Published in final edited form as:

AIDS Behav. 2019 June ; 23(6): 1541–1551. doi:10.1007/s10461-019-02395-x.

The Intersection of HIV, Social Vulnerability, and Reproductive Health: Analysis of Women Living with HIV in Rio de Janeiro, Brazil from 1996 to 2016

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Abstract

Comprehensive care for sexual and reproductive health (SRH) and social needs for women living with HIV remains limited globally. We aimed to assess trends in baseline sociodemographic, clinical, sexual, and reproductive characteristics among a cohort of HIV-infected women in Rio de Janeiro from 1996 to 2016. Participants were stratified into four time periods based on year of enrollment; we compared cross-sectional data from each period. Of 1361 participants (median age 36), most were black or mixed race (60.1%), unemployed (52.1%), and without secondary education (54%). Adolescent pregnancy was common (51.5%), and 18.3% reported sexual debut at < 15 years old. Nearly half (45.2%) had < 5 lifetime sexual partners, yet prior syphilis and oncogenic human papillomavirus prevalence were 10.9% and 43.1%, respectively. Lifetime prevalence of induced abortion was 30.3%, and 16% used no contraceptive method. Future research should explore interactions between social vulnerability, HIV, and poor SRH outcomes and healthcare models to alleviate these disparities.

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Publisher's Note Springer Nature remains neutral with regard to jurisdictional claims in published maps and institutional affiliations. Compliance with Ethical Standards

Conflict of interest The authors have no conflicts of interest to declare.

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

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

Resumen

La atención integral de la salud sexual y reproductiva (SSR) y necesidades sociales para las mujeres que viven con VIH ha estado limitada al nivel global. Nuestro objetivo fue evaluar las tendencias de características sociodemográficas, clínicas, sexuales y reproductivas en una cohorte de mujeres infectadas por VIH en Río de Janeiro entre 1996 y 2016. Los participantes se estratificaron en cuatro períodos de tiempo según el año de enrolamiento; comparamos datos transversales de cada período. De 1361 participantes (mediana de edad 36), la mayoría eran negras o de raza mixta (60,1%), desempleadas (52,1%) y no tenían educación secundaria (54%). El embarazo en la adolescencia fue común (51,5%) y el 18,3% reportaron iniciación sexual antes de los 15 años de edad. Casi la mitad (45,2%) tenían menos de 5 parejas sexuales durante sus vidas, sin embargo, la prevalencia de la sífilis previa y del virus del papiloma humano oncogénico fue del 10,9% y 43,1%, respectivamente. La prevalencia de vida de aborto inducido fue 30,3% y el 16% no utilizaron ningún método anticonceptivo. Futuras investigaciones deberían explorar las interacciones entre la vulnerabilidad social, el VIH y los resultados adversos de SSR y los modelos de cuidado de la salud para aliviar estas disparidades.

Keywords

HIV; Sexual and reproductive health; Women; Disparities; Brazil; VIH; Salud sexual y reproductiva; Mujeres; Disparidades; Brasil

Introduction

In 2016, more than half of the 34.5 million adults living with HIV worldwide were women [1]. Brazil's epidemic has reflected global epidemiology, with dramatic increases in HIV/AIDS cases among women from the mid-1990s to early-2000s [2, 3]. In 2015, women accounted for approximately 35% of AIDS cases in Brazil [2]. Although the past two decades have seen incredible gains in HIV outcomes, healthcare models have not adequately integrated the myriad of social, sexual and reproductive health needs of women living with HIV [4–6]. Therefore, international organizations have recently called for a “woman-centered” approach to HIV care that comprehensively incorporates social determinants and reproductive services [4, 7].

The improved life expectancy and overall health that accompanies HIV treatment advances has important implications for sexual and reproductive health (SRH). Reproductive desires for HIV-infected individuals are similar to HIV-uninfected peers [8, 9] and, as maternal-to-child HIV transmission has been greatly reduced, women living with HIV are increasingly choosing to have children [10]. Yet, accommodating these changing attitudes can be challenging for health services. Women living with HIV report negative interactions with providers regarding provision of options for healthy pregnancy and contraception, as well as unaddressed mental health and social issues [11]. Compared to Brazilian men living with HIV, women experience lower HIV treatment adherence and quality of life [12, 13].

Interactions between biological, behavioral, cultural, and structural factors contribute to women's vulnerability to HIV infection. As such, women living with HIV may have

complex psychosocial needs arising from both their social circumstances and stigmatization related to HIV disease. Gender-based violence reduces engagement for women living with HIV at multiple levels of the care continuum [14], and may be a particularly salient issue for the Latin American region, where high rates of intimate partner violence, sexual assaults, and femicide have been documented [15, 16]. Women experience disproportionate financial barriers to accessing HIV care that can be exacerbated by gendered norms such as childcare responsibilities, financial dependence, and restricted personal autonomy [17]. Furthermore, women worldwide report social stigma as a major obstacle to accessing HIV services, which may be related to oppressive views of female sexuality that can limit HIV disclosure and care-seeking behaviors [17, 18].

