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Sex and Race Disparities in Mortality and Years of Potential Life Lost Among People With HIV: A 21-Year Observational Cohort Study

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Background. Since the availability of antiretroviral therapy, mortality rates among people with HIV (PWH) have decreased; however, this does not quantify premature deaths among PWH, and disparities persist.

Methods. We examined all-cause and premature mortality among PWH receiving care at the Vanderbilt Comprehensive Care Clinic from January 1998 to December 2018. Mortality rates were compared by demographic and clinical factors, and adjusted incidence rate ratios (aIRRs) were calculated using multivariable Poisson regression. For individuals who died, age-adjusted years of potential life lost (aYPLL) per total person-years living with HIV were calculated from US sex-specific life tables, and sex and race differences were examined using multivariable linear regression.

Results. Among 6531 individuals (51% non-Hispanic [NH] White race, 40% NH Black race, 21% cis-gender women, 78% cis-gender men) included, 956 (14.6%) died. In adjusted analysis, PWH alive in the most recent calendar era (2014–2018) had decreased risk of mortality compared with those in the earliest calendar era (1998–2003; aIRR, 0.22; 95% CI, 0.17–0.29), and women had increased risk of death compared with men (aIRR, 1.31; 95% CI, 1.12–1.54). Of those who died, Black women had the highest aYPLL (aIRR, 592.5; 95% CI, 588.4–596.6), followed by Black men (aIRR, 470.7; 95% CI, 468.4–472.9), White women (aIRR, 411.5; 95% CI, 405.6–417.4), then White men (aIRR, 308.6; 95% CI, 308.0–309.2). In adjusted models, higher YPLL remained associated with NH Black race and cis-gender women, regardless of HIV risk factor.

Conclusions. Despite marked improvement over time, sex disparities in mortality as well as sex and race disparities in YPLL remained among PWH in this cohort.

Keywords. HIV; health care disparities; mortality; premature mortality; years of potential life lost.

With the success of antiretroviral therapy, people with HIV (PWH) in the United States have nearly normal life expectancies, particularly among those with early diagnosis and treatment [1]. In the United States, rates of death among people diagnosed with HIV have decreased by 36.6% from 2010 to 2018, driven primarily by decreases in the HIV-related mortality rate of those connected to care and the shift toward earlier initiation of antiretroviral therapy [2]. Notably, this mortality benefit relies on retention of individuals at each step of the HIV care continuum; however, disparities across the continuum by sex and race persist [1, 3].

These sex and race disparities among PWH have been evident since the beginning of the epidemic, but the persistence of these disparities represents one of the most important challenges of the HIV epidemic today [4]. Minority groups are disproportionately affected by HIV, with the highest prevalence of HIV by race in the United States in 2019 seen in Black/African American persons [5]. Delays in HIV diagnosis are seen in females, Black and Hispanic/Latino individuals, and older persons [6]. Discontinuity of care has also been shown to be higher in Black individuals compared with non-Black individuals, which contributes to differences in long-term outcomes [7]. Among PWH in care in the United States, female sex and Black race have been associated with higher mortality risk [8, 9].

The intersection of sex and racial disparities is particularly pertinent to HIV care in the US South, which continues to have the highest incidence of HIV and rate of HIV-related deaths [2, 5]. The US South includes rural areas with high HIV prevalence,

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less access to health care providers, and higher HIV stigma, all of which contribute to worse outcomes for PWH and increased disparities [10, 11]. This was seen in a study reported by our group in 2009 that showed a significantly increased risk of mortality among women at the Vanderbilt Comprehensive Care Clinic (VCCC) after adjusting for race [12].

While examination of mortality rates is an important metric, it does not capture the burden of early deaths in these communities. Consequently, there has been a growing interest in monitoring premature mortality, which emphasizes the concept that the time lost by death at a young age is an important measurement of the impact of disease [13]. One method for assessing this impact is measurement of years of potential life lost by each death, which quantifies the years a person would have been expected to live if they had not died prematurely. Rates of years of potential life lost in different groups can be calculated to allow for comparison. In the era of antiretrovirals in the United States, deaths related to untreated HIV are more commonly seen in vulnerable populations and tend to result in death at a younger age when compared with deaths from chronic diseases [14]. There are few epidemiologic studies that focus specifically on years of potential life lost for people with HIV in the United States connected to care.

This study examined race and gender/sex differences in mortality rates and years of potential life lost among PWH at the VCCC from 1998 to 2018. We hypothesized that mortality rates and rates of years of potential life lost, as a measure of premature mortality, have improved over time but that differences by race and sex persist.

METHODS

Study Population

We conducted a retrospective cohort study of adults (≥18 years of age) receiving care at the Vanderbilt Comprehensive Care Clinic (VCCC) in Nashville, Tennessee, between January 1, 1998, and December 31, 2018. The VCCC provides HIV subspecialty and primary care for PWH. We included PWH who had established care at the clinic between 1998 and 2018 and had at least 2 provider visits in the first year of care. Individual-level data elements were collected systematically from electronic medical record review by dedicated research staff throughout the observation period. Data elements included demographic variables (race, ethnicity, birth sex, gender, self-reported HIV acquisition risk factors), HIV clinical variables (year of HIV diagnosis, history of AIDS-defining illnesses, CD4 lymphocyte counts, and HIV RNA values), comorbidities and coinfections (including hepatitis C infection and noncommunicable diseases), and date of death (mortality). Throughout the observation period, mortality data were collected routinely by periodic linkage with national registries (the National and Social Security Death Indices) and by clinic outreach, including direct reports from families and newspapers obituaries. Internal analyses comparing clinic records and national death registries have validated very high capture (98.7%) of death events among clinic patients [15]. Cause of death data were systematically recorded by clinic providers and research staff based upon thorough medical record review and death certificate data, when available, throughout the study period. Deaths without any available cause of death information were classified as due to unknown causes.

