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Impact of community antiretroviral therapy coverage on HIV incidence in Kenyan female sex workers: A fifteen year prospective cohort study

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Abstract

Objective—To test the hypothesis that increasing community ART coverage would be associated with lower HIV incidence in female sex workers (FSWs) in Mombasa District, Kenya.

Design—Prospective cohort study.

Methods—From 1998–2012, HIV-negative FSWs were asked to return monthly for an interview regarding risk behavior and testing for sexually transmitted infections including HIV. We

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Disclosure

R.S.M. has received honoraria for invited lectures and consulting as well as donated study product for a trial of treatment of vaginal infections from Embil Pharmaceutical Company. R.S.M. currently receives research funding from Hologic/Gen-Probe for a study of human papilloma virus screening. All other authors report nothing to disclose.

RSM, BAR, KM, GJ-S, WJ, and JO designed the study. RSM, PC, KM, BM, KO-D, WJ, and DK collected and managed the data. BAR performed the statistical analysis and KO-D created the figure. All authors contributed to interpretation of the data. RSM prepared the initial draft manuscript. All authors contributed to editing and approved the final version of the manuscript.

evaluated the association between community ART coverage and FSW's risk of becoming HIV infected using Cox proportional hazards models adjusted for potential confounding factors.

Results—1,404 FSWs contributed 4,335 woman-years of follow-up, with 145 acquiring HIV infection (incidence 3.35/100 woman-years). The ART rollout began in 2003. By 2012, an estimated 52% of HIV-positive individuals were receiving treatment. Community ART coverage was inversely associated with HIV incidence (adjusted hazard ratio [aHR] 0.77; 95% confidence interval [95%CI] 0.61–0.98; $p=0.03$), suggesting that each 10% increase in coverage was associated with a 23% reduction in FSWs' risk of HIV acquisition. Community ART coverage had no impact on HSV-2 incidence (aHR 0.97; 95% CI 0.79–1.20; $p=0.8$).

Conclusions—Increasing general population ART coverage was associated with lower HIV incidence in FSWs. The association with HIV incidence, but not HSV-2 incidence, suggests that the effect of community ART coverage may be specific to HIV. Interventions such as pre-exposure prophylaxis and antiretroviral-containing microbicides have produced disappointing results in HIV prevention trials with FSWs. These results suggest that FSWs' risk of acquiring HIV infection might be reduced through the indirect approach of increasing ART coverage in the community.

Keywords

Antiretroviral therapy; HIV; transmission; women; sex worker; Africa

BACKGROUND

The HPTN-052 trial demonstrated that early initiation of antiretroviral therapy (ART) in HIV-serodiscordant couples reduced HIV transmission by 96% compared to standard ART initiation [1]. Observational data from discordant couples, including a meta-analysis of nine studies, also showed a significant, though more modest, 42% reduction in HIV transmission when the HIV-positive partner was on ART [2]. Large ecological studies have found associations between community ART coverage, community viral load, and incident HIV infections at the community level [3, 4]. One study examined the association between community ART coverage and individual-level HIV risk [5]. This study demonstrated that for each 10% increase in ART coverage, there was a significant 14% decline in the risk of HIV acquisition in uninfected individuals.

The effect of community ART coverage on individual-level risk of HIV acquisition in female sex workers (FSWs) has not been evaluated. This question has important implications for HIV prevention. Female sex workers are disproportionately affected by HIV, stigmatized, difficult to reach, and may be resistant to prevention efforts targeted to the general population [6]. Although they represent only ~1% of the general population, FSWs account for about 14% of new HIV infections in high-prevalence countries like Kenya [7]. We hypothesized that increasing community ART coverage would be associated with lower HIV incidence in FSWs in Mombasa District (now Mombasa subcounty), Kenya, independent of their individual-level risk factors for HIV acquisition.

METHODS

Population and procedures

Between February, 1993 and December, 2012, we recruited FSWs using procedures that remained constant throughout the enrollment period. Outreach meetings were conducted at bars around Mombasa District one to two times each month. The meetings were coordinated through peer leaders who helped to identify venues and notify colleagues of meetings. Outreach staff provided a talk on a health topic requested by women in the community, as well as general information about the research clinic. Interested women were provided with a referral card and invited to visit the research clinic, located in the Ganjoni Municipal Communicable Disease Control Centre. Ganjoni Clinic has been a primary venue for FSW sexually transmitted infection (STI) testing and treatment in Mombasa for over 25 years.

