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Lung Cancer Mortality Associated With Smoking and Smoking Cessation Among People Living With HIV in the United States

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Editor's Note

Supplemental content

IMPORTANCE Lung cancer has become a leading cause of death among people living with human immunodeficiency virus (HIV) (PLWH). Over 40% of PLWH in the United States smoke cigarettes; HIV independently increases the risk of lung cancer.

OBJECTIVE To project cumulative lung cancer mortality by smoking exposure among PLWH in care.

DESIGN Using a validated microsimulation model of HIV, we applied standard demographic data and recent HIV/AIDS epidemiology statistics with specific details on smoking exposure, combining smoking status (current, former, or never) and intensity (heavy, moderate, or light). We stratified reported mortality rates attributable to lung cancer and other non–AIDS-related causes by smoking exposure and accounted for an HIV-conferred independent risk of lung cancer. Lung cancer mortality risk ratios (vs never smokers) for male and female current moderate smokers were 23.6 and 24.2, respectively, and for those who quit smoking at age 40 years were 4.3 and 4.5. In sensitivity analyses, we accounted for nonadherence to antiretroviral therapy (ART) and for a range of HIV-conferred risks of death from lung cancer and from other non–AIDS-related diseases (eg, cardiovascular disease).

MAIN OUTCOMES AND MEASURES Cumulative lung cancer mortality by age 80 years (stratified by sex, age at entry to HIV care, and smoking exposure); total expected lung cancer deaths, accounting for nonadherence to ART.

RESULTS Among 40-year-old men with HIV, estimated cumulative lung cancer mortality for heavy, moderate, and light smokers who continued to smoke was 28.9%, 23.0%, and 18.8%, respectively; for those who quit smoking at age 40 years, it was 7.9%, 6.1%, and 4.3%; and for never smokers, it was 1.6%. Among women, the corresponding mortality for current smokers was 27.8%, 20.9%, and 16.6%; for former smokers, it was 7.5%, 5.2%, and 3.7%; and for never smokers, it was 1.2%. ART-adherent individuals who continued to smoke were 6 to 13 times more likely to die from lung cancer than from traditional AIDS-related causes, depending on sex and smoking intensity. Due to greater AIDS-related mortality risks, individuals with incomplete ART adherence had higher overall mortality but lower lung cancer mortality. Applying model projections to the approximately 644 200 PLWH aged 20 to 64 in care in the United States, 59 900 (9.3%) are expected to die from lung cancer if smoking habits do not change.

CONCLUSIONS AND RELEVANCE Those PLWH who adhere to ART but smoke are substantially more likely to die from lung cancer than from AIDS-related causes.

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Antiretroviral therapy (ART) has dramatically improved the life expectancy of people living with human immunodeficiency virus (HIV) (PLWH), with a concomitant shift in morbidity and mortality from AIDS to non-AIDS diseases.[1,2] Much of the non-AIDS disease burden is tobacco-related. Over 40% of PLWH in the United States smoke cigarettes, more than double the smoking prevalence in the general population.[3-7] Among PLWH undergoing ART, smoking now reduces life expectancy more than HIV itself.[8-10]

Tobacco use and HIV together may accelerate the development of lung cancer.[11-14] The risk of lung cancer is increased by the presence of HIV through mechanisms likely involving chronic inflammation, immunomodulation, and other infections.[11,15-19] Lung cancer is the leading cause of cancer death among PLWH undergoing ART and is among the leading causes of death overall in this population.[13,20]

Despite the high smoking prevalence and the risk of lung cancer and other tobacco-related diseases, smoking cessation programs generally have not been successfully implemented in HIV care. As the population of PLWH in the United States ages, estimates of projected comorbidities can help guide where to direct attention and resources in HIV care. We sought to understand the likely impact of smoking cessation on lung cancer mortality among PLWH in HIV care in the United States. We compared the risk of lung cancer death against the risks of death from other causes as a function of smoking exposure.

Key Points

Question What is the risk of lung cancer death by smoking exposure for a person living with human immunodeficiency virus (HIV)?