Patient Consent

This study was approved by the Vanderbilt University Medical Center Institutional Review Board, and a waiver of consent was obtained. All study activities were compliant with the Declaration of Helsinki.

Unadjusted and Adjusted Mortality Trends

Person-time of observation was defined by date of clinic entry and continued until first occurrence of date of death or December 31, 2018. Loss to follow-up was defined as last clinic visit >1 year before date of death or date of administrative censoring (December 31, 2018). Age-period tables were created by stratifying person-time contributed across age and calendar periods (1998–2003, 2004–2008, 2009–2013, and 2014–2018). Trends in probability of mortality in each calendar era were examined by demographic characteristics including age, gender (including cis-gender men, cis-gender women, and transgender women), race/ethnicity (non-Hispanic White, non-Hispanic Black, and other), HIV acquisition risk factors, and CD4 cell count at clinic entry using univariate and multivariable Poisson regression with robust variance. Multivariable models examining trends by gender and race/ethnicity across calendar eras included covariates selected a priori: calendar era, age at calendar era start, injection drug use as an HIV acquisition risk factor, anemia at clinic entry, documented year of HIV diagnosis, history of AIDS-defining illness at clinic entry, any history of chronic hepatitis C virus (HCV) coinfection, CD4 cell count at clinic entry, and HIV RNA at clinic entry. We multiplied imputed (n = 5 replications) missing laboratory data at clinic entry (CD4 cell count, HIV RNA, and hemoglobin) for multivariable models including variables for death, age, year of clinic entry, sex, HIV acquisition risk factor, race, and antiretroviral therapy (ART). Continuous covariates were included using restricted cubic splines using 3 knots to relax linearity assumptions. Effect modification was examined using 2-way interactions of calendar era with gender and with race/ethnicity.

Years of Potential Life Lost

For individuals who died, YPLL were calculated using the expected years of life remaining for an individual at the time of their death by referencing US sex-specific period life tables by age and year of death [16, 17]. Sex at birth was used for all

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individuals, regardless of gender, and the life tables were not stratified by race. This method has been employed in multiple other studies and more accurately accounts for life expectancy in older adults and sex differences when compared with subtracting age at death from a standard predicted life expectancy [3, 14, 18].

Crude YPLL rate was calculated for each sex and race/ethnic group as total years of potential life lost among those who died per 1000 person-years of time living with HIV among individuals in each demographic in the cohort. Total person-years living with HIV for the denominator was calculated from age at HIV diagnosis to age at death or censoring (December 31, 2018). To account for the younger age distribution among PWH, age-adjusted YPLL (aYPLL) rates and 95% CIs were calculated by direct standardization to the 2000 US census population using the modified gamma-distribution method of Tiwari et al. [19, 20].

To further investigate sex and racial disparities among individuals who had died, we used multivariable linear regression to examine predictors of YPLL. Multivariable models examined differences in predicted YPLL by HIV acquisition risk factor and race/ethnicity, adjusting for age at HIV diagnosis, CD4 lymphocyte count at clinic entry, HIV RNA at clinic entry, history of HCV coinfection, and year of clinic entry.

All analyses were conducted in Stata (StataCorp, College Station, TX, USA).

RESULTS

There were 6539 individuals who established care at the VCCC from 1998 to 2018 who met inclusion criteria. Of the total, 5 individuals were missing age at clinic entry; 2 intersex individuals and 1 transgender male were excluded, leaving 6531 individuals and 57 548 total person-years of follow-up included in the analyses (Table 1). The cohort was approximately half non-Hispanic White, and 78% were cis-gender men. Less than 1% of the cohort were transgender women. Injection drug use as an HIV acquisition risk factor was reported in ~9% of all individuals. Overall, >90% of all individuals received ART during follow-up at the VCCC. From clinic entry, the median person-time of observation was 8.2 years, and overall 41% of individuals had no clinic visits within 1 year of censoring or 1 year of death. Of the 6531 PWH, 956 (14.6%) died. From clinic records and death certificate data, nearly a third of all deaths were from unknown causes, and 24% were due to AIDS. Characteristics of all included individuals by race/ethnicity are described in Supplementary Table 1. Demographic and clinical characteristics of individuals contributing person-time across calendar years (1998–2003, 2004–2008, 2009–2013, 2014–2018) are shown in Supplementary Table 2. From the earliest to the most recent period, the distribution of total person-time shifted to older ages, increasingly other race/ethnicity, increasingly male sex, and a higher median CD4 cell count at clinic entry.

Mortality Trends

Unadjusted mortality rates by demographic and clinical characteristics are shown in Figure 1. Overall, unadjusted mortality rates dramatically decreased during the study period across all demographic and clinical characteristics including age, gender, race/ethnicity, history of injection drug use and HCV coinfection, and CD4 cell count at clinic entry. For age, race, injection drug use, and CD4 cell count at clinic entry, mortality rates not only declined, but disparities between groups narrowed over time. Differences in crude mortality rates among PWH by history of HCV coinfection persisted across the study period. Results of multivariable analyses examining mortality risk are shown in Table 2. After adjusting for age, gender, race/ethnicity, history of injection drug use, anemia at clinic entry, year of HIV diagnosis, history of AIDS-defining illness, HCV coinfection, CD4 cell count, and HIV RNA at clinic entry, PWH in the most recent calendar era (2014–2018) had a 78% decreased probability of death during this time period compared with the probability of death of individuals in the earliest calendar era (1998–2003). In adjusted models, compared with those of non-Hispanic White race/ethnicity, individuals of other (including Hispanic) race/ethnicity had a 44% decreased risk of death overall, and there was no statistical difference in mortality risk comparing PWH of non-Hispanic White or Black race/ethnicity. Compared with cis-gendered men, cis-gender women had a 31% increased risk of mortality in adjusted analyses. Neither the interactions between calendar era and gender nor the interactions between calendar era and race/ethnicity were statistically significant.

