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Homelessness at Diagnosis is Associated with Death among People with HIV in a Population-Based Study of a U.S. City

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Abstract

Objective: San Francisco (SF), California, has experienced a 44% reduction in new HIV diagnoses since 2013 supported by its "Getting to Zero" initiative; however, the age-adjusted mortality rate in people with HIV (PWH) has not decreased. We sought to identify factors associated with death among PWH in SF.

Design: Population-based incidence-density case-control study

Methods: Among PWH in the SF HIV surveillance registry, a random sample of 48 decedents from July 1, 2016 to May 31, 2017 were each matched to 2-3 controls who were alive at the date of death (108 controls matched on age and time since diagnosis). Covariates included demographics, substance use, housing status, medical conditions, and care indicators from the study population. We used matched-pair conditional logistic regression to examine factors associated with mortality.

Results: Of the 156 PWH in the study, 14% were African-American, 14% Latino, and 8% female sex. In adjusted analysis, factors associated with higher odds of death included: homelessness at HIV diagnosis [adjusted odds ratio (AOR)=27.4 95% confidence interval (CI)=3.0-552.1], prior-year injection drug use (AOR=10.2 95% CI=1.7-128.5), prior-year tobacco use (AOR=7.2 95% CI=1.7-46.9), being off ART at any point in the prior year (AOR=6.8; 95% CI=1.1-71.4), and being unpartnered vs. married/partnered (AOR=4.7; 95% CI=1.3-22.0).

Conclusions: People homeless at HIV diagnosis had 27-fold higher odds of death compared to those with housing; substance use and retention on ART in the prior year are other important intervenable factors. New strategies to address these barriers, and continued investment in supportive housing and substance use treatment, are needed.

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Keywords

Mortality; HIV; homelessness; substance use; antiretroviral therapy; preventable mortality

Introduction:

Getting to Zero San Francisco (GTZ-SF), a multisector consortium formed in 2013, seeks to dramatically reduce HIV-associated deaths among people with HIV (PWH), new HIV infections, and HIV-related stigma [1–3]. Although SF has experienced a 44% reduction in HIV diagnoses and a 25% decline in HIV-related fatality rate since 2013, the overall age-adjusted mortality rate did not change among PWH over this period, likely related to increasing deaths from non-HIV related cancers and substance use [3–5]. Furthermore, given the association between homelessness and poor HIV outcomes,[6] there is concern that limited progress on homelessness in SF and nationally could also limit the impact of GTZ-SF, and future impact of U.S. End the HIV Epidemic programs, on the health of PWH [1, 7, 8].

The goal of this investigation was to identify factors associated with death among PWH using an incidence-density case-control study, to inform programs designed to meet the GTZ-SF goal of reducing preventable deaths among PWH. We hypothesized that substance use, housing status, and mental health would contribute to increased odds of HIV mortality.

Methods:

Sampling and data collection

Among PWH in the SF Department of Public Health surveillance registry July 1, 2016 to May 31, 2017, a random sample of 50 decedents was drawn from the overall total of 171 decedents for enhanced mortality review. Then, 2-3 persons living with HIV were selected as controls using incidence-density sampling to match to decedents based on age +/−three years and date of diagnosis +/−six months [9–11]. The death date of the matched decedent was defined as the “index date” for both decedents and matched controls. Of this sample, two individuals (>90 years-old) were excluded due to not having matched any living controls. Two percent of potential controls were also not able to be sampled due to receiving care at a site at which surveillance staff did not have access.

Demographics, transmission group, housing status at diagnosis, and CD4-counts and HIV viral load (both prior year) were extracted from the surveillance database. Surveillance definitions categorized PWH in transmission groups [3]. Chart review was performed starting three years prior to the index date for cases and controls. Substance use and current housing status was extracted in the 12-months prior. Individuals were classified as unpartnered vs. partnered/married in the prior year. Mental health diagnoses and comorbid medical conditions were extracted based on ICD 9/10 codes or chart documentation by the provider. Being off ART was defined as any time off ART in the 12-months prior to the index date. Missed visits were defined as a no-show visit without cancelling in advance [12]. Retained in care was defined as having attended two in-person visits at least 90 days apart over 12-

months[13]. The underlying cause of death was obtained from the National Death Index-Plus [14].

