Supplemental Methods

*HIV/AIDS Cancer Match Contributing Registries*

The HIV/AIDS Cancer Match Study is a record linkage study of HIV and cancer registries in the U.S. ([www.hivmatch.cancer.gov](http://www.hivmatch.cancer.gov). Data from 8 U.S. states (i.e., Colorado, Connecticut, Georgia, Maryland, Michigan, New Jersey, New York and Texas) and Puerto Rico were included in this analysis.

*Joinpoint Analysis and Assessment of Heterogeneity by Registry*

Joinpoint regression (1) was used to identify the presence of statistically significant changes in the slope of time trends in crude cancer incidence rates in each age and risk-group stratum, and, if a significant change was present, calendar years prior to the Joinpoint were excluded from all analyses for that cancer site. Joinpoints were detected in 2002 for NHL among 35-44 year-olds, in 2009 for anal cancer among 45+ year-old MSMs, and in 2005 for liver cancer among 65+ year-old PWIDs. Models for NHL were restricted to ≥2002. Restricting anal and liver cancer models to ≥2009 and ≥2005, respectively, resulted in too few cases; therefore, the full time period (i.e., 2000-2012) was used in the projection of these two cancers. Of note, the Joinpoint trends in the most recent time period were not statistically significant for either of these cancer sites. In addition, data from 2000 were excluded from Hodgkin lymphoma models due to an extremely high rate observed in that year.

For each cancer type, heterogeneity by registry was assessed by including an interaction term between registry and calendar year in the Poisson model. Significant heterogeneity was only observed for NHL and the other combined cancer category. After excluding the registries with the most extreme trends (i.e., Maryland for NHL, New Jersey for other cancers combined), no notable differences in projected incidence rates were observed, so all registries were retained in the main analysis.

*Comparison of Modeled and Projected Rates with General Population Rates*

For cancers known to be elevated in HIV-infected people (i.e., KS, NHL, cervical cancer, anal cancer, lung cancer, liver cancer, oral cavity and pharynx cancer, and Hodgkin lymphoma (2)) it was assumed *a priori* that future cancer rates would never be lower than rates observed in the general population. Therefore, any projected rate that was lower than the age-specific rate observed for the U.S. general population, based on data from 18 cancer registries in the Surveillance, Epidemiology and End Results program (SEER-18) in 2013 (3), was reset to the SEER rate with an upper confidence limit estimated from the Poisson model and a lower confidence limit estimated from SEER data. If the modeled upper confidence limit was lower than the SEER estimate, the SEER upper confidence limit was utilized. Likewise, as PLWH have a deficit of prostate, breast and colon cancers (2, 4), we assumed that the age-specific rates of these cancers would never exceed those in SEER-18.

*HIV Optimization and Prevention Economics (HOPE) model*

The number of PLWH in the U.S. during 2006-2030 was estimated with the dynamic, compartmental HIV Optimization and Prevention Economics (HOPE) model, which simulates the sexually active U.S. population years beginning in 2006 (5, 6). The population is stratified into 195 subpopulations by transmission group (gay, bisexual, and other men who have sex with men [collectively referred to as MSM], persons who inject drugs [PWID], or heterosexuals); sex (male or female); race/ethnicity (black, Hispanic/Latino, or white/other racial-ethnic groups combined, of which whites comprised 89%); age-group (13–17, 18–24, 25–34, 35–44, 45–64, and 65+ years of age); male circumcision status (circumcised or uncircumcised); and HIV risk level (low or high) as defined for this model based on previously published methods (7, 8). The force of HIV infection, or the rate at which susceptible individuals acquire HIV infection, is a function of HIV prevalence among their partners and the transmission risk from sexual and needle contacts with HIV-infected partners.