Female sex workers who were HIV-negative and 18 years old were invited to participate in a prospective open cohort study of risk factors for HIV acquisition as previously described [8]. All participants self-reported exchanging sex for cash or in-kind payment. The majority of women reported working in bars, where they met local male clients [9]. At enrollment and monthly follow-up visits, women were interviewed to ascertain demographic information, medical history, and sexual risk behavior. The women also had a monthly physical examination with collection of blood and genital specimens for diagnosis of HIV and STIs. Risk reduction counseling and condoms were provided at each visit, and STIs were treated according to Kenyan national guidelines. Ethical approval for the study was obtained from the University of Washington Human Subjects Research Committee, the Fred Hutchinson Cancer Research Center Institutional Review Board, and the Kenyatta National Hospital Ethics and Research Committee. All participants provided written informed consent.

Serology and microbiology

Screening for HIV was performed by enzyme linked immunosorbent assay (ELISA). The Detect HIV1–2 ELISA (Biochem Immunosystems) was used from February 1993 through January 2010. Pishtaz HIV 1,2 ELISA (Pishtaz Teb Diagnostics) was used for the remainder of this study. All positive screening ELISA tests were confirmed with a second ELISA (Recombigen HIV 1–2 [Cambridge Biotec] from February 1993 through August 2004, Biorad HIV 1–2 [Biorad Laboratories] from September 2004 through May 2006, and Vironostika HIV-1 Uni-Form II Ag/Ab [bioMerieux] after June 2006).

Screening for STIs included examination of a vaginal saline wet preparation at X40 magnification to identify motile *Trichomonas vaginalis* parasites. Bacterial vaginosis (BV) was diagnosed by vaginal Gram stain [10]. Culture of cervical secretions for *Neisseria gonorrhoeae* was performed on modified Thayer-Martin media. Cervicitis was defined as the presence of an average of 30 polymorphonuclear leukocytes per high-power field of Gram stained cervical secretions. Beginning in 2006, additional testing for *N. gonorrhoeae* and *Chlamydia trachomatis* was performed using the Gen-Probe APTIMA Combo-2 Assay (Hologic/Gen-Probe). Serological testing for HSV-2 was performed using a type-specific

HSV-2 gG based ELISA (HerpeSelect 2, Focus Diagnostics). Index values ≥ 2.1 were considered positive [11].

Estimation of HIV prevalence and ART coverage in Mombasa District

The prevalence of HIV in adults (15–64 years) in Mombasa District was estimated to be the same as the national HIV prevalence for Kenya; prevalence in Mombasa has mirrored national trends throughout the epidemic, and national data are more complete. Prevalence data from 1998–2006 came from online resources [12], 2007–2011 from the most recent Kenya AIDS Epidemic Update [7], and 2012 from the Kenya AIDS Indicator Survey (KAIS) conducted in that year [13]. Sensitivity analyses substituting Coast Province data for national data to estimate HIV prevalence utilized data from KAIS 2007 and KAIS 2012 [13, 14]. Most communities in Mombasa County traditionally circumcise men [15]. Over 94% of men who participated in a national survey in 2009 reporting that they had been circumcised.

Mombasa's population was taken from Kenya National Bureau of Statistics (KNBS) census data for 1999 and 2009 [16]. The population in non-census years was calculated using the KNBS estimate of 3.51% annual population growth. To estimate the number of people living with HIV in Mombasa, we multiplied the HIV prevalence by the population for each year. Population ART coverage was calculated by dividing the number of people on treatment by the total number living with HIV. Kenya's National AIDS and STD Control Programme (NASCOP) provided the number of people on treatment in Mombasa District for 2011 and 2012 (PC and DK). There are no centralized records of district-level ART coverage for earlier years. The first public ART program in Mombasa was established in 2003, so we assumed 0% ART coverage in 2002, then used linear interpolation to estimate the number of people on treatment from 2002–2011. Examination of plots of the total number of people treated with ART in Kenya from both NASCOP (2004–2012; PC and DK) and the Presidents Emergency Program for AIDS Relief (2004–2013) show close approximation to this linear increase (Pearson's correlation coefficients 0.998 and 0.993, respectively) [17].

Kenyan guidelines for ART initiation in 2003 recommended treatment for patients with CD4 cell counts <200 cells/ μ L or World Health Organization (WHO) stage IV disease. Guidelines were modified in 2005, adding a recommendation to initiate treatment in patients who had WHO stage III disease together with CD4 cell counts <350 cells/ μ L. In 2011, guidelines were further modified to recommend ART initiation for all patients with CD4 <350 cells/ μ L, regardless of disease stage. There was no recommendation for use of antiretroviral medications for pre-exposure prophylaxis during the period of this study.

