HHS Public Access

Author manuscript

*AIDS*. Author manuscript; available in PMC 2023 July 15.

Published in final edited form as:

*AIDS*. 2022 July 15; 36(9): 1279–1286. doi:10.1097/QAD.0000000000003249.

# Years of life lost to cancer among the US HIV population, 2006–2015

**Qianlai LUO, Ph.D.**[1], **Ruth M. PFEIFFER, Ph.D.**[*,2], **Anne-Michelle NOONE, Ph.D.**[3], **Marie-Josèphe HORNER, Ph.D.**[1], **Eric A. ENGELS, M.D., M.P.H.**[1], **Meredith S. SHIELS, Ph.D.**[*,1]

[1]Infections and Immunoepidemiology Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, MD, USA

[2]Biostatistics Branch, Division of Cancer Epidemiology and Genetics, National Cancer Institute, Rockville, MD, USA

[3]Division of Cancer Control and Population Sciences, National Cancer Institute, Rockville, MD, USA

## Abstract

**Objectives:** We estimated years of life lost (YLLs) to all causes of death and years of life lost to cancer among persons living with human immunodeficiency virus (HIV; PLWH) in the United States (US).

**Design:** Linked HIV and cancer registry data from the HIV/AIDS Cancer Match Study were used to identify incident cancers and deaths among PLWH in 11 regions of the US during 2006–2015.

**Methods:** Mean YLL (MYLL) to all causes of death and MYLL to cancer during 2006–2015 were derived from the restricted mean survival estimated from Cox proportional hazards regression models. MYLLs were then upweighted to the national population of PLWH to obtain all-cause total years of life lost (TYLL) and cancer-related TYLL in the US during 2006–2015.

**Results:** Among 466,234 PLWH in the study population, 25,772 (5.5%) developed cancer during 2006–2015. Nationally, an estimated 134,986 years of life were lost to cancer of all types during 2006–2015 among PLWH, representing 9.6% of TYLL to all causes. Non-Hodgkin lymphoma (NHL), Kaposi sarcoma (KS), anal cancer, and lung cancer were the four largest cancer contributors (45% of TYLL to cancer). The largest fraction of TYLL occurred among Black PLWH, men who have sex with men, and PLWH aged 40–59 years old.

**Conclusion:** PLWH have higher mortality rates after developing cancer. NHL, KS, and anal and lung cancers were large contributors to years of life lost to cancer in the U.S. population of PLWH,

Corresponding author: Qianlai Luo, Ph.D., Postdoctoral Fellow, qianlai.luo@nih.gov Phone: 240-276-5754, Address: Infections and Immunoepidemiology Branch, Division of Cancer Epidemiology & Genetics National Cancer Institute, 9609 Medical Center Dr. Rm. 6E234, Rockville, MD 20850, USA.

[*]Indicates that authors contributed equally.

Potential conflicts of interest

We declare no competing interests.

highlighting opportunities to reduce cancer mortality through improved access to antiretroviral treatment, prevention, and screening.

### Keywords

human immunodeficiency virus; persons living with HIV; years of life lost; cancer; restricted mean survival; United States

## Introduction

Persons living with human immunodeficiency virus (HIV; PLWH) have an elevated risk of certain cancers compared to the general population, largely due to immunosuppression and co-infection with oncogenic viruses such as Kaposi sarcoma-associated herpesvirus, hepatitis C virus, and human papillomavirus.[1-4] In the US, since the introduction of combination antiretroviral therapy (ART), which suppresses HIV replication and improves immune function, life expectancy of PLWH has been significantly prolonged.[5] PLWH are aging, and cancer rates and the number and types of cancers that occur among PLWH are changing over time.[6]

Cancer-specific mortality is also higher among PLWH compared to cancer patients without HIV.[7, 8] There are various possible explanations, including suppressed immune function, but also screening and treatment disparities between cancer patients with and without HIV.[7, 9-18] Though cancer-attributable mortality rates have declined over time, cancer has caused a growing fraction of deaths among US PLWH in the ART era, with 17.1% of deaths in 2011–2015 attributable to cancer.[19]

To further illustrate the impact of cancer mortality among PLWH, we used years of life lost (YLL) due to cancer, an informative metric for assessing deaths due to cancer among PLWH.[20] YLL estimates can help in allocating resources and designing prevention programs for PLWH to maximize the number of life years gained.[21, 22] In this study, we used data from the National Cancer Institute's HIV/AIDS Cancer Match (HACM) Study and national HIV surveillance data to estimate YLL due to cancer among all PLWH in the United States from 2006 to 2015, as well as by population subgroups and for select cancer sites.

## Methods

### Data sources

**HIV/AIDS Cancer Match Study—**Data on HIV and cancer during 2006–2015 were obtained from the HACM Study, a record linkage study of population-based HIV and cancer registries in 11 U.S. regions (https://www.hivmatch.cancer.gov/sites.html). The included population-based cancer registries and year ranges covered were Colorado (2006–2015), Connecticut (2006–2015), Washington, D.C. (2007–2015), Georgia (2006–2012), Louisiana (2006–2015), Maryland (2008–2012), Michigan (2006–2015), New Jersey (2006–2012), New York (2006–2012), North Carolina (2006–2014), Puerto Rico (2006–2012), and Texas (2006–2015).

