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Predictive Factors for HIV Seroconversion Among Women Attending an Urban Health Clinic: a Matched Case Control Study in Atlanta, GA

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Master of Public Health

Epidemiology

_____

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Predictive Factors for HIV Seroconversion Among Women Attending an Urban Health Clinic: a Matched Case Control Study in Atlanta, GA

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An abstract of

A thesis submitted to the Faculty of the
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Abstract

Predictive Factors for HIV Seroconversion Among Women Attending an Urban Health Clinic: a Matched Case Control Study in Atlanta, GA

By Pauline Harrington

Objective: To more accurately predict women at greatest risk for HIV, we conducted an individually-matched case control study using data from women who attended an urban health clinic in Atlanta, GA to identify risk factors associated with HIV seroconversion.

Methods: We obtained data from women who sought care at Fulton County Board of Health Sexual Health Clinic between 2011 and 2016. Cases were women who seroconverted before 2018 but after having at least one clinician assisted visit (CAV) with the clinic prior to their date of HIV diagnosis. Controls were women who visited the clinic in this same time frame but remained HIV negative. Controls were individually matched to cases in a 2:1 matching ratio on race, age at first CAV (± one year of age), and date of first CAV (± three calendar months). Clinical characteristics and risk factors between cases and controls were compared using Chi-square and Fisher's exact tests. Bivariate and multivariate conditional logistic regression were performed to develop a model for predicting probability of HIV seroconversion. We evaluated our predictive model using the global null hypothesis.

Results: Having a history of gonorrhea, multiple gonorrhea episodes, a history of syphilis, a greater number of sex partners in the past 2 months, anal sex, history of injection drug or crack cocaine use, a history of exchanging drugs/money for sex, and heterosexual sex with more than one sex partner in the last month were independently associated with HIV seroconversion. After conducting backward selection from a fully adjusted model, the predictors that remained in the model were: having a history of syphilis, anal sex, and injection drug or crack cocaine use. We obtained the following formula: ln(odds HIV seroconversion)= 1.596 (history of syphilis) + 1.073 (anal sex) + 3.459 (injection drug or crack cocaine use). Women having all of those risk factors were six times more likely to seroconvert than similar women without any of those factors.

Conclusion: Our results offer clinical insights into which women are most at-risk for HIV, and therefore best candidates for initiating HIV prevention interventions like pre-exposure prophylaxis (PrEP) for HIV within a HIV "hotspot" in the South.

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Background/Literature Review

In the early 1990's, limited research existed regarding human immunodeficiency virus (HIV) among women (1). Over the past 20 years, it has been recognized that the burden of HIV among women has grown considerably. In 2016, women made up about a quarter of the newly diagnosed HIV cases in the U.S. (1 – 5). An estimated 85% of these new infections among women are acquired through heterosexual transmission (4).

HIV in women is disproportionately concentrated among poor urban women of racial/ethnic minority groups (2, 6, 7). Eighty percent of HIV infections in women are among non-Hispanic Black and Hispanic women, who make up roughly one-third of the American female population (8, 9). For African American women, HIV/acquired immunodeficiency syndrome (AIDS) is a leading cause of death, and their risk of HIV is 20 times that of white women's risk (7, 8, 10, 11).

The southern region of the U.S. has the highest incidence rate of HIV infection in the country, with its rate increasing faster than that of any other region in the country (12, 13). The South contains 37% of the U.S. population, but accounts for 44% of people living with diagnosed HIV (1, 12). Specifically, new HIV diagnoses among Black women are increasing in the South (14).

Georgia ranks 3rd highest in lifetime HIV risk in the U.S. (10). Fulton County is in the top 3 counties in Georgia with the highest HIV burden and is ranked 6th among all counties in the U.S. for highest rate of new HIV diagnoses in the U.S. (15). In 2019, it was named one of 48 "hotspot" counties most necessary to target in the HHS Ending the HIV Epidemic campaign (16). While the county holds 10% of Georgia's population, it

accounts for 25% of its HIV cases (15). Fifteen percent of HIV cases in Fulton County are among women (15). Among these women, 83% of the new HIV cases are non-Hispanic Black women and 95% are as a result of heterosexual contact (15).