Data analysis

Statistical analyses were performed using SPSS Version 22.0 (IBM) and Stata Version 13.1 (StataCorp). All HIV-negative women who were either continuing participants or enrolled on or after January 1st 1998 and provided 1 follow-up visit were included in analyses. This provided 5 years of pre-ART follow-up (1998–2003), avoiding the initial 4 years of enrollment (1993–1997), during which accrual of lower risk women predictably led to a

reduction in overall incidence [18]. Women were included in analyses up to HIV seroconversion or their last follow-up visit, whichever occurred first.

The association between community ART coverage and HIV acquisition was evaluated using Cox proportional hazards regression. Although the main covariate of interest, community ART coverage, was measured at an ecological level, the unit of analysis was the individual FSWs. The base model included two variables, community HIV prevalence and ART coverage. The latter variable was scaled to each 10% change in overall community coverage. Both variables were analyzed as time varying by calendar year. A multivariate model was constructed to control for known or suspected potential confounding factors that were selected *a priori*. These included baseline educational level (≤ 8 vs. >8 years), parity (≤ 2 vs. >2), workplace (bar vs. nightclub vs. other), and vaginal washing practices (none vs. water only vs. soap or other substances). The multivariate model also included time-varying adjustment for years of sex work (≤ 1 , >1 to ≤ 5 , >5 to ≤ 10 , and >10), contraceptive method (no contraception or tubal ligation, oral contraceptive pills, depot medroxyprogesterone acetate, Norplant, and intrauterine device), number of sex partners in the last week (≤ 1 vs. >1), sexual frequency in the last week (≤ 1 vs. >1), episodes of unprotected sex in the last week (0 vs. ≥ 1), and presence of genital tract conditions (BV, *T. vaginalis*, *C. trachomatis*, *N. gonorrhoeae*, cervicitis, and genital ulcer disease). We also included time varying adjustment for herpes simplex virus type-2 (HSV-2) serostatus. Adjustment for time-varying age categories was dropped from the multivariate model, as this variable was collinear with years of sex work, and the latter was more strongly associated with HIV risk. To test the specificity of the community ART coverage effect on HIV incidence, we used the same analytical approach to examine the association between community ART coverage and HSV-2 incidence.

Continuous measures were dichotomized using cutoffs based on our prior analyses [19]. As in prior studies, the analyses included an effect window of 60 days to capture the influence of other genital tract infections on HIV susceptibility. For sexual behaviors, an average was calculated for each year of follow-up to capture average behavior over time.

Of the variables included in the multivariate model for 23,570 visits, only contraceptive method, missing at 32 (0.1%) visits, and HSV-2 status missing at 52 (0.2%) visits, had missing data. Thus, all analyses were complete case with no adjustment for missing data.

RESULTS

Between January 1998 and December 2012, 4,920 women were screened, and 1,929 (39%) were HIV-negative. Of the HIV-negative women, 1,777 (92%) returned to clinic for a baseline HIV-negative visit and 1,404 (73%) contributed at least one follow-up visit to the survival analyses. Baseline characteristics of the cohort are shown in Table 1.

Participants in this analysis contributed a median of 7 (IQR 3–18) visits and a median of 17 (IQR 5–53) months of follow-up. A total of 23,570 visits were accrued, representing 4,335 woman-years of follow-up. One hundred and forty five women acquired HIV infection (3.35/100 woman-years; 95%CI 2.85–3.93/100 woman-years). The annual incidence of HIV

in the sex worker cohort is shown graphically in Figure 1, together with annual prevalences of adult (15–64 years old) HIV infection and ART coverage in Mombasa District. The estimated HIV prevalence peaked in 2000 at 13.4%, and then declined over the next 12 years to 5.6% in 2012. The ART rollout began in 2003, increasing through 2012, when an estimated 52% of HIV infected individuals were receiving treatment.

There was no significant association between community HIV prevalence and FSWs' risk of HIV infection in the base model (hazard ratio [HR] 0.97, 95% confidence interval [CI] 0.87–1.09), as shown in Table 2. On the other hand, community ART coverage was significantly inversely associated with HIV incidence (HR 0.70; 95%CI 0.56–0.88; $p=0.002$). This association remained significant after adjustment for potential confounding factors, as detailed in the methods (adjusted HR [aHR] 0.77; 95%CI 0.61–0.98; $p=0.03$), suggesting that each 10% increase in community ART coverage was associated with a 23% reduction in the relative hazard for FSWs becoming HIV infected. To determine whether the source of Mombasa District HIV prevalence data influenced the results, we performed a sensitivity analysis substituting data from the Kenya AIDS Indicator Surveys of 2007 and 2012 for the NASCOP data. This analysis produced very similar results, in which the effect of ART on HIV incidence remained significant (aHR 0.79; 95%CI 0.62–1.00; $p=0.05$).

