AIDS Behav
DOI 10.1007/s10461-011-9981-3

ORIGINAL PAPER

High Pregnancy Intentions and Missed Opportunities for Patient–Provider Communication About Fertility in a South African Cohort of HIV-Positive Women on Antiretroviral Therapy

Sheree R. Schwartz · Shruti H. Mehta · Taha E. Taha · Helen V. Rees · Francois Venter · Vivian Black

Abstract High fertility intentions amongst HIV-positive women have been reported elsewhere. Less is known about how clinical and HIV treatment characteristics correlate with fertility intentions. We use cross-sectional baseline data from a prospective cohort study to assess pregnancy intentions and patient–provider communication around fertility. Non-pregnant, HIV-positive women aged 18–35 on ART were recruited through convenience sampling at Johannesburg antiretroviral (ART) treatment facilities. Among the 850 women in this analysis, those on efavirenz had similar fertility intentions over the next year as women on nevirapine-based regimens (33% vs. 38%). In multivariate analysis, recent ART initiation was associated with higher current fertility intentions; there was no association with CD4 cell count. Forty-one percent of women had communicated with providers about future pregnancy options. Women on ART may choose to conceive at times that are sub-optimal for maternal, child and partner health outcomes and should be routinely counseled around safer pregnancy options.

Some of the preliminary analysis of data was presented in poster form at the XVIII International AIDS Conference in Vienna, Austria, 18–23 July 2010. The poster abstracts were entitled *Fertility intentions by antiretroviral regimen among women in inner-city Johannesburg (*abstract THPE0784) and *Communication between patients and providers about HIV and fertility in inner city Johannesburg, South Africa* (abstract THPE0650).

S. R. Schwartz (✉) · H. V. Rees · F. Venter · V. Black
Wits Reproductive Health & HIV Institute, Hillbrow Health Precinct, University of the Witwatersrand, Johannesburg, South Africa
e-mail: sschwartz@rhru.co.za

S. R. Schwartz · S. H. Mehta · T. E. Taha
Department of Epidemiology, Johns Hopkins Bloomberg School of Public Health, Baltimore, MD, USA

Keywords HIV-1 infection · Antiretroviral therapy · Fertility intentions · Prevention of mother-to-child transmission · South Africa

Introduction

Global roll-out of antiretroviral therapy (ART) to treat HIV infection has been extensive over the last few years and many individuals in resource-limited settings now have access to ART services. In South Africa alone, nearly one million people were on ART by the end of 2009 [1]. Improved access to treatment results in new prospects for long-term survival for these patients [2].

Prevention of mother-to-child transmission (PMTCT) programs have been highly effective in reducing mother-to-child transmission (MTCT) of HIV [3] and have nearly eliminated the risk of infection in developed countries with well functioning health systems [4]. Vertical transmission rates should continue to decline globally as national treatment programs expand and women initiate ART earlier [5].

As a result of these advances in ART roll-out and scale-up of PMTCT successes, women on ART now face difficult decisions about their reproductive futures, including how to address concerns over the safety of conceiving on ART. There is a growing body of evidence indicating that HIV-infection reduces but does not eliminate fertility desires, and that ART initiation may be associated with an increase in fertility intentions [6, 7]. Studies in Sub-Saharan Africa have reported a range of 7–45% of HIV-infected women desire to have more children at some point in the future [8–10]. There is less evidence, however, on how HIV-positive women are planning for pregnancy, and whether measures are being taken by ART patients to advance safer conception.

Published online: 09 June 2011

Patient–provider communication about fertility, including provider monitoring of pregnancy intentions and provision of preconception counseling in HIV-positive populations, is a necessary component of effective HIV treatment and prevention. Amongst the benefits of better communication are decreased risk of horizontal transmission to partners and decreased risk of super-infection through promotion of safer sexual practices [11], as well as decreased risk of vertical transmission to infants, conception on appropriate ART drugs and conception under 'optimal' health conditions [12]. However, little is known on HIV patient–provider communication about fertility and future pregnancy options and what is available suggests that communication is poor [9, 13, 14].

Opportunities may exist to improve HIV prevention efforts through better patient–provider communication and management of fertility-related issues as part of routine HIV care. These opportunities may be identified through an assessment of fertility intentions and HIV treatment characteristics. For example, CD4 cell count and time-on-ART provide insight as to a patients' clinical readiness to conceive, while assessment of contraceptive use and fertility intentions measure the unmet need for family planning in this population.

In the South African context of which this study takes place, an assessment of fertility intentions across ART regimens also offers a good *proxy indicator* of provider knowledge and management of patients' fertility intentions. Intention to conceive on the ART drug efavirenz (EFV) would indicate inadequate patient–provider communication around fertility plans, as EFV is contraindicated for women at risk of pregnancy under both former and current South African national treatment guidelines due to teratogenicity concerns [15]. While recent research suggests that these concerns may be unwarranted [16, 17], these safety data were not available to providers at the time of study enrollment and have not yet prompted a change in South African national guidelines.

The purpose of this analysis is to assess pregnancy intentions and patient–provider communication around fertility concerns in order to identify ways to reduce HIV transmission and improve routine HIV treatment management for HIV-positive women on ART in South Africa.

Methods

Study Population

This is an analysis of data collected at enrollment into an ongoing observational cohort study of HIV-positive women on ART. The cohort study was designed to examine longitudinal fertility intentions, contraceptive use, ART regimen assignment and incidence of pregnancy during 1 year of follow-up in women at various stages of ART.