Years of Potential Life Lost

For the premature mortality analysis, 96 individuals, 29 of whom died during the study period, did not have a date of HIV diagnosis available and were excluded, leaving 6435 individuals and a total of 927 deaths available for YPLL analyses. Age-standardized YPLL per 1000 person-years were significantly higher for females than males (606.9; 95% CI, 604.7–609.1; vs 366.8; 95% CI, 365.8–367.9). Overall, aYPLL were higher for non-Hispanic Black individuals compared with non-Hispanic White individuals (509.7; 95% CI, 508.2–511.2; vs 395.1; 95% CI, 393.1–397.2). Crude YPLL results are shown in Supplementary Table 3. When the cohort was stratified by race/ethnicity and sex, Black women had the highest aYPLL (592.5; 95% CI, 588.4–596.6), followed by Black men (470.7; 95% CI, 468.4–472.9), White women (411.5; 95% CI, 405.6–417.4), and lastly White men (308.6; 95% CI, 308.0–309.2) (Figure 2). For these calculations, 55 White women in the ≥50-years age group were excluded because their years of life lost was greater than the person-years they contributed after

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Table 1. Demographic and Clinical Characteristics of Persons With HIV by Gender

	Cis-gender Men n = 5108 (78%)	Cis-gender Women n = 1372 (21%)	Transgender Women n = 51 (1%)
Age at HIV diagnosis, median [IQR], y	31.1 [25.4–39.6]	32.2 [25.2–40.7]	27.2 [20.4–34.8]
Age at clinic entry, median [IQR], y	37.4 [29.5–45.3]	37.4 [28.9–45.5]	33.6 [24.3–42.4]
Race/ethnicity, No. (%)	…	…	…
Non-Hispanic White	2772 (54.3)	509 (37.1)	16 (31.4)
Non-Hispanic Black	1856 (36.3)	747 (54.5)	30 (58.8)
Other	480 (9.4)	116 (8.5)	5 (9.8)
Hispanic ethnicity, No. (%)	325 (6.4)	80 (5.8)	3 (5.9)
Sex/HIV acquisition risk factor, No. (%)	…	…	…
Men who have sex with men & TGW	3648 (71.4)	0 (0)	51 (100)
Heterosexual women	0 (0)	1224 (81.9)	0 (0)
Heterosexual men	779 (15.3)	0 (0)	0 (0)
Other/unknown/IDU men	681 (13.3)	0 (0)	0 (0)
Other/unknown/IDU women	0 (0)	248 (18.1)	0 (0)
Injection drug use as HIV acquisition risk factor, No. (%)	412 (8.1)	144 (10.5)	3 (5.9)
Year of HIV diagnosis, median [IQR]	2005 [98–11]	2003 [98–08]	2008.5 [00–13]
ART-naïve at clinic entry, No. (%)	2400 (47.0)	614 (44.8)	29 (56.9)
History of AIDS-defining event at clinic entry,[a] No. (%)	713 (14.0)	151 (11.0)	7 (13.7)
Anemia at clinic entry,[b] No. (%)	903 (20.1)	414 (35.8)	9 (18.0)
CD4 cell count nadir at clinic entry, median [IQR], cells/μL	344 [155–549]	347.5 [174–594]	293 [164–536]
CD4 cell count at clinic entry,[c] median [IQR], cells/μL	377 [185–581]	389.5 [197–633]	357 [216–595]
Log_{10} HIV RNA at clinic entry,[d] median [IQR]	4.28 [2.60–4.94]	4.01 [2.60–4.75]	4.29 [1.67–4.96]
Received ART at clinic during follow-up, No. (%)	4602 (90.1)	1246 (90.8)	50 (98.0)
Comorbidities at clinic entry,[e] No. (%)	…	…	…
Anxiety	369 (7.2)	91 (6.6)	2 (3.9)
Atherosclerosis	165 (3.2)	35 (2.6)	2 (3.9)
Chronic kidney disease	106 (2.1)	24 (1.8)	3 (5.9)
Chronic liver disease	52 (1.0)	18 (1.3)	0 (0)
Congestive heart failure	35 (0.7)	8 (0.6)	1 (2.0)
Diabetes	215 (4.2)	93 (6.8)	2 (3.9)
Hyperlipidemia	384 (7.5)	79 (5.8)	4 (7.8)
Hypertension	733 (14.4)	271 (19.8)	7 (13.7)
Malignancy	200 (3.9)	34 (2.5)	2 (3.9)
Mood disorder	900 (17.6)	300 (21.9)	10 (19.6)
Other psychiatric disorder	66 (1.3)	17 (1.2)	1 (2.0)
Post-traumatic stress disorder	48 (0.9)	19 (1.4)	2 (3.9)
Schizophrenia	50 (1.0)	22 (1.6)	0 (0)
Hepatitis C virus coinfection ever, No. (%)	633 (12.4)	226 (16.5)	8 (15.7)
Substance use ever, No. (%)	2067 (40.5)	494 (36.0)	27 (52.9)
Smoking ever, No. (%)	2461 (48.2)	608 (44.3)	26 (51.0)
Alcohol ever, No. (%)	2820 (55.2)	534 (38.9)	29 (56.9)
Insurance at clinic entry,[f] No. (%)	…	…	…
Ryan White or none/self-pay	2174 (42.6)	454 (33.1)	27 (52.9)
Medicaid/Medicare/VA	482 (9.4)	339 (24.7)	9 (17.7)
Private/commercial	1132 (22.2)	137 (10.0)	8 (15.7)
Unknown/missing	1320 (25.8)	442 (32.2)	7 (13.7)
Years of follow-up from clinic entry, median [IQR]	7.93 [3.57–13.24]	9.36 [4.40–13.78]	4.70 [2.37–8.17]
Lost to follow-up,[g] No. (%)	2124 (41.6)	552 (40.2)	14 (27.5)
Total died, No. (%)	709 (13.9)	243 (17.7)	4 (7.8)
Cause of death,[h] No. (%)	…	…	…
AIDS	151 (21.3)	79 (32.5)	0 (0)
Sudden death	35 (4.9)	8 (3.3)	0 (0)
Cancer	105 (14.8)	18 (7.4)	2 (50)
Cardiovascular disease	46 (6.5)	17 (7.0)	0 (0)
Liver disease	36 (5.1)	9 (3.7)	0 (0)
Trauma/accident/suicide	30 (4.2)	11 (4.5)	0 (0)

