

High Incidence of Intended Partner Pregnancy Among Men Living With HIV in Rural Uganda: Implications for Safer Conception Services

Angela Kaida, PhD,^a Jerome Kabakyenga, MBChB,^b Mwebesa Bwana, MBChB,^{b,c} Francis Bajunirwe, MD, PhD,^b Winnie Muyindike, MBChB, MMED,^{b,c} Kara Bennett, MSc,^d Annet Kembabazi, MSc,^b Jessica E. Haberer, MD,^e Yap Boum, PhD,^{b,f} Jeffrey N. Martin, MD, MPH,^g Peter W. Hunt, MD,^g David R. Bangsberg, MD, MPH,^{b,h} and Lynn T. Matthews, MD, MPHⁱ

Background: Many men with HIV express fertility intentions and nearly half have HIV-uninfected sexual partners. We measured partner pregnancy among a cohort of men accessing antiretroviral therapy in Uganda.

Methods: Self-reported partner pregnancy incidence and blood-work (CD4, HIV-RNA) were collected quarterly. Interviewer-administered questionnaires assessed men's sexual and reproductive health annually and repeated at time of reported pregnancy (2011–2015). We measured partner pregnancy incidence overall, by pregnancy intention and by reported partner HIV serostatus. We assessed viral suppression (≤ 400 copies/mL) during the periconception period. Cox proportional hazard regression with repeated events identified predictors of partner pregnancy.

Results: Among 189 men, the baseline median age was 39.9 years (interquartile range: 34.7–47.0), years on antiretroviral therapy was 3.9 (interquartile range: 0.0–5.1), and 51% were virally suppressed. Over 530.2 person-years of follow-up, 63 men reported 85 partner pregnancies (incidence = 16.0/100 person-years); 45% with HIV-serodifferent partners. By 3 years of follow-up, 30% of men reported a partner pregnancy, with no difference by partner HIV serostatus ($P = 0.75$). Sixty-nine percent of pregnancies were intended, 18%

wanted but mistimed, and 8% unwanted. Seventy-eight percent of men were virally suppressed before pregnancy report. Men who were younger [adjusted hazard ratio (aHR): 0.94/yr; 95% confidence interval (CI): 0.89 to 0.99], had incomplete primary education (aHR: 2.95; 95% CI: 1.36 to 6.40), and reported fertility desires (aHR: 2.25; 95% CI: 1.04 to 4.85) had higher probability of partner pregnancy.

Conclusions: A high incidence of intended partner pregnancy highlights the need to address men's reproductive goals within HIV care. Nearly half of pregnancy partners were at-risk for HIV, and one-quarter of men were not virally suppressed during periconception. Safer conception care provides opportunity to support men's health and reproductive goals, while preventing HIV transmission to women and infants.

Key Words: HIV, men, ART, safer conception, pregnancy, Uganda
(*J Acquir Immune Defic Syndr* 2019;81:497–507)

INTRODUCTION

Globally, millions of men and women living with HIV want to have children and an estimated half have HIV-uninfected sexual partners.^{1–6} For the majority, achieving pregnancy involves condomless sex, presenting risks of HIV transmission to uninfected partners and infants. To achieve global 90-90-90 goals and eliminate perinatal HIV transmission, comprehensive HIV treatment and prevention strategies are needed that address the reproductive rights and desires of HIV-affected men and women.¹

A range of safer conception strategies create opportunities to support individuals and couples to meet reproductive goals with minimal HIV risk.¹ These strategies include sustained use of antiretroviral therapy (ART) with viral suppression by the partner living with HIV and/or pre-exposure prophylaxis (PrEP) by the HIV-uninfected partner, which effectively eliminate HIV transmission risk during condomless sex.^{7–11} Treatment for sexually transmitted infections may further reduce HIV risk.¹ For HIV-serodifferent couples in which the female partner is living with HIV, male medical circumcision and home insemination reduce sexual HIV transmission while allowing for conception.¹ For men living with HIV (MLWH), sperm washing with insemination offers additional options when such services are available and accessible.^{12,13}

Received for publication December 8, 2018; accepted March 11, 2019.

From the ^aFaculty of Health Sciences, Simon Fraser University, Burnaby, British Columbia, Canada; ^bFaculty of Medicine, Mbarara University of Science and Technology (MUST), Mbarara, Uganda; ^cDepartment of Medicine, Mbarara Regional Referral Hospital, Mbarara, Uganda; ^dBennett Statistical Consulting, Ballston Lake, NY; ^eDepartment of General Medicine, Massachusetts General Hospital (MGH) Global Health, Boston, MA; ^fEpicentre, Médecins Sans Frontières (MSF), Yaoundé, Cameroon; ^gDepartment of Medicine, University of California at San Francisco (UCSF), San Francisco, CA; ^hSchool of Public Health, Oregon Health Sciences University, Portland, OR; and ⁱDivision of Infectious Diseases, MGH Global Health, Boston, MA.

Presented in part at the International AIDS Conference (AIDS 2016); July 18–22, 2016; Durban, South Africa (Oral Poster Abstract THPDC0106). Supported by NICHD (R21-HD069194), NIMH (R01-MH54907, K23-MH095655, K24-MH87227), NIH P30-AI027763, and the Canada-Sub Saharan Africa (CANSSA) HIV/AIDS Network.

The authors have no conflicts of interest to disclose.

Correspondence to: Angela Kaida, PhD, Faculty of Health Sciences, Simon Fraser University, Blusson Hall Rm 10522, 8888 University Drive, Burnaby, BC V5A 1S6, Canada (e-mail: kangela@sfu.ca).

Copyright © 2019 Wolters Kluwer Health, Inc. All rights reserved.

Although increasing attention has focused on improving access to safer conception care for women,^{14–16} less is known about the needs of men. In Uganda^{2,3,5} and globally,¹ approximately half of MLWH have HIV-uninfected partners¹⁷ and an estimated 30%–50% of MLWH desire children. Yet globally, heterosexual men are poorly engaged in HIV care¹⁸ and largely absent from sexual and reproductive health programming.¹⁹ Men are less likely than women to engage in HIV care, initiate ART, and achieve a suppressed HIV viral load,^{18,20} which compromises their health and survival outcomes and exposes potential pregnancy partners to HIV. Constructs of masculinity contribute to men's control of many relationship and reproductive decisions,²¹ and accordingly, women report limited power within sexual relationships.²² Such gender and power inequities contribute to strong gender-normative expectations for childbearing, regardless of HIV status and risk.^{21,23} Despite these gender dynamics, safer conception interventions have primarily focused on women.^{15,16} Previous work in Uganda highlights that MLWH are eager to discuss their reproductive goals with providers^{1,23,24}; however, providers are unlikely to initiate such discussions in part because little is known about men's reproductive health needs.²⁵

Given men's often dominant role in couple decision-making regarding reproductive goals, plans, and practice, including uptake of HIV-prevention strategies,^{1,24} new approaches are required to inform safer conception services that include men. To inform the design and implementation of such services, we measured partner pregnancy incidence, intention, and predictors among MLWH enrolled in HIV care in rural Uganda.