Findings In this microsimulation model–based analysis, cumulative lung cancer mortality by age 80 years for men and women who entered HIV care in the United States at age 40 years and continued to smoke an average number of cigarettes daily was 23.0% and 20.9%, respectively; if they quit smoking, the respective risks decreased to 6.1% and 5.2%. Those who continued to smoke were 6 to 13 times more likely to die from lung cancer than from traditional AIDS-related causes.

Meaning Smoking cessation should be a priority in the care of people living with HIV.

Methods

Analytic Overview

We used the Cost-Effectiveness of Preventing AIDS Complications (CEPAC)-US model, a validated, widely published Monte Carlo microsimulation of HIV disease and treatment.[10,21-23] After populating the model with published data, we projected lung cancer mortality among PLWH in HIV care according to smoking exposure. We defined smoking exposure by both smoking status (current, former, or never) and, for current and former smokers, intensity (heavy, moderate, or light) based on number of cigarettes per day. We accounted for competing risks of death from AIDS-related and non-AIDS-related causes, the latter stratified by smoking exposure. We modeled cohorts of 1 million men or women of a particular smoking exposure entering HIV care at a specific age (eg, 30, 40, or 50 years).

The primary outcome was cumulative lung cancer mortality by age 80 years. We combined the model-generated estimates with published epidemiologic data to project the total expected lung cancer deaths among PLWH in care in the United States.

Model Overview

For this analysis, an individual enters the model at the time of linkage to HIV care and is followed until death or age 80 years, whichever comes first. The model draws randomly from user-defined initial distributions of CD4 count and HIV RNA and tracks clinical outcomes as an individual transitions monthly through states of disease progression and treatment. Probabilities of transition between HIV-related health states depend on factors including current CD4 count and HIV RNA. All individuals are ART eligible, regardless of CD4 count.[24] An individual may die from an AIDS-related cause (opportunistic infection or chronic AIDS-related disease), lung cancer, or another non-AIDS-related cause (eg, cardiovascular disease; eFigure 1 in the Supplement). Model details are available at http://www.massgeneral.org/mpec/cepac/.

Cohort Stratifications

We simulated cohorts stratified by sex, age at entry to HIV care, and smoking exposure (eg, current moderate smokers, former heavy smokers). We assumed no change in smoking status or intensity stratification over time. Former smokers are stratified by past smoking intensity. Within each cohort of former smokers, all individuals stop smoking at the same age (at entry to HIV care, except in sensitivity analysis, in which they quit later) and remain abstinent. We did not evaluate those who had quit smoking before entering HIV care.

Lung Cancer Mortality

We derived lung cancer mortality probabilities by sex, age, and smoking exposure. For current smokers, risks depend on smoking intensity. At the time of quitting smoking, risks decrease to those of former smokers and depend on age at cessation and prior smoking intensity.

Lung Cancer–Deleted, Non–AIDS-Related Mortality

We applied probabilities of non-AIDS-related death from all causes besides lung cancer (eg, other cancers, cardiovascular disease) by sex, age, and smoking exposure. Risks for current and former smokers are stratified in a similar manner to lung cancer risks. We additionally stratified former smokers' risks by years since cessation, in accordance with available data.[25]

Antiretroviral Therapy and HIV Care

In the pre-ART era, smoking was not an important driver of mortality among PLWH.[26] Untreated individuals were unlikely to survive long enough to develop lung cancer. Recognizing that smoking emerges as an important competing risk in the presence of virologic suppression, we assumed, in the base case, complete ART adherence and no loss to follow-up from HIV care. These in-care individuals are more likely to participate in a smoking cessation intervention. In sensitivity

Table 1. Input Parameters for Model Simulations of Smoking and Lung Cancer Among People Living With HIV in the United States