Women living with HIV experience high rates of interpersonal violence, substance use, and mental illness that may contribute to greater vulnerability and adverse health outcomes [19, 20]. Globally, living with HIV has been associated with persistent SRH disparities in quality of contraceptive methods, unintended pregnancy, and induced abortion [21–23]. Brazilian literature presents similar findings: HIV-infected women had earlier sexual initiation, more illicit substance use, higher rates of sexually transmitted infections (STIs), and were more often victims of sexual violence compared to HIV-uninfected women [24]. Other Brazilian studies have found disparities in reproductive outcomes like unplanned pregnancy and abortion [6], and highlighted social vulnerabilities of young HIV-infected women [25]. While these studies characterize women living with HIV during specific time periods, there is limited information on the evolution of sociodemographic characteristics and SRH outcomes in Brazil.

To better implement international recommendations for woman-centered HIV services, it is important to understand how these characteristics have changed over the years and describe the current needs of women living with HIV. We analyzed data from the Instituto Nacional de Infectologia Evandro Chagas, Fundação Oswaldo Cruz (INI-Fiocruz) women's cohort in Rio de Janeiro, Brazil. Our objectives were to describe sociodemographic, clinical, sexual, and reproductive characteristics of the INI-Fiocruz cohort and to assess trends in these baseline characteristics from 1996 to 2016. These findings can be used to improve understanding of social needs and SRH disparities among women living with HIV, and to suggest possible directions for optimizing HIV care and service delivery for this population. Analyzing trends over time also allows us to describe changes in the characteristics of interest and to hypothesize about the potential effects of Brazilian policies and programs designed to advance HIV treatment and promote women's health.

Methods

Study Population and Procedures

The INI-Fiocruz women's cohort was established in 1996 as an open cohort of HIV-infected women. The observational cohort is clinic-based, and serves women from the city of Rio de Janeiro and surrounding metropolitan areas. Women with documented HIV infection were invited to enroll, and informed consent was obtained from all individual participants. Participants were excluded from this analysis if they were: < 18 years old, not enrolled in the HIV clinical cohort at INI-Fiocruz, or had incomplete baseline questionnaires. Study visits

occurred every 6–12 months, and consisted of structured interviews, clinical and laboratory assessments, and gynecologic exam with specimen collection and cervical cytology. Face-to-face interviews collected information on socioeconomic characteristics, substance use, sexual and reproductive history, and HIV disease history.

Study Definitions

Cohort enrollment was defined as the first study visit date. Self-reported race/skin color was categorized as: white, black, mixed, or other. For cases of unknown HIV exposure route, women without identifiable risk factors of injection drug use (IDU), transfusion, or vertical transmission were assumed to be exposed through sexual contact. Baseline CD4⁺ T lymphocyte count and HIV-1 RNA were defined as the value recorded closest to enrollment date, within a window of 180 days before or after enrollment. Use of antiretroviral therapy (ART) at cohort entry was defined as the regimen initiated before the enrollment date with an end date occurring after enrollment. Combination antiretroviral therapy (cART) use was defined as any exposure to at least one ART backbone drug (nucleoside reverse transcriptase inhibitor [NRTI]) and at least one ART core drug class (non-NRTI, protease inhibitor, or integrase strand transfer inhibitor).

STI co-infections were classified as prevalent if diagnosed any time before enrollment and up to 30 days after enrollment. Prior syphilis was diagnosed by positive treponemal antibody test (FT-ABS or TPHA). Human papillomavirus (HPV) was assessed using hybrid capture II technique (Digene Inc.). Oncogenic strains included HPV types 16, 18, 31, 33, 35, 39, 45, 51, 52, 56, 58, 59, and 68. As routine HPV sample processing ceased in 2013, women enrolling in 2013 or later were censored for this variable. Gonorrhea and chlamydia infections were only assessed by self-report, and were therefore excluded.

Adolescent pregnancy was defined as pregnancy between 10 and 19 years of age [26]. Contraceptive methods were assessed for pre-menopausal women who were sexually active within the past year, and were based on current method at enrollment. Methods were categorized hierarchically (i.e., if dual methods were used, participants were categorized by the most effective method). Participants were asked about condom use as a method of contraception, in addition to use for STI prevention. Dual methods were defined as use of barrier contraception plus another effective method, including: intrauterine devices (IUDs), oral contraceptive pills (OCPs), injectable contraceptives, and tubal ligation.