METHODS

Study Design and Participants

This study was conducted in Mbarara District, a rural setting (population 418,200) located approximately 265 km southwest of Kampala, Uganda. In Uganda, HIV prevalence among adult men (aged 15–64 years) is 4.7% compared with 7.6% among adult women.²⁰ The estimated total fertility rate in Mbarara is 7.0 children per woman, and the regional adult HIV prevalence is 7.9%, among the highest in the country.²⁰

Study participants were enrolled in the Uganda AIDS Rural Treatment Outcomes (UARTO) prospective cohort study between 2005 and 2012 with follow-up until September 2015. Treatment-naïve men and women living with HIV were recruited from the HIV treatment clinic at Mbarara Regional Referral Hospital, which offers comprehensive HIV care at no cost to patients. Clients who were 18 years of age or older and living within 60 km of the clinic were eligible to enroll in this cohort.

All participants provided voluntary written informed consent. Study procedures were approved by the Institutional Ethics Review Boards of Mbarara University of Science and Technology (Uganda), Partners Human Research Committee at Massachusetts General Hospital (Boston, USA), and Simon Fraser University (Burnaby, Canada). Consistent with national guidelines, approvals were also obtained from the

Uganda National Council for Science and Technology and the Research Secretariat in the Office of the President.

Procedures

All cohort participants completed phlebotomy (CD4 cells/mm³, HIV-RNA) and interviewer-administered questionnaires, detailing mental and physical health, behavior, and pregnancy incidence (self or partner), quarterly. Annual questionnaires assessed sociodemographics.

In October 2011, the Reproductive Health Component study of the cohort was initiated to assess additional sexual and reproductive health outcomes, relationship dynamics, fertility desires, and attitudes and feelings about reported pregnancies. Between 2011 and 2015, all male participants completed the Reproductive Health Component questionnaire annually. Every 3 months (quarterly), male participants were asked about partner pregnancy. For men reporting a new pregnancy at any quarterly assessment, the Reproductive Health Component questionnaire was then repeated, thus potentially preceding the next scheduled annual questionnaire. Procedures for female UARTO participants are detailed elsewhere.²⁶

Questionnaires were developed by Ugandan and global experts in HIV and sexual and reproductive health. Questionnaires were translated from English into Runyankole, the dominant local language, and then back-translated into English. Questionnaires (available in English and Runyankole) were administered by bilingual interviewers who had completed extensive training in survey administration. Consistent with research site standards, participants were given a small honorarium for their participation and reimbursed for transportation costs at each study visit.

Inclusion and Exclusion Criteria

Starting in 2005, 235 men and 524 women living with HIV were enrolled in the parent cohort study. This analysis of partner pregnancy incidence includes male participants who completed the Reproductive Health Component questionnaire at least once (considered the “baseline” visit), beginning from October 2011 with follow-up to September 2015. All men, regardless of reported sexual activity, were included in the partner pregnancy analysis. We excluded 1 participant who reported a vasectomy before study enrolment.

Measures

Primary Outcomes

At each quarterly study visit, men reported on partner pregnancies and partnership characteristics among up to 4 sexual partners in the previous year or since the previous visit. For each reported partner pregnancy, men were asked to report the pregnancy outcome. Among reported live births, men were asked about infant HIV testing and status within 1 year. Although relying on men's report of partner pregnancy is likely to underestimate true pregnancy incidence, we identified this as the best option to assess partner pregnancy because we were (1) concerned about limiting partner

pregnancy data to the small proportion of couples who are able to present to care together and (2) interested in understanding partner pregnancy incidence from the perspective of MLWH.

Partner pregnancy incidence rate was computed using person-time methods. For time-to-event analyses, we analyzed the time to the first reported pregnancy. For those with an event (ie, partner pregnancy), the event time was based on the date that the participant first reported a pregnant partner. For those who did not have a pregnant partner during the course of follow-up, person-time was censored at the last UARTO study visit. For both those with events and those censored, the start time was the first completion of the Reproductive Health Component questionnaire. Thus, time-to-event was calculated as the number of months from first completion of the Reproductive Health Component questionnaire through to either the first report of pregnancy or the last study visit.

The pregnancy partner's HIV serostatus was assessed at the first report of pregnancy, as reported by the male partner in response to a question about their partner's HIV status at the last sexual encounter. We identified pregnancies within HIV-seroconcordant (ie, HIV-positive pregnancy partner) or HIV-serodifferent (HIV-negative or HIV status unknown pregnancy partner) partnerships. For 4 participants' missing data on pregnancy partner's HIV status, we extrapolated a partner's HIV status by assessing relationship and partner HIV status at the visits immediately before and after the visit where a pregnancy was reported. All reported partner pregnancies were assumed to be fathered by the male participant reporting them.

We assessed the proportion of pregnancies where the male index partner had laboratory confirmation of viral suppression (HIV-RNA \leq 400 copies/mL) during the periconception period, defined as viral suppression at the closest study visit before the first pregnancy report. For participants reporting partner pregnancy at ART initiation, we assumed an unsuppressed viral load.

At the first report of pregnancy, we assessed the participant's attitudes and feelings about the pregnancy²⁷ (ie, "Thinking back to just before she got pregnant, how did you feel about her becoming pregnant?") as well as his thoughts of his partner's attitudes and feelings. A pregnancy was considered "intended" if the participant reported "I wanted to get pregnant sooner" or "I wanted to get pregnant then"; considered "mistimed" if he reported "I wanted to get pregnant later"; or "unwanted" if he reported "I did not want her to be pregnant then or at any time in the future." Both mistimed and unwanted pregnancies were classified as unintended (vs intended) pregnancies.²⁸ We also assessed whether the participant (or his partner) was "trying" to get pregnant (Yes vs No) and how happy he felt when he found out that his partner was pregnant (5-point Likert scale from "Very Unhappy" to "Very Happy").

Covariates

We examined the association of incident partner pregnancy with baseline and time-updated variables, including sociodemographic characteristics (age, marital status,

employment, education, and household income), sexual and reproductive history (number of children fathered, fertility desire, number of sexual partners in the 12 months before interview, HIV-serostatus disclosure to primary sexual partner, and knowledge of partner's HIV serostatus), and HIV clinical history confirmed using clinical chart review and laboratory data (time on ART, CD4 at ART initiation, most recent CD4, and most recent viral load). Socioeconomic status was assessed using the Filmer–Pritchett Asset Index, which estimates wealth based on asset ownership and housing characteristics, with higher scores indicative of greater wealth.²⁹

Statistical Analysis

We compared baseline characteristics of men who did and did not report partner pregnancy using the Pearson χ^2 test or Fisher exact test for categorical variables and the Wilcoxon rank-sum test for continuous variables.

We used Kaplan–Meier methods to measure time to the first partner pregnancy overall and by pregnancy partner HIV serostatus. A log-rank test assessed differences.

Cumulative incidence of partner pregnancies was calculated as the total number of partner pregnancies reported over the follow-up period (including multiple unique pregnancies per male participant) by person-years (PYs) of follow-up. No person-time was eliminated from the denominator while his partner was pregnant, given that some men reported (or may have had) multiple partners and that we had incomplete data on the length of each pregnancy.

