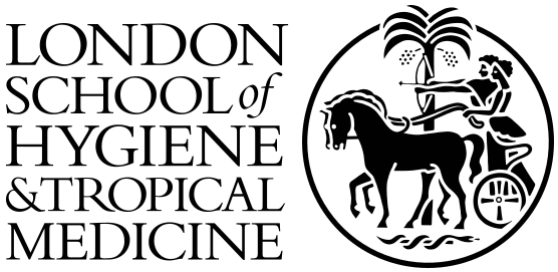

Title: The mediating role of partner selection in the association between transactional sex and HIV incidence among young women

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Running head: Transactional sex and HIV: causal pathways

Abstract

Objective: In sub-Saharan Africa, transactional sex is associated with an increased risk of HIV infection in adolescent girls and young women, but the mechanisms for this relationship remain unclear. We hypothesise that young women who report transactional sex may have multiple partners and older partners, thereby increasing their HIV risk.

Setting*:* We used longitudinal data from the HPTN 068 trial in rural South Africa where young women aged 13-20 who were HIV-negative at enrolment (n=2362) were followed approximately annually for up to 6 years.

Methods: We used the parametric g-formula to estimate the total effect of time-varying, frequent transactional sex (receipt of gifts/money at least weekly vs monthly or less) on HIV incidence and the controlled direct effect for mediation in a simulated cohort using 20,000 bootstrapped observations. We calculated rates and hazard ratios over the entire study period.

Results: The hazard ratio for the total effect of frequent transactional sex on HIV incidence was 1.56 (95% CI: 1.28, 1.85). However, this effect was mediated by partner age (>5+) and number of partners (>1) and the hazard ratio was attenuated to 1.09 (95% CI: 0.90, 1.28) when setting both partner age and partner number constant.

Conclusion: Both partner age difference and partner number mediate the relationship between transactional sex and incident HIV infection. Through this mediation analysis, we provide important longitudinal evidence to suggest that young women who engage in frequent transactional sex select multiple partners, often older male partners that may be part of higher risk sexual networks.

Keywords: adolescent girls, young women, transactional sex, mediation analysis, causal pathways, HIV incidence, older partners, multiple partners.

Introduction

In sub-Saharan Africa (SSA) adolescent girls and young women (hereafter young women) aged 15-24 bear a disproportionate burden of the HIV epidemic; over 25% of new HIV infections in this region occur in this population [1]–[3]. Transactional sex defined as a 'non-commercial, non-marital sexual relationships motivated by an implicit assumption that sex will be exchanged for material support or other benefits' is considered to be a contributing factor to the high HIV infection rates observed among young women in the region [4]–[7]. Both cross-sectional [6], [8] and longitudinal evidence [7], [9] has demonstrated that young women reporting transactional sex are at a higher risk of HIV acquisition. In addition, prior analysis of these data by Kilburn et al (2018) found that the effect of transactional sex is particularly driven by relationships in which a sexual partner provides money and/or gifts frequently, meaning at least weekly, as opposed to monthly [7].

Structured by gender inequality, transactional sex takes place across a range of economic contexts; from those characterised by poverty and insecure livelihoods to those marked by income inequality and consumerist aspirations [10]. The discourse around women's motivations for engaging in transactional sex have included: fulfilment of basic needs in impoverished settings; the expectation that men should provide for their partners in relationships; and efforts to improve one's social status [4], [12], [13]. Not all sexual relationships characterised by or involving transactional sex are risky for HIV infection. Qualitative evidence suggests that transactional sex is an expectation embedded in adolescent romantic relationships; only certain aspects related to male provision or dependence on partners for money or material support, result in young women's weakened negotiating position within the relationship that make it risky for HIV infection [11].

Transactional sex is also associated with other dimensions of HIV risk in women. These include different forms of partner violence and abuse [12], [13], alcohol consumption or patronising venues that serve alcohol [15], [16], and non-use or inadequate use of condoms, although there is no clear association with condom use, possibly due to reporting and measurement bias [17], [18]. Further, there is evidence that young women who report transactional sex are more likely to have multiple partners [12], [14], and to have older partners [13]. On the other hand, a study by Jewkes et al (2012) in South Africa showed an increase in incident HIV among young women who reported transactional sex with an on-going or once off partner. This finding was independent of partner number or age.[9]. Therefore, the question still remains as to why transactional sex is risky for HIV

In particular, examining the causal pathways between transactional sex and increased HIV risk is important for improving the health and well-being of young women in SSA, and for improving our HIV prevention response. Longitudinal evidence examining the pathway from transactional sex to HIV acquisition is limited. A cross-sectional study from Swaziland suggests a measure of gender inequality—constrained agency of young women — and offers an explanation of the pathway [21]. This was further clarified by a cross-sectional analysis in rural South Africa that found that young women who engage in transactional sex are at risk for HIV due to their choice of partners and the sexual networks of those partners [6].