Generally, behavioral risk factors for HIV include injection drug use, exchanging sex for drugs and money, inconsistent condom use, and having a high number of sexual partners (2, 4, 9, 10, 17, 18). Demographic risk factors include poverty, race, unstable housing situation, and psychological distress/mental health (2, 4, 9, 10, 17, 18). Studies have shown that women have a higher physiological risk of contracting HIV and other sexually transmitted infections (STI) compared to men since the vagina is an ideal environment for bacteria and viruses to thrive (19 – 21). Additionally, having a STI increases the risk of acquiring HIV (19, 21, 22). Because women are less likely to experience or recognize symptoms for STIs than me, many infections go untreated for longer, thus making women more susceptible to HIV (19, 21, 22).

While risk factors for HIV among MSM (men who have sex with men) have been well-characterized, less is known about HIV risk factors for women specifically (8). As evidenced by how the same STIs can differentially affect HIV risk in men versus women, HIV risk factors can be similar between genders, but not entirely the same. Despite the high HIV burden among minority women, very few epidemiologic studies have assessed risk factors for HIV among Black women in the U.S., and more specifically among Black women within HIV "hotspots" in the South (14). Using clinical data obtained on women seeking care at the Fulton County Board of Health Sexual Health Clinic from 2011 – 2016, the goal of this matched case control study was to identify factors associated with

HIV seroconversion in an effort to more effectively identify women at greatest risk for HIV and guide them towards strategies to prevent HIV acquisition.

Methods

Study design and population

Cases and controls for this retrospective matched case-control study were selected from the population of women who sought care at the Fulton County Board of Health (FCBOH) Sexual Health Clinic (SHC) between 2011 to 2016. A case was defined as any woman who seroconverted before 2018 but after having at least one clinician assisted visit (CAV) on record prior to her date of HIV diagnosis. All HIV-negative women seeking care at the SHC during this timeframe of interest were examined for potential inclusion as cases. Exclusion criteria included: having an HIV diagnosis prior to 2011, being diagnosed with HIV in the same month and year as the first visit to the SHC, and not having a CAV on record prior to date of HIV diagnosis. HIV status was confirmed on all women via a cross-check with the Enhanced HIV/AIDS Reporting System (eHARS) database facilitated through a data request to the Georgia Department of Public Health.

All women who remained HIV negative (as verified via eHARs) between 2011 to 2016 and had at least one CAV on record were considered for selection as controls. Controls were individually matched to cases in a 2:1 matching ratio on race, age at first CAV (± one year of age), and date of first CAV (± three calendar months). Matching on date of first CAV was to control for variations in clinic-level factors such as any changes in personnel, patient triage processes and/or electronic health records (EMR) documentation that could have affected collection and documentation of patient data. This study protocol was reviewed and approved by both the institutional review boards of the Georgia Department of Public Health and Emory University.

Statistical analysis

Demographic and risk factor data were obtained from electronic SHC medical records associated with the first CAV visit on record for all women who visited the SHC within the timeframe of interest (2011 – 2016). Demographic data included age, race, and ethnicity. Risk factor data included history and number of STI episodes and gynecological infections (e.g. gonorrhea, chlamydia, trichomoniasis, syphilis, and bacterial vaginosis), self-reported sexual behaviors (e.g. sex of sexual partners, number of sex partners, condom use, type of sex, sexual contact with high HIV risk, exchanging drugs/money for sex, and heterosexual sex in the last month), and self-reported drug use (e.g. injecting drug or crack cocaine use). Because no women in our sample had more than one episode of syphilis, no analyses beyond simply having a history of syphilis were conducted. Due to substantial missingness of data on the condom use variables, we created a secondary summary condom variable to describe consistent vs. inconsistent condom use. This variable utilized any available data from the three original condom use variables: condom use during last sex (answer options including: yes or no), condom use during regular sex (answer options including: always, never, or sometimes), and condom use during casual sex (answer options including: always, never, or sometimes). If the participant used a condom during their last sexual encounter, always used a condom during regular sex, and always used a condom during casual sex, then they were considered to have consistent condom use. If one or two of these variables was missing but any others reflected consistent condom use based on the previously listed criteria, they were also considered a consistent condom user. If a participant responded to any of the original condom use variables with responses that indicated anything less than routine

use (e.g. they did not used a condom during last sexual encounter, never uses a condom during regular sex, and sometimes uses a condom during casual sex), then they were categorized as an inconsistent condom user.