Parameter	Patient Characteristic Category				Source
HIV- and ART-related parameters	Base case				
CD4 count at entry to HIV care, cells/μL, mean (SD)	360 (280)				Althoff et al[32]
First-line ART suppression (dolutegravir/abacavir/lamivudine), <50 copies/mL at 48 wk, %	87				Walmsley et al[33] and Raffi et al[34]
Virologic failure for suppressed patients (dolutegravir/abacavir/lamivudine), % per month	0.1				Raffi et al[35]
Smoking and non-AIDS-related parameters	Men		Women		
Cigarettes per day at age 40 years, No.[a]					Rosenberg et al[25]
Heavy smokers	35		28		
Moderate smokers	18		14		
Light smokers	2		2		
Lung cancer mortality RR vs never smokers					Thun et al[36]
Current smokers					
Heavy smokers	32.4		36.1		
Moderate smokers	23.6		24.2		
Light smokers	15.8		16.7		
Former smokers (quit at age 40 years)					
Heavy smokers	5.8		6.8		
Moderate smokers	4.3		4.5		
Light smokers	2.9		3.1		
Lung cancer mortality RR, people with HIV vs HIV-uninfected people (independent of smoking)[b]	1.7		1.7		Sigel et al[11]
Lung cancer–deleted, non–AIDS-related mortality RR, people with HIV vs HIV-uninfected people (independent of smoking)[c]	1.0		1.0		Triant et al,[37] Freiberg et al,[38] and Althoff et al[39]
Monthly lung cancer–deleted, non–AIDS-related mortality probability in men only,[d] $\times 10^{-4}$	Age 40 y	Age 50 y	Age 60 y	Age 70 y	Rosenberg et al[25]
Current smokers					
Heavy smokers	6.1	8.6	17.1	40.1	
Moderate smokers	3.9	7.0	16.2	38.6	
Light smokers	3.0	5.4	11.2	26.7	
Former smokers (quit at age 40 years)					
Heavy smokers	6.1	5.6	9.0	20.3	
Moderate smokers	3.9	4.3	7.9	19.2	
Light smokers	3.0	3.5	7.1	18.6	
Never smokers	1.7	2.7	6.7	18.5	

Abbreviations: ART, antiretroviral therapy; HIV, human immunodeficiency virus; RR, risk ratio.

[a] The number of cigarettes per day changes with age, based on published data (Supplement).

[b] In sensitivity analysis, we varied the HIV-associated lung cancer mortality risk ratio from 1.0 to 1.9.[11]

[c] In sensitivity analysis, we varied the HIV-associated, lung cancer–deleted, non–AIDS-related mortality risk ratio from 1.0 to 1.7.[37-39]

[d] Assumes age at smoking initiation is 15 years. Mortality probabilities for women, based on published data, are slightly lower.[25]

analysis, we relaxed this assumption, accounting for reported rates of ART nonadherence and loss to follow-up (Supplement).[27] Additional specifications are described elsewhere.[23,27]

Model Validation

There are few published data on smoking-related mortality specific to PLWH. We therefore pursued 2 validation strategies. First, we compared our model-generated cumulative lung cancer mortality among HIV-uninfected people to results reported in general population studies in Western Europe.[28,29] Second, we compared our model-generated cumulative lung cancer mortality among PLWH (accounting for ART nonadherence and loss to follow-up) with the modeled cumulative lung cancer incidence reported by the North American AIDS Cohort Collaboration on Research and Design (NA-ACCORD) (Supplement).[30,31]

Input Parameters

Cohort Characteristics

We simulated PLWH reflecting those initiating HIV care in the United States[25,32-39] (**Table 1** and Supplement). In the base case, we assumed the same CD4 distribution regardless of cohort age at entry to care.