Invasive cancer sites were defined using a modified version of SEER site recodes.[23] YLL were estimated for all cancers combined and separately for common cancer types (Kaposi sarcoma, non-Hodgkin lymphoma, cervix, lung and bronchus, anal, Hodgkin lymphoma, liver, breast, prostate, colon and rectum, other). The analysis was restricted to individuals older than 20 years during follow-up due to the low number of HIV and cancer cases among persons younger than 20 years old.

**The US national HIV population—**Data on the number of PLWH and the number of incident HIV cases each year in the US was obtained from the Centers for Disease Control and Prevention's (CDC) National HIV Surveillance System and the National Center for HIV/AIDS, Viral Hepatitis, STD, and TB Prevention's AtlasPlus.[24, 25]

## Statistical analysis

To estimate the total years of life lost (TYLL) among the national population of PLWH between 2006 and 2015, we first estimated the mean years of life lost (MYLL) due to cancer per PLWH in the HACM Study, and then weighted the estimated MYLL to the US national PLWH population.[26, 27]

**MYLL to cancer—**We estimated MYLL due to cancer per PLWH as the difference in survival, also known as restricted mean survival time, between two scenarios. We compared the observed restricted mean survival time in the cohort with a hypothetical scenario in which individuals did not develop cancer.[26-28] Calculation of MYLL was done in three steps: estimation of the survival models, prediction of survival curves, followed by integration and subtraction.

**1. Estimation of the survival models:** We fit Cox regression models with calendar year as the time scale to estimate the impact of cancer on survival. Follow-up for each person started on the latest of three dates: (1) registry start date, (2) the earliest of HIV report or AIDS diagnosis date, and (3) age 20. Follow-up ended at death or at the end of registry coverage. To facilitate weighting of MYLL from the HACM Study to the US national population of PLWH, we generated 10 mutually exclusive cohorts in the HACM Study based on year of HIV diagnoses: the first cohort (2006) included PLWH who were diagnosed during or prior to the end of year 2006; cohorts of later years (2007–2015) were limited to persons newly diagnosed with HIV in each of those years. Covariates included age at the beginning of follow-up (in categories 20–29, 30–39, 40–49, 50–59, and >60 years old), a variable that combined sex and risk group (men who have sex with men [MSM], male persons who inject drugs [PWID], all other males, female PWID, all other females), race/ethnicity (non-Hispanic White [i.e., White], non-Hispanic Black [i.e., Black], Hispanic, other/unknown/multiple), registry, and a time-varying dichotomous variable for cancer status (0 vs. 1). Cancers were included up to five years prior to the start of follow-up, as the mortality associated with cancer usually occurs within five years after cancer diagnoses.[19] For the 2006 cohort only, the Cox model also included a time-varying categorical variable for time since HIV diagnosis (<2, 2–6, 7–10, 11–18, and >18 years).

**2. Prediction:** For each PLWH we predicted two survival curves with coefficients estimated from the Cox models—curve-α and curve-β for the person's observed follow-up time. Curve-α was computed using the estimated baseline hazard and the individual's covariate values; curve-β was similarly estimated, except here the value for cancer status was set to zero for everyone in the cohort. For those who never developed cancer during follow-up, the two curves were the same.

**3. Integration and subtraction:** For each cohort (i.e., years 2006–2015), the area under the averaged survival curve-α's, $S\bar{\alpha}$, was estimated by integrating the averaged survival probabilities at each event-time over the follow-up period. The area under the averaged curve-β's, $S\bar{\beta}$, was estimated similarly. For each cohort, the difference between $S\bar{\beta}$ and $S\bar{\alpha}$ (shadowed area ABC in Figure 1) was the MYLL due to cancer among PLWH in that cohort, restricted to its follow-up period.

MYLL due to cancer per person were estimated overall, for each cancer type, and in age, race/ethnicity, and sex/risk subgroups using the HACM study. When estimating MYLL for each type of cancer, individuals were additionally censored at first cancer diagnosis of any other cancer type. MYLL due to cancer among population subgroups (by race/ethnicity [White, Black, and Hispanic], risk groups [MSM/PWID/Other], age groups [20–39, 40–59, and 60+ years old]) were estimated similarly in stratified analyses. For MYLL to cancer by age group, time-updated age was additionally included as an entry and exit criteria in the Cox regression models. For some of the more recent cohorts in stratified analyses, data were sparse, and Cox regression among subgroups required collapsing of some covariate categories. In those cases, we did sensitivity analyses. Examples for sensitivity analyses included the following: treating age as a continuous variable; re-categorizing race/ethnicity (for stratified analyses by risk group) as White, Black, Hispanic/Other; re-categorizing risk group (for stratified analyses by race) as MSM, all PWID, and all others; and removing the registry variable as a covariate.

**All-cause MYLL and proportion of MYLL that was due to cancer—**We estimated the all-cause MYLL for each cohort, represented by the total area above the averaged curve-α's in Figure 1 (area ACD). We then estimated the proportion of all-cause MYLL that was due to cancer for each cohort by dividing the shadowed area in Figure 1 (area ABC) by all-cause MYLL (area ACD). All-cause MYLL and the proportion of it that was due to cancer were estimated overall, for each race/ethnicity, and for sex/risk group.