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Table 1. Continued

	Cis-gender Men n = 5108 (78%)	Cis-gender Women n = 1372 (21%)	Transgender Women n = 51 (1%)
Other infections	20 (2.8)	9 (3.7)	0 (0)
Pulmonary disease	13 (1.8)	6 (2.5)	0 (0)
Renal disease	6 (0.9)	5 (2.1)	0 (0)
Other non-AIDS causes	15 (2.1)	3 (1.2)	0 (0)
Unknown	252 (35.5)	78 (32.1)	2 (50)

Abbreviation: ART, antiretroviral therapy; IDU, injection drug use; IQR, interquartile range; TGW, transgender women; VA, Veteran Affairs.

[a]Includes AIDS-defining events diagnosed before or within 30 days of clinic entry.

[b]Anemia at clinic entry defined as hemoglobin <13 g/dL for males, <12 g/dL for females for values obtained closest to clinic entry, no more than 6 months before to 30 days after clinic entry. Missing for n = 830.

[c]CD4 cell count: values obtained closest to clinic entry, no more than 6 months before to 30 days after clinic entry. Missing for n = 159.

[d]HIV RNA at clinic entry: values obtained closest to clinic entry, no more than 6 months before to 30 days after clinic entry. Missing for n = 389.

[e]Comorbidity diagnosed before or within 30 days of clinic entry. Other psychiatric disorders include adjustment disorder, dementia, mental retardation, cognitive decline, personality disorder, psychosis. Schizophrenia includes schizoaffective disorder and schizophrenia. Atherosclerosis includes cerebrovascular disease, coronary artery disease, and peripheral vascular disease.

[f]Lowest insurance status at time of first clinic visit or within 30 days of first appointment.

[g]Lost to follow-up defined as either (1) clinic visit >1 year before 12/31/2018 or (2) date of last clinic visit >1 year before 12/31/2018 and date of death >1 year after last clinic visit.

[h]Patients with an AIDS-defining event, AIDS, or HIV-causing specific diseases listed as primary or secondary cause of death categorized as AIDS death. Sudden death includes primary cause listed as sudden death. Cancer includes any cancer diagnosis listed as primary or secondary cause (regardless of AIDS), cardiovascular disease includes coronary artery disease, cerebrovascular disease, hypertension, arrhythmia, cardiac arrest, cardiomyopathy, myocarditis. Liver includes chronic hepatitis, cirrhosis, hepatic failure, chronic liver disease due to alcoholism. Trauma/accident includes suicides, overdoses, trauma, hyperthermia. Other infections include infections not qualifying as AIDS-defining event. Pulmonary includes chronic lung diseases, pulmonary embolism, pulmonary hypertension, pneumonitis, etc. Other non-AIDS includes alcoholism, dementia not specified to be HIV-related, hemorrhage, diabetes. Unknown includes documented unknown cause or unspecified HIV disease listed as cause. No missing cause of death.

HIV diagnosis, artifactually yielding negative aYPLL for this group. Furthermore, after excluding those with unknown or other HIV risk factors, aYPLL were higher for heterosexual women (486.1; 95% CI, 485.2–486.9) than for men regardless of their sexual HIV acquisition risk factor. Among men, heterosexual men had higher aYPLL when compared with men who have sex with men (351.8; 95% CI, 350.9–352.7; vs 263.3; 95% CI, 262.7–263.8). In multivariable linear regression (Table 3), after adjusting for age at HIV diagnosis, CD4 cell count at clinic entry, HIV RNA at clinic entry, any history of HCV coinfection, and year of clinic entry, increased YPLL were associated with non-Hispanic Black individuals and cis-gender women, regardless of HIV acquisition risk factor.

DISCUSSION

In the analysis of mortality and years of potential life lost in this clinic population, we found that PWH in the most recent calendar era (2014–2018) had a 78% decreased risk of mortality compared with the earliest calendar era (1998–2003). Women were found to have significantly higher adjusted mortality and premature mortality compared with men. While Black individuals did not have significantly higher mortality rates, they were found to have higher rates of premature mortality, and these rates were highest in Black women.

