

Factors related to non-adherence to lung cancer screening across multiple screening time points

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Key Points

Question

What factors and longitudinal patterns are associated with patient non-adherence to lung cancer screening across multiple screening time points?

Findings

In this cohort study, Lung-RADS score at baseline was most associated with of patient non-adherence to the recommended follow-up. Non-adherence increased over time for patients who received consecutive Lung-RADS 1 or 2 screens.

Meaning

Our approach suggests that patients with consecutive negative screens (Lung-RADS 1 or 2) are more likely to become non-adherent and may benefit from outreach and education.

Abstract

Importance

Screening with low-dose computed tomography has been shown to reduce mortality from lung cancer but in clinical trials, the adherence rate to follow-up recommendations was over 90%. Adherence to Lung-RADS recommendations, however, has been low in practice. Identifying patients who are at risk of being non-adherent to screening recommendations can enable personalized outreach to improve overall screening adherence.

Objective

To identify factors associated with patient non-adherence to Lung-RADS recommendations across multiple screening time points.

Design

This is an observational cohort study.

Setting

This study was conducted at a single academic medical center across ten geographically distributed sites where lung cancer screening is offered.

Participants

This study enrolled 2496 individuals who underwent low-dose computed tomography screening for lung cancer at our institution between July 31, 2013 and Nov 30, 2021.

Exposures

Multivariable logistic regression was used to identify significant risk factors of patient non-adherence to baseline Lung-RADS recommendations. A generalized estimating equations model was used to assess whether the pattern of longitudinal Lung-RADS score was associated with patient non-adherence over time.

Main Outcome(s) and Measure(s)

Non-adherence was defined as failing to complete a recommended or more invasive follow-up examination (i.e., diagnostic dose chest computed tomography [CT], positron emission tomography-CT, tissue sampling as opposed to low dose CT) within 15 months (Lung-RADS 1 or 2), 9 months (Lung-RADS 3), 5 months (Lung-RADS 4A), and 3 months (Lung-RADS 4B/X).

Results

Among 1979 eligible patients, 56.1% were ≥ 65 years at baseline screen, 59.4% were male, and 77.1% were White. We identified six patient-related variables associated with non-adherence to baseline Lung-RADS recommendations. The Lung-RADS score was the most influential factor. Among eligible patients who had completed at least two screening examinations (n=830), the adjusted odds of being non-adherent to the Lung-RADS recommendations at the following screening increased in patients with consecutive Lung-RADS 1-2 screens (adjusted odds ratio: 1.38, 95% confidence interval: 1.12, 1.69).

Conclusions and Relevance

In this retrospective cohort study, patients with consecutive negative screens were more likely to be non-adherent. These individuals are potential candidates for tailored outreach to improve adherence to recommended annual lung cancer screening.

Introduction

Screening with low-dose computed tomography (LDCT) effectively reduces mortality from lung cancer by at least 20% in large randomized clinical trials where adherence rates were over 90%¹.² The Lung CT Screening Reporting & Data System (Lung-RADS), released in 2014, has become a nationally-accepted standard for lung cancer screening (LCS) CT reporting and management recommendations³. The follow-up recommendations are to continue annual LDCT screening in patients with Lung-RADS scores 1-2; in patients with Lung-RADS score 3-4, early or more aggressive follow-up is advised, which may entail an LDCT in 6 months, an LDCT in 3 months, a chest CT, a positron emission tomography-CT (PET-CT), or tissue sampling⁴. Notably, patient adherence in clinical practices is substantially lower than the over 90% adherence rates in clinical trials. Our systematic review and meta-analysis found that patient adherence to baseline Lung-RADS recommendations was 57-65% in clinical LCS programs, with a significantly lower annual adherence rate among patients with Lung-RADS 1-2 (45-49%) as opposed to early follow-up adherence among Lung-RADS 3-4 (74-78%)⁵. Similarly, a recent study reported adherence to recommendations from baseline and first annual screen were 48% and 44%, respectively, among patients with Lung-RADS 1-2 scores in a large national cohort (N=30,166)⁶. Failing to maintain annual adherence to LCS recommendations may diminish the ability of clinical screening programs to achieve the same mortality benefits found in large clinical trials. Patients with interval lung cancers, diagnosed between screening episodes following a preceding negative screen (Lung-RADS 1-2), are more likely to be aggressive, emphasizing the importance of regular screening intervals⁷.