Cohort Stratifications by Smoking Exposure

Smoking intensity for current and former smokers was based on number of cigarettes per day as derived by Rosenberg et al,[25] who categorized US smokers into quintiles of cigarettes per day stratified by sex, age, and 5-year birth cohort, through the year 2000.[25] Among current and former smokers, we considered the fifth, third, and first quintiles to be heavy, moderate, and light smokers. For example, among 40-year-old men, heavy, moderate, and light smokers consumed 35, 18, and 2 cigarettes per day, respectively (Table 1). These quantities changed with age according to published data (Supplement).[25]

Lung Cancer Mortality

To derive monthly lung cancer mortality by smoking exposure, we combined US general population data on lung cancer mortality rates in 2000 (to match the latest year of the lung cancer–deleted life tables[25]), lung cancer mortality risk ratios for current and former smokers (further stratified by smoking intensity) vs never smokers, and the proportions of current, former, and never smokers in the population (Supplement).[25,36,40-42] Compared with never smokers, the lung cancer mortality risk ratio for male and female current moderate smokers was 23.6 and 24.2, respectively, and for those who quit at age 40 years, it was 4.3 and 4.5.

The derived smoking exposure-stratified lung cancer rates were not specific to PLWH. Therefore, in the base case, we accounted for an HIV-associated independent risk of lung cancer by multiplying the derived rates by 1.7. This was the multivariable-adjusted risk ratio (PLWH vs HIV-uninfected people) reported by the Veterans Aging Cohort Study,[11] the largest study of the association between HIV and lung cancer.

Lung Cancer–Deleted, Non–AIDS-Related Mortality

We applied lung cancer–deleted, non–AIDS-related mortality probabilities (eg, from other cancers and cardiovascular disease) based on published lung cancer–deleted life tables through 2000 (Supplement).[25] Mortality risks were stratified by sex, age, and smoking exposure. In the base case, we assumed no HIV-associated increase in these causes of death. We did not specify the cause of death within this group; estimates would have been inaccurate owing to the absence of many cause-deleted life tables.

Sensitivity Analysis

To understand the robustness of our findings under parameter uncertainty, we performed sensitivity analyses with alternative assumptions and parameter estimates. These included (1) accounting for reported rates of ART nonadherence and loss to follow-up from HIV care, which increase AIDS-related death risk; (2) varying the HIV-associated risk ratio for lung cancer from 1.0 to 1.9[11]; (3) varying initial CD4 count at entry to HIV care, which affects AIDS-related death risk; and (4) varying when former smokers quit: 10 or 20 years after entering HIV care, rather than at the time of entering care.

Our base case did not include a link between HIV and other non–AIDS-related causes of death (besides lung cancer). This reflected the inconsistency of reported smoking-adjusted, HIV-associated risks of death from these causes. However, we conducted an additional sensitivity analysis using a multiplicative risk factor of 1.7 to increase the independent effect of HIV on other non–AIDS-related mortality, including that from other cancers and cardiovascular disease. This value highlighted the reported HIV-conferred risk of myocardial infarction and matched the HIV-associated lung cancer risk ratio we applied in the base case.[37-39,43]

Population-Level Impact

We derived the number of current, former, and never smokers among PLWH aged 20 to 64 years in HIV care in the United States by sex and 5-year age increment (the overall prevalence of current, former, and never smokers among PLWH was approximately 42%, 20%, and 37%, respectively, in 2009).[3,31] Accounting for reported rates of ART nonadherence and loss to follow-up from care, we used model-generated cumulative lung cancer mortality for each sex, age, and smoking stratum to derive the expected total number of lung cancer deaths by age 80 years among PLWH in HIV care in the United States. To examine the potential impact of a smoking cessation intervention, we estimated the reduction in lung cancer deaths if 20% of current smokers in each sex and age cohort were to quit smoking (Supplement).

Results

Model Validation

For HIV-uninfected people, model-generated cumulative lung cancer mortalities by age 75 years for current heavy smokers were 24.5% and 19.5% for men and women, respectively; these values are similar to those reported in the United Kingdom, 24.4% and 18.5% (eTables 1 and 2 in the Supplement).[28] For 20-year-old PLWH in the United States, our model-generated cumulative lung cancer mortality by age 75 years was 5.0%, while the modeled cumulative lung cancer incidence reported by NA-ACCORD was 3.7% (Supplement).[30]