The prevalence of HIV among women in the United States has increased dramatically since the beginning of the epidemic, and women now make up 21% of PWH in the United States [5]. While the incidence rate of HIV among men has decreased from 2015 to 2019, it has remained stable among women, who primarily acquire HIV through heterosexual contact and intravenous drug use [5]. Many women face unique challenges and discrimination as a result of race, ethnicity, and sex, as well as higher rates of poverty and lack of access to care [21]. Women have been shown to be less likely than men to maintain viral suppression and also have delays in HIV diagnosis, which may be a reflection of access to care and adequacy of public health efforts and resources [6, 22]. Pre-exposure prophylaxis (PrEP) for HIV is another area where uptake among women has been poor, which is in some part due to low awareness [22]. Women, especially in the Southern United States, also experience higher levels of HIV-related stigma due to gender expectations and the moral stigmatization of "sexual promiscuity" [23]. Interestingly, counties with a relatively high prevalence of HIV in women compared with men are concentrated in the US South, and these counties have higher percentages of the general population living below the federal poverty level with less than a high school education [11]. More than half of new HIV diagnoses in 2018 were in the US South, an area with underlying unequal access to health care and HIV treatment services [10]. The compounding of these factors may ultimately contribute to worse outcomes for women with HIV in the South.

Our analysis found that of individuals who have died, Black women with HIV were particularly impacted by increased years of potential life lost. Racial disparities in HIV diagnosis are especially pronounced in women, with Black women accounting for 58% of HIV diagnoses among women, but making up 14% of the female population in the United States. The incidence of HIV by race in the United States is highest among Black individuals; it is 8 times the rate for a White person—a disparity that has not significantly improved from 2015 to 2019 [5].

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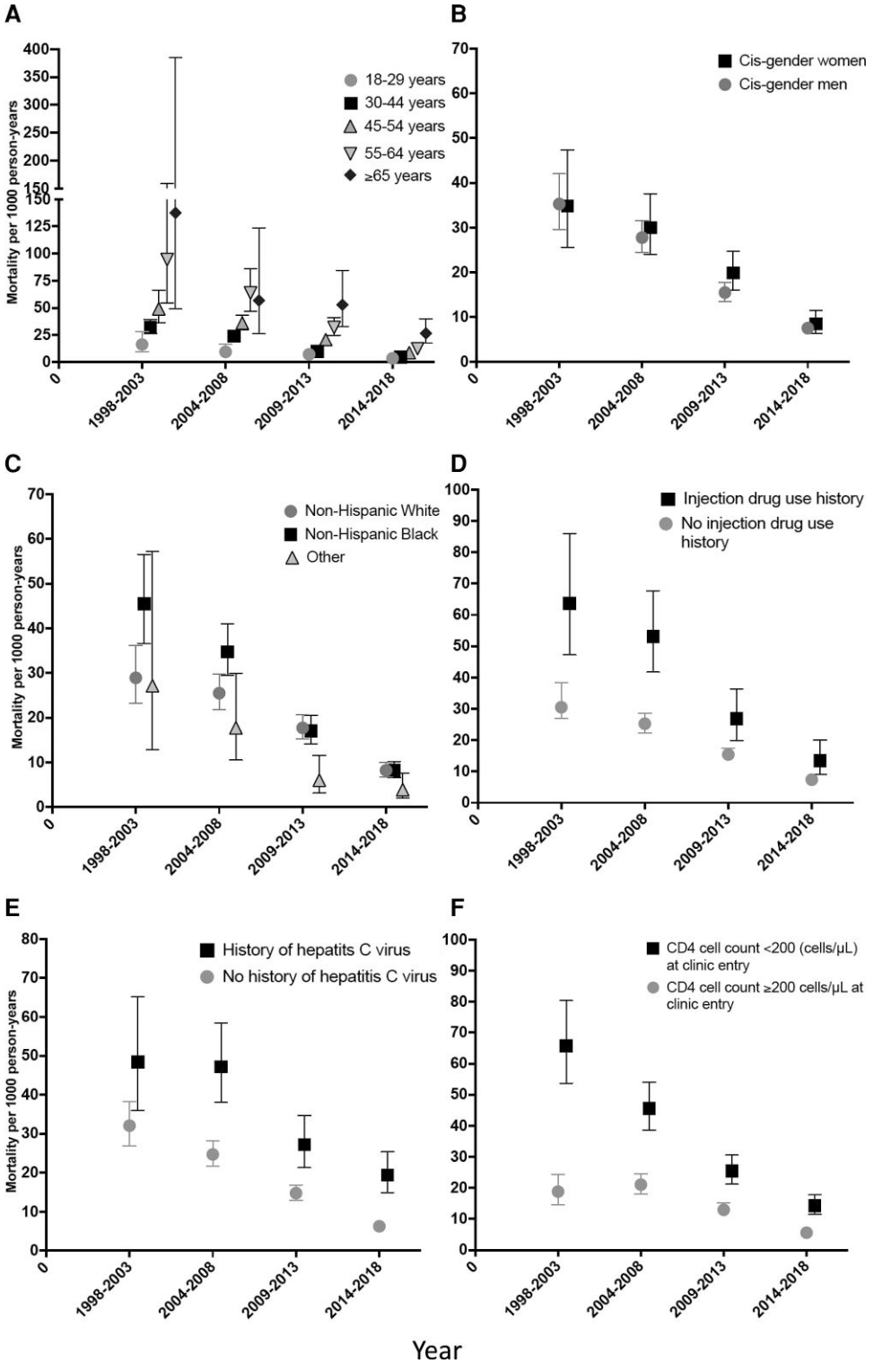

Figure 1. Unadjusted mortality rates by calendar era among individuals cared for at the VCCC, 1998–2018, by demographic and clinical characteristics, including (A) age during calendar era, (B) gender, (C) race/ethnicity, (D) history of injection drug use as HIV acquisition risk factor, (E) any history of hepatitis C virus infection, and (F) CD4 cell count at clinic entry. The 1998–2003 calendar era includes 1737 individuals, 4722.44 person-years, and 166 deaths. The 2004–2008 calendar era includes 3176 individuals, 11 044.57 person-years, and 313 deaths. The 2009–2013 calendar era includes 4285 individuals, 17 436.78 person-years, and 287 deaths. The 2014–2018 calendar era includes 5765 individuals, 24 313.98 person-years, and 190 deaths.

