MAJOR ARTICLE

Low Rates of Contraception Use in Women With Human Immunodeficiency Virus

Manasa Bhatta,[1,2] Aihua Bian,[3] Jamison Norwood,[4] Bryan E. Shepherd,[3] Imani Ransby,[4] Jeffrey Nelson,[4] Megan Turner,[4] Timothy R. Sterling,[4] and Jessica L. Castilho[4,5]

[1]School of Medicine, Vanderbilt University, Nashville, Tennessee, USA, [2]Department of Medicine, Icahn School of Medicine at Mount Sinai, New York, New York, USA, [3]Department of Biostatistics, Vanderbilt University Medical Center, Nashville, Tennessee, USA, [4]Division of Infectious Disease, Department of Internal Medicine, Vanderbilt University Medical Center, Nashville, Tennessee, USA, and [5]Department of Health Policy, Vanderbilt University Medical Center, Nashville, Tennessee, USA

Background.   Women with human immunodeficiency virus (WWH) have low rates of hormonal or long-acting contraceptive use. Few studies have described contraception use among WWH over time.

Methods.   We examined contraception (including all forms of hormonal contraception, intrauterine devices, and bilateral tubal ligations) use among cisgender women aged 18–45 years in care at Vanderbilt's human immunodeficiency virus (HIV) clinic in Nashville, Tennessee, from 1998 through 2018. Weighted annual prevalence estimates of contraception use were described. Cox proportional hazards models examined factors associated with incident contraception use and pregnancy.

Results.   Of the 737 women included, median age at clinic entry was 31 years; average follow-up was 4.1 years. At clinic entry, 47 (6%) women were on contraception and 164 (22%) were pregnant. The median annual percentage of time on any contraception use among nonpregnant women was 31.7% and remained stable throughout the study period. Younger age was associated with increased risk of pregnancy and contraceptive use. Psychiatric comorbidity decreased likelihood of contraception (adjusted hazard ratio [aHR], 0.52 [95% CI {confidence interval}, .29–.93]) and increased likelihood of pregnancy (aHR, 1.77 [95% CI, .97–3.25]). While not associated with contraceptive use, more recent year of clinic entry was associated with higher pregnancy risk. Race, substance use, CD4 cell count, HIV RNA, smoking, and antiretroviral therapy were not associated with contraception use nor pregnancy.

Conclusions.   Most WWH did not use contraception at baseline nor during follow-up. Likelihood of pregnancy increased with recent clinic entry while contraception use remained stable over time. Continued efforts to ensure access to effective contraception options are needed in HIV clinics.

Keywords.   contraception; family planning; HIV; pregnancy; women.

Women make up nearly one-quarter of all people living with human immunodeficiency virus (HIV) in the United States (US) and >50% of people living with HIV worldwide [1, 2]. Globally, 25% of new HIV infections are in young women of reproductive age between 15 and 24 years [3]. Regardless of HIV infection, family planning is important for all women to attain their desired number of children and determine timing of pregnancies [4]. However, more than half of the pregnancies among women with HIV (WWH) are unintended [5, 6]. In the US, age-adjusted abortion rates among women without HIV have decreased over time, but those for WWH have remained stable [7]. Recent questions surrounding dolutegravir and risk of

neural tube defects have brought contraception among WWH back into focus [8, 9]. Prevention of unintended pregnancy is an important strategy in preventing mother-to-child transmission of HIV [10]. Furthermore, unplanned pregnancy in women with HIV has been shown to be a predictor of poor HIV and mental health outcomes in mothers [11, 12]. Thus, it is important to provide WWH with access to effective contraception not only to optimize perinatal health, but also to reduce maternal morbidity and allow WWH to achieve their reproductive health goals [5, 13].

Studies have suggested that WWH have low rates of hormonal contraception and long-acting reversible contraception (LARC) use [14–16]. In one study of women with HIV in the US from 1994 to 2005, use of barrier methods were reported in <40% of clinic visits, hormonal methods in <10%, and no contraception in >30% of visits [17]. In another study of privately insured women in the US, WWH on antiretroviral therapy (ART) had 50% lower odds of using short-acting hormonal contraception, such as oral contraception or vaginal rings, than those not on ART, which may be in part due to concerns regarding drug–drug interactions [18]. A recent clinical trial that required some form of contraception use in WWH initiating

ART described that between 2009 and 2011, permanent contraception use was common while use of other effective contraception methods was low [19]. However, these studies span an earlier and shorter time periods, limiting evaluation of contraception initiation and trends in use over time.