Our aim is to investigate whether the association between frequent transactional sex and HIV acquisition is mediated by young women having multiple and older sexual partners given their role in influencing young women's HIV risk. We have conceptualised multiple sexual partners as being on the pathway between frequent transactional sex and HIV, as young women might engage in transactional acts with multiple partners, primarily motivated by the need to obtain items or status [4]. For older partners, young women who report frequent transactional sex are more likely to have age-disparate partnerships, due to the following reasons: young women may pick older partners due to men's ability to provide gifts and money to the young women, for their social and educational maturity, for the belief that they are better sexual partners, and they may be perceived as more marriageable [15]–[17]. There is usually an established power dynamic between these older men and young women in turn making it more difficult for young women to negotiate safe sexual behaviour, especially in transactional relationships [18].

To our knowledge, there are no longitudinal studies that formally test these causal pathways [4]. Hence, our aim is to address this knowledge gap by using longitudinal data collected from a randomised controlled trial with young rural South African women.

Methods

Study Population and Sample

This paper is a secondary analysis of longitudinal data of participants enrolled in a phase 3, individually randomised conditional cash transfer (CCT) trial in rural South Africa (HPTN 068). The primary objective of the trial was to determine whether providing cash transfers, conditional on school attendance, reduced the risk of HIV acquisition in young women aged 13-20 years. Data collection was conducted in rural Mpumalanga Province,

South Africa [19]–[21]. Further details on the study design, questionnaires and laboratory procedures are available in the baseline and main trial publications [22], [23].

The trial included young women living in 28 villages within the Agincourt Health and Socio- Demographic Surveillance System (AHDSS) area run by the MRC/Wits Rural Public Health and Health Transitions Research Unit [24]. At baseline, the trial enrolled 2533 young women in grades 8, 9, 10, or 11 at selected schools within the AHDSS study site. Participants were excluded if they were pregnant or married at baseline. Participants were seen annually from baseline at 12, 24, and 36 months until the study completion date or their planned high-school completion date, whichever came first [23]. One additional visit took place 1–2 years after the study ended (a post-intervention visit) for all participants; thus participants could have up to four follow-up visits over 6 years [7]. Young women were in different grades at enrolment and could have had fewer than four visits if they were expected to graduate before the end of the study period. Each annual study visit included an audio computer-assisted self-interview (ACASI) with the young woman and HIV testing for those who were negative at the previous visit. An additional HIV test was conducted for some girls around the time of expected graduation from high school or when the study was completed to capture more person-time in the study, if eligibility was met (termed the 'graduation visit'). This test was typically around 6 months after the previous annual visit [23].

To measure HIV incidence and mediation, our analytical sample (n=2362) included participants who were HIV negative at baseline enrolment and had at least one follow-up visit [7]. We did not exclude sexually inactive young women as a meaningful proportion of the incident HIV infections (20%) occurred in those that did not report any sexual activity and we wanted to extrapolate findings to all young women [7]. Kilburn et al's (2018) paper that showed whether there is an association between transactional sex and HIV incidence used the same dataset and provides a sensitivity analysis that shows the association among only those who reported ever having sex (*Appendix Table A1*) [7].

Measures

The outcome variable, *HIV incidence* was determined using HIV tests conducted at baseline and at each follow-up visit. HIV testing procedures included using two HIV rapid tests performed in parallel followed by a confirmatory test, if one or both rapid results were HIV reactive. Detailed procedures for HIV testing and laboratory procedures are described in the trial paper [23].

Our exposure variable is *frequent transactional sex* as Kilburn et al (2018) showed not only an association between transactional sex and HIV incidence in this cohort, but that the effect was strongest among those who engaged in transactional sex with frequent exchanges [7]. Frequent exchanges were defined as receiving money weekly or gifts 'often' or 'always', in contrast to infrequent exchanges (having received money once or monthly and gifts 'a few times' or 'once' or 'none'). We constructed a binary exposure variable for this analysis to equal 1 for transactional sex with a partner that gave money or gifts frequently (*frequent transactional sex*) and 0 if either 1) no transactional sex; or 2) transactional sex with infrequent exchange (*infrequent transactional sex*). Further, in modelling the exposures and outcomes for the simulations, we included a dummy variable for infrequent transactional sex so that 'none' served as reference group.

We defined the mediator of *having an older partner* as having had at least one sexual or nonsexual partner >5 years older at each follow-up visit. Partners with whom there was no reported sexual relationship were included to account for potential misreporting about sexual behaviours. The mediator of the *number of sexual partners* was defined as having zero, 1 or >1 sex partners in the 12 months prior to each follow-up visit.

We selected confounders based on previous literature on transactional sex and HIV infection and our directed acyclic graph (shown as Appendix 2). We included the exposure-outcome baseline confounders of age of young woman, intervention arm assignment to account for the original trial design, and quartiles of per-capita household consumption. Time-varying controls include schooling (high school attainment vs. enrolled in high school), ever pregnant, physical intimate partner violence (IPV), Herpes Simplex Virus-2. We also included the exposure-outcome and mediator-outcome time-varying confounders for depression from the Center for Epidemiologic Studies depression scale (CES-D), a 20 item scale with a cut-off score >=16 [25], and wealth quartiles, represented as the lag of time-varying log of per capita expenditure in all models. The construction of the specific variables – schooling, IPV and per-capita household consumption – has been referenced in earlier papers [7], [26].