Comparisons of characteristics between cases and controls were analyzed using Chi-squared test or Fisher's exact test for categorical variables to assess factors associated with seroconversion. Variables with a p-value less than 0.1 were considered statistically significant and evaluated in bivariate analysis. To establish a model for predicting probability of an HIV seroconversion in the studied population, we conducted conditional logistic regression to assess factors independently associated with HIV seroconversion. Variables found to have a significant relationship with seroconversion (p-value less than 0.1) in bivariate analyses were included in an adjusted model; variables were then evaluated for significance using backward elimination (using a p-value less than 0.05 as criteria to stay in the model) to obtain a parsimonious predictive model. To evaluate whether all regression coefficients are zero in this predictive model, we analyzed the joint significance of the parameters in the model by using the global null hypothesis. Statistical analyses were performed using SAS 9.4 (SAS Institute; Cary, NC).

Results

A total of 18,878 women sought care at FCBOH SHC between 2011 and 2016. Five-hundred and three (3%) were excluded due to being HIV positive prior to their first encounter with the SHC during this timeframe of interest (Figure 1). Ninety-four more (0.5%) were excluded for being HIV positive on their first encounter at the clinic. Of the remaining women, 110 seroconverted between 2011 – 2018. Of these, 30 (27%) were excluded due to not having a CAV on record with the SHC prior to the date of HIV diagnoses. From the remaining 18,171 women who remained HIV negative for the duration of this timeframe, 3,753 (21%) were ineligible for control selection because they did not have a CAV on their first visit the SHC in the timeframe of interest. The remaining 14,418 women comprised the pool of possible controls. Two controls per case were then randomly selected from a list of eligible controls meeting the matching criteria for each case, resulting in a total of 160 controls.

Compared to controls, cases were more likely to have had a history of gonorrhea ($p=0.04$), more gonorrhea episodes ($p=0.09$), a history of syphilis ($p=0.02$), a greater number of sex partners in the past 2 months ($p=0.02$), anal sex ($p=0.05$), history of injection drug or crack cocaine use ($p<0.0001$), history of exchanging drugs/money for sex ($p=0.02$), and heterosexual sex with more than one sex partner in the last month ($p=0.05$) (Table 1).

In our bivariate conditional logistic regression analyses, all of the aforementioned factors were independently associated with HIV seroconversion (Table 2). The strongest predictors were injection drug/crack cocaine use (OR=20.5, 95% CI: 2.6, 159.8), having

exchanged drugs or money for sex (OR= 3.6, 95% CI: 1.2, 10.7), history of syphilis (OR=3.6, 95% CI: 1.2, 10.7), and anal sex (OR=2.2, 95% CI: 0.9, 5.4). After conducting backward selection from a fully adjusted model, the predictors that remained in the model were: having a history of syphilis, anal sex, and injection drug or crack cocaine use. We obtained the following formula: ln(odds HIV seroconversion)= 1.596 (history of syphilis) + 1.073 (anal sex) + 3.459 (injection drug or crack cocaine use). Using this model, we found that women who had a history of syphilis, had anal sex, and used injection drugs or crack cocaine were 6.2 times more likely to HIV seroconvert than women who did not have any of these risk factors. We used the global test hypothesis to conclude that all of the coefficients within the model are statistically significantly different than zero (p-value <0.0001), indicating there is a joint effect of all explanatory variables in the model.

Discussion

The objective of this study was to analyze and identify factors associated with HIV seroconversion among women seeking care at the Fulton County Board of Health Sexual Health Clinic from 2011 – 2016 in an effort to more accurately predict which women are at greatest risk for HIV. We found that having a history of syphilis, anal sex, and injection drug or cocaine use were the strongest predictive factors for HIV; women having all of those risk factors were six times more likely to seroconvert than similar women without any of those factors.

As previously reported, general risk factors for HIV include STI history and injection drug or crack cocaine use (2, 19, 21, 22). Our study also aligns with these findings; having a STI history, specifically syphilis, and injection drug or crack cocaine use were risk factors for HIV seroconversion among this population of women. Additionally, in previous studies, it has been found that condomless anal sex is a risky sexual behavior that results in HIV acquisition; an estimated 40% of HIV cases among 18 to 34-year-old women is due to anal sex (3). Our results again indicate that anal sex is a risk factor for HIV seroconversion among women.