There is currently little longitudinal data about contraception use among WWH in the US. There is especially a need for a better understanding of healthcare for WWH in the southeastern US, where the epidemic is disproportionately female [1]. This study evaluated trends and factors associated with contraceptive use among cisgender WWH in a southeastern US HIV clinic.

METHODS

Our study population consisted of WWH seen at the Vanderbilt Comprehensive Care Center (VCCC) in Nashville, Tennessee, between 1 January 1998 and 31 December 2018. The VCCC provides comprehensive primary and specialty care to adults living with HIV. Women's healthcare routinely provided at the VCCC includes cervical cancer screening, screening for sexually transmitted infections, mammogram referrals, prenatal care in conjunction with Vanderbilt Maternal Fetal Medicine, and family planning services, including preconception and contraception counseling, prescriptions, and administration of injectable contraception. Injectable contraception and referrals for bilateral tubal ligation (BTL) have been available in the clinic since the beginning of the study period. Intrauterine devices (IUDs) and hormonal implants have been available in clinic since 2008. Routine follow-up care for patients occurs every 3–6 months. For most women seen at the clinic, the VCCC serves as their primary care clinic. Demographic, clinical, medication (including hormonal contraception use), and laboratory data are routinely abstracted from electronic medical records by data management specialists for research purposes; fields with conflicting results or high rates of error are validated.

This retrospective cohort study included all cisgender women with HIV aged 18–45 years with at least 2 clinic visits within their first year of care seen at VCCC between 1 January 1998 and 31 December 2018. Women with a history of BTL, hysterectomy, or diagnosis of breast, cervical, or ovarian cancer before clinic entry were excluded. Follow-up time was censored at first occurrence of age 45 years; last visit if before 31 December 2018; diagnosis of breast, cervical, or ovarian cancer; hysterectomy; 31 December 2018; or death. Person-time during pregnancies was censored, and observation-time of women who were pregnant at the time of clinic entry began after completion of the pregnancy.

Our primary outcome of interest was initiation of a World Health Organization tier 1 or tier 2 contraception method. Contraception used included oral, transdermal, vaginal ring, and injectable hormonal contraception (tier 2) as well as IUDs, hormonal implants, and BTL (tier 1) [20]. Start and stop dates of tier 2 contraception, IUDs, and hormonal implants were abstracted from medication lists and reviewed in cases of conflicting results. When >1 type of contraception was listed as occurring, the highest-tier use was used. We excluded hormonal contraception with <1 month of documented use. Injectable contraception data were adjusted to demonstrate contraception coverage for 3 months with each injection, when needed. IUD and implant data with duration of use less than a year were reviewed. Tier 3 contraception data (including male condoms, female condoms, withdrawal, spermicides, sponges, and fertility awareness–based methods) were not available, nor was information regarding frequency of sexual activity or desire for pregnancy.

We first calculated the annual prevalence of contraception use over the study period. Percentage of time per year using contraception was calculated using total duration on contraception divided by total duration of follow-up after excluding periods of pregnancy. Overall proportion of total person-time per year using contraception by BTL, implant/IUD, injectable hormonal contraception, oral contraception, or no contraception use was plotted graphically. We used the longitudinal data to calculate the frequency of transition between various states, including tier 1 contraception, tier 2 contraception, pregnancy, and no reliable contraception method. Transition periods between states <30 days were excluded.

We next examined demographic and clinical factors associated with prevalent contraception use (including tiers 1 and 2 as a composite outcome) among women in the cohort. We used multivariable logistic regression models to determine factors associated with contraception use and pregnancy at the time of clinic entry in cross-sectional analyses. For the former analysis, women pregnant at clinic entry were excluded. Covariates of interest in this analysis included baseline CD4 cell count (as a continuous covariate, square-root transformed), undetectable HIV RNA (<400 copies/mL), age at first visit, year of first visit, race/ethnicity, and psychiatric comorbidity at baseline, including adjustment disorder, anxiety, mood disorders (depression and bipolar affective disorders), psychosis, schizophrenia, and personality disorders. To avoid assuming a linear relationship, continuous covariates were included in the models with nonlinear terms [21].