LCS is nascent as a preventive measure in the United States; as such, barriers to LCS have been incompletely investigated. Patient-level barriers include unawareness of screening benefits and risks, perceptual barriers such as fear of cancer diagnosis and perceived stigma, screening-related cost concerns, and challenges in accessing imaging sites⁸. Identifying factors that affect patient adherence to Lung-RADS recommendations can help clinicians better understand who would benefit from outreach strategies to improve adherence⁹. These factors may be used to identify patients that are at risk for non-adherence. Given that patient characteristics in clinical LCS programs vary across institutions, clinical risk stratification models that aid in the identification of potentially non-adherent patients could result in more aggressive, tailored approaches and thus improve the mortality benefit of screening. To our knowledge, no studies have investigated risk factors of patient non-adherence to Lung-RADS recommendations over multiple screening intervals. Specifically, Lung-RADS scores may vary over time. Previous work has shown that Lung-RADS score was a significant risk factor of non-adherence to baseline Lung-RADS recommendations⁵, however, evidence on whether longitudinal patterns of Lung-RADS scores affect the risk of non-adherence to screening in the future is lacking.

This study aims to identify risk factors of patients at risk for non-adherence to Lung-RADS recommendations at baseline and across multiple time points. In Experiment 1, we investigate whether patient demographics, socioeconomic status, and health status are risk factors of non-adherence to baseline Lung-RADS recommendations. Experiment 2 adjusts for significant risk factors from Experiment 1 to evaluate the hypothesis that adherence increases/decreases as Lung-RADS score upgrades/downgrades and adherence is stable when Lung-RADS scores remain unchanged.

Methods

Patient enrollment

Institutional review board (IRB) approval was obtained at University of California, Los Angeles to conduct this retrospective study, and informed consent was waived (IRB#19-000627). We included 2860 patients who underwent at least one LDCT screening examination at our institution from July 31, 2013 to Nov 30, 2021 (last follow-up date: Dec 8, 2021), with ten geographically distributed sites where LCS is offered. Lung-RADS scores were retrospectively assigned to LDCT screens performed prior to the release date of Lung-RADS version 1.0¹⁰ by a board-certified thoracic radiologist (DRA). Patient exclusion criteria are summarized in **Figure 1**. Annual screens or early follow-up LDCT screens were excluded if patients were greater than 80 years old at the time of screen (n=69), the screen was a Lung-RADS 0 (n=8), or the screen was incorrectly ordered for non-screening purposes (n=25). Additional details are reported in **eAppendix 1** in the supplement, such as identification of screen-eligible patients and intervention for adherence. This study followed the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) reporting guideline for cohort studies.

Data collection

Patient characteristics at the time of their baseline screen were obtained by medical abstraction from our institution's electronic health record, including an existing registry of patients who undergo LCS. Baseline factors of interest included Lung-RADS score, age, sex, race/ethnicity, education level, family history of lung cancer, smoking status, primary insurance status, age-adjusted Charlson Comorbidity Index (CCI)¹¹, distance to screening center, median family

income, area deprivation index (ADI) state rank¹², and type of referring physician. Race and ethnicity data were obtained from a self-reported questionnaire administered prior to the LDCT screening examination that was stored as a discrete series of the screening exam in our picture archiving and communication system. When such data were missing from the questionnaire, data in the electronic medical record were extracted. The ‘Other’ race/ethnicity category included American Indian or Alaska Native, Native Hawaiian or Pacific Islander, more than one race, or other racial and ethnic groups not otherwise stated. Age-adjusted CCI was grouped into three categories: low (0-1), intermediate (2-3), and high (≥ 4)¹¹. Median family income was mapped with the 2010 Census data using the home zip code. Distance to screening center was estimated between the home zip code and the zip code of the screening center. We dichotomized the following variables: ADI state rank, median family income, and distance to screening center: low/short ($\leq$ median) and high/long ($>$ median). Elective imaging examinations, such as LDCT screening examinations, were suspended at the beginning of the COVID-19 pandemic (i.e., from Mar 19, 2020 to May 19, 2020) at our institution to conserve healthcare resources and minimize the risk of viral transmission. To account for the potential impact of this pause in elective imaging examinations on patient adherence, we included one variable indicating whether the date of the expected follow-up examination fell within the two-month pause period or not.

