Does ART change partnership dynamics and HIV risk behaviours among PLWH? A cohort study in KwaZulu-Natal, South Africa

Authors: McGrath N1, 2, 3, Grapsa E3

1 University of Southampton, Southampton, UK; 2 Africa Health Research Institute, KwaZulu-Natal, South Africa; 3 Institute Of Social And Economic Research, Rhodes University, South Africa*.*

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Introduction

Modelling studies incorporating sexual behaviour change among HIV-infected individuals due to ART separately from sexual behaviour change among HIV-uninfected individuals due to the availability of ART predict that even small increases in partner acquisition and partner dissolution rates will reduce the overall impact of antiretroviral (ART) rollout on HIV incidence at the population-level [1, 2]. In sub-Saharan Africa, the majority of men and women of reproductive age are in heterosexual monogamous sexual partnerships [3]. Studies examining the risk of partnership dissolution associated with HIV have consistently reported that serodiscordant relationships in which the woman was HIV-positive were the most likely to dissolve [4-6]. Higher dissolution rates are likely to lead to increased acquisition of new partnerships over time. For an HIV-infected adult, forming new partnerships requires repeated HIV disclosure and condom use negotiation to prevent onward HIV transmission. In Africa, few sources of longitudinal data are available with which to estimate partnership acquisition and dissolution rates among HIV-infected individuals, and the impact of ART on these rates.

With respect to the association between antiretroviral treatment and subsequent sexual behavior, a review by Venkatesh et al, 2011, found that only one study out of 17 in African populations reported a finding of higher risk sexual behaviours, specifically increased unprotected sex, among HIV-infected individuals after ART initiation [7]. However, other than cross-sectional reports of type of partnership, partner’s HIV status and multiple partnerships, limited partnership characteristics were available for risk factor analysis [8-11]. Relationship dynamics play a role in the acceptability of condoms within partnerships [12], and HIV disclosure [13]. Among HIV serodiscordant couples, desire for future children together, being co-parents of living children and couples without an income where the male was the individual with HIV are associated with lower risk of partnership dissolution [6, 14]. Venkatesh et al, 2011, propose a conceptual model for the way in which partnership (dyadic) factors such as non-disclosure of HIV status and fertility desires are associated with increased sexual risk behaviours while other partnership factors such as condom use within the partnership are associated with decreased sexual risk behaviours in the context of ART availability[7].

We use detailed longitudinal data from a prospective cohort conducted in rural KwaZulu-Natal, South Africa between 2009 and 2013 to investigate the impact of ART on partnership acquisition and dissolution rates among HIV-infected individuals. We also examine the changes in sexual behaviours, specifically sexual activity, unprotected sex, and levels of sexual activity, associated with taking ART.

Methods

The cohort study has been described elsewhere [15, 16]. Men and women attending one of three primary health care clinics within the HIV Treatment and Care Programme in the Hlabisa sub-district of Umkhanyakude in northern KwaZulu Natal, South Africa [17] with CD4<200 cell/ml (‘ART-eligible’ at enrolment) or CD4>500 cell/ml (ART-ineligible at enrolment, referred to as ‘pre-ART’) were eligible for the study between January 2009 and March 2011 if resident within the Africa Centre Demographic Surveillance Area, and not currently pregnant (women). A questionnaire was administered at enrolment and 6-monthly through 36 months or October 2012. Demographic and social variables as well as details regarding up to three sexual partnerships in the last six months, sexual activity and condom use data were collected at each study visit. Participants who reported an ongoing partnership were asked additional questions about the quality of those relationships and their fertility intentions with their current main partner. Scales from the literature were adapted to measure gender norms [18], HIV stigma [19], And relationship quality [20]. Further details are given in Fladseth et al, 2015 [21]. This paper addresses one of the specific objectives of the cohort study, to compare sexual behaviour and partner change over a three year period among ART initiators and those not yet eligible for ART [15]. The cohort study was given ethics approval by the University of KwaZulu-Natal (ref BF083/08) and London School of Hygiene and Tropical Medicine (ref 5413).

Outcomes

We calculate crude partnership acquisition and dissolution rates and consider the impact of ART on five outcomes.

*Partner acquisition*: Participants were considered at risk of acquiring a new partner from study enrolment and censored at last study visit.

*Partnership dissolution:* All ongoing partnerships at enrolment and new partnerships were considered at risk of dissolution from the enrolment date and reported date of relationship start respectively. Dissolution date was calculated as the date of last sex prior to break up if the participant reported sex with this partner since prior visit, or the date of the previous visit if this partnership was reported as ongoing at the previous visit and there had been no sex within this partnership between the previous visit and break-up.

*Frequency of sexual activity in the last month:* The question ‘How many times have you had sexual intercourse with this partner in the last month?’ was asked for each partner.