We used multivariable Cox proportional hazards models to examine factors associated with initiating contraception and with incident pregnancy during follow-up in time-to-event analyses. We excluded women who were pregnant at clinic entry from the time to pregnancy analysis, and we excluded women who used contraception at clinic entry from the time to contraception analysis. Multivariable models included age at clinic entry, race/ethnicity, year of clinic entry, psychiatric diagnosis at clinic entry, smoking history (ever/never, documented at any point during follow-up), substance use history (ever/

never, documented at any point during follow-up), and time-varying CD4 cell count (square-root transformed), undetectable HIV type 1 (HIV-1) RNA (<400 copies/mL), and ART use. Rather than exclude women with missing laboratory data in the multivariable model, missing baseline HIV-1 RNA and CD4 data were multiply imputed (25 replications), using predictive models based on other covariates and the outcome. Estimates from the imputation-specific analyses were then combined using the Rubin rule [22]. Cumulative incidence of initiation of contraception was estimated using Kaplan-Meier methods from two different starting points: (1) from clinic entry among women not on contraception and not pregnant at baseline and (2) from the point of finishing their first pregnancy during follow-up.

All analyses were conducted in R version 3.6.2 software, and analysis code is available online at https://biostat.app.vumc.org/ArchivedAnalyses. All P values were 2-sided.

Patient Consent Statement

As this study used only deidentified, retrospective data abstracted from medical records, patient consent was not required. The design of the work was approved by Vanderbilt University Institutional Review Board local and conforms to standards currently applied in the US.

RESULTS

In total, 1017 women aged 18–45 years at clinic entry were seen at the VCCC between 1998 and 2018. We excluded 280 WWH due to hysterectomy or BTL prior to clinic entry. Overall, we included 737 women in our study.

The baseline characteristics of the women in our cohort are in Table 1. The median age at clinic entry was 31 years, and women were followed for a median of 4.1 years. Most women were of Black race. There were 159 (22%) women with a psychiatric diagnosis at baseline, and 262 (36%) reported substance use in the past. At time of clinic entry, 285 (39%) women were on ART. Median CD4 count at time of clinic entry was 408 cells/μL. Median proportion of follow-up time on ART was 0.64 (interquartile range [IQR], 0.10–0.90).

At clinic entry, 164 (22%) women were pregnant and 47 (6%) were using tier 1 or 2 contraception. Of the women on contraception at baseline, half were using injectable contraception. The results of the multivariable logistic regression analysis to determine factors associated with contraception use and pregnancy at clinic entry are shown in Table 2. Younger age and higher CD4 cell count at baseline were associated with higher likelihood of contraception use and higher likelihood of pregnancy at clinic entry.

The annual proportions of nonpregnant person-time on contraceptives during the study period are shown in Figure 1. Overall, the median annual percentage of time on any

Table 1. Demographic and Clinical Characteristics of the Cohort

Characteristic	All Women (N = 737)
Age, years, at clinic entry, median (IQR)	31 (25–37)
Race	
Black	426 (58)
White	263 (36)
Other or unknown	48 (7)
Hispanic ethnicity	41 (6)
Contraception use at clinic entry	
None	526 (72)
Pregnant	164 (22)
Oral contraception	19 (3)
Injectable contraception	23 (3)
Intrauterine device	5 (1)
BMI, kg/m^2, at clinic entry[a], median (IQR)	28 (23–34)
Year of clinic entry, median (IQR)	2007 (2002–2011)
Year of clinic entry	
1998–2002	212 (29)
2003–2007	190 (26)
2008–2012	174 (24)
2013–2018	161 (22)
Psychiatric comorbidity at clinic entry[b]	159 (22)
History of substance use at any time	262 (36)
History of smoking at any time	307 (42)
ART use at clinic entry	285 (39)
CD4 count, cells/μL, at clinic entry[c], median (IQR)	408 (223–635)
Log$_{10}$ HIV RNA, copies/mL, at clinic entry[d], median (IQR)	3.94 (2.60–4.71)
AIDS-defining event at or before clinic entry	70 (9)
Years of follow-up, median (IQR)	4.1 (1.3–8.1)
Died during follow-up	104 (14)

Data are presented as No. (%) unless otherwise indicated.

Abbreviations: ART, antiretroviral therapy; BMI, body mass index; HIV, human immunodeficiency virus; IQR, interquartile range.

[a]BMI at clinic entry available for 650 women.

[b]Psychiatric comorbidities included diagnoses of adjustment disorder, anxiety, mood disorders (depression and bipolar affective disorders), psychosis, schizophrenia, and personality disorders recorded at or within 30 days of clinic entry.