Where our study deviates from previous studies is in regard to risk posed by exchanging drugs or money for sex. While this has been a significant risk factor in other studies of HIV acquisition, this variable failed to maintain significance in a model adjusting for other risk factors (6). One hypothesis for why this could be is that other studies that have explored behavioral risk factors for HIV or other STIs have obtained their study participants from more community-based venues rather than health clinics. In

a community-based study where women were recruited from their residences in New York City, heterosexual women who exchange money or goods for sex were found to be at high risk for HIV acquisition (24). Another study based in in Houston, Texas, where they recruited participants from fast-food restaurants, residences, bars, street corners, and post offices, also found that exchanging money or drugs for sex leads to high-risk sexual behaviors, and therefore results in increased risk for HIV infection (25). By having identified study subjects from a health clinic, we may have introduced a bias towards women more likely to seek any type of health care which may have resulted in a selection bias against women working in the sex trade. The Centers for Disease Control and Prevention claim that persons who exchange money/drugs for sex are less likely to seek healthcare because they are unsure where to access services (26). Furthermore, since there is a strong correlation between those who exchange money or drugs for sex and those who are injection drug or crack cocaine users (26), our predictive model may still encompass women in who engage in exchanging money or drugs for sex that way.

While this study aligns with existing literature that anal sex, injection drug or crack cocaine use, and history of syphilis are strong predictors of HIV, our results indicate that these risk factors are strongly associated with HIV among this particular high-risk population of women in Fulton County. These results help discern the risk factors that are necessary to focus preventative interventions for women, and more specifically underserved Black women, in Fulton County, but also potentially other "hotspots" of HIV in the South.

Limitations

This study has some important limitations. First, among our initial cohort of women, there may have been additional seroconversions if the woman moved out of state. We were only able to verify HIV status among women who remained in Georgia during the period of interest With that said, because we were able to verify the HIV status of all women in the initial cohort through a cross-check with Georgia's eHARs database, we do feel confident in the HIV statuses of all women selected for this study, assuming they remained Georgia residents for the entire follow-up period. Another limitation is that we can only draw conclusions on women who seek care at FCBOH, a safety net health clinic which has a high burden of homeless and low SES patients. For the purposes of identifying women at greatest risk for HIV in Atlanta, the population this clinic serves are precisely the women at greatest risk for HIV in Atlanta: young, Black women (10). Additionally, we only looked at one snapshot in time. We obtained our cases and controls from 2011 – 2016, which means some of the women we excluded for only coming into FCBOH once could have actually been returning clients, having had their first visit before our timeframe of interest. And lastly, all variables related to sexual behaviors, history of STIs and drug use captured during a CAV visit are self-reported by the patients, thus introducing recollection and social desirability biases. Because the data collected on these sensitive topics were obtained during a clinical encounter, we hope the confidentiality of this setting contributed to patients' willingness to report on these topics with higher degrees of honesty than had the data been collected in other more public venues.

Conclusion

Understanding what factors place women at risk for HIV is a timely topic as we embark on a national goal to end the HIV epidemic in the U.S. within 10 years (16). Using our predictive model, we can more accurately identify women at risk for HIV seroconversion in Fulton County, GA, one of the 48 "hotspots" for HIV incidence. Early identification can hopefully result in getting more at-risk women on pre-exposure prophylaxis (PrEP) and considering additional positive modifications to their sexual practices (16).

Future Directions

A study published in 2018 by Sales et al. established that there was no valid HIV risk assessment tool for identifying women who are at high risk for HIV seroconversion (10). The assessment tool used for MSM leaves out important risk factors unique to women, such as substance abuse, gender-based violence, and intimate partner violence (10, 20). While we lacked any data on violence for the women included in this sample, that is an area worth exploring, perhaps by adding questions about violence and abuse to the series of questions that SHC clinicians ask during a CAV. Additionally, PrEP awareness and promotion for MSM has increased rapidly in the Southern U.S. as a result of the current HIV epidemic, but the few studies that have focused on women show low PrEP awareness (10). In 2014, a study was done that concluded less than 10% of women at high risk for HIV seroconversion had heard of PrEP (10). The intention of this study – to identify risk factors for HIV seroconversion among women and to build a predictive model for HIV based upon those factors – was to contribute to the clinic's ability to not only more accurately identify women at greatest risk, but to quantify that increased risk. The quantification of that risk allows clinicians to be able to tell female patients how much more at risk they are for HIV because they have certain factors. This awareness may then be beneficial to affecting change in risk behaviors or accepting new preventive health measures like PrEP.

