Antiretroviral therapy initiation in Kenyan female sex workers is not associated with increased sexual risk taking

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STROBE 2007 (v4) checklist of items to be included in reports of observational studies in epidemiology*

Checklist for cohort, case-control, and cross-sectional studies (combined)

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Antiretroviral therapy initiation in Kenyan female sex workers is not associated with increased sexual risk taking in a retrospective case-control study.

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Author contributions: EM, PT, WJ, JK, LG, and RK designed the study. EM, LRM, AK, NN, and RK analyzed the data. CW and JK managed the clinical cohorts. All authors contributed to the writing and editing of the manuscript.

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Data sharing statement: There are no additional data available.

ARTICLE SUMMARY

Article Focus:

- Impact of starting antiretroviral therapy (ART) on sexual risk-taking behaviour in female sex workers (FSW), an important potential source of onward HIV transmission.

Key Messages:

- ART initiation was not associated with increased risk taking or STI incidence.

- Both of these declined over time, most likely as a result of risk reduction counseling.

Strengths and Limitations:

- Strengths include a relevant population, longitudinal follow-up, and inclusion of biological measures of risk-taking (STI incidence).

- Limitations include relatively small study groups and limited sampling time points.

ABSTRACT

Objectives: Although antiretroviral therapy (ART) prolongs life and reduces infectiousness, in some contexts it has been associated with increased sexual risk taking.

Design: Retrospective case-control study.

Setting: Nairobi-based dedicated female sex worker (FSW) clinic.

Participants: HIV-infected FSW before and after ART initiation (n=62); HIV-infected and uninfected control FSWs not starting ART during the same follow-up period (n=40).

Intervention: Initiation of ART.

Primary outcome measures: Self-reported condom use, client numbers, and STI incidence over the study period (before and after ART initiation in cases).

Results: Sexual risk-taking behaviour with casual clients did not increase after ART initiation; condom use increased and STI incidence decreased in both cases and controls, likely due to successful cohort-wide HIV prevention efforts.

Conclusions: ART provision was not associated with increases in unsafe sex in this core transmission group.

MAIN TEXT

ART provision may have dichotomous effects on HIV transmission. While ART reduces blood and genital tract viral load, and therefore infectiousness(1), it has also been associated with reduced safe sex practices(2-4) and increases in STI incidence(5). Although this has not been the experience to date in resource-poor countries(6), it could become an issue as access expands(7), and merits further study. Models suggest that if safe sex practices are not maintained, then HIV transmission may increase despite ART-associated reductions in genital tract virus levels(8). A recent study in Kenyan sex workers with relatively low rates of partner exchange showed no change in risk-taking following ART(9), but these findings need to be confirmed in a high partner exchange setting.

Female sex workers (FSWs) play a key role in HIV epidemic spread in sub-Saharan Africa(10) during both early and late epidemic phases(7) due to multiple partners, high rates of HIV and sexually transmitted infections (STIs), and an inability to negotiate safer sex practices(10-12). HIV prevention in this group may be the highest impact intervention in developing countries(13). Therefore, ART programs targeting FSW may not only preserve life, but also reduce HIV transmission at a population level. However, it will be critical to ensure that sexual disinhibition does not counteract these beneficial effects.

We assessed the impact of ART on sexual behaviour within an established cohort of FSWs from Nairobi, Kenya in a retrospective case-control study. Institutional Review Boards at Kenyatta National Hospital, and the Universities of Manitoba and Toronto approved the study, and all participants gave written, informed consent prior to participation. Each participant completed a

standardized questionnaire and physical exam every six months. Self-reported risk-taking data included the number of clients (casual and regular) and condoms used per week. Percentage condom use with casual clients was calculated from reported client and condom numbers, with maximum usage arbitrarily set at 98%. Risk reduction services provided to all participants included peer and clinic-based counseling, provision of free condoms, and STI management according to Kenyan guidelines. Non-parametric statistical comparisons between groups and within an individual were performed using PASWStatistics 18.0.

All HIV-infected FSWs initiating ART during 2001-2006 with ≥ 1 year of follow-up were included as cases (n=62). Since sexual risk-taking may change over time in the cohort as a whole, HIV-infected ART-naïve and HIV-uninfected FSWs enrolled in the cohort for a similar duration were selected as controls (n=20 each). Cases and controls were generally comparable at baseline, but cases reported higher condom use with casual clients (mean 97.8% vs. 95.7%; p=0.01) and had a trend to a lower number of unprotected sex acts over the past year (23.0 vs. 34.1; p=0.14, Table 1). The proportion of participants reporting a regular client was similar (cases 58% vs. controls 65%; p=0.62), and condoms were rarely used with regular clients (cases 23.2% vs. controls 9.6%; p=0.13).