**TYLL due to cancer nationally from 2006 to 2015—**MYLL estimates from the HACM Study were then multiplied by US national level estimates of the total HIV+ population sizes to compute the total years of life lost (TYLL) due to cancer among PLWH in the US between January 2006 and December 2015, accounting for PLWH's HIV status (incident or prevalent) and differential follow-up time. The exact computation was based on

$$TYLL = MYLL_{2006} * N_{(prevalent\ and\ incident\ hiv\ in\ 2006)} + \sum_{i=2007}^{2015} MYLL_i * N_{(incident\ hiv\ in\ year\ i)} \quad (1)$$

From 2008 on, all states had implemented name-based HIV infection reporting, allowing for national reporting of HIV diagnoses and prevalence.[29] For 2006 and 2007, 37 and 40 states' data were available, respectively. The total number of prevalent and incident PLWH in the US in 2006 and 2007 were estimated by first calculating the fraction of national PLWH in these states in 2008, and then multiplying the partial estimates from 2006 and 2007 by the inverse of these ratios to upweight them to represent the whole US PLWH population.

We also estimated all-cause TYLL from 2006 to 2015 and calculated the national proportion of all-cause TYLL that was due to cancer, both overall and by race and sex/risk group.

We used Stata 16 to run the analyses.[30]

## Results

During 2006–2015, there were 25,772 cancers and 62,232 deaths among 466,234 PLWH in the HACM Study. Seventy-four percent of PLWH in HACM were male and 26% were female (Table 1). At beginning of follow-up, 43% of PLWH were 20–39-years-old, 52% were 40–59-years-old, and 5% were older than 60 years. Forty-six percent were Black, 23% were White, and 27% were Hispanic. Thirty-eight percent were MSM and 20% were PWID.

Hazard ratios (HRs) for the risk of death across characteristics among PLWH in each of the 10 cohorts are presented (see Table, Supplemental Digital Content 1). Risk of death was higher among PWID (vs. MSM), Black PLWH (vs. White PLWH), older age groups (vs. 20–29-year-olds) and among those with a cancer diagnosis (vs. no cancer). Having a cancer diagnosis was associated with increased risk of death across cohorts. For example, in the 2006 cohort, a prior cancer diagnosis was associated with HR=6.7 (95% CI: 6.3 to 6.9).

### MYLL due to cancer and all-cause MYLL in the HACM Study during 2006–2015

The MYLL due to cancer per PLWH in the HACM Study for each cohort, overall, and in subgroups are presented (see Table, Supplemental Digital Content 2). MYLL due to cancer was greater for earlier cohorts due to longer follow up. MYLL increased with age. By risk group, MYLL due to cancer was highest among PWID. By race/ethnicity, MYLL due to cancer was highest among White PLWH for all cohorts except cohort 2006, in which Black PLWH had the highest MYLL. MYLL due to any cancer was 41.3 days for the 2006 cohort, 30% of which were due to AIDS-defining cancers. Sensitivity analyses after recoding covariates in some recent cohorts with sparse data resulted in nearly no change of MYLL estimates (results not shown). The all-cause MYLL per PLWH, by race/ethnicity, and by sex/risk group in the HACM Study for each cohort are presented (see Table, Supplemental Digital Content 3). For cohort 2006 (10-year follow-up), which included prevalent and incident PLWH in 2006, 386 days were lost due to cancer per White PLWH, 491 days were lost due to cancer per Black PLWH, and 377 days were lost due to cancer per Hispanic/other racial/ethnic group PLWH.

### TYLL due to cancer and all-cause TYLL in the US during 2006–2015

Among PLWH in the US during 2006–2015, an estimated 135,000 TYLL were lost due to cancer, with 32% of the TYLL due to AIDS-defining cancers and 68% to non-AIDS-defining cancers (Table 2, Figure, Supplemental Digital Content 4). There were an estimated 23,400 YLL due to cancer among PLWH between 20–39 years of age (17%), 91,200 among PLWH aged 40–59 (68%), and 20,400 among PLWH aged 60 or older (15%). By race/ethnicity, an estimated 72,600 YLL due to cancer occurred among Black PLWH (54%), followed by 37,200 among White PLWH (28%) and 21,700 among Hispanic PLWH (16%). By risk group, an estimated 73,400 YLL due to cancer occurred among MSM (54%), 14,600 among PWID (11%), and 46,900 among all other risk groups (35%).

By cancer type, 27,700 YLL were due to NHL (21% of TYLL due to cancer), 12,800 YLL were due to KS (10%), 9,700 YLL due to anal cancer (7%), and 9,000 YLL due to lung cancer (7%) (Table 2, Figure, Supplemental Digital Content 5). The remaining cancer types accounted for 55% of TYLL due to cancer.

Among PLWH in the US during 2006–2015, an estimated 1,443,500 YLL due to any cause occurred, compared to a scenario where no deaths occurred (Table 3). Cancer contributed 9.6% of the all-cause TYLL. By race/ethnicity, cancer contributed 10.6% of the TYLL among White PLWH, 9.0% among Black PLWH, and 8.7% among Hispanics/other PLWH (Table 3, Figure S3). By risk group, cancer contributed 11.6% of the TYLL among MSM, 7.1% among PWID, and 9.4% among all other PLWH (Table 3, Figure, Supplemental Digital Content 6).