To echo Hodder et al., further research is necessary to find successful interventions that decrease women's HIV risk in the U.S., and these interventions need to be feasible to target vulnerable populations, such as Black women (8). Our findings will help other local public health practices to use existing EMR data to predict which women

are at high risk for HIV seroconversion and target those individuals for PrEP use. Our findings are especially important for the HIV hotspot of Atlanta, GA, since often women with HIV or at risk for HIV in this area are overshadowed by the MSM population.

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Tables

Table 1. Clinical characteristics of 80 cases (HIV seroconversion) and 160 matched control subjects

Characteristic		Cases (n=80) Number (%)	Controls (n=160) Number (%)	p
Age*		32 (20)	31 (19)	N/A
Race				
	Black/African American	74 (93)	148 (93)	N/A
	White	6 (7)	12 (7)	
Ethnicity				
	Hispanic	1 (1)	6 (4)	0.43
	Non-Hispanic	79 (99)	154 (96)	
History of gonorrhea				
	No	43 (54)	108 (68)	0.04
	Yes	37 (46)	52 (32)	
Number of gonorrhea episodes				
	0	43 (55)	108 (69)	0.09
	1	25 (32)	39 (25)	
	2	8 (10)	8 (5)	
	3	2 (3)	1 (1)	
History of chlamydia				
	No	36 (46)	80 (51)	0.46
	Yes	43 (54)	78 (49)	
Number of chlamydia episodes				
	0	36 (48)	80 (52)	0.87
	1	30 (40)	51 (33)	
	2	6 (8)	15 (10)	
	3	3 (4)	6 (4)	
	4	0 (0)	1 (1)	
History of trichomoniasis				
	No	47 (59)	105 (66)	0.30
	Yes	33 (41)	55 (34)	
Number of trichomoniasis episodes				
	0	47 (64)	105 (68)	0.63
	1	20 (27)	38 (24)	

	2	4 (6)	10 (6)	
	3	1 (1)	1 (1)	
	4	1 (1)	0 (0)	
	≥5	1 (1)	1 (1)	
History of bacterial vaginosis				
	No	51 (64)	98 (62)	0.75
	Yes	29 (36)	61 (38)	
Number of bacterial vaginosis episodes				
	0	51 (67)	98 (66)	0.88
	1	16 (21)	31 (21)	
	2	2 (3)	7 (5)	
	3	2 (3)	7 (5)	
	4	2 (3)	2 (1)	
	≥5	3 (3)	4 (2)	
History of syphilis				
	No	70 (88)	152 (96)	0.02
	Yes	10 (12)	7 (4)	
Sex with				
	Both	4 (5)	4 (2)	0.58
	Females	2 (2)	3 (2)	
	Males	74 (93)	153 (96)	
Number of sex partners in the past 2 months				
	0	8 (10)	10 (6)	0.02
	1	46 (58)	111 (70)	
	2	12 (15)	23 (14)	
	3	2 (3)	10 (6)	
	4	4 (5)	1 (1)	
	≥5	7 (9)	4 (3)	
Number of sex partners in the past 12 months				
	0	0 (0)	2 (1)	0.38
	1	32 (41)	77 (49)	
	2	20 (25)	44 (28)	
	3	9 (11)	15 (9)	
	4	5 (6)	6 (4)	
	≥5	13 (17)	14 (9)	
Consistent condom use				
	No	72 (90)	145 (91)	0.88