Statistical Analysis

Descriptive analyses were performed on baseline data for women entering the cohort from May 1996 to June 2016, according to 5-year inclusion periods (1996–2000, 2001–2005, 2006–2010, 2011–2016). Trends were assessed by enrollment period, using Chi squared test for trend in proportions for categorical variables and Poisson linear regression models for continuous variables. We conducted sub-analyses of selected SRH variables, stratified by age at enrollment and treatment status (ART use vs. no ART). Chi squared tests were used for categorical variables and Kruskal–Wallis tests for continuous variables. R (version 3.3.1) was used for all analyses.

Results

Overall, 1361 women met inclusion criteria (Fig. 1). The median and interquartile range (IQR) age at enrollment was 36.2 (29.6, 43.6) years, and median age increased over time from 34.1 to 37.9 years between the first and last periods (p value 0.004). Most participants were black or mixed race (60.1%), unemployed (52.1%), and had < 9 years of education (54%). Increasing proportions of non-white women were enrolled (p-value 0.002), and educational attainment rose over the study period with significantly more women completing 9–11 years of education (p-value < 0.001) (Table 1).

Nearly half of women (42.3%) were current or former smokers, and smoking declined over the study period (p-value 0.021 for current smokers). Exposure to HIV through IDU was 0.4% (Table 2), and marijuana and inhaled cocaine both had a lifetime prevalence of 11.4%. Lifetime history of sexual or physical violence was 38.5%, with 16% and 31.4% reporting exposure to sexual and physical violence, respectively. Sexual violence significantly decreased over time from 27.8 to 10.8% between first and last periods (p-value < 0.001), while physical violence remained unchanged (26.2% vs. 26.4%, p-value 0.841) (Table 1).

Most women (96.3%) were exposed to HIV through sexual contact, while 3.2% were exposed through blood transfusion or vertical transmission. The proportion of women on cART at enrollment increased from 23.2 to 69.3% between the first and last periods (p-value < 0.001) (Table 2). This increase in use of treatment is reflected in the median CD4⁺ T lymphocyte count and the proportion of participants with HIV-1 RNA < 400 copies/mL at enrollment, both of which also increased significantly over time (p-value < 0.001 for both). Median (IQR) time between HIV diagnosis and cohort entry was 1.5 (0.6, 4.6) years.

Overall, 18.3% initiated sexual activity before the age of 15, and age at sexual debut significantly decreased over time (p-value < 0.001). Median (IQR) age at first pregnancy was 19 (17, 22) years, and 62 women (4.6%) experienced pregnancy before age 15. The prevalence of adolescent pregnancy and birth were 51.5% and 39.2%, respectively, and both increased significantly over time (p-value 0.008, < 0.001).

Most women (75.5%) were sexually active within the past year, and 79.4% reported 10 or fewer lifetime partners. Prior syphilis and oncogenic HPV infections remained stable with total prevalence at 10.9% and 43.1%, respectively (p-value 0.079, 0.208). Barrier methods were the dominant form of contraception (42.8%), while 16% used no method. Tubal ligation was the primary method for 23.3%, and use was unchanged over the study period (p-value 0.079). Hormonal methods and IUDs were used by 14.6% of women, and this proportion increased over time (p-value 0.009). Use of dual methods was 9% overall, but increased from 6.3 to 14% between the first and last periods (p-value < 0.001) (Table 3).

Gravidity decreased (p-value 0.034), but parity remained relatively stable over time with a median (IQR) of 2 (1, 3) (p-value 0.146). Lifetime history of induced abortion was 30.3% for all women in our sample, and 33.4% among women with a past pregnancy (Table 3). History of spontaneous abortion increased over time (p-value 0.002), but pregnancies ending in either spontaneous or induced abortion decreased significantly (from 55 to 41.2% between first and last periods, p-value < 0.001).

Discussion

Our study used two decades of observation to construct a profile of 1361 women living with HIV in Rio de Janeiro and to describe the baseline demographic, social, sexual, and reproductive characteristics of the women's cohort over time. Overall, INI-Fiocruz women living with HIV are a socially vulnerable population. Participants were frequently exposed to physical and sexual violence, experienced sexual debut and childbearing at an early age, had a high burden of STIs, and reported elevated rates of tobacco and illicit substance use compared to women of unknown HIV-status in Brazil [27, 28]. There was an unmet need for family planning, reflected by the low use of dual contraception and high prevalence of induced abortion. We observed dramatic improvements in HIV disease parameters over time (as increasing proportions of women were on cART and had higher CD4⁺ T lymphocyte counts and lower HIV-1 RNA levels), likely resulting from Brazil's successful HIV/AIDS policies [29].

