $P = 0.3$) and *N. gonorrhoeae* (3.6 versus 9.8%; $P = 0.2$), but not for *T. vaginalis* (10.8 versus 9.8%) or genital ulcers (1.1 versus 0%), although reported consistent condom use (82.6 versus 79%) was not different between these two groups.

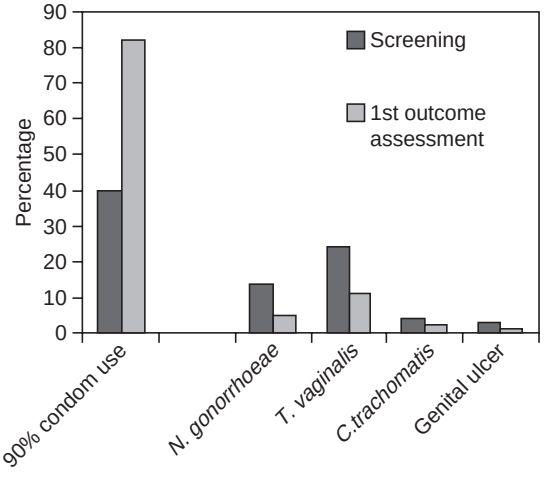

Fig. 2. Comparison of reported condom use and STD prevalence in the cross-sectional study and at the first outcome assessment of the interventional study among female sex workers who had at least one outcome assessment (n = 225). The rate of reported condom use refers to the last working day for the cross-sectional study and to the approximately 6 month period between enrollment and the first outcome assessment for the first outcome assessment.

No significant difference was detected between women in the intensive and the basic strategy in mean number of visits between enrollment and the first 6 monthly outcome assessment (mean 3.8 versus 4.1; $P = 0.2$). However, compared with women in the basic strategy, women in the intensive strategy had more frequently received treatment for *T. vaginalis* (mean 0.9 versus 0.3 episodes; $P = 0.0001$) and for *N. gonorrhoeae* and *C. trachomatis* (mean 2.3 versus 0.6 episodes; $P = 0.0001$). As shown in Fig. 3, women in the intensive strategy had a lower prevalence of *T. vaginalis* compared with women in the basic strategy at the first (14 versus 7%; $P = 0.07$) and second (11 versus 6%; $P = 0.5$) outcome assessment, while there were no differences for other STD: *N. gonorrhoeae* (4 versus 6% at first assessment and 6 versus 4% at the second), C. trachomatis (3 versus 1% at first assessment and 0 versus 4% at the second) and genital ulcers (1 versus 1% at first assessment and 0 versus 2% at the second).

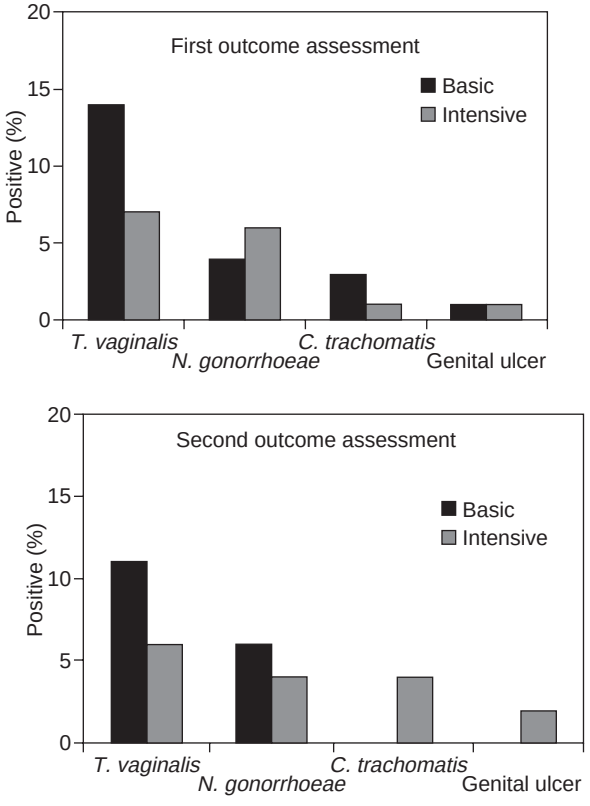

Fig. 3. Comparison of the STD prevalence in the basic and intensive STD diagnosis and treatment strategy groups at the first (n = 117 and 108, respectively) and second outcome assessments (n = 58 and 56, respectively).

