Low Rates of Lung Cancer Screening Referrals in Patients With Human Immunodeficiency Virus: A Correlational Study

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Abstract
People living with HIV (PLWH) have an increased risk of lung cancer compared to the general population. In 2013, the United States Preventive Services Task Force (USPSTF) released their lung cancer screening (LCS) guidelines. However, the impact of these guidelines has not been well established in PLWH. The objective of this retrospective descriptive study is to evaluate the frequency of lung cancer screening referrals and factors associated with LCS referrals using the 2013 USPSTF screening guidelines in at-risk PLWH. We collected demographic and clinical information on PLWH from electronic medical records from July 2016 to July 2018. Descriptive statistics, chi-square tests, t-tests, Wilcoxon rank sum tests, and Fisher’s exact tests were used for analysis. Only 14% of patients who met 2013 USPSTF screening guidelines were referred for screening. Patients who received a referral were more likely to have received tobacco cessation counseling. Patients who received and completed a referral were more likely to have hepatitis C infection. Quality improvement strategies are needed to improve rates of LCS in PLWH.

Keywords
lung cancer, cancer screening, Human Immunodeficiency Virus, people living with human immunodeficiency virus (PLWH), U.S. Preventive Services Task Force

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Introduction
The introduction of combination antiretroviral therapy (cART) has led to a decrease in morbidity and mortality from Human Immunodeficiency Virus (HIV). In the United States, treatment with cART in people living with HIV (PLWH) has led to a near-normal life expectancy.1 As PLWH live longer, there has been an increased incidence of chronic and age-related diseases, such as malignancy and specifically non-AIDS defining cancers (NADCs) as compared to the pre-antiretroviral era.2 The risk for NADCs among PLWH varies from an increase of 2- to 5-fold for melanoma, lung cancer, and hepatocellular carcinoma and up to 10- to 30-fold for Hodgkin’s lymphoma and anal cancer relative to the general population. Additionally, other prevalent risk factors in PLWH may contribute to the increased risk for specific cancers, such as smoking, alcohol consumption, human papillomavirus (HPV) infection, and hepatitis C (HCV) infection.3

Lung cancer is a common NADC diagnosis that occurs at younger ages, progresses rapidly, is diagnosed mostly in later stages, and has increased mortality in PLWH.4 While the main risk factor is likely increased tobacco use, HIV infection itself may be an independent risk factor for the development of lung cancer.5 HIV infection can also lead to immune system dysfunction and a state of chronic inflammation.6 In addition,
a decreased immunological defense system may lead to re-
curring infections, such as bacterial pneumonia, which can
further contribute to chronic inflammation. Both of these
immunological and infectious factors are associated with the
development of lung cancer in PLWH. As lung cancer be-
comes prevalent in PLWH, it is imperative that providers focus
on diagnostic strategies to decrease the overall morbidity and
mortality.

Smoking cessation is an essential intervention in the
prevention of lung cancer and is required by Medicare for all
current smokers, including PLWH. Smoking is highly prev-
alent among PLWH with 50–70% reporting smoking ciga-
rettes daily compared to 17.8% of the United States general
adult population. Many PLWH have contemplated smoking
cessation (60–70%) or have tried to stop at least once (50–
75%). Smoking cessation could lead to a 34% decreased risk
of development of NADCs, including lung cancer. The
European AIDS Clinical Society (EACS) has recently es-
stablished smoking cessation guidelines specifically for
PLWH.

In addition to smoking cessation, lung cancer screening
(LCS) is an important tool in assessing at-risk PLWH. The
U.S. Preventive Services Task Force (USPSTF) released LCS
recommendations in 2013 which have been recently updated
in March 2021. Their 2013 recommendations called for an
annual screening for lung cancer with low-dose computed
tomography in patients 55 to 80 years of age who have a 30
pack-year smoking history and who currently smoke or have
quit within the past 15 years. The updated recommendations
for 2021 include expanding both the age range (50 to 80 years
of age) and pack-year history (20 pack-years). Given that
PLWH are at an increased risk for lung cancer, it is vital to
identify methods for implementation of LCS as part of primary
HIV care. HIV clinics provide comprehensive care to PLWH
including screening for hepatitis, tuberculosis, sexually
transmitted diseases, and cancer including cervical cancer.
For federally funded clinics, these services are usually tracked
and reported to the HIV and AIDS Bureau as part of annual
measures. However, there is a paucity of data on the current
state of LCS in PLWH in the United States. We therefore
conducted a retrospective study to determine the frequency of
and factors associated with LCS using the 2013 USPSTF
guidelines in at-risk PLWH.