The cohort underwent several sociodemographic changes: median age and years of education increased over time, and increasing proportions of black and mixed race women were enrolled. These changes mirror the Brazilian epidemic, as recent trends toward increasing AIDS incidence among women over age 55, non-white race, and higher educational status have been observed [2, 6, 25, 30]. Changes in educational attainment may be reflective of increasing age and/or overall improvements in education for women in Brazil [31]. Despite these educational advances, INI-Fiocruz participants remained socioeconomically disadvantaged as most women were unemployed and without secondary education.

Slightly more women in our cohort reported sexual initiation before age 15 compared to women in the general population (18.4% vs. 15.4%) [32]. This is consistent with results from other women's HIV cohorts in Brazil that demonstrate earlier sexual debut for HIV-infected women than for their HIV-uninfected counterparts [6, 24, 25]. Early sexual debut represents a public health concern as sexual activity at younger ages is more likely to be non-consensual and unprotected [33]. Interventions targeting young women are needed in Brazil, as new AIDS diagnoses increased 12.9% for women aged 15–19 from 2006 to 2015 [2]. Adolescent birth was also common in our cohort (39.2%) and increased significantly over time. Our trends contrast with national data, which show decreasing prevalence from 23.5 to 19.2% between 2000 and 2011 [34]. This disparity could be partially attributed to lower socioeconomic status, which has been associated with teenage pregnancy and elevated fertility rates in Brazil [34, 35], or to cohort effects as median age at cohort enrollment increased over time in our sample.

We observed a large burden of prior syphilis and HPV in our population, underscoring the importance of regular gynecologic care for women living with HIV. Prior syphilis infections were higher in our population (10.9%) compared to a prevalence study among Brazilian postpartum women (1.02%), and were similar to other reports of HIV-infected women in Brazil (9.9%) [36, 37]. Our cohort's oncogenic HPV prevalence (43.1%) was similar to international HIV cohorts using comparable laboratory techniques (49.5–51.8%) [38, 39], but higher than previous studies among Brazilian women of unknown HIV status in the

general population (20–24.6%) [40–42]. While sexual risk behavior may partially explain these findings, immuno-suppression in HIV infection can also lead to reduced HPV clearance [43]. Women in our cohort generally had fewer lifetime partners compared to the Brazilian general population—15.9% INI-Fiocruz versus 26.3% of Brazilian women reporting > 10 lifetime partners [32]. This finding suggests that other sexual risk behaviors (e.g., inconsistent condom use, early sexual debut) may be important predictors of both HIV and STI risk in this population. In addition, there is evidence to suggest that individual socioeconomic and community-level factors like violent crime and high unemployment may contribute to elevated HIV/STI risk, and should be explored further in our cohort [44–46]. Risk factor identification is especially needed for syphilis in Brazil as incidence among women has been rising, significant morbidity is associated with untreated infection, and there is a paucity of literature specific to women living with HIV [47].

Use of highly-effective contraception at cohort entry was low in our sample (37.9%), as women mainly relied on condoms or used no method. A national survey of reproductive-aged, married women in Brazil found that 53.3% used highly-effective methods (27.4% OCPs, 25.9% female sterilization) [48]. While use of hormonal and dual methods in our cohort improved over time, dual use remained well below what is reported nationally (9% vs. 27%) [49]. These findings are consistent with U.S. studies reporting disparities in contraceptive quality for HIV-infected women [21]. Given the reality that women may experience difficulties with condom negotiation and consistent use, the World Health Organization recommends that women living with HIV be counseled on the full range of contraceptive options [4]. Potential barriers to uptake of effective methods (such as cost, limited access, medication non-adherence, or cultural norms) should be explored to help women living with HIV achieve their desired family size. Integration of family planning with HIV care provides a model to increase accessibility and potentially improve reproductive health outcomes [4, 50].

In the INI-Fiocruz women's cohort the prevalence of lifetime induced abortion was 30.3%, compared to 13–15% reported in Brazilian national surveys of urban women aged 18–39 and 17.5% for HIV-infected women in Brazil [51, 52]. Induced abortion is illegal in Brazil (except in cases of rape, danger to the woman's life, or fetal anencephaly) and is often performed under unsafe conditions [23, 53]. Given this reality, substantial underreporting or misreporting of induced abortions as spontaneous is likely. Previous literature indicates that the decision to terminate pregnancy can be influenced by both HIV diagnosis and life circumstances such as age, prior births, and partner stability [10, 23, 54]. The same contexts of vulnerability (e.g., social instability, marginalization) may place women at risk for both HIV infection and abortion [23]. As such, socioeconomic disparities may partially explain our cohort's elevated prevalence. Induced abortion prevalence decreased over time in our population, which could be a consequence of decreasing sexual violence, improved HIV control, or educational advancement among INI-Fiocruz women, as educational status has been correlated with contraceptive knowledge and fewer unplanned pregnancies [55].