Generalized estimating equation Poisson models were used to calculate partner pregnancy incidence rates (per 100 PYs) with 95% confidence intervals (CIs). We used modified Poisson generalized estimating equation methods accounting for repeated measures to assess and compare the proportion of all pregnancies occurring within HIV-seroconcordant and HIV-serodifferent partnerships where the male index partner was virally suppressed.

Cox proportional-hazards regression was used to produce unadjusted estimates of the association between baseline covariates and hazard of partner pregnancy. A multivariable model investigated independent baseline and time-updated predictors of partner pregnancy. Time-updated variables included the following: Asset Index, HIV-serostatus disclosure, knowledge of primary partner's HIV status, primary partner's HIV status, fertility desire, CD4, and viral suppression. For the latter 3 variables, we imputed missing data with the last observation (within 12 months of the visit) carried forward. For time-updated viral load, only values reported within 14 months of the first pregnancy report visit were included. We selected 14 months since viral load testing is typically performed annually in most clinical settings in sub-Saharan Africa and allowing a 2-month window around a scheduled study visit.

The final model was conducted using a backward stepwise elimination technique, whereby the least significant variable was dropped until the final model had the optimum (minimum) Akaike information criterion while maintaining covariates with type III *P* values <0.20 .³⁰

TABLE 1. Baseline Characteristics of Men Living With HIV and Receiving ART, Overall and by Partner Pregnancy After Study Enrollment, Uganda (n = 189)

Variable	Overall (n = 189), n (%), Median [IQR]	Total, n	Partner Pregnancy After Study Enrollment		P
			Yes (n = 63), n (%) or Median [IQR]	No (n = 126), n (%) or Median [IQR]	
Age, yr	39.9 [34.7 to 47.0]	189	36.7 [32.1 to 41.9]	42.5 [36.4 to 48.7]	<0.001
Currently married	140 (77%)	183	54 (90%)	86 (70%)	0.003
Employed	171 (93%)	183	55 (92%)	116 (94%)	0.532
Education: <primary 7 (vs ≥P7)	93 (49%)	189	40 (63%)	53 (42%)	0.008
Monthly household income (UGX)	170,000 [80,000 to 300,000]	152	200,000 [80,000 to 330,000]	150,000 [85,000 to 300,000]	0.396
Filmer-pritchett asset index	-0.2 [-1.2 to 1.5]	180	-0.5 [-1.3 to 1.2]	-0.1 [-1.1 to 1.6]	0.219
No. of children fathered*	4 [2 to 6]	183	4 [2 to 5.5]	4 [2 to 6]	0.229
Fertility desire†		173			0.010
Desires a(nother) child	57 (33%)		23 (49%)	34 (27%)	
Does not desire a(nother) child/ Undecided	116 (67%)		24 (51%)	92 (73%)	
Sexual partners in previous 12 mo		188			0.065
0	20 (11%)		3 (5%)	17 (14%)	
1	133 (71%)		44 (70%)	89 (71%)	
≥2	35 (19%)		16 (25%)	19 (15%)	
HIV Disclosure to primary partner‡	143 (88%)	162	56 (97%)	87 (84%)	0.020
Know partner's HIV status‡	135 (80%)	169	53 (88%)	82 (75%)	0.046
Time on ART, yr	3.9 [0 to 5.1]	189	1.9 [0 to 4.1]	4.1 [0 to 5.1]	0.005
CD4 at ART initiation (cells/mm ³)	175 [86 to 277]	152	203 [111 to 292]	164 [75 to 255]	0.078
Most recent CD4 (cells/mm ³)	319 [235 to 424]	186	299 [243 to 393]	328 [230 to 443]	0.452
Most recent HIV-RNA suppressed (≤400 copies/mL)§	74 (51%)	144	23 (45%)	51 (55%)	0.298
Most recent HIV-RNA suppressed (≤400 copies/mL) among men on ART for ≥3 mo	74 (90%)	82	23 (96%)	51 (88%)	0.426

P values that are <0.05 are bolded.

*Excludes current pregnancies.

†Excludes n = 16 participants with missing responses because they reported a partner pregnancy at baseline and did not report on fertility desires.

‡Of those who report having a primary sexual partner.

§Of n = 45 men with missing VL data at baseline, all were on ART with a minimum duration of use of 1.5 years.

Given that among men with nonmissing VL data, 90% who had been on ART for ≥3 months had HIV-RNA suppression, the true proportion of men with HIV-RNA suppression at baseline overall is likely higher than the 51% reported here.

RESULTS

Overall, 189 MLWH completed the Reproductive Health Component questionnaire at least once and were included in this analysis (ie, 189/235; 80% of all men enrolled in UARTO). Men included in this analysis (n = 189) were more likely to be married (56% vs 33%; $P = 0.005$) and have a higher asset index (median scores of -0.20 vs -1.10; $P = 0.005$) at UARTO enrollment, compared with men who were excluded (n = 46). We detected no differences between groups in terms of age, education, employment status, income, or number of children.

Baseline Characteristics

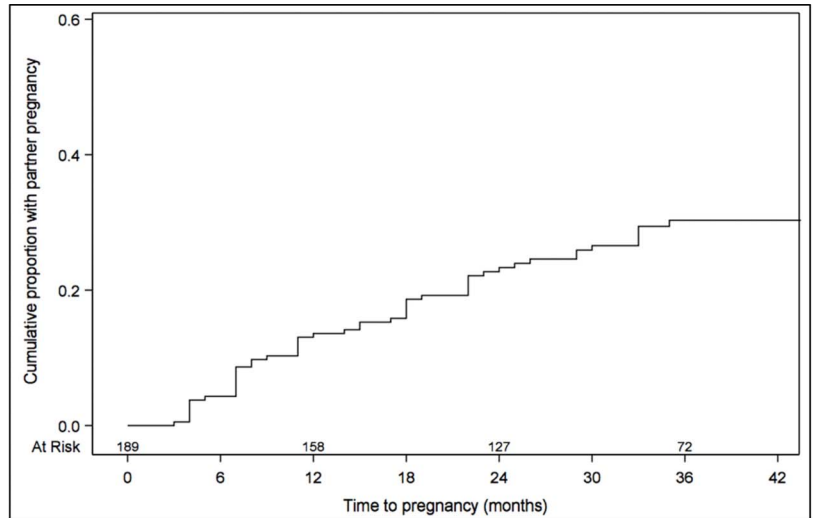
At first completion of the Reproductive Health Component questionnaire (ie, baseline), the median age was 39.9 years [interquartile range (IQR): 34.7–47.0], 93% of men were employed, 49% had not completed primary education, the median monthly household income was 170,000 UGX (~\$99 USD) (IQR: 80,000–300,000), and a median asset index score of -0.2 (IQR: -1.2 to 1.5). The median number of previous

live births was 4 (IQR: 2–6), and 33% reported desiring a child now or in the future (ie, fertility desire). Most (77%) were married, and 19% reported 2 or more sexual partners in the 12 months before interview. Of men with a sexual partner, 88% had disclosed their HIV serostatus to their partner and 80% knew their partner's HIV serostatus. Median years since HIV diagnosis was 4.9 (IQR: 2.5–6.4), median years on ART was 3.9 (IQR: 0–5.1), and median CD4 at ART initiation was 175 (IQR: 86–277). Overall, 51% of men were virally suppressed, including 90% of those on ART for ≥3 months (Table 1).

