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Fertility intentions and clinical care attendance among women living with HIV in South Africa

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Abstract

Poor HIV care retention impedes optimal treatment outcomes in persons living with HIV. Women trying to become pregnant may be motivated by periconception horizontal and vertical transmission concerns and thus more likely to attend HIV care visits than women not trying to conceive. We estimated the effect of fertility intentions on HIV care attendance over 12 months among non-pregnant, HIV-positive women aged 18–35 years who were on or initiating antiretroviral therapy in Johannesburg, South Africa. The percentage of women attending an HIV care visit decreased from 93.4% in the first quarter to 82.8% in the fourth quarter. Fertility intentions were not strongly associated with care attendance in this cohort of reproductive-aged women; however, attendance declined over time irrespective of childbearing plans. These findings suggest a need for reinforced efforts to support care engagement and risk reduction, including safer conception practices for women wishing to conceive.

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Compliance with Ethical Standards

Conflict of interest: The authors declare that they have no conflict of interest.

Ethical approval: All procedures performed in studies involving human participants were in accordance with the ethical standards of the institutional and/or national research committee and with the 1964 Helsinki declaration and its later amendments or comparable ethical standards.

Informed consent: Informed consent was obtained from all individual participants included in the study

Keywords

fertility intentions; antiretroviral therapy; retention; engagement in care; safer conception

Introduction

Sustained engagement in HIV care is required for optimal clinical and prevention outcomes. Although advances in global antiretroviral therapy (ART) programs have expanded treatment availability for persons living with HIV (1), poor attendance at clinical care visits, high loss to follow-up, and inadequate ART use continue to impede efforts to optimize treatment and prevention worldwide (2, 3).

One factor that that may influence engagement in care is decision-making around childbearing. Women who are trying to conceive have different clinical needs than women not trying to become pregnant (4), potentially precipitating differences in the frequency with which women attend HIV clinical care visits. Women who are conscious of their pregnancy plans may be motivated to adopt healthier behaviors in the preconception period (5), including improved ART adherence to maintain their own physical health. Concerns about horizontal transmission (6, 7) or mother-to-child transmission (8) may also motivate women who are planning to conceive to have a more consistent relationship with HIV care, particularly among those who discussed their fertility intentions with a provider or those who were counseled on reducing transmission risk during an earlier pregnancy.

In South Africa and other sub-Saharan African settings, research around ART adherence and periconception HIV care retention is largely framed around prevention of mother-to-child transmission (PMTCT) (9–11), and relatively few studies have explicitly evaluated HIV treatment outcomes in women outside of the pregnancy and postpartum periods (10, 12–14). In particular, few studies have explicitly assessed the relationship between fertility intentions and retention in HIV care. Here, we estimated the effect of fertility intentions on attendance at HIV clinical care visits among HIV-positive women on ART in Johannesburg, South Africa.

Methods

Study Setting, Population and Procedures

We performed a secondary analysis of longitudinal data from a prospective cohort study conducted in Johannesburg between 2009 and 2011. This original study was designed to estimate the 12-month incidence of pregnancy in HIV-positive women on ART. Full descriptions of study procedures and eligibility criteria have been published elsewhere (15–19). Briefly, non-pregnant, sexually active women between the ages of 18 and 35 years receiving ART care at one of four public community or primary health clinics were eligible for participation if they had not been pregnant in the last three months; were not breastfeeding; had not had a previous tubal ligation, hysterectomy, or bi-lateral oophorectomy; and had not been diagnosed as permanently infertile. Pregnancy was assessed using a urine-based pregnancy test (One Step hCG Urine Pregnancy Test, Atlas

Link Technology, Beijing) at enrollment. After providing written informed consent, eligible women completed an interviewer-administered questionnaire. Questionnaires assessed demographic characteristics, fertility history and intentions, contraceptive use, and sexual risk behaviors. ART regimen information, CD4 cell count and viral load data were abstracted through medical records, pharmacy, and laboratory records.

Study follow-up visits coincided with routine HIV care visits, every 1–3 months based on clinic protocol and ART supply. During follow-up visits, women were assessed for pregnancy (via urine-based pregnancy test) and updated HIV-associated clinical characteristics were recorded (i.e., CD4 count and HIV viral load). Current contraceptive use and fertility intentions were assessed at each visit using a short questionnaire.