Statistical Analysis

To explore the mediating effect of frequent transactional sex on HIV incidence, we used an adaptation to the parametric g-formula for mediation analysis that allows us to empirically model both time-varying confounding and mediators within longitudinal, survival data [27]. We examined total effects and controlled direct effects

(CDE) of mediators of interest. Mediator effects were examined both separately and jointly in a simulated cohort of 400 estimates using approximately 20,000 bootstrapped samples (inflating the original baseline sample by 8).

Using the counterfactual approach to causal mediation, we define the total effect as the Hazard Ratio (HR) of the effect of frequent transactional sex on incident HIV, if it were possible to observe all participants under each possible exposure plans: Y(1) = frequent transactional sex and Y(0) = no frequent transactional sex. Mediators in this model are left at the natural value they would have taken under each exposure plan [28]. We estimated the CDEs of the two mediators (older partners and number of sexual partners) on the relationship between frequent transactional sex and incident HIV. CDEs are defined as the effect of exposure on an outcome while keeping the mediator 'controlled' at level M for everyone, but switching exposure from control, Y(0), to treatment, Y(1). Mediation is the attenuation of the total effect closer to the null (i.e., the HR of the CDE is closer to 1). We also attempted to estimate the CDE for the mediators, condom use and low sexual power, but did not include them in the final model due to measurement concerns and issues with missing values (see 'discussion').

In general, CDEs require fewer assumptions about no measured confounding of exposure and outcome relationships than the natural direct and indirect effects. In particular, the CDE does not require that mediator-outcome confounders are unaffected by prior exposure, a difficult assumption to demonstrate without randomisation of mediators [29]. In our study, CDEs represent the hypothetical scenario if we were able to set mediators to a riskier level in the sample (e.g. increasing number of sexual partners). We examined the CDE under several different 'scenarios' including (1) setting all young women to have an older partner; (2) setting young women to have one sexual partner (3) setting young women to have more than one sexual partner; (4) setting all young women to have both an older partner and more than one sexual partner. We checked for interactions between the exposure and mediators and are not including them due to sparse data.

In order to estimate the total effect and the CDEs using the parametric g-formula, we undertook the following steps (details in *Appendix 1*): first, we expanded the dataset to eight times the sample size (around 20,000 observations) and pulled a random sample with replacement [29], [30]. Next, we fitted pooled logistic regression models (ordered logit model for number of sexual partners) for every time-varying outcome, exposure, and confounder used in the analysis. Third, using Monte Carlo simulation, we used baseline confounders and coefficients obtained from the logit models in the first step to simulate the predicted probabilities of every time-

varying outcome across each of the four follow-up time points. We repeated this process under each exposure plan, Y(1) and Y(0), to estimate the risk of HIV incidence across both potential outcomes. We then used this predicted HIV incidence to estimate the HR of the total effect and CDEs using Cox Proportional Hazard models. We also report the rate of HIV incidence per person year and the difference between them taken as an average across the simulated sample. We repeated all steps for each hypothetical scenario to estimate the CDEs. We calculated 95% confidence intervals (CI) of rates, hazard ratios and rate differences using the standard deviation of the point estimate from 400 simulated samples. We used STATA version 15.1 for all analyses.

Results

Table 1 provides baseline characteristics for the entire sample (n=2362) of young women. At baseline, the median age was 15 years, 26.2% reported ever having sex and the median age of first sex was 16 years. With a low proportion of sexually active participants in the entire sample, sexual behaviours such as past year transactional sex (n=82 [3.6%]) and frequent transactional sex (n=38 [1.7%]) were low. Further, of all young women, 5.6% (n=129) reported having a partner >5 years older, 20.4% (n = 476) had one partner, 73.6% (n = 1715) had zero partners and 5.9% (n=138) had more than one partner in the past year.

Table 2 provides mean characteristics of young women by frequency of transactional sex across time. For this table, we split the table into two study visit periods: during the main trial (3 years) and post-intervention visit (one year). A higher percentage of young women who reported frequent transactional sex during the main and post-intervention trial had an older partner (>5 years older) (29%.versus 0.7%), and higher mean numbers of sexual partners compared to those that reported infrequent or no transactional sex (mean: 1.2 versus 0.3). For sexually active young women, the proportion using condoms during last sex was almost the same between those engaging in frequent or infrequent transactional sex across study periods. Further, those that did not report frequent transactional sex had higher sexual relationship power compared to those that reported frequent transactional sex (57.7% versus 36.7%) in the main trial period. In addition, Table 2 shows that a higher proportion of young women that engaged in frequent transactional sex had older partners (>5 years older) and number of partners in the post-intervention visit compared to the main trial. We have included sample observations of our key covariates through 2 x 2 tables (cross-tabulations) to demonstrate that the cells of our covariates have sufficient sample numbers. This table, included as Appendix 3, shows the exposure (frequent transactional sex) by each confounder and mediators (older partner and multiple partners) by each confounder, pooled over all intervals.