Several baseline characteristics (including younger age, being married, lower education, fertility desire, HIV disclosure, knowledge of partner's HIV status, and fewer years on ART) were associated ($P < 0.05$) with reporting a partner pregnancy after study enrollment.

Partner Pregnancy Incidence

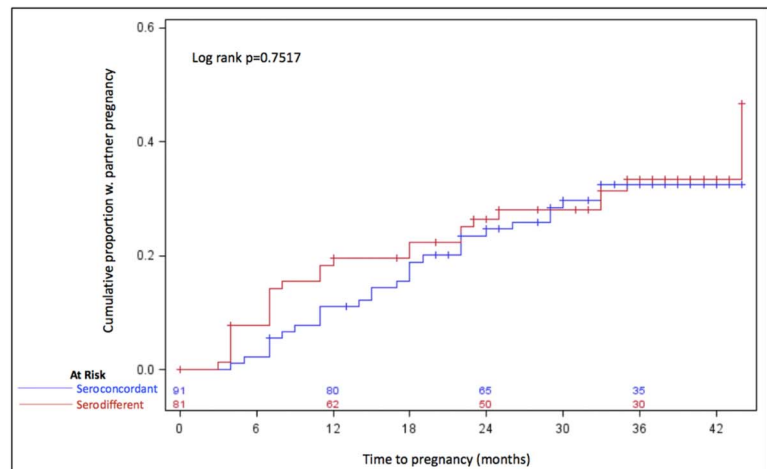
Among 189 men followed over 530.2 PYs, 63 men (33%) reported at least 1 partner pregnancy. Of these, 46 (73%) reported 1, 12 (19%) reported 2, and 5 (8%) reported 3 incident



Summary of the Number of Censored and Uncensored Values*			
Total	Pregnancy	Censored	Percent Censored
189	53	136	71.96%

* Note: Of the 63 participants with at least 1 pregnancy, 10 only had a pregnancy at baseline and did not have a subsequent pregnancy over the follow-up so are included as censored/nonevents in the survival analysis.

A



Summary of the Number of Censored and Uncensored Values*					
Stratum	Partnership HIV status	Total	Pregnancy	Censored	Percent Censored
1	HIV-seroconcordant	91	28	63	69.23%
2	HIV-serodifferent	81	25	56	69.14%
Total		172	53	119	69.19%

* Note: 17 observations with invalid time, censoring, or strata values were excluded from this analysis. HIV serodifferent partnerships included men living with HIV who reported HIV-negative or HIV status unknown pregnancy partners. HIV seroconcordant partnerships included men living with HIV who reported HIV-positive pregnancy partners.

B

FIGURE 1. A, Probability of partner pregnancy over time reported by men living with HIV on ART, Uganda. B, Probability of partner pregnancy over time reported by men living with HIV on ART by partnership HIV status (HIV seroconcordant vs HIV serodifferent), Uganda.

partner pregnancies, totaling 85 pregnancies (partner pregnancy incidence rate = 16.0 per 100 PYs; 95% CI: 13.0 to 19.8).

The 85 pregnancies resulted in 62 live births (73%). Among the 62 live births, 17 participants (27%) reported knowing the infant’s HIV testing status. Among these 17 infants, only 11 men knew the test results and reported that

the infant tested HIV negative. Thus, of 62 live births, 18% of infants were known to be HIV negative, whereas the HIV status of the remaining 82% was unknown by the male pregnancy partner.

By 1, 2, and 3 years after first completion of the Reproductive Health Component questionnaire, the

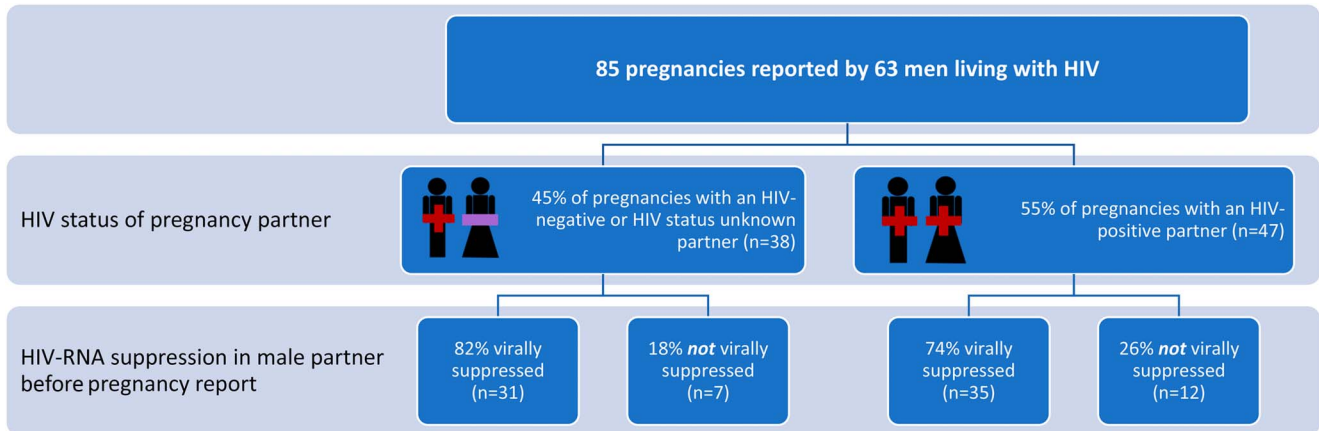


FIGURE 2. Male partner viral suppression (HIV-RNA ≤ 400 copies/mL) before report of pregnancy, by pregnancy partner HIV serostatus, Uganda.

cumulative probability of partner pregnancy was 14%, 23%, and 30%, respectively. No difference in time to the first pregnancy was detected by pregnancy partner HIV serostatus ($P = 0.75$) (Figs. 1A, B).

Pregnancy Partner HIV Serostatus and Viral Suppression

Of 85 pregnancies, 38 (45%) occurred with an HIV-serodifferent partner (including 24/38 with a known HIV-negative partner), whereas 47 (55%) occurred with an HIV-seroconcordant partner. The male partner was not virally suppressed at the study visit before pregnancy report in 19 (22%) of all pregnancies, including 7 (18%) and 12 (26%) of pregnancies that occurred with an HIV-serodifferent or HIV-seroconcordant partner, respectively ($P = 0.46$) (Fig. 2).

Of the 19 pregnancies where the male partner was not virally suppressed during the periconception period, 10 were reported at UARTO enrollment and assumed to be not virally suppressed (given that cohort enrollment coincided with ART initiation, as per the study design). For the remaining 9 pregnancies, the median viral load of men who were not virally suppressed was 4.38 \log_{10} copies/mL (IQR: 4.12–5.52) and the median time between the viral load assessment and first report of pregnancy was 3.82 months (IQR: 3.68–4.31). For all virally suppressed participants, the median time between the viral load assessment and first report of pregnancy was 7.33 months (IQR: 3.78–10.86).