*Sexual activity in the last month:* The frequency of sexual activity in the last month response was coded into a binary indicator representing sex in the last month: Yes (1) vs No (0).

*Unprotected sex in the last month:* Those who were sexually active in the last month, were asked ‘On how many of these occasions did you and your partner use condoms throughout?’ was asked. A binary indicator represented unprotected sex in last month (1) vs condoms were used in all reported sex acts (0).

 Statistical analyses

R version 3.1.3 was used for all analyses [22]. Partnership acquisition and dissolution rates were calculated using the R package ‘epicalc’[23]. The `survival’ and `coxme’ R packages [24, 25] were used to fit multivariable Cox regression models [26, 27] with and without frailties, and to test the proportional hazards assumption. For the acquisition model, we used a counting process formulation extension of the Cox model by Andersen and Gill [28] to incorporate all acquisitions observed during follow-up including repeated events within an individual. The time at risk for each individual is calculated as time since enrolment or last event, breaking the total time at risk for any individual with multiple events into multiple intervals of risk. For dissolution, one record per partnership was used, allowing partnership level covariates to vary between partnerships for a participant. Initially, Cox PH models with frailties were fitted to allow for individual random effects. However, the variance of frailties was not statistically significant and a robust variance (WLW estimator, [29]) was used instead to account for clustering within individuals.

Generalized linear mixed models with a logit link, using the ‘lme4’ R package [30, 31] were used to model the odds of sexual activity in the last month and the odds of unprotected sex among partnerships sexually active in the last month, with individual random effects to capture variation between participants. Finally, in order to model the number of sex acts in the last month in ongoing partnerships (count data), we fitted a negative binomial (NB) model with random effects and a log link function (log-linear model) using the ‘glmmADMB’ R package [32, 33]. The NB model was used to account for over-dispersion and the relatively high number of zeros in the outcome. Initially included as dummy variables representing each visit, estimates suggested that time could be reasonably represented by one indicator in each model: 6 or more months after first report vs first report of partnership.

Individual and partnership characteristics, and whether a relationship was ongoing at enrolment, were considered in models for the outcome of dissolution and all sexual activity outcomes i.e. all partnership-level analyses. For acquisition only individual level variables were considered.

In building a multivariable model for each outcome we used a combination of forward and backward selection and both p-value and AIC criteria to identify significant predictors in a final parsimonious model. In all final models we controlled for age (four categories: 18-21 years, 22-29 years, 30-40 years and >40 years), time in the study and participant’s sex. We had previously shown that, controlling for gender, there were few differences at baseline between the two ART groups. However, the pre-ART group was significantly more likely to have been sexually active in the last month than the ART-eligible group, suggesting they might be more physically well [16]. We considered an interaction term between ART-group and time in the study to allow the association between ART and each sexual behavior outcome to vary over time [34]. Given that the analyses were at the partnership level, first report of partnership was synonymous with enrolment for most but not all of the partnerships. The analyses for each sexual behaviour outcome were repeated among partnerships ongoing at enrolment only and the results remained virtually unchanged. Thus, we refer to the time of first report of partnership as enrolment and time after first report as ‘during follow-up’.

A small number in the ART-eligible group never started ART while in follow-up. Similarly, a small proportion of the pre-ART group started ART during the study. Analyses for each outcome were repeated excluding those in the ART-eligible group who never started ART and censoring those in the pre-ART group who became ART-eligible at their ART initiation date. Exclusion of this subset did not substantively change the results, therefore we kept the larger sample size for all analyses to increase power.

Descriptive analyses examined disclosure and knowledge of partner status across ART groups at enrolment and over time, among ongoing partnerships and new partnerships separately.

Results

Six hundred and thirty-two participants were enrolled, 385 in the ART-eligible group (37% male) and 247 in the pre-ART group (14% male). The CD4 test result used to define enrolment group was a median 22 days before enrolment, interquartile range (IQR) (15,36) for the ART-eligible group and 16 days, IQR (14, 27) for the pre-ART group, and all were ART naive prior to that CD4 test. Median CD4 count at enrolment was 133 cells/µl, IQR (76, 175) and 632 cells/µl, IQR (559, 768) for the ART-eligible and pre-ART groups respectively. The median time to ART initiation among the ART-eligible group was 15 days, IQR (7, 28) after enrolment. Median age and interquartile range (IQR) were 35 years, (29, 43) and 34 years, (27, 43) in the ART-eligible and pre-ART groups respectively. The median duration of follow-up was 2.97 years, IQR (2.44, 3.02) and 2.87 years, IQR (1.99, 3.01), p=0.007, and the median lifetime number of sexual partners was 3, IQR (2, 6) and 3 IQR (2, 4), for ART-eligible and pre-ART groups respectively.

