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Deaths Due to Screenable Cancers Among People Living With HIV Infection, Florida, 2000–2014

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Abstract

Introduction—Because of antiretroviral therapy, people living with HIV infection are surviving longer and are at higher risk for chronic diseases. This study's objective was to assess the magnitude of deaths due to cancers for which there are screening recommendations for people living with HIV in Florida.

Methods—Florida Department of Health Enhanced HIV/AIDS Reporting System data were matched with Department of Health Vital Records and the National Death Index to identify deaths and their causes through 2014. The sex-specific and cause-specific mortality rates and indirect standardized mortality ratios (SMRs, using U.S. mortality rates as a standard) were calculated during 2016 for people reported with HIV infection 2000–2014.

Results—Despite the competing risk of HIV mortality, among the 25,678 females, there was a higher risk of cervical (SMR=6.32, 95% CI=4.63, 8.44), colorectal (SMR=2.05, 95% CI=1.44, 2.83), liver (SMR=8.96, 95% CI=5.39, 14.03), and lung (SMR=5.82, 95% CI=4.80, 6.96) cancer mortality and lower risk of breast cancer mortality (SMR=0.57, 95% CI=0.42, 0.76). Among 63,493 males, there was a higher risk of liver (SMR=5.50, 95% CI=4.47, 6.70) and lung (4.63, 95% CI=4.11, 5.19) cancer mortality. Among males, the lung cancer SMR significantly declined 2000–2014 ($p<0.05$), but was still high in 2012–2014 (SMR=3.59, 95% CI=2.87, 4.43).

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Conclusions—These results indicate the importance of primary and secondary cancer prevention during primary care for people living with HIV infection.

INTRODUCTION

Because of antiretroviral therapy, people living with HIV infection (PLHIV) can have near normal life expectancies.¹ Furthermore, as mortality due to HIV decreased, a higher proportion of mortality is due to non-HIV causes,^{2–4} heightening the need to effectively prevent and manage chronic disease.² Increased cancer incidence among PLHIV has been documented in several studies.^{5–8} Less has been reported about cancer mortality, but two studies found elevated mortality among people with AIDS (PWA) for some cancers including lung and liver.^{3,9} This study's objective is to assess the magnitude of mortality during 2000–2014 due to screenable cancers among PLHIV (with and without AIDS) in Florida, where 10.5% of PLHIV in the U.S. live.¹⁰

METHODS

Deaths and their causes through December 2014 were obtained by matching Florida Department of Health Enhanced HIV/AIDS Reporting System records with Florida Department of Health Vital Records and the National Death Index. The dataset included de-identified records of Florida residents reported in Enhanced HIV/AIDS Reporting System 2000–2014 with an HIV diagnosis meeting the Centers for Disease Control and Prevention case definition.^{11–13} Underlying causes were classified as follows with ICD-10¹⁴: HIV/AIDS (B20–B24), breast cancer (C50), cervical cancer (C53), colorectal cancer (C18–C20), liver cancer (C22), lung cancer (C33–C34), other cancers (all other C codes), external causes such as accidents and suicides (all S, T, V, W, X, and Y codes), and other medical conditions (all other codes). Cancers with established screening recommendations were chosen.^{15–16}

Statistical Analysis

Crude cause-specific mortality rates, stratified by sex, were calculated during 2016 for each year by dividing number of deaths due to a specific cause by number of person-years. Three- and 15-year averages were calculated. The indirect standardized mortality ratios (SMRs) were calculated using age-adjusted, cause-specific U.S. cancer mortality rates for each of the years 2000–2013 as the standard.¹⁷ Because of the unavailability of 2014 U.S. rates, the 2012 and 2013 average was used for 2014. U.S. rates were multiplied by the number of person-years in the cohort for each year to obtain the expected number of deaths. The observed number of deaths was divided by the expected number for each cancer cause stratified by sex. Linear trend was assessed by modeling the natural logarithm of individual yearly rates or ratios using ordinary least squares.¹⁸ Analyses were conducted using SAS, version 9.4, and Open Epi, version 3.01. The Florida International University IRB approved the study, and the Florida Department of Health IRB deemed it non-human subjects research.

RESULTS

Of 89,171 people diagnosed with HIV 2000–2014 in Florida, 28.8% were female. Among females, there were 5,121 deaths (59.5% HIV, 8.2% cancer, 27.6% other medical, and 4.7% external causes) (Table 1). Among males, there were 11,568 deaths (57.4% HIV, 9.1% cancer, 26.6% other medical, and 6.9% external causes). Total and crude mortality rates due to HIV infection and for other medical conditions declined over time for males and females ($p<0.05$), and rates due to other cancers and external causes declined for males ($p<0.05$).

Indirect SMRs indicated that for females, risk of breast cancer was lower in the cohort relative to the U.S. female population (Table 2). However, female SMRs for the 2000–2014 period were significantly elevated for cervical, colorectal, liver, and lung cancer. None had a significant linear trend.

