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Molecular Epidemiology of Individuals Experiencing Unstable Housing or Living Homeless at HIV Diagnosis: Analysis of HIV Surveillance Data in King County, Washington

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Abstract

We examined patterns of genetic clustering among individuals diagnosed with HIV between 2010 and 2018 using data from King County, Washington's National HIV Surveillance System. Among 2,371 individuals newly diagnosed with HIV, 231 (10%) experienced unstable housing or were living homeless at the time of diagnosis. Among the 1,658 (70%) people with an available HIV-1 *pol* gene sequence, 1,071 (65%) were identified to be part of 296 genetic clusters. In our analysis, housing status was not associated with genetic clustering (OR 1.02; 95%CI:0.75,1.39). After adjusting for demographic and behavioral factors, people who were living homeless at HIV diagnosis had 35% lower odds of being identified as part of a genetic cluster (AOR 0.65; 95%CI:0.44,0.95) compared to people with stable housing. Our findings highlight that people experiencing unstable housing are disproportionately burdened by HIV, and that within this population in King County, being in a genetic cluster is predominantly associated with substance use.

Keywords HIV · Molecular epidemiology · Housing instability · Homelessness · Genetic clusters

Introduction

In recent years, there has been an increase in HIV outbreaks among people experiencing unstable housing or living homeless across the United States, including in Massachusetts, Florida, Pennsylvania, and Seattle.[1–5] Lack of stable housing is a barrier to adequate HIV medical care, including access and adherence to antiretroviral treatment (ART) and sustained viral suppression.[6, 7] Several studies based in New York City and San Francisco demonstrate that unstable housing is associated with a reduced likelihood of viral suppression and increased likelihood of low CD4 cell counts, and that people who are unstably housed or living homeless when newly diagnosed with HIV are also more likely to be concurrently diagnosed with AIDS.[8–11] In addition, New York City's HIV Housing Assistance program observed a strong dose-response relationship between stable housing and viral suppression: the proportion of individuals who achieved viral suppression was lowest among individuals in emergency housing/shelters, increased among those in transitional housing and permanent housing, and was highest among those in independent living.[11, 12] Additional studies demonstrate that unstable housing is associated with increased likelihood of hospitalization, emergency department visits, and premature mortality for people living with HIV (PLWH).[10, 13, 14].

In King County, WA, which includes the city of Seattle, an estimated 12% of all PLWH were living homeless in 2017, defined as living in a shelter, a single-room occupancy hotel, on the street, or in parks, tents, vehicles, or other places not meant for human habitation.[15] Similar to other urban counties, homelessness is a growing and persistent

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public health concern in King County. On any given night in 2018, approximately 12,000 residents were living homeless in King County, a 20% increase since 2015.[16, 17] Housing instability disproportionately affects populations who are also vulnerable to HIV acquisition, including racial, ethnic, sexual and gender minorities: 27% of people living homeless in King County were Black and 15% were Hispanic or Latinx (compared to 6% and 9% of the general King County population, respectively); 18% identified as lesbian, gay or bisexual; and 8% identified as transgender, genderqueer or non-binary.[16] Unstable housing is also a common experience among people who inject drugs (PWID). In a 2017 survey of King County syringe services program clients, the majority were living homeless or unstably housed (43% and 26%, respectively).[15–17].

HIV genomic epidemiology uses viral evolutionary information encoded in HIV genetic sequences to understand transmission dynamics. At the fundamental level, if two or more individuals have genetically similar HIV sequences, this suggests that they likely share a close epidemiological connection. These methods can reveal HIV transmission networks that include populations vulnerable to HIV acquisition, and, related to the current study, can potentially assess whether people experiencing unstable housing or living homeless experience higher rates of HIV transmission than other populations. Variation in how frequently certain subpopulations (defined by demographic or behavioral factors) are identified to be part of a genetic similarity cluster can either be due to variation in transmission rates or variation in the time between HIV acquisition and sequence collection, as sequences sampled soon after HIV acquisition are more likely to cluster.[18, 19] Importantly, variability in the time from HIV acquisition to sequence collection can reflect variation in rates of HIV testing and diagnosis.

