



Changing Causes of Death for People With HIV

Mortality has declined overall, especially for AIDS-related causes and liver disease, but disparities persist.

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All-cause mortality dropped among people with HIV in high-income countries over the past three decades, and the causes of death are shifting, but all groups have not benefited equally, according to recent studies.

Mortality rates for people with HIV began to decline dramatically with the advent of highly active [antiretroviral therapy](#) (ART) in the mid-1990s. Since then, death rates have continued to fall as treatment has gotten more effective and easier to take. Today, people who start treatment promptly can have [a near-normal life expectancy](#). What's more, the causes of death have evolved over time as the HIV population ages.

As described in [The Lancet HIV](#), Adam Trickey, PhD, of the University of Bristol in the United Kingdom, and colleagues looked at longitudinal trends in cause-specific mortality among people with HIV in North America and Europe who started treatment between 1996 and 2020.

The analysis included more than 189,000 people ages 16 or older in 17 cohorts that contributed data to the Antiretroviral Therapy Cohort Collaboration. A total of 16,832 people (9%) died during the study period, and 13,180 deaths were retrospectively classified by cause. The researchers did not rely solely on death certificates, which might have erroneously listed HIV as a cause of death if the person was HIV positive, but also took into account recent CD4 counts and AIDS diagnosis.

Over the entire period, the most common causes of death were AIDS (25%), non-AIDS and non-liver-related cancers (14%) and cardiovascular or heart disease (8%). The all-cause mortality rate fell by half, from 16.8 deaths per 1,000 person-years during 1996–1999 to 7.9 per 1,000 during 2016–2020. The decline was steepest in the youngest age group (those ages 16 to 39).

The proportion of deaths due to AIDS declined dramatically, from 49% during 1996–1999 to 16% during 2016–2020. Mortality due to other specific causes also fell. Deaths due to cardiovascular causes, non-AIDS/non-liver malignancies and liver disease fell even as the population aged. The declines in cause-specific mortality were likely attributable in part to changes in treatment

guidelines to recommend starting ART sooner, the availability of more effective and less toxic regimens and better care in general for people with HIV, the study authors suggested. The decline in cardiovascular mortality, which was most marked among men who have sex with men, might reflect improvements in cardiovascular care for the general population or perhaps reduced toxicity of ART regimens.

Mortality due to non-AIDS infections and accidents or suicide also declined. The only increases in mortality were due to central nervous system causes, respiratory illnesses and substance use. However, the latter can be difficult to classify due to overlaps with accidental overdose and suicide. Although the last follow-up date was April 2020, deaths due to COVID-19 are not mentioned.

While the news is good overall, some groups did not benefit as much, especially people who acquired HIV through injection drug use. Within this group, the mortality rate for men decreased only slightly, while the mortality rate for women increased. For most causes of death, reductions in mortality were larger in North America than in Europe. Substance use mortality, however, fell in Europe while rising in North America. Among the population at large, opioid-related mortality is more than 10 times higher in North America compared with the European Union and medication-assisted treatment for opioid use is less widely available, according to the study authors.

“People with histories of substance use conditions have higher rates of homelessness and other comorbidities and often experience additional barriers and stigma while attempting to access care,” they wrote. “This indicates that targeted interventions, such as addressing social determinants of health and bringing comorbidity care to needle and syringe dispensing locations, are required for people who acquired HIV through injection drug use.”

The researchers suggested that most of their findings are likely generalizable to other high-income countries, such as Australia and Japan, although some particular trends—for example, substance use deaths—might be context-specific.

“Although mortality among people with HIV on ART has decreased, there is still higher mortality among people with HIV than among the general population, due both to the consequences of HIV infection and to a higher prevalence of comorbidities and risk behaviors among people with HIV,” the authors concluded. “Although there were reductions in rates of non-AIDS-related mortality, such as cancer and cardiovascular disease, non-AIDS deaths make up an increasingly large proportion of mortality among people with HIV. Expanding access to prevention, screening and treatment of these conditions is required to close the gap of comorbidity prevalence between adults with and those without HIV, and funders should recognize this.”

Causes of Death in the United States

Other recent analyses shed more light on changing causes of death among people with HIV in the United States.

According to the latest [HIV Epidemiology Report from the San Francisco Department of Public](#)

[Health](#), 77% of deaths in 2021 were due to non-HIV-related causes. Accidents (20%) were the leading non-HIV-related cause of death during 2018–2021, including 18% of deaths due to drug overdose, exceeding non-AIDS cancers (16%) and heart disease (15%). Just 3% of deaths were attributed to COVID and less than 2% to liver disease.