For males, liver and lung SMRs were significantly elevated for the 2000–2014 period. However, there was a statistically significant decline in SMRs for lung cancer.

DISCUSSION

In this cohort, HIV mortality during 2000–2014 significantly declined. Females and males had elevated risk of mortality due to liver and lung cancer. Among females there was also an elevated risk of colorectal and cervical cancer.

Among males and females, there was a large SMR for lung cancer mortality. Although the SMR for lung cancer declined over time among males, the 2012–2014 lung cancer SMR remained considerable (3.59). The findings are consistent with studies that found elevated lung cancer mortality among PWA^{3,9} and PLHIV.¹⁹ Declining SMRs could be due to a temporal decline in smoking, better antiretroviral therapy coverage, earlier diagnosis, or better treatment in this population. Although no information is available about smoking prevalence among PLHIV in Florida, studies of other PLHIV populations have found high smoking prevalence even though many PLHIV smokers reported contemplating tobacco cessation.^{20–22} Results indicate that PLHIV providers should assess tobacco use, offer tobacco cessation options, and consider lung cancer screening, as recommended for the general population by the U.S. Preventive Services Task Force.¹⁵

A significantly elevated colorectal SMR for 2000–2014 was only seen among females consistent with a study of PWA.⁹ The U.S. Preventive Services Task Force recommends colorectal cancer screening for adults aged 50–75 years.¹⁵

The elevated risk of liver cancer mortality among PLHIV in this cohort is consistent with the excess risk reported among PWA.^{3,9} Among 113 liver cancer deaths observed, 26 (23.0%) had hepatitis C, and 1 (0.9%) had hepatitis B listed as a contributing cause. Most cases had no contributing causes; thus, viral hepatitis may have been responsible for a larger proportion of liver cancer deaths, although alcohol use, higher among PLHIV than the general population,²³ is likely also responsible.²⁴ The Infectious Diseases Society of America recommends hepatitis B and C screening for PLHIV.¹⁶

Females had lower risk of breast cancer mortality relative to the U.S. population. Lower breast cancer incidence was reported in two large studies of women with HIV/AIDS.^{25,26} Possible explanations are discussed elsewhere.²⁶ It would be important to assess breast cancer mortality in a multistate study.

Limitations

First, only cancer mortality could be examined; increased mortality can result from elevated incidence or late diagnosis, factors amenable to improved screening, as well as inadequate treatment or poor treatment response,^{27–29} problems requiring other interventions. Furthermore, there was no information about CD4 nadir or duration of uncontrolled viral suppression, which likely changed over time. Second, only underlying cause of death was examined. ICD-10 classifies deaths with both HIV and cervical (and several other cancers) causes as having an HIV (B20–24) underlying cause instead of the respective cancer code.³⁰ To assess how this could have affected observed cancer mortality, all deaths were reclassified with an HIV underlying cause and any contributing cancer cause as a cancer death. This led to an increase in all cancer SMRs. For breast cancer, the SMR increased from 0.57 (95% CI=0.42, 0.76) to 0.67 (95% CI=0.51, 0.87), but remained protective. Third, SMRs could not be calculated stratified by sex and race/ethnicity because of the small number of deaths. Race/ethnicity-stratified SMRs might have been slightly lower for some cancers (e.g., colorectal cancer because non-Hispanic blacks are overrepresented among PLHIV³¹ and at higher risk of colorectal cancer death³²). However, the race/ethnicity effects would be small relative to the large HIV SMRs. Finally, the general Florida population has a slightly lower risk for cancer mortality (170.0 deaths per 100,000 people) compared with the U.S. (178.7 deaths per 100,000 people).³² Therefore, SMRs would have been slightly greater had the Florida population been the comparison group.

CONCLUSIONS

Relative to the general population, PLHIV were at higher mortality risk due to screenable cancers with the exception of breast cancer. These results suggest that efforts should be enhanced to improve cancer screening and primary preventive measures, such as tobacco cessation efforts.

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Number of Deaths and Crude Mortality Rate Among People Diagnosed With HIV Infection