Patient outcome

The patient outcome of the study was non-adherence, defined as failing to comply with follow-up recommendations based on Lung-RADS category, factoring in some time allowance from the recommended period. Adherence was defined for Lung-RADS 1-2 as completing the next annual screen within 12 months + 3 months; for Lung-RADS 3, completing a recommended repeat

LDCT within 6 months + 3 months; for Lung-RADS 4A, completing an LDCT within 3 months + 2 months; and for Lung-RADS 4B/X, completing more aggressive diagnostic workup (i.e., diagnostic CT chest, PET-CT, or tissue sampling) within 3 months of the abnormal screen (see **eFigure 1** in the Supplement). Patients were considered adherent if they completed a more invasive (i.e., diagnostic CT chest, PET-CT, or tissue sampling as opposed to LDCT) follow-up examination within the defined time intervals.

Statistical analyses

In Experiment 1, we used a multivariable logistic regression model to identify significant risk factors of non-adherence to baseline Lung-RADS recommendations. Patients who had missing values in some characteristics were excluded from the analysis. A comparison of the observed baseline characteristics between included and excluded patients is shown in **eTable 1** in the Supplement. No significant differences were found for any variables except the family history of lung cancer. A sensitivity analysis was implemented using multiple imputation (i.e., the ‘mice’¹³ package in R) data and found similar results.

In Experiment 2, we examined whether baseline Lung-RADS score and a pattern of subsequent Lung-RADS scores were associated with non-adherence to Lung-RADS recommendations over time. Patients who underwent at least two screening examinations were included in this analysis. The Lung-RADS score was binary (1-2 vs. 3-4). A Lung-RADS 1 or 2 screen was defined as a negative screen and a Lung-RADS 3 or 4 screen was defined as a positive screen. Patients were categorized into subgroups based on their longitudinal patterns of Lung-RADS scores (see **eTable 2** in the Supplement): unchanged, upgraded (negative to positive), and downgraded

(positive to negative). Patients whose Lung-RADS scores were first upgraded and then downgraded or vice versa were excluded (n=25). These patients may have more complex changes in health status (e.g., first upgraded then downgraded: health status got worse then became better) than those with monotonic or no changes in Lung-RADS scores (e.g., downgraded: health status became better). A generalized estimating equations (GEE) model with a logit link and an unstructured working correlation accounted for repeated measurements within the same patient was used. The fixed effects included in this model were baseline Lung-RADS score (1-2 vs. 3-4), longitudinal patterns of Lung-RADS scores (changed vs. unchanged), screening time point (T0, T1, T2), three two-way interaction terms, one three-way interaction term among the three variables, and significant baseline risk factors from Experiment 1 (i.e., z test, two-sided p-value<0.05). Less than 10% of patients who had missing values of some risk factors were excluded from this analysis. No significant differences in the observed variables were found between the included and excluded patients.

Python version 3.7.3 and R version 3.6.1¹⁴ were used for data analyses.

Results

Among the 2496 eligible patients, 1979 had no missing values in all baseline characteristics (**Figure 1**). The majority had a negative baseline screen (83.9%), were ≥ 65 years of age (56.1%), male (59.4%), White (77.1%), and former smokers (61.1%). Patient characteristics at the baseline screen are summarized in **Table 1**. The mean follow-up time was 1.78 years (range: 0.25 to 3.75, see **eTable 4** in the Supplement for details). Eighty-one patients (3.2%) were diagnosed with primary lung cancers during follow-up.

Lung-RADS score at baseline was most associated with non-adherence to baseline Lung-RADS recommendations

Among the 1979 patients, the rates of non-adherence to baseline Lung-RADS recommendations were 70.5% (1170/1660), 46.1% (71/154), 32.3% (32/99), and 19.7% (13/66) for Lung-RADS 1-2, 3, 4A, and 4B/X, respectively. The odds of being non-adherent among patients with a positive baseline Lung-RADS score decreased compared with those with a negative baseline score (referent: 1-2, 3: adjusted odds ratio [aOR]: 0.35, 95% confidence interval [CI] 0.25, 0.50, 4A: aOR: 0.21, 95% CI: 0.13, 0.33, and 4B/X: aOR: 0.10, 95% CI: 0.05, 0.19) (see **Table 2**). Lower odds of non-adherence were also observed among patients with a postgraduate degree (referent: college graduate, aOR:0.70, 95% CI 0.53, 0.92), with family history of lung cancer (referent: no, aOR: 0.74, 95% CI 0.59, 0.93), in the high age-adjusted CCI category (referent: low, aOR:0.67, 95% CI 0.46, 0.98), in the high-income category (referent: low, aOR: 0.79, 95% CI: 0.65, 0.98), and referred by physicians from pulmonary or thoracic-related departments (i.e., Thoracic Oncology/Radiology/Surgery) (referent: other department, aOR: 0.56, 95% CI 0.44, 0.73). These significant baseline risk factors were used as inputs into multiple machine learning classifiers that predict patient non-adherence with the top performing model achieving a sensitivity of 0.94 in sensitivity, specificity of 0.71, and accuracy of 0.72 on the hold-out test data (see **eAppendix 2** in the Supplement).