Fertility intentions were measured at enrollment using three questions that asked about current and future childbearing plans. Women were first asked if they were trying to conceive at time of interview (yes/no). Those who said no were then asked if they were planning to conceive in the next 12 months (yes/no/uncertain). Those who said no or were uncertain were then asked if they were planning to conceive someday in the future (yes/no/uncertain).

During follow-up, women were only asked if they were trying to conceive at the time of each HIV clinical care visit (yes/no).

Exposure and Outcome Definitions

We created three dichotomous exposure variables for fertility intentions: two time-fixed variables based on assessments at enrollment and one time-varying variable based on assessments across follow-up. We first created a time-of-enrollment variable reflecting *short-term* plans for childbearing. Those reporting at enrollment that they were currently trying to conceive, as well as those who answered “yes” or “uncertain” to the question about plans to conceive in the next 12 months, were classified as having short-term plans for childbearing. Those who answered “no” at enrollment to questions about current or 12-month conception plans were classified as not having short-term plans for childbearing. We constructed a second dichotomous time-of-enrollment variable to reflect *any* plans for childbearing, classifying those answering “yes” or “uncertain” to any of the three questions about conception intentions (at time of interview, in the next 12 months, or someday in the future) as having plans for childbearing; those answering “no” to all three fertility intentions questions were classified as not having plans for childbearing. Third, we created a time-varying dichotomous variable reflecting current fertility intentions, basing classifications on the single yes/no question assessing current conception attempts at the time of interview in each quarter. In sensitivity analyses, women with uncertain fertility intentions (time-fixed variables only) were re-classified as having no plans to conceive.

To estimate the effect of each categorization of fertility intentions on attendance at HIV clinical care visits, we constructed an analytic cohort in which each woman was followed from study enrollment through the completion of 12 months of follow-up or until date of censoring if she became pregnant or died. We partitioned the 12-month follow-up period into three-month intervals (quarters). Attendance at HIV clinical care visits was assessed

dichotomously in each quarter: a woman was classified as having attended a visit in a given interval if she attended one or more routine HIV clinical care visits in that interval.

Statistical Analysis

Demographic and clinical characteristics of women at enrollment were described using proportions for categorical variables and medians for continuous variables. Chi-square tests were used to compare the differences in proportions between groups for categorical variables, and Wilcoxon signed-rank sum tests were used for continuous data (= 0.05).

We used an extension of the modified Poisson regression model (20, 21) to estimate risk ratios for the association between care attendance and each exposure variable. To estimate risk differences, we fit Poisson models with an identity link and a robust variance estimator under a generalized estimating equations (GEE) framework (22). For each comparison, an exchangeable correlation structure was specified to account for within-subject correlation between outcomes (multiple intervals of potential care attendance per woman) (23). To ensure temporality in our analysis of time-varying fertility intentions – that is, to ensure that the fertility intentions measure preceded a given care attendance measure – we included a time lag. More specifically, we assessed attendance quarterly among women who reported they were either trying or not trying to conceive at their visit in the previous quarter.

To determine whether the relationship between fertility intentions (assessed at enrollment) and care attendance varied by treatment experience, we considered potential effect measure modification (EMM) by ART duration and CD4 count (using most recently collected CD4 [median time since CD4 testing 3.2 months (IQR 2, 5)]) assessed at enrollment. To assess EMM by ART duration, we compared women who had initiated or reinitiated ART within three months of study enrollment (recent initiators) with those who had been on ART for more than three months (ART experienced). CD4 count was categorized as <200 or ≥200 cells/ml. To formally test for EMM, we included an interaction term between the time-fixed dichotomized exposure measures of fertility intentions and each of the proposed modifiers. We considered both the magnitude and precision of stratum-specific estimates when making a final determination of EMM.

All analyses were conducted using SAS statistical software (SAS, version 9.4, Cary, NC).