Base Case

Among men, cumulative lung cancer mortality by age 80 years for heavy, moderate, and light current smokers entering HIV care at age 40 years was 28.9%, 23.0%, and 18.8%, respectively; for heavy, moderate, and light former smokers who quit smoking at age 40 years, it was 7.9%, 6.1%, and 4.3%; and for never smokers, it was 1.6%. Among women, the corresponding respective cumulative lung cancer mortality for heavy, moderate, and light current smokers was 27.8%, 20.9%, and 16.6%; for heavy, moderate, and light former smokers who quit at age 40 years, it was 7.5%, 5.2%, and 3.7%; for never smokers, it was 1.2% (**Table 2** and **Figure 1**). Cumulative lung cancer mortality for ART-adherent current and never smokers varied little by age at entry to HIV care, with slightly higher results among those entering care at older ages owing to survival bias (Table 2).

Risk of Mortality From Lung Cancer vs Other Causes

Risks of mortality from lung cancer vs other causes varied by smoking exposure. For men who entered HIV care at age 40 years, adhered to the ART regimen, and continued to smoke at a moderate ("average") level, cumulative mortality from lung cancer was 10 times that from AIDS-related causes (23.0% vs 2.3%; **Figure 2**A). The mortality for former smokers in this

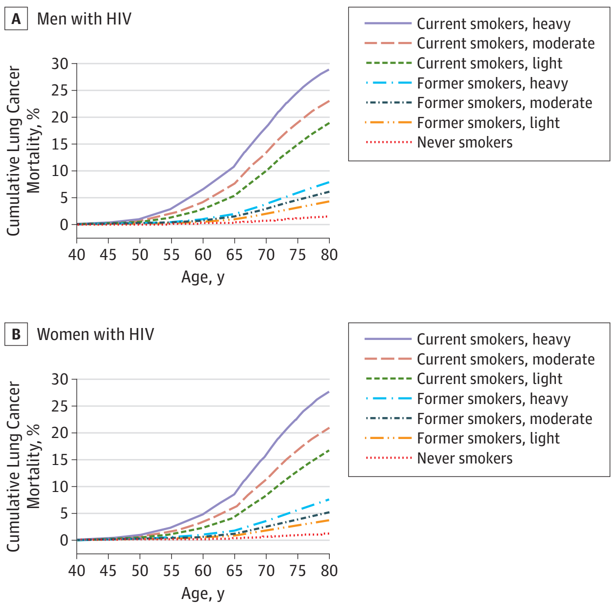
Table 2. Model-Generated Cumulative Lung Cancer Mortality by Age at Entry to HIV Care and Smoking Exposure[a]

	Cumulative Lung Cancer Mortality by Age 80 y, %					
	Enter at Age 30 y		Enter at Age 40 y (Base Case)		Enter at Age 50 y	
Smoking Exposure	Men	Women	Men	Women	Men	Women
Current smokers, heavy	28.2	27.1	28.9	27.8	30.9	28.3
Current smokers, moderate	22.4	20.3	23.0	20.9	24.0	21.0
Current smokers, light	18.4	16.2	18.8	16.6	19.4	16.8
Former smokers, heavy	4.2	2.9	7.9	7.5	13.5	11.6
Former smokers, moderate	3.2	2.0	6.1	5.2	10.6	8.2
Former smokers, light	2.1	1.4	4.3	3.7	7.7	6.0
Never smokers	1.5	1.2	1.6	1.2	1.6	1.2

Abbreviation: HIV, human immunodeficiency virus.