Discussion

This intervention study in female sex workers in Abidjan has shown that intervening with an integrated approach including health education, condom distribution and regular STD screening and treatment (which is not dependent on sophisticated laboratory procedures) reduces the incidence of HIV infection. The results are compatible with the incidence of HIV infection being further reduced by an intensive diagnosis and treatment strategy, although the difference in HIV seroincidence between the two groups was too small for such reductions to be reliably detected in the present study.

The intervention study started about 18 months after the cross-sectional study and some of the women who had been screened before the start of the intervention study later enrolled in the intervention study. Other female sex workers who had been screened after the start of the intervention study enrolled in the intervention study more than 2 weeks after their initial screening. These two factors have resulted in a quasi-experimental design in which it was possible to compare female sex workers exposed to the intervention with women who had not.

The rate of follow-up of female sex workers in this intervention study was low, consistent with observations in other studies [17]. The considerable loss to follow-up may be explained by the high mobility of female sex workers in West Africa [18,19] and possibly by factors related to the procedures required by the research itself. The low follow-up rate has important implications for the applicability of the intervention. Indeed 58% of female sex workers were exposed to the intervention for less than 6 months, precluding an assessment of HIV incidence in these women, suggesting either that they had left the study area or that the intervention was not attractive.

The overall estimate of the HIV-1 incidence rate of 8.5/100 person-years among female sex workers in Abidjan is low compared with that described in Thailand (24–29/100 person-years [17]) and in Kenya (42/100 person-years [20]) but comparable to that in Kinshasa (8/100 person-years [8]). The 6.5/100 person-years incidence of HIV-1 during the intervention study was much lower than the 16.3/100 person-years incidence before the intervention study. This reduction may be a consequence of both an increase in condom use and a reduction in the prevalence of STD, linked to lower susceptibility. As observed in the Kinshasa study, regular attendance during the intervention study was associated with a lower HIV incidence rate. The non-significant association of regular attendance with lower rates of gonorrheal and chlamydia infection, but not with increased condom use, may suggest that regular attenders were less susceptible to HIV infection because of lower STD rates.

The lower HIV incidence in the intensive strategy compared with the basic strategy, although not statistically significant, also suggests that the presence of STD in HIV-seronegative individuals facilitates the acquisition of HIV infection [8]. Indeed, STD were more frequently treated in women in the intensive strategy than in women in the basic strategy, although there tended to be a difference between women in the intensive and the basic strategy only in the prevalence of trichomoniasis, not other STD. The strong association of gonococcal infection and trichomoniasis with incidence of HIV infection may reflect facilitation of HIV transmission in the presence of these infections, but it could also be a marker of increased sexual exposure. Indeed, sexual exposure was inadequately assessed at enrollment as self-reported consistent condom use referred to the last working day only. In the absence of a significant difference between the two STD diagnosis and treatment strategy groups, the comparison of the HIV incidence rates before and during the intervention study does not allow us to disentangle the effect of health education and provision of condoms [5,21–23] from the effect of STD diagnosis and treatment [8,9]. Although *T. vaginalis, N. gonorrhoeae* and *C. trachomatis* were significantly more frequently treated in women in the intensive strategy than in women in the basic strategy, there were divergent relative risks for STD prevalence, with only the prevalence of *T. vaginalis* lower in the intensive arm. The Mwanza study suggests that the reduction in HIV incidence can be attributed to both a reduction in prevalence of STD and a reduction in the duration of symptomatic STD [24].

Since the incidence rate of HIV-1 infection among initially HIV-2-seropositive women was higher than among initially HIV-seronegative women, these data do not support the hypothesis that HIV-2 protects against infection with HIV-1 [25]; the data are in agreement with four other studies in West Africa that failed to show such a protective effect [26–29]. While our study is limited by the use of dual seroreactivity to indicate dual infection, the great majority of Abidjan female sex workers with dual seroreactivity have been shown to have dual infection [30].

In conclusion, an integrated approach to HIV prevention that included health education, condom distribution and regular STD screening and treatment lowered the HIV incidence significantly in a cohort of female sex workers in Abidjan. The basic STD diagnosis and treatment strategy appears to be slightly less effective, though not statistically significant, compared with the intensive strategy in lowering STD prevalence and HIV incidence. Finally, considering that female sex

workers and their clients are a driving force of the HIV epidemic in many countries throughout the world, national AIDS control programs should consider adopting as policy the type of integrated approach used in this intervention study for HIV prevention in these high-risk populations, although research and surveillance should be continued to determine the most effective ways to deliver this approach.