At enrollment, 487 ongoing partnerships were reported among 467 participants (270 among ART-eligible and 197 pre-ART). Fourteen participants were in more than one partnership at enrolment (11 ART-eligible and 3 pre-ART). 587 participants had at least one follow-up visit and an opportunity to report a change in partnership status. During the study, 68 participants died (84% of these were in the ART-eligible group), 19 out-migrated from the health district and were lost to follow-up (32% of these were in the ART-eligible group), one (ART-eligible) went to prison and was unavailable for interview, and 33 (64% of these were in the ART-eligible group) refused to continue follow-up before their final visit. Ninety-four percent of the ART-eligible group started ART, a median 15 days after enrolment, IQR (7, 28); and 39 (16%) of the pre-ART group progressed to become ART-eligible and initiated ART during the analysis period, a median 19 months after enrolment, IQR (13, 24).

*Partner acquisition:* 161 new partnerships were observed among 132 individuals during follow-up. In the final multivariable Cox model (Table 1), participants had an increased hazard of acquiring a new partner if they were <30 years old, with those aged 18-21 years almost two times more likely compared to 22-29 year olds; had >3 lifetime partners, had no partner at enrolment, had ever taken alcohol, and had not disclosed their HIV status to anyone. There was no significant difference in acquisition hazard by ART group or sex.

*Partnership dissolution:* A total of 565 partnerships (404 ongoing at enrolment and 161 new during follow-up) among 466 participants contributed to this analysis. One hundred and ninety-two partnerships dissolved during follow-up. In the final multivariable Cox model (Table 2), partnerships had an increased hazard of dissolution if partners were not residing together, if the quality of the relationship was low and if the participant had ever taken alcohol. Partnerships of more than 5 years duration at first report were significantly less likely to dissolve than partnerships of <1 year duration. There was no significant difference in dissolution hazard between ART groups, men and women, or by age.

*Sexual activity in the last month:* In the final multivariable model (Table 3), the estimated odds of having had sex in the last month for participants in the ART-eligible group were approximately half of those in the pre-ART group at enrolment, aOR=0.51, 95%CI(0.31, 0.81). In contrast, during follow-up, the odds ratio is 0.91, 95%CI(0.61, 1.34). The model also estimated a lower odds for participants reporting that they had not used condoms (during last sex with partner or never used), participants believing that their partner had sex with someone else and participants not living with their partner. On the other hand, knowing partner’s HIV status and wanting to have more children were associated with higher odds of having sex in the last month. Individuals in a new relationship rather than a relationship ongoing at enrolment and those who had argued with their partner recently were also more likely to be sexually active in the last month.

*Unprotected sex acts in the last month:* Table 4 presents the final model for the odds of unprotected sex in the last month among partnerships that reported sexual activity in the last month. There were no significant differences between the two ART groups at enrolment aOR=1.10, 95%CI(0.57, 2.12), while during follow-up the odds of unprotected sex were significantly lower for partnerships of ART-eligible participants compared to pre-ART participants, a0R=0.26, 95%CI(0.15, 0.43). Significantly lower odds of unprotected sex in the last month were also associated with the participant having more equitable gender norms, not living with their partner, and having disclosed their HIV status to the partner. Higher odds of unprotected sex were associated with the involvement of alcohol at last sex, ever having had unwanted sex within the partnership, desire to have (more) children with partner, and the partner having ever performed a physical act of violence towards the participant. Unprotected sex with a partner who is HIV-negative or has unknown HIV status is considered risky sex. Of the total sexual acts by participants in the ART-eligible group, 5.5% were categorized as risky acts, compared to 13.2% of the sexual acts in the pre-ART group, p<0.0001. Thirty-three percent (186) of the 565 partnerships reported unprotected sex at least once, 104 (56%) of them had risky sex, the rest had unprotected sex with a partner known to have HIV.

*Frequency of sex acts in the last month:* In the final multivariable negative binomial model (Table 5), the number of sex acts was 23% lower among the ART-eligible group compared to the pre-ART group at enrolment, aIRR=0.77, 95%CI(0.65, 0.91); whereas during follow-up, the ratio was no longer significantly different from 1.0, aIRR=0.97, 95%CI(0.88, 1.08). The number of sex acts in the last month was higher when more children were wanted and among new partnerships. The number of sex acts in the last month was lower with more equitable gender norms, when condom use were not used at every sex act, when unwanted sex had ever happened within the partnership, when the participant believed their partner had sex with others, and when the couple were not living together.