While substantial SRH disparities were still present in later cohort years, we observed significant improvements in use of dual contraceptive methods, lifetime abortion prevalence, and sexual violence over time. In 2004, the Brazilian government established a national

Comprehensive Women's Health Policy to promote sexual and psychosocial women's health [56]. Expanded contraceptive access, particularly among women of lower socioeconomic status, resulting from the policy likely contributed to the SRH improvements we observed. Reductions in the cohort's prevalence of sexual violence could be attributed, in part, to the policy's provisions and to 2006 legislation combating gender-based violence. Analysis of nationally-representative household survey data showed reductions in intimate partner violence following the law's implementation [57]. Yet, prevalence of physical violence in our cohort did not diminish and sexual abuse remains unacceptably high, particularly compared to HIV-uninfected women of similar social circumstance in Brazil [6, 24]. As violence can impact psychological health and limit health-promoting behaviors, linking to supportive services is an important component of comprehensive care for women living with HIV [4].

Our study has several limitations. The INI-Fiocruz women's cohort uses open enrollment procedures, and our study population may lack generalizability to other HIV-infected populations because of non-probabilistic sampling. Our use of face-to-face interviews for data collection may have introduced social desirability bias, leading to underreporting of potentially stigmatizing activities like substance use and induced abortion. Women also received treatment through the HIV clinical cohort at Fiocruz prior to women's cohort enrollment, which potentially biases baseline HIV clinical values. We performed stratified analysis of key SRH variables (prior syphilis, parity, lifetime abortion, contraception) by treatment status and did not find significant differences. Age at cohort enrollment increased over time, potentially reflecting different reproductive life stages of study participants. Therefore, we would expect variables measuring cumulative incidence to increase over time (e.g., prior syphilis, parity, lifetime abortion). We conducted sub-analyses of reproductive variables and found no significant differences in time trends with age stratification. We had limited information on whether prior events occurred before or after HIV diagnosis because women were enrolled an average of 1.5 years after HIV diagnosis. These limitations did not impact our overall objective to describe baseline characteristics of women living with HIV to better anticipate their social and SRH needs.

Conclusions

Our analysis revealed a population of highly vulnerable women, with complex social and SRH histories at cohort entry. Integrating services like domestic violence support, specialized gynecologic care, and family planning into routine HIV care could reduce barriers to access and more fully address the spectrum of health needs for women living with HIV. While certain indicators improved over time, much work remains to address the root causes of social vulnerability that place women at risk for HIV infection and SRH disparities. Future research should explore the syndemic interactions between social vulnerability, HIV disease, and poor SRH outcomes that we described, and develop strategies for advancing social progress to improve overall health for women living with HIV.

Acknowledgements

We would like to thank the INI-Fiocruz study participants and staff who devoted their time and efforts to make this project possible. We would also like to thank Eddy Segura for his assistance with abstract translation.

Funding This work was supported in part by the Doris Duke Charitable Foundation through a grant supporting the Doris Duke International Clinical Research Fellows Program at the University of California San Francisco. CMZ is a Doris Duke International Clinical Research Fellow. This work was also supported by the US National Institute of Health Grants NIH R25 MH087222 to JLC and K23 AI110532 to JEL. RBDB acknowledges funding from the Research Funding Agency of the State of Rio de Janeiro (FAPERJ) E-26/203.154/2017 and from the National Council of Technological and Scientific Development (CNPq) 310541/2017-4.

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Fig. 1.
Enrollment flowchart, INI-Fiocruz women's cohort, 1996–2016

Table 1
Sociodemographic and behavioral characteristics at baseline by study period, INI-Fiocruz women's cohort, 1996–2016