Table 3 displays the total effect and CDEs of frequent transactional sex on HIV incidence by different levels of mediators. The total effect in Table 3 indicates that if the mediators had taken on their natural values (represented by the coefficients that the simulation model shows before we set the mediators), the incidence rate of HIV per person year over six years of follow-up was ~5% if all young women had frequent transactional sex and ~3% if all had infrequent or no transactional sex. The HR for the total effect was 1.56 (95% CI 1.28, 1.85). Table 3 also shows the CDE for the effect of frequent transactional sex on HIV incidence under different scenarios, such as having an older partner >5 years, having one sex partner and more than one sex partner, each individually. We observed attenuation from the total effect (as HR reaches 1) for CDEs after setting individual mediators to: all young women have an older partner (HR: 1.38; 95% CI: 1.17, 1.59), sex partner number is set to one partner (HR 1.23; 95% CI 1.00, 1.46) and then more than one sex partner (HR: 1.22; 95% CI 1.00, 1.45), as also depicted in Figure 2.

Furthermore, when jointly setting the two mediators – having an older partner and more than one sex partner – CDEs are strongly attenuated in comparison to the total effect. In this joint scenario, the HR is the closest to one out of all scenarios (HR 1.09, 95% CI: 0.90, 1.28) (see Table 3). This result is also demonstrated by the cumulative incidence curves in Figure 1, Panel B. When we set the mediators, the curves for frequent and no frequent transactional sex (either none or non-frequent exchanges) with HIV incidence are uniform during years 1-3 especially (during the main trial) and diverge later during the post-intervention study period.

Discussion

This longitudinal mediation analysis examined the pathways between frequent transactional sex and HIV incidence among a sample of secondary school young women aged 13-20 in rural South Africa. Young women's partner characteristics, such as having an older partner (>5 years) and the number of sexual partners in the past year mediated the relationship between frequent transactional sex and incident HIV, suggesting that a large proportion of the effect of frequent transactional sex on HIV acquisition is the result of partner selection. To our knowledge, this is the first study that uses formal mediation analysis methods to delineate the causal pathways between transactional sex and HIV incidence. Previous research has shown that a partner age difference of 5-10 years is associated with higher HIV risk [31]–[33] and that young women who engage in transactional sex tend to have a higher number of sexual partners compared to those that do not engage in transactional sex, thus increasing their HIV risk [34]. Further, evidence from South Africa shows that young women's negotiating power

for condom use is often compromised by partner age disparities and economic dependence that increases HIV risk [33], [35].

We also observed that young women who engaged in more frequent transactional sex reported lower sexual relationship power than those who engaged less or not at all. In this study, we saw this particularly among younger women as part of the main trial study visits. Not seen here, but shown in other studies, females in multiple and concurrent relationships report less consistent condom use and are more likely to report transactional sex, and difficulty in both negotiating condoms and not being able to influence timing and nature of sex [36]. In this analysis, young women engaging in frequent transactional sex have a higher risk of HIV. These young women may be more dependent on male partners, thus reducing their decision-making power when practising safer sex. In addition, when male partners provide money/gifts frequently, the imbalance in power may be more acute, as shown by qualitative research in South Africa [37]. This finding aligns with research by Luke (2011) in Kenya that demonstrates that resources obtained from within the relationship decrease young women's negotiating power [17]. Furthermore, Luke's (2005) research on the value of transfers and condom use showed that the larger the value of the gift, the less likely safer sex would be practised [38]. Our results also suggest that young females with multiple partners might be part of a network of higher-risk male partners that increase their exposure to HIV, as has been shown through an ecological analysis of epidemiological data in 14 West African countries [39], [40]. These high-risk male partners are likely older men with their own networks of sexual partners who may have more power in relationships, thus compromising young women's ability to negotiate condom use [35], [41], [42].

As far as we know, this paper is one of the only longitudinal studies that formally tests the mechanisms through which transactional sex increases HIV acquisition in young women. It is based on a biological outcome measure of HIV, not self-reported sexual behaviours. However, there are a few limitations to consider. We recognise that violations or near violations of positivity can be of concern in this causal analysis given the small proportion of young women who, at baseline, report any transactional sex, who report sex with older partners, and who report multiple sex partners. This can cause some participants to have high probability, as fewer individuals within a given covariate stratum have the exposure. Hence, the probability of those 'rare' individuals who do have the exposure become more extreme. To show that there has not been a violation of positivity, we have included a table (Appendix 3) that indicates that the cells for our covariates have sufficient sample numbers. Furthermore, our models converge, and the standard errors and coefficients are reasonable suggesting that data sparsity is not