*Disclosure to partner and knowledge of partner status*: Among ongoing partnerships at enrolment, 346 (71%) participants had already disclosed their HIV status to their partner and 63 more (13%) disclosed during follow-up, with no difference between ART groups (p=0.79 and p=0.22 respectively). Two hundred and twenty participants (45%) knew their partner status at enrolment, p=0.11 for this proportion across the ART groups, and a further 114 (23%) learned their partner’s status during follow-up – 80 (28%) in the ART-eligible group and 34 (17%) in the pre-ART group, p=0.006. Among partnerships initiated during follow-up, 93 (58%) had disclosed their HIV status to their partner and 61 (38%) knew their partner’s HIV status by the time of first report of the new relationship, and there was no difference by ART group (p=0.16 and p=0.32 respectively). A further 20 (12%) disclosed their HIV status after first report while still in relationship and study follow-up, and 18 (11%) learned their partner’s HIV status.

Discussion

In this long-term follow-up study being on ART was not associated with increased partner acquisition or partnership dissolution rates. Partner acquisition rate estimates in this study are 2-3 times lower than those estimated for the general population in the same area, in contrast dissolution rate estimates were 3-4 times higher [35]. It is difficult to compare the proportion of partnerships that dissolved in this study with other studies because of differences in the study population and duration of follow-up. Both a study in Nairobi with 1-2 years follow-up and a randomized trial measuring life events 6 months after voluntary counselling and testing in Kenya, Tanzania, and Trinidad reported approximately one quarter of partnerships had dissolved, compared to 34% of all couples in our study [4, 6]. These previous studies did not report dissolution rates.

By ART group, we observed no difference in HIV disclosure and knowledge of partner HIV status. The proportion disclosing to, or knowing the HIV status of a partner did not differ between new and established partnerships either, contrary to our *a priori* hypothesis that HIV disclosure may be easier in new partnerships post linkage to care. Being on ART was not associated with increased sexual risk behaviours, consistent with other shorter-term studies in Africa [8, 36-38] that have also shown reductions in sexual risk behaviours with ART. Indeed, reports of unprotected sex were significantly lower among the ART group during follow-up, a reassuring finding given the WHO recommends ART initiation upon HIV diagnosis [39] which will result in many more people on ART.

This study provides evidence that relationship-level characteristics determine partnership dissolution, the odds and frequency of sexual activity and the odds of unprotected sex, all of which influence onward HIV transmission. Living with a partner, longer partnership duration and higher reported relationship quality were associated with lower risk of partnership dissolution. Living with a partner and wanting more children with that partner were associated with increased odds and frequency of sexual activity, and higher odds of unprotected sex. Other relationship-level characteristics were found to be significantly associated with at least one of the sexual behaviour outcomes, including believing their partner had not had sex with others in the last 6 months (higher odds and frequency of sexual activity) and being in a new partnership (higher odds and frequency of sexual activity).

The odds of unprotected sex were higher within partnerships if a partner had ever insisted to have sex when the participant didn’t want to, had ever been physically violent towards the participant, alcohol was involved in last sex, and the participant had inequitable gender norms. The odds of unprotected sex were lower when the participant had disclosed their HIV status to their partner. Kerridge et al, 2014, report similar findings regarding alcohol use and unprotected sex in Uganda and suggested that HIV programmes promoting condom use combine alcohol reduction messaging and address gender norms [40]. Clinic staff could tailor messages regarding HIV disclosure, condom use and partner testing by routinely asking questions about ongoing and new partners. Staff could also identify individuals needing support around physical and sexual violence. Discussing relationships in the clinic setting could also identify individuals who wants children with their partner and would benefit from fertility support services.

Advancing our knowledge of partnerships and sexual behaviour in an HIV care context, this study has some limitations. All interviews were face-to-face or by phone which may have resulted in social desirability bias, particularly in reports of condom use and HIV disclosure [41-43]. In addition, this study population may not be representative with respect to partnership acquisition and dissolution of individuals with HIV who are not engaged in the HIV clinic. Capturing sexual activity, frequency of sex acts and condom coverage over the short period of one month before interview limited several analyses to focus only on those partnerships that were ongoing in the month before interview and these may not have been representative of all partnerships that occurred in the study. However, asking participants about sexual acts more than one month ago would have potentially introduced recall bias. Neither disease stage at enrolment nor history of illness in the year prior to enrolment were available, thus we are unable to explore to what extent the effect of ART was due to an overall health improvement in the ART group.

In Africa there is much more that can be provided by way of support for HIV disclosure and sexual risk reduction, and promotion of couples-testing and positive couple-relationships over the course of HIV care. The repeated interaction with the clinics required for HIV treatment and CD4 count and viral load measurement provide an opportunity for strategies similar to the ‘Making every contact count’ [44] advocated by National Health Service England which promotes delivery of brief advice at every opportunity to improve health and wellbeing. With HIV now a chronic disease, this study highlights the opportunities to respond to changing partnership dynamics of individuals in HIV care services.

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