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Table 2. Univariate and Multivariable[a] Incidence Rate Ratios of Mortality Risk

	IRR (95% CI)	*P* Value	aIRR (95% CI)	*P* Value
Calendar era	…		…	
1998–2003	1		1	
2004–2008	0.81 (0.67–0.97)	.025	0.85 (0.69–1.04)	.121
2009–2013	0.47 (0.39–0.57)	<.001	0.48 (0.38–0.60)	<.001
2014–2018	0.22 (0.18–0.27)	<.001	0.22 (0.17–0.29)	<.001
Race/ethnicity	…		…	
Non-Hispanic White	1		1	
Non-Hispanic Black	1.14 (1.00–1.30)	.048	0.97 (0.84–1.12)	.686
Other	0.49 (0.36–0.68)	<.001	0.56 (0.40–0.79)	.001
Gender	…		…	
Cis-gender men	1		1	
Cis-gender women	1.17 (1.01–1.35)	.037	1.31 (1.12–1.54)	.001
Transgender women	0.84 (0.31–2.25)	.724	1.33 (0.45–3.88)	.603

Abbreviations: aIRR: adjusted incidence rate ratio; IRR, incidence rate ratio.

[a]Poisson regression models with robust variance used. Multivariable Poisson model included multiple imputation to account for missing laboratory data at clinic entry (CD4 cell count, HIV RNA, and hemoglobin) and included the following covariates: calendar era, age at calendar era start, race/ethnicity, gender, injection drug use as HIV acquisition risk factor, anemia at clinic entry, year of HIV diagnosis, history of AIDS-defining event at clinic entry, CD4 cell count at clinic entry, HIV RNA at clinic entry, and any history of hepatitis C virus coinfection. Age at calendar era start, year of HIV diagnosis, CD4 cell count at clinic entry, HIV RNA at clinic entry examined using restricted cubic splines with 3 knots.

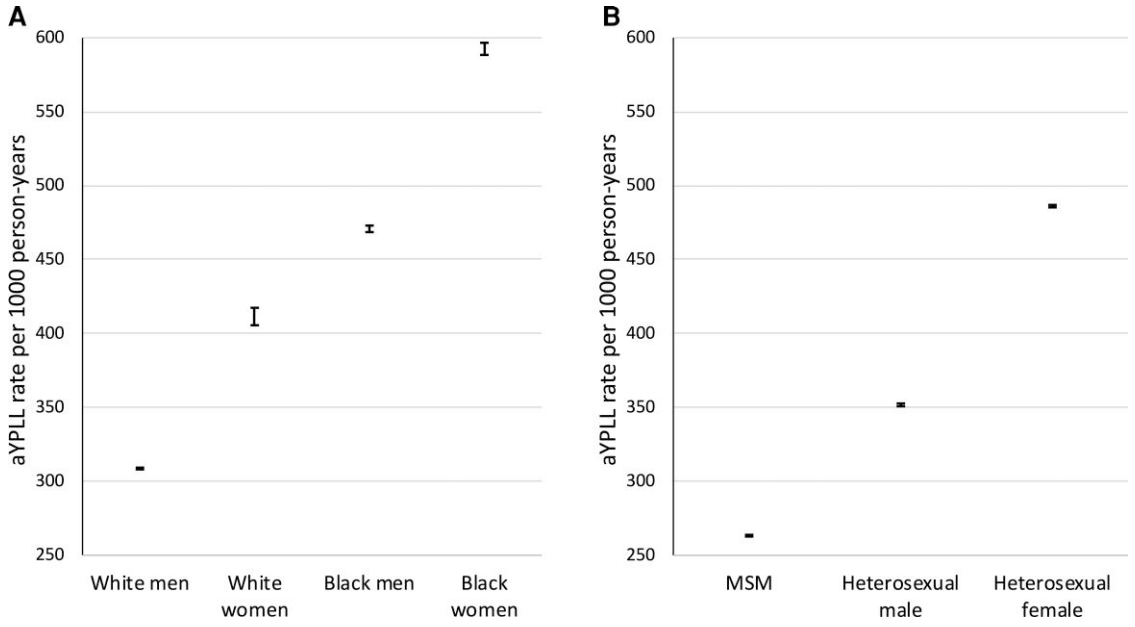

Figure 2. Age-adjusted years of potential life lost rates (95% CI) among individuals cared for at the VCCC who died during the study period (1998–2018), by (A) sex and race/ethnicity and (B) HIV acquisition risk factor. Abbreviations: aYPLL, age-adjusted years of potential life lost; MSM, men who have sex with men; VCCC, Vanderbilt Comprehensive Care Clinic.

There have been improvements in decreasing time to HIV diagnosis and viral suppression, which have led to decreases in the absolute and relative differences in HIV-related deaths among Black persons and Hispanic/Latino persons compared with White persons [2]. Our study found similar decreases in mortality rates by race in our population of PWH, which is consistent with recent data from 2010 to 2017 in the United States [2]. Even with these improvements, we found that Black individuals who died in our cohort had more years of potential life lost over the study period, though mortality was similar. This discrepancy between mortality and years of potential life lost emphasizes the importance of exploring outcome measures beyond mortality. These differences in aYPLL were consistent with a study from Florida that examined

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Table 3. Univariate and Multivariable[a] Linear Regression for Years of Potential Life Loss for Those who Died[b]

	Average Years of Potential Life Lost (95% CI)	*P* Value	Adjusted Average Years of Potential Life Lost (95% CI)	*P* Value
HIV acquisition risk factor	…	…	…	…
MSM & transgender women	32.39		36.7	
Heterosexual cis-gender women	36.76 (29.67–38.41)	<.001	42.28 (41.50–43.29)	<.001
Heterosexual cis-gender men	29.5 (27.68–31.31)	.002	37.19 (36.06–38.31)	.396
Other/IDU cis-gender men	31.78 (30.18–33.38)	.457	37.95 (36.84–38.97)	.015
Other/IDU cis-gender women	38.09 (35.81–40.38)	<.001	42.87 (41.42–44.32)	<.001
Race/ethnicity	…	…	…	…
Non-Hispanic White	32.82		36.7	
Non-Hispanic Black	33.31 (32.07–34.56)	.434	37.47 (36.73–38.21)	.042
Hispanic ethnicity/other	34.54 (31.35–37.72)	.291	37.71 (35.9–39.52)	.274

Abbreviations: IDU, injection drug use; MSM, men who have sex with men; PWH, people with HIV.