an issue. Relatedly, as noted in Kilburn et al (2018), there might have been underreporting or misreporting of sexual behaviours, especially as we found incident HIV among young women that did not report ever having sex. This was despite the use of ACASI to minimise reporting bias. However, we conducted a sensitively analysis among sexually active girls only and found similar results. There might have been some misreporting when it came to sexual partner number and partner age difference, in particular, due to issues of social-desirability and recall bias. If we assume that young women are not telling the truth, for example, they are reporting having a lower number of partners or underestimating their partner's age, it might result in underestimating the effect. However, there is no reason to suspect that misreporting of sexual activity would be associated with HIV status, as HIV testing occurred after young women had answered the ACASI questions. We had also planned to include condom use as a mediation variable, but the condom use variable showed collinearity with older partners and multiple sexual partners. Given that our results show that almost all the mediation was through older partners and partner number, we extrapolated that lack of condom use within such partnerships might increase HIV risk but we could not explicitly test it in our model. Further, we planned to test low sexual relationship power using the sexual relationship power scale (SRPS) but had issues with a high percentage of missing values that could not be addressed with multiple imputation methods. However, again we can extrapolate how low power relates to older partners and condom use negotiation to explain the mechanism further. Finally, our analysis assumes no unmeasured confounding that is impossible to assess in the data. However, we explored measured confounding by examining the effect of adding and removing different variables to our models.

Conclusion

In order to reduce the burden of HIV faced by young women in SSA, we need to examine transactional sex and the pathways to HIV infection. Our analysis demonstrates that for young women engaging in frequent transactional sex, having older and multiple sexual partners helps explain their increased HIV risk. This might be due to the underlying risk profile of these older men that young women have as sexual partners and the density of sexual networks. Interventions addressing transactional sex should target young women and men's gendered expectations of male provision [4] and promote notions of equitable relationships that include critical reflections on agency and power to influence young women's choice in partners [29][43][44]. Furthermore, programmes that tackle relationship dynamics, individual beliefs and psycho-social aspects of adolescence, alongside economic opportunities for young women transitioning to adulthood are promising, especially if tailored to the socio-economic context to reduce reliance on risky partnerships [45]. From a research perspective, using improved

measures for transactional sex to capture primary motivations is important to understand risk and having better measures for sexual relationship power might enable further confirmation of these pathways [46]. Research should also focus on influences that shape engagement in transactional sex and the underlying developmental trajectories of these young women within overarching systems of gendered social and economic inequalities in different contexts.

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The funder of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The corresponding author had full access to all the data in the study and had final responsibility for the decision to submit for publication.

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In text tables and figures

Table 1. Baseline characteristics of HIV negative young women aged 13-20 in Agincourt, South Africa with at least one follow-up visit (N=2362)

	Median (IQR) or n (%)
Young women's age at baseline (years)	15 (14, 17)
Average monthly per capita Household expenditure (South African Rand)	289.2 (184.5, 477.6)
Ever had sex	618 (26.2)
Age in years at first sex (sexually active girls)	16 (14, 16)
CCT beneficiary arm	1,215 (51.4)
Older partner (5+ years)	129 (5.6)
Sex partner number	
0	1,715 (73.6)
1	476 (20.4)
>2	138 (5.9)
Prevalent HSV-2 infection	90 (3.8)
Ever pregnant	192 (8.2)
Any alcohol use	51 (2.2)
Double or single orphan	468 (20.0)
Physical IPV	245 (10.6)
Condom use at last sex (sexually active girls)	426 (69.5)
High relationship power (sexually active girls)	227 (37.9)
Children's depression inventory score ≥ 16	415 (18.5)
Any transactional sex past 12 months	82 (3.6)
Frequent transactional sex past 12 months	38 (1.7)

Notes: [1.] Baseline data collection occurred between March 2011-December 2012. [2.] Ever transactional sex is operationalised as whether a young woman reported that she felt that she had to have sex with a male partner who gave her money or gifts. [3.] Frequent transactional sex is defined as transactional sex with a partner that frequently provided material items (gave money weekly and gifts 'often' or 'always'). These frequent exchanges are in comparison to infrequent exchanges, defined as having received money once or monthly and gifts 'a few times' or 'once' infrequently. [4.] We report on the Children's depression inventory score at baseline, but used the Center for Epidemiologic Studies Depression Scale (cutoff score>=16) in the models.

Table 2: Mean characteristics of young women by whether she engaged in frequent transactional sex across study visits

	During the main trial (3 visits)		**Post-intervention (1 visit)**	
	Frequent transactional sex		Frequent transactional sex	
	Yes	No	Yes	No
Age	17.9	16.9	20.3	20.1
Condom use during last sex (sexually active girls)	73.1%	73.3%	74.8%	79.2%
High sexual relationship power (sexually active girls)	36.7%	57.7%	53.0%	56.4%
Ever pregnant	55.0%	15.0%	55.3%	35.9%
Older partner (5+ years older)	29.0%	0.7%	40.6%	21.7%
Number of partners (mean)	1.2	0.3	1.3	0.7
Alcohol use	4.3%	1.7%	6.4%	4.2%
Physical IPV	39.1%	21.9%	17.6%	8.5%

*Notes***:** During the main trial there were 449 observations over the 3 follow-up visits defined as having frequent transactional sex and 2314 that did not have frequent transactional sex. At the post-intervention visit 188 young women reported frequent transactional sex and 1571 that did not have frequent transactional sex.