The total population (people living with HIV [PLWH] and those susceptible) transitions among the 25 compartments, which are defined by disease progression and continuum-of-care stage, and moves into (upon attaining age 13) and out of the model via aging and death. The model uses differential equations to represent the progression of the HIV-uninfected and HIV-infected populations between compartments. Differential equations in the model are solved using MATLAB software (MathWorks; Natick, Massachusetts). Additional model details, including definitions of all subpopulations and compartments and descriptions of the model’s differential equations, force of infection calculations, model inputs and sources, calibration, validation, and other model methods, assumptions, and specifications are published in a full technical report on the HOPE model (5, 6) This model assumes that no new infections occur among or are caused by those in the over 65 age group. The HOPE model has been shown to closely match published HIV surveillance estimates. For example, the latest 2014 estimates from CDC for 13-64 year-olds were 1,107,700 for overall HIV prevalence and 37,600 for overall HIV incidence (9), and the model predictions were 1,042,140 and 35,761, respectively.

To consider the uncertainty of the HIV prevalence for 2006-2030 due to the values of the parameters, we ran the HOPE model using 10 additional sets of values for those inputs that, like the set used in the base case analysis, approximated the targeted surveillance measures. To generate each of the 10 sets, we went through a calibration process, which was also used to generate the base case inputs. The process that was applied to calibrate the model is outlined in Sections 11.1.1 to 11.1.4 of the published technical report (6). We report the range of the HIV population estimates across those runs.

Supplemental Table 1. Description of Joinpoint analyses and modeling decisions by cancer site and age-group.

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| Cancer Type | Age-groups | N | Significant Joinpoint (year) | Annual Percent Change (p-value) | Estimate Replaced with SEER 2013 Rate (years)\*\*\* |
| AIDS-defining cancers | |  |  |  |  |
| Kaposi sarcoma |  |  |  |  |  |
| MSM\* | 18-34 | 642 | No | -5.0 (p<0.001) | No |
|  | 35-44 | 904 | No | -5.2 (p<0.001) | No |
|  | 45+ | 511 | No | -8.0 (p<0.001) | No |
| Non-MSM\* | 18-34 | 194 | No | -5.2 (p=0.01) | No |
|  | 35-44 | 420 | No | -8.8 (p<0.001) | No |
|  | 45+ | 420 | No | -11.3 (p<0.001) | No |
| NHL\* | 18-24 | 86 | No | -11.1 (p=0.001) | No |
|  | 25-34 | 529 | No | -5.1 (p<0.001) | No |
|  | 35-44 | 1660 | Yes (2002) | -6.2 (p<0.001) | No |
|  | 45-64 | 2403 | No | -9.0 (p<0.001) | Yes (2028-30) |
|  | 65+ | 168 | No | -12.7 (p<0.001) | Yes (2014-30) |
| Cervical Cancer‡ | 25-34 | 75 | No | -8.7 (p<0.001) | Yes (2030) |
|  | 35-44 | 252 | No | -8.7 (p<0.001) | Yes (2027-30) |
|  | 45+ | 209 | No | -8.7 (p<0.001) | Yes (2025-30) |
| Non-AIDS-defining Cancers | |  |  |  |  |
| Lung Cancer\*‡ | 35-44 | 278 | No | -9.1 (p<0.001) | Yes (2025-30) |
|  | 45-64 | 1857 | No | -5.6 (p<0.001) | Yes (2020-30) |
|  | 65+ | 360 | No | -7.9 (p<0.001) | Yes (2011-30) |
| Prostate cancer\*‡ | 35-44 | 52 | No | 8.7 (p=0.050) | Yes (2002-30) |
|  | 45-64 | 1116 | No | 3.5 (p<0.001) | Yes (2024-30) |
|  | 65+ | 381 | No | 1.2 (p=0.45) | No |
| Anal Cancer |  |  |  |  |  |
| MSM‡ | 25-34 | 58 | No | -2.7 (p=0.005) | No |
|  | 35-44 | 330 | No | -2.7 (p=0.005) | No |
|  | 45+ | 537 | Yes (2009)\*\* | -2.7 (p=0.005) | No |
| Non-MSM | 25-34 | 26 | No | 1.4 (p=0.32) | No |
|  | 35-44 | 158 | No | 1.4 (p=0.32) | No |
|  | 45+ | 333 | No | 1.4 (p=0.32) | No |
| Liver Cancer |  |  |  |  |  |
| PWID‡ | 35-44 | 38 | No | 0.8 (p=0.51) | No |
|  | 45-64 | 577 | No | 0.8 (p=0.51) | No |
|  | 65+ | 48 | Yes (2005)\*\* | 0.8 (p=0.51) | No |
| Non-PWID‡ | 35-44 | 73 | No | -1.4 (p=0.92) | No |
|  | 45-64 | 350 | No | -1.4 (p=0.92) | No |
|  | 65+ | 49 | No | -1.4 (p=0.92) | No |
| Hodgkin lymphoma† | 18-34 | 155 | No | -4.4 (p<0.001) | No |
|  | 35-44 | 324 | No | -4.4 (p<0.001) | No |
|  | 45+ | 440 | No | -4.4 (p<0.001) | No |
| Oral cavity/pharynx cancers‡ | 35-44 | 105 | No | -1.5 (p=0.175) | No |
|  | 45-64 | 555 | No | -1.5 (p=0.175) | No |
|  | 65+ | 59 | No | -1.5 (p=0.175) | No |
| Breast cancer‡ | 25-44 | 206 | No | -1.4 (p=0.24) | No |
|  | 45-64 | 436 | No | -1.4 (p=0.24) | No |
|  | 65+ | 48 | No | -1.4 (p=0.24) | No |
| Colon cancer\*‡ | 25-44 | 58 | No | -4.7 (p=0.22) | No |
|  | 45-64 | 325 | No | 0.01 (p=0.99) | No |
|  | 65+ | 117 | No | -6.0 (p=0.028) | No |
| All Other Cancers\* | 18-34 | 269 | No | -5.3 (p=0.002) | No |
|  | 35-44 | 1019 | No | -3.1 (p=0.001) | No |
|  | 45-64 | 3379 | No | -2.0 (p<0.001) | No |
|  | 65+ | 579 | No | -3.4 (p=0.008) | No |