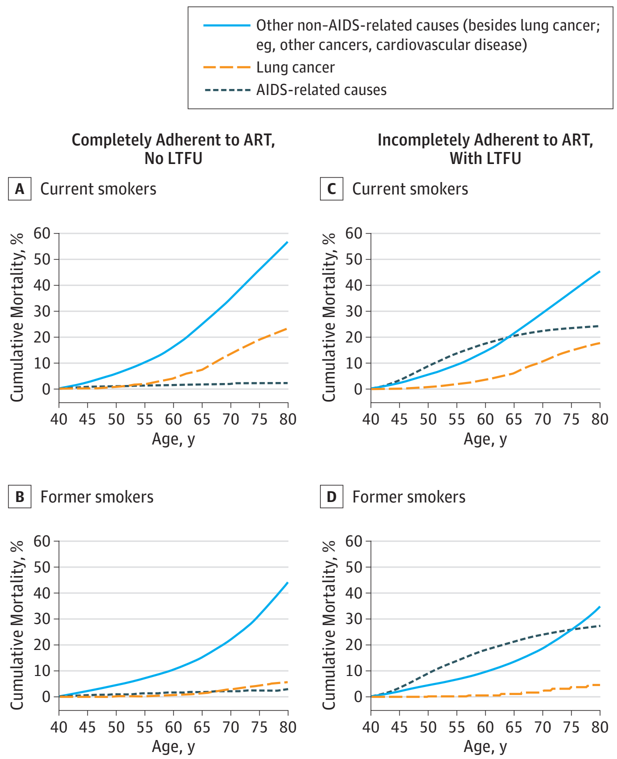
[a] Individuals in the simulation model were assumed to enter HIV care at the specified age and to remain in the model until death or age 80. These model simulations assumed complete adherence to antiretroviral therapy and no loss to follow-up from HIV care. Current smokers continued smoking until the end of follow-up. Former smokers quit at the time of entering HIV care (ie, at model entry).

Figure 1. Cumulative Lung Cancer Mortality for People Entering HIV Care at Age 40 Years by Smoking Exposure



Individuals in the simulation model were assumed to enter human immunodeficiency virus (HIV) care at age 40 years and to remain in the model until death or age 80 years. Current smokers continued smoking until the end of follow-up. Former smokers quit at age 40 years and remained abstinent. "Number at risk" tables are not needed here. The graphs represent model-generated outcomes, each line a simulated cohort of 1 million people entering HIV care at age 40 years. The number at risk are the number of people still alive at each time point, with no other form of censoring.

Figure 2. Cumulative Mortality by Cause Among Men Entering HIV Care at Age 40 Years



ART indicates antiretroviral therapy; LTFU, loss to follow-up. The intensity of smoking (number of cigarettes per day) was considered to be moderate ("average"). Current smokers continued smoking until the end of follow-up. Former smokers quit at age 40 years and remained abstinent. "Number at risk" tables are not needed here. The graphs represent model-generated outcomes, each line a simulated cohort of 1 million people entering HIV care at age 40 years. While some people are lost to follow-up from clinical care (in the sensitivity analyses that allow for loss to follow-up), the model still keeps track of them, recording when and how they die, so they are not lost from the model or from the results. The number at risk are the number of people still alive at each time point, with no other form of censoring.

category is illustrated in Figure 2B, and for never smokers, it is illustrated in eFigure 2A in the Supplement. For women who entered HIV care at age 40 years, adhered to the ART regimen, and continued to smoke at a moderate ("average") level, cumulative mortality from lung cancer was 8 times that from AIDS-related causes (20.9% vs 2.5%). Depending on sex and smoking intensity, ART-adherent smokers were 6 to 13 times more likely to die from lung cancer than from AIDS-related causes. For 40-year-old ART-adherent men who were current moderate smokers, the combined cumulative mortality from lung cancer and other non-AIDS-related causes—both of which were increased by smoking—was approximately 35 times that from AIDS-related causes (79.9% vs 2.3%); for women in this

Table 3. Effect of Varying the HIV-Associated Mortality Risk Ratios Among Current Smokers for Lung Cancer and for Other Non–AIDS-Related Causes[a]

HIV-Associated Mortality Risk Ratios	Cumulative Mortality by Age 80 y (Men/Women), %		
	Lung Cancer	Other Non–AIDS-Related Causes[b]	AIDS-Related Causes[c]
Lung cancer, 1.7; other non–AIDS-related causes, 1.0[d]	23.0/20.9	56.9/45.7	2.3/2.5
Lung cancer, 1.0; other non–AIDS-related causes, 1.0	14.6/13.0	61.3/48.6	2.4/2.5
Lung cancer, 1.0; other non–AIDS-related causes, 1.7	10.7/10.5	78.0/66.6	2.1/2.3
Lung cancer, 1.7; other non–AIDS-related causes, 1.7	16.9/16.8	73.3/63.1	2.1/2.3

Abbreviation: HIV, human immunodeficiency virus.