Patients with consecutive negative screens were more likely to be non-adherent at the follow-up screening

Nine hundred and fifteen patients had two or three adherence statuses and monotonic changes in Lung-RADS scores over time, 91% (n=830) of them had no missing values in all significant baseline risk factors from Experiment 1 (see **Figure 1**). Most patients (79.2%) were in the unchanged category (631 negative, 26 positive); 11.3% and 9.5% were in the downgraded and upgraded categories, respectively. Patient baseline characteristics stratified by patterns of subsequent Lung-RADS scores are shown in **Table 3**. Fewer patients were ≥ 65 years of age in the negative screen-unchanged group compared to the other three groups combined (54% vs. 66%, $p=0.002$) and were referred by pulmonary medicine or thoracic-related subspecialists (16% vs. 24%, $p=0.011$).

For patients with a negative screen at baseline, results from the GEE model suggested that the odds of being non-adherent to the Lung-RADS recommendations at the second screening increased in the unchanged-negative category (aOR: 1.38, 95% CI: 1.12, 1.69) but decreased in the upgraded category (aOR: 0.29, 95% CI: 0.14, 0.60) (see **Table 4**). For those with a positive baseline screen, the odds of being non-adherent at the following negative screening increased (aOR: 5.08, 95% CI: 1.28, 20.1). There was no significant change in adherence in the unchanged-positive category at the second screen. In addition, no significant difference in adherence at the third screen was found across four subgroups.

Discussion

As the volume of patients participating in clinical LCS practices increases, the challenge of addressing low adherence to Lung-RADS recommendations is magnified, as observed among patients with negative screens in this study. Identifying risk factors of non-adherence may help

resource-constrained health systems to direct targeted outreach to patients who are at a higher risk of non-adherence and thus likely to receive the greatest benefit from targeted interventions. Appointment reminders and/or LCS educational materials sent to patients by mail or via patient health portals in the electronic medical record as well as reinforcement of LCS-related benefits by the screening program are possible interventions to mitigate non-adherence.

Our findings that Lung-RADS scores and type of referring physician were associated with patient non-adherence to baseline Lung-RADS recommendations aligned with previous studies¹⁵⁻¹⁷. The baseline Lung-RADS score was the most important variable when estimating whether a patient would be adherent in returning for their initial follow-up screening exam. Patients with a negative baseline screen are at high risk for non-adherence. A study by Wildstein et al.¹⁸ found that higher education level (e.g., individuals with at least a college degree) was associated with annual adherence to LCS, though the study was conducted prior to the release date of the Lung-RADS recommendations. Our study found that a positive family history of lung cancer ($p<0.01$), comorbidity (high vs. low score $p=0.04$), and lower income ($p=0.03$) were statistically significant risk factors of non-adherence at the first follow-up, a finding that has not been previously reported in LCS literature. These risk factors have been previously studied in colorectal and breast cancer screening^{19, 20, 21}, but with sometimes conflicting results, as in the case of medical comorbidity^{19, 20}. As such, further investigation on the clinical significance of these risk factors is necessary.

The major contribution of this study lies in the identification of changes in Lung-RADS scores as the driving risk factor of non-adherence to LCS across multiple screening time points. Our

analysis provides insights into which groups of patients may be more likely to be non-adherent in subsequent screening exams. For example, if patients have had consecutive negative screens, their adherence diminishes over time. Individuals in this group tend to be younger in age at baseline and referred by physicians from non-pulmonary or thoracic-related departments. These observations help to inform which patients are at highest risk of non-adherence to annual screening, which can delay the diagnosis of lung cancer^{7, 22}. Of note, cancers first observed on incidence screens tend to be faster growing and more aggressive in behavior than those identified at prevalence screens⁷, increasing the importance of adherence to follow-up recommendations. The GEE model also suggests that patients with a positive baseline screen followed by a negative screen may also need assistance in maintaining adherence at the first annual screen (i.e., non-adherence increased over time). However, further investigation is needed, given the wide confidence interval. Our findings regarding changes in adherence as patients undergo subsequent screens underscore the need for screening programs to provide ongoing patient education and reminders, and facilitate adherence by providing screening locations near the patient, and to minimize patient inconvenience through timely scheduling and efficient patient through-put.