Weights

To address potential selection bias in this analysis we constructed two sets of weights. First, to account for the possibility of informative censoring (whereby censoring due to pregnancy or death was associated with the exposure/outcome) we calculated time-varying inverse probability of censoring weights. Pooled logistic regression models were used to estimate censoring weights for each exposure, and weights were stabilized and multiplied over time (24). Second, in our analysis of time-varying fertility intentions, we applied inverse probability of selection weights to account for missing exposure information due to a missed visit in the prior interval (25). The probability of having an observed exposure measure was modeled as a function of age, CD4 count and having prior children, and weights were stabilized by the marginal probability of having an exposure measure that was observed.

To account for confounding, we used stabilized inverse probability of exposure weights (IPW) to calculate weighted risk ratios and risk differences (26). A minimally sufficient set of covariates for attendance and each categorization of fertility intentions was identified using a causal directed acyclic graph (27). Covariates in the minimally sufficient set were measured at enrollment and included age, marital status, ART duration, partner fertility intentions and having prior children. Our use of censoring weights and selection weights informed our decision to use IPW instead of other adjustment methods. For each exposure, IPW were stabilized by the marginal probability of having that exposure and weights were truncated at the 5th and 95th percentiles to further improve stability.

Results

We enrolled 850 women between August 2009 and January 2010 and followed them for up to 12 months. Over the 12-month follow-up period, 149 women (17.5%) became pregnant and contributed a median of 6.2 months (IQR 4, 9) of follow-up before they were censored. No deaths were reported during follow-up. Twenty-eight (3.8%) women did not return to care after their initial study visit. Women were a median of 30.4 years old at enrollment (IQR 27, 33) and fewer than half were married or co-habiting (44.5%) (Table 1). Most (89.4%) had previously been pregnant. Median time since HIV diagnosis was 24.0 months (IQR 12, 48), and median time since ART initiation was 13.2 months (IQR 5, 24).

Approximately half (46.6%) of women reported having short-term plans for childbearing (either trying to become pregnant at time of interview or sometime within the next 12 months) at enrollment, including 12.4% who were trying to conceive at enrollment. Compared to women without plans to conceive in the short term, women with short-term childbearing plans were more likely to be married/co-habiting (50.3% vs. 39.4%), less likely to have been previously pregnant (82.6% vs. 95.3%), and less likely to be taking hormonal contraception (18.4% vs. 33.3%). The proportion of women who had achieved viral suppression (<50 copies/ml) was similar in both groups.

The overall probability of attending an HIV clinical care visit decreased from 93.4% in the first quarter to 82.8% in the fourth quarter. When we compared women with short-term plans for childbearing at enrollment to those without short-term plans, we detected no difference in attendance in unweighted and weighted models (Table 2). When we compared women with any plans for childbearing at enrollment to those reporting no such plans, care attendance was also similar between groups. Results did not change substantively in sensitivity analyses where women with uncertain fertility intentions were re-classified as having no plans to conceive (Online Appendix 1). In our assessment of time-varying fertility intentions, women who were trying to conceive at a particular visit were slightly more likely to attend an HIV clinical care visit in the following quarter than women who were not trying to conceive at that time (RR 1.03 (95% CI 1.00, 1.06); RD 0.03 (95% CI 0.00, 0.05)). However, attendance was >80.0% in the fourth quarter for both groups. There did not appear to be modification by ART duration or CD4 count (Online Appendix 2).

Discussion

In this study of South African women on ART, we expected that women with immediate or short-term plans to conceive would exhibit greater care engagement than those with less proximal plans to become pregnant. Instead, we observed comparable engagement overall between these groups over the subsequent year. Care attendance in the subsequent quarter was marginally greater among women currently trying to conceive at a given visit compared to women who were not trying to conceive, but the estimated incremental difference in retention may not be programmatically meaningful in this population.

Maternal concerns around mother-to-child transmission are thought to motivate care attendance during pregnancy in some HIV-positive women (8, 13, 28–30), and we expected that women in our study would demonstrate similar health-seeking behaviors in the periconception period. Additionally, concerns about horizontal transmission to HIV-uninfected partners during attempts to become pregnant could prompt better attendance at HIV clinical care visits among women trying to conceive (6, 7). However, we found little difference in care attendance among women with and without plans for childbearing (short-term or any), an indication that fertility intentions may not markedly impact care attendance in this population.