No significant change in casual client numbers was seen during the year after starting ART in cases (19.9/week pre- vs. 21.9 post-ART; p=0.17), in condom use with casual clients (97.8% both pre- and post-ART; p=0.66), or in the number of unprotected sex acts with casual clients (23.7/year pre- vs. 24.7 post-ART; p=0.26). Condom use increased in controls (mean 95.7% vs. 97.6%; p=0.14), so that although casual client numbers increased over the study period from 19.4

to 24.5 per week (p=0.002), there was a trend to reduced unprotected sex acts with casual clients during the latter year (34.1 vs. 29.5; p=0.10).

There was some evidence to suggest an increase in condom use with regular clients, using the semi-quantitative measure, in both cases (3.91 versus 3.98, p=0.06) and controls (3.80 versus 3.93, p=0.05). The mean number of regular clients remained unchanged in cases (0.64 versus 0.43, p=0.13) and controls (0.55 versus 0.60, p=0.25), although controls had more regular partners during follow-up (0.60 vs. 0.43, p=0.04).

Social desirability or fear of being taken off ART could associate with false reporting of sexual behaviour by FSWs, and so STI rates were also examined. Combining TV and NG data in all participants, 12/102 FSW were STI-positive during the year pre-ART, compared to 8/102 post-ART (p=0.346). This included 6/62 cases and 6/40 controls pre-ART, and 4/62 cases and 4/40 controls post-ART. The period prevalence of *N. gonorrhea* declined from 4.6% to 1.1% in the periods before and after ART initiation (p=0.02, Wilcoxon test); this decrease was apparent in both cases (6/78, 7.7%, pre-ART; versus 1/76, 1.3%, post-ART) and controls (3/116, 2.6%, pre-ART; versus 1/110, 0.9%, post-ART).

In summary, we found no increase in sexual risk-taking in FSW who initiated ART, either using self-reported behaviour or STI rates. This was in the context of clinic and peer-based risk-reduction services offered to all participants. The latter may be important, since studies in Uganda(14) and Kenya(9, 15) showed increases in safe sex practices following ART initiation in conjunction with risk-reduction services, while in Cote d'Ivoire there was an increase in

unprotected sex post-ART in their absence(16). This suggests that ART should be combined with risk-reduction services where possible. A prior Kenyan FSW study also reported no increased risk after ART initiation(9, 15), although in that cohort less than a third of participants reported >1 partner over the past week, compared to a mean of >20 casual clients in our study.

Several factors may potentially impact sexual practices in FSW participants, including nation-wide HIV education campaigns associated with national declines in HIV prevalence(17, 18) and a cohort-wide risk reduction program(19). Although we found no change in HIV risk behaviour after starting ART, these factors could have masked increases in risk relative to other cohort participants after ART initiation. To rule out this possibility we assessed a control group of 40 FSW followed over a similar time span, both HIV infected ART-naïve and HIV-uninfected, and found no evidence that this was the case.

In conclusion, we found no evidence for alterations in sexual behaviour after starting ART in Kenyan FSWs with very high partner exchange rates. Since FSWs may act as an important core HIV transmission group in the region, and since ART has been shown to reduce HIV transmission(20, 21), ART provision for FSWs in conjunction with risk-reduction services should be considered an important strategy to reduce HIV transmission at a population level.

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Table 1. Longitudinal comparison of sexual risk-taking behaviour and STI period prevalence between cases and controls

Variable	Group	Before ART	After ART	P value
No. unprotected acts with casual partners/year	Cases	23.05	24.72	p=0.57
	Controls	34.08	29.49	p=0.62
Condom use with casual clients	Cases	3.91	3.98	p=0.06
	Controls	3.80	3.93	p=0.05
Condom use with regular clients	Cases	0.24	0.39	p=0.16
	Controls	0.12	0.13	p=0.79
Number of casual clients (/day)	Cases	3.93	4.12	p=0.13
	Controls	4.11	4.43	p=0.43
Number of regular clients	Cases	0.64	0.43	p=0.13
	Controls	0.55	0.60	p=0.26
NG/TV period prevalence	Cases	9.7%	6.5%	p=0.53
	Controls	15%	10%	p=0.48
NG period prevalence	Cases	7.7%	1.3%	p=0.025
	Controls	2.6%	0.9%	p=0.32

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ARTICLE SUMMARY

Article Focus:

- Impact of starting antiretroviral therapy (ART) on sexual risk-taking behaviour in female sex workers (FSW), **which could have an important impact on HIV transmission to clients.**

Key Messages:

- ART initiation was not associated with increased risk taking or STI incidence.
- Both of these declined over time, most likely as a result of risk reduction counseling.

Strengths and Limitations:

- Strengths include a relevant population, longitudinal follow-up, and inclusion of biological measures of risk-taking (STI incidence).
- Limitations include relatively small study groups and limited sampling time points.