Materials and Methods

We conducted a retrospective chart review study of PLWH
who were identified as potential candidates for LCS between
July 1, 2016, and July 1, 2018. Initial screening included
patients aged 55–80 with a confirmed diagnosis of HIV, who
were actively receiving care at a Midwestern HIV clinic as-
associated with an academic hospital, to establish continuity of
care at the clinic. Exclusion criteria consisted of those who had
never smoked, were deceased, had an unknown smoking
pack-year history, and/or a prior lung cancer diagnosis.
Universal sampling included all patients during this period
who met inclusion/exclusion criteria were included.

We then divided the patients into 2 groups: those who met
the 2013 USPSTF Lung Cancer Screening guidelines of
being 1) an adult aged 55–80, 2) had a 30-pack-year smoking
history, currently smoking or quit within the past 15 years,
and 3) were in good health and can have curative lung
surgery and those who did not meet the 2013 USPSTF LCS
guidelines (Figure 1). Both groups were included for addi-
tional analysis.

Information obtained from the electronic medical record
included the following: demographic information such as age,
sex, race/ethnicity, HIV risk factor, and federal poverty level
(FPL); clinical information including comorbid diabetes,
hypertension, cardiovascular disease, current or history of
hepatitis B and/or C, liver disease, and kidney disease was
obtained based on corresponding ICD-10 codes; substance use
information including tobacco use, history, and quit date,
whether they had received tobacco cessation counseling, al-
cohol use, and illicit drug use; and HIV-related information
such as date of HIV diagnosis and laboratory information
including most recent HIV viral load and CD4 T-cell count. In
addition to automatic prompts to screen for and record
smoking status in the electronic medical records system,
medical providers in our clinic conduct tobacco cessation
counseling during each medical visit. Patients who express an
interest in quitting are referred to the clinical pharmacist for
continued counseling, follow-up, and pharmacological man-
gement. All patient information obtained was de-identified.
We collected information on LCS referrals including the
provider who ordered the screening and the status of com-
pletion of screening during the aforementioned time period.
The American College of Radiology Lung-Reporting and
Data System (Lung-RADS) recommendations were used for
assessment and management after completion of initial LCS in
those who met 2013 USPSTF LCS guidelines. The study
was approved by the institutional review board.

Subjects were divided into groups for comparison based on
whether they received a screening referral. A screening re-

ferral is made after a shared-decision visit between the patient
and provider to proceed with a low-dose CT for further
evaluation. Those who were given a screening referral were
further divided by whether they completed the screening.
Groups were initially compared on age, sex, sexual orienta-
tion, race, poverty level, insurance status, alcohol and other
substance use, smoking history, comorbidities, CD4 T-cell
count, HIV viral load, duration of HIV, and frequency of
healthcare visits using descriptive statistics. Differences be-
tween those who were given a referral or not were evaluated
using Wilcoxon rank-sum tests and either chi-square tests or
Fisher’s exact tests, as appropriate. Differences between those
who did and did not complete screening after receiving a
referral were compared using either Fisher’s exact tests or
Wilcoxon rank-sum tests. All analyses were completed using
STATA version 16.1 (StataCorp, College Station, TX).
Results

Of 347 patients included based on initial screening criteria, 91 patients were excluded because of having never smoked (8), were deceased (38), had an unknown smoking pack-year history (39), and/or a prior lung cancer diagnosis (6). Of the remaining 256 patients, the mean (SD) for age was 61(5) with an age range of 55–78. There were 104 patients (41%) who met the 2013 USPSTF lung cancer screening recommendations while the other 152 patients did not. Regardless of whether patients met USPTSF criteria, 22/256 (9%) of patients had a screening/referral order with 12/22 (55%) being completed. Patients who completed low-dose computed tomography (LDCT) 12/256 (4.7%) were considered as having completed LCS. In patients who did not meet USPTSF criteria, 8/152 (5%) had a screening/referral ordered with 2/8 (25%) being completed. In patients meeting USPTSF criteria, 14/104 (14%) had a screening/referral ordered with 10/14 (71%) being completed. Of those 10 that were completed, 2 (20%) were classified as “Negative,” while the other 8 (80%) were “Other” and consisted of 2 “Category Lung-RADS 1,” 5 “Category Lung-RADS 2,” and 1 “Category Lung-RADS 3.” An infectious disease provider ordered 12 (55%) screenings while a non-infectious disease provider ordered 10 (45%).