	1996–2000	2001–2005	2006–2010	2011–2016	Total	p-value trend	Linear coefficient (95% CI)
Demographics							
Age							
Median (IQR)	34.1 (27.8,41.3)	37.3 (32.1, 43.5)	34.9 (28.8, 43.6)	37.9 (31.1, 45.9)	36.2 (29.6, 43.6)	0.004	1.03 (1.01–1.04) ^a
18–24	36 (11.9)	17 (6.9)	51 (11.5)	36 (9.7)	140 (10.3)	0.774	
25–34	126 (41.7)	85 (34.6)	171 (38.7)	108 (29.1)	490 (36)	0.004	
35–44	96 (31.8)	97 (39.4)	126 (28.5)	129 (34.8)	448 (32.9)	0.926	
45	44 (14.6)	47 (19.1)	94 (21.3)	98 (26.4)	283 (20.8)	< 0.001	
Skin color							
White	159 (52.6)	116 (47.2)	112 (25.3)	129 (34.8)	516 (37.9)	< 0.001	
Black	54 (17.9)	49 (19.9)	102 (23.1)	102 (27.5)	307 (22.6)	0.002	
Mixed	89 (29.5)	79 (32.1)	205 (46.4)	138 (37.2)	511 (37.5)	0.002	
Other	0 (0)	2 (0.8)	23 (5.2)	2 (0.5)	27 (2)		
Education							
Illiterate	13 (4.3)	5 (2)	10 (2.3)	13 (3.5)	41 (3)	0.613	
Literate and < 4 years	66 (21.9)	57 (23.2)	78 (17.6)	57 (15.4)	258 (19)	0.010	
4–8 years	122 (40.4)	61 (24.8)	142 (32.1)	111 (29.9)	436 (32)	0.035	
9–11 years	74 (24.5)	92 (37.4)	160 (36.2)	143 (38.5)	469 (34.5)	< 0.001	
12 years	26 (8.6)	23 (9.3)	51 (11.5)	44 (11.9)	144 (10.6)	0.113	
Missing	1 (0.3)	8 (3.3)	1 (0.2)	3 (0.8)	13 (1)		
Employment							
Unemployed	148 (49)	142 (57.7)	230 (52)	189 (50.9)	709 (52.1)	0.946	
Sporadic work	43 (14.2)	31 (12.6)	37 (8.4)	31 (8.4)	142 (10.4)	0.004	
Regular work	111 (36.8)	71 (28.9)	150 (33.9)	108 (29.1)	440 (32.3)	0.120	
Missing	0 (0)	2 (0.8)	25 (5.7)	43 (11.6)	70 (5.1)		
Substance use							
Smoking status							
Current smoker	74 (24.5)	58 (23.6)	93 (21)	65 (17.5)	290 (21.3)	0.021	

	1996–2000	2001–2005	2006–2010	2011–2016	Total	p-value trend	Linear coefficient (95% CI)
Former smoker	72 (23.8)	59 (24)	92 (20.8)	63 (17)	286 (21)	0.019	
Never smoker	155 (51.3)	129 (52.4)	254 (57.5)	241 (65)	779 (57.2)	< 0.001	
Missing	1 (0.3)	0 (0)	3 (0.7)	2 (0.5)	6 (0.4)		
Lifetime history of marijuana							
Yes	37 (12.3)	28 (11.4)	46 (10.4)	44 (11.9)	155 (11.4)	0.801	
No	264 (87.4)	218 (88.6)	386 (87.3)	324 (87.3)	1192 (87.6)	0.939	
Missing	1 (0.3)	0 (0)	10 (2.3)	3 (0.8)	14 (1)		
Lifetime history of inhaled cocaine							
Yes	40 (13.2)	31 (12.6)	46 (10.4)	38 (10.2)	155 (11.4)	0.158	
No	261 (86.4)	215 (87.4)	386 (87.3)	330 (88.9)	1192 (87.6)	0.300	
Missing	1 (0.3)	0 (0)	10 (2.3)	3 (0.8)	14 (1)		
History of violence							
Lifetime history of physical violence							
Yes	79 (26.2)	87 (35.4)	163 (36.9)	98 (26.4)	427 (31.4)	0.841	
No	214 (70.9)	151 (61.4)	266 (60.2)	270 (72.8)	901 (66.2)	0.633	
Missing	9 (3)	8 (3.3)	13 (2.9)	3 (0.8)	33 (2.4)		
Lifetime history of sexual abuse							
Yes	84 (27.8)	41 (16.7)	53 (12)	40 (10.8)	218 (16)	< 0.001	
No	212 (70.2)	199 (80.9)	385 (87.1)	330 (88.9)	1126 (82.7)	< 0.001	
Missing	6 (2)	6 (2.4)	4 (0.9)	1 (0.3)	17 (1.2)		

^aFor this variable overall age was divided by 5; coefficients represent 5-year age increases

Table 2

HIV clinical characteristics at baseline by study period, INI-Fiocruz women's cohort, 1996–2016