[c]CD4 cell count at clinic entry available for 733 women.

contraception use among nonpregnant women was 31.7% (IQR, 31.1%–32.3%) and was stable throughout the study period. Tubal ligation was the most frequently used contraception method with a median annual percentage of time on tubal ligation of 18.8% (IQR, 18.3%–21.2%). Annual percentage of time on oral contraception decreased over time, whereas use of IUD increased over time since 2010 to 5.8% at end of follow-up. Supplementary Figure 1 shows the frequency of observed transitions between tier 1 contraception, tier 2 contraception, no tier 1 or 2 contraception, and pregnancy. Most frequent transitions were between tier 2 contraception to no contraception and between no contraception to pregnancy.

Among the 526 women not on contraception nor pregnant at clinic entry, 142 (27%) women initiated contraception (42% started with injection, 31% started with oral medication, 20% started with a BTL, and 6% with IUD) and 84 (16%) became

Table 2. Univariate and Multivariable Logistic Regression Models of Factors Associated With Contraception Use[a] and Pregnancy at Clinic Entry

Characteristic	Contraception Use (n = 47)				Pregnancy (n = 164)			
	OR (95% CI)	PValue	aOR[b] (95% CI)	PValue	OR (95% CI)	PValue	aOR[b] (95% CI)	PValue
Age (ref: 25 years)		.003		.007		<.001		<.001
20 years	1.56 (.96–2.54)		1.43 (.87–2.35)		1.22 (.88–1.70)		1.16 (.83–1.62)	
30 years	0.65 (.45–.95)		0.70 (.48–1.03)		0.67 (.54–.83)		0.69 (.55–.87)	
35 years	0.45 (.28–.73)		0.48 (.29–.80)		0.28 (.20–.39)		0.29 (.20–.41)	
Year (ref: 2008)		.13		.12		.01		.03
2003	0.70 (.48–1.02)		0.67 (.46–.98)		0.83 (.68–1.03)		0.78 (.63–.98)	
2013	1.13 (.73–1.75)		1.01 (.63–1.61)		1.33 (1.04–1.72)		1.20 (.90–1.59)	
Black race	1.28 (.69–2.38)	.44	1.10 (.58–2.10)	.77	0.89 (.62–1.26)	.50	0.86 (.58–1.26)	.43
Psychiatric comorbidity[c]	0.86 (.42–1.74)	.67	1.03 (.49–2.18)	.93	0.85 (.56–1.28)	.44	1.16 (.73–1.84)	.53
CD4 count (ref: 350 cells/µL)		.01		.01		<.001		<.001
200 cells/µL	0.64 (.44–.93)		0.66 (.45–.97)		0.57 (.46–.71)		0.65 (.51–.82)	
500 cells/µL	1.37 (1.11–1.69)		1.35 (1.09–1.68)		1.27 (1.13–1.44)		1.16 (1.02–1.32)	
700 cells/µL	1.70 (1.22–2.39)		1.74 (1.20–2.52)		1.09 (.86–1.38)		0.92 (.70–1.20)	
HIV RNA ≥400 copies/mL	0.93 (.47–1.85)	.85	1.40 (.49–2.18)	.41	0.71 (.49–1.05)	.09	0.69 (.44–1.09)	.11

Abbreviations: aOR, adjusted odds ratio; CI, confidence interval; HIV, human immunodeficiency virus; OR, odds ratio.

[a]Contraception use at baseline analyses excluded women who were pregnant at baseline.

[b]Multivariable models included the following covariates: age, year, race, psychiatric comorbidity, CD4 cell count, and HIV RNA.

[c]Psychiatric comorbidities included diagnoses of adjustment disorder, anxiety, mood disorders (depression and bipolar affective disorders), psychosis, schizophrenia, and personality disorders recorded at or within 30 days of clinic entry.

pregnant during follow-up. There were no events of vertical transmission among women who were pregnant when they enrolled in care nor those who became pregnant during follow-up. The results of our multivariable Cox proportional hazards model to assess factors associated with incident contraception use and incident pregnancy are shown in Figure 2. Younger baseline age was significantly associated with higher hazard of incident pregnancy (*P* < .001) and initiating contraception (*P* = .001). More recent year of clinic entry was associated with higher chance of incident pregnancy (*P* = .008) but not contraception initiation (*P* = .11). Compared to women without documented psychiatric comorbidity at clinic entry, women with a psychiatric comorbidity had 48% lower risk of incident contraception use.

