HIV Incidence in Women at Risk for HIV Acquisition in the United States: HPTN 064 (ISIS Study)

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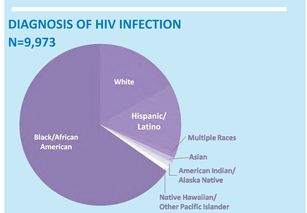
W-159

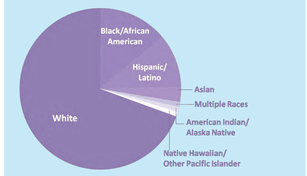
HPTN 064

BACKGROUND

- Approximately 25% of new HIV infections in the US occur in women; 66% of those are in black women (Figure 1).[1]
- Women acquire HIV infection most commonly through heterosexual transmission (Figure 2)
- Limited availability of HIV incidence has impeded design of prevention interventions and trials for US women at risk for HIV acquisition.
- Past efforts have failed to identify populations of US women with sufficient HIV incidence to enable conduct of HIV prevention trials with an HIV incidence endpoint.
- We assessed HIV incidence and factors that may impact HIV risk among US women using novel recruitment strategies and innovative methods of incidence determination.

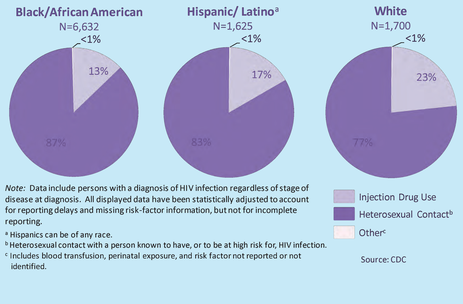
Figure 1: Diagnoses of HIV Infection and Population Among Adult and Adolescent Females by Race/ Ethnicity, 2009—40 States[1]





Source: CDC

Figure 2: Diagnoses of HIV Infection among Adult and Adolescent Females, by Race/Ethnicity and Transmission Category, 2009 – 40 States and 5 U.S. Dependent Areas[2]



Note: Data include persons with a diagnosis of HIV infection regardless of stage of disease at diagnosis. All displayed data have been statistically adjusted to account for reporting delays and missing risk-factor information, but not for incomplete reporting.

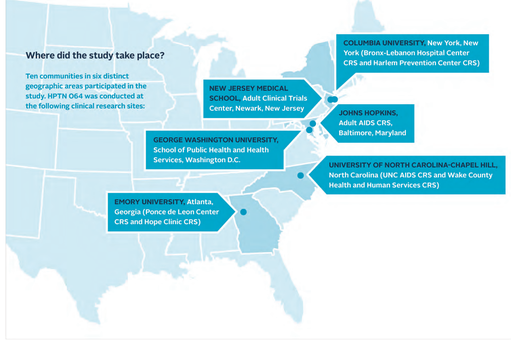
[a] Hispanics can be of any race.
[b] Heterosexual contact with a person known to have, or to be at high risk for, HIV infection.
[c] Includes blood transfusion, perinatal exposure, and risk factor not reported or not identified.

Source: CDC

STUDY DESIGN

- Multi-site, longitudinal cohort study with prospective and retrospective components.
- Eligible women were enrolled from 10 US communities (in six geographic locations) with relatively high reported HIV prevalence (Figure 3).
- Detailed ethnographic mapping identified recruitment venues frequented by women within areas of participating communities with high HIV prevalence and poverty rates.

Figure 3: ISIS Study Sites



METHODS

Study Design

- Participants were followed from 6-12 months
- Rapid HIV testing at baseline and every 6 months
- Audio computer-assisted self interviews (ACASI) at baseline, and every 6 months
  - ACASI domains included: socio-economic factors, food insecurity, mental health (depression and post-traumatic stress disorder), perceived general health status, sexual behavior (including concurrency), history of sexually transmitted infections (STIs), domestic violence, and social support.
- Monthly phone contacts and updates of locator information encouraged.
- Qualitative substudy consisting of semi-structured interviews and focus groups was conducted in four communities.
- HIV incidence was assessed in four ways (See Poster W-229 for more details): Analysis of (1) recent infection at enrollment, among women who had a positive Western blot (WB) at enrollment (HIV+); recent infection was analyzed using a multi-assay algorithm (MAA, window period estimated to be between 3 and 9 months) that defines recent infection as BED capture immunoassay (BED) <1.0 normalized optical density units (OD-n) + avidity index <80% (using an avidity assay based on the BioRad ½+0 ELISA) + CD4 cell count > 200 cells/mm^3 + viral load > 400 copies/ml, (2) acute infection at enrollment (HIV RNA positive with an non-reactive EIA or a reactive EIA with a negative or indeterminate WB, identified using the ARCHITECT HIV Ag/Ab Combo HIV assay [COMBO] or an unpooled HIV RNA assay), (3) HIV seroconversion (rapid testing with WB confirmation), and (4) acute infection at study exit (acute infection as defined above), identified using the COMBO assay).