ABSTRACT

Objectives: Although antiretroviral therapy (ART) prolongs life and reduces infectiousness, in some contexts it has been associated with increased sexual risk taking.

Design: Retrospective case-control study.

Setting: Nairobi-based dedicated female sex worker (FSW) clinic.

Participants: HIV-infected FSW before and after ART initiation (n=62); HIV-infected and uninfected control FSWs not starting ART during the same follow-up period (n=40).

Intervention: Initiation of ART.

Primary outcome measures: Self-reported condom use, client numbers, and STI incidence over the study period (before and after ART initiation in cases).

Results: Sexual risk-taking behaviour with casual clients did not increase after ART initiation; condom use increased and STI incidence decreased in both cases and controls, likely due to successful cohort-wide HIV prevention efforts.

Conclusions: ART provision was not associated with increases in unsafe sex **in this FSW population.**

MAIN TEXT

Female sex workers (FSWs) play a key role in HIV epidemic spread in sub-Saharan Africa(1) during both early and late epidemic phases(2) due to multiple partners, high rates of HIV and sexually transmitted infections (STIs), and in many instances their ability to negotiate safer sex practices are compromised(1, 3, 4). HIV prevention in this group may be the highest impact intervention in developing countries(5). Therefore, ART programs targeting FSW may not only preserve life, but also reduce HIV transmission at a population level. However, it will be critical to ensure that sexual disinhibition does not counteract these beneficial effects.

ART provision **appears to have contradictory effects** on HIV transmission. While ART reduces blood and genital tract viral load, and therefore infectiousness(6), it has also been associated with reduced safe sex practices(7-9) and increases in STI incidence in some settings(10). **Reasons for behavioural disinhibition could be several, including a feeling of improved health after ART initiation.** Although this increase has not been the experience to date in resource-poor countries(11), it could become an issue as access expands(2), and **further studies are needed to understand the extent to which these initial observations are generalizable. Mathematical** models suggest that if safe sex practices are not maintained, then HIV transmission may increase despite ART-associated reductions in genital tract virus levels(12). A recent study in Kenyan sex workers with relatively low rates of partner exchange showed no change in risk-taking following ART(13), but these findings need to be confirmed in a high partner exchange setting.

In the current study, we assessed the impact of ART on sexual behaviour within an established cohort of FSWs from Nairobi, Kenya in a retrospective case-control study. Institutional Review Boards at Kenyatta National Hospital, and the Universities of Manitoba and Toronto approved the study, and all participants gave written, informed consent prior to participation. Each participant completed a standardized questionnaire and physical exam every six months. Self-reported risk-taking data included the number of clients (casual and regular) and condoms used per week. Percentage condom use with casual clients was calculated from reported client and condom numbers, with maximum usage arbitrarily set at 98%. Risk reduction services provided to all participants included peer and clinic-based counseling, provision of free condoms, and STI management according to Kenyan guidelines. Non-parametric statistical comparisons between groups and within an individual were performed using PASWStatistics 18.0. **Self-reported sexual behaviour data were collected at two time-points six months apart prior to ART initiation, and at two time-points after: means of continuous variables were calculated for each period, and changes within an individual compared by using the Wilcoxon signed rank test. Categorical variables were compared by Mann-Whitney.**

RESULTS

All HIV-infected FSWs initiating ART during 2001-2006 with ≥ 1 year of follow-up were included as cases (n=62). Since sexual risk-taking may change over time in the cohort as a whole, HIV-infected ART-naïve and HIV-uninfected FSWs enrolled in the cohort for a similar duration were selected as controls (n=20 each). Cases and controls were generally comparable at baseline, but cases reported higher condom use with casual clients (mean 97.8% vs. 95.7%; p=0.01) and had a trend to a lower number of unprotected sex acts over the past year (23.0 vs.

34.1; p=0.14, Table 1). The proportion of participants reporting a regular client was similar (cases 58% vs. controls 65%; p=0.62), and condoms were rarely used with regular clients (cases 23.2% vs. controls 9.6%; p=0.13).

No significant change in casual client numbers was seen during the year after starting ART in cases (19.9/week pre- vs. 21.9 post-ART; p=0.17, **Table 2**), in condom use with casual clients (97.8% both pre- and post-ART; p=0.66), or in the number of unprotected sex acts with casual clients (23.7/year pre- vs. 24.7 post-ART; p=0.26). Condom use increased in controls (mean 95.7% vs. 97.6%; p=0.14), so that although casual client numbers increased over the study period from 19.4 to 24.5 per week (p=0.002), there was a trend to reduced unprotected sex acts with casual clients during the latter year (34.1 vs. 29.5; p=0.10).