[a]Multivariable linear regression models examined clinical and demographic factors associated with years of potential life lost among 879 PWH who died during follow-up and had complete data. Multivariable linear regression model included the following covariates: HIV acquisition risk factor, race/ethnicity, age at HIV diagnosis, CD4 cell count at clinic entry, HIV RNA at clinic entry, any history of hepatitis C virus infection, and year of clinic entry.

[b]Regression was centered on reference individual: White MSM individual, diagnosed with HIV at age 30, no history of hepatitis C, entered clinic in 2008 with CD4 500 and logVL 4.

YPLL among PWH throughout the state from 2000 to 2009 [14]. In the United States, there are stark differences in life expectancy by race, with Black Americans having lower life expectancies at birth than their White counterparts, and health disparities likely play a part in these outcomes [17, 24]. Our study focused on individuals with HIV and found similar disparities by race through the lens of years of potential life lost.

Most health disparities are a result of social determinants of health. Indeed, in our study we observed differences by race and sex with regards to burden of noninfectious comorbidities and health insurance at clinic entry, clinical factors often closely associated with adverse social determinants of health and mortality [25–27]. This is also highlighted by the higher rates of HIV diagnoses in areas with a higher percentage of individuals living below the federal poverty level, a higher percentage of individuals with less than a high school diploma, a lower median household income, and a lower percentage of those with insurance coverage [28]. The persistence of racial segregation has also been shown to be a factor in decreased survival after AIDS diagnosis [29]. The challenges experienced by women and Black Americans require an intersectional approach to addressing the social determinants of health that create and reinforce these inequities, and further investigation into how underlying societal and structural determinants of health continue to drive disparities in long-term outcomes of PWH are needed. While the observational period for this analysis concluded before the COVID-19 pandemic, future studies are urgently needed to examine how the recent pandemic may have exacerbated disparities in mortality and YPLL among PWH in the United States.

This study is limited by its analysis being from 1 center in the US South, a region with higher mortality rates in the general population compared with the United States [30]. Additionally, we were unable to analyze mortality by cause of death due to lack of consistent reporting of these data. In the assessment of years of potential life lost, due to the small number of deaths in the cohort, especially among older individuals, we were unable to assess changes in premature mortality over time or assess differences in age-adjusted rates by other factors. Though there was high loss to follow up in this cohort over the long follow-up period, the high capture of the end point of death allowed for robust analysis of mortality and years of potential life lost, regardless of the individuals' involvement in care at our clinic. Our data are limited by lack of information on transition of care to other clinics, and, therefore, loss to clinical follow-up in our cohort may not accurately reflect disengagement from HIV care overall. Future analyses of the impact of care engagement and mortality outcomes among PWH where care transitions are accounted for are needed. Ideally, we would have been able to collect data on social determinants of health, such as insurance status, income, and education level, that could be factored into the analysis. Future studies that can incorporate individual-level and/or area-level measures of these important factors are needed to better understand persistent disparities in outcomes among PWH. Our analyses were also limited by the small numbers of transgender individuals captured in our cohort, affecting our ability to examine mortality and YPLL among this vulnerable population of PWH often at increased risk of poor retention and lack of virologic suppression [31, 32]. Capture of transgender status using routine electronic medical records is often challenging given lack of standardized reporting [31]. Despite review of provider notes to validate gender status, it also possible that our analysis was affected by misclassification of gender status of some individuals included [31]. Further studies of larger cohorts with complete capture of gender are needed for investigation of mortality trends among transgender individuals with HIV in the United States.

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CONCLUSIONS

In conclusion, though there have been significant strides in decreasing mortality among PWH connected to care in the United States South from 1998 to 2018, inequities persist, especially for Black Americans and women. It is important to further dissect mortality rates by utilizing methods in assessing years of potential life lost and quality of life. Additional research is needed to identify factors associated with persistent inequities and assessment of targeted interventions at the individual and community levels.

Supplementary Data

Supplementary materials are available at *Open Forum Infectious Diseases* online. Consisting of data provided by the authors to benefit the reader, the posted materials are not copyedited and are the sole responsibility of the authors, so questions or comments should be addressed to the corresponding author.