Attitudes and Feelings About the Pregnancy

Of 72 pregnancies with nonmissing responses, 50 (69%) were reported as intended, 13 (18%) were mistimed, and 6 (8%) were unwanted [the remaining 3 (4%) “didn’t care”]. Similarly, 53 (74%) of men reported that his partner intended the pregnancy, 12 (17%) that his partner mistimed the pregnancy, and 4 (6%) that his partner did not want the pregnancy. For 49 (68%) of the pregnancies, men reported “trying” for pregnancy, and for 56 (80%), men reported that his partner was trying for pregnancy (Fig. 3). For 55 (77%) of the

pregnancies, men reported that they were very happy ($n = 30$; 42%) or happy ($n = 25$; 35%) when they found out about their partner’s pregnancy. The remaining 17 (24%) were not sure ($n = 4$; 6%), unhappy ($n = 6$; 8%), or very unhappy ($n = 7$; 10%).

Feelings about the pregnancy strongly correlated with reports about pregnancy intention. Of men reporting that the pregnancy was intended, 44/50 (88%) were happy or very happy when they found out about the pregnancy, compared with 8/13 (62%) of men reporting a mistimed pregnancy and 1/6 (17%) of men reporting an unwanted pregnancy.

Predictors of Partner Pregnancy

Factors associated with increased risk of partner pregnancy included younger age of the male partner, being married, having a primary school education or less, and reporting a desire for a child (ie, fertility desire) at the study visit before pregnancy report.

In the adjusted model, younger age (aHR: 0.94 per year, 95% CI: 0.89 to 0.99), having not completed primary education (aHR: 2.95, 95% CI: 1.36 to 6.40), and reporting fertility desires at a study visit before the first pregnancy report (aHR: 2.25, 95% CI: 1.04 to 4.85) predicted increased probability of partner pregnancy. No HIV-related treatment factors predicted partner pregnancy (Table 2).

DISCUSSION

This is among the first studies to assess partner pregnancy incidence among MLWH and accessing ART in an HIV-endemic setting. We found a high incidence of partner pregnancy (16.0 per 100 PYs), a majority of which ($\geq 69\%$) were reported as intended or perceived as intended by both pregnancy partners. Nearly one-third of men reported at least 1 partner pregnancy within 3 years of follow-up, nearly half of which occurred with HIV-seronegative or unknown serostatus partners (ie, HIV-serodifferent partnerships). In almost one-quarter of pregnancies, men were not virally suppressed in the visit before pregnancy report. The observed high prevalence of intended pregnancy and suboptimal viral suppression in the periconception period

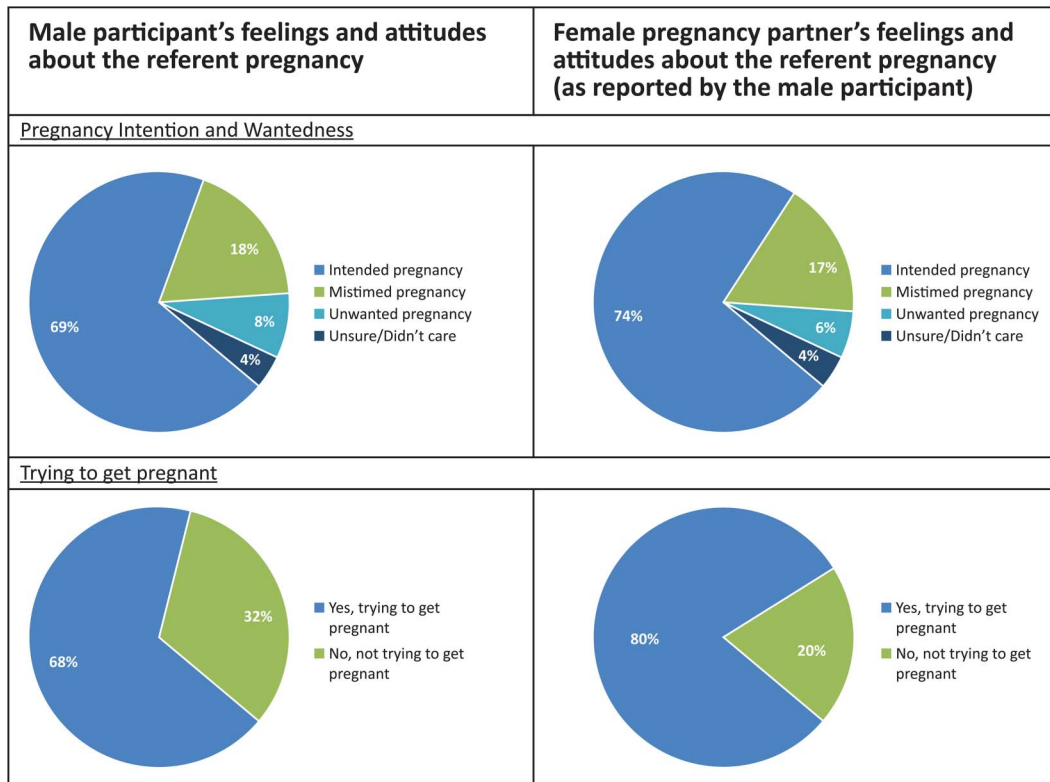


FIGURE 3. Pregnancy intention and wantedness at the first report of pregnancy (n = 72 partner pregnancies among men living with HIV).

underscore a need to address the reproductive goals of men who have sex with women, within HIV care.

Our reported partner pregnancy incidence is higher than the 10.3 per 100 PY incidence rate reported in the Partners PrEP study, which included 1785 HIV-uninfected female partners of MLWH in Kenya and Uganda,³¹ and is nearly double that reported by women living with HIV from this same cohort (9.40 per 100 woman-years).³² Reasons for this difference may have stemmed from our capture of pregnancies among up to 4 sexual partners (19% of men reported 2 or more sexual partners at baseline) and our capture of partner pregnancy from men enrolled in an observational cohort study, rather than a controlled clinical trial. Despite a higher observed pregnancy incidence than previous studies, our estimates likely underestimate true partner pregnancy incidence given expected underreporting of partner pregnancy because of men's lower awareness of early stage pregnancies and stigma toward people living with HIV having children. True partner pregnancy incidence among MLWH is, however, likely lower than the general population of Uganda (where the general fertility rate is 189 per 1000 women aged 15–44)³³ given known behavioral and biological effects of HIV and/or ART use on male infertility.³⁴

ART-mediated HIV-RNA suppression effectively eliminates HIV transmission during condomless sex.⁹ In this cohort of men who knew their HIV serostatus, were engaged in HIV care, and on ART, 22% had detectable HIV-RNA in the study visit before pregnancy report. Suboptimal viral suppression during the periconception period presents risks to

the health of MLWH and their female partners. For HIV-negative female partners, recent data suggest that such risks are particularly elevated during pregnancy and postpartum when HIV acquisition probability per condomless sex act increases significantly.³⁵ In 26% of pregnancies with a female HIV-seroconcordant partner, the male partner was not virally suppressed during the periconception period. In 3/12 of these pregnancies, the male partner had been on ART for ≥ 6 months, highlighting the importance of viral load monitoring to ensure that HIV-seroconcordant couples are also optimally supported on ART before conception attempts.