There were 366 women who were initially HSV-2 seronegative, of whom 107 became HSV-2 seropositive during 553 person-years of follow-up (19.34/100 person years). In contrast to our findings for HIV incidence, community ART coverage was not associated with HSV-2 incidence in the base model (HR 0.97; 95%CI 0.79–1.20; $p=0.8$). This finding remained non-significant after adjustment for the same set of cofactors included in our multivariate model for HIV-1 incidence (aHR 0.99, 95%CI 0.78–1.25; $p=0.9$).

DISCUSSION

This 15-year prospective study demonstrated a strong association between community ART coverage and the risk of HIV acquisition in Kenyan FSWs. Each 10% increase in community ART coverage was associated with a 23% decrease in the relative hazard for becoming HIV infected. These findings remained significant after careful individual-level adjustment for potential confounding factors. The association with HIV incidence, but not HSV-2 incidence, suggests that the effect of community ART coverage may be specific to HIV. In fact, community ART coverage had virtually no effect on HSV-2 incidence, and the confidence intervals around this effect exclude the point estimate for the effect of community ART coverage on HIV incidence. To our knowledge, this is the first study to investigate the effect of community ART coverage on the risk of HIV in FSWs. Future studies in different populations of high-risk women will help to determine the degree to which these findings are generalizable in other high and lower HIV prevalence settings.

It is notable that HIV incidence in this cohort began to decline after 1999, while ART did not become available at any appreciable level until 2003. This observation highlights an important point. Our analysis does not demonstrate that community ART coverage was the only factor driving the reduction in HIV incidence. As noted in other studies in Kenya, ongoing changes in the cohort's demographics, risk behaviors, STI rates, contraceptive

choices, intravaginal practices, immunogenetic shifts in at-risk women, HIV-prevention efforts in the community, and other factors are likely to have contributed [20, 21]. Our data are consistent with observations of regional HIV incidence trends in Africa, which noted declines since the mid-1990's, likely due to multiple factors including the effects of HIV prevention programs supporting behavioral change, condom use, and syndromic management of STIs [20–22]. Two crucial features of this analysis of Mombasa FSWs support our ability to examine a possible effect of ART on transmission in the context of these ongoing changes. First, women in the Mombasa Cohort had consistent access to high-quality prevention interventions including risk reduction education, condom promotion and free condoms, free laboratory screening and treatment for STIs, and regular HIV testing throughout the analysis period. Second, because our data allow individual-level adjustment for key variables including sexual risk behaviors, condom use, STIs, and other biological and behavioral exposures, this analysis is able to show that community ART coverage may be an independent predictor of lower HIV incidence in FSWs. Our approach makes no assumptions about lower or upper thresholds for the effect of community ART coverage on HIV incidence in sex workers.

There is strong biological plausibility, as well as observational [3, 4], modeling [23], and randomized trial evidence supporting the role of ART in reducing HIV infectivity and decreasing transmission [1, 2]. The single previous study that examined individual-level HIV risk in relation to community ART coverage demonstrated a 14% decrease in general population HIV incidence for every 10% increase in ART coverage [5]. Both in FSWs and the general population, the average risk of sexual contact with an untreated partner would be expected to decline with increasing ART coverage. The resulting decline in population HIV incidence could be enhanced by community-level factors including decreases in the incidence of highly transmissible acute infections and disruption of transmission within sexual networks including concurrent partnerships [24, 25].

In this analysis, there was no significant association between population HIV prevalence and HIV incidence in FSWs. This may be a result of the inaccuracy and imprecision inherent in using population HIV prevalence as a proxy for the prevalence of HIV in clients of FSWs. We may also have lacked power to demonstrate a significant association. Related to this, the rate of decline in HIV prevalence in the general population was not as marked as the rate of increase in ART coverage in HIV-positives (Figure 1). Antiretroviral therapy effectively transitions HIV-infected sexual partners to being similar to HIV-uninfected partners in terms of infectiousness, making it conceptually similar to an accelerated decline in HIV prevalence.

This study had a number of strengths. Prospective data collection with frequent follow-up provided good precision for estimating the time of HIV acquisition. In addition, while community ART coverage is necessarily an ecological-level exposure, the study design facilitated careful individual-level adjustment for variables that could have biased the association between ART coverage and HIV risk. Importantly, the measure of community ART coverage would capture both biological effects of treatment on infectiousness and ART-associated behavior changes in the community such as increased HIV testing, disclosure, and changes in risk behavior. The 15-year follow-up and large sample size

facilitated a unique longitudinal analysis with sufficient power to evaluate the impact of ART coverage on HIV incidence. The continuous open cohort design minimized the risk of observing the expected decline in HIV incidence when following a closed cohort [18]. Finally, the inclusive approach to enrollment of HIV-negative FSWs, excluding only those too young to participate, is likely to make these results generalizable to other populations of high-risk women in Africa. Additional analyses from other groups who have conducted open cohort studies of FSWs over periods spanning the pre- and post-ART rollout will be important for examining the presence and magnitude of this association in other populations.