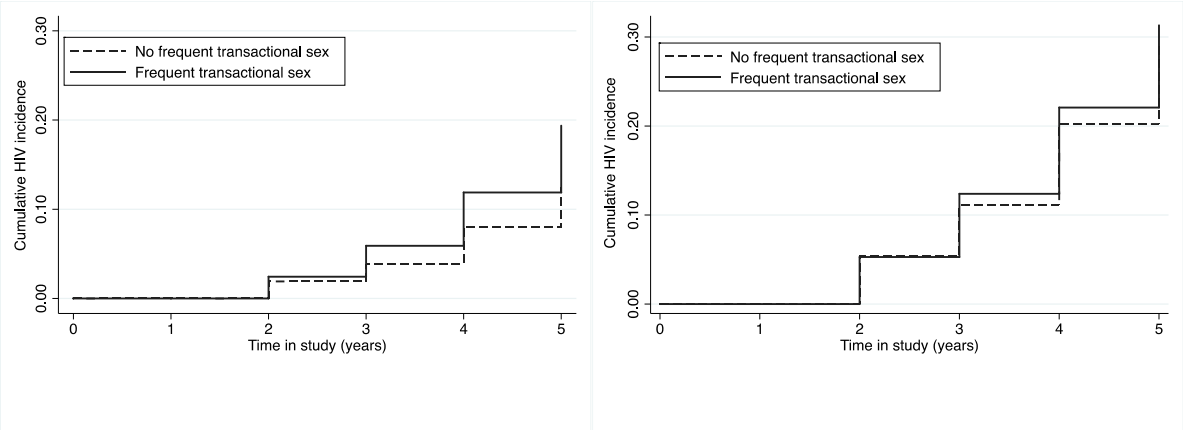
Table 3: Total and Controlled Direct Effect (CDE) of frequent transactional sex on HIV incidence by different levels of mediators (partner number and partner age difference)

	HIV		
	Incidence Rate (%)	**RD (95% CI)**	**HR (95% CI)**
Total effect			
Frequent TS (weekly)	5.0	1.8 (1.2–2.2)	1.56 (1.28–1.85)
Non-frequent TS or none	3.3		
CDE: having an older partner			
Frequent TS (weekly)	7.3	2.0 (1.4–2.6)	1.38 (1.17–1.59)
Non-frequent TS or none	5.3		
CDE: having 1 sex partner			
Frequent TS (weekly)	4.9	0.8 (0.3–1.5)	1.23 (1.00–1.46)
Non-frequent TS or none	4.0		
CDE: having more than 1 sex partner			
Frequent TS (weekly)	6.1	1.0 (0.4–1.7)	1.22 (1.00–1.45)
Non-frequent TS or none	5.1		
CDE: having older partner and more than one sex partner			
Frequent TS (weekly)	8.9	0.7 (-0.1–1.5)	1.09 (0.90–1.28)
Non-frequent TS or none	8.2		

Notes: Incidence Rates, Rate Differences (RD), and Hazard Ratios (HR) calculated from 400 Monte Carlo simulations with 20,000 observations randomly pulled with replacement from all follow-up visits (main trial and post-intervention).

