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Evidence for HIV transmission across key populations: a longitudinal analysis of HIV and AIDS rates among Black people who inject drugs and Black heterosexuals in 84 large U.S. metropolitan areas, 2008–2016

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Abstract

Purpose: To assess cross-population linkages in HIV/AIDS epidemics, we tested the hypothesis that the number of newly diagnosed AIDS cases among Black people who inject drugs (PWID) was positively related to the natural log of the rate of newly diagnosed HIV infections among Black non-PWID heterosexuals in 84 large U.S. metropolitan statistical areas (MSAs) in 2008–2016.

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Methods: We estimated a multilevel model centering the time-varying continuous exposures at baseline between the independent (Black PWID AIDS rates) and dependent (HIV diagnoses rate among Black heterosexuals) variables.

Results: At MSA level, baseline (standardized β = 0.12) Black PWID AIDS rates and change in these rates over time (standardized β = 0.11) were positively associated with the log of new HIV diagnoses rates among Black heterosexuals. Thus, MSAs with Black PWID AIDS rates that were 1 standard deviation=higher at baseline also had rates of newly diagnosed HIV infections among Black non-PWID heterosexuals that were 10.3% higher. A 1 standard deviation increase in independent variable over time corresponded to a 7.8% increase in dependent variable.

Conclusions: Black PWID AIDS rates may predict HIV rates among non-PWID Black heterosexuals. Effective HIV programming may be predicated, in part, on addressing intertwining of HIV epidemics across populations.

Keywords

HIV; AIDS; Cross-population transmission; Black PWID; Black heterosexuals; Metropolitan statistical area

In 2019, the U.S. Department of Health and Human Services announced an initiative to reduce new infections in the country by at least 90% by 2030 [1]. Emerging evidence suggests that our ability to accomplish this ambitious goal may be strengthened by better understanding and intervening in HIV transmission dynamics across key populations bearing the disproportionate burden of the infection. One such population are Black heterosexual men and women—although Black people constitute only 13% of the U.S. population, HIV cases attributed to heterosexual transmission among Black people comprised 62% of all new HIV diagnoses in this transmission category in 2018. [15]. The role of structural determinants, including structural racism, in driving HIV rates among Black heterosexuals is well established [2–6]. However, scientific knowledge on the population-level influences of HIV infections in other epidemiological groups on HIV rates among Black heterosexual adults is limited.

The possibility of HIV transmission between key populations has been widely acknowledged for decades and is supported by empirical data from individual-level network and phylogenetic studies. Network-level studies show that many PWID are likely to have sexual relationships with noninjecting partners, including men who have sex with men (MSM) and heterosexuals [7–10]. Likewise, molecular HIV surveillance data indicate that 49% of HIV-infected male PWID in the U.S. had genetic viral sequences linked to MSM and 25% linked to female noninjecting heterosexuals [11], suggesting considerable HIV transmission links between individuals from various key populations. Although these findings provide rigorous evidence of transmission links between individuals belonging to different subpopulations, there is still a need to assess epidemiologic linkages at the population level because HIV is a population-level phenomenon, shaped not only by individual-level transmission, but also by place characteristics and other structural determinants. Population-level studies of cross-population HIV linkages may lay the

foundation for future research investigating the role of structural variables in creating and shaping these linkages within and across populations.

However, population-level data investigating the extent to which HIV or AIDS rates in one population may influence HIV rates in another population are limited. One such study was a lagged cross-sectional analysis of U.S. metropolitan statistical areas (MSAs) that found that HIV prevalence among PWID may influence later AIDS incidence and mortality among non-PWID heterosexuals [12]. This same cross-sectional analysis also found that the several PWID-focused interventions (i.e., syringe service programs presence, HIV testing rates among PWID, and drug treatment coverage of PWID) were inversely associated with AIDS incidence and death rates among non-PWID heterosexuals in large U.S. MSAs [12]. Another ecological study found moderate albeit nonsignificant correlation between the proportion of surveyed MSM who also reported having sex with women and the percentage of HIV cases attributed to heterosexual contact among women in 12 U.S. cities [13].

Our study extends this nascent line of inquiry by analyzing the longitudinal association between HIV epidemics among Black PWID and Black non-PWID heterosexuals. Our analysis relies on the hierarchical classification of transmission categories by the Centers for Disease Control and Prevention (CDC), in which the “heterosexual contact” category excludes PWID and MSM [14]. We focus on Black heterosexuals because they experience higher rates of newly diagnosed HIV infections compared with other heterosexual populations [14]. Similarly, we chose Black PWID as another population of interest because according to 2018 data, Black men and women constitute almost half (47.8%) of 117,710 people living with HIV whose infection has been attributed to injection drug use [15]. Here, we test two main hypotheses (Fig. 1): (1) the number of AIDS diagnoses among Black PWID is positively related to rates of newly diagnosed HIV among Black heterosexuals in MSAs over time, and (2) this association stronger in MSAs with higher racial residential segregation or with higher rates of non-HIV sexually transmitted infections (STIs) among Black people. We test the latter interactions because research suggests that (1) sexual networks are more assorted by race/ethnicity in segregated MSAs [6], creating conditions in which Black heterosexuals who do not inject drugs might be more likely to partner with Black PWID; and (2) higher STI rates among Black people may facilitate the cross-population spread of HIV because STIs increase physiological susceptibility to sexual transmission of HIV [16].