Using HIV surveillance data and genomic epidemiology methods, this study aimed to characterize individuals who were unstably housed or living homeless at HIV diagnosis and their patterns of genetic clustering, compared to individuals who are presumed to be stably housed, in King County, WA.

Methods

HIV surveillance data, including HIV-1 *pol* gene sequences, are collected as part of routine clinical care and public health surveillance undertaken by Public Health-Seattle & King County (PHSKC). We used these de-identified data from King County's National HIV Surveillance System (NHSS) from 2010 to 2018 to identify King County residents newly diagnosed with HIV. Additionally, PHSKC attempts to contact all persons newly diagnosed with HIV to offer partner services. Partner services interviews collect additional information on sexual behavior, substance use, and housing status. Sexual behavior questions include history of transactional sex (e.g. ever given/received money or drugs in exchange for sex), and sex with a person who used injection drugs. Substance use questions include any injection drug use, and specific drug use (e.g., methamphetamine use) in the past year. HIV sequences were linked to demographic, clinical, and epidemiological information in the NHSS and collected during partner services interviews.

We used both NHSS and partner services data to identify participants who were unstably housed or living homeless at diagnosis. In the NHSS, PHSKC identified individuals who were living homeless or staying in shelters based on their reported address at diagnosis. During partners services interviews, individuals are also asked whether their housing situation in the last 3 months was *stable/permanent, unstable/non-permanent, institutionalized*, or *other*. We assumed that individuals who were not categorized as living homeless in the NHSS and who self-reported *stable/permanent* housing in partner services interviews were stably housed at diagnosis. However, because not all individuals complete a partner services interview, we were unable to verify the housing status for some individuals. Thus, ascertainment of housing status was incomplete, and we likely under-reported the number of individuals who are homeless. We define people as presumably housed if they self-reported *stable/permanent* housing or for whom we do not know their housing status. In our primary analyses, we compared individuals who were unstably housed or living homeless at diagnosis to individuals we presume to be stably housed. Sensitivity analyses were conducted comparing individuals who were homeless at diagnosis, those who were known to be stably housed (via self-report during partner services interviews), and those with unknown housing status. We characterized participant's demographic, behavioral, and clinical characteristics and tested for statistical significance of differences using χ^2 tests with a significance level of 0.05. In order to account for an up-to 18-month delay in reported deaths, vital status was ascertained as of December 2017.

HIV-1 sequences from the protease and reverse transcriptase (PR/RT) region of the *pol* gene were aligned with the HXB2 reference genome using the MAFTT algorithm.[20] We identified genetic similarity clusters of two or more individuals using Tamura-Nei (TN93) pairwise genetic distance with a 0.02 threshold. At this distance threshold, belonging to a cluster is consistent with being closely epidemiologically connected, either directly or indirectly.[18, 21].

To assess factors associated with being a genetic cluster, we use univariate and multivariate logistic regression analysis. For a given factor, a higher odds of being in a genetic cluster can be interpreted as an increased likelihood

of onward HIV transmission within the sampled population, relative to individuals without that factor. Since variability in the time from HIV acquisition to sequence collection is strongly associated with clustering, we estimated the adjusted odds ratio (AOR) for clustering using logistic regression adjusted for early HIV (defined as having a CD4 count > 500 cells/mm^3 at diagnosis) as well as other potential confounders, including: transmission category (men who have sex with men (MSM), PWID, MSM-PWID, heterosexual, and other/unknown transmission), behaviors associated with HIV acquisition (methamphetamine use, sex with a PWID, and transactional sex), year of diagnosis, age, race, ethnicity, and country of birth (born in the USA or born outside of the USA). We conducted a collinearity analysis since several of these variables were likely to be highly correlated; please see the Digital Supplement for these details. We performed sensitivity analyses using genetic distance thresholds of 0.015 and 0.01, and additional sensitivity analyses that excluded data from 2018, due to an HIV outbreak in north Seattle among cisgender women who exchanged sex and PWID also living homeless.[1, 5] This study received ethical approval from Washington State and University of Washington Institutional Review Boards.