Study participants were recruited through convenience sampling from four government-run ART outpatient clinics in inner city Johannesburg, South Africa. Clinics included two ART initiation sites and two associated ART maintenance sites where patients continue treatment after they are determined to be clinically stable and responsive to ART. We included both types of clinics in order enroll a study population with a variety of ART-experiences. Although in theory patients are down-referred to maintenance sites once stable, in practice some patients attending ART initiation sites have been recently initiated and others have been on ART for several month or even years and have not been down-referred due to clinic oversight, potential complications or risks that may require physician attendance, or patient resistance to being down-referred.

Women were eligible to participate in the study if they were aged 18–35 years, not pregnant at time of enrollment, currently on or being initiated onto ART at time of study enrollment and sexually active within the past 12 months. Women who had given birth during the previous 3 months or who had been previously sterilized, undergone a hysterectomy or were otherwise diagnosed as permanently infertile were not eligible for study participation. The study protocol was approved by the University of the Witwatersrand Human Research Ethics Committee (*M090719*).

South African National Treatment Guidelines

HIV care and antiretrovirals are provided free of charge by the government in South Africa for anyone with a CD4 cell count $\leq$200 cells/μl or with a WHO-classified AIDS defining illness. First line therapy includes a non-nucleoside reverse transcriptase inhibitor ([NNRTI], either EFV or nevirapine [NVP]), and two nucleoside analog reverse transcriptase inhibitors (NRTIs). EFV is the preferred NNRTI because it has been associated with lower hepatotoxicity concerns and is better tolerated with tuberculosis treatment. Guidelines, however, indicate NVP regimen assignment for women initiating treatment during pregnancy and for women 'posing a pregnancy risk'. Second line therapy replaces the NNRTI with the protease inhibitor (PI) lopinavir/ritonavir as well as two NRTIs and is most commonly used in cases of virologic failure due to suspected drug resistance, in persons with severe NNRTI-induced hepatotoxicity or for conception/pregnancy planning in women initiated and stable on EFV with higher CD4 cell counts.

Data Collection

Participant enrollment and baseline data collection were conducted between August 2009 and January 2010.

Approximately 9,000 persons were receiving care at the study sites at the time of study enrollment and around 3,000 of these patients were women meeting the study's age eligibility criteria. A total of 850 women were targeted for enrollment into the prospective cohort study. Site specific enrollment targets were proportional to clinic size. Recruitment at each site took place over 2–3 months; enrollment closed at each site when site targets were met. All women appearing younger than 50 years old attending the clinic during the site enrollment period were approached and invited by research assistants to participate in a study related to reproductive health and experiences on ART. Interested individuals were provided additional information and underwent further screening in a private room on-site. Those meeting eligibility criteria were fully informed about the study and consented to participate. Testing to exclude pregnancy followed the informed consent process. All non-pregnant, consented individuals were enrolled into the study and baseline interviews were conducted by research assistants in participants' language of choice (English, Zulu or Sotho).

Baseline information included participant demographics, health status, reproductive history, fertility desires and intentions, sexual behavior and contraceptive use, relationship dynamics and communication with providers around fertility. Interviews averaged 30 min in length. Additional clinical and laboratory data, including CD4 cell count and ART regimens were confirmed through medical record review by the project coordinator and research assistants; pharmacy and laboratory records were used to settle any data discrepancies. Referral for regimen changes and counseling were provided as necessary following baseline interviews.

Fertility intentions were assessed using varying time horizons of participant intent. Participants were first asked if they were *currently* trying to conceive (yes/no). Those not trying to conceive were asked if they intended to conceive during *the next 12 months* (yes/no/don't know). Those indicating 'no' or 'don't know' were further asked if they thought that they would try to conceive someday in the future.

Statistical Analysis

Bivariate comparisons of medians, proportions and distributions across multiple groups were compared using Wilcoxon-rank sum tests, equality of proportions tests and chi-squared statistics respectively. Univariate and multivariate poisson regression models using robust variance estimators were applied to calculate prevalence ratios (PRs) and adjusted prevalence ratios (aPRs) with 95% confidence intervals (CIs) [18]. Poisson regression was used because of the high prevalence of the outcome (>10%). Variables were included in the multivariate models based on prior literature, clinical relevance and associations with the outcome in the univariate models ($P < 0.10$).

Twenty-three participants (3%) were missing data for income. We used multiple imputation (MI) to restore missing income values in the regression models under the assumption that income data was missing at random, dependent upon employment status [19]. Only employment was associated with missing income in our dataset; those employed were *more* likely to report their income. MI was performed using five draws for each missing value from a distribution of income values that were modeled on employment, financial dependence on partner, government grant status, education, relationship status, age and current fertility intentions.

Data were analyzed using Stata version 11.1 (*StataCorp, College Station, Texas, USA*).

Results

Among 907 women on ART consented to participate, 57 (6%) were excluded as further screening established that eligibility criteria were not met, including 38 women who tested pregnant prior to conducting the baseline interview and were referred for appropriate care. The remaining 850 (94%) women were included in this analysis.

Description of Population

Table 1 presents participant characteristics by ART treatment regimens at time of enrollment. Ninety-five percent ($n = 804$) of study participants were on first-line ART ($n = 445$ on NVP; $n = 359$ on EFV), while 46 participants were on second-line regimens. Comparing participants on first-line ART regimens, women on NVP-based regimens were younger, had fewer children, had more recently tested positive for HIV and were more likely to have first tested positive during pregnancy than participants on EFV-based regimens. Participants on first-line regimens had a shorter duration of time-on-ART than women on second-line regimens (1.4 vs. 1.8 years, $P = 0.04$) and were more likely to have a living child (79% vs. 63%, $P < 0.01$).