## Discussion

We found that in the US, 135,000 years of life were lost due to cancer among PLWH during 2006–2015. Cancer contributed 9.6% of the TYLL lost from any cause. NHL and KS, the two most common AIDS-defining cancers among PLWH, were responsible for 30% of TYLL due to cancer, followed by anal cancer and lung cancers, which contributed an additional 14% of TYLL to cancer. The greatest proportion of YLL due to cancer occurred among 40–59-year-olds, Black PLWH, and MSM.

Consistent with previous research focused on cancer mortality, NHL and lung cancer were big contributors of TYLL due to cancer among PLWH in the U.S.[7, 31] In addition, we also found anal cancer to be a big contributor of TYLL (bigger than lung cancer). This is likely due to the average age that these cancers were diagnosed: 43 years old for anal cancer as opposed to 54 years old for lung cancer. Although KS was not found to be as big a contributor to deaths among PLWH in previous studies, KS contributed 10% of TYLL due to cancer during 2006–2015 in our study.[31] It is important to note that KS is strongly associated with immune suppression among PLWH, with rates highest among PLWH who have not received effective antiretroviral therapy to treat HIV. Therefore, the strong association between a KS diagnosis and death may be partly explained by the immune suppression rather than by KS itself.

PLWH have elevated incidence of many cancer types, especially those with viral causes.[4] Cancer risk has declined in the ART era for several virus-related cancers and lung cancer.[4] Recent findings from large trials further confirmed that early diagnosis of HIV infection and an earlier initiation of ART can reduce incidence of multiple major cancers among PLWH.[32] Sustained low plasma HIV viral load was associated with reduction in anal cancer incidence among PLWH.[33, 34] KS and NHL are essentially preventable with ART. These deaths and YLL could be eliminated if established treatment guidelines were followed, including timely HIV diagnosis and referral to care.[35, 36] HPV vaccination is expected to reduce risk of HPV-related cancers.[37] Cigarette smoking is the predominant risk factor for lung cancer, and smoking prevalence is elevated among PLWH.[38] Smoking cessation should be emphasized in this population, and more information is needed on the possible utility of lung cancer screening with low-dose CT scans in this population.[38]

TYLL due to cancer depends on the number of PLWH with cancer and the survival experience after cancer diagnosis of PLWH. MYLL to cancer were highest among the oldest age group, as cancer incidence and mortality generally increases with age; however, given that the largest fraction of PLWH was in the 40–59 age group (60%), PLWH in this age group had the highest TYLL to cancer. Mortality associated with cancer is highest within 5 years of cancer diagnosis. Our study focused on measuring TYLL over a defined calendar period and captured almost all cancer-related deaths, especially for people who entered early. However, our results underestimate YLL due to cancer over a lifetime, as we were unable to follow every PLWH in the study from HIV report to death.

We found the largest proportions of TYLL to cancer occurred among Black PLWH (54%) and among MSM (54%), reflecting the high population fractions of PLWH that were Black (50%) and that were MSM (56%). Cancer incidence and mortality rates among PLWH have been reported to vary by racial/ethnic group and risk group. For example, NHL and anal cancer rates were higher among White PLWH than among Black PLWH, and White PLWH had a lower percentage of excess cancer cases for lung cancer compared Black PLWH.[39] Non-White PLWH have higher mortality rates compared to White PLWH for both NHL and anal cancer.[7] Lung cancer mortality was similar between non-White and White PLWH.[7] By risk group, MSM have higher anal and KS cancer rates.[34, 39] PWID have higher lung cancer rates, due to higher smoking prevalence.[40] We were unable to examine the intersection of race/ethnicity and risk group in this analysis due to sparse numbers in some categories. These differences highlight the need to better understand disparities in cancer incidence and mortality rates among PLWH by racial/ethnic group and by risk group.

This study has several strengths. The HACM Study is the largest study of cancer risk among PLWH in the world, and our approach of up-weighting to the US HIV population allowed for nationally-representative estimates. HACM comprises over half of PLWH in the US, and its large sample size allowed us to estimate MYLL and TYLL due to cancer in racial/ethnic and HIV risk groups. Our approach accommodated time-dependent variables and was statistically powerful because it relies on semi-parametric modeling using data from the entire curve rather than single time points.

One limitation was that follow-up time ended in 2015. Thus, the interpretation of our YLL estimates is limited to 2006–2015. In addition, sparse data for some cancer types in cohorts with shorter follow-up did not allow us to reliably generate estimates of YLL due to specific cancer types. However, given that the national number of PLWH in year 2006 (around 1,000,000 in 2006 in the US) significantly outweighs the size of subsequent yearly national incident HIV population (around 50,000), and the declining trend in restricted MYLL for shorter follow-ups, we expect the impact of sparse data on our estimates of TYLL for some cancer types in more recent cohorts to be minimal. In addition, individual-level information on HIV strains, HIV treatment and adherence, and behaviors are not available in our dataset.

In conclusion, between 2006 and 2015, nearly 135,000 years of life were lost due to cancer among PLWH in the United States. Though rates of certain cancers have declined among PLWH during the ART era, cancer risk remains elevated among PLWH, and more progress in cancer prevention and early detection is needed to prevent future YLL due to cancer in this population.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

## Acknowledgments

Funding: This work was supported by the Intramural Research Program of the National Cancer Institute.