There were limitations to this analysis, some of which could have inflated the apparent effect of community ART coverage on HIV incidence. First, changes may have occurred in the community over time that influenced HIV incidence through mechanisms that are independent of ART coverage. Because we did not have data on spatial distribution of ART coverage within Mombasa District, we could not adjust for calendar time as a reflection of other factors that might have changed such as blood safety, injection safety, migration, and seroadaptive behavior. Second, sexual risk behaviors were self-reported. Prior research has demonstrated that reported risk behaviors are predictive of markers of unprotected sex in this cohort [26]. Nonetheless, some mis-reporting due to social desirability bias or inaccurate recall can be anticipated. Third, we measured community ART coverage, rather than ART coverage specifically in the clients of FSWs. Clients may, in fact, be from elsewhere, and may have higher or lower rates of ART coverage. Importantly, ART coverage in Mombasa mirrored coverage nationally, as detailed in the methods. In addition, community ART coverage could impact FSW incidence indirectly, through reductions in the incidence and prevalence of HIV in clients. Fourth, this analysis did not have a pre-specified sample size. Rather, we chose to analyze data over a fixed time period that encompassed 5 years prior to the introduction of large-scale ART programs in Mombasa and 10 years of increasing ART coverage. Almost 20% of women who were HIV-negative at baseline did not return for follow-up. We have previously shown that women lost to follow-up from this cohort tend to have lower risk behavior, but that loss of these women did not bias the effect estimates of risk factors for HIV [27]. Still, we cannot rule out attrition as a source of bias. Fifth, FSWs who joined the cohort may differ from non-enrolled FSWs in the community. This would not influence the study's internal validity, but could limit generalizability. Finally, this analysis relied on census and HIV program data for estimates of HIV prevalence and ART coverage [12–14, 16]. Since there was no centralized reporting of district-level ART coverage prior to 2011, we used linear interpolation to estimate coverage between the pre-ART period (0% before 2002) and 2011. As detailed in the methods, the increase in ART coverage in Kenya did closely parallel this assumption of linearity. In addition, the findings were robust to sensitivity analyses in which community HIV prevalence and the resulting proportion of HIV-positive individuals on ART were derived using different sources.

Key populations including FSWs have been directly targeted with HIV prevention interventions since early in the epidemic. Declines in HIV incidence prior to the ART rollout may well have resulted from programs focused on behavior change, condom use, STI treatment, and HIV testing. On the other hand, direct antiretroviral-based interventions such as pre-exposure prophylaxis and antiretroviral-containing microbicides, which have

demonstrated efficacy in other populations [28, 29], have produced disappointing results in HIV prevention trials with FSWs [30, 31]. Our present study suggests that in the setting of ongoing high-quality direct prevention services, FSWs risk of acquiring HIV infection might be further reduced through the indirect approach of increasing ART coverage in the community. Modeling studies have reached similar conclusions about the complementary effects of condom use and STI treatment on HIV incidence in FSWs, even when ART is available [32]. This effect could result in further declines in HIV incidence in the general population, as fewer new infections would be transmitted from HIV-positive FSWs. In this context, increasing ART coverage to include all adults with CD4 counts <500 cells/ μ L, as recommended by WHO and adopted in Kenya in 2014 [33], could provide a substantial HIV prevention benefit.

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REFERENCES

1. Cohen MS, Chen YQ, McCauley M, Gamble T, Hosseinipour MC, Kumarasamy N, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011; 365:493–505. [PubMed: 21767103]
2. Anglemyer A, Rutherford GW, Horvath T, Baggaley RC, Egger M, Siegfried N. Antiretroviral therapy for prevention of HIV transmission in HIV-discordant couples. *Cochrane Database Syst Rev*. 2013; 4:CD009153. [PubMed: 23633367]
3. Montaner JS, Lima VD, Barrios R, Yip B, Wood E, Kerr T, et al. Association of highly active antiretroviral therapy coverage, population viral load, and yearly new HIV diagnoses in British Columbia, Canada: a population-based study. *Lancet*. 2010; 376:532–539. [PubMed: 20638713]
4. Das M, Chu PL, Santos GM, Scheer S, Vittinghoff E, McFarland W, et al. Decreases in community viral load are accompanied by reductions in new HIV infections in San Francisco. *PLoS ONE*. 2010; 5:e11068. [PubMed: 20548786]
5. Tanser F, Barnighausen T, Grapsa E, Zaidi J, Newell ML. High coverage of ART associated with decline in risk of HIV acquisition in rural KwaZulu-Natal, South Africa. *Science*. 2013; 339:966–971. [PubMed: 23430656]
6. Baral S, Beyrer C, Muessig K, Poteat T, Wirtz AL, Decker MR, et al. Burden of HIV among female sex workers in low-income and middle-income countries: a systematic review and meta-analysis. *Lancet Infect Dis*. 2012; 12:538–549. [PubMed: 22424777]
7. National AIDS Control Council, National AIDS/STD Control Programme. Kenya AIDS epidemic update 2011. Nairobi, Kenya: 2012.