Consistent with other short-term estimates of retention in South Africa (31), overall HIV care attendance in our study population remained >80% at the end of 12 months. As follow-up began at study entry and not at a more clinically meaningful milestone (e.g., HIV diagnosis, linkage to care, ART initiation) (32), our population may have been biased towards women already enrolled and retained into long-term HIV care. As such, the relatively high proportion of attendance may have attenuated the magnitude of our effect estimates (33), thus affecting this study's ability to identify differences in care attendance by different childbearing plans. In subgroup analysis among women who had recently initiated ART, however, estimates were largely similar to results in the full cohort, although precision was limited.

A strength of this study was our use of prospectively collected and time-updated measures of current fertility intentions that preceded pregnancy assessment, which may have reduced potential exposure misclassification (34, 35). Though dynamic, fertility intentions are often not assessed routinely within the context of HIV clinical care (36, 37), and so we also considered baseline (time-fixed) fertility intentions measures pertaining to less proximal time horizons that enabled us to assess a range of childbearing scenarios and their respective effects on HIV care attendance. Furthermore, although more multidimensional measures of fertility intentions may provide additional insights into women's family planning needs (38, 39), the measures of fertility intentions included in this study were highly predictive of pregnancy incidence among women with stated intentions to conceive in this study population (15, 16).

This analysis has some limitations. First, women in this study who missed one or more routine HIV care visits may have engaged in care elsewhere without our knowledge (40). However, attendance was relatively high among all participants, minimizing the likelihood

that any misclassification of missed visits would have biased the overall interpretation of our results (33). Second, our assessment of attendance using quarterly visits may have disregarded circumstances in which women were advised to return to care more than three months after a given visit. Because date of next clinic visit was not routinely collected during the study period, a “days late” or “missed appointments” definition of care disengagement was not possible (41). Third, questions regarding exposure to safer conception services were administered only at the end of follow-up (17), and thus we were unable to ascertain whether or not safer conception knowledge modified the relationship between fertility intentions and care attendance in this analysis. Fourth, data included in this study were collected prior to South African national service delivery guidelines around earlier thresholds for treatment initiation, and thus the generalizability of our results to the modern era of universal treatment is uncertain. Finally, we cannot discount the possibility of unmeasured confounding, although all confounders identified by our directed acyclic graph were included in final models.

While retention remained relatively high in this population, by just 12 months attendance was predicted to have decreased to approximately 80% irrespective of childbearing plans. To the extent that routine HIV care visits present opportunities to offer contraceptive counseling and pregnancy testing, missed visits may prevent women in this population from fully meeting their family planning needs. We have previously reported both a high probability of unmet need for contraception (19) and a high incidence of unplanned pregnancy in this cohort (16). Though an assessment of unmet need for contraception and its relationship with care attendance was beyond the scope of this analysis, only 26% of women reported using a method of hormonal contraception to prevent pregnancy at enrollment. Contraceptive use among those without more immediate plans for pregnancy was notably only 33%.

Our findings reaffirm the need for expanded efforts to help women to remain engaged in HIV care, including during the periconception period. Routine screening of fertility intentions, accompanied by rapid referrals for safer conception, may offer the potential to improve periconception care engagement and HIV transmission prevention in South Africa. Safer conception services, which support the reproductive goals of HIV-positive women and their partners, can reduce the risks of HIV transmission through pregnancy and pregnancy attempts, identify and treat sexually transmitted infections, and potentially engage sexual partners to optimize care delivery (42). For women who are already attending routine HIV care visits in the periconception period, safer conception counseling can promote ART adherence and encourage limiting pregnancy attempts until viral suppression can be achieved and maintained. Viral suppression prevalence was just 71% among women with short-term plans to conceive in this study, highlighting the need for reinforced efforts to support care engagement and risk reduction strategies during periconception. While safer conception has been found to be both acceptable and feasible in South Africa (43), services remain largely unavailable outside of research settings (4). Our study contributes to a growing body of evidence that supports routine implementation of safer conception services during periconception to increase care engagement and optimize HIV prevention in this population.

In summary, our findings suggest that women with plans for pregnancy have comparable engagement in care to other women. However, we report a non-trivial decline in attendance over a 12-month period among both women with and without plans for childbearing, as well as a suboptimal viral suppression prevalence among women with plans to conceive. Efforts to ensure sustained care engagement and treatment adherence after ART initiation, particularly during periconception, remain critical.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Table 1.