QL and MSS wrote the first draft of the manuscript. EAE and MSS conceptualized this analysis. QL, RMP, and MSS did the statistical analysis. All authors contributed to the study design, data analyses, interpretation of results, discussion, revision of manuscript, and approved the final version of this manuscript. EAE and MSS, who are principal investigators in the HIV/AIDS Cancer Match Study, acquired the data, obtained funding, and supervised the study.

The authors gratefully acknowledge the support and assistance provided by individuals at the following state HIV/AIDS and cancer registries: Colorado, Connecticut, District of Columbia, Georgia, Louisiana, Maryland, Michigan, New Jersey, New York, North Carolina, Puerto Rico, and Texas. We also thank Timothy McNeel at Information Management Services for programming support.

The views expressed in this paper are those of the authors and should not be interpreted to reflect the views or official policies of the National Cancer Institute, Centers for Disease Control and Prevention or the Department of Health and Human Services, HIV/AIDS or cancer registries, or their contractors, nor does the mention of trade names, commercial practices, or organizations imply endorsement by the U.S. Government. This research was supported in part by the Intramural Research Program of the National Cancer Institute.

The following cancer registries were supported by the cooperative agreement funded by the Centers for Disease Control and Prevention, National Program of Cancer Registries: Colorado (NU58DP006347-01), Georgia (5U58DP003875-01), Louisiana (NU58DP006332-03-00), Maryland (NU58DP006333), Michigan (17NU58DP006334), New Jersey (NU58/DP003931-05-00), New York (6NU58/DP006309), North Carolina (1NU58DP006281), Texas (1NU58DP006308). District of Columbia is supported by the Centers for Disease Control and Prevention cooperative agreement DP006302.

The following cancer registries were supported by the SEER Program of the National Cancer Institute: Connecticut (HHSN261201300019I), Louisiana (HHSN261201800007I/ HHSN26100002), New Jersey (HHSN261201300021I, N01-PC-2013-00021), and New York (HHSN261201800009I). The New Jersey State Cancer Registry was also supported by the state of New Jersey, the Maryland Cancer Registry was supported by the State of Maryland and the Maryland Cigarette Restitution Fund, the Louisiana Tumor Registry was also supported by the state of Louisiana (0587200015), and the New York State Cancer Registry was also supported by the state of New York.

The following HIV registries were supported by HIV Incidence and Case Surveillance Branch of the Centers for Disease Control and Prevention, National HIV Surveillance Systems: Colorado (NU62PS003960),

Connecticut (5U62PS001005-05), Louisiana (NU62PS924522-02-00), Michigan (U62PS004011-02), New Jersey (U62PS004001-2), New York (NU62PS924546-02-00; PS18-1802: Integrated HIV Surveillance and Prevention Programs for Health Departments, National Center for HIV, Viral Hepatitis, STD, and TB Prevention (NCHHSTP)).

## References:

1. Chan DP, Sun HY, Wong HT, Lee SS, Hung CC. Sexually acquired hepatitis C virus infection: a review. Int J Infect Dis 2016; 49:47–58. [PubMed: 27270138]
2. Denny LA, Franceschi S, de Sanjosé S, Heard I, Moscicki AB, Palefsky J. Human papillomavirus, human immunodeficiency virus and immunosuppression. Vaccine 2012; 30 Suppl 5:F168–174. [PubMed: 23199960]
3. Gonçalves PH, Uldrick TS, Yarchoan R. HIV-associated Kaposi sarcoma and related diseases. Aids 2017; 31(14):1903–1916. [PubMed: 28609402]
4. Hernández-Ramírez RU, Shiels MS, Dubrow R, Engels EA. Cancer risk in HIV-infected people in the USA from 1996 to 2012: a population-based, registry-linkage study. Lancet HIV 2017; 4(11):e495–e504. [PubMed: 28803888]
5. Antiretroviral Therapy Cohort C. Life expectancy of individuals on combination antiretroviral therapy in high-income countries: a collaborative analysis of 14 cohort studies. Lancet 2008; 372(9635):293–299. [PubMed: 18657708]
6. Shiels MS, Engels EA. Evolving epidemiology of HIV-associated malignancies. Curr Opin HIV AIDS 2017; 12(1):6–11. [PubMed: 27749369]
7. Coghill AE, Pfeiffer RM, Shiels MS, Engels EA. Excess Mortality among HIV-Infected Individuals with Cancer in the United States. Cancer epidemiology, biomarkers & prevention : a publication of the American Association for Cancer Research, cosponsored by the American Society of Preventive Oncology 2017; 26(7):1027–1033.
8. Coghill AE, Shiels MS, Suneja G, Engels EA. Elevated Cancer-Specific Mortality Among HIV-Infected Patients in the United States. J Clin Oncol 2015; 33(21):2376–2383. [PubMed: 26077242]
9. Crepaz N, Dong X, Wang X, Hernandez AL, Hall HI. Racial and Ethnic Disparities in Sustained Viral Suppression and Transmission Risk Potential Among Persons Receiving HIV Care - United States, 2014. MMWR Morb Mortal Wkly Rep 2018; 67(4):113–118. [PubMed: 29389918]
10. Simoni JM, Huh D, Wilson IB, Shen J, Goggin K, Reynolds NR, et al. Racial/Ethnic disparities in ART adherence in the United States: findings from the MACH14 study. J Acquir Immune Defic Syndr 2012; 60(5):466–472. [PubMed: 22595873]
11. Kimmel AD, Masiano SP, Bono RS, Martin EG, Belgrave FZ, Adimora AA, et al. Structural Barriers to Comprehensive, Coordinated HIV Care: Geographic Accessibility in the US South. AIDS Care 2018; 30(11):1459–1468. [PubMed: 29845878]
12. Masiano SP, Martin EG, Bono RS, Dahman B, Sabik LM, Belgrave FZ, et al. Suboptimal geographic accessibility to comprehensive HIV care in the US: regional and urban–rural differences. J Int AIDS Soc 2019; 22(5).
13. Meditz AL, MaWhinney S, Allshouse A, Feser W, Markowitz M, Little S, et al. Sex, Race, and Geographic Region Influence Clinical Outcomes Following Primary HIV-1 Infection. J Infect Dis 2011; 203(4):442–451. [PubMed: 21245157]
14. Adimora AA, Ramirez C, Schoenbach VJ, Cohen MS. Policies and politics that promote HIV infection in the Southern United States. AIDS 2014; 28(10):1393–1397. [PubMed: 24556871]
15. Bradley H, Hall HI, Wolitski RJ, Van Handel MM, Stone AE, LaFlam M, et al. Vital Signs: HIV diagnosis, care, and treatment among persons living with HIV--United States, 2011. MMWR Morb Mortal Wkly Rep 2014; 63(47):1113–1117. [PubMed: 25426654]
16. Suneja G, Boyer M, Yehia BR, Shiels MS, Engels EA, Bekelman JE, et al. Cancer Treatment in Patients With HIV Infection and Non-AIDS-Defining Cancers: A Survey of US Oncologists. J Oncol Pract 2015; 11(3):e380–387. [PubMed: 25873060]
17. Suneja G, Coghill A. Cancer care disparities in people with HIV in the United States. Curr Opin HIV AIDS 2017; 12(1):63–68. [PubMed: 27753654]