Inclusion Criteria and Definitions

Eligible individuals were:

- 18 to 44 years of age.
- Self-identified as being a woman (transgender individuals were eligible).
- Had reported unprotected (i.e., without a condom) vaginal and/or anal sex with a man in the 6 months prior to enrollment.
- Resided in a census tract or zip code with high HIV prevalence and poverty (referred to as primary prevention area, PPA).
- Reported at least one of the following:
  1. Individual risk factor: Reported one or more of the following in the past 6 months, except for incarceration which could have occurred within the past 5 years: a) illicit injection and/or noninjection drug use (e.g. heroin, cocaine, crack cocaine, methamphetamine, and/or prescription drugs used outside the oversight of a medical professional), b) alcohol dependence (defined as CAGE Score ≥ 2)[3], c) binge drinking defined as four or more drinks at one time, d) incarceration (jail and/or prison ≥ 24 hours), e) history of self-reported STIs: gonorrhea, Chlamydia, trichomonas, or syphilis, f) exchange of sex for commodities (e.g. drugs, money, shelter).
  2. Sexual partner risk factor: Reported male sexual partner in the past 6 months with a history of the following (in past 6 months, except for incarceration which could have occurred within the past 5 years): reported history of use of illicit injected or noninjected drugs, and/or STIs, and/or HIV seropositive diagnosis, and/or incarceration, and/or history of binge drinking defined as 5 or more drinks at one time and/or alcohol dependence (defined as CAGE Score ≥ 2)[3].

Exclusion criteria

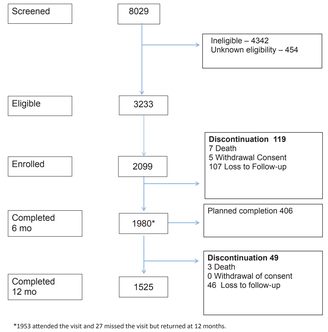
- Self-reported history of a previous positive HIV test.
- Current enrollment in an HIV prevention trial or current/past participation in an HIV vaccine trial.
- Intention to move or travel for more than two consecutive months during the follow-up period.

RESULTS

Screening and enrollment took place between May 2009 and August 2010. 8,029 women were screened and 2,099 women were enrolled (Figure 4).

- 88% black, 8% white, 12% Hispanic.
- 44% with annual household income <$10,000.
- Characteristics and risk behaviors are shown (Table 1).
- Thirty-two women (1.5%) were newly diagnosed as HIV-infected at enrollment (baseline). Two additional women had acute infection at baseline (estimated annual incidence 2.52%, 95% CI: 0.60-10.7). Four women acquired HIV during follow-up (estimated annual incidence 0.24%,95% CI: 0.09-0.65). The annual incidence estimate based on acute infection at enrollment was significantly higher than the annual incidence estimate based on seroconversion (P=0.027) (Table 3).
- High mortality rate of participants; ten participants died during follow-up with age-adjusted mortality rate of 0.61%/year, (expected mortality rate of this age cohort is 0.11%/year.[4]
- HIV incidence in HPTN 064 (ISIS) was substantially (5 times) higher than CDC 2009 annual HIV incidence estimate overall for US black women (0.05%)[5] and comparable to estimated HIV adult incidence rates in parts of sub-Saharan Africa (Congo 0.28% and Kenya 0.53%),[6] underscoring the substantial HIV transmission to US women that is occurring.

Figure 4: Study Flow Chart: Recruitment, Retention and Discontinuation Reasons



*1953 attended the visit and 27 missed the visit but returned at 12 months.

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RESULTS (cont.)

Table 1: Baseline Characteristics of the Study Cohort n=2,099

		Number[a]	% [or IQR][a]
Age		29[b]	[23-38][b]
Race[c]	Black	1851	88.2
	White	163	7.8
	Other	152	7.2
Hispanic Ethnicity		245	12
Education	Less than high school graduation	777	37.0
	High school graduation	772	36.8
	Education beyond high school	550	26.2
Marital Status	Single/Separated/Divorced/Widowed	1258	59.9
	Married/Not married, living with partner	638	30.4
	Other/Unknown	203	9.7
Annual Household Income	<$10,000	932	44.4
	$10,000 - $20,000	225	10.7
	>$20,000	197	9.4
	Unknown	745	35.5
Food Insecurity	Concerned about having sufficient food for self and/or family	971	46

[a] Number and percentage are shown for all variables except for age.
[b] Median and interquartile range are shown for age.
[c] Participants could report more than one race.