Cause of death (ICD-10)	Time period of death									
	2000–2002		2003–2005		2006–2008		2009–2011		2012–2014	
	Deaths, N	Average Mortality Rate ^a	Deaths, N	Average Mortality Rate ^a	Deaths, N	Average Mortality Rate ^a	Deaths, N	Average Mortality Rate ^a	Deaths, N	Average Mortality Rate ^a
Females										
HIV (B20–24)	370	3,230.0	640	2,173.8	807	1,908.2	649	1,242.3	583	988.5
Cancers (total)	29	253.2	63	214.0	92	217.5	103	197.2	132	223.8
Breast (C50)	2	17.5	7	23.8	11	26.0	12	23.0	14	23.7
Cervical (C53)	4	34.9	5	17.0	13	30.7	11	21.1	10	17.0
Colorectal (C18–C20)	1	8.7	5	17.0	6	14.2	9	17.2	13	22.0
Liver (C22)	1	8.7	1	3.4	1	2.4	8	15.3	6	10.2
Lung (C33–C34)	5	43.6	21	71.3	25	59.1	23	44.0	38	64.4
Other cancers ^b	16	139.7	24	81.5	36	85.2	40	76.5	51	86.5
Other medical ^c	146	1,274.5	237	805.0	309	730.7	345	660.4	374	634.1
External (All S, T, V, W, X, and Y codes)	17	148.4	46	156.2	50	118.2	61	116.8	68	115.3
Total	562	4,906.1	986	3,349.1	1,258	2,974.6	1,158	2,216.6	1,157	1,961.8
Males										
HIV (B20–24)	973	4,300.4	1,462	2,389.3	1,675	1,806.3	1,338	1,107.2	1,186	821.2
Cancers (total)	87	384.5	175	286.0	219	236.2	290	240.0	291	201.5
Colorectal (C18–C20)	2	8.8	11	18.0	11	11.9	20	16.6	20	13.8
Liver (C22)	2	8.8	15	24.5	23	24.8	32	26.5	24	16.6
Lung (C33–C34)	24	106.1	41	67.0	59	63.6	81	67.0	81	56.1
Other cancers ^b	59	260.8	108	176.5	126	135.8	157	129.9	166	114.9
Other medical ^c	341	1,507.1	535	874.3	692	746.3	736	609.1	776	537.3
External (All S, T, V, W, X, and Y codes)	63	278.4	120	196.1	199	214.6	199	164.7	211	146.1
Total	1,464	6,470.4	2,292	3,745.8	2,785	3,003.3	2,563	2,121.0	2,464	1,706.1

Notes: Boldface indicates statistical significance ($p < 0.05$) for linear trend between five time periods (2000–2002, 2003–2005, 2006–2008, 2009–2011, 2012–2014).

Other medical includes all non-external causes that were not any of the codes listed above.

Other cancers are all other C codes.

Number deaths per 100,000 person-years

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Table 2
Indirect Standardized Mortality Ratio (SMR) Among People Diagnosed With HIV Infection Relative to U.S. Population

Specific cancer mortality (ICD 10 codes)	Time period					
	2000–2002 SMR (95% CI) ^a	2003–2005 SMR (95% CI)	2006–2008 SMR (95% CI)	2009–2011 SMR (95% CI)	2012–2014 SMR (95% CI)	2000–2014 SMR (95% CI)
Females						
Breast (C50)	0.54 (0.09–1.79)	0.70 (0.31–1.39)	0.68 (0.36–1.19)	0.54 (0.29–0.92)	0.50 (0.28–0.81)	0.57 (0.42–0.76)
Cervical (C53)	9.19 (3.18–24.12)	4.78 (1.83–11.08)	8.49 (4.82–14.45)	6.07 (3.21–10.62)	5.05 (2.54–8.91)	6.32 (4.63–8.44)
Colorectal (C18–C20)	1.49 (0.07–7.05)	2.55 (0.92–5.54)	1.81 (0.74–3.78)	1.91 (0.93–3.51)	2.18 (1.21–3.61)	2.05 (1.44–2.83)
Liver (C22)	18.88 (0.50–98.64)	5.99 (0.25–24.66)	3.07 (0.17–16.44)	14.69 (7.43–30.38)	7.43 (3.04–15.60)	8.96 (5.39–14.03)
Lung (C33–C34)	6.49 (2.29–13.85)	9.37 (6.07–14.34)	6.56 (4.35–9.57)	4.26 (2.77–6.29)	5.40 (3.90–7.37)	5.82 (4.80–6.96)
Males						
Colorectal (C18–C20)	0.95 (0.16–3.15)	1.77 (0.93–3.08)	1.04 (0.55–1.80)	1.33 (0.83–2.01)	0.99 (0.62–1.50)	1.18 (0.92–1.50)
Liver (C22)	4.77 (0.84–16.52)	9.89 (5.81–16.12)	7.66 (4.98–11.32)	6.27 (4.37–8.75)	3.24 (2.13–4.75)	5.50 (4.47–6.70)
Lung (C33–C34)	9.16 (6.05–13.53)	5.59 (4.08–7.55)	4.83 (3.72–6.20)	4.74 (3.79–5.86)	3.59 (2.87–4.43)	4.63 (4.11–5.19)

Note: Boldface indicates statistical significance ($p < 0.05$) for linear trend between five time periods (2000–2002, 2003–2005, 2006–2008, 2009–2011, 2012–2014).

^a SMRs were calculated using the age-adjusted, cause-specific U.S. cancer mortality rates for the age groups <20, 20–49, 50–64, 65–74, >75 years for each of the years 2000–2013 as the standard.¹¹ Because the 2014 U.S. rates were not available, the 2012–2013 average for the U.S. standard population was used in the SMR calculations for 2012–2014.