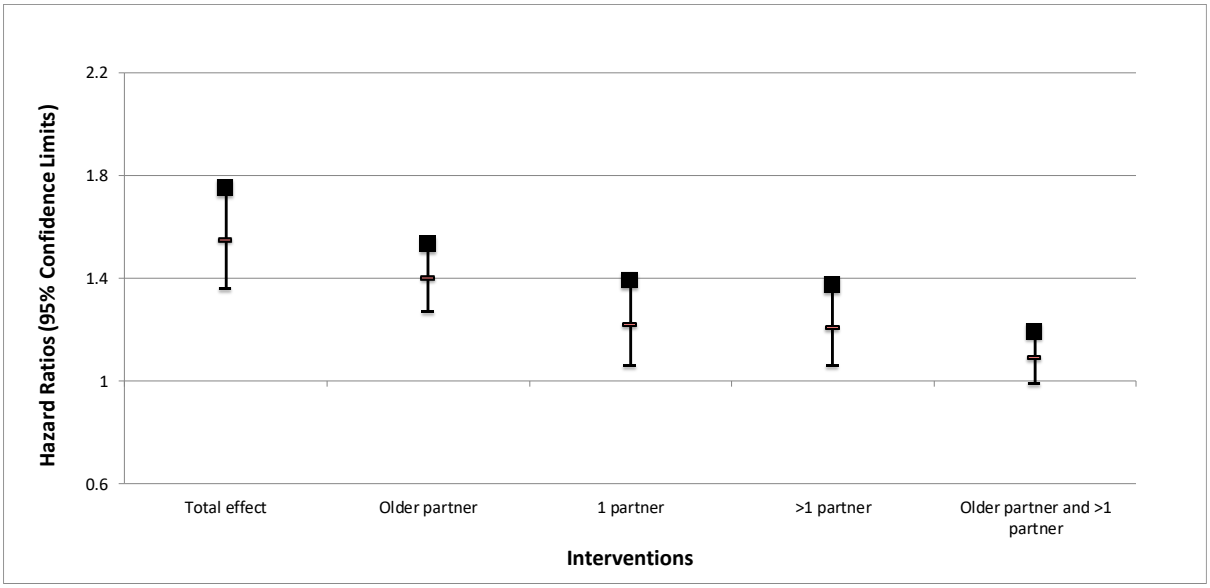
FIGURES

Figure 1: Cumulative HIV incidence by frequent transactional sex and by time since study enrolment in a Monte Carlo sample of 20,000 observations accounting for confounding. Panel A illustrates the total effect of the frequent transactional sex on HIV. Panel B illustrates the CDE under the condition that young women have an older partner and have more than one sex partner.



Panel A Panel B

Figure 2: Controlled Direct Effects (CDEs) showing the effect of transactional sex on HIV incidence under different scenarios using older partner and partner number as mediators



Appendix 1:

Steps for G-formula mediation of frequent transactional sex on HIV incidence:

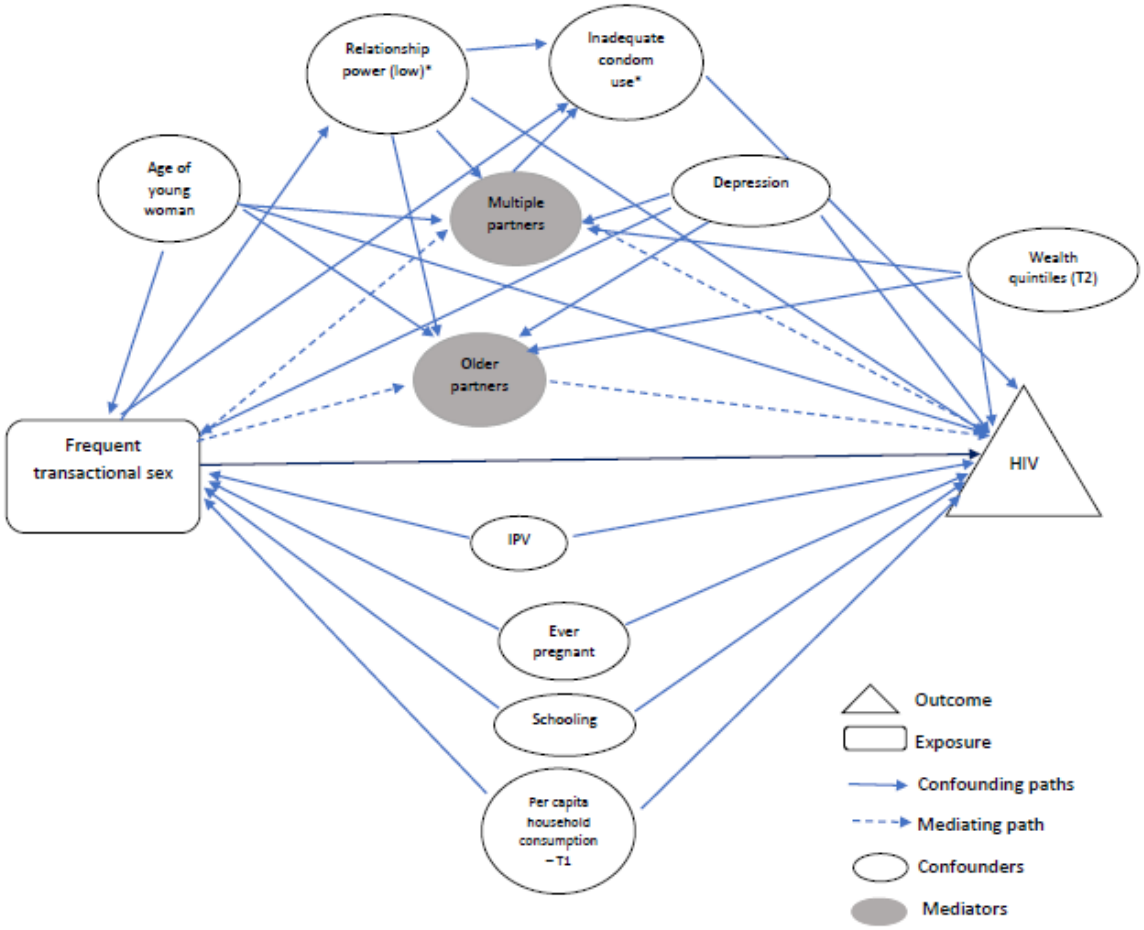
Analysis performed using Stata 15.1

1) Increase the sample size by expanding the original baseline sample to 8 times its size (N=~20,000) in order to reduce Monte Carlo error. Then merge follow-up visit data in for each participant creating a longitudinal data set for estimation of regression models in Step 2 and time-to-event analysis in Step 3.
2) Run separate pooled logistic regression models (or ordered logit for categorical variables) for each of the following time-varying variables: outcome, mediators, mediator-outcome confounders and exposure-mediator confounders. Each model is adjusted to control for baseline confounding and a sufficient set of time-varying covariates. One confounder model (*in school* for our analysis), is adjusted only for baseline confounders in order to simulate time-varying covariates in Step 3.
    a. Save all coefficients from each model in separate matrices
3) Simulate the time-varying variables based on the coefficients saved in the matrices from Step 2:
    a. Set the exposure variable