Finally, cumulative incidence of contraception use during follow-up was markedly higher following a woman's first pregnancy during follow-up compared to overall cumulative incidence among all women not pregnant or on contraception at clinic entry (Figure 3). Ten years after their first pregnancy in care, the cumulative incidence of contraception initiation was 85.8% (95% confidence interval [CI], 78.3%–90.8%); among women not on contraceptives or pregnant at baseline, the cumulative incidence of contraception initiation was only 46.0% (95% CI, 38.3%–52.7%).

DISCUSSION

Overall, our analysis demonstrated a persistently low proportion of WWH in our clinic who used contraception over time. Sterilization was the most common form of contraceptive used over the observation period, while LARC usage remained infrequent over time. Patient factors most associated with decreased likelihood of contraception initiation among WWH in our cohort were older age and psychiatric comorbidity. However, younger age, psychiatric comorbidity, and more recent year of clinic entry were associated with increased likelihood of pregnancy; and women who became pregnant during follow-up had a higher cumulative incidence of contraception initiation following pregnancy than the larger cohort of women who were not on contraceptives nor pregnant at enrollment. These findings provide longitudinal data to suggest that among WWH, there may be a widening gap between higher fertility and stagnant contraception use, particularly among younger women and those with psychiatric comorbidity.

Between 1998 and 2018, use of tier 1 and tier 2 contraception among WWH in our cohort remained stable and persistently low. The most commonly used form of contraception during all years of follow-up was tubal ligation, with rates of oral hormonal contraception decreasing over time. Rates of IUD usage increased over time but still remained low by the end of follow-up. These observations mirror previous findings that WWH in the US may be less likely to utilize LARC and hormonal contraception but have had persistently high rates of tubal ligations [14–16, 19]. In
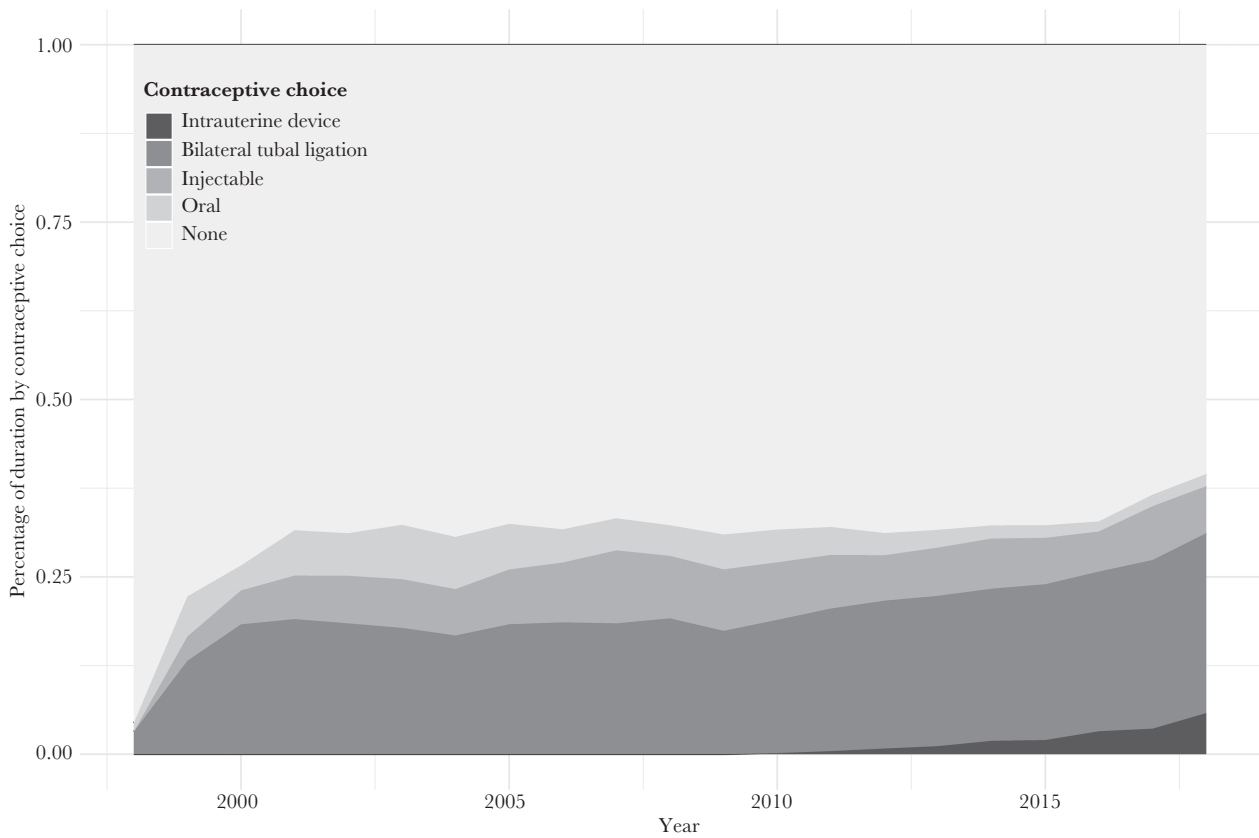
Contraceptive choice among female patients living with HIV
1998 to 2018

