OXFORD

JNCI J Natl Cancer Inst (2018) 110(9): djy030

doi: 10.1093/jnci/djy030
First published online February 26, 2018
Editorial

EDITORIAL

Opportunities to Understand Unique Cancer Risks in Global HIV-Infected Populations

Marie-Josèphe Horner, Satish Gopal

See the Notes section for the full list of author's affiliations.
Correspondence to: Satish Gopal, MD, MPH, UNC Project-Malawi, Private Bag A-104, Lilongwe, Malawi (email: satish_gopal@med.unc.edu).

In this issue, Coghill and colleagues (1) describe reduced incidence of three common screen-detectable cancers among people living with HIV relative to the general population of the United States. Findings from the population-based HIV/AIDS Cancer Match Study show a 37% reduced incidence of breast cancer, 52% reduced incidence of prostate cancer, and 31% to 49% reduced incidence of rectal cancer, proximal colon, and distal colon cancer, respectively, among people living with HIV.

Coghill et al. further investigate whether observed deficits in the incidence of breast, prostate, and colorectal cancers are consistent across tumor stage and size, as stage and size distribution may be impacted by differential application of cancer screening in HIV-infected and HIV-uninfected populations. For example, if reduced incidence of these cancers in HIV-positive populations is due to lower uptake of cancer screening, an excess of advanced stage disease and larger tumors would be observed in people with HIV. Conversely, a stage shift toward earlier-stage disease and smaller tumor size could result from higher screening rates among HIV-infected populations engaged in regular care than the general population. With the exception of late-stage breast cancer, which did not show a statistically significant association, the observed reduced incidence of breast, prostate, and colorectal cancers was consistent across local, regional, and distant tumor stages, as well as small, medium, and large tumors, suggesting that reduced risk for these cancers in people with HIV cannot be explained solely by population-level screening effects.

Furthermore, the study addressed whether inverse risk associations could be artifacts of the study design itself or confounded by unmeasured risk factors (1). Advanced analytic approaches examined several scenarios and conditions that would need to occur to replicate the magnitude of inverse risk associations observed in this study. Under different scenarios, the level of measurement error and confounding required to generate such strong inverse associations are essentially implausible. These findings taken together suggest a putative direct effect of HIV infection and its sequelae on reduced risk for these three common cancers without known oncogenic virus associations. Further investigations are needed to elucidate the underlying molecular mechanisms of how immune dysfunction, duration and class of antiretroviral therapy, and infection with HIV itself may impact disease pathogenesis and to translate these etiologic mechanisms into the clinical and public health realms.

Importantly, while people living with HIV experience a lower risk of breast, prostate, and colorectal cancers in the United States, they continue to experience increased mortality after cancer diagnosis compared with their HIV-uninfected counterparts, even after accounting for stage and receipt of cancer therapy (2,3). HIV-infected individuals with breast cancer experience 2.6 times greater cancer-specific mortality, and those with colorectal cancer experience 1.5 times greater mortality (3). In light of worse cancer outcomes and evolving cancer risk among aging HIV-infected populations in the United States treated ever earlier with antiretroviral therapy (4), early detection and primary prevention of cancer remain important priorities for people living with HIV. Currently, breast, prostate, and colorectal cancer screening recommendations by the US Preventive Task Force (USPSTF) for the general population are usually applied to people living with HIV (5). However, few studies have specifically examined the uptake, efficacy, or cost-effectiveness of mammography, prostate-specific antigen, or colonoscopy screening in HIV-infected individuals, and such data could inform more tailored cancer screening recommendations for people living with HIV (6). Such data could also inform the next phase of efforts to reduce health disparities and inequities across the entire HIV care continuum (7), including access to preventive services for chronic diseases and quality cancer care for people living with HIV regardless of age and background.