8. Martin HL Jr, Nyange PM, Richardson BA, Lavreys L, Mandaliya K, Jackson DJ, et al. Hormonal contraception, sexually transmitted diseases, and risk of heterosexual transmission of human immunodeficiency virus type 1. *J Infect Dis*. 1998; 178:1053–1059. [PubMed: 9806034]
9. McClelland L, Wanje G, Kashonga F, Kibe L, McClelland RS, Kiarie J, et al. Understanding the context of HIV risk behavior among HIV-positive and HIV-negative female sex workers and male bar clients following antiretroviral therapy rollout in Mombasa, Kenya. *AIDS Educ Prev*. 2011; 23:299–312. [PubMed: 21861605]
10. Nugent RP, Krohn MA, Hillier SL. Reliability of diagnosing bacterial vaginosis is improved by a standardized method of gram stain interpretation. *J Clin Microbiol*. 1991; 29:297–301. [PubMed: 1706728]
11. Mujugira A, Morrow RA, Celum C, Lingappa J, Delany-Moretlwe S, Fife KH, et al. Performance of the Focus HerpeSelect-2 enzyme immunoassay for the detection of herpes simplex virus type 2 antibodies in seven African countries. *Sex Transm Infect*. 2011; 87:238–241. [PubMed: 21307152]
12. AVERT.org. [Accessed on February 22, 2014] Estimated national HIV prevalence in Kenya: Sentinel surveillance 1990 – 2006. Available at: <http://www.avert.org/media/content/graphs/hiv-prevalence-graph.gif>.
13. National AIDS and-STI Control Programme, Ministry of Health Kenya. Kenya AIDS Indicator Survey 2012: Final Report. Nairobi, Kenya: 2013.
14. National AIDS and-STI Control Programme, Ministry of Health Kenya. Kenya AIDS Indicator Survey 2007: Final Report. Nairobi, Kenya: 2009.
15. National AIDS Control Council, National AIDS/STD Control Programme, UNAIDS. [Accessed on April 16th 2015] HIV and AIDS profile: Mombasa County. 2012. p. 1-6. Available at: <http://www.nacc.or.ke/countyprofiles/Mombasa%20County%20Profile.pdf>.
16. Kenya National Bureau of Statistics. [Accessed on February 25, 2014] Mombasa County. 2013. Available at: <http://www.citypopulation.de/php/kenya-admin.php?adm2id=01>.
17. The United States President's Emergency Plan for AIDS Relief. [Accessed on June 14, 2014] Annual reports to congress on the President's Emergency Plan for AIDS Relief. 2014. Available at: <http://www.pepfar.gov/reports/progress/index.htm>.
18. Baeten JM, Richardson BA, Martin HL, Nyange PM, Lavreys L, Ngugi EN, et al. Trends in HIV-1 incidence in a cohort of prostitutes in Kenya: implications for HIV-1 vaccine efficacy trials. *J Acquir Immune Defic Syndr*. 2000; 24:458–464. [PubMed: 11035617]
19. McClelland RS, Sangare L, Hassan WM, Lavreys L, Mandaliya K, Kiarie J, et al. Infection with *Trichomonas vaginalis* Increases the Risk of HIV-1 Acquisition. *J Infect Dis*. 2007; 195:698–702. [PubMed: 17262712]
20. Kimani J, Kaul R, Nagelkerke NJ, Luo M, MacDonald KS, Ngugi E, et al. Reduced rates of HIV acquisition during unprotected sex by Kenyan female sex workers predating population declines in HIV prevalence. *AIDS*. 2008; 22:131–137. [PubMed: 18090401]
21. Luchters S, Chersich MF, Rinyiru A, Barasa MS, King'ola N, Mandaliya K, et al. Impact of five years of peer-mediated interventions on sexual behavior and sexually transmitted infections among female sex workers in Mombasa, Kenya. *BMC Public Health*. 2008; 8:143. [PubMed: 18445258]
22. UNAIDS/WHO. Report on the global HIV/AIDS epidemic. Geneva: 1998. p. 1-72.
23. Shannon K, Strathdee SA, Goldenberg SM, Duff P, Mwangi P, Rusakova M, et al. Global epidemiology of HIV among female sex workers: influence of structural determinants. *Lancet*. 2014
24. Pilcher CD, Tien HC, Eron JJ Jr, Vernazza PL, Leu SY, Stewart PW, et al. Brief but efficient: acute HIV infection and the sexual transmission of HIV. *J Infect Dis*. 2004; 189:1785–1792. [PubMed: 15122514]
25. Morris M, Kretzschmar M. Concurrent partnerships and the spread of HIV. *Aids*. 1997; 11:641–648. [PubMed: 9108946]
26. McClelland RS, Richardson BA, Wanje GH, Graham SM, Mutunga E, Peshu N, et al. Association Between Participant Self-Report and Biological Outcomes Used to Measure Sexual Risk Behavior in Human Immunodeficiency Virus-1-Seropositive Female Sex Workers in Mombasa, Kenya. *Sex Transm Dis*. 2011; 38:429–433. [PubMed: 21217420]