Figure 1. Proportion of person-time by contraception use of nonpregnant women per calendar year, weighted by individual observation time per year. Source: North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) Vanderbilt. Abbreviations: HIV, human immunodeficiency virus.
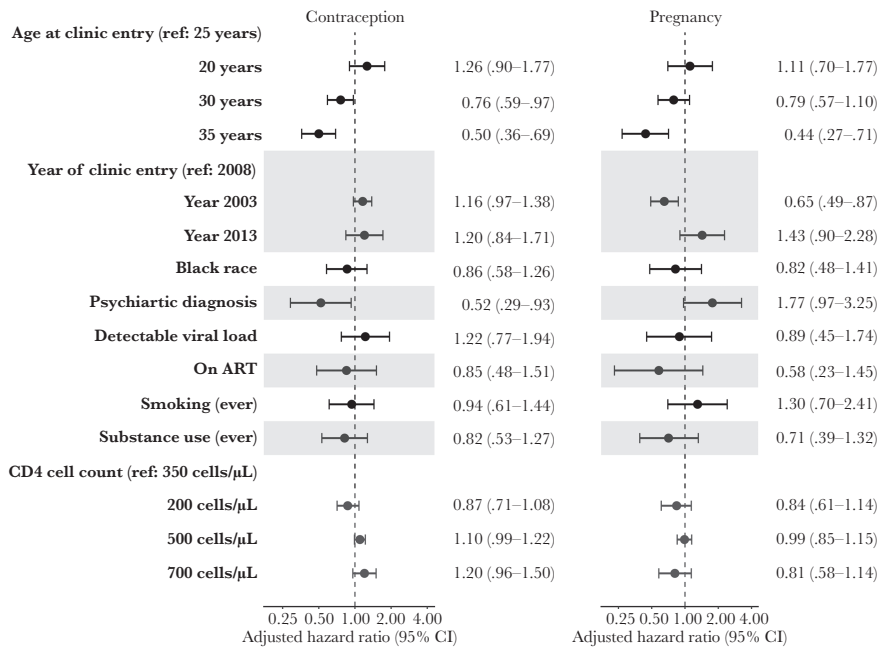

	Contraception	Pregnancy
Age at clinic entry (ref: 25 years)		
20 years	1.26 (.90–1.77)	1.11 (.70–1.77)
30 years	0.76 (.59–.97)	0.79 (.57–1.10)
35 years	0.50 (.36–.69)	0.44 (.27–.71)
Year of clinic entry (ref: 2008)		
Year 2003	1.16 (.97–1.38)	0.65 (.49–.87)
Year 2013	1.20 (.84–1.71)	1.43 (.90–2.28)
Black race	0.86 (.58–1.26)	0.82 (.48–1.41)
Psychiartic diagnosis	0.52 (.29–.93)	1.77 (.97–3.25)
Detectable viral load	1.22 (.77–1.94)	0.89 (.45–1.74)
On ART	0.85 (.48–1.51)	0.58 (.23–1.45)
Smoking (ever)	0.94 (.61–1.44)	1.30 (.70–2.41)
Substance use (ever)	0.82 (.53–1.27)	0.71 (.39–1.32)
CD4 cell count (ref: 350 cells/μL)		
200 cells/μL	0.87 (.71–1.08)	0.84 (.61–1.14)
500 cells/μL	1.10 (.99–1.22)	0.99 (.85–1.15)
700 cells/μL	1.20 (.96–1.50)	0.81 (.58–1.14)