Analysis

Unadjusted and adjusted conditional logistic regression was performed to assess risk factors for mortality. The adjusted model was initially constructed using all prognostic covariates that were significantly associated with death at the $p<0.05$ level in the unadjusted models. A manual forward stepwise process was employed, and covariates were retained in the multivariate model at the $p<0.10$ level.

In-depth chart-review of the contribution of substance use, mental health, or housing to circumstances of death

In addition to the case-control study's assessment of factors associated with increased odds of death, an in-depth chart review was performed to understand the absolute proportion of deaths in which three specific factors contributed to the circumstances of death: substance use (including tobacco), mental health, and/or unstable housing. Two HIV physicians independently reviewed each record and evaluated if these conditions contributed to the circumstances of the individual's death, with discrepancies going to a third review.

Results:

The study population included 156 individuals, 48 decedents and 108 matched controls. Overall, 14% of the sample were African-American, 14% Latino; 8% were female sex. The median time from HIV diagnosis was 228 months (interquartile range (IQR): 152-304), median CD4 prior to death was 398 (IQR: 180-617), and median CD4 at diagnosis was 417 (IQR: 224-612). Overall, 25% of the decedents compared with 4% of the controls were homeless at diagnosis. **(**Table 1**)**.

Causes of death

In the decedents, 27% had an HIV-related condition as the underlying cause of death, 15% non-AIDS cancer, 15% overdose/substance use, 10% cardiovascular disease, 4% trauma/accident, 4% suicide, 4% hepatitis B or C, 4% other liver disease, 4% non-AIDS infectious disease, 2% chronic obstructive pulmonary disease, 2% renal disease, and 9% other.

Factors associated with death in case-control analysis

The factors associated with death in unadjusted analysis are listed in Table 2. Factors associated with death in the unadjusted but not adjusted analysis included: non-injection illicit drug use [unadjusted odds ratio (OR)=8.6 95% confidence interval (CI)=3.2-37.8], alcohol use disorder (OR=3.3 95% CI=1.5-7.7), people who inject drugs (PWID) vs. men who have sex with men (MSM; OR=6.3; 95%CI=1.5-31.5) and MSM-PWID vs. MSM (OR 4.6; 95% CI=1.5-15.7), homeless in the prior year (OR 9.5; 95% CI=1.9-90.9), schizophrenia (OR=18.5 95% CI=2.4-828.2), bipolar disorder (OR=5.7; 95% CI=1.3-34.6), and missing a primary care visit in the prior year (OR=4.6; 95% CI=1.9-12.3).

In adjusted analysis, factors associated with death included: homelessness at diagnosis [adjusted OR (AOR)=27.4 95% CI=3.0-552.1], past-year injection drug-use (IDU; AOR=10.2 95% CI=1.7-128.5), tobacco use (AOR=7.2 95% CI=1.7-46.9), not using ART at any point in the prior year (AOR=6.8; 95% CI=1.1-71.4), and being unpartnered/living alone vs. married/partnered (AOR=4.7; 95% CI=1.3-22.0) **(**Table 2**)**. In an alternate modelling strategy including transmission group rather than current IDU, homelessness at diagnosis remained associated (AOR 18.3; 95%CI=2.6-271.6). When excluding homelessness at diagnosis from the adjusted model, the AOR for current homelessness was 3.4 (95% CI=0.47-40.1).

In-depth chart-review for contribution of substance use, mental health, or housing to death

After performing an in-depth review of circumstances that may have contributed to death, substance use contributed for 60% of the decedents, mental illness for 34%, and housing status for 30%. At least one of the factors contributed to death for 65% of the decedents.

Discussion:

In a contemporary population-based study in a U.S. city, homelessness at diagnosis was associated with 27-fold higher independent odds of death. In the in-depth chart review, housing status contributed to the circumstances of death for 30% of decedents, echoing other cohorts[15–17]. Supportive housing improves care outcomes across the disease course and is associated with lower mortality among PWH [16–18]. “Housing First,” a policy that prioritizes provision of supportive housing prior to substance use abstinence, first implemented in SF in 2004, increases long-term housing stability and decreases substance use [19]. However, housing supply remains far too limited [18]. Given the independent association of both homelessness and substance use with death, increasing supportive housing may be particularly effective. The intersection of mental health, housing, and substance use on the pathway to preventable deaths is complex and may be best addressed by multi-component interventions. For instance, an intervention that combined housing, case management, and behavioral interventions decreased hospitalizations in adults with chronic medical illnesses [20], and a comprehensive housing program for PWH and severe mental illness was associated with improved AIDS-free survival [21]. Housing is a key social determinant of health for PWH:[16–18] continued investment in supportive housing will likely be needed to meet the U.S. End the Epidemic goals.