Acknowledgments

We thank K. M. Yeboué, J.-M. N'Gbichi, M. N'Krumah, C. Kouakou-Kantiono and T. Aka for their daily efforts at Clinique de Confiance; K. Brattegaard, Y. M. Hoyi, M.-J. Teurquetil, M.-L. Adom, D. Soroh, D. Yavo, L. Ya, C. Kouyaté and S. Koblavi for laboratory support; B. Gbaye, R. Traoré, J. Patrick Whitaker, J.-L. Njampo and B. Bondo Monga for data management; D. Djéha of the Côte d'Ivoire Ministry of Health for support; J. Vielfont of the Institute of Tropical Medicine for logistical support; M. A. Clottey (deceased), the peer educators, A. Tiémelé and the staff of the PPP, the Programme National de lutte contre le SIDA and les Maladies Sexuellement Transmissible et la Tuberculose for their appreciated collaboration; and D. Avondts, R. Colebunders, R. Coutinho, D. Mabey, A. Meheus and P. Vanderstuyft for review of earlier drafts of the manuscript.

Sponsorship: This work was supported in part by Nationaal Fonds voor Wetenschappelijk Onderzoek, Brussels; World Health Organization, Geneva; European Community Programme on Science and Technology for Development, Brussels; UNAIDS, Geneva; and Vlaamse Interuniversitaire Raad, Brussels. During part of the study P. D. Ghys was a scholar of the American Foundation for AIDS Research, San Francisco, USA.