Adjusted hazard ratio (95% CI)

Figure 2. Multivariable proportional hazard models for contraception initiation and for pregnancy. Models included 526 women not on contraception nor pregnant at clinic entry, of whom 142 initiated contraception and 84 became pregnant during follow-up. Multivariable models included the following covariates: age at clinic entry, year of clinic entry, race, psychiatric comorbidity at clinic entry, any history of substance use, any history of smoking, time-varying antiretroviral therapy use, time-varying human immunodeficiency virus RNA ≥400 copies/mL, and time-varying CD4 cell count. Abbreviations: ART, antiretroviral therapy; CI, confidence interval.
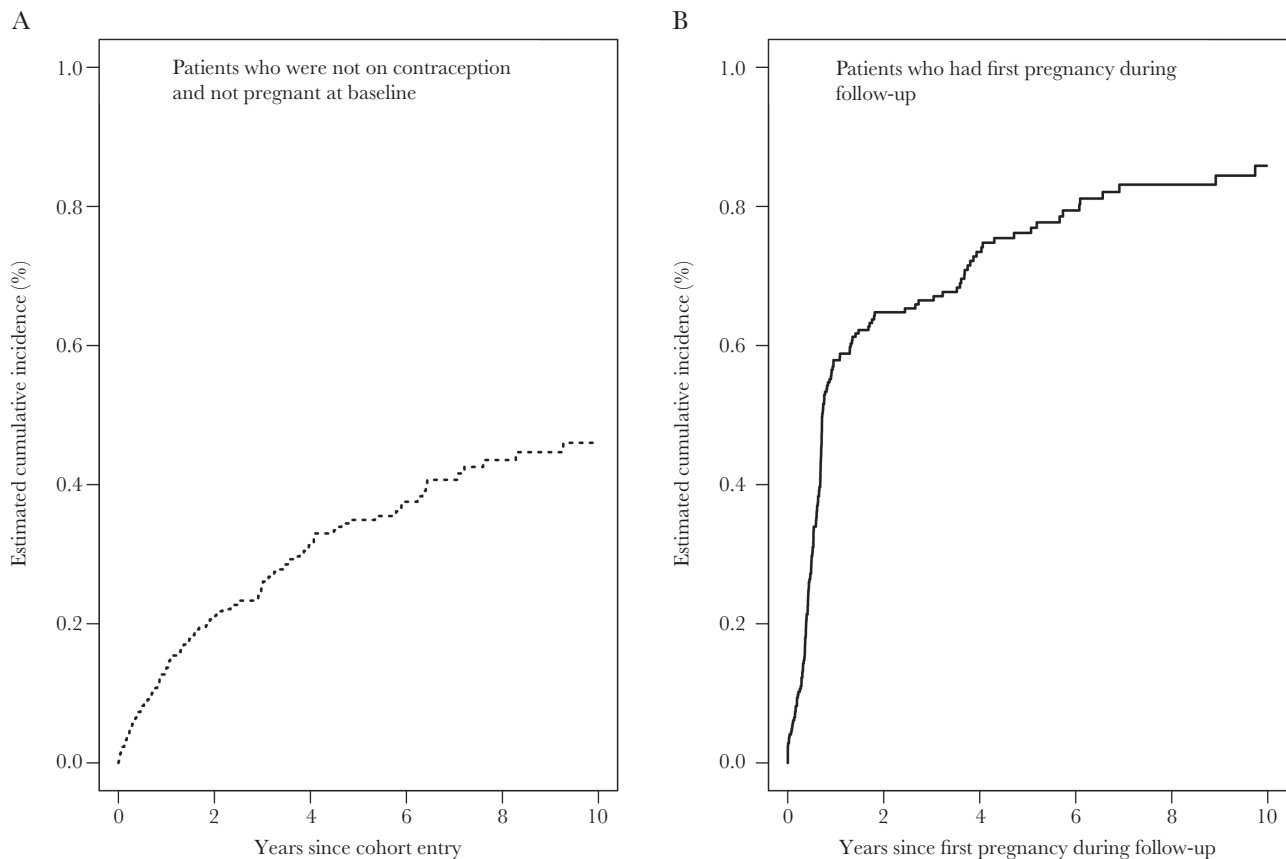
Figure 3. Estimated cumulative incidence of contraception use among patients who were not on contraception and not pregnant at baseline (*A*) and patients who had first pregnancy during follow-up (*B*).