Results

Between January 2010 and December 2018, 2,371 people were newly diagnosed with HIV in King County, among whom 1,380 (58%) completed a partner services interview. Among individuals who completed a partner services interview, 200 were unstably housed and 1,180 had stable or permanent housing. An additional 31 individuals were reported to be living homeless at diagnosis in the NHSS but did not complete a partner services interview. There were 960 (40%) individuals for whom we are unable to determine their housing status at diagnosis. Overall, 10% (231/2,371) of all people newly diagnosed with HIV experienced unstable housing or were living homeless at diagnosis. The annual proportion of new diagnoses among people who were living homeless ranged between 6% and 11% from 2010 to 2017, and increased sharply to 20% in 2018, coinciding with an HIV outbreak among people living homeless (Fig. 1).[1].

Individuals who were unstably housed or living homeless at diagnosis were more likely to be American Indian/Alaskan Native (7% v. 4%, p-value 0.016) and cisgender women (20% v. 11%, p-value 0.002) and less likely to be Asian (3% v. 8%, p-value 0.005) compared to presumably housed individuals (Table 1). People experiencing unstable housing or living homeless were more likely to report injection drug use (40% v. 10%, p-value < 0.001) and less likely to be MSM (59% v. 75%, p-value < 0.001) than presumably

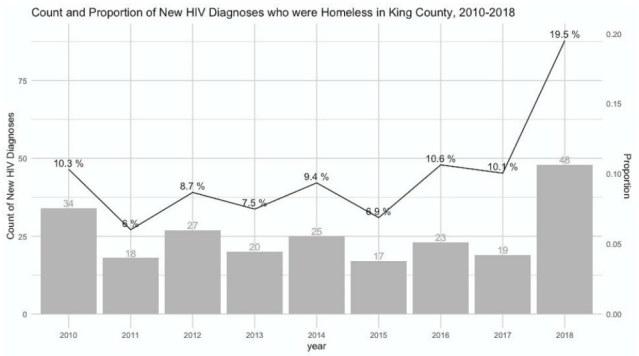

Fig. 1 Count and Proportion of People with New HIV Diagnoses in King County, WA who were Unstably Housed or Living Homeless at Diagnosis, 2010–2018

housed persons. Notably, approximately a third of MSM who were homeless at diagnosis also reported injection drug use (MSM-PWID), compared to just 9% of MSM who were presumably housed at HIV diagnosis. People experiencing unstable housing or living homeless were also more likely to report some sexual behaviors and substance use typically associated with HIV acquisition, including: sex with a PWID (30% v. 7%, p-value < 0.001), giving someone money or drugs in exchange for sex (5% v. 2%, p-value 0.025), receiving money or drugs in exchange for sex (14% v. 4%, p-value < 0.001), sex with both men and women (23% v. 14%, p-value < 0.001), and methamphetamine use in the past year (44% v. 13%, p-value < 0.001). Individuals who were unstably housed or living homeless at diagnosis were more than twice as likely to be deceased as of December 2017 (9% v. 4%, p-value 0.004) compared to those who were presumed stably housed.

People who were unstably housed or living homeless at diagnosis were more likely to have an available HIV sequence (85% v. 68%, p-value < 0.001) than those who were stably housed. Among the 1,658 (70%) people newly diagnosed with HIV with an available PR/RT *pol* gene sequence, we found that 1,071 (65%) individuals were identified to be part of 296 distinct genetic clusters of two or more individuals. The proportion of PLWH with an HIV sequence who were also in a genetic similarity cluster was similar for unstably housed and presumably housed PLWH (66% v. 64%).