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References

1. Samji H, Cescon A, Hogg RS, et al. Closing the gap: increases in life expectancy among treated HIV-positive individuals in the United States and Canada. PLoS One **2013;** 8:e81355.
2. Bosh KA, Johnson AS, Hernandez AL, et al. Vital signs: deaths among persons with diagnosed HIV infection, United States, 2010–2018. MMWR Morb Mortal Wkly Rep **2020;** 69:1717–24.
3. Harrison KMD, Song R, Zhang X. Life expectancy after HIV diagnosis based on national hiv surveillance data from 25 states, United States. J Acquir Immune Defic Syndr **2010;** 53:124–30.
4. Castilho JL, Melekhin V V, Sterling TR. Sex differences in HIV outcomes in the highly active antiretroviral therapy era: a systematic review. AIDS Res Hum Retroviruses **2014;** 30:446–56.
5. Centers for Disease Control and Prevention. Estimated HIV incidence and prevalence in the United States, 2015–2019. HIV Surveill Suppl Rep **2021;** 26:1–81.
6. Hall HI, Song R, Szwarcwald CL, Green T. Brief report: time from infection with the human immunodeficiency virus to diagnosis, United States. J Acquir Immune Defic Syndr **2015;** 69:248–51.
7. Rebeiro PF, Abraham AG, Horberg MA, et al. Sex, race, and HIV risk disparities in discontinuity of HIV care after antiretroviral therapy initiation in the United States and Canada. AIDS Patient Care STDS **2017;** 31:129–44.
8. Kitahata MM, Gange SJ, Abraham AG, et al. Effect of early versus deferred antiretroviral therapy for HIV on survival. N Engl J Med **2009;** 360:1815–26.
9. Allgood KL, Hunt B, Rucker MG. Black:White disparities in HIV mortality in the United States: 1990–2009. J Racial Ethn Heal Disparities **2015;** 3:168–75.
10. Sullivan PS, Satcher Johnson A, Pembleton ES, et al. Epidemiology of HIV in the USA: epidemic burden, inequities, contexts, and responses. Lancet **2021;** 397: 1095–106.
11. Breskin A, Adimora AA, Westreich D. Women and HIV in the United States. PLoS One **2017;** 12:e0172367.
12. Lemly DC, Shepherd BE, Hulgan T, et al. Race and sex differences in antiretroviral therapy use and mortality among HIV-infected persons in care. J Infect Dis **2009;** 199:991–8.
13. Martinez R, Soliz P, Caixeta R, Ordunez P. Education corner reflection on modern methods: years of life lost due to premature mortality—a versatile and comprehensive measure for monitoring non-communicable disease mortality. Int J Epidemiol **2019;** 48:1367–76.
14. Trepka MJ, Niyonsenga T, Fennie KP, McKelvey K, Lieb S, Maddox LM. Sex and racial/ethnic differences in premature mortality due to HIV: Florida, 2000–2009. Public Health Rep **2015;** 130:505–13.
15. Davidson A, Turner M, Kheshti A, Sterling TR, Raffanti SP, Castilho JL. Cause of death discrepancies: an internal review of data collection methods of Vanderbilt Comprenshive Care Clinic and the National Death Index. Poster presentated at: 64th Annual Student Research Day at Meharry Medical College; Nashville, TN. **March 11, 2020**.
16. Anderson RN. United States life tables, 1998. Natl Vital Stat Rep **2001;** 48:1–40.
17. Arias E, Xu J. United States life tables, 2018. Natl Vital Stat Rep **2020;** 69:1–45.
18. Bergen H, Hawton K, Waters K, et al. Premature death after self-harm: a multicentre cohort study. Lancet **2012;** 380:1568–74.
19. Tiwari RC, Clegg LX, Zou Z. Efficient interval estimation for age-adjusted cancer rates. Stat Methods Med Res **2006;** 15:547–69.
20. Fay MP, Feuer EJ. Confidence intervals for directly standardized rates: a method based on the gamma distribution. Stat Med **1997;** 16:791–801.
21. Aziz M, Smith KY. Challenges and successes in linking HIV-infected women to care in the United States. Clin Infect Dis **2011;** 52(Suppl 2):S231–7.
22. Adimora AA, Ramirez C, Poteat T, et al. HIV and women in the USA: what we know and where to go from here. Lancet **2021;** 397:1107–15.
23. Darlington CK, Hutson SP. Understanding HIV-related stigma among women in the Southern United States: a literature review. AIDS Behav **2017;** 21:12–26.
24. GBD US Health Disparities Collaborators. Life expectancy by county, race, and ethnicity in the USA, 2000–19: a systematic analysis of health disparities. Lancet **2022;** 400:25–38.
25. Bisquera A, Turner EB, Ledwaba-Chapman L, et al. Inequalities in developing multimorbidity over time: a population-based cohort study from an urban, multiethnic borough in the United Kingdom. Lancet Reg Heal Eur **2021;** 12:100247.
26. Nanditha NGA, Zheng G, Tafessu HM, et al. Disparities in multimorbidity and mortality among people living with and without HIV across British Columbia's health regions: a population-based cohort study. Can J Public Health **2021;** 112:1030–41.
27. Jabs AW, Jabs DA, Van Natta ML, Palella FJ, Meinert CL. Insurance status and mortality among patients with AIDS. HIV Med **2018;** 19:7–17.
28. Centers for Disease Control and Prevention. Social determinants of health among adults with diagnosed HIV infection, 2018. HIV Surveill Suppl Report **2020;** 25:134.
29. Fennie KP, Lutfi K, Maddox LM, Lieb S, Trepka MJ. Influence of residential segregation on survival after AIDS diagnosis among non-Hispanic Blacks. Ann Epidemiol **2015;** 25:113–9.e1.
30. US Burden of Disease Collaborators, Mokdad AH, Ballestros K, et al. The state of US health, 1990–2016: burden of diseases, injuries, and risk factors among US states. J Am Med Assoc **2018;** 319:1444–72.
31. Poteat T, Hanna DB, Rebeiro PF, et al. Characterizing the human immunodeficiency virus care continuum among transgender women and cisgender women and men in clinical care: a retrospective time-series analysis. Clin Infect Dis **2020;** 70:1131–8.
32. Santos GM, Wilson EC, Rapues J, Macias O, Packer T, Raymond HF. HIV treatment cascade among transgender women in a San Francisco respondent driven sampling study. Sex Transm Infect **2014;** 90:430–3.

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