Tobacco use’s association with mortality is supported by increasing deaths from tobacco-related cancers such as lung and oropharyngeal cancer among PWH [3, 22]. U.S. PWH on ART are more likely to smoke than the general population and smoking cessation interventions reduce mortality [23]. IDU’s association with mortality mirrors the findings of prior cohorts, contributing to death via overdose, hepatitis C, and decreased care engagement [24–26]. In the in-depth review, substance use contributed to the circumstances of death for a majority (60%). Opioid use disorder treatment is associated with decreased mortality in the general population, and improved viral suppression and ART initiation among PWH [5, 27–30]. Stimulant use is increasing among San Francisco MSM [3], and interventions to treat stimulant use disorder merit additional research.

Schizophrenia and bipolar disorder were associated with mortality in unadjusted, but not adjusted analyses; while in the in-depth review, mental illness contributed to the circumstances of death for greater than a third of decedents. The impact of severe mental illness (SMI) on mortality may have been mediated by increased substance use and/or decreased ART use in the adjusted analysis. Death due to substance use outpaces suicide in its contribution to excess mortality among people with schizophrenia [31]. Smoking cessation and substance use treatment can reduce mortality among people with SMI[31, 32].

The association between being unpartnered and mortality has been noted in studies in the general population and among PWH [33–35]. Provision of social support services may particularly benefit older PWH living alone, who may suffer health consequences of geriatric conditions such as falls and neurocognitive issues without additional support [36].

Finally, not using ART in the prior year was associated with death. Retaining PWH on ART remains a challenge across the United States, particularly in populations with severe mental illness, substance use challenges, and housing instability, with new strategies needed [37]. Continued investment in reengagement programs, such as the Getting to Zero-SF navigation program, particularly for individuals who miss or do not attend primary care visits, can potentially improve ART persistence in this population [3, 38, 39].

The limitations of this study included the inability to access records at some sites, although this affected a small subset. Assessment of covariates was limited by provider documentation, and therefore the prevalence of factors and their impact on mortality, such as substance use and homelessness, may have been underestimated. Another limitation is the time elapsed between homelessness at diagnosis and death. Current homelessness was also associated with near ten-fold higher odds of mortality in unadjusted analysis although confidence intervals were wide in adjusted analysis. Homelessness at diagnosis, which was assessed through proactive questioning rather than chart review, yielded more precise estimates, and thus was favored in this analysis. Although it is likely that homelessness across the disease courses negatively impacts the health of PWH, it is also possible that the time of diagnosis may be a critical period for homelessness' impact on health, such as through delayed ART initiation [3]. In addition, the sample size was small and may not be generalizable to other populations.

In conclusion, despite progress supported by Getting to Zero programs, potentially preventable deaths occurred for more than half of participants (i.e. HIV, substance use, suicide, violence, Hepatitis B/C, and potentially-preventable cancers). The intersection of housing, substance use, and mental illness contribute to challenges in maintaining PWH on treatment and demonstrate the HIV epidemic's disproportionate impact on vulnerable populations. In addition to continued investment in medical interventions, implementation of comprehensive social services with known efficacy such as supportive housing, substance use and mental health treatment, as well as investment in developing new strategies, will be needed to dramatically reduce preventable deaths.

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Table 1.

Characteristics of decedents and matched controls among persons with HIV, San Francisco, CA, July 1, 2016-May 31, 2017.