Table 2: Reported Characteristics at Baseline

FACTOR	NUMBER	% or [IQR]
Any illicit drug (excluding cannabis)[1]	576	27.4
Cocaine use[1]	365	17.4
Opioid use[1]	260	12.4
Binge drinking[1,2]	827	39.4
Intravenous drug use	84	4
STI[3] (one or more)	324	15.4
Exchange sex	776	37
Number of partners in past 6 months	2	[1 – 3]
Condom used at last vaginal sex	376	18
HIV status of man with whom had last vaginal sex unknown	865	41
Condom used at last anal sex	143	18

[1] At least monthly
[2] Four or more drinks on one occasion
[3] Gonorrhea, syphilis, trichomonas, or chlamydia

Table 3: HIV Incidence Estimates*

Events Analyzed	# women analyzed	# events	Window period	Annual incidence estimate	95% CI
Acute infection at enrollment	2,064	2	2 weeks	2.52%**	0.60-10.7%
Seroconversion	1,951	4	--	0.24%**	0.09-0.65%
Recent infection at enrollment	32 HIV+	2	3 months	0.36%	0.08-1.61%
	2067 HIV-		6 months	0.18%	0.40-0.80%
			9 months	0.12%	0.03-0.53%
Acute infection at study exit	1,913	0	2 weeks	0.0%	0.0-4.09%

* 32 HIV+ women tested with the MAA; 2067 seronegative women.
** P=0.027

Table 4: Univariate Analysis of Potential Factors Associated with HIV Infection *Relative Risk (95% Confidence Interval)*

Participant Risk Factors	Prevalent HIV Infection (n=30)	Incident HIV Infection (n=8)
Substance Use[a]	2.52 (1.22, 5.21)[b]	0.57 (0.06, 3.18)
Concurrency[a]	1.13 (0.55, 2.33)	0.57 (0.06, 3.16)
HS education (≥ HS vs. < HS)	0.59 (0.29, 1.20)	0.97 (0.09, 6.26)
HS+ education (> HS vs. ≤ HS)	0.43 (0.15, 1.24)	0.93 (0.09, 5.20)
Income <$10K vs. >$20K	2.53 (0.33, 19.34)	0.64 (0.05, 33.52)
Food Insecurity[a]	0.57 (0.27, 1.21)	1.88 (0.37, 12.07)
Anal Sex[a]	0.59 (0.27, 1.33)	1.62 (0.30, 8.69)
Binge Drinking[a]	1.31 (0.64, 2.67)	0.90 (0.14, 4.64)
Age (27-33 vs. 18-26)	5.83 (1.22, 27.96)[b]	0.84 (0.08, 5.89)
Age (34+ vs. 18-26)	11.54 (2.71, 49.05)[b]	0.57 (0.05, 3.94)
Depressive symptoms	1.45 (0.68, 3.07)	1.09 (0.17, 5.60)
PTSD (pos vs. neg)[a]	0.63 (0.26, 1.54)	0.80 (0.08, 4.50)
Any History of Abuse	0.43 (0.18, 1.04)	1.01 (0.16, 5.20)
History of Childhood Abuse	0.93 (0.46, 1.91)	3.64 (0.65, 36.93)
Partners' Risk Factors		
Illicit Drug Use (Injection or noninjection)[a]	1.57 (0.77, 3.19)	1.08 (0.17, 5.56)
Incarceration[c]	0.61 (0.30, 1.25)	0.70 (0.13, 3.74)
Reported STI[a]	0.97 (0.30, 3.17)	0.0 (0.0, 5.13)
HIV Seropositive Diagnosis	8.19 (2.64, 25.42)[b]	0.0 (0.0, 47.90)
Binge Drinking[a]	1.82 (0.84, 3.96)	1.31 (0.26, 8.44)
Alcohol Dependence[a]	1.42 (0.70, 2.88)	1.42 (0.27, 7.64)

*Abbreviations: HS: high school; HS+: education beyond high school: K: thousands; PTSD: post-traumatic stress disorder; pos: positive; neg: negative; STI: sexually transmitted infection. Illicit drug use and binge drinking are at least weekly. The numbers shown are relative risk with 95% confidence intervals shown in parentheses.
[a] Within the previous 6 months.
[b] p<0.05
[c] Within the previous 5 years.

LIMITATIONS

- Few incident infections limited ability to identify specific risk factors associated with HIV transmission (Table 4).
- These results, are not generalizable to the general population of women as participant eligibility determined by geographic location and presence of personal or partner HIV risks.

CONCLUSIONS

- HIV incidence in the HPTN 064 (ISIS) cohort was substantially (5 times) higher than CDC 2009 annual HIV incidence estimate overall for US black women, suggesting that novel recruitment methods were successful in identifying US women at increased risk for HIV acquisition and underscoring the importance of focusing prevention efforts among similar populations in the US.
- Thirty-two women (1.5%) entered the study unaware of their HIV infection, suggesting that testing programs must improve coverage.
- While known HIV infection in a sexual partner was strongly associated with HIV infection in this study, more than 40% of women were unaware of their partner's HIV status, again emphasizing the importance of testing strategies as outlined in the National AIDS Strategy.[7]

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