18. Suneja G, Shiels MS, Angulo R, Copeland GE, Gonsalves L, Hakenewerth AM, et al. Cancer treatment disparities in HIV-infected individuals in the United States. J Clin Oncol 2014; 32(22):2344–2350. [PubMed: 24982448]
19. Horner MJ, Shiels MS, Pfeiffer RM, Engels EA. Deaths attributable to cancer in the United States HIV population during 2001-2015. Clin Infect Dis 2020.
20. Romeder JM, McWhinnie JR. Potential years of life lost between ages 1 and 70: an indicator of premature mortality for health planning. Int J Epidemiol 1977; 6(2):143–151. [PubMed: 892979]
21. Morrow RH, Bryant JH. Health policy approaches to measuring and valuing human life: conceptual and ethical issues. Am J Public Health 1995; 85(10):1356–1360. [PubMed: 7573617]
22. Hyder AA, Rotllant G, Morrow RH. Measuring the burden of disease: healthy life-years. Am J Public Health 1998; 88(2):196–202. [PubMed: 9491007]
23. Surveillance Research Program DoCCaPS, National Cancer Institute. Site Recode ICD-O-3/WHO 2008 Definition. In.
24. Centers for Disease Control and Prevention. Estimated HIV incidence and prevalence in the United States, 2010–2016. In: HIV Surveillance Supplemental Report 2019;24(No 1): February, 2019; 2019.
25. Centers for Disease Control and Prevention. NCHHSTP AtlasPlus. Updated 2019. In; 2019.
26. Royston P, Parmar MK. The use of restricted mean survival time to estimate the treatment effect in randomized clinical trials when the proportional hazards assumption is in doubt. Stat Med 2011; 30(19):2409–2421. [PubMed: 21611958]
27. Royston P, Parmar MK. Restricted mean survival time: an alternative to the hazard ratio for the design and analysis of randomized trials with a time-to-event outcome. BMC Med Res Methodol 2013; 13:152. [PubMed: 24314264]
28. Dehbi HM, Royston P, Hackshaw A. Life expectancy difference and life expectancy ratio: two measures of treatment effects in randomised trials with non-proportional hazards. BMJ 2017; 357:j2250. [PubMed: 28546261]
29. Centers for Disease Control and Prevention. Surveillance Systems. In.
30. StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC.
31. Engels EA, Yanik EL, Wheeler W, Gill MJ, Shiels MS, Dubrow R, et al. Cancer-Attributable Mortality Among People With Treated Human Immunodeficiency Virus Infection in North America. Clin Infect Dis 2017; 65(4):636–643. [PubMed: 29017269]
32. Borges ÁH, Neuhaus J, Babiker AG, Henry K, Jain MK, Palfreeman A, et al. Immediate Antiretroviral Therapy Reduces Risk of Infection-Related Cancer During Early HIV Infection. Clin Infect Dis 2016; 63(12):1668–1676. [PubMed: 27609756]
33. Guiguet M, Boué F, Cadranel J, Lang JM, Rosenthal E, Costagliola D. Effect of immunodeficiency, HIV viral load, and antiretroviral therapy on the risk of individual malignancies (FHDH-ANRS CO4): a prospective cohort study. The Lancet Oncology 2009; 10(12):1152–1159. [PubMed: 19818686]
34. Hernandez-Ramirez RU, Qin L, Lin H, Leyden W, Neugebauer RS, Althoff KN, et al. Association of Immunosuppression and Human Immunodeficiency Virus (HIV) Viremia With Anal Cancer Risk in Persons Living With HIV in the United States and Canada. Clin Infect Dis 2020; 70(6):1176–1185. [PubMed: 31044245]
35. Dubrow R, Qin L, Lin H, Hernandez-Ramirez RU, Neugebauer RS, Leyden W, et al. Association of CD4+ T-cell Count, HIV-1 RNA Viral Load, and Antiretroviral Therapy With Kaposi Sarcoma Risk Among HIV-infected Persons in the United States and Canada. J Acquir Immune Defic Syndr 2017; 75(4):382–390. [PubMed: 28394855]
36. Hernandez-Ramirez RU, Qin L, Lin H, Leyden W, Neugebauer RS, Althoff KN, et al. Association of immunosuppression and HIV viraemia with non-Hodgkin lymphoma risk overall and by subtype in people living with HIV in Canada and the USA: a multicentre cohort study. Lancet HIV 2019; 6(4):e240–e249. [PubMed: 30826282]
37. Zizza A, Banchelli F, Guido M, Marotta C, Di Gennaro F, Mazzucco W, et al. Efficacy and safety of human papillomavirus vaccination in HIV-infected patients: a systematic review and meta-analysis. Sci Rep 2021; 11(1):4954. [PubMed: 33654181]