There were 62 clusters with at least one person who was unstably housed or living homeless at diagnosis, 21 of which included two or more individuals who were living homeless at diagnosis. Overall, PLWH who were living homeless at diagnosis and who were also identified to be part of a genetic cluster mostly (62%, 80/129) were part of small clusters of 3 or fewer people. The largest overall genetic cluster included 237 people and was mostly comprised of MSM (78%), MSM-PWID (9%), and PWID (5%).

In addition, 32 (14%) people in this large cluster were unstably housed or living homeless at diagnosis, a quarter (25%, 32/129) of all people living homeless who were identified to be part of a genetic cluster. Similar to the overall characteristics of people in this cluster, these 32 individuals were mostly MSM (n = 18, 56%) and MSM-PWID (n = 8, 25%) who were living homeless. The annual number of new HIV diagnoses that were identified to be linked to this large cluster fell dramatically from 2010 to 2018 (Digital Supplement). The second largest cluster including people living homeless represents the 2018-19 outbreak in north Seattle, and was comprised mostly of cisgender women and individuals diagnosed in 2018. In our analysis, this genetic cluster included 17 people, 12 of whom were unstably housed or living homeless, 14 of whom were PWID, and 3 of whom reported heterosexual transmission only.

In univariate models among all PLWH, early HIV, methamphetamine use, reporting sex with a PWID, transactional sex, and being born in the US were all significantly associated with being identified as part of a genetic cluster (Table 2). In contrast, heterosexual transmission, age > 45 years, as well as Asian and Black race were all associated with a lower odds of being identified as part of a genetic cluster. Housing status was not associated with genetic clustering in the univariate model (OR 1.02; 95% CI: 0.75, 1.39).

In the multivariate model among all PLWH, individuals who were unstably housed or living homeless at HIV diagnosis had a 35% lower odds of being identified as part of a genetic cluster (AOR 0.65; 95% CI: 0.44, 0.95) compared to people we presumed to be stably housed, after adjusting for early stage of HIV, transmission category, methamphetamine use, sex with a PWID, transactional sex, age, race, ethnicity, country of birth, and year of diagnosis. When we restricted our analysis to examine correlates of being in a genetic cluster just among PLWH who were living homeless, we observe that methamphetamine use (aOR 3.82; 95% CI: 1.40, 10.46) and reporting sex with a PWID in the last year (aOR 7.82; 95% CI: 1.74, 35.12) were the only factors associated with a higher odds of being identified as part of a genetic cluster.

Sensitivity analyses using more conservative genetic distance thresholds obtained similar results. Excluding data from 2018, when the outbreak of HIV among heterosexual PWID experiencing unstable housing or living homeless was identified, resulted in the odds that people living homeless belonged to a cluster (AOR 0.48, 95% CI: 0.32, 0.72) moving away from the null. This suggests that, prior to this outbreak, unstable housing was associated with a 52% lower odds of being in a genetic cluster.

Discussion

Our findings suggest that people experiencing unstable housing or living homeless in King County are very vulnerable to HIV acquisition, as they are disproportionately burdened by incident HIV. Over the past decade, 10% of new HIV diagnoses were among people experiencing unstable housing or living homeless, despite comprising < 1% of King County's overall population. Outside of a previously described outbreak, we did not observe that populations living homeless were more likely to be in a genetic cluster, suggesting they do not have higher rates of onward HIV transmission compared to those who were stably housed. Our findings suggest that the genetic clustering that does exist within this population in King County is predominantly associated with methamphetamine and injection drug use.

Genomic epidemiology has increasingly been used to identify HIV clusters among PWID, many of whom are also living homeless. This analysis was strengthened by the high proportion of unstably housed individuals who had an available HIV sequence (85%), which likely results from the high proportion of PLWH who are living homeless and receive care at a Ryan White funded HIV clinic (Madison Clinic, the largest HIV clinic in the Northwestern US) at Harborview Medical Center (the county hospital) and other public clinics that specialize in HIV/AIDS care.