Abbreviations: Surveillance, Epidemiology, and End Results Program, SEER; Men who have sex with men, MSM; Non-Hodgkin’s Lymphoma, NHL; Persons who inject drugs, PWID;

\*Time trends differed significantly across age-groups, so trends were projected separately for each age-group.

† 2000 excluded due to extreme estimates.

\*\*Though a Joinpoint was identified, data were too sparse for forecasting if the calendar years were limited.

‡The cancer incidence rates in the youngest age-group(s) were assumed to be zero due to the limited number of reported cases: cervix (n=1); anal cancer MSM (n=2), anal cancer non-MSM (n=0), lung (n=10), liver PWID (n=0), liver non-PWID (n=2), oral cavity/pharynx (n=7), prostate (n=2), breast (n=2), colon cancer (n=0).

\*\*\* For cancers known to be elevated in PLWH, it was assumed *a priori* that future cancer rates would never be lower than rates observed in the general population. Therefore, any projected rate that was lower than the 2013 age-specific rate in the Surveillance, Epidemiology and End Results program (SEER-18) data (as a proxy for the US general population) was reset to the SEER rate. Likewise, as PLWH have a lower risk of prostate, breast and colon cancers for unclear reasons, we assumed that the age-specific rates of these cancers would never exceed those in SEER-18.