Fertility Intentions

Overall, 12% ($n = 105$) of participants were trying to conceive at the time of enrollment. Amongst those not currently trying to conceive, 36% ($n = 268$) planned on conceiving in the next year (Fig. 1) and a further 37% ($n = 272$) indicated plans to conceive someday in the future. Women on NVP were more likely to be actively trying to conceive than their counterparts on EFV-based

Table 1 Description of baseline characteristics of cohort participants by ART regimen

Characteristics at time of study enrollment	All participants ($n = 850$)	Estimates by baseline antiretroviral regimen			*P*-value[a]
		Nevirapine-based regimens ($n = 445$)	Efavirenz-based regimens ($n = 359$)	Protease-inhibitor regimens ($n = 46$)	
Median age, years (IQR)	30.4 (27.4–32.9)	29.6 (26.8–32.3)	31.3 (28.3–33.4)	29.6 (27.2–33.3)	<0.001
Employed, *n* (%)	510 (60.0)	264 (59.3)	219 (61.0)	27 (58.7.0)	0.629
Education completed, *n* (%)					
None–grade 10	218 (25.7)	101 (22.7)	99 (27.6)	18 (39.1)	0.104
Grade 11–12	528 (62.1)	294 (66.1)	211 (58.8)	23 (50.0)	
Post-grad degree or certificate	104 (12.2)	50 (11.2)	49 (13.6)	5 (10.9)	
Median monthly income, USD (IQR)	270 (149–473)	270 (149–459)	270 (162–473)	291 (149–527)	0.497
Median years since HIV diagnosis (IQR)	2.0 (1.0–4.0)	1.9 (1.0–4.0)	2.3 (1.0–4.0)	2.9 (1.4–4.3)	0.003
Median years on ART (IQR)	1.1 (0.4–2.0)	1.0 (0.4–1.8)	1.1 (0.4–2.1)	1.7 (0.9–2.9)	0.228
Median CD4 count at enrollment, cells/μl (IQR)	312 (178–462)	312 (179–457)	312 (174–466)	309 (199–492)	0.994
CD4 at enrollment, *n* (%)					
≤200 cells/μl	259 (30.5)	135 (30.3)	112 (31.2)	12 (26.1)	0.399
201–350 cells/μl	229 (26.9)	115 (25.9)	99 (27.6)	15 (32.6)	
351–500 cells/μl	182 (21.4)	106 (23.8)	68 (18.9)	8 (17.4)	
>500 cells/μl	180 (21.2)	89 (20.0)	80 (22.3)	11 (23.9)	
Recruitment site, *n* (%)					
ART initiation site	525 (61.8)	271 (60.9)	208 (57.9)	46 (100.0)	0.395
ART down-referral site	325 (38.2)	174 (39.1)	151 (42.1)	0 (0.0)	
In a relationship, *n* (%)	789 (92.8)	409 (91.9)	335 (93.3)	45 (97.8)	0.451
Married/Cohabitating, *n* (%)	378 (44.5)	210 (47.2)	147 (41.0)	21 (45.7)	0.077
Median number of living children (IQR)	1 (1–2)	1 (1–2)	1 (1–2)	1 (0–1)	<0.001
≥1 living child, *n* (%)	666 (78.4)	336 (75.5)	301 (83.8)	29 (63.0)	0.004
≥1 living child with *current* partner, *n* (%)[b]	324 (41.1)	167 (40.8)	141 (42.1)	16 (35.6)	0.729
Pregnant at time of HIV diagnosis, *n* (%)	271 (31.9)	153 (34.4)	100 (27.9)	18 (39.1)	0.048
Using hormonal contraception, *n* (%)	243 (28.6)	133 (29.9)	96 (26.7)	14 (30.4)	0.326

IQR interquartile range

[a] *P*-values represent differences between NVP and EFV users ($n = 804$). Patients on protease inhibitors are not represented in these values. Values were determined using Wilcoxon-rank sums tests for equality of medians, equality of proportions tests and chi-squared statistics for categorical comparisons as appropriate

[b] Restricted to participants in a current relationship ($n = 789$)

regimens ($n = 61$ [14%] NVP vs. $n = 31$ [9%] EFV, $P = 0.03$). Women on PI-based regimens were more likely to be trying to conceive at baseline than those on first-line regimens (28% vs. 11%, $P < 0.01$). However, amongst women not currently trying to conceive, women on EFV-based regimens were equally likely to indicate plans to conceive in the next year as women on NVP-based regimens (33% EFV vs. 38% NVP, $P = 0.18$) or PI-based regimens (39%, $P = 0.48$).

Characteristics associated with fertility intentions in univariate and multivariate analyses are presented in Table 2. We restricted models to women in relationships ($n = 789$, 93%) in order to assess partnership characteristics associated with fertility intentions. After adjusting for other factors, women *currently* trying to conceive were more likely to be financially dependent upon their partner [aPR 1.55, 95% CI 1.03–2.34]. Having more children was associated with lowered *current* fertility intentions. Women who did not have children with their current partner were 2.5 times more likely [aPR 2.55, 95% CI 1.37–4.75] to be trying to conceive than women who already had a child with their current partner, irrespective of her overall number of living children. Furthermore, women were over 60% more likely [aPR 1.64, 95% CI 1.00–2.68] to report that they were trying to conceive if they knew their partner to be HIV-positive as compared to HIV-negative.