contrast, rates of sterilization have decreased from 37% to 28% and LARC usage increased from 6% to 14% from 2008 to 2014 among all US women aged 15–44 years using any contraception [23]. Several factors may be contributing to persistent barriers to contraception use among WWH in the US, including hesitancy to discuss family planning with one's physician [24]. WWH have historically faced recommendations from providers to select permanent contraception methods to prevent vertical transmission, which may continue to affect patient–provider discussions today [25]. Furthermore, one study that surveyed women in the US who underwent BTL revealed that WWH were more likely to experience regret after undergoing the procedure [15]. Potential drug–drug interactions between ART and hormonal contraception may contribute to hesitancy among patients and providers to use certain contraception methods [26]. Current US Department of Health and Human Services guidelines state that all WWH who are sexually active but do not desire pregnancy should be offered effective and available contraceptive methods. WWH can use all available contraceptive methods (oral, injectable, implant, IUD, etc) after consideration of potential drug–drug interactions [27].

Compared to older women, younger WWH were more likely to initiate contraception. Previous studies of contraception use among WWH also reported younger age, higher CD4 cell count, and longer duration of HIV diagnosis as factors associated with higher odds of contraception use [28, 29]. Our study did not show associations of time-varying CD4 cell count nor HIV viral load with initiation of contraception, though women with higher CD4 count were more likely to be on contraception at clinic entry, perhaps related to prior access to care. Our study is novel in its findings regarding psychiatric comorbidity and risk of reproductive health outcomes. In our study, psychiatric comorbidity was associated with decreased likelihood of initiating contraception and increased risk of pregnancy. While few studies have described contraception use among women with psychiatric comorbidities in general, some have suggested that women with anxiety and depression have increased ambivalence about pregnancy [30–32]. Our results suggest that non-HIV health factors (such as psychiatric comorbidities) may contribute more to contraception initiation than HIV disease biomarkers. We did not observe differences in likelihood of contraception in our cohort by race/ethnicity nor year of clinic entry. While race has not been described as a factor associated with contraceptive use in WWH in the US, previous studies in women in the general population have suggested delayed contraception initiation among Black women [33, 34]. We also

observed that of all women in the clinic, those who had a pregnancy during follow-up had a higher cumulative incidence of contraception use. This likely reflects contraception counseling received during obstetric care, with many women initiating contraception postpartum based on current recommendations from the American College of Obstetrics and Gynecology to avoid short interpregnancy intervals [35].

While younger women in our cohort had higher likelihood of initiating contraception, they also had increased likelihood of incident pregnancy. Women with psychiatric comorbidity also had increased likelihood of incident pregnancy despite lower likelihood of initiating contraception. Previous studies have shown that women with a history of mental health disorders are more likely to report unintended pregnancies than those without mental illness [36–38]. Furthermore, psychiatric comorbidities during pregnancy are associated with increased risk of pregnancy-related morbidity, as are unintended pregnancies [39, 40]. In addition to younger age, our study showed higher CD4 cell count to be associated with increased likelihood of pregnancy at baseline. The reason for this is unclear, though it may indicate previous engagement in HIV care in women with known pregnancy. The similar patient factors associated with likelihood of initiation of contraception and incident pregnancy observed in our study highlight an important population for family planning counseling and education.

While our study is strengthened by a diverse cohort and 20 years of longitudinal data, there are important limitations to consider. This was a single-site study in the US and may be limited in generalizability to other populations of WWH. Our sample size limited our ability to compare factors associated with use of specific contraception methods, such as patient factors specifically associated with tubal ligation, IUD, or oral/injectable forms of contraception. Data on use of tier 3 contraception forms (such as condoms), sexual activity patterns, and desire for pregnancy were also not available—thus, findings may underestimate contraception use in this population. Furthermore, our methodology was limited by the inability to abstract contraception adherence from the medical records. Last, our data were limited with regards to longitudinal economic and behavioral determinants of health, including measures of poverty, substance use, trauma, or other factors that may affect reproductive health and choices of WWH.

In conclusion, WWH in our study had persistently low rates of contraception use over time with persistently low uptake of LARCs and higher rates of tubal ligation, contrary to the general population. These findings highlight a need for improving reproductive health services in care for WWH, particularly those with comorbid psychiatric disorders. Further studies using survey and qualitative methods are needed to characterize contraception preferences and barriers to reproductive healthcare among WWH in the US.

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