Methods

We tested our hypotheses in an ecologic cohort study of large U.S. MSAs spanning 2005—2016 but at the MSA, rather than at the individual level of analysis. MSAs were included in the cohort if they had populations >500,000 in 1990. Although 96 MSAs met this eligibility criterion, 12 MSAs were missing data on key covariates reducing our final cohort to 84 MSAs. An MSA is defined as an area containing “…at least one urbanized area that has a population of at least 50,000 [and] counties having a high degree of social and economic integration with the central [urbanized] county…”[17] (p.82238). The parent study spans 1992—2016 [18], so we used 1993 MSA boundaries throughout the study period.

Measures

Outcome—The outcome was the rate of newly diagnosed cases of HIV among Black heterosexuals aged 15—64 years in each year and MSA, as expressed in the following formula:

$$\frac{\text{No. of new HIV diagnoses among Black adults and adolescents with infection attributed to heterosexual contact}_{\text{YeariMSAj}}}{(\text{No. residents aged 15 to 64 years who are Black} - \text{No. Black MSM})_{\text{YeariMSAj}}} \times 100{,}000$$

For each MSA and year (2008—2016), the CDC provided data on the number of newly diagnosed cases of HIV among Black heterosexuals derived from the confidential name-based National HIV Surveillance System (NHSS). The number of Black MSM was estimated following an approach published by Tempalski et al [19].

Independent variable—Our focal independent variable (IV) was the rate of Black PWID AIDS diagnoses per100,000 Black adults aged 15—64 years (hereafter referred to as the "Black PWID AIDS rate"), calculated as follows:

$$\frac{\text{No. of new AIDS diagnoses among Black PWID}_{\text{YeariMSAj}}}{(\text{No. residents aged 15 to 64 years who are Black} - \text{No. Black MSM})_{\text{YeariMSAj}}} \times 100{,}000$$

We conceptualize this exposure as a proxy indicator for cross-population transmission potential because it may indicate that there is a higher population viral load and higher infectivity of PWID living with HIV, reflecting inadequate access to or utilization of antiretroviral treatment by PWID [20]. We assume that this variable reflects the transmission potential better than the rate of PWID living with HIV because individuals living with HIV who are not progressing to AIDS may be more likely to have low or undetectable viral loads than those who progressed to AIDS.

Data on the number of newly diagnosed AIDS cases among Black PWID for each MSA and year (2005—2013 to accommodate for the potential time lag of 3 years between the IV and dependent variable [DV]) were also provided by the CDC based on NHSS reporting (CDC imputes transmission category for cases without a reported risk factor) [14].

Covariates—Characteristics of MSAs that might confound the relationship of interest were chosen based on empirical and theoretical literature and included demographic and socioeconomic characteristics; governmental expenditures on health and community services; affordable housing; measures of war on drugs expenditures, policing, and criminal justice practices; services targeting PWID; and other epidemiologic covariates [21—28]. Supplemental Table S1 provides detailed description of measures and their data sources.

Possible effect modifiers—As discussed previously, we explored two sets of possible effect modifiers to test if the magnitude of the association between the Black PWID AIDS rate and the rate of newly diagnosed cases of HIV among Black heterosexuals depended on Black residential isolation [2] and the rates of primary and secondary syphilis, gonorrhea, and chlamydia among Black adolescents and adults.

Analysis—We used descriptive statistics to summarize each variable's distribution. We used a three-stage model building process: first, modeling temporal changes in the outcome (Stage 1); second, selecting covariates for the final model (Stage 2); and third, conducting multivariable analyses (Stage 3). We selected a multilevel linear modeling (MLM) approach because it accounts for correlation of clustered observations (i.e., time within MSAs) [29].

Our study sought to analyze a census, rather than a sample, of all MSAs with a population of 500,000 or larger; therefore, *P* values and confidence intervals cannot be used for inferential purposes (we report them as heuristic guides only) [30,31]. We therefore determined substantive significance using the magnitude of association. Associations were deemed substantively significant if a standardized coefficient for a variable was ≥|0.10| in the final model [32].

Stage 1: Modeling change in the outcome over time—We log transformed the outcome to linearize its relationship with covariates because of its skewed distribution. All models (Stages 1—3) used two-level MLM to account for the clustering of annual observations within MSAs. We visually inspected plots of each covariate over time and tested linear, quadratic, and cubic time functions and selected the time function with the smallest Akaike information criterion.