Sixteen men (25% of all men who reported partner pregnancy) reported a pregnant partner at ART initiation. Furthermore, among those men accessing ART, less time on ART was associated with reporting a partner pregnancy. These findings highlight the importance of counseling all MLWH early and often about their reproductive goals and offering support to help them achieve desired pregnancy as safely as possible, to maximize their own health, and that of their partners and families.²⁴ Offering reproductive health counseling at each stage of the HIV cascade of care, including at diagnosis, may help normalize such discussions such that both men and their providers become more comfortable routinely discussing reproductive goals. Counseling should include simple safer conception messages about delaying condomless sex until HIV-RNA suppression is achieved or ≥ 6 months on ART, consistent with national HIV treatment guidelines.³⁶

TABLE 2. Cox Proportional Hazards Regression of Baseline and Time-Updated Factors Associated With Partner Pregnancy Among Men Living With HIV and on ART in Mbarara, Uganda (n = 181)

Variable	Unadjusted HR (95% CI)	P	Adjusted HR (95% CI)	P
Age at baseline (per yr)	0.93 (0.90 to 0.96)	<0.001	0.94 (0.89 to 0.99)	0.012
Currently married	2.40 (1.02 to 5.62)	0.044	Not selected	
Employed	0.67 (0.24 to 1.87)	0.445	0.33 (0.08 to 1.47)	0.146
Education: incomplete primary school	1.89 (1.08 to 3.29)	0.025	2.95 (1.36 to 6.40)	0.006
Asset index, time-updated	1.06 (0.91 to 1.25)	0.451	1.14 (0.96 to 1.35)	0.137
No. of children fathered			Not selected	
0	1.14 (0.24 to 5.48)	0.873		
1–3	2.20 (0.94 to 5.13)	0.068		
4–6	1.86 (0.78 to 4.42)	0.162		
≥7	Reference			
Fertility desire, time-updated		0.003		0.039
No/undecided	Reference		Reference	
Yes	2.46 (1.37 to 4.43)		2.25 (1.04 to 4.85)	
Sexual partners in previous 12 mo			Not selected	
None	Reference			
1	1.93 (0.59 to 6.26)	0.276		
≥2	3.47 (1.00 to 11.99)	0.050		
Disclosed HIV status to partner, time-updated	0.68 (0.21 to 2.21)	0.516	Not selected	
Know partner's HIV status before pregnancy report, time-updated	0.96 (0.38 to 2.44)	0.924	2.38 (0.77 to 7.40)	0.134
Partner's HIV status, time-updated		0.665	Not selected	
HIV-uninfected or unknown	Reference			
HIV-infected	0.88 (0.49 to 1.57)			
Time on ART (per yr), at baseline	0.89 (0.80 to 1.00)	0.045	Not selected	
CD4 per 50 cells/mm ³ , time-updated	0.99 (0.91 to 1.07)	0.703	Not selected	
VL suppressed (≤400 copies/mL), time-updated	0.80 (0.37 to 1.76)	0.585	Not selected	

Baseline refers to entry into the Reproductive Health Component study.

P values that are <0.05 are bolded.

HR, hazard ratio.

Given that 20% of men reported not knowing their primary partner's HIV status, there remains a need to encourage partner HIV testing (individually or within couples-based testing programs) and offering ART if she is living with HIV or PrEP if she is HIV negative. Moreover, considering that 67% of men reported not desiring a child at baseline and nearly one-quarter of pregnancies were mistimed or unwanted, there is a clear need for integrated family planning services that include men within HIV testing and treatment programs. Across these efforts, additional provider training on initiating discussions about reproductive goals with their male clients is necessary.

Qualitative data from this site²³ and elsewhere³⁷ reveal that men may prioritize achieving reproductive goals before disclosing their HIV status or initiating ART, to maximize reproductive options. Thus, unambiguous messaging is needed regarding the survival and HIV prevention benefits of ART initiation, including the option of realizing fatherhood goals without risking HIV transmission to their partner or child. In the context of growing recognition of Undetectable = Untransmittable (#UequalsU)³⁸ and gender gaps, whereby more women initiate ART and suppress viral load thus offering HIV prevention benefits to male partners, but not vice versa,³⁹ it is critical that these messages permeate beyond

the clinic and into the community to promote uptake of HIV testing and early linkage and engagement in HIV treatment and prevention. Such work focusing on MLWH who have sex with women remains rare, but essential.

At baseline, one-third of men reported wanting to have a child now or in the future. Although there is a relationship between fertility desire and actual fertility, a sizable proportion of men do not express fertility desires but subsequently report a partner pregnancy. Our findings suggest, however, that after the male partner is aware of a pregnancy, he is likely to identify that pregnancy as intended, with only 8% of pregnancies reported as unwanted. These findings deviate from research among women living with HIV, whereby an estimated 50%–86% of pregnancies are reported unintended after the pregnancy is established.^{1,32} Reasons for this difference have not been fully elucidated, although previous work has shown that MLWH report higher fertility desire⁶ and less stigma when expressing fertility goals than women,⁴⁰ both of which may contribute to a larger proportion of partner pregnancies described as intended and wanted.

Most men reported having disclosed their HIV serostatus to his pregnancy partner. Although this prevalence of HIV status disclosure is likely inflated because of social desirability reporting biases,²³ it nonetheless suggests

a tremendous opportunity for male-inclusive safer conception programming in this setting. Many safer conception strategies require (ie, home insemination or condomless sex timed to peak fertility) or at least benefit (ie, adherence to ART or PrEP) from couple's mutual disclosure of HIV status. In our cohort, the conditions to support couples-based, male-inclusive programming are evident.

Nearly three-quarters of reported pregnancies ended in a live birth. This finding is likely an overestimate given that men may not be aware of partner pregnancies that end within the first trimester. Men's awareness of infant HIV testing and serostatus outcomes was low; only 18% of men knew the HIV testing results of their infants (all HIV negative). These data provide additional evidence for the need to actively engage men in counseling and promote family health during periconception (ie, being virally suppressed before conception attempts, HIV-serostatus disclosure, and couples-based HIV testing), antenatal (ie, supporting clinical and social aspects of maternal care, promoting ART adherence), and postnatal (ie, supporting maternal ART/PrEP adherence, infant HIV testing and care, infant feeding choices, and retention in care) periods, to improve maternal, partner, and infant outcomes.