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | 2010 | | 2020 | | 2030 | |
|  | N | % | N | % | N | % |
| Total | 1,127,669 |  | 1,161,947 |  | 1,091,827 |  |
| Sex |  |  |  |  |  |  |
| Male | 846,197 | 75.0% | 879,868 | 75.7% | 838,770 | 76.8% |
| Female | 281,472 | 25.0% | 282,079 | 24.3% | 253,057 | 23.2% |
|  |  |  |  |  |  |  |
| Age group, years |  |  |  |  |  |  |
| 18–24 | 73,130 | 6.5% | 40,260 | 3.5% | 21,550 | 2.0% |
| 25–34 | 212,100 | 18.8% | 157,330 | 13.5% | 111,310 | 10.2% |
| 35–44 | 301,590 | 26.7% | 254,290 | 21.9% | 204,400 | 18.7% |
| 45–64 | 444,710 | 39.4% | 520,050 | 44.8% | 520,470 | 47.7% |
| 65+ | 96,139 | 8.5% | 190,017 | 16.4% | 234,097 | 21.4% |
|  |  |  |  |  |  |  |
| Race/ethnicity |  |  |  |  |  |  |
| Non-Hispanic black | 481,535 | 42.7% | 472,273 | 40.6% | 419,535 | 38.4% |
| Hispanic | 218,971 | 19.4% | 228,199 | 19.6% | 216,506 | 19.8% |
| Non-Hispanic white/other | 427,163 | 37.9% | 461,475 | 39.7% | 455,786 | 41.7% |
|  |  |  |  |  |  |  |
| Risk Group |  |  |  |  |  |  |
| MSM | 624,456 | 55.4% | 677,332 | 58.3% | 665,471 | 61.0% |
| PWID | 193,630 | 17.2% | 174,103 | 15.0% | 148,579 | 13.6% |
| Heterosexual | 309.583 | 27.5% | 310,512 | 26.7% | 277,777 | 25.4% |
| Abbreviations: Men who have sex with men, MSM; Persons who inject drugs, PWID | | | | | | |

Supplemental Table 2. Characteristics of modeled adult U.S. HIV population in 2010, 2020 and 2030.

Supplemental Table 3. Minimum and maximum estimates for the adult U.S. HIV population by calendar year.

|  |  |  |  |
| --- | --- | --- | --- |
| Year | Estimated Number  of PLWH | Minimum  Estimate | Maximum  Estimate |
| 2006 | 1,063,089 | 1,058,806 | 1,063,091 |
| 2007 | 1,083,294 | 1,080,005 | 1,085,508 |
| 2008 | 1,100,540 | 1,098,408 | 1,107,386 |
| 2009 | 1,115,194 | 1,114,485 | 1,127,652 |
| 2010 | 1,127,669 | 1,122,937 | 1,143,608 |
| 2011 | 1,138,033 | 1,135,849 | 1,154,345 |
| 2012 | 1,146,495 | 1,142,227 | 1,164,294 |
| 2013 | 1,152,985 | 1,145,083 | 1,164,667 |
| 2014 | 1,157,701 | 1,150,285 | 1,170,579 |
| 2015 | 1,160,646 | 1,150,527 | 1,174,673 |
| 2016 | 1,163,729 | 1,146,365 | 1,178,523 |
| 2017 | 1,165,314 | 1,141,017 | 1,181,120 |
| 2018 | 1,165,445 | 1,134,735 | 1,182,647 |
| 2019 | 1,164,345 | 1,127,537 | 1,183,059 |
| 2020 | 1,161,947 | 1,119,647 | 1,182,577 |
| 2021 | 1,158,499 | 1,111,107 | 1,181,218 |
| 2022 | 1,154,081 | 1,102,013 | 1,179,068 |
| 2023 | 1,148,743 | 1,092,395 | 1,176,197 |
| 2024 | 1,142,497 | 1,082,290 | 1,172,599 |
| 2025 | 1,135,609 | 1,071,792 | 1,168,422 |
| 2026 | 1,127,914 | 1,060,843 | 1,163,570 |
| 2027 | 1,119,687 | 1,049,509 | 1,158,147 |
| 2028 | 1,110,830 | 1,037,915 | 1,152,268 |
| 2029 | 1,101,618 | 1,025,998 | 1,145,881 |
| 2030 | 1,091,827 | 1,013,812 | 1,139,042 |

Supplemental Figure Legend

Supplemental Figure 1. Age-specific estimated and projected cancer incidence rates among adults living with HIV, 2006-2030. Solid lines represent rates and dotted lines represent 95% confidence intervals. MSM: men who have sex with men; PWID: persons who inject drugs.

Supplemental Figure 2. Proportions of total cancer burden by cancer type among adults living with HIV in the U.S., during 2010 and 2030, and in the general population of the U.S. in 2010. General population estimates were calculated with data from the Surveillance, Epidemiology and End Results Program. NHL: non-Hodgkin lymphoma; KS: Kaposi sarcoma; PLWH: persons living with HIV.

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