Stage 2: Covariate selection—We centered each time-varying continuous covariate at baseline to aid interpretation. Centering produced variable "dyads" for each time-varying covariate, with one variable capturing the baseline value and another capturing annual change in the variable (year minus baseline). To illustrate, the IV was modeled as two variables: (1) baseline (i.e., circa 2005) rate of Black PWID AIDS diagnoses; (2) annual change since baseline in the rate of Black PWID AIDS diagnoses; together, these two variables constitute a dyad capturing the rate of Black PWID AIDS diagnoses. To account for unobserved state-level characteristics, we included a state fixed effect in all models. We report findings using magnitudes of association and standardized coefficients, obtained by creating Z-scores for variables, in bivariate and multivariable analyses [30,31].

We did not expect changes in the focal IV to have an instantaneous effect on the outcome, so we introduced a 3-year lag between Black PWID AIDS rates and the rates of newly diagnosed cases of HIV among Black heterosexuals. We tested the model without structural covariates with various time lags between the IV and DV and found that 3-year lag model had the largest standardized coefficient compared with the models with 1- and 2-year lags.

We used MLM to regress annual heterosexual HIV diagnosis rates on time (operationalized as years since baseline) and the lagged Black PWID AIDS rate dyad (baseline and annual change since baseline). Next, we added possible confounders, one "dyad" (i.e., baseline and annual change since baseline variables for the characteristic of interest) at a time. To determine which putative covariate might actually confound the relationship between the rates of PWID AIDS and heterosexual new HIV diagnoses, we used a rule of thumb: if the magnitude of the focal relationship changed by ≥10% across the models with and without the putative confounder dyad, this dyad was considered a potential confounder and added to the multivariable model [33]. As we operationalized Black PWID AIDS rate using a

baseline and annual change since baseline dyad, we determined whether 10% change occurred in the sum of absolute magnitudes of the standardized coefficients for Black PWID AIDS rate dyad. We used this rule of thumb for all covariates except for epidemiologic covariates (AIDS diagnoses among Black heterosexuals and HIV prevalence among MSM), which we decided a priori to include in the multivariable model because of their importance as potential confounders of epidemiologic cross-population associations.

Stage 3: Multivariable analysis—We used multivariable MLM to test the relationship between the rates of Black PWID AIDS diagnoses and the rates of HIV diagnoses among Black heterosexuals, controlling for confounders selected in Stage 2. We tested the multivariable model for multicollinearity using condition index and variance decomposition proportions [34]. As we log transformed the outcome, we used back transformation of the unstandardized coefficients to calculate percent change in heterosexual new HIV diagnoses rate per one-unit increase in the rate of PWID AIDS diagnoses [35]. We report percent change in the outcome per 1 standard deviation (SD) increase in covariates.

Once we had constructed the final multivariable model, we tested possible moderation of the focal relationship by Black residential isolation and annual rates of syphilis, chlamydia, and gonorrhea among Black adults by testing the substantive significance of the interaction term between these covariates and the IV dyad using the standardized coefficient cut point $\geq|0.10|$.

Sensitivity analyses—We assessed the sensitivity of our final multivariable model to the possible misclassification of HIV transmission routes that may introduce measurement error to our IV and DV. Specifically, the number of AIDS cases among Black PWID may be underestimated because of underreporting of HIV transmission via injecting drug use, whereas the number of diagnoses of HIV infection attributed to heterosexual transmission may be overestimated because individuals who contract HIV via same-sex intercourse (men) or injecting drug use may report a heterosexual route of transmission to avoid disclosing stigmatized practices. Although evidence of such misclassification is limited for the United States, reports from the United Kingdom and other countries suggest that it is a possible scenario [36—38]. Specifically, we tested various scenarios where the number of Black PWID AIDS cases was 5%, 10%, and 20% higher, and the rate of new HIV diagnoses among Black heterosexuals was 5%, 10%, and 20% lower than actual data.

We conducted our analyses in SAS 9.4 (SAS Institute Inc., Cary, NC).

Results

In 2005, the median rate of Black PWID AIDS diagnoses across the 84 MSAs was 8.8 per 100,000 Black heterosexual population (25th and 75th percentiles: 5.3/100,000, 17.6/100,000; SD: 11.8/100,000); this rate decreased by more than two-thirds by 2013 to 2.9/100,000 (25th and 75th percentiles for change over time [the difference between the last observation and baseline values]: −12.0/100,000, −3.1/100,000; SD: 9.5/100,000). The median rate of newly diagnosed HIV infections among Black heterosexuals decreased from 25.2/100,000 (25th and 75th percentiles: 16.2/100,000, 42.7/100,000; SD: 27.3) in 2008 to

15.1/100,000 (25^{th} and 75^{th} percentiles for the change over time: −20.1/100,000, −2.6/100,000; SD: 17.3) in 2016. Descriptive statistics for covariates are presented in Table 1.

Bivariate analyses

In the model adjusted for time and state fixed effects, both the lagged baseline measure of the main IV and the measure of change over time in this variable (rate of AIDS diagnoses among Black PWID/100,000 Black heterosexuals) were positively associated with the outcome (log of the rate of new HIV diagnoses/100,000 Black heterosexuals). The standardized coefficients for the IV dyad ($\beta = 0.40$ for baseline; $\beta = 0.11$ for change score) were above the cutoff point ($\geq|0.10|$) for substantive significance in this model. Bivariate relationships for all covariates are presented in Supplemental Table S2.