Despite observing a lower odds of genetic clustering among sequences from people who were unstably housed at diagnosis in our multivariate analysis, our retrospective application of genetic clustering methods was still able to identify the 2018-19 outbreak in north Seattle among a community of PWID and cisgender women engaged in sex work who were also living homeless.[1, 5] This outbreak was first identified by PHSKC through partner services interviews, and later the scale of the outbreak was confirmed through the use of HIV genetic sequences.[5, 22] The local newspaper's messaging around this particular HIV outbreak, which named the street on which this outbreak occurred, has received significant criticism from HIV advocates, who state that this type of disclosure presents the potential risk of violence for PLWH.[23] This example underscores the importance that all outbreak investigations—both those identified through traditional epidemiological methods as well as those identified using HIV genetic sequences—consider the potential role of media in disseminating stigmatizing information and prioritize the confidentiality of the affected communities. At the same time, PHSKC's response resulted in a significant expansion of services and HIV prevention infrastructure in the north Seattle, which was geographically far from most of the low-barrier and low-cost HIV prevention and treatment services in central Seattle. These expanded services included a mobile clinic, mobile

Table 1 Characteristics of People Newly Diagnosed with HIV in King Country, WA, 2010–2018

		Unstably Housed or Living Homeless at Diagnosis	Presumed to be Stably Housed at Diagnosis	Chi-Square Test Statistic	p-value
N		231	2140		
Age at diagnosis (n,%)					
	< 25	35 (15.2)	349 (16.3)	2.99	0.392
	25–34	74 (32.0)	785 (36.7)		
	35–44	60 (26.0)	480 (22.4)		
	> 45	62 (26.8)	526 (24.6)		
Gender (n,%)					
	Cisgender Men	182 (78.8)	1873 (87.5)	15.31	**0.002**
	Cisgender Women	46 (19.9)	241 (11.3)		
	Transgender Men	0 (0.0)	4 (0.2)		
	Transgender Women	3 (1.3)	22 (1.0)		
Race[a] (n,%)					
American Indian/Alaska Native		17 (7.4)	78 (3.6)	5,84	**0.016**
Asian		6 (2.6)	179 (8.4)	7.86	**0.005**
Black		65 (28.1)	487 (22.8)	1.82	0.178
Native Hawaiian/ Pacific Islander		2 (0.9)	41 (1.9)	0.74	0.390
White		145 (62.8)	1431 (66.9)	0.26	0.608
Unknown		12 (5.2)	96 (4.5)	0.09	0.762
Hispanic/Latinx Ethnicity		22 (9.5)	284 (13.3)	0.18	**0.183**
Country of Birth (n,%)					
	USA	189 (81.8)	1439 (67.2)	22.81	**< 0.001**
	Foreign	38 (16.5)	547 (25.6)		
	Missing	4 (1.7)	154 (7.2)		
Transmission Category (n,%)					
	MSM	93 (40.3)	1460 (68.2)	208.76	**< 0.001**
	MSM-PWID	44 (19.0)	149 (7.0)		
	PWID	48 (20.8)	61 (2.9)		
	Heterosexual	16 (6.9)	145 (6.8)		
	Other/Unknown	30 (13.0)	325 (15.2)		
Sexual Behavior (n,%)					
	Sex with both men and women[b]	54 (23.4)	288 (13.5)	15.82	**< 0.001**
	Sex with a PWID[c,d]	60 (30.0)	81 (6.9)	107.44	**< 0.001**
	Gave money or drugs in exchange for sex[b,d]	10 (5.0)	27 (2.3)	5.04	**0.025**
	Received money or drugs in exchange for sex[b,d]	27 (13.5)	41 (3.5)	39.98	**< 0.001**
Substance Use (n,%)					
	Methamphetamine use[c,d]	87 (43.5)	156 (13.2)	117.94	**< 0.001**
First CD4 cell count (n,%)					
	< 200	40 (17.3)	488 (22.8)	3.55	0.169
	200–499	87 (37.7)	828 (38.7)		
	≥ 500	92 (39.8)	774 (36.1)		
Deceased as of 2017[e] (n,%)		16 (8.7)	76 (3.9)	8.29	**0.004**
Completed a partner services interview (n,%)		200 (86.6)	1180 (55.1)	83.43	**< 0.001**
Has a PR/RT Sequences (n,%)		196 (84.8)	1462 (68.3)	26.31	**< 0.001**
HIV subtype[f] (n,%)					