	1996–2000	2001–2005	2006–2010	2011–2016	Total	p-value trend	Linear coefficient (95% CI)
Total	302	246	442	371	1361		
Route of HIV exposure							
Sexual	284 (94)	240 (97.6)	430 (97.3)	357 (96.2)	1311 (96.3)	0.121	
Injection drug use	4 (1.3)	1 (0.4)	1 (0.2)	0 (0)	6 (0.4)		
Other ^a	14 (4.6)	5 (2)	11 (2.5)	14 (3.8)	44 (3.2)		
CD4 ⁺ T lymphocyte count							
Median (IQR)	361 (184, 554)	345 (208, 506)	462 (317, 631)	486 (270, 730)	421 (251, 608)	< 0.001	1.13 (1.12–1.15) ^b
< 200	77 (25.5)	52 (21.1)	44 (10)	55 (14.8)	228 (16.8)	< 0.001	
200–499	116 (38.4)	113 (45.9)	199 (45)	120 (32.3)	548 (40.3)	0.115	
500	91 (30.1)	58 (23.6)	190 (43)	166 (44.7)	505 (37.1)	< 0.001	
Missing	18 (6)	23 (9.3)	9 (2)	30 (8.1)	80 (5.9)		
HIV-1 RNA (copies/mL)							
< 400	48 (15.9)	116 (47.2)	236 (53.4)	255 (68.7)	655 (48.1)	< 0.001	
400	158 (52.3)	104 (42.3)	184 (41.6)	84 (22.6)	530 (38.9)	< 0.001	
Missing	96 (31.8)	26 (10.6)	22 (5)	32 (8.6)	176 (12.9)		
ART use							
No ART	111 (36.8)	103 (41.9)	228 (51.6)	114 (30.7)	556 (40.9)	0.465	
ART but not cART	121 (40.1)	6 (2.4)	2 (0.5)	0 (0)	129 (9.5)		
cART	70 (23.2)	137 (55.7)	212 (48)	257 (69.3)	676 (49.7)	< 0.001	

^a Other exposures include: blood transfusion and maternal-to-child transmission^b For this variable CD4⁺ T lymphocyte count was divided by 50; coefficients represent 50 count changes

Table 3

Sexual and reproductive history at baseline by study period, INI-Fiocruz women's cohort, 1996–2016

	1996–2000	2001–2005	2006–2010	2011–2016	Total	p-value trend	Linear coefficient (95% CI)
Total	302	246	442	371	1361		
Age at first sexual intercourse							
Median (IQR)	17 (15, 20)	17 (15, 19)	16 (15, 18)	16 (15, 18)	17 (15, 18)	< 0.001	– 0.97 (– 0.96 to – 0.98)
< 15	41 (13.6)	34 (13.8)	89 (20.1)	85 (22.9)	249 (18.3)	< 0.001	
15–19	181 (59.9)	154 (62.6)	298 (67.4)	244 (65.8)	877 (64.4)	0.053	
20	77 (25.5)	54 (22)	47 (10.6)	40 (10.8)	218 (16)	< 0.001	
Missing	3 (1)	4 (1.6)	8 (1.8)	2 (0.5)	17 (1.2)		
Age at first pregnancy							
Median (IQR)	20 (17, 23)	19 (17, 21)	18 (17, 21.5)	19 (17, 21)	19 (17, 22)	0.020	– 0.99 (– 0.98 to – 1.00)
< 20	136 (45)	120 (48.8)	247 (55.9)	198 (53.4)	701 (51.5)	0.008	
20	142 (47)	94 (38.2)	152 (34.4)	124 (33.4)	512 (37.6)	< 0.001	
Never pregnant	18 (6)	25 (10.2)	35 (7.9)	47 (12.7)	125 (9.2)	0.010	
Missing	6 (2)	7 (2.8)	8 (1.8)	2 (0.5)	23 (1.7)		
Age at first birth							
Median (IQR)	21 (18, 24)	20 (18, 23)	19 (17, 23)	19 (17, 23)	20 (17, 23)	0.001	– 0.98 (– 0.97 to – 0.99)
< 20	101 (33.4)	79 (32.1)	193 (43.7)	161 (43.4)	534 (39.2)	< 0.001	
20	156 (51.7)	120 (48.8)	172 (38.9)	144 (38.8)	592 (43.5)	< 0.001	
Never pregnant or gave birth	40 (13.2)	39 (15.9)	70 (15.8)	64 (17.3)	213 (15.7)	0.172	
Missing	5 (1.7)	8 (3.3)	7 (1.6)	2 (0.5)	22 (1.6)		
Sexual partners in the past year							
0	64 (21.2)	68 (27.6)	78 (17.6)	92 (24.8)	302 (22.2)	0.875	
1	205 (67.9)	143 (58.1)	313 (70.8)	235 (63.3)	896 (65.8)	0.935	
2	31 (10.3)	24 (9.8)	40 (9)	37 (10)	132 (9.7)	0.843	
Missing	2 (0.7)	11 (4.5)	11 (2.5)	7 (1.9)	31 (2.3)		
Lifetime partners							
1	33 (10.9)	27 (11)	22 (5)	28 (7.5)	110 (8.1)	0.018	
2–4	136 (45)	96 (39)	153 (34.6)	120 (32.3)	505 (37.1)	< 0.001	
5–10	83 (27.5)	77 (31.3)	153 (34.6)	152 (41)	465 (34.2)	< 0.001	