Multivariable analysis

The relationships between the measures of Black PWID AIDS diagnoses at baseline and the rate of new HIV diagnoses among Black heterosexuals and between change since baseline in AIDS diagnoses and the rate of new HIV diagnoses among Black heterosexuals remained positive and substantively significant (i.e., absolute value of the standardized coefficient $\beta \geq 0.10$) in the multivariable model that controlled for quadratic time, state fixed effects, and multiple covariates. The magnitude of the association for the standardized baseline exposure coefficient decreased (to $\beta = 0.12$), whereas the coefficient for change over time remained the same ($\beta = 0.11$); both coefficients were above the substantive significance cutoff ($\geq|0.10|$; Table 2). Back transformation of the model results suggests that MSAs with Black PWID AIDS rates that were 1 SD (11.8/100.000) above the mean in 2005 had the rates of newly diagnosed HIV infections that were 10.3% higher in 2008 (Table 3). Similarly, MSAs that experienced a 1 SD (9.5/100.000) increase in Black PWID AIDS rates over time (2005—2013) had 7.8% more new HIV cases per 100,000 Black heterosexuals over 2008—2016. The multivariable analysis also demonstrated positive and substantively significant associations between some structural covariates and the outcome. Specifically, positive associations were established for the percent of Black adults without a high school diploma (baseline $\beta = 0.16$; change since baseline $\beta = 0.18$), and Black/White poverty ratio (baseline $\beta = 0.17$; change since baseline $\beta = 0.07$).

Moderation analyses

We found evidence for effect moderation by STI rates (Table 3). Specifically, baseline gonorrhea rates and chlamydia rates as well as change over time in chlamydia rates moderated the relationship between baseline AIDS rates and the outcome (interaction term coefficients: $\beta = -0.17$ for baseline gonorrhea rate; $\beta = -0.13$ for baseline chlamydia rate; $\beta = -0.10$ for change in chlamydia rate). Notably, and in contrast to our hypotheses, the focal relationship was attenuated, where STI rates were higher or rising. The test of interaction for Black isolation revealed that this covariate did not moderate the focal relationship.

Sensitivity analyses showed that the multivariable model findings are robust to adjusting the IV (Black PWID AIDS diagnoses) and DV (the rate of new HIV diagnoses among Black heterosexuals) data for misclassification by 5%. The strengths of association diminished in

scenarios with higher misclassification rates and were especially susceptible to misclassification in the rate of new HIV diagnoses among Black heterosexuals (Supplemental Table S3).

Discussion

Our analysis is the first longitudinal population-based study of the possible epidemiologic links between AIDS rates among PWID and HIV rates among noninjecting heterosexuals; it is also the first study of cross-population associations focusing on Black MSA residents, a vulnerable population. In 84 MSAs covering 65% of the U.S. Black population in 2016, we found that both baseline and change in the rate of newly diagnosed AIDS cases among Black PWID were positively associated with the rate of newly diagnosed HIV infections among Black heterosexual adults and adolescents. Specifically, we found that, on average, a 1 SD (9.5/100,000) increase in the Black PWID AIDS rates over time corresponds to 7.8% increase in the rate of new HIV diagnoses among Black heterosexuals. Our hypotheses that segregation and STI rates might strengthen these relationships were not supported.

The study corroborates emerging evidence from past epidemiologic studies linking HIV transmission between PWID and heterosexuals in the United States. As noted, a lagged cross-sectional MSA-level analysis reported positive associations between the prevalence of HIV-positive PWID in 1992 and AIDS incidence rate among heterosexuals in 2006–2008 [12]. In addition, our results are aligned with the findings of a genetic HIV surveillance study reporting a large percentage of similar HIV genetic sequences among male PWID and female heterosexuals [11].

Findings from network studies may help explain these associations. These studies have found that PWID have dense sexual connections (often involving unprotected sex) with non-PWID, including people who use drugs without injecting them [8,39]. There is, though, a dearth of network studies elucidating factors influencing sexual transmission of HIV between PWID and heterosexuals who do not use drugs, including demographic characteristics of bridging networks, condom use prevalence, concurrency, and serosorting. Future research should explore these topics.

More research is also needed to identify biological and structural factors facilitating HIV transmission between Black PWID and heterosexuals. Our study tested whether racial residential segregation and epidemics of STIs might amplify the PWID/heterosexual relationship. We found no evidence that this relationship was stronger in MSAs that were more segregated. A molecular HIV surveillance study found that 81% of HIV infections among Black people are linked to other Black people [11]. Possibly, centuries of structural discrimination have created multiple processes-including but not limited to residential segregation-that create racially assortative sexual partnerships among Black Americans, including partnerships that span key populations regardless the level of segregation.