Table 1 (continued)

	Unstably Housed or Living Homeless at Diagnosis	Presumed to be Stably Housed at Diagnosis	Chi-Square Test Statistic	p-value
B	179 (91.3)	1279 (87.5)	0.11	0.738
Other	17 (8.7)	183 (12.5)		
HIV sequence appears in a genetic cluster[f] (n,%)	129 (65.8)	942 (64.0)	0.01	0.908

MSM, men who have sex with men; PR/RT, protease/reverse transcriptase; PWID, people who inject drugs

[a] Categories are not exclusive. Note that 120 (5%) of individuals are multiracial.

[b] Ever

[c] In the past year

[d] Among individuals with a partner services interview

[e] Data are restricted to 2010–2017 to account for an up-to 18-month delay in reported vital status

[f] Among individuals with an available PR/RT sequence

syringe services programs, and direct outreach to communities of people living homeless and engaged in sex work for HIV and Hep C screening and condom distribution. This outbreak also resulted in expanded local guidelines to recommend that medical providers offer PrEP to women who exchange sex, particularly individuals who inject drugs or who are living homeless.[1, 5, 22].

Our results highlight that PLWH who have overlapping marginalizing experiences that place them at increased risk of criminalization—namely people who report methamphetamine use, transactional sex, injection drug use—are significantly more likely to be identified as part of a genetic cluster. This is particularly important given community concerns about the use of MHS data for cluster detection and response.[24] People living with and at risk for HIV acquisition in King County and nationally have expressed confidentiality concerns related to cluster detection and response, which they fear could increase their vulnerability to criminalization and further stigmatize community members who disproportionately experience policing.[25, 26] Although the behavior of PLWH is criminalized in the majority of US states, recent legislation within WA state and King County has significantly minimized the risk of criminalization for PLWH in King County.[27] In 2020, WA state passed legislation that reduced intentional HIV exposure from a felony to a misdemeanor and the city of Seattle repealed two prostitution and drug traffic loitering laws. In addition, PHSKC has data protections that prevent MHS data from being shared with court/legal systems, police, or immigration and customs enforcement (i.e. ICE). Nonetheless, these findings highlight that PLWH who are identified to be part of genetic clusters are members of communities that are already more likely to experience multiple axes of stigma.

Given that people in our study who were unstably housed or living homeless at diagnosis had a high prevalence of behaviors that were independently associated with genetic clustering in our analysis, it was surprising that we did not observe elevated rates of clustering within that population in either univariate or multivariate models. One explanation could be that while these factors do place people experiencing unstable housing or living homeless at increased risk of HIV acquisition, onward HIV transmission occurs infrequently within this population. Alternatively, our findings may be affected by how individuals are defined as unstably housed or living homeless in the NHSS and partner services interviews, the lack of specificity in our measures of behavioral risk, or the failure to include individuals who transmit/acquire HIV from people living homeless in our sample of HIV sequences. Although our study has a high sampling coverage compared to other molecular HIV studies, we were still missing HIV sequence data for 30% of new HIV diagnoses. Regardless, our findings highlight that HIV disproportionately affects individuals who face housing insecurity, and that unstably housed PLWH experience higher rates of mortality, social marginalization and syndemic factors (e.g. transactional sex, injection drugs use).