Women on ART for 1–2 years and >2 years were 44 and 20% less likely respectively, to be *currently* trying to conceive than women initiated onto ART in the past year

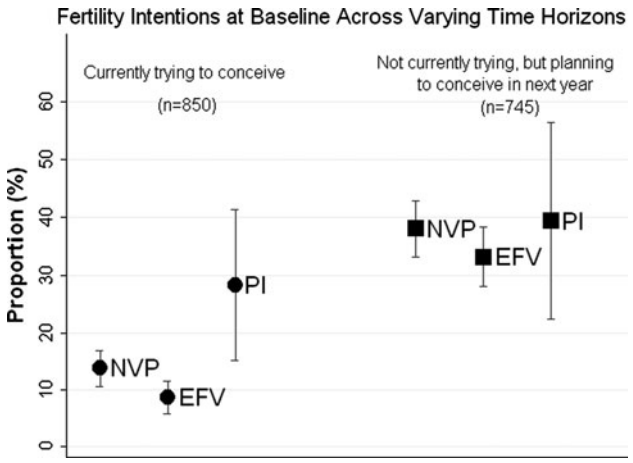

Fig. 1 Patient fertility intentions by antiretroviral regimen over varying time horizons. *Circles* and *bars* represent point estimates and 95% confidence intervals for prevalence of fertility intentions at baseline

[aPR 0.56, 95% CI 0.35–0.91; aPR 0.80, 95% CI 0.49–1.32]. Notably age and CD4 cell count were not statistically significantly associated with *current* fertility intentions. ART regimen assignment was not included in these models as regimen assignment should be a consequence rather than a predictor of fertility intentions.

Based on the multivariate findings, we explored in greater depth the *current* fertility intentions of these same women in relationships according to important clinical characteristics. Women on ART for <6 months were equally likely to be *currently* trying to conceive as women on ART for ≥6 months ($P = 0.41$). Furthermore, despite the wide range of CD4 cell counts in our cohort [3–1451 cells/μl], 31% of the women *currently* trying to conceive had a CD4 count ≤200 cells/μl and 63% had CD4 counts ≤350 cells/μl.

Given these results we assessed whether the non-clinical predictors of *current* fertility intentions differ by time-on-ART. In a stratified analysis (*results not shown*), we found that the *number* of children a woman has is significantly and negatively associated with current fertility intentions amongst women on ART for ≤1 year, whereas having *a child with one's current partner*, rather than prior parity, was a more significant predictor of fertility intentions amongst women on ART for >1 year. Additionally we observed that having a known HIV-positive partner was positively associated with *currently* trying to conceive amongst recent ART initiators, whereas there was no association between fertility intentions and partner's HIV-status amongst more experienced ART users (>1 year).

When considering fertility intentions *in the next year*, socioeconomic factors were not associated with fertility intentions in the adjusted analysis (Table 2). Number of living children was negatively associated with plans to conceive. Both not having a child with a current partner and being married or cohabitating with one's partner were positively associated with fertility intentions (Table 2). We observed no significant relationship between time-on-ART or CD4 cell count and intent to conceive.

Overall, 75% of women reported that they plan to conceive at some point in the future. Of those planning to conceive again or for the first time, the desire to lead a normal life was the most common reason identified for wanting to conceive (91%). Partner desires for children (44%) and not having a child with a current partner (39%) were also identified as important reasons. Partner desires for children were very high among participants, with 72% of the 789 women in relationships reporting that their partner wanted more children. Fears of losing their partner if they do not conceive were expressed by 20% of women in relationships and 15% of women were worried that their partner may take on another woman if she did not become pregnant. The top three fears around having children were infecting the baby with HIV (22%), financial concerns (19%) and that pregnancy would cause their HIV disease to advance (19%).

Amongst women not *currently* trying to conceive, 32% were using a hormonal method of contraception or another modern, non-barrier method and a further 39% of women reported consistent condom use (dual use was reported by 15% of participants). Nearly three out of ten women (29%) demonstrated an unmet need for family planning.

Patient–Provider Communication

Less than half (41%) of women reported that an ART health care provider had spoken with them about their options should they want to conceive in the future. In univariate analysis, higher income and being on a PI-based regimen were positively associated with patient–provider communication about pregnancy (Table 3), however, neither of these associations were statistically significant predictors in the multivariate model of a provider having talked to a woman about future pregnancy options. There were no other predictors of patient–provider communication.

A higher percentage of women (67%) indicated that a provider or counselor had talked to them about PMTCT. When providers did talk to women about PMTCT, women displayed higher levels of knowledge about the likelihood of MTCT ($P < 0.01$) (Fig. 2). Women pregnant at the time of HIV diagnosis or since diagnosis (n = 380) demonstrated higher knowledge about PMTCT than those who had not been pregnant since HIV-diagnosis ($P = 0.01$).

Around one-third of women (35%) knew that EFV was contra-indicated during pregnancy. Women on EFV did *not* have higher knowledge about potential risks of conceiving on EFV as compared to women on NVP ($P = 0.90$).