The finding that higher STI rates attenuated the association between the baseline number of newly diagnosed AIDS cases among Black PWID and new HIV diagnoses among Black heterosexuals is unanticipated because STIs create physiological vulnerability to

transmitting and acquiring HIV. Possibly, MSAs with higher background STI prevalence may have implemented more intensive prevention programs targeting at-risk groups who might be bridging PWID and heterosexuals. In addition, we did not have data to test interactions with STIs such as herpes simplex virus (not a mandatorily reportable infection in all states in the United States) that are the strongest risk factor for HIV transmission [40]. Future studies should investigate whether Black residents' access to HIV and other STI prevention, testing, and treatment services moderates HIV transmission between Black PWID and heterosexuals.

Our findings of the positive associations between structural covariates (educational attainment among Black people and Black/White poverty ratio) and the outcome of interest are well aligned with the literature on structural determinants of high burden of HIV among Black people [4,41,42]. However, these results need to be interpreted with caution because our modeling steps were not aimed at assessing the independent effects of these covariates.

Overall, the finding of association of HIV-related outcomes between Black PWID and Black heterosexuals should not be interpreted as an evidence of Black PWID risky behaviors being the reason behind high HIV rates among Black heterosexuals. It would be inaccurate and counterproductive to put the blame for HIV transmission on Black PWID population or on any other population bearing disproportionate burden of the infection. Black PWID are heavily stigmatized population exposed to a high risk of HIV because of a host of structural determinants, including structural racism and racialized war on drugs, determinants that create risk environment and increase the risk of transmission irrespective of individual behaviors [43,44].

Strengths and limitations

Our findings are generalizable to the 65% of the U.S. Black population who live in the MSAs studied here. The main IV and DV data are derived from the confidential name-based NHSS. Cases reported to NHSS undergo both inter- and intra-state deduplication. Possible underreporting of HIV diagnoses and misclassification of cases by transmission category may, however, have biased our results-for example, our sensitivity analysis demonstrated that the bias can be toward the null if the proportion of new HIV diagnoses misattributed to heterosexual transmission (IV) is higher than 5%. Because of the ecological nature of the study, our findings should be interpreted as population-level associations not generalizable to individuals. We were unable to compare the cross-population associations across specific age groups or separately for Black men and women because the CDC can only share MSA-level surveillance data for various transmission groups by one demographic characteristic at a time. As Black women are almost twice as likely to contract HIV via heterosexual transmission than Black men [15], exploring the cross-population linkages among Black people via biological sex and gender lenses is especially important. Our outcome measure of new HIV diagnoses among Black heterosexuals includes both transmission from PWID and non-PWID individuals, which may attenuate the magnitude of the relationship of interest. The use of various sources of data to create our focal variables and covariates might have affected the reliability of our data. The study findings have limited generalizability to smaller MSAs and to rural areas.

Implications for public health practice and research

Our study adds to existing knowledge on cross-population HIV linkages and strengthens the argument that engaging Black PWID in the HIV prevention and care cascade as prescribed by the U.S. government's 2019 strategic HIV initiative pillars (i.e., early diagnosis, adequate treatment, effective prevention) [1] may also help curb down HIV incidence among Black non-PWID heterosexuals. Further research on factors facilitating cross-population interactions of HIV transmission among Black PWID and Black heterosexuals (and across other key populations), including structural barriers to HIV-related care, is warranted to inform the development of these interventions and programs. The findings from this research may also improve the accuracy of effectiveness and cost-effectiveness estimates of evidence-based interventions recommended by the CDC [45]. Current cost-effectiveness and effectiveness studies that limit their focus to an intervention's impact on the single target population may considerably underestimate its cost-effectiveness and effectiveness by omitting its impacts on other, epidemiologically linked populations. Integrating a cross-population perspective into HIV-related programming and research may create more efficient targeting of resources by recognizing potential transmission linkages within and between key populations.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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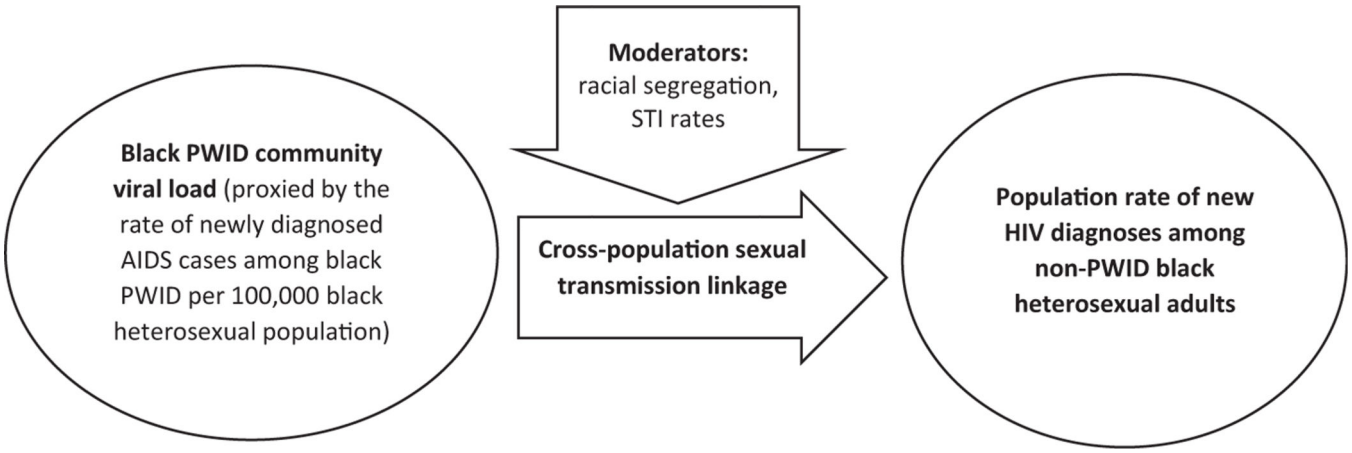