References

1. Koffi K, Gershy-Damet G-M, Peeters M, Soro B, Rey J-L, Delaporte E. **Rapid spread of HIV infections in Abidjan, Ivory Coast, 1987–1990.** *Eur J Clin Microbiol Infect Dis* 1992, **11**:271–273.
2. Ghys PD, Diallo MO, Ettiègne-Traoré V *et al.* **Genital ulcers associated with human immunodeficiency virus-related immunosuppression in female sex workers in Abidjan, Ivory Coast.** *J Inf Dis* 1995, **172**:1371–1374.
3. Sassan-Morokro M, Greenberg AE, Coulibaly I-M *et al.* **High rates of sexual contact with female sex workers, sexually transmitted diseases, and condom neglect among HIV-infected and uninfected men with tuberculosis in Abidjan, Côte d'Ivoire.** *J Acquir Immune Defic Syndr* 1995, **11**:183–187.
4. Schutz R, Savarit D, Kadjo J-C *et al.* **Excluding blood donors at high risk of HIV infection in a west African city.** *BMJ* 1993, **307**:1517–1519.
5. Ngugi EN, Plummer FA, Simonsen JN *et al.* **Prevention of transmission of human immunodeficiency virus in Africa: effectiveness of condom promotion and health education among prostitutes.** *Lancet* 1988, **ii**:887–890.
6. Cameron DW, Simonsen JN, D'Costa LJ *et al.* **Female to male transmission of human immunodeficiency virus type 1: risk factors for seroconversion in men.** *Lancet* 1989, **ii**:403–407.
7. Plummer FA, Simonsen JN, Cameron DW *et al.* **Cofactors in male-female sexual transmission of human immunodeficiency virus type 1.** *J Inf Dis* 1991, **163**:233–239.
8. Laga M, Alary M, Nzila N *et al.* **Condom promotion, sexually transmitted diseases treatment, and declining incidence of HIV-1 infection in female Zairian sex workers.** *Lancet* 1994, **344**:246–248.
9. Grosskurth H, Mosha F, Todd J *et al.* **Impact of improved treatment of sexually transmitted diseases on HIV infection in rural Tanzania: randomised controlled trial.** *Lancet* 1995, **346**:530–536.
10. Laga M. **STD control for HIV prevention – it works!** *Lancet* 1995, **346**:518–519.
11. World Health Organization. *Management of patients with sexually transmitted diseases. Report of a WHO Study Group.* (WHO Technical report Series No 810) Geneva: World Health Organization; 1992.
12. Diallo MO, Ghys PD, Vuylsteke B *et al.* **Evaluation of simple diagnostic algorithms for *Neisseria gonorrhoeae* and *Chlamydia trachomatis* cervical infections in female sex workers in Abidjan, Côte d'Ivoire.** *Genitourin Med* 1998, **74**(special issue: Sexually Transmitted Infections):S106–S111.
13. Kanki P, Mboup S, Marlink R *et al.* **Prevalence and risk determinants of human immunodeficiency virus type 2 (HIV-2) and human immunodeficiency virus type 1 (HIV-1) in West African female prostitutes.** *Am J Epidemiol* 1992, **136**:895–907.
14. van Dyck E, Piot P, Meheus A. *Bench-level laboratory manual for sexually transmitted diseases.* (WHO/VDT/89.443) Geneva: World Health Organization, 1989.
15. de Cock KM, Porter A, Kouadio J *et al.* **Rapid and specific diagnosis of HIV-1 and HIV-2 infections: an evaluation of testing strategies.** *AIDS* 1990, **4**:875–878.
16. Nkengasong JN, Maurice C, Koblavi S *et al.* **Field evaluation of a combination of monospecific enzyme-linked immunosorbent assays for the type-specific diagnosis of human immunodeficiency virus type 1 (HIV-1) and HIV-2 infections in HIV-seropositive persons in Abidjan, Ivory Coast.** *J Clin Microbiol* 1998, **36**:123–127.
17. Weniger BG. **Experience from HIV incidence cohorts in Thailand: implications for HIV vaccine efficacy trials.** *AIDS* 1994, **8**:1007–1010.
18. Pickering H, Quigley M, Hayes RJ, Todd J, Wilkins A. **Determinants of condom use in 24000 prostitute/client contacts in The Gambia.** *AIDS* 1993, **7**:1093–1098.
19. Decosas J, Kane F, Anarfi JK, Sodji KDR, Wagner HU. **Migration and AIDS.** *Lancet* 1995, **346**:826–828.
20. Fowke KR, Nagelkerke NJD, Kimani J *et al.* **Resistance to HIV-1 infection among persistently seronegative prostitutes in Nairobi, Kenya.** *Lancet* 1996, **348**:1347–1351.
21. Fischbacher CM, Njeru JM. **Impact of improved condom supply on condom use by prostitute women.** *AIDS* 1994, **8**:856–857.
22. Ford K, Wirawan DN, Fajans P, Meliawan P, MacDonald K, Thorpe L. **Behavioral interventions for reduction of sexually transmitted disease/HIV transmission among female commercial sex workers and clients in Bali, Indonesia.** *AIDS* 1996, **10**: 213–222.
23. Ngugi EN, Wilson D, Sebstad J, Plummer FA, Moses S. **Focused peer-mediated educational programs among female sex workers to reduce sexually transmitted disease and human immunodeficiency virus transmission in Kenya and Zimbabwe.** *J Inf Dis* 1996, **174**(Suppl 2):S240–S247.
24. Mayaud P, Mosha F, Todd J *et al.* **Improved treatment services significantly reduce the prevalence of sexually transmitted diseases in rural Tanzania: results of a randomized controlled trial.** *AIDS* 1997, **11**:1873–1880.
25. Travers K, Mboup S, Marlink R *et al.* **Natural protection against HIV-1 infection provided by HIV-2.** *Science* 1995, **268**: 1612–1615.
26. Aaby P, Poulsen A-G, Larsen O *et al.* **Does HIV-2 protect against HIV-1 infection?** *AIDS* 1997, **11**:939–940.
27. Ariyoshi K, Schim van der Loeff M, Sabally S, Cham F, Corrah T, Whittle H. **Does HIV-2 infection provide cross-protection against HIV-1 infection?** *AIDS* 1997, **11**:1053–1054.
28. Wiktor SZ, Nkengasong JN, Ekpini ER *et al.* **Lack of protection**

against HIV-1 infection among women with HIV-2 infection. *AIDS* 1999, **13**:695–699.
29. Norrgren H, Andersson S, Biague AJ *et al.* **Trends and interaction of HIV-1 and HIV-2 in Guinea-Bissau, west Africa: no protection of HIV-2 against HIV-1 infection.** *AIDS* 1999, **13**:701–707.
30. Ishikawa K, Fransen K, Ariyoshi K *et al.* **Improved detection of HIV-1 proviral DNA in dually seroreactive individuals.** *AIDS* 1998, **12**:1419–1425.