Table 2 Prevalence ratios (PRs) and adjusted PRs (aPRs) for correlates of current and future fertility intentions among women in relationships

	PRs for trying to get pregnant now[a] ($n = 789$)				PRs for intentions to get pregnant in the next year[a,b] ($n = 684$)			
	Univariate PR [95% CI]	*P*-value	Multivariate aPR [95% CI]	*P*-value	Univariate PR [95% CI]	*P*-value	Multivariate aPR [95% CI]	*P*-value
Age (per 5 years)	0.82 [0.66–1.03]	0.084	1.03 [0.82–1.30]	0.785	0.87 [0.76–0.98]	0.026	1.04 [0.93–1.17]	0.483
Employed								
Yes	0.80 [0.56–1.15]	0.229			0.91 [0.75–1.11]	0.363		
No	REF	–			REF	–		
Education completed								
None–grade 10	REF	–			REF	–		
Grade 11–12	0.72 [0.49–1.06]	0.094			0.87 [0.69–1.09]	0.227		
Post grad degree/ certificate	0.61 [0.32–1.18]	0.142			1.10 [0.82–1.49]	0.517		
Income, log (USD)[c]								
log (income)	1.18 [0.98–1.43]	0.083	1.12 [1.01–1.37]	0.248	1.06 [0.95–1.19]	0.265		
$(\log(\text{income}))^2$	1.07 [1.02–1.11]	0.004	1.05 [1.01–1.10]	0.027	1.02 [0.99–1.05]	0.315		
Financially dependent on partner								
Yes	1.42 [0.97–2.09]	0.070	1.55 [1.03–2.34]	0.036	0.96 [0.79–1.17]	0.703		
No	REF	–	REF	–	REF	–		
Years since HIV diagnosis	0.97 [0.90–1.06]	0.528	–	–	0.99 [0.95–1.03]	0.636		
Time on ART								
<1 year	REF	–	REF	–	REF		REF	–
1–2 years	0.54 [0.34–0.88]	0.013	0.56 [0.35–0.91]	0.020	0.84 [0.67–1.05]	0.125	1.03 [0.82–1.31]	0.778
>2 years	0.81 [0.53–1.24]	0.335	0.80 [0.49–1.32]	0.388	0.70 [0.53–0.91]	0.007	0.86 [0.65–1.14]	0.303
CD4 category at enrollment								
≤200	1.05 [0.64–1.73]	0.833	0.65 [0.38–1.10]	0.107	1.57 [1.17–2.09]	0.002	1.20 [0.88–1.64]	0.245
201–350	1.16 [0.71–1.90]	0.559	0.96 [0.59–1.58]	0.883	1.35 [1.00–1.84]	0.052	1.20 [0.90–1.59]	0.216
351–500	0.70 [0.39–1.29]	0.253	0.69 [0.40–1.20]	0.188	1.01 [0.72–1.43]	0.948	0.97 [0.71–1.33]	0.851
>500	REF	–	REF	–	REF	–	REF	–
Number of living children								
None	REF		REF		REF		REF	
One	0.40 [0.28–0.59]	<0.001	0.50 [0.34–0.73]	<0.001	0.57 [0.50–0.68]	<0.001	0.65 [0.54–0.79]	<0.001
Two or more	0.18 [0.10–0.30]	<0.001	0.29 [0.15–0.55]	<0.001	0.25 [0.19–0.33]	<0.001	0.32 [0.23–0.44]	<0.001
Married/cohabitating								
Yes	1.45 [1.01–2.08]	0.044	1.37 [0.90–2.08]	0.141	1.24 [1.02–1.50]	0.033	1.50 [1.25–1.80]	<0.001
No	REF	–	REF	–	REF	–	REF	–
No children with current partner								
No children with partner	3.61 [2.19–5.95]	<0.001	2.55 [1.37–4.76]	0.003	2.15 [1.71–2.71]	<0.001	1.59 [1.23–2.07]	<0.001
1+ child with partner	REF	–	REF	–	REF	–	REF	–
Disclosed HIV status to partner								
Yes	1.13 [0.70–1.81]	0.627			1.00 [0.78–1.27]	0.974		
No	REF	–			REF	–		
Partner HIV status								
Negative	REF	–	REF	–	REF	–	REF	–
Positive	1.70 [1.05–2.75]	0.032	1.64 [1.00–2.68]	0.049	0.98 [0.78–1.23]	0.841	1.05 [0.85–1.31]	0.624
Unknown	1.16 [0.68–1.96]	0.593	1.24 [0.75–2.08]	0.403	0.76 [0.59–0.99]	0.039	0.87 [0.69–1.11]	0.258

Table 2 continued

	PRs for trying to get pregnant now[a] ($n = 789$)				PRs for intentions to get pregnant in the next year[a,b] ($n = 684$)			
	Univariate PR [95% CI]	*P*-value	Multivariate aPR [95% CI]	*P*-value	Univariate PR [95% CI]	*P*-value	Multivariate aPR [95% CI]	*P*-value
PMTCT knowledge								
High	0.70 [0.49–1.01]	0.056	0.85 [0.60–1.21]	0.363	0.81 [0.66–0.98]	0.035	0.90 [0.75–1.09]	0.276
Low	REF	–			REF	–	REF	–

[a] Prevalence ratios (PRs) and adjusted PRs (aPRs) estimated using robust poisson regression models

[b] Models restricted to those *not currently* trying to conceive

[c] Income is logarithmically transformed and centered at the mean ($e^{5.43}$ = USD $228). The centered, logarithmic term was subsequently squared to generate the quadratic term

Women on PI-based regimens had a slightly higher knowledge of EFV contraindication ($P = 0.07$).

In terms of conversations about contraception, 94% of women reported that a provider had spoken to them about using condoms, however less than half (48%) of women reported that an HIV provider had discussed hormonal methods of contraception with them.

Discussion

Overall, women in this study had high fertility intentions with nearly half (44%) interested in pregnancy within the next year. Fertility intentions were high regardless of current ART regimens or presenting clinical characteristics. Improving patient–provider communication regarding future pregnancy options could help women to better time their pregnancies for optimal health outcomes.