Fig. 1.

Cross-population HIV transmission from Black PWID living with AIDS to non-PWID Black heterosexual adults.

Table 1

Rates of diagnosis of HIV infection attributed to heterosexual contact per 100,000 Black adults and adolescents aged 15—64 y over time and possible structural covariates: 84 large U.S. metropolitan statistical areas, 2008—2016[*]

	Mean	SD	Median	25th percentile	75th percentile
HIV diagnosis per 100,000 Black heterosexual adults					
Baseline (2008)	33.55	27.33	25.16	16.22	42.68
Change between 2008 and 2016	−12.44	17.28	−10.05	−20.12	−2.60
AIDS diagnosis among Black PWID per 100,000 Black heterosexual adults					
Lagged baseline (2005)	12.49	11.82	8.75	5.33	17.56
Change between 2005 and 2013	−8.77	9.49	−5.83	−11.99	−3.07
Adult population size					
Lagged baseline (2005)	1,331,159.90	1,222,995.00	943,631.50	543,583.50	1,530,782.50
Change between 2005 and 2013	104,871.48	129,989.71	60,500.50	23,070.00	149,619.00
Black adult population size					
Lagged baseline (2005)	187,101.36	255,671.20	88,595.50	38,481.00	192,009.00
Change between 2005 and 2013	19,583.52	37,907.40	7096.50	3264.50	24,560.00
Population density (over square miles)					
Lagged baseline (2005)	979.17	1721.74	541.55	346.20	1016.48
Change between 2005 and 2013	56.98	70.16	49.94	20.09	75.55
Percentage of population aged 15—29 y					
Lagged baseline (2005)	30.93	2.57	30.73	29.38	32.31
Change between 2005 and 2013	−0.05	1.01	−0.10	−0.64	0.61
Percentage of Black population aged 15—29 y					
Lagged baseline (2005)	35.27	2.64	35.15	33.42	36.70
Change between 2005 and 2013	−0.24	1.00	−0.17	−0.97	0.36
Black male—female sex ratio					
Lagged baseline (2005)	0.96	0.21	0.87	0.84	1.00
Change between 2005 and 2013	0.00	0.08	0.01	0.00	0.03
Percentage of Black population employed					
Lagged baseline (2005)	59.71	6.07	60.95	56.18	63.59
Change between 2005 and 2013	0.05	2.03	0.06	−1.30	1.52

	Mean	SD	Median	25th percentile	75th percentile
Ratio of percentage of Black to White population employed					
Lagged baseline (2005)	0.96	0.10	0.96	0.90	1.02
Change between 2005 and 2013	0.04	0.03	0.04	0.01	0.06
Percentage of Black adults without a high school diploma					
Lagged baseline (2005)	18.92	5.09	19.05	15.38	22.27
Change between 2005 and 2013	−5.08	1.75	−5.20	−6.36	−4.04
Ratio of percentage of Black to White adults without a high school diploma					
Lagged baseline (2005)	1.97	0.57	1.89	1.58	2.23
Change between 2005 and 2013	0.12	0.19	0.11	−0.02	0.24
Percentage of Black population in poverty					
Lagged baseline (2005)	21.45	6.40	20.89	17.42	25.86
Change between 2005 and 2013	1.16	2.30	1.27	−0.11	2.56
Ratio of percentage of Black to White population in poverty					
Lagged baseline (2005)	2.85	0.68	2.74	2.43	3.21
Change between 2005 and 2013	−0.39	0.27	−0.38	−0.54	−0.23
Gini index					
Lagged baseline (2005)	0.45	0.02	0.44	0.43	0.46
Change between 2005 and 2013	0.01	0.01	0.02	0.01	0.02
Health expenditures per capita ($)					
Lagged baseline (2005)	132.29	136.80	92.36	47.70	188.83
Change between 2005 and 2013	7.28	160.99	8.31	−3.03	35.41
% without health insurance					
Lagged baseline (2005)	19.39	5.70	18.32	14.58	22.75
Change between 2005 and 2013	0.76	2.45	1.04	−0.69	2.25
Housing/community expenditures per capita ($)					
Lagged baseline (2005)	221.95	922.89	102.67	78.12	154.18
Change between 2005 and 2013	−107.18	1218.62	22.29	3.51	45.64
Percentage of low-income households with rent >30% of income					
Lagged baseline (2005)	72.20	3.44	71.73	69.62	74.20
Change between 2005 and 2013	−2.60	3.02	−2.46	−4.53	−0.53
Police per 1000 population					