	Yes	8 (10)	15 (9)	
Vagina to penis sex				
	No	1 (1)	4 (2)	0.67
	Yes	79 (99)	156 (98)	
Anal sex				
	No	68 (86)	148 (94)	0.05
	Yes	11 (14)	10 (6)	
Sexual contact with bisexual male				
	No	79 (99)	159 (99)	1.00
	Yes	1 (1)	1 (1)	
Sexual contact with injection drug user				
	No	80 (100)	160 (100)	1.00
	Yes	0 (0)	0 (0)	
Sexual contact with known HIV positive person				
	No	80 (100)	160 (100)	1.00
	Yes	0 (0)	0 (0)	
Injecting drug or crack cocaine use				
	No	69 (86)	158 (99)	<0.0001
	Yes	11 (14)	2 (1)	
Exchanged drugs/money for sex				
	No	71 (89)	155 (97)	0.02
	Yes	9 (11)	5 (3)	
Heterosexual sex with more than 1 sex partner in last month				
	No	51 (64)	121 (76)	0.05
	Yes	29 (36)	39 (24)	

Cases and controls matched by age, race, and date of first CAV visit.

*Reported as median (IQR)

Table 2. Bivariate and multivariate effects of risk factors for HIV seroconversion among women seeking care at FCBOH Sexual Health Clinic, 2011 – 2016

Risk Factor	Crude OR (95% CI)	Fully adjusted OR (95% CI)	Final Predictive OR (95% CI)
History of gonorrhea	1.8 (1.0, 3.0)	0.7 (0.2, 3.2)	-
Number of gonorrhea episodes	1.7 (1.1, 2.5)	1.7 (0.6, 4.9)	-
History of syphilis	3.1 (1.1, 8.6)	4.6 (1.3, 16.5)	4.9 (1.4, 16.9)
Number of sex partners in the past 2 months	1.3 (1.0, 1.6)	1.0 (0.7, 1.4)	-
Anal sex	2.2 (0.9, 5.4)	3.1 (1.0, 9.9)	2.9 (1.0, 8.3)
Injecting drug or crack cocaine use	20.5 (2.6, 159.8)	24.6 (2.5, 239.8)	34.8 (3.7, 328.1)
Exchanged drugs/money for sex	3.6 (1.2, 10.7)	2.3 (0.5, 11.4)	-
Heterosexual sex with more than 1 sex partner in last month	1.8 (1.0, 3.2)	1.1 (0.5, 2.4)	-

Figures and Figure Legends

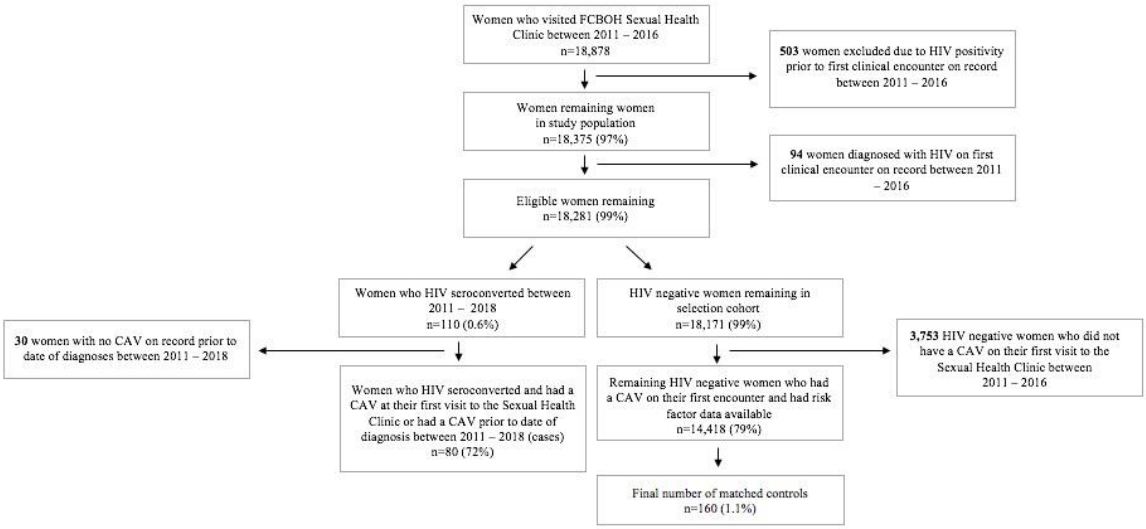

Figure 1. Flow diagram for inclusion and exclusion of participants.