As has been documented elsewhere, immediate and 1 year fertility intentions were negatively associated with number of living children and having a child with a current partner [8, 9, 20]. Unlike other studies, we found no association between age and fertility intentions [20]. This finding is not surprising as many other studies included women aged 15–44, whereas we have restricted enrollment to women in their prime reproductive years (18–35).

Other studies have focused less on clinical characteristics and their implications for appropriate pregnancy planning. In particular, it is concerning that participants' most recent CD4 cell count was not associated with immediate plans to conceive. Of women who were *currently* trying to conceive, 31% had a CD4 count ≤200 cells/μl and 63% had CD4 counts ≤350 cells/μl. This is disconcerting as lower maternal CD4 cell count, independent of maternal viral load and infants' HIV-status, has been associated with greater infant mortality [21] and risk for MTCT [5].

Our findings also suggest that those initiating ART in the past year were more likely to be currently trying to conceive than more treatment-experienced participants. Time-on-ART, however, was not strongly associated with more distal fertility intentions. This may indicate changes in perceived urgency to conceive as women become more confident in their long-term survival prospects. This finding reinforces the need for proactive provider counseling regarding future pregnancy options and proper pregnancy planning. Delaying conception until viral load suppression is achieved not only reduces MTCT risk, but is important for reducing horizontal transmission in discordant partnerships [5, 22, 23]. In this population, the women on ART for <6 months, who are the most likely to have not yet achieved virologic suppression, were just as likely to be *currently* trying to conceive as women on ART for ≥6 months.

Fertility intentions by drug regimen assignment provide another way of evaluating patient–provider communication and treatment management around fertility issues. Although few women on EFV-based regimens were *currently* trying to conceive in this study, fertility intentions over the next year were similar between EFV and NVP treatment groups. This is contrary to what we might expect to see—much higher fertility intentions in women on NVP-based regimens as compared to EFV-based regimens. This suggests that providers may periodically assess immediate fertility intentions, but may not be routinely considering longer term plans. Longer term fertility intentions are important to consider as pregnancy prevention efforts may actually depend on medium to long-term fertility plans. We see evidence of this in our participants as hormonal contraception uptake is highest in women who report wanting no more children in the future (40%), followed by women who want more children someday but not in the next year (36%), followed by those wanting to conceive in the next year (23%) and those currently trying to conceive (4%).

Table 3 Correlates of communication between patients and providers regarding future fertility ($n = 850$)

	Univariate PR [95% CI][a]	*P*-value	Multivariate aPR [95% CI][a]	*P*-value
Age (years)[b]				
18–25 years	1.17 [0.99–1.38]	0.068	1.16 [0.97–1.39]	0.108
>25–35 years	0.98 [0.95–1.01]	0.180	0.98 [0.95–1.02]	0.372
Employed				
Yes	1.09 [0.92–1.29]	0.322		
No	REF	–		
Education completed				
None–grade 10	REF	–		
Grade 11–12	0.90 [0.74–1.08]	0.249		
Post grad degree/certificate	1.05 [0.81–1.36]	0.724		
Income, (log USD/mo)				
log (income)	1.08 [1.00–1.17]	0.041	1.08 [0.98–1.18]	0.127
Time on ART				
<1 year	REF	–	REF	–
1–2 years	0.85 [0.70–1.04]	0.115	0.84 [0.63–1.12]	0.242
>2 years	0.93 [0.77–1.14]	0.505	0.91 [0.65–1.26]	0.566
CD4 category at enrollment				
≤200	1.02 [0.81–1.27]	0.895	0.95 [0.66–1.37]	0.780
201–350	0.98 [0.78–1.24]	0.882	0.96 [0.69–1.34]	0.815
351–500	0.82 [0.63–1.07]	0.139	0.82 [0.58–1.15]	0.249
>500	REF	–	REF	–
Married/cohabitating				
Yes	1.16 [0.98–1.36]	0.076	1.11 [0.89–1.39]	0.343
No	REF	–	REF	–
Regimen				
Nevirapine-based	REF	–	REF	–
Efavirenz-based	0.95 [0.80–1.13]	0.574	0.96 [0.77–1.21]	0.759
Protease-inhibitor	1.34 [1.00–1.78]	0.048	1.38 [0.91–2.12]	0.132
Fertility intentions				
Currently trying to conceive	0.93 [0.72–1.21]	0.585	0.86 [0.61–1.22]	0.396
Not currently trying	REF	–	REF	–
Type of ARV clinic				
ARV initiation site	REF	–		
Down-referral site	.88 [0.74–1.04]	0.128		

[a] Prevalence ratios (PRs) and adjusted PRs (aPRs) estimated using robust poisson regression models

[b] Age modeled continuously as a spline term with a knot at 25 years; results reported are for each individual linear segment

We do not conclude that all women of reproductive age be initiated on NVP rather than EFV-based regimens, as there are other clinical reasons for which EFV may be a preferred drug [24]. However, fertility intentions across varying time horizons should be assessed and frequently revisited during routine HIV management visits. Given that many women may fear provider disapproval of plans to conceive, provider initiation of these conversations is essential.

We also observed low levels of reported patient–provider communication around future pregnancy options. Surprisingly we found no significant predictors of patient–provider communication, including ART regimen assignment, fertility intentions, age, marital status, prior parity, ART duration or CD4 cell count.

Poor patient–provider communication is not likely to decrease the risk of pregnancy, but rather increases the risk that pregnancies will occur without adequate knowledge and thus under sub-optimal circumstances. With proper counseling and low-cost techniques, women can reduce the risk of horizontal transmission to an uninfected partner or their own risk of super-infection [11] by reducing the frequency of unprotected sexual exposure [25]. Preconception counseling is further warranted as a strategy for PMTCT and to ensure that women are conceiving on ART regimens recommended for use during pregnancy.