	Mean	SD	Median	25th percentile	75th percentile
Lagged baseline (2005)	2.50	1.17	2.22	1.87	2.78
Change between 2005 and 2013	−0.15	0.27	−0.14	−0.26	−0.03
Police expenditures per capita ($)					
Lagged baseline (2005)	439.20	1808.05	233.36	185.58	289.84
Change between 2005 and 2013	−216.79	2389.60	44.60	24.13	62.51
Hard drug arrest rate per 10,000 adults					
Lagged baseline (2005)	27.41	19.70	20.57	15.23	32.22
Change between 2005 and 2013	−6.67	10.00	−4.31	−10.68	0.04
% incarcerated					
Lagged baseline (2005)	0.86	0.72	0.71	0.50	0.99
Change between 2005 and 2013	−0.04	0.15	−0.04	−0.10	0.03
% jail incarcerated					
Lagged baseline (2005)	0.34	0.16	0.31	0.24	0.43
Change between 2005 and 2013	−0.04	0.07	−0.02	−0.07	0.00
% Black jail incarcerated					
Lagged baseline (2005)	1.25	0.57	1.12	0.86	1.52
Change between 2005 and 2013	−0.06	1.25	−0.24	−0.39	−0.08
Syringe exchange presence					
Lagged baseline (2005), *n* (%)	24 (28.57)				
Black PWID treatment coverage per 100,000 Black PWID					
Lagged baseline (2005)	265.15	681.17	64.00	22.00	203.00
Black PWID HIV testing per 10,000 Black adults					
Lagged baseline (2005)	5.25	5.30	3.34	1.52	7.63
Change between 2005 and 2013	−2.08	5.88	−1.15	−5.06	0.92
% isolated Black residents					
Lagged baseline (2005)	35.48	19.46	37.40	17.74	48.30
Change between 2005 and 2013	−2.77	2.12	−2.71	−4.41	−1.14
Black heterosexual people living with AIDS per 100,000 Black					
Lagged baseline (2005)	201.29	197.36	136.88	86.87	235.23
Change between 2005 and 2013	53.39	39.56	45.94	30.90	69.35
MSM HIV prevalence					

	Mean	SD	Median	25th percentile	75th percentile
Lagged baseline (2005)	15.55	1.97	15.61	14.71	16.41
Change between 2005 and 2013	4.57	1.92	4.31	3.44	5.63

Correlates were lagged because we did not expect a change in the correlates to have an instantaneous effect on the outcome.

* 2008—2016 is the time frame for the outcome. Correlates were lagged 3 years and reflect 2005—2013.

Table 2

Multilevel multivariable modeling of logged* rates of diagnosis of HIV infection attributed to heterosexual contact (per 100,000 Black adults and adolescents aged 15—64 y), 84 large MSAs, 2008—2016†

Independent variable	Multivariable model standardized β (CI)§	Multivariable model % change‡ per SD increase (CI)§
AIDS diagnosis among Black PWID per 100,000 Black heterosexual adults		
Lagged baseline (2005)	0.12 (−0.03, 0.28)//	10.25 (−1.02, 21.63)
Change since baseline	0.11 (0.03, 0.18)//	7.80 (2.80, 12.83)
Structural covariates		
Black adult population size per 100,000		
Lagged baseline (2005)	0.24 (0.10, 0.37)//	17.46 (6.84, 28.53)
Change since baseline	−0.05 (−0.13, 0.04)	−4.15 (−8.10, 0.70)
Ratio of percentage of Black to White population employed		
Lagged baseline (2005)	−0.01 (−0.15, 0.14)	−3.04 (−7.51, 10.12)
Change since baseline	0.02 (−0.05, 0.09)	−0.24 (−2.48, 9.59)
Percentage of Black adults without a high school diploma		
Lagged baseline (2005)	0.16 (−0.02, 0.35)//	7.54 (−6.03, 21.46)
Change since baseline	0.18 (0.03, 0.33)//	13.45 (3.90, 23.44)
Ratio of percentage of Black to White adults without a high school diploma		
Lagged baseline (2005)	0.09 (−0.03, 0.20)	6.45 (−2.18, 16.42)
Change since baseline	−0.13 (−0.23, −0.03)//	−7.57 (−10.44, −3.47)
Ratio of percentage of Black to White population in poverty		
Lagged baseline (2005)	0.17 (0.01, 0.33)//	12.48 (−0.61, 27.91)
Change since baseline	0.07 (0.01, 0.14)	4.18 (−0.30, 9.61)
Gini index		
Lagged baseline (2005)	−0.02 (−0.14, 0.11)	−0.93 (−2.18, 79.73)
Change since baseline	0.03 (−0.07, 0.13)	2.87 (−0.64, 59,504.81)
Percentage of isolated Black residents		
Lagged baseline (2005)	0.01 (−0.18, 0.20)	−1.94 (−16.07, 12.32)