This study had several limitations. It is likely that we have under-ascertained the number of individuals who were unstably housed or living homeless at diagnosis. Most unstably housed individuals (200 out of 231) were identified through partner services interviews and not in NHSS; thus, ascertainment of housing status was likely incomplete. In addition, homelessness is often a transient state, and our study only captured housing status at diagnosis. We also were unable to determine other situational factors that may influence a person's vulnerability to HIV, including whether or not people were sheltered (e.g. living in an emergency shelter or vehicle) or unsheltered (e.g. living on the street or in a tent), chronically homeless, or had access to syringe services or PrEP.

Our analysis is also vulnerable to some degree of misclassification of the exposure variable and other covariates since HIV surveillance data is collected at the time of HIV diagnosis rather than at the time of HIV acquisition or onward transmission (which are unknown); although, this is a general limitation of public health surveillance data.

Table 2 Factors associated with being part of a genetic cluster among PLWH with an available PR/RT HIV sequence, King County, WA, 2010–2018

		All PLWH (N = 1,658)		PLWH Unstably Housed or Living Homeless at Diagnosis (N = 196)	
		Univariate	Multivariate	Univariate	Multivariate
		OR (95% CI)	AOR (95% CI)	OR (95% CI)	AOR (95% CI)
Unstably housed or living homeless at diagnosis		1.02 (0.75, 1.39)	**0.65 (0.44, 0.95)**	--	--
Early HIV[a]		**2.09 (1.67, 2.62)**	**1.66 (1.29, 2.12)**	**2.81 (1.49, 5.31)**	**2.88 (1.28, 6.47)**
Transmission Category					
	MSM	ref	ref	ref	ref
	MSM-PWID	1.37 (0.92, 2.04)	0.72 (0.46, 1.14)	2.28 (0.93, 5.60)	1.39 (0.45, 4.34)
	PWID	1.39 (0.85, 2.29)	0.96 (0.54, 1.67)	**2.65 (1.09, 6.44)**	1.39 (0.45, 4.34)
	Heterosexual	**0.45 (0.31, 0.65)**	0.95 (0.64, 1.51)	0.37 (0.11 1.23)	0.64 (0.15, 2.81)
	Other/Unknown	**0.23 (0.17, 0.31)**	**0.47 (0.33, 0.66)**	**0.21 (0.07, 0.58)**	0.42 (0.12 1.48)
Behaviors					
	Methamphetamine use (past year)	**3.56 (2.45, 5.18)**	**2.09 (1.33, 3.27)**	**6.68 (3.22, 13.86)**	**3.82 (1.40, 10.46)**
	Sex with a PWID (past year)	**5.86 (3.20, 10.7)**	**3.41 (1.70, 6.89)**	**14.82 (4.42, 49.65)**	**7.82 (1.74, 35.12)**
	Transactional Sex[b]	**1.96 (1.20, 3.18)**	0.98 (0.55, 1.73)	1.71 (0.72, 4.05)	0.74 (0.22, 2.48)
Age					
	<25	ref	ref	ref	ref
	25–34	0.88 (0.64, 1.20)	0.85 (0.60, 1.20)	0.94 (0.37, 2.42)	0.49 (0.15, 1.68)
	35–44	0.79 (0.57, 1.10)	0.87 (0.60, 1.27)	0.60 (0.23, 1.57)	0.60 (0.16, 2.21)
	>45	**0.64 (0.46, 0.89)**	0.75 (0.52, 1.08)	0.71 (0.27, 1.84)	0.94 (0.26, 3.40)
Race					
	White	ref	ref	ref	ref
	American Indian/Alaska Native	1.09 (0.65, 1.83)	0.88 (0.52, 1.50)	0.80 (0.28, 2.34)	1.58 (0.40, 6.24)
	Asian	**0.56 (0.38, 0.82)**	0.81 (0.52, 1.26)	0.25 (0.04, 1.58)	0.60 (0.06, 5.97)
	Black	**0.27 (0.22, 0.35)**	**0.36 (0.27, 0.48)**	**0.33 (0.17, 0.64)**	**0.47 (0.20, 1.12)**
	Native Hawaiian/Pacific Islander[c]	1.02 (0.49, 2.13)	1.36 (0.64, 2.88)	--	--
Ethnicity					
Non-Hispanic/Latinx		ref	ref	ref	ref
Hispanic/Latinx		0.80 (0.62, 1.03)	0.85 (0.62, 1.16)	**0.17 (0.06, 0.46)**	**0.18 (0.05, 0.68)**
USA born		**3.54 (2.81, 4.47)**	**2.20 (1.62, 2.97)**	**6.25 (2.60, 15.04)**	1.92 (0.58, 6.44)
Year of diagnosis[d]		**0.94 (0.90, 0.97)**	0.96 (0.92, 1.000)	1.11 (1.00, 1.24)	1.09 (0.95, 1.26)