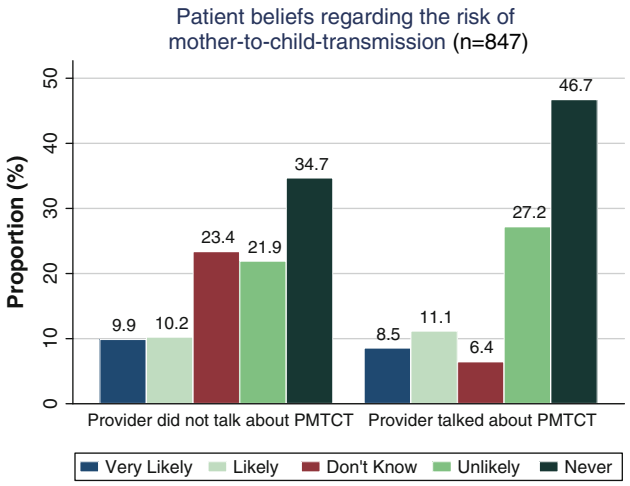

Fig. 2 Patients' understanding about the likelihood of mother-to-child transmission of HIV, according to whether or not the ART clinic providers have discussed PMTCT with patients

Our study is primarily comprised of women on first-line ART. It is interesting that women on second line regimens had somewhat higher fertility intentions and levels of knowledge about EFV contraindication. While this could indicate that women have been switched to second line regimens as part of fertility planning, our baseline data do not support this notion. A similar number of women on PI-regimens were initiated on EFV (51%) *vs.* NVP-base regimens (49%) ($P = 0.75$) and according to medical records, 90% of women were changed to second line therapy due to side effects and treatment failure.

Our analysis does have some limitations. This analysis is cross-sectional and does not directly assess changes in individual fertility intentions and provider communication over time. Subsequent analyses will be able to address this issue in our cohort once the longitudinal data collection is complete. Additionally, our study uses a convenience sample of women recruited in ART facilities. While all women meeting eligibility criteria were invited to participate, there may be a self-selection bias such that those wanting more children may have been more likely to participate, thus increasing the overall prevalence of positive fertility intentions in our study. We attempted to minimize this bias by using recruitment messages targeting women's ART treatment experiences and general assessment of reproductive health concerns of women on ART. Furthermore, our prevalence estimates for fertility intentions in the next year are well within the range of what have been previously documented. We believe that the high prevalence of women hoping to conceive someday in the future largely reflects the younger age range selected for this cohort and universal ART coverage within the cohort and further highlights the importance of assessing multiple time horizons when assessing fertility intentions.

While we recognize that South Africa is different than most other resource-limited settings in its use of EFV as part of first-line regimens, these results remain important as South Africa has the largest HIV burden in the world. Furthermore, the use of EFV as a proxy indicator in this study speaks to a general lack of communication between patients and providers about fertility which is likely to extend beyond South African borders.

Strengths of this analysis include the large size of the cohort and the inclusion of women both recently initiating ART and already stable on treatment. Our analysis is based on multi-site data and is linked to clinical and treatment records.

In conclusion, there is a need for more frequent provider-initiated monitoring of patients' fertility intentions and counseling about pregnancy options. Preconception counseling is the best way to prevent both vertical and horizontal transmission amongst women who desire more children in the future. An important finding was that women with low CD4 cell counts, who for their own health and for transmission reasons should not be getting pregnant, are trying to conceive. Proper timing of pregnancy needs to be a part of routine counseling and should be emphasized.

As ART services continue to roll-out in resource limited contexts, particularly those with high fertility rates and in which reproduction is so highly valued, preparing and planning for pregnancy is not a luxury expense, but a necessary component of HIV treatment and prevention. More research is needed on preconception counseling approaches and the best ART treatment options for HIV-positive women planning to conceive in limited resource settings. The needs of men and HIV-negative women in serodiscordant relationships should also be considered in future studies.

Acknowledgments We thank all of our participants for sharing their time and experiences and the study staff for their efforts and dedication to the participants. The Pregnancy Intentions and Incidence Study is supported by the Wits Reproductive Health & HIV Institute at the University of the Witwatersrand and the United States Centers for Disease Control (CDC) public health dissertation grant *1R36PS001584-01*. SS received support from grant *1R36PS001584-01*, the Johns Hopkins Bloomberg School of Public Health, Department of Epidemiology Doctoral Student Fund and the Johns Hopkins Bloomberg School of Public Health, Global Field Experience Fund. Our research was conducted in clinics supported by PEPFAR and the United States Agency for International Development. All authors contributed to the study design. SS and VB oversaw data collection. SS conducted the analysis with assistance from SM and TT. SS drafted the manuscript and all authors contributed substantially to the editing of the manuscript. Some parts of this analysis were presented in posters at the International AIDS Society Conference in Vienna, Austria (July 2010).

Conflict of interest None to declare.