According to New York City’s latest [HIV Surveillance Annual Report](#), the two leading causes of death among people with HIV in 2021 were non-AIDS cancers and cardiovascular disease. The report notes that 8% of deaths that year were due to COVID, making it the third most common cause of death, down from 18% in 2020, when it was the second most common cause. Accidents were the fourth leading cause, but this apparently does not include drug overdose. “Use of or poisoning by psychoactive substances” was the 10th leading cause of death 2019 but was not listed in 2020 or 2021.

As described in [Clinical Infectious Diseases](#), Catherine Bielick, MD, of the University of Virginia in Charlottesville, and colleagues described national hospitalization and in-hospital mortality rates due to HIV-related opportunistic infections (OIs) in the United States during 2011–2018, based on data from the [National Inpatient Sample](#).

During this period, there were an estimated 1,710,164 hospital discharges for people with HIV. Of these, 154,430 were associated with an OI, of which 9,336 led to death in the hospital. The OI-related hospitalization rate fell from 27.3 per 1,000 people with HIV in 2011 to 16.5 per 1,000 in 2018, but the proportion of in-hospital deaths remained stable at 6%. Younger age, nonwhite race/ethnicity and lack of health insurance were risk factors for OI-related hospitalization, while older age, male sex, Latino ethnicity and lack of insurance were risk factors for OI-related mortality.

“Our findings indicate an ongoing need for continued funding of HIV testing, health insurance for all people with HIV, OI screening initiatives, review of current prophylaxis guidelines and recruitment of more HIV clinicians,” the study authors concluded.

Mortality Trends in Switzerland

Finally, Marc Weber, an internal medicine resident at University Hospital Zurich, and colleagues assessed changing causes of death in the Swiss HIV Cohort Study, highlighting trends in a country that monitors and manages its HIV epidemic within a single robust health care system.

This analysis, also [published in Clinical Infectious Diseases](#), included 1,630 deaths reported between 2005 and 2022. Across the entire study period, 9% of deaths were classified as HIV/AIDS-related. The leading causes of death were non-AIDS/non-liver cancers (23%), liver disease (10%) and cardiovascular disease (10%). The median age at death increased from 45 during 2005–2007 to 61 during 2020–2022.

HIV/AIDS-related mortality decreased most steeply, falling from 19% of all deaths during 2005–2007 to 4% during 2020–2022. Of the deaths attributed to HIV/AIDS, 42% were due to AIDS-defining OIs, 44% to AIDS-defining cancers and 15% to other AIDS-defining conditions. Among the

10 HIV/AIDS-related deaths during 2020–2022, eight were due to non-Hodgkin lymphoma. Men who have sex with men and those with a nadir (lowest-ever) CD4 count below 50 were more likely to die of AIDS-related causes, while those with a lower cumulative viral load were less likely.

The share of liver-related deaths also decreased dramatically, from 15% during 2005–2007 to just 2% during 2020–2022. More than 80% of the 166 liver-related deaths were due to hepatitis C-related cirrhosis, liver cancer or liver failure. Seventeen deaths were due to hepatitis B and 16 were due to nonviral causes of liver failure. The researchers attributed the decline in liver-related deaths to the advent of direct-acting antiviral therapy for hepatitis C, harm reduction programs for people who inject drugs and a nationwide program to eliminate hepatitis C among men who have sex with men.

In contrast, non-AIDS/non-liver cancer deaths doubled, rising from 15% of all deaths during 2005–2007 to 31% during 2020–2022. Lung cancer was the most common cause, followed by pancreatic cancer. As expected, the risk of cancer-related death rose with increasing age.

Cardiovascular deaths remained relatively stable at just over 11%, despite the aging HIV population. Ischemic heart disease and stroke were the most common causes. Thanks to the substantial progress in reducing HIV/AIDS-related and liver-related deaths, the causes of death among people with HIV gradually aligned with those of general population, namely cardiovascular disease and non-AIDS cancer, the researchers noted. Although the study period extended to 2022, COVID was not mentioned as a cause of death.

“The proportionally decreasing HIV/AIDS and liver-related deaths showcase the effectiveness of ART, comprehensive HIV patient care and interventions targeting hepatitis C virus coinfection,” the study authors wrote. “Future research should focus on managing cancer and cardiovascular-related conditions as the new leading causes of death among people with HIV. Comprehensive health care strategies focusing on non-AIDS-related comorbidities, cancer management and sustaining liver and cardiovascular health are needed to bridge the ongoing health disparities between people with HIV and the general population.”