Limitations

This study has some limitations. Several potential risk factors were not considered in our investigation due to a lack of data. Carter-Harris et al.²³ proposed additional important precursors to LCS behaviors, including patient psychological, cognitive, social and environmental factors as well as healthcare provider recommendations. These variables were previously shown to be associated with behaviors in the lung or other types of cancer screening²⁴⁻³¹. Unlike immutable factors such as race/ethnicity, psychological and cognitive factors can change over time,

providing opportunities for an outreach interventions. Other potential risk factors are social determinants of health variables^{32, 33}. Moreover, it was not possible to track patients who had permanently moved, but continued LCS at outside institutions. The risk factors we assessed were limited to data elements that were captured routinely in the medical records. Future work is needed to evaluate other life circumstances (e.g., personal such as health (e.g., had other medical issues, LCS was not a priority) and later emergence, family, social/economic), professional activities (e.g., workload), and social environmental factors (e.g., childcare and family responsibilities) that might affect adherence.

The lack of primary care physician involvement may be another major determinant of patients' adherence behaviors in LCS. Primary care physicians may be less familiar with LCS, its relative risks and benefits, and eligibility requirements for reimbursement as compared to other cancer screening examinations. Although annual review of preventive health measures is inherent to primary care, LCS is nascent in practice and there are myriad reasons why primary care referrals may be associated with less adherence. Relative to other preventive measures, LCS requires a greater time commitment for shared decision making, smoking cessation counseling, and formal documentation. Our study only examined a high-level variable to distinguish primary care and subspecialty referrals, which cannot capture nuances of physician awareness or practice constraints.

In the future, the findings of this study can be incorporated into a temporal model that helps evaluate adherence status at each screening time point, adding time-varying variables into the temporal model to achieve better performance by considering the changes in patients' health statuses at each screen (e.g., age-adjusted CCI, smoking status, and insurance status). Finally, the use of specific types of outreach intervention (e.g., reminders, consultations, educational

materials) to improve adherence will vary based on the underlying reason why an individual may be non-adherent. While reminders and educational outreach have been helpful in other screening contexts^{34, 35}, a greater understanding of the psychological, cognitive, social and healthcare provider factors that influence screening adherence may be essential to optimize outreach interventions. Further studies that explicitly examine these factors are needed.

Conclusions

We identify risk factors in patients at risk of non-adherence to Lung-RADS recommendations across three screening time points. We show that the Lung-RADS score at baseline was the most important risk factor of non-adherence in the initial follow-up screen. Patients with consecutive negative screens were at the greatest risk of being non-adherent in a subsequent screen. Our study provides evidence that can be used as the basis of a decision support tool to estimate non-adherent patients across multiple time points and inform future outreach interventions designed to improve patient adherence to LCS.

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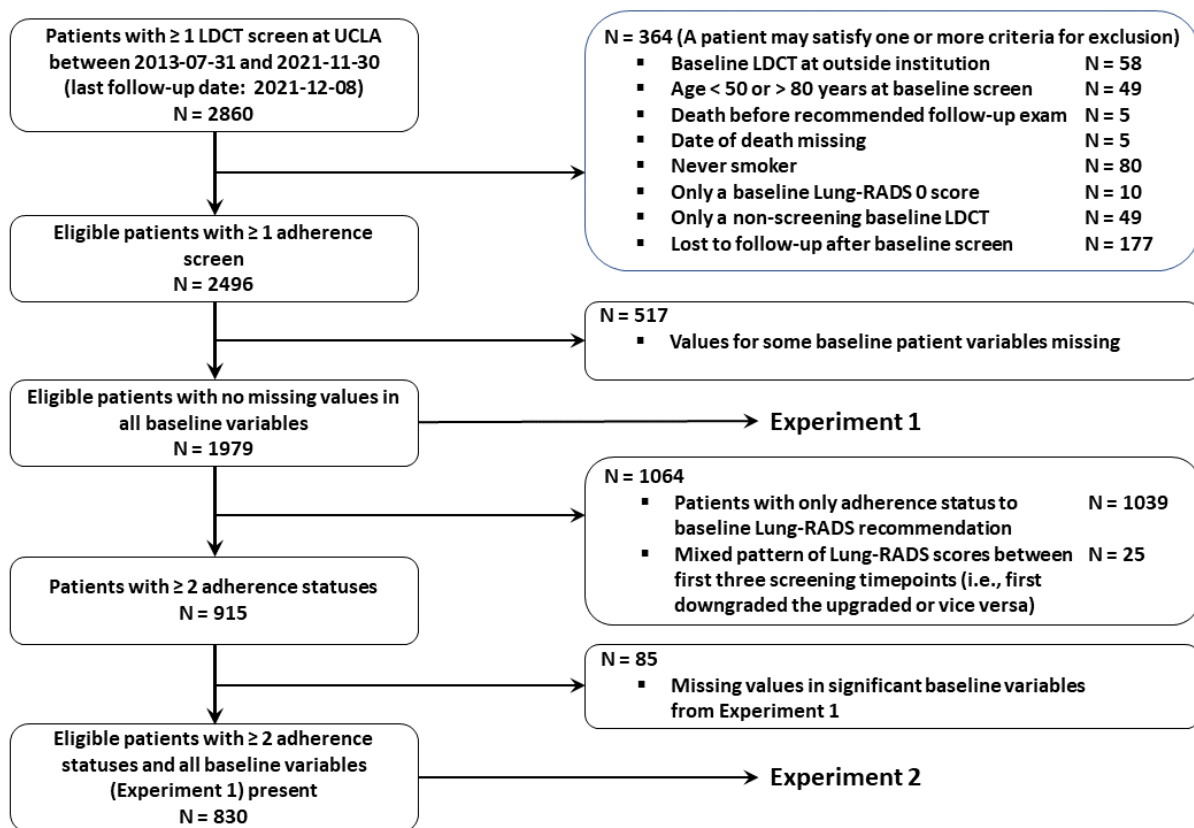