References

1. Republic of South Africa. South Africa UNGASS country progress report on the declaration of commitment on HIV/AIDS, 2010 report. 2010. Available from http://www.unaidsrstesa.org/files/u1/southafrica_2010_country_progress_report_en.pdf.
2. Brinkhof MW, Boulle A, Weigel R, Messou E, Mathers C, Orrell C, et al. Mortality of HIV-infected patients starting antiretroviral therapy in sub-Saharan Africa: comparison with HIV-unrelated mortality. PLoS Med. 2009;6:e1000066.
3. Shapiro RL, Hughes MD, Ogwu A, Kitch D, Lockman S, Moffat C, et al. Antiretroviral regimens in pregnancy and breast-feeding in Botswana. N Engl J Med. 2010;362:2282–94.
4. Centers for Disease Control and Prevention (CDC). Achievements in public health. Reduction in perinatal transmission of HIV infection–United States, 1985–2005. MMWR Morb Mortal Wkly Rep 2006;55:592–7.
5. Hoffman RM, Black V, Technau K, van der Merwe KJ, Currier J, Coovadia A, et al. Effects of highly active antiretroviral therapy duration and regimen on risk for mother-to-child transmission of HIV in Johannesburg, South Africa. J Acquir Immune Defic Syndr. 2010;54:35–41.
6. Taulo F, Berry M, Tsui A, Makanani B, Kafulafula G, Li Q, et al. Fertility intentions of HIV-1 infected and uninfected women in Malawi: a longitudinal study. AIDS Behav. 2009;13(Suppl 1):20–7.
7. Maier M, Andia I, Emenyonu N, Guzman D, Kaida A, Pepper L, et al. Antiretroviral therapy is associated with increased fertility desire, but not pregnancy or live birth, among HIV+ women in an early HIV treatment program in rural Uganda. AIDS Behav. 2009;13(Suppl 1):28–37.
8. Kaida A, Laher F, Strathdee SA, Janssen PA, Money D, Hogg RS, et al. Childbearing intentions of HIV-positive women of reproductive age in Soweto, South Africa: the influence of expanding access to HAART in an HIV hyperendemic setting. Am J Public Health. 2010;101(2):350–8.
9. Cooper D, Moodley J, Zweigenthal V, Bekker LG, Shah I, Myer L. Fertility intentions and reproductive health care needs of people living with HIV in Cape Town, South Africa: implications for integrating reproductive health and HIV care services. AIDS Behav. 2009;13(Suppl 1):38–46.
10. Homsy J, Bunnell R, Moore D, King R, Malamba S, Nakityo R, et al. Reproductive intentions, outcomes among women on antiretroviral therapy in rural Uganda: a prospective cohort study. PLoS ONE. 2009;4:e4149.
11. Smith D, Wong J, Hightower G, Ignacio C, Koelsch K, Daar E, et al. Incidence of HIV superinfection following primary infection. JAMA. 2004;292(10):1177–8.
12. Aaron EZ, Criniti SM. Preconception health care for HIV-infected women. Top HIV Med. 2007;15:137–41.
13. Orner P, Cooper D, Myer L, Zweigenthal V, Bekker LG, Moodley J. Clients' perspectives on HIV/AIDS care and treatment and reproductive health services in South Africa. AIDS Care. 2008;20:1217–23.
14. Finocchario-Kessler S, Dariotis JK, Sweat MD, Trent ME, Keller JM, Hafeez Q, et al. Do HIV-infected women want to discuss reproductive plans with providers, and are those conversations occurring? AIDS Patient Care STDS. 2010;24:317–23.
15. De Santis M, Carducci B, De Santis L, Cavaliere AF, Straface G. Periconceptional exposure to efavirenz and neural tube defects. Arch Intern Med. 2002;162:355.
16. Ford N, Mofenson L, Kranzer K, Medu L, Frigati L, Mills EJ, et al. Safety of efavirenz in first-trimester of pregnancy: a systematic review and meta-analysis of outcomes from observational cohorts. AIDS. 2010;24:1461–70.
17. Bera E, McCausland K, Nonkwelo R, Mgudlwa B, Chacko S, Majeke B. Birth defects following exposure to efavirenz-based antiretroviral therapy during pregnancy: a study at a regional South African hospital. AIDS. 2010;24:283–9.
18. Zou G. A modified poisson regression approach to prospective studies with binary data. Am J Epidemiol. 2004;159(7):702–6.
19. Rubin D. Multiple imputation for non-response in surveys. New York: Wiley; 2004.
20. Nattabi B, Li J, Thompson SC, Orach CG, Earnest J. A systematic review of factors influencing fertility desires and intentions among people living with HIV/AIDS: implications for policy and service delivery. AIDS Behav. 2009;13:949–68.
21. Chilongozi D, Wang L, Brown L, Taha T, Valentine M, Emel L, et al. Morbidity and mortality among a cohort of human immunodeficiency virus type 1-infected and uninfected pregnant women and their infants from Malawi, Zambia, and Tanzania. Pediatr Infect Dis J. 2008;27:808–14.
22. Garcia PM, Kalish LA, Pitt J, Minkoff H, Quinn TC, Burchett SK, et al. Maternal levels of plasma human immunodeficiency virus type 1 RNA and the risk of perinatal transmission. Women and Infants Transmission Study Group. N Engl J Med. 1999;341:394–402.
23. Quinn TC, Wawer MJ, Sewankambo N, Serwadda D, Li C, Wabwire-Mangen F, et al. Viral load and heterosexual transmission of human immunodeficiency virus type 1. Rakai Project Study Group. N Engl J Med. 2000;342:921–9.
24. Nachega JB, Hislop M, Dowdy DW, Gallant JE, Chaisson RE, Regensberg L, et al. Efavirenz versus nevirapine-based initial treatment of HIV infection: clinical and virological outcomes in Southern African adults. AIDS. 2008;22:2117–25.
25. Matthews LT, Mukherjee JS. Strategies for harm reduction among HIV-affected couples who want to conceive. AIDS Behav. 2009;13(Suppl 1):5–11.