Table 1 compares patient demographic and clinical information by whether a patient received an LCS referral. The proportions having a history of tobacco cessation counseling during screening (95% for those with a referral vs 73% for those without, Fisher’s exact test $P = .019$), having a comorbid current or history of Hepatitis C infection (45% for those with a referral vs 16% for those without, $X^2(1, N = 256) = 11.3, P = .001$), and the number of visits in 2017 to 2018 (mean of 12.0 for those with a referral vs mean of 9.0 for those without, $Z = −2.24, P = .025$) were the only statistically significant differences noted between the groups. Table 2 compares patient demographic and clinical information by whether the referred patients completed LCS. Rates of comorbid current or past history of Hepatitis C infection were significantly higher among those who completed referral (67% vs 20%, Fisher’s exact test $P = .043$).

Discussion

Our study evaluated the factors associated with referral and completion of LCS in PLWH in a Midwestern HIV clinic. Our main finding was a low rate of LCS referral and completion in PLWH. In addition, tobacco cessation counseling was associated with increased rates of LCS referral. Interestingly, hepatitis C infection was associated with both increased rates of LCS referral and completion. Identification of factors associated with LCS is important as it can aid in development of strategies to improve LCS in PLWH.

In this retrospective study, we evaluated PLWH who received LCS referral and those who completed referral. Two groups were established: patients who met and those who did not meet the 2013 USPSTF guidelines. Lung cancer screening referrals and completion were low in both groups with slightly higher referral rate in those who met the 2013 USPSTF guidelines. Lung cancer screening rates in PLWH are not well characterized compared to the general population. The National Lung Cancer Screening trial evaluated LCS for detection of malignancy and mortality reduction in the general population. This data was later used for development of the 2013 USPSTF guidelines. However, after implementation there have been limited data on the rates of LCS. In 2016, an analysis of the Lung Cancer Screening Registry was conducted to determine the rates of screening in the general US population who met the 2013 USPSTF recommendations. The rates for LCS were 2.0% in the general population and 2.1% in the Midwest. Compared to the general population in the Midwest, our clinic population had an increased rate of LCS (2% vs 10%) in PLWH who met the 2013 USPSTF LCS guidelines. Engagement in healthcare among PLWH is greater than the general population. However, the rates among both groups are low and highlight the need for an emphasis in

![Flow Chart of Lung Cancer Screening Criteria.](figure1.png)
preventative care in general and specialty care medicine. Nevertheless, adherence to LCS recommendations in PLWH remains low and warrants further investigation to identify barriers to screening referral and completion.

Lung cancer screening and tobacco cessation counseling are part of the lung cancer prevention and management paradigm. However, their utility and implementation are not well understood. Tobacco cessation counseling is addressed prior to LCS referral. The observed association between tobacco cessation counseling and referral for LCS suggests that these strategies are being utilized for LCS prevention (Table 1). A study by Cao et al suggested that there are more health benefits from intervention methods, such as cessation counseling, compared to screening alone.18 Conversely,
tobacco cessation counseling was not associated with completion of LCS. This is likely multifactorial including lack of patient adherence or provider follow-up during the screening process. However, these factors were not assessed in our study. Currently, the National Cancer Institute-Lung Population-based Research to Optimize the Screening Process Initiative is evaluating the use of cessation programs during LCS. A study utilized an opt-out strategy during LCS where patients were able to see their provider and a tobacco treatment counselor during their visit, which led to increased referrals for LDCT and increased patient satisfaction with counseling services. Ultimately, other barriers exist that prevent effective implementation of tobacco cessation during LCS, such as patient motivation and provider reimbursement, that future studies can provide further input into.