27. Graham SM, Raboud J, McClelland RS, Jaoko W, Ndinya-Achola J, Mandaliya K, et al. Loss to follow-up as a competing risk in an observational study of HIV-1 incidence. *PLoS One*. 2013; 8:e59480. [PubMed: 23555041]
28. Grant RM, Lama JR, Anderson PL, McMahan V, Liu AY, Vargas L, et al. Preexposure chemoprophylaxis for HIV prevention in men who have sex with men. *N Engl J Med*. 2010; 363:2587–2599. [PubMed: 21091279]
29. Abdool Karim Q, Abdool Karim SS, Frohlich JA, Grobler AC, Baxter C, Mansoor LE, et al. Effectiveness and safety of tenofovir gel, an antiretroviral microbicide, for the prevention of HIV infection in women. *Science*. 2010; 329:1168–1174. [PubMed: 20643915]
30. Van Damme L, Corneli A, Ahmed K, Agot K, Lombaard J, Kapiga S, et al. Preexposure prophylaxis for HIV infection among African women. *N Engl J Med*. 2012; 367:411–422. [PubMed: 22784040]
31. Marrazzo JM, Ramjee G, Richardson BA, Gomez K, Mgodhi N, Nair G, et al. Tenofovir-based preexposure prophylaxis for HIV infection among African women. *N Engl J Med*. 2015; 372:509–518. [PubMed: 25651245]
32. Steen R, Hontelez JA, Veraart A, White RG, de Vlas SJ. Looking upstream to prevent HIV transmission: can interventions with sex workers alter the course of HIV epidemics in Africa as they did in Asia? *AIDS*. 2014; 28:891–899. [PubMed: 24401648]
33. Kenya Ministry of Health, National AIDS and STI Control Program (NASCOP). Guidelines on Use of Antiretroviral Drugs for Treating and Preventing HIV Infection: A rapid advice. Nairobi, Kenya: Kenya Ministry of Health; 2014. p. 1-40. Nairobi, Kenya.

Figure 1.

In this figure, the total height of the colored bars represents the estimated prevalence of HIV in adults (15–64 years old) Mombasa District for each year. The red segment of the bar represents the estimated proportion of the population that is not on ART, while the green segment represents the estimated proportion of the population that is on ART. Data sources for the population of Mombasa, HIV prevalence, and ART coverage are detailed in the Methods section of the paper. The black dots connected by the black line show the calculated HIV incidence in this prospective open cohort study of female sex workers in Mombasa. Dashed black lines show the upper and lower bounds of the 95% confidence interval around the point estimate of HIV incidence. Numerical data corresponding to each year are presented in the column directly below that year. The figure demonstrates that HIV incidence began to decline even before the ART rollout began, with substantial additional reductions in HIV incidence with increasing ART coverage. The downward and upward spikes in incidence in 2001 and 2009, respectively, most likely represent normal variation in incidence in our data.

Definitions for Table at base of figure: Pop % HIV+ not on ART, percentage of the general population that is HIV-positive and not on antiretroviral therapy; Pop% HIV+ on ART, percentage of the general population that is HIV-positive and is on antiretroviral therapy; % HIV+ on ART, percentage of the HIV-positive population that is on ART.