38. Reddy KP, Kong CY, Hyle EP, Baggett TP, Huang M, Parker RA, et al. Lung Cancer Mortality Associated With Smoking and Smoking Cessation Among People Living With HIV in the United States. JAMA Intern Med 2017; 177(11):1613–1621. [PubMed: 28975270]

39. Robbins HA, Pfeiffer RM, Shiels MS, Li J, Hall HI, Engels EA. Excess cancers among HIV-infected people in the United States. J Natl Cancer Inst 2015; 107(4).

40. Sigel K, Makinson A, Thaler J. Lung cancer in persons with HIV. Curr Opin HIV AIDS 2017; 12(1):31–38. [PubMed: 27607596]

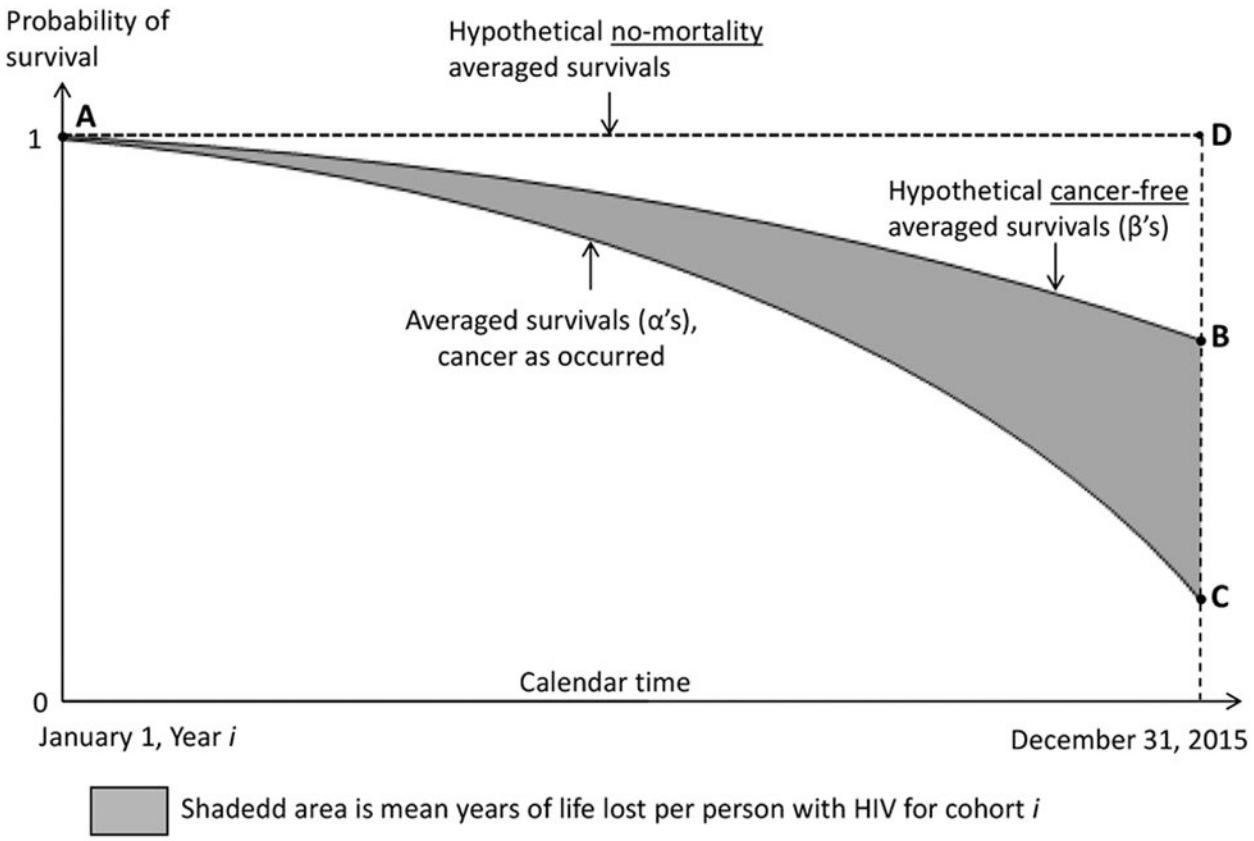


**Figure 1. Illustration of calculation of MYLL for cohort year i**

Shaded area is mean years of life lost per person with HIV for cohort *i*

Note. The curve AC represents the averaged survival experience of individuals as occurred. The curve AB represents the averaged survival experience of individuals who were cancer free during follow-up. The area ABC represents the mean years of life lost to cancer per person between January 1, year *i* and December 31, 2015.