Characteristics at enrollment of 850 women with HIV taking ART in Johannesburg, 2009–2011

	Overall N=850 (100.0%)		Short-term childbearing plans N=396 (46.6%)		Long-term or no childbearing plans N=454 (53.4%)		
	Median	**IQR**	**Median**	**IQR**	**Median**	**IQR**	**p-value**[a]
Age (years)	30.4	27–33	30.0	28–33	31.0	28–34	0.55
No. living children	1.0	1–2	1.0	0–1	2.0	1–2	<0.01
Months since HIV diagnosis	24.0	12–48	24.0	12–48	24.5	12–48	0.11
CD4 count, cells/ml	312.0	178–462	270.5	169–425	345.5	196–492	<0.01
Months on ART	13.2	5–24	10.8	3–22	14.0	7–27	<0.01
	n	%	n	%	n	%	
Married/cohabitating	378	44.5	199	50.3	179	39.4	<0.01
Ever pregnant	760	89.4	327	82.6	433	95.3	<0.01
Trying to conceive, currently	105	12.4	105	26.5	0	0	.
Taking hormonal contraception	224	26.4	73	18.4	151	33.3	<0.01
Pregnant at HIV diagnosis	271	31.9	84	21.2	187	41.2	<0.01
Viral load <50 copies/ml[b]	618	74.1	277	71.2	341	76.6	0.07

Abbreviations; IQR: Interquartile Range, No: Number, ART: Antiretroviral therapy

[a]Chi-square tests were used to compare the differences in proportions between groups for categorical variables, and Wilcoxon signed-rank sum tests were used for continuous data (= 0.05).

[b]n=834

Table 2.

Unweighted and Weighted Risk Ratios (RRs), Risk Differences (RDs) and 95% CIs for the effect of fertility intentions on quarterly attendance at HIV clinical care visits among 850 women with HIV taking ART in Johannesburg, 2009–2011

	Unweighted		Weighted	
	RR (95% CI)	**RD (95% CI)**	**RR (95% CI)**	**RD (95% CI)**
Short-term childbearing plans [a]				
yes	0.98 (0.96, 1.00)	−0.02 (−0.05, 0.01)	0.99 (0.96, 1.02)	−0.01 (−0.05, 0.02)
no	REF	REF	REF	REF
Any childbearing plans [b]				
yes	1.00 (0.97, 1.03)	0.00 (−0.04, 0.03)	1.01 (0.96, 1.06)	0.01 (−0.05, 0.06)
no	REF	REF	REF	REF
Currently trying to conceive (time-varying) [c]				
yes	1.01 (0.98, 1.04)	0.01 (−0.02, 0.04)	1.03 (1.00, 1.06)	0.03 (0.00, 0.05)
no	REF	REF	REF	REF

Abbreviations. RR: risk ratio; RD: risk difference; CI: confidence interval; ART: Antiretroviral therapy

[a] Weighted effect estimates account for censoring (mean=1.01; range 0.37–2.26) and confounding by age (≤30, >30 years), marital status (married or co-habitating/not married or co-habitating), time on ART (initiated ART ≤3 vs. >3 months before enrollment), partner fertility intentions (no partner, partner does not desire a/another child, partner unsure, partner desires a/another child) and any prior living children (yes/no) (mean=0.99; range 0.49–4.18)

[b] Weighted effect estimates account for censoring (mean=1.00; range 0.40–1.73) and confounding by age (≤30, >30 years), marital status (married or co-habitating/not married or co-habitating), time on ART (initiated ART ≤3 vs. >3 months before enrollment), partner fertility intentions (no partner, partner does not desire a/another child, partner unsure, partner desires a/another child) and any prior living children (yes/no) (mean=0.97; range 0.34–3.19)

[c] Weighted effect estimates account for censoring (mean=1.00; range 0.42–1.86), selection (mean=1.04; range 0.54–1.65), and confounding by age (≤30, >30 years), marital status (married or co-habitating/not married or co-habitating), time on ART (initiated ART ≤3 vs. >3 months before enrollment), partner fertility intentions (no partner, partner does not desire a/another child, partner unsure, partner desires a/another child) and any prior living children (yes/no) (mean=0.97; range 0.26–1.93)