Younger age, less education, and reports of fertility desire independently predicted incident partner pregnancy, consistent with findings among women living with HIV and HIV-uninfected populations.³² All MLWH should receive routine counseling regarding reproductive goals; however, these data suggest that younger men and those who express fertility desires are key populations for this counseling. The association with lower education highlights the need for innovative reproductive health messaging initiatives, to support and engage men with lower literacy. Our team²³ and others⁴¹ have adapted safer conception messaging into visuals and vignettes, interpretable by lower-literacy populations. Additional tools are warranted. Notably, no partnership-related characteristics or HIV-related clinical factors predicted incident partner pregnancy.

Strengths and Limitations

We enrolled MLWH rather than couples and did not attempt to trace pregnancy partners; we were thus unable to conduct pregnancy testing in the female partner. Consequently, limitations of this study include reliance on self-report of partner pregnancy and the probable underestimation of partner pregnancy incidence and overestimation of the proportion of pregnancies ending in live birth. Self-report of other key variables (pregnancy intention, partner HIV serostatus, and disclosure to partner) is subject to social desirability reporting bias, but likely reflects participants' perceptions of HIV risk. Although we used a standard approach to assessing intention after pregnancy was established,²⁸ this may have yielded an overestimate of intended pregnancy. For disclosure analyses, we assumed that the "pregnancy partner" was the "primary sexual partner." This was the case for all but 4 reported pregnancies. In only one of these cases, however, disclosure status differed between the primary and pregnancy partners. Among participants assessed to be virally sup-

pressed during the periconception period, half of the viral load assessments occurred >7 months before the pregnancy report, presenting risk of misclassification bias. We may have therefore overestimated the proportion of pregnancies where the male partner was virally suppressed. Moving forward, safer conception counseling programs might consider adapting viral load monitoring guidelines to offer testing more regularly for those who may benefit from additional support while trying to conceive. Relatedly, our assessment of HIV-RNA suppression in the male partner before pregnancy by partner HIV-serostatus report yielded small cell sizes, subject to low precision of estimates. Our study inclusion criteria (eg, living within 60 km of the HIV clinic) may have contributed to an overestimation of the reported viral suppression rate compared with that expected in the general population. In general, this analysis was conducted among MLWH who had overcome practical and structural barriers to HIV testing and initiating ART. Thus, these results may not be generalizable to MLWH who are not engaged in HIV care.

Our analysis provides a longitudinal assessment of partner pregnancy incidence in a large cohort of men initiated on ART in rural Uganda, where both HIV prevalence and fertility rates are high.²⁰ As we struggle to engage and retain men into HIV care,^{42,43} these findings should inform the design and implementation of HIV prevention programming that acknowledges and supports the reproductive goals of men. In November 2016, we initiated a pilot safer conception program aimed at engaging MLWH in Mbarara. Preliminary findings suggest acceptability and feasibility of the program.⁴⁴

The evidence supporting the need, demand, and feasibility for safer conception services, and potential benefits, is now extensive.¹ Excellent safer conception guidelines are available to support adoption into routine clinical care,⁴⁵⁻⁴⁷ including a global consensus statement on safer conception care cowritten by experts in HIV and reproductive health.¹ However, there remains insufficient action on converting evidence into practice in Uganda and elsewhere. Given the high pregnancy incidence and high rate of viral nonsuppression observed here, we must act now to integrate the services that we know will prevent HIV transmission and support the reproductive goals and rights of women and men living with or affected by HIV.

CONCLUSIONS

Safer conception approaches can extend the reach of HIV prevention initiatives to meet the needs of the millions of HIV-affected individuals and couples who desire children. Such efforts can minimize risks to maternal, partner, and infant health while helping to normalize sex, pregnancy, and family building in the context of HIV. By normalizing sexual and reproductive desires, we can support global efforts to increase HIV testing, linkage, and engagement in care to meet the 90-90-90 goals and eliminate perinatal transmission.⁴⁸ Proactively including heterosexual MLWH in this effort is long overdue.

ACKNOWLEDGMENTS

The authors acknowledge the many contributors to this study including men living with HIV and their families, the UARTO Reproductive Health Component research team, and the ISS clinic physicians and staff.