**Table 1.**

HACM population characteristics, all cohorts, January 2006 –December 2015.

| Characteristics | Total | % |
|---|---|---|
| Number of subjects | 466,234 | 100.00% |
| *Age at study entry* | | |
| 20–29 | 82,006 | 17.59% |
| 30–39 | 118,461 | 25.41% |
| 40–49 | 160,868 | 34.50% |
| 50–59 | 81,132 | 17.40% |
| 60+ | 23,767 | 5.10% |
| *Race/ethnicity* | | |
| Non-Hispanic white | 115,810 | 24.84% |
| Non-Hispanic black | 214,138 | 45.93% |
| Hispanic | 126,602 | 27.15% |
| Other | 9,684 | 2.08% |
| *Risk group/sex* | | |
| MSM, non-PWID | 176,691 | 37.90% |
| Male PWID | 68,763 | 14.75% |
| All other male | 98,224 | 21.07% |
| Female PWID | 24,545 | 5.26% |
| All other females | 98,011 | 21.02% |
| *Diagnosed with cancer during follow-up* | | |
| Any first cancer | 25,772 | 5.53% |
| Kaposi sarcoma | 3,011 | 0.65% |
| Non-Hodgkin lymphoma | 5,155 | 1.11% |
| Cervix uteri | 574 | 0.12% |
| Lung and bronchus | 2,257 | 0.48% |
| Anal | 1,600 | 0.34% |
| Hodgkin lymphoma | 1,160 | 0.25% |
| Liver | 1,125 | 0.24% |
| Breast | 946 | 0.20% |
| Prostate | 2,155 | 0.46% |
| Colon and rectum | 1,131 | 0.24% |
| Other | 6,658 | 1.43% |
| No cancer | 440,462 | 94.47% |

Note: MSM: men who have sex with men. PWID: persons who inject drugs.

**Table 2.**

Total years of life lost (TYLL) to cancer by subgroups, and by cancer types in the total U.S. population of people living with HIV between 2006 and 2015

| | Subgroup | TYLL to cancer | % of TYLL to any cancer |
|---|---|---|---|
| | Overall | 135,000 | 100.0% |
| Age | 20–39 | 23,400 | 17.3% |
| | 40–59 | 91,200 | 67.5% |
| | 60+ | 20,400 | 15.1% |
| Race | Non-Hispanic white | 37,200 | 27.5% |
| | Non-Hispanic black | 72,600 | 53.8% |
| | Hispanic | 21,700 | 16.1% |
| Risk group | MSM, non-PWID | 73,400 | 54.4% |
| | PWID | 14,600 | 10.8% |
| | All other | 46,900 | 34.7% |
| Cancer type | AIDS-defined cancer | | |
| | Non-Hodgkin lymphoma | 27,800 | 20.5% |
| | Kaposi sarcoma | 12,800 | 9.5% |
| | Cervix Uteri | 2,600 | 1.9% |
| | Non-AIDS-defined cancer | | |
| | Anal | 9,700 | 7.2% |
| | Lung and bronchus | 9,000 | 6.6% |
| | Colon and rectum | 6,000 | 4.4% |
| | Hodgkin Lymphoma | 5,000 | 3.7% |
| | Liver | 4,500 | 3.3% |
| | Breast | 3,800 | 2.8% |
| | Prostate | 2,600 | 1.9% |
| | Other | 35,000 | 25.9% |

Note: TYLL: total years of life lost. MSM: men who have sex with men. PWID: persons who inject drugs.

**Table 3.**

Total all-cause years of life lost, and its proportion that was lost to cancer by subgroups in the total U.S. population of people living with HIV between 2006 and 2015

| | Group | TYLL to any cause (column %) | TYLL to cancer | Proportion of TYLL to any cause that were lost to cancer (row %) |
|---|---|---|---|---|
| Overall | | 1,443,500 (100%) | 135,000 | 9.6% |
| Race | Non-Hispanic white | 351,700 (24.4%) | 37,200 | 10.6% |
| | Non-Hispanic black | 809,200 (56.1%) | 72,600 | 9.0% |
| | Hispanic | 24,900 (17.3%) | 21,700 | 8.7% |
| Risk group | MSM, non-PWID | 634,700 (47.4%) | 73,400 | 11.6% |
| | PWID | 204,700 (15.3%) | 14,600 | 7.1% |
| | All other | 498,700 (37.3%) | 46,900 | 9.4% |

Note: TYLL: total years of life lost. MSM: men who have sex with men. PWID: persons who inject drugs.