We should also emphasize that high-quality epidemiologic studies similar to the work by Coghill et al. are urgently needed to describe risk patterns in other populations, notably in low- and middle-income countries, where the global HIV epidemic is most concentrated (8). An emerging global public health question is whether HIV-cancer associations observed in Western settings will be replicated in Africa during the current era of

Received: January 30, 2018; **Accepted:** February 2, 2018

increasing access to antiretroviral therapy and rapidly improving life expectancy for HIV-infected populations (9,10). This is an essential question for ministries of health across the continent, which are tasked with safeguarding public health with many competing priorities and limited resources. Notably, African populations with HIV differ dramatically from high-income countries with respect to demographic, behavioral, and other cancer risk factors, and the continent overall is undergoing marked demographic shifts with major population growth and aging. Beyond the well-described burden of AIDS-defining malignancies, few studies have examined the effects of HIV and antiretroviral therapy on the risk of developing non-AIDS-defining cancers in the African setting, or prognosis following a cancer diagnosis. These questions will be critical and highly dynamic in the coming decades, and robust cancer surveillance should be prioritized within global efforts to scale up HIV treatment and prevention.

In summary, high-quality descriptive epidemiology like the work of Coghill and colleagues, coupled with molecular studies, can provide etiologic insights into the unique cancer risk patterns observed in HIV-infected individuals in the United States and worldwide. These insights can ultimately translate into more effective clinical management of HIV-infected patients with cancer and more efficient allocation of scarce public health resources to prevent cancer in this vulnerable population. Continued progress toward these goals is important for all countries where HIV and cancer are major public health problems, regardless of World Bank income level classification.

Notes

Affiliations of authors: Epidemiology, Gillings School of Global Public Health (MJH, SG), Lineberger Comprehensive Cancer Center (SG), and UNC Institute for Global Health and Infectious Diseases (SG), University of North Carolina at Chapel Hill, Chapel Hill, NC; UNC Project-Malawi, Lilongwe, Malawi (MJH, SG); Malawi Cancer Consortium and Regional Center of Research Excellence for Non-Communicable Diseases, Lilongwe, Malawi (SG); Department of Medicine, University of Malawi College of Medicine, Blantyre, Malawi (SG).

The authors have no conflicts of interest to disclose.

References

1. Coghill AE, Engels EA, Schymura MJ, et al. Risk of breast, prostate, and colorectal cancer diagnoses among HIV-infected individuals in the United States. *J Natl Cancer Inst*. 2018;110(9):959–966.
2. Coghill AE, Pfeiffer RM, Shiels MS, et al. Excess mortality among HIV-infected individuals with cancer in the United States. *Cancer Epidemiol Biomarkers Prev*. 2017;26(7):1027–1033.
3. Coghill AE, Shiels MS, Suneja G, et al. Elevated cancer-specific mortality among HIV-infected patients in the United States. *J Clin Oncol*. 2015;33(21):2376–2383.
4. Hernandez-Ramirez RU, Shiels MS, Dubrow R, et al. 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.
5. Mani D, Aboulafia DM. Screening guidelines for non-AIDS defining cancers in HIV-infected individuals. *Curr Opin Oncol*. 2013;25(5):518–525.
6. Goedert JJ, Hosgood HD, Biggar RJ, et al. Screening for cancer in persons living with HIV infection. *Trends Cancer*. 2016;2(8):416–428.
7. Centers for Disease Control and Prevention. Understanding the HIV care continuum. https://www.cdc.gov/hiv/pdf/library/factsheets/cdc-hiv-care-continuum.pdf. Accessed January 28, 2018.
8. UNAIDS. Global AIDS update 2016. http://www.unaids.org/sites/default/files/media_asset/global-AIDS-update-2016_en.pdf. Accessed on January 28, 2018.
9. UNAIDS. Access to antiretroviral therapy in Africa. Status report on progress towards the 2015 targets. http://www.unaids.org/sites/default/files/media_asset/20131219_AccessARTAfricaStatusReportProgresstowards2015Targets_en_0.pdf. Accessed January 28, 2018.
10. Reniers G, Slaymaker E, Nakiyingi-Miiro J, et al. Mortality trends in the era of antiretroviral therapy: Evidence from the Network for Analysing Longitudinal Population based HIV/AIDS data on Africa (ALPHA). *AIDS*. 2014;28(Suppl 4):S533–S542.