REFERENCES

- Matthews LT, Beyeza-Kashesya J, Cooke I, et al. Consensus statement: supporting safer conception and pregnancy for men and women living with and affected by HIV. *AIDS Behav*. 2018;22:1713–1724.
- Beyeza-Kashesya J, Ekstrom AM, Kaharuzi F, et al. My partner wants a child: a cross-sectional study of the determinants of the desire for children among mutually disclosed sero-discordant couples receiving care in Uganda. *BMC Public Health*. 2010;10:247.
- Homsy J, Bunnell R, Moore D, et al. Reproductive intentions and outcomes among women on antiretroviral therapy in rural Uganda: a prospective cohort study. *PLoS One*. 2009;4:e4149.
- Myer L, Morroni C, Rebe K. Prevalence and determinants of fertility intentions of HIV-infected women and men receiving antiretroviral therapy in South Africa. *AIDS Patient Care STDS*. 2007;21:278–285.
- Nakayiwa S, Abang B, Packer L, et al. Desire for children and pregnancy risk behavior among HIV-infected men and women in Uganda. *AIDS Behav*. 2006;10(suppl 4):S95–S104.
- Nattabi B, Li J, Thompson SC, et al. 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;13:949–968.
- Baeten JM, Donnell D, Ndase P, et al. Antiretroviral prophylaxis for HIV prevention in heterosexual men and women. *N Engl J Med*. 2012;367:399–410.
- Cohen MS, Chen YQ, McCauley M, et al. Prevention of HIV-1 infection with early antiretroviral therapy. *N Engl J Med*. 2011;365:493–505.
- Rodger AJ, Cambiano V, Bruun T, et al. Sexual activity without condoms and risk of HIV transmission in serodifferent couples when the HIV-positive partner is using suppressive antiretroviral therapy. *JAMA*. 2016;316:171–181.
- Thigpen MC, Kebaabetswe PM, Paxton LA, et al. Antiretroviral preexposure prophylaxis for heterosexual HIV transmission in Botswana. *N Engl J Med*. 2012;367:423–434.
- Cohen MS, Chen YQ, McCauley M, et al. Antiretroviral therapy for the prevention of HIV-1 transmission. *N Engl J Med*. 2016;375:830–839.
- Pollock LC, Weber S, Kaida A, et al. HIV-affected couples and individuals who desire children should be offered options for safer conception. *J Int AIDS Soc*. 2017;20:22155–22162.
- Zafer M, Horvath H, Mmeje O, et al. Effectiveness of semen washing to prevent human immunodeficiency virus (HIV) transmission and assist pregnancy in HIV-discordant couples: a systematic review and meta-analysis. *Fertil Steril*. 2016;105:645–655.e642.
- Schwartz SR, Bassett J, Holmes CB, et al. Client uptake of safer conception strategies: implementation outcomes from the Sakh'umndeni Safer Conception Clinic in South Africa. *J Int AIDS Soc*. 2017;20(suppl 1):43–51.
- Wagner GJ, Linnemayr S, Goggin K, et al. Prevalence and correlates of use of safer conception methods in a prospective cohort of Ugandan HIV-affected couples with fertility intentions. *AIDS Behav*. 2017;21:2479–2487.
- Goggin K, Hurley EA, Beyeza-Kashesya J, et al. Study protocol of “Our Choice”: a randomized controlled trial of the integration of safer conception counseling to transform HIV family planning services in Uganda. *Implement Sci*. 2018;13:110.
- Eyawo O, de Waal D, Ford N, et al. HIV status in discordant couples in sub-Saharan Africa: a systematic review and meta-analysis. *Lancet Infect Dis*. 2010;10:770–777.
- Auld AF, Shiraishi RW, Mbofana F, et al. Lower levels of antiretroviral therapy enrollment among men with HIV compared with women—12 countries, 2002–2013. *MMWR Morb Mortal Wkly Rep*. 2015;64:1281–1286.
- UNAIDS. Male engagement in the HIV response—a platform for action. 2016. Available at: http://www.unaids.org/sites/default/files/media_asset/JC2848_en.pdf. Accessed May 1, 2017.
- UPHIA. Uganda population-based HIV impact assessment UPHIA 2016–2017: summary sheet of preliminary findings. 2017. Available at: <http://www.afro.who.int/sites/default/files/2017-08/UPHIA%20Uganda%20factsheet.pdf>. Accessed April 8, 2017.
- Courtenay WH. Constructions of masculinity and their influence on men's well-being: a theory of gender and health. *Soc Sci Med*. 2000;50:1385–1401.
- Blanc AK. The effect of power in sexual relationships on sexual and reproductive health: an examination of the evidence. *Stud Fam Plann*. 2001;32:189–213.
- Matthews LT, Burns BF, Bajunirwe F, et al. Beyond HIV-serodiscordance: partnership communication dynamics that affect engagement in safer conception care. *PLoS One*. 2017;12:e0183131.
- Khidir H, Psaros C, Greener L, et al. Developing a safer conception intervention for men living with HIV in South Africa. *AIDS Behav*. 2018;22:1725–1735.
- Matthews LT, Bajunirwe F, Kastner J, et al. “I always worry about what might happen ahead”: implementing safer conception services in the current environment of reproductive counseling for HIV-affected men and women in Uganda. *Biomed Res Int*. 2016;2016:4195762.
- Nieves CI, Kaida A, Seage GR III, et al. The influence of partnership on contraceptive use among HIV-infected women accessing antiretroviral therapy in rural Uganda. *Contraception*. 2015;92:152–159.
- Rogers MM, Ahluwalia IB, Melvin CL. The pregnancy risk assessment monitoring system (PRAMS). *J Womens Health*. 1998;7:799–801.
- Santelli J, Rochat R, Hatfield-Timajchy K, et al. The measurement and meaning of unintended pregnancy. *Perspect Sex Reprod Health*. 2003;35:94–101.
- Filmer D, Pritchett LH. Estimating wealth effects without expenditure data—or tears: an application to educational enrollments in states of India. *Demography*. 2001;38:115–132.
- Lima VD, Geller J, Bangsberg DR, et al. The effect of adherence on the association between depressive symptoms and mortality among HIV-infected individuals first initiating HAART. *AIDS*. 2007;21:1175–1183.
- Mugo NR, Hong T, Celum C, et al. Pregnancy incidence and outcomes among women receiving preexposure prophylaxis for HIV prevention: a randomized clinical trial. *JAMA*. 2014;312:362–371.
- Kaida A, Matthews LT, Kanters S, et al. Incidence and predictors of pregnancy among a cohort of HIV-positive women initiating antiretroviral therapy in Mbarara, Uganda. *PLoS One*. 2013;8:e63411.
- Uganda Bureau of Statistics (UBOS) and ICF. *Uganda Demographic and Health Survey 2016: Key Indicators Report*. 2017. Available at: https://www.ubos.org/onlinefiles/uploads/ubos/pdf%20documents/Uganda_DHS_2016_KIR.pdf. Accessed January 19, 2019.
- Pilat A, Discher T, Lochnit G, et al. Semen quality in HIV patients under stable antiretroviral therapy is impaired compared to WHO 2010 reference values and on sperm proteome level. *AIDS*. 2014;28:875–880.
- Thomson KA, Hughes J, Baeten JM, et al. Increased risk of female HIV-1 acquisition throughout pregnancy and postpartum: a prospective pericoital act analysis among women with HIV-1 infected partners. *J Infect Dis*. 2018;218:16–25.
- Ministry of Health Republic of Uganda. Consolidated guidelines for prevention and treatment of HIV in Uganda. 2016. Available at: <http://library.health.go.ug/publications/service-delivery-diseases-control-prevention-communicable-diseases/hivaids/consolidated>. Accessed October 1, 2017.
- Matthews LT, Crankshaw T, Giddy J, et al. Reproductive decision-making and periconception practices among HIV-positive men and women attending HIV services in Durban, South Africa. *AIDS Behav*. 2013;17:461–470.
- Prevention Access Campaign. Risk of sexual transmission of HIV from a person living with HIV who has an undetectable viral load: messaging primer and consensus statement. 2016. Available at: <https://www.preventionaccess.org/consensus>. Accessed August 23, 2018.
- Vandormael A, Akullian AN, Dobra A, et al. Sharp decline in male HIV incidence in a rural South African population (2004–2015). *CROI 2018, 4–7 March 2018*. Boston, MA; 2018.
- Cooper D, Harries J, Myer L, et al. “Life is still going on”: reproductive intentions among HIV-positive women and men in South Africa. *Soc Sci Med*. 2007;65:274–283.
- Brown J, Njoroge B, Akama E, et al. A novel safer conception counseling toolkit for the prevention of HIV: a mixed-methods evaluation in Kisumu, Kenya. *AIDS Educ Prev*. 2016;28:524–538.

42. Adeyeye AO, Stirratt MJ, Burns DN. Engaging men in HIV treatment and prevention. *Lancet*. 2018;392:2334–2335.
43. UNAIDS. Reaching out to men and boys: addressing a blind spot in the response to HIV. 2017. Available at: http://www.unaids.org/sites/default/files/media_asset/blind_spot_en.pdf. Accessed November 1, 2017.
44. Young CR, Bwana M, Hock RS, et al. Implementation of a safer conception program for HIV-affected men and women in Uganda. *AIDS* 2018, 23–27 July 2018. Amsterdam, Netherlands; 2018.
45. Davies NECG, Ashford G, Bekker LG, et al. Guidelines to support HIV-affected individuals and couples to achieve pregnancy safely: update 2018. *South Afr J HIV Med*. 2018;19:915.
46. Fakoya A, Lamba H, Mackie N, et al. British HIV Association, BASHH and FSRH guidelines for the management of the sexual and reproductive health of people living with HIV infection 2008. *HIV Med*. 2008;9: 681–720.
47. Loutfy M, Kennedy VL, Poliquin V, et al. No. 354-Canadian HIV pregnancy planning guidelines. *J Obstet Gynaecol Can*. 2018;40: 94–114.
48. UNAIDS. 90-90-90: An ambitious treatment target to help end the AIDS epidemic. 2014. Available at: http://www.unaids.org/sites/default/files/media_asset/90-90-90_en_0.pdf. Accessed September 14, 2015.