Independent variable	Multivariable model standardized β (CI)[§]	Multivariable model % change[‡] per SD increase (CI)[§]
Change since baseline	0.10(0.01,0.18)[//]	6.55 (0.99, 12.29)
Black heterosexual people living with AIDS per 100,000 Black heterosexual adults		
Lagged baseline (2005)	0.20 (0.04, 0.36) [//]	15.95 (4.13, 27.76)
Change since baseline	0.03 (−0.06, 0.11)	0.24 (−5.4, 5.89)
MSM HIV prevalence		
Lagged baseline (2005)	−0.03 (−0.12, 0.07)	−0.68 (−7.51, 6.4)
Change since baseline	−0.03 (−0.10, 0.04)	−2.25 (−6.81, 2.41)
Time		
Time	0.13 (−0.05, 0.30)	7.03 (−267.48, 24.06)
Time squared	0.02 (−0.04, 0.08)	4.76 (−2154.26, 15.76)

We assessed multicollinearity diagnostics using variance decomposition proportions (VDP) > .5 associated with confidence indices (CI) > 15. Bivariate and multivariate models include a state covariate and quadratic time.

[*] We natural log transformed the outcome to linearize its relationship with covariates.

[†] 2008—2016 is the time frame for the outcome. We lagged covariates 3 y because we did not expect an instantaneous effect on the outcome.

[‡] Back transformation performed on unstandardized model coefficients to obtain correct estimates of percent change.

[§] We determined substantive significance using a priori cutoff for the magnitude of the standardized coefficient ≥ |0.10|, and not a CI, as described in the methods. CIs are provided as a heuristic.

[//] Significant at the a priori cutoff of the standardized coefficient ≥|0.10|.

Table 3

Interaction[*] testing for multivariable modeling of logged[†] rates of diagnosis of HIV infection attributed to heterosexual contact (per 100,000 Black adults and adolescents aged 15—64 y) in 84 large MSAs, 2008—2016[‡]

Independent variable, effect modifiers and interactions	Models without and with effect modifiers, standardized β (CI)				
	No effect modifiers	% Black residential isolation effect modifier	Black syphilis rate per 100,000 Black adults effect modifier	Black gonorrhea rate per 100,000 Black adults effect modifier	Black chlamydia rate per 100,000 Black adults effect modifier
AIDS diagnoses among Black PWID[§] per 100,000 Black heterosexual adults (independent variable)					
Lagged baseline (2005)	0.12 (−0.03, 0.28)[§]	0.11 (−0.06, 0.27)[§]	0.11 (−0.04, 0.26)[§]	0.09 (−0.06, 0.24)	0.12 (−0.04, 0.27)[§]
Change since baseline	0.11 (0.03, 0.18)[§]	0.13 (0.03, 0.22)[§]	0.10 (0.03, 0.18)[§]	0.12 (0.03, 0.2)[§]	0.09 (0.01, 0.17)
Effect modifier dyads					
Lagged baseline (2005)		−0.02 (−0.21, 0.17)	0.20 (0.09, 0.3)[§]	0.0 (−0.11, 0.12)	−0.05 (−0.17, 0.07)
Change since baseline		0.09 (0.0, 0.18)	0.02 (−0.05, 0.08)	0.01 (−0.05, 0.07)	0.0 (−0.06, 0.06)
Interaction effects					
AIDS diagnosis among Black PWID[§] per 100,000 Black heterosexual adults baseline[§] effect modifier baseline		−0.08 (−0.19, 0.03)	0.03 (−0.09, 0.16)	−0.17 (−0.32, −0.02)[§]	−0.13 (−0.28, 0.02)[§]
AIDS diagnosis among Black PWID[§] per 100,000 Black heterosexual adults change[§] effect modifier baseline		−0.02 (−0.10, 0.05)	−0.01 (−0.07, 0.05)	−0.01 (−0.1, 0.09)	−0.02 (−0.09, 0.05)
AIDS diagnosis among Black PWID[§] per 100,000 Black heterosexual adults baseline[§] effect modifier change		−0.04 (−0.14, 0.07)	−0.04 (−0.13, 0.05)	−0.02 (−0.13, 0.08)	−0.10 (−0.2, 0.0)[§]
AIDS diagnosis among Black PWID[§] per 100,000 Black heterosexual adults change[§] effect modifier change		−0.06 (−0.16, 0.03)	−0.01 (−0.08, 0.06)	−0.03 (−0.12, 0.06)	−0.02 (−0.11, 0.06)

Models include state covariate and quadratic time.

[*] For each effect modifier, we added the effect modifier baseline and change since baseline effect modifier dyad, along with effect modifier interactions with Black PWID AIDS diagnosis to the multivariate model.

[†] We natural log transformed the outcome to linearize its relationship with covariates.

[‡] 2008–2016 is the time frame for the outcome. We lagged covariates 3 y because we did not expect an instantaneous effect on the outcome.

[§] Significant at the a priori cutoff for the standardized coefficient ≥ |0.10|.