Characteristic	Decedents N=48 (%)	Controls N= 108 (%)
Female sex at birth	5 (10)	7 (6)
Race/ethnicity: White	31 (65)	65 (60)
African-American	8 (17)	14 (13)
Latino	4 (8)	17 (16)
Other/Multiple	5 (10)	12 (11)
Age (at death or at index date): * <40	2 (4)	6 (6)
40-49	9 (19)	16 (15)
50-59	15 (31)	34 (31)
60-69	15 (31)	37 (34)
70+	7 (15)	15 (14)
Months since diagnosis (median, IQR) *	243 (168-318)	214 (136-292)
CD4 count at diagnosis (median, IQR)	437 (274-600)	407 (204-610)
HIV Transmission group: MSM	23 (48)	84 (78)
PWID	8 (17)	5 (5)
MSM-PWID	13 (27)	11 (10)
Heterosexual	3 (3)	6 (6)
None reported	1 (2)	2 (2)
Homeless at any point (prior year)	11 (23)	3 (3)
Homeless at diagnosis	12 (25)	4 (4)
Unpartnered vs. married/partnered	18 (31)	18 (17)
Alcohol use disorder (prior year)	12 (25)	7 (6)
Tobacco use (prior year)	23 (48)	22 (20)
Injection drug use (prior year)	6 (13)	2 (2)
Non-injection illicit drug use (prior year)	19 (40)	10 (9)
Schizophrenia	8 (17)	1(1)
Bipolar Disorder	7 (15)	3 (3)
Depressive disorder (active prior year)	17 (35)	33 (31)
Not retained in care [1]	28 (58)	46 (43)
Missed primary care visits in prior year (median, IQR) [2]	1 (0-2)	0 (0-0)
CD4 count prior to death; median (IQR)	398 (180-617)	581 (426-795)
Not on ART at any time in prior year	13 (27)	10 (10)

MSM: men who have sex with men; PWID: people who inject drugs; ART: antiretroviral therapy; IQR: interquartile range

* Matching criteria

[1] Attending two visits per year at least 90 days apart

[2] Missed visits indicates a scheduled visit to which the patient no-showed without cancelling

Table 2:

Unadjusted and adjusted odds ratios and 95% confidence intervals for death among people with HIV, San Francisco, CA, July 1, 2016-May 31, 2017[1]

Characteristic	Unadjusted OR (95% CI)	Adjusted OR (95% CI)
Female sex at birth	1.85 (0.43-7.54)	-
Race/ethnicity: White	Ref.	-
African-American	1.58 (0.46-5.58)	-
Latino	0.54 (0.13-1.80)	-
Other/Multiple	0.81 (0.20-1.82)	-
HIV transmission group: MSM	Ref.	-
PWID	**6.28 (1.53-31.52)**	-
MSM-PWID	**4.58 (1.50-15.68)**	-
Heterosexual	2.13 (0.30-12.58)	-
None	2.81 (0.05-56.84)	-
Homeless at any point (prior year)	**9.45 (1.94-90.87)**	-
Homeless at diagnosis	**13.47 (2.94-125.44)**	**27.36 (3.03-552.14)**
Unpartnered vs. married/partnered	**2.71 (1.18-6.42)**	**4.70 (1.28-21.96)**
Tobacco use (prior year)	**6.00 (2.24-20.26)**	**7.22 (1.67-46.90)**
Injection drug use (prior year)	**10.95 (3.18-37.79)**	**10.18 (1.65-128.50)**
Non-injection illicit drug use (prior year)	**8.64 (3.19-29.31)**	-
Alcohol use disorder (prior year)	**3.29 (1.48-7.74)**	-
Schizophrenia	**18.49 (2.44-828.20)**	-
Bipolar disorder	**5.69 (1.28-34.58)**	-
Active depressive disorder (prior year)	0.84 (0.41-1.71)	-
Not retained in care[2]	1.85 (0.87-4.05)	-
Any missed primary care visits[3]	**4.61 (1.92-12.25)**	-
CD4 count <200 within year of death	3.61 (0.95-15.40)	-
CD4 count at diagnosis per 100 cells	1.01 (0.93-1.30)	
Not on ART at any point in prior year	**3.86 (1.30-12.82)**	**6.80 (1.05-71.43)**
Unsuppressed HIV viral load (prior year)	1.84 (0.41-8.26)	-

Bold text indicates p<0.05; OR: Odds ratio; CI: Confidence interval; MSM: men who have sex with men; PWID: people who inject drugs; ART: antiretroviral therapy

[1]Among people with HIV in San Francisco, a random sample of decedents was matched to controls based on age +/− 3 years and date of diagnosis +/− 6 months.

[2]Attending two visits per year at least 90 days apart in the prior 12-months

[3]Missed visits indicate a missed scheduled visit that the patient did not attend or cancel in the prior 12-months.