[a] The model-generated results are for people who entered HIV care at age 40 years and were followed up until death or age 80 years. These simulations assumed moderate ("average") intensity of smoking, based on number of cigarettes per day. Individuals continued smoking until the end of follow-up. The HIV-associated mortality risk ratios represent the independent risk conferred by HIV, compared with HIV-uninfected people, of mortality from either lung cancer or other non–AIDS-related causes. A mortality risk ratio of 1.0 indicates no increased risk for a person with HIV compared with an HIV-uninfected person of otherwise similar characteristics.

[b] Non–AIDS-related causes of death include cardiovascular disease and cancers besides lung cancer.

[c] AIDS-related causes of death include opportunistic infections and chronic AIDS-related conditions such as wasting.

[d] Base case.

category, it was approximately 27 times higher (66.6% vs 2.5%) (eTable 3 in the Supplement). See eTable 4 in the Supplement for results for different ages at entry to HIV care.

Sensitivity Analysis

For the sensitivity analyses described in the Methods section, we report instances where input data were most uncertain and/or where variation in the underlying parameter had a material impact on our findings. Results of other sensitivity analyses (including varying CD4 count at entry to HIV care and timing of smoking cessation) are reported in the Supplement.

Incomplete Adherence and Loss to Follow-up

When we accounted for reported rates of ART nonadherence and loss to follow-up from HIV care, cumulative lung cancer mortality among moderate smokers decreased, and cumulative AIDS-related mortality increased (Figure 2C and D). The results for never smokers are depicted in eFigure 2B in the Supplement. For men who were current heavy smokers, cumulative lung cancer mortality (22.7%) was similar to AIDS-related mortality (23.0%); for women, the corresponding results were 21.6% vs 25.5% (eTable 5 in the Supplement).

Varying HIV-Associated Risks of Lung Cancer and of Other Non–AIDS-Related Mortality

Model-generated cumulative mortality varied depending on the HIV-associated risk ratios applied for lung cancer and for other non-AIDS-related causes. For male and female current moderate smokers, cumulative lung cancer mortality varied from 10.5% to 23.0%, and cumulative other non-AIDS-related mortality varied from 45.7% to 78.0%. The lower numbers reflected scenarios assuming no direct influence of HIV on these causes of death (**Table 3**).

Population-Level Impact

Applying sex- and age-specific, model-projected results to the approximately 644 200 PLWH aged 20 to 64 years in care in the United States (including current, former, and never smokers), 59 900 lung cancer deaths by age 80 years are expected (9.3% of this population) if smoking status does not change. If 20% of the 273 200 current smokers quit, their lung cancer risk would decrease to that of former smokers, and 6900 (11.5%) lung cancer deaths could be averted.

Discussion

Using a microsimulation model, we found that ART-adherent PLWH in the United States who smoke cigarettes are 6 to 13 times more likely to die from lung cancer than from AIDS-related causes. Even when accounting for reported rates of ART nonadherence and loss to follow-up, we found that nearly 10% of PLWH initially linked to HIV care (including both smokers and nonsmokers) are expected to die from lung cancer if smoking habits do not change. Smoking cessation could substantially reduce lung cancer risk for an individual and avert many lung cancer deaths at the population level.