Table 2. Demographic and Clinical Characteristics of Patients Referred and Completed Lung Cancer Screening.

|                          | Total N (%) | Missing | Completed Mean (SD) or n (%) | Not Complete Mean (SD) or n (%) | P-value |
|--------------------------|-------------|---------|------------------------------|----------------------------------|---------|
| Age, years               | 22          | 0       | 60.5 (3.8)                   | 61.1 (3.3)                       | .618    |
| Sex/Gender               |             |         |                              |                                  |         |
| Male                     | 18 (82)     | 0       | 10 (83)                      | 8 (80)                           | 1.000   |
| Female                   | 4 (18)      |         | 2 (17)                       | 2 (20)                           |         |
| Transgender, male to female | 0 (0)      |         | 0 (0)                        | 0 (0)                            |         |
| Heterosexual             | 9 (45)      | 2       | 4 (36)                       | 5 (56)                           | .653    |
| MSM (males only)         | 11 (69)     | 2       | 7 (78)                       | 4 (57)                           | .596    |
| Race/Ethnicity           |             |         |                              |                                  |         |
| Non-Hispanic White       | 11 (50)     | 0       | 5 (42)                       | 6 (60)                           | .691    |
| Non-Hispanic Black       | 9 (41)      |         | 6 (50)                       | 3 (30)                           |         |
| Other                    | 2 (9)       |         | 1 (8)                        | 1 (10)                           |         |
| Poverty level            |             |         |                              |                                  |         |
| Less than 100% of FPL    | 10 (48)     | 1       | 6 (55)                       | 4 (40)                           | .850    |
| 100–200% of FPL          | 8 (38)      |         | 4 (36)                       | 4 (40)                           |         |
| Over 200% FPL            | 3 (14)      |         | 1 (9)                        | 2 (20)                           |         |
| Insurance                |             |         |                              |                                  |         |
| Private                  | 11 (50)     | 0       | 4 (33)                       | 7 (70)                           | .198    |
| Medicare/Medicaid/VA     | 11 (50)     |         | 8 (67)                       | 3 (30)                           |         |
| RW/Pending/None          | 0 (0)       |         | 0 (0)                        | 0 (0)                            |         |
| Alcohol use              | 13 (59)     | 0       | 7 (58)                       | 6 (60)                           | 1.000   |
| Illegal drug use         | 10 (48)     | 1       | 3 (27)                       | 7 (70)                           | .086    |
| Tobacco cessation counseling | 21 (95) | 0       | 11 (92)                      | 10 (100)                         | 1.000   |
| HIV disease duration, yearsa | 21 (95) | 1       | 20.8 (7.5)                   | 16.4 (8.8)                       | .121b   |
| Care interval, years     | 21 (95)     | 1       | 4.6 (8.9)                    | 2.7 (3.2)                        | 1.000b  |
| Diabetes                 | 6 (27)      | 0       | 5 (42)                       | 1 (10)                           | .162    |
| Hypertension             | 13 (59)     | 0       | 8 (67)                       | 5 (50)                           | .666    |
| Cardiovascular disease   | 4 (18)      | 0       | 2 (17)                       | 2 (20)                           | 1.000   |
| Liver disease            | 1 (5)       | 0       | 0 (0)                        | 1 (10)                           | .455    |
| Hepatitis B              | 1 (5)       | 0       | 0 (0)                        | 1 (10)                           | .455    |
| Hepatitis C              | 10 (45)     | 0       | 8 (67)                       | 2 (20)                           | .043    |
| Kidney disease           | 2 (9)       | 0       | 1 (8)                        | 1 (10)                           | 1.000   |
| CD4 T-cell count         |             |         |                              |                                  |         |
| 0–200                    | 1 (5)       | 0       | 0 (0)                        | 1 (10)                           | .481    |
| 201–350                  | 1 (5)       |         | 1 (8)                        | 0 (0)                            | .000    |
| 351–500                  | 2 (9)       |         | 2 (17)                       | 0 (0)                            |         |
| 501+                     | 18 (82)     |         | 9 (75)                       | 9 (90)                           |         |
| HIV viral load >200      | 1 (5)       | 0       | 1 (8)                        | 0 (0)                            | 1.000   |
| # Of HIV primary visits  | 22 (100)    | 0       | 2.9 (1.3)                    | 3.4 (0.8)                        | .425b   |
| Number of visits 2017–2018 (Any) | 22 (100) | 0       | 13.1 (9.7)                   | 10.8 (9.0)                       | .337b   |