Table 1

Baseline characteristics (n=1,404)

Variable	Median (IQR) or Number (%)
Age	28 (24, 33)
Education (years)	8 (7,11)
Workplace	
Bar	895 (63.7%)
Nightclub	368 (26.2%)
Duration of sex work (years)	4.7 (2.5, 8.4)
Ever pregnant	1,210 (86.2%)
Parity	2 (1, 3)
Contraceptive method	
None/Condoms only	835 (59.5%)
Combined oral contraceptive pills	125 (8.9%)
Depot medroxyprogesterone acetate	327 (23.3%)
Intrauterine contraceptive device	26 (1.9%)
Tubal ligation	33 (2.3%)
Norplant	49 (3.5%)
Other	9 (<1%)
Vaginal Washing	
None	99 (7.1%)
Water only	371 (26.4%)
Soap or other substance*	934 (66.5%)
Alcohol use (any)	1067 (76.0%)
Number of sex partners in the past week	1 (1, 2)
Number of sex acts in the past week	2 (1, 3)
Unprotected sex in the past week (any)	402 (29%)
Genital Tract Infections	
<i>Neisseria gonorrhoeae</i>	32 (2.3%)
<i>Chlamydia trachomatis</i> [†]	4 (2.1%)
<i>Trichomonas vaginalis</i>	58 (4.1%)
Cervicitis	42 (3.0%)
Bacterial vaginosis	448 (31.9%)
Herpes simplex virus type 2 seropositive	1144 (82%)

IQR, interquartile range

* Of the 934 women using soap or other substances for vaginal washing, 663 used soap, 57 used antiseptic, 23 used detergents, and 191 used "other" substances for which no further information was provided.

[†] Among 193 women tested for *Chlamydia trachomatis* infection at baseline; this testing was initiated in 2006.

Table 2

Univariate and multivariate analysis of association between community antiretroviral therapy coverage and HIV incidence in female sex workers

Variable	Univariate HR (95% CI)	Univariate p-value	Multivariate HR (95% CI)	Multivariate p-value
ART coverage*	0.70 (0.56, 0.88)	0.002	0.77 (0.61, 0.98)	0.03
HIV prevalence*	0.97 (0.87, 1.09)	0.6	1.06 (0.94, 1.19)	0.3
Contraception				
None	1.0		1.0	
OCP	1.31 (0.70, 2.46)	0.4	1.03 (0.53, 1.99)	0.9
DMPA	2.30 (1.62, 3.25)	<0.001	2.03 (1.42, 2.90)	<0.001
IUD	0.85 (0.12, 6.15)	0.9	0.90 (0.12, 6.53)	0.9
Norplant	0.68 (0.17, 2.76)	0.6	0.76 (0.18, 3.12)	0.7
Education 8 years	0.90 (0.64, 1.25)	0.5	0.82 (0.58, 1.15)	0.3
Parity >2	1.06 (0.75, 1.49)	0.8	0.94 (0.65, 1.35)	0.7
Workplace				
Bar	1.0		1.0	
Nightclub	0.41 (0.25, 0.68)	<0.001	0.58 (0.34, 1.01)	0.05
Other	0.87 (0.46, 1.66)	0.7	1.65 (0.81, 3.36)	0.2
Vaginal washing				
None	1.0		1.0	
Water only	4.46 (1.06, 18.62)	0.04	4.16 (0.99, 17.53)	0.05
Soap/Other	5.63 (1.39, 22.79)	0.02	5.01 (1.23, 21.47)	0.03
Genital tract infection [†]	2.17 (1.54, 3.05)	<0.001	2.03 (1.42, 2.88)	<0.001
HSV-2 seropositive	2.69 (1.32, 5.52)	0.007	2.42 (1.17, 5.03)	0.02
Years of sex work				
1	1.0		1.0	
>1 and <5	0.52 (0.28, 0.94)	0.03	0.47 (0.25, 0.87)	0.02
5 and <10	0.34 (0.18, 0.65)	0.001	0.29 (0.15, 0.58)	<0.001
10	0.15 (0.07, 0.34)	<0.001	0.14 (0.06, 0.32)	<0.001
>1 Sex partner	0.59 (0.39, 0.90)	0.01	0.74 (0.43, 1.26)	0.3
>1 Sex act	0.86 (0.62, 1.20)	0.4	1.10 (0.72, 1.69)	0.6
Unprotected sex	0.84 (0.60, 1.17)	0.3	1.13 (0.68, 1.87)	0.6
Age [‡]			NA	NA
<25 years	1.0			
25–29 years	0.90 (0.54, 1.52)	0.7		
30–34 years	0.54 (0.30, 0.95)	0.03		
35–39 years	0.50 (0.27, 0.91)	0.03		
40 years	0.37 (0.19, 0.73)	0.004		

* Base model for these two variables includes both of them. Hazard ratios for community antiretroviral therapy coverage are reported per 10% increase in coverage.

[†] Includes *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, *Trichomonas vaginalis*, cervicitis by Gram stain, and bacterial vaginosis

[‡]Excluded from multivariate model due to collinearity with years of sex work

ART, antiretroviral therapy; DMPA, depot medroxyprogesterone acetate; HR, hazard ratio; HSV-2, herpes simplex virus type-2; IUD, intrauterine device; OCP, oral contraceptive pill

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