AOR, adjusted odds ratio; CI, confidence interval; MSM, men who have sex with men; OR, odds ratio; PLWH, people living with HIV; PWID, people who inject drugs

[a] Defined as a CD4 count > 500 cells/mm^3 at diagnosis

[b] Ever giving or receiving money or drugs in exchange for sex

[c] Among Native Hawaiian/Pacific Islander PLWH who were also living homeless, all individuals with an available sequence appeared in a genetic cluster which results in high collinearity. Thus, this variable was omitted from the subanalysis.

[d] Reference year is 2010

Additionally, since the time between HIV acquisition and diagnosis is variable, we are unable to determine if this misclassification is differential or non-differential and are unable to predict the direction of misclassification bias. Cluster-based analyses are also vulnerable to confounding by sampling coverage and time from HIV acquisition to sample collection. Our measure of early HIV (CD4 count > 500 cells/mm^3 at diagnosis) is imperfect, and thus there may be residual confounding by time from acquisition to sample collection. Last, Since King County was one of the first counties in the U.S. to achieve the UNAIDS 90-90-90 targets, and has been experiencing an overall decline in HIV incidence since 2014, these findings may not be generalizable to other regions of the US.[1].

Our findings highlight that people experiencing unstable housing or living homeless in King County are disproportionately impacted by HIV, but do not have an increased likelihood of onward HIV transmission or being identified in genetic clusters compared to PLWH with stable housing. These findings underscore the importance of prioritizing HIV interventions for people experiencing unstable housing, and run counter to prejudicial stereotypes about people who live homeless and their role in HIV transmission. To date, HIV prevention and strategies to retain people living homeless in HIV care across the US have included: the provision of on-site medication storage (or "lockers") for PrEP and ART medicines, accessible syringe services and outreach programs, mobile ART/PrEP delivery, integrated housing and HIV services, low barrier HIV care clinics, and access to medical providers with whom individuals living homeless feel safe and respected.[28–31] Existing studies also highlight the importance of upstream interventions, such as rental assistance, housing-first and rapid supportive housing models to improve outcomes among people newly diagnosed with HIV.[32–37] Future areas of research should examine modifiable factors that may increase likelihood of HIV outbreaks among homeless communities—such as encampment sweeps, during which people's possessions, including medicines (PrEP, ART, naloxone), and safe injection supplies are lost—as well as interventions that increase access to biomedical interventions and engagement in care.

Abbreviations

AOR	adjusted odds ratio
ART	antiretroviral treatment
CI	confidence interval
HIV	human immunodeficiency virus
MSM	men who have sex with men
NHSS	National HIV Surveillance System
PrEP	pre-exposure prophylaxis
PR/RT	protease/reverse transcriptase
PWID	people who inject drugs

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Declarations

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