There was some evidence to suggest an increase in condom use with regular clients in both cases (3.91 versus 3.98, p=0.06) and controls (3.80 versus 3.93, p=0.05). The mean number of regular clients remained unchanged in cases (0.64 versus 0.43, p=0.13) and controls (0.55 versus 0.60, p=0.25), although controls had more regular partners during follow-up (0.60 vs. 0.43, p=0.04). **It should be noted that condom use with regular partners remained infrequent in all groups; specific interventions to increase this in FSW populations could have important public health benefits.**

Social desirability or fear of being taken off ART could associate with false reporting of sexual behaviour by FSWs, and so STI rates were also examined. Combining Trichomonas vaginalis (TV) and *Neisseria gonorrhea* (NG) data in all participants, 12/102 FSW were STI-positive

during the year pre-ART, compared to 8/102 post-ART (p=0.346). This included 6/62 cases and 6/40 controls pre-ART, and 4/62 cases and 4/40 controls post-ART. The period prevalence of *N. gonorrhea* declined from 4.6% to 1.1% in the periods before and after ART initiation (p=0.02, Wilcoxon test); this decrease was apparent in both cases (6/78, 7.7%, pre-ART; versus 1/76, 1.3%, post-ART) and controls (3/116, 2.6%, pre-ART; versus 1/110, 0.9%, post-ART).

In summary, we found no increase in sexual risk-taking in FSW who initiated ART, either using self-reported behaviour or STI rates. This was in the context of clinic and peer-based risk-reduction services offered to all participants. The latter may be important, since studies in Uganda(14) and Kenya(13, 15) showed increases in safe sex practices following ART initiation in conjunction with risk-reduction services, while in Cote d'Ivoire there was an increase in unprotected sex post-ART in their absence(16). This suggests that ART should be combined with risk-reduction services where possible. A prior Kenyan FSW study also reported no increased risk after ART initiation(13, 15), although in that cohort less than a third of participants reported >1 partner over the past week, compared to a mean of >20 casual clients in our study.

Several factors may potentially impact sexual practices in FSW participants, including nation-wide HIV education campaigns **that could be associated** with national declines in HIV prevalence(17, 18) and a cohort-wide risk reduction program(19). Although we found no change in HIV risk behaviour after starting ART, these factors could have masked increases in risk relative to other cohort participants after ART initiation. To rule out this possibility we assessed a control group of 40 FSW followed over a similar time span, both HIV infected ART-naïve and HIV-uninfected, and found no evidence that this was the case.

In conclusion, we found no evidence for alterations in sexual behaviour after starting ART in Kenyan FSWs with very high partner exchange rates. **FSWs through their profession may act as an important core HIV transmission group in the region.** Since ART has been shown to reduce HIV transmission(20, 21), ART provision for FSWs in conjunction with risk-reduction services should be considered an important strategy to reduce HIV transmission at a population level.

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TABLE 1. Baseline characteristics of study groups.

Characteristic (median, range)	Cases starting ART (N=62)	HIV-infected controls (N=20)	HIV-uninfected controls (N=20)
Age (years)	41 (26-61)	38 (27-48)	41 (27-61)
Duration of sex work (years)	14 (2-41)	13 (1-28)	11 (2-33)
Clients per week	16 (4-80)	20 (3-51)	19 (2-45)
Condom use (%)	98 (86-98)**	98 (75-98)	98 (50-98)
Unprotected sex acts (past year)	16 (4-160)	21 (3-195)	24 (4-171)
Regular partner (proportion)	36/62 (58%)	12/20 (60%)	14/20 (70%)
Condom with regular partner (%)	23	8	11
CD4 T cell count	205 (70-1028)**	557 (243-1082)	1100 (631-1692)

**Mann-Whitney P≤0.01 for cases vs. controls.

TABLE 2. Longitudinal assessment of risk-taking and STI prevalence in FSW over time.

Variable	Before ART	After ART	P value
CASES			
No. unprotected acts with casual partners/year	23.05	24.72	0.57
Condom use with casual clients (Scale 1-4)	3.91	3.98	0.06
Condom use with regular clients (Scale 1-4)	0.24	0.39	0.16
Mean Number of casual clients per day	3.93	4.12	0.13
Mean Number of regular clients per day	0.64	0.43	0.13
NG/TV period prevalence (%)	9.7%	6.5%	0.53
NG period prevalence (%)	7.7%	1.3%	0.03
CONTROLS			
No. unprotected acts with casual partners/year	34.08	29.49	0.62
Condom use with casual clients (Scale 1-4)	3.80	3.93	0.05
Condom use with regular clients (Scale 1-4)	0.12	0.13	0.79
Mean Number of casual clients per day	4.11	4.43	0.43
Mean Number of regular clients per day	0.55	0.60	0.26
NG/TV period prevalence (%)	15%	10%	0.48
NG period prevalence (%)	2.6%	0.9%	0.32