    For each follow-up time point (Visits 2 through 5):

    b. Simulate time-varying confounder variables using coefficients obtained from Step 2, baseline variables and prior simulated time-varying variables in the simulation
    c. Simulate mediators using coefficients obtained from Step 2 time-varying confounder variables already simulated
    d. Simulate HIV incidence using all new unconfounded variables and the coefficients obtained from Step 1.
4) Reshape the new data set into long format and replace HIV status to be missing for individuals after the first infected incidence to replicate a survival data set.
5) Generate the effect size of transactional on HIV
    a. First, set the exposure to either 1 and then 0, run saving separate data sets with simulated values under each exposure scenario
    b. Append the separate data sets
    c. Use the indicator exposure variable for transactional sex in an unadjusted Cox model with simulated HIV as the outcome.
    d. Save the Hazard Ratio from each Cox model and the rates of HIV under each exposure.
    e. Calculate and save risk ratios using the HIV rates under each exposure.
6) Run Steps1 through 5, 400 times to generate a simulated sample of 400 effect estimates (starting with a new bootstrap sample of the original sample each time per Step 1).
7) Use the standard deviation of the simulated samples (each N=400) to calculate the standard errors and confidence intervals.
8) Rerun steps 1-7, setting the mediators at different values to estimate each relevant effect described in the text (total effect and controlled direct effects).

Appendix 2: Directed Acyclic Graph of relationship between frequent transactional sex and HIV infection



Appendix 3: Outcome and Mediators with all confounders - full sample (including baseline)

Confounders	Frequent transactional sex			Older partners			Multiple partners			
	No	**Yes**	**Total**	**No**	**Yes**	**Total**	**0**	**1**	**>2**	**Total**
Young women's age										
13	1098	30	1128	1079	78	1157	937	174	55	1166
14	1987	68	2055	1968	139	2107	1590	414	100	2104
15	1990	108	2098	1995	201	2196	1412	623	155	2190
16	1643	110	1753	1608	268	1876	988	715	161	1864
17	1076	84	1160	1052	167	1219	563	490	152	1205
18	452	46	498	424	113	537	181	273	80	534
19	220	24	244	212	42	254	73	136	43	252
20	85	12	97	90	20	110	36	62	10	108
21	2	0	2	2	1	3	0	2	1	3
Total	8553	482	9035	8430	1029	9459	5780	2889	757	9426
Av monthly/ capita HH exp – 2nd quartile										
No	6418	355	6773	6303	791	7094	4341	2173	561	7075
Yes	2130	127	2257	2122	238	2360	1435	715	196	2346
Total	8548	482	9030	8425	1029	9454	5776	2888	757	9421
Av monthly/ capita HH exp– 3rd quartile										
No	6430	352	6782	6338	750	7088	4375	2130	561	7066
Yes	2118	130	2248	2087	279	2366	1401	758	196	2355
Total	8548	482	9030	8425	1029	9454	5776	2888	757	9421
Av monthly/ capita HH exp – 4th quartile										
No	6369	380	6749	6281	810	7091	4214	2268	582	7062
Yes	2179	102	2281	2144	219	2363	1564	620	175	2359
Total	8548	482	9030	8425	1029	9454	5776	2888	757	9421
Prevalent HSV-2										
No	8012	412	8424	7953	850	8803	5578	2564	634	8776
Yes	529	70	599	466	177	643	196	320	122	638
Total	8541	482	9023	8419	1027	9446	5774	2884	756	9414
Schooling										
Graduated	310	47	6177	252	121	6088	94	213	61	368
Enrolled	5867	391	438	5836	755	876	3874	2152	537	6563
Total	6177	438	6615	6088	876	6964	3968	2365	598	598
CCT beneficiary arm										
Control	4100	264	8553	4034	523	4557	2716	1430	393	4539
Intervention	4453	218	482	4396	506	4902	3064	1459	364	4887
Total	8553	482	9035	4557	4902	9459	5780	2889	757	9426
Ever pregnant										
No	7089	225	7314	7084	529	7613	5467	1698	436	7601
Yes	1464	257	1721	1346	500	1846	313	1191	321	1825
Total	8553	482	9035	8430	1029	9459	5780	2889	757	9426
Physical IPV										
No	7171	336	7507	7091	759	7850	5089	2220	524	7833
Yes	1306	146	1452	1269	269	1538	620	666	233	1519
Total	8477	482	8959	8360	1028	9388	5709	2886	757	9352
Children's depression inventory score ≥ 16										
16 or lower	4323	245	5981	4281	528	4809	2899	1555	342	4796
Higher than 16	1658	175	420	1618	310	1928	948	727	240	1915
Total	5981	420	6401	5899	838	6737	3847	2282	582	6711