All tests are Fisher’s exact tests except as noted. Abbreviations: MSM; men who have sex with men, FPL; federal poverty level, VA; Tricare/Veterans Administration, RW; Ryan White Part C—a federal grant that is awarded to HIV clinic.

a of July 1, 2018.
b Wilcoxon rank-sum test.
Patient demographic and clinical information were evaluated to identify specific factors that are associated with LCS referral and completion. Hepatitis C infection was significantly associated with referral and completion for LCS. Approximately a third of PLWH in the US have HIV/HCV co-infection. This population has an increased morbidity and mortality when compared to HIV or HCV mono-infections. In addition, tobacco use in patients with HIV/HCV co-infection was significantly higher at 48% compared to the national rate of 14%. Providers interacting with this population may focus on medical management of HIV/HCV co-infection to reduce morbidity and mortality. Specifically, during treatment for HCV, patients are more likely to interact with the medical system. The duration of treatment for HCV is approximately 12–24 weeks and thus leads to additional opportunities for healthcare maintenance management and follow-up, including LCS. Overall, the association of HCV with LCS in our study may be multifactorial and requires further evaluation.

Important limitations of our study design are the relatively small sample size within a 2-year time period and retrospective collection of data from the electronic health record. Statistical analysis of a small sample size does not allow for multivariable analysis. It would be important to study robust HIV clinics and evaluate LCS rates and referral, including significant variables that may influence these two. In addition, this is a single center study and certain variables may be noted compared to other centers which does not allow for generalization of these results. Collection of data from the electronic health record may have limited our ability for effective assessment and evaluation. For example, data entry of tobacco use and history is self-reported and is entered by various healthcare professionals and can limit data quality and accuracy. Free text fields can lead to incorrectly recorded data about smoking pack-years or years since quitting in evaluation for LCS. Therefore, LCS rates may be adversely affected due to under- or over-reported rates of pack-year history. In addition, we were not able to determine the status of hepatitis C whether it was a current or historic infection. Our study was conducted at a single academic medical center in the Midwest, and the results may not be generalizable to all PLWH. Lastly, we did not evaluate the patient’s beliefs and attitudes toward LCS and tobacco cessation counseling. Prior research has shown that patient-related barriers often impact adherence with LCS. Patients are less likely to participate in screening due to the associated financial burdens of screening, lack of education about lung cancer, concerns about radiation exposure from CT imaging, and if they are an active smoker. In future studies, these limitations should be considered and evaluated to improve our understanding of LCS in PLWH.

As a result of this study, opportunities arise for quality improvement initiatives and continued research within our patient population for improved LCS. Integration of tobacco cessation counseling for prevention of and management during LCS can aid in reducing mortality in PLWH. Future studies should include assessment of patient’s attitudes and beliefs toward LCS and tobacco cessation counseling to determine which personal factors may be associated with LCS.

In conclusion, the rates of LCS in PLWH are inadequate and create an opportunity for quality improvement programs in HIV clinics. Currently, the 2021 USPSTF guidelines for LCS have expanded the inclusion criteria of patients recommended for screening. However, the guidelines used for the general population may not be sufficient for certain populations, such as PLWH who have increased risk for malignancy due to underlying disease factors. This discrepancy highlights the need for continued research in PLWH to determine if specific LCS guidelines may be needed in the future. Subsequently, providers must be aware of maintaining adherence to the current USPSTF guidelines to provide adequate and optimal care to at-risk PLWH. Overall, improving rates of LCS in PLWH is imperative as it is considered a standard of care for healthcare maintenance.

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Ethics Statement
Ethical approval to report this case was obtained from University of Nebraska Medical Center IRB (# 019-19-EP). All procedures in this study were conducted in accordance with the University of Nebraska Medical Center (# 019-19-EP) approved protocols. Informed consent for patient information to be published in this article was not obtained as the study was eligible for a waiver for informed consent due the only record linking the subject and the research would be the informed consent form and the principal risk would be potential harm resulting from a breach of confidentiality.

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