	1996–2000	2001–2005	2006–2010	2011–2016	Total	p-value trend	Linear coefficient (95% CI)
11	47 (15.6)	39 (15.9)	75 (17)	55 (14.8)	216 (15.9)	0.908	
Missing	3 (1)	7 (2.8)	39 (8.8)	16 (4.3)	65 (4.8)		
Prior syphilis							
Yes	20 (6.6)	35 (14.2)	48 (10.9)	45 (12.1)	148 (10.9)	0.079	
No	244 (80.8)	205 (83.3)	385 (87.1)	289 (77.9)	1123 (82.5)	0.633	
Missing	38 (12.6)	6 (2.4)	9 (2)	37 (10)	90 (6.6)		
Prevalent oncogenic HPV ^a							
Yes	144 (47.7)	100 (40.7)	183 (41.4)	61 (43)	488 (43.1)	0.208	
No	156 (51.7)	137 (55.7)	237 (53.6)	71 (50)	601 (53.1)	0.935	
Missing	2 (0.7)	9 (3.7)	22 (5)	10 (7)	43 (3.8)		
Contraceptive method ^b							
Tubal ligation	51 (24.9)	51 (31.5)	65 (19.9)	53 (21.2)	220 (23.3)	0.079	
Hormonal and IUD	27 (13.2)	9 (5.6)	55 (16.9)	47 (18.8)	138 (14.6)	0.009	
Barrier	91 (44.4)	67 (41.4)	142 (43.6)	104 (41.6)	404 (42.8)	0.671	
Other less effective method	5 (2.4)	1 (0.6)	2 (0.6)	2 (0.8)	10 (1.1)		
No method	29 (14.1)	33 (20.4)	46 (14.1)	43 (17.2)	151 (16)	0.772	
Missing	2 (1)	1 (0.6)	16 (4.9)	1 (0.4)	20 (2.1)		
Dual contraceptive use ^b							
Yes	13 (6.3)	5 (3.1)	32 (9.8)	35 (14)	85 (9)	< 0.001 ^c	
No	190 (92.7)	156 (96.3)	278 (85.3)	214 (85.6)	838 (88.9)		
Missing	2 (1)	1 (0.6)	16 (4.9)	1 (0.4)	20 (2.1)		
Gravidity							
Median (IQR)	3 (2, 4)	3 (2, 4)	2 (1, 4)	2 (1, 4)	3 (1, 4)	0.034	−0.97 (−0.94 to −1.00)
0	18 (6)	25 (10.2)	35 (7.9)	47 (12.7)	125 (9.2)	0.010	
1–2	124 (41.1)	89 (36.2)	189 (42.8)	139 (37.5)	541 (39.8)	0.728	
3	160 (53)	132 (53.7)	218 (49.3)	185 (49.9)	695 (51.1)	0.290	
Parity							
Median (IQR)	2 (1, 3)	2 (1, 3)	2 (1, 3)	2 (1, 3)	2 (1, 3)	0.146	1.03 (0.99–1.06)
0	40 (13.2)	39 (15.9)	70 (15.8)	64 (17.3)	213 (15.7)	0.172	
1–2	177 (58.6)	130 (52.8)	232 (52.5)	181 (48.8)	720 (52.9)	0.017	

	1996–2000	2001–2005	2006–2010	2011–2016	Total	p-value trend	Linear coefficient (95% CI)
3	85 (28.1)	77 (31.3)	140 (31.7)	126 (34)	428 (31.4)	0.111	
Lifetime history of induced abortion							
Yes	125 (41.4)	91 (37)	115 (26)	82 (22.1)	413 (30.3)	< 0.001	
No	172 (57)	151 (61.4)	325 (73.5)	286 (77.1)	934 (68.6)	< 0.001	
Missing	5 (1.7)	4 (1.6)	2 (0.5)	3 (0.8)	14 (1)		
Lifetime history of spontaneous abortion							
Yes	47 (16.5)	39 (17.6)	112 (27.5)	84 (25.9)	282 (22.8)	0.002	
No	232 (81.7)	178 (80.5)	293 (72)	237 (73.1)	940 (76.1)	< 0.001	
Missing	5 (1.8)	4 (1.8)	2 (0.5)	3 (0.9)	14 (1.1)		

^aThere were 229 (16.8%) women enrolled in 2013 or later who were excluded from this variable, as HPV results were not routinely collected after this time

^bThere were 302 (22.2%) women who were not sexually active within the past year and 224 (16.5%) post-menopausal women who were excluded from analysis of this variable. There were 3 IUD users total, who were grouped with hormonal contraceptive users. None of the women in our sample used implants. Other less effective methods included spermicide, withdrawal, and rhythm methods

^cFisher's exact test