People with HIV whose virus is suppressed now have a life expectancy approaching that of HIV-uninfected people.[44] However, life expectancy gaps persist, and smoking is a key driver of this difference.[45] This smoking footprint will likely grow as PLWH age and develop lung cancer and other smoking-associated diseases. Lung cancer was already the leading cause of death in a study of PLWH in France in 2010; the smoking prevalence among PLWH is similar in France and the United States.[3,20,46]

In stratifying mortality risks by smoking status and intensity, our results can inform important conversations between clinicians and PLWH who smoke, helping both clinician and patient understand the patient's risks of different diseases and the potential benefits of smoking cessation. Recognizing the increased risk of death from lung cancer vs that from traditionally feared AIDS-related causes may motivate a smoker to quit smoking,[47] although this is not always the case. Our analyses also accounted for the smoking-conferred increase in risk of death from causes besides lung cancer and AIDS—this includes other cancers, other lung diseases, and cardiovascular disease. Our results provide evidence for HIV care programs and policymakers to include smoking cessation interventions as a key component of the comprehensive care of PLWH. Though smoking cessation is challenging, smoking prevalence among the US general population has decreased substantially in recent decades, from 42% in 1965 to 15% in 2015.[7,48] While the current smoking prevalence among PLWH is much higher than that among HIV-uninfected people, a similar proportion of smokers in the 2 groups want to quit, offering hope for a potential decrease in smoking prevalence in PLWH as well.[49]

Perhaps counterintuitively, lung cancer risk is linked to adherence to HIV therapy. Those who are not ART-adherent are more likely to die of AIDS-related causes before developing lung cancer. Nonetheless, even when accounting for reported rates of ART nonadherence and loss to follow-up from HIV care, we found that for male heavy smokers, the risk of dying from lung cancer is similar to the risk of dying from AIDS-related causes.

Limitations

Our results are subject to limitations inherent in the assumptions and simplifications of any model-based study. These include the following: (1) using data from the US general population in 2000 in the absence of smoking-stratified lung cancer data for PLWH; (2) uncertainty around the HIV-conferred risk of lung cancer, which could be lower or higher than what we applied in this analysis, and could vary by age[11,13-17,50]; (3) assuming no relationship between CD4 count and lung cancer risk, given conflicting reports affected by confounders such as smoking intensity[15,19,51-54]; (4) assuming that the HIV-associated increase in lung cancer mortality is similar to the increase in incidence, since median survival after lung cancer diagnosis is short[11,40]; (5) not accounting for disparities between PLWH and HIV-uninfected people in mortality after lung cancer diagnosis[17,55-58]; (6) not examining race: African American men are overrepresented among PLWH in the United States and may be more susceptible to lung cancer than people of other races[31,59]; (7) not differentiating by HIV transmission risk category: the national survey data for smoking prevalence among PLWH indicated little difference by sexual transmission risk category, but there were few injection drug users[3]; (8) not accounting for possibly higher average daily cigarette consumption among PLWH who smoke compared with HIV-uninfected people who smoke[11]; (9) assuming, in the base case, that smoking status does not change over time; and (10) not examining a potential impact on mortality from lung cancer screening with computed tomography.[60,61] Estimating smoking-attributable mortality for various diseases would be informative, but the data for non-AIDS, non-lung cancer outcomes were too limited to do so. The smoking-conferred risk of death from smoking-related diseases may be even greater than that applied in our analyses, especially in PLWH.[43] Though the model-generated estimates may be influenced by input parameter uncertainty, the magnitude of smoking-related harm with respect to lung cancer and other non-AIDS-related mortality, and the magnitude of the benefit from smoking cessation, remain robust, as shown in our sensitivity analysis.

Conclusions

In conclusion, there is a large expected burden of lung cancer among PLWH in the United States because (1) the smoking prevalence is very high in this population; (2) HIV itself increases the risk of lung cancer; and (3) PLWH are increasingly living long enough to develop lung cancer. For PLWH who adhere to ART, smoking is a much greater threat to their health than HIV itself. Clinicians caring for PLWH should offer guideline-based behavioral and pharmacologic treatments for tobacco use.[62] Lung cancer is now a leading cause of death among PLWH, but smoking cessation can greatly reduce the risk. Lung cancer prevention, especially through smoking cessation, should be a priority in the comprehensive care of PLWH.

ARTICLE INFORMATION

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