Figure 1. The flow diagram of patient enrollment. LDCT: low-dose computed tomography; Lung-RADS: Lung CT Screening Reporting & Data System.

Table 1. Baseline patient characteristics (Experiment 1).

Variable	Individual, No. (%)		
	Overall (N=1979)	Adherent (n=693)	Non-adherent (n=1286)
Lung-RADS			
1-2	1660 (83.9)	490 (70.7)	1170 (91.0)
3	154 (7.8)	83 (12.0)	71 (5.5)
4A	99 (5.0)	67 (9.7)	32 (2.5)
4B/X	66 (3.3)	53 (7.6)	13 (1.0)
Age in years			
<65	868 (43.9)	268 (38.7)	600 (46.7)
≥65	1111 (56.1)	425 (61.3)	686 (53.3)
Sex			
Female	803 (40.6)	276 (39.8)	527 (41.0)
Male	1176 (59.4)	417 (60.2)	759 (59.0)
Race/ethnicity			
Asian	169 (8.5)	59 (8.5)	110 (8.6)
Black	130 (6.6)	49 (7.1)	81 (6.3)
Hispanic/Latino	111 (5.6)	35 (5.1)	76 (5.9)
White	1526 (77.1)	540 (77.9)	986 (76.7)
Other ^a	43 (2.2)	10 (1.4)	33 (2.6)
Education level			
Less than college	958 (48.4)	337 (48.6)	621 (48.3)
College Graduate	590 (29.8)	186 (26.8)	404 (31.4)
Postgraduate	431 (21.8)	170 (24.5)	261 (20.3)
Family history of lung cancer			
Yes	466 (23.5)	187 (27.0)	279 (21.7)
No	1513 (76.5)	506 (73.0)	1007 (78.3)
Smoking status			
Current	769 (38.9)	246 (35.5)	523 (40.7)
Former	1210 (61.1)	447 (64.5)	763 (59.3)
Primary insurance			
Medicare/Medicaid	830 (41.9)	328 (47.3)	502 (39.0)
Private or Commercial	1121 (56.6)	358 (51.7)	763 (59.3)
Other ^b	28 (1.4)	7 (1.0)	21 (1.6)
Age adjusted CCI			
Low (0-1)	287 (14.5)	72 (10.4)	215 (16.7)
Intermediate (2-3)	1152 (58.2)	403 (58.2)	749 (58.2)
High (≥4)	540 (27.3)	218 (31.5)	322 (25.0)

Table 1. Baseline patient characteristics (Experiment 1) (Continued).

Variable	Individual, No. (%)		
	Overall (N=1979)	Adherent (n=693)	Non-adherent (n=1286)
Distance to screening center ^c			
Short ($\leq$ median)	994 (50.2)	346 (49.9)	648 (50.4)
Long ($>$ median)	985 (49.8)	347 (50.1)	638 (49.6)
Median household income ^c			
Low ($\leq$ median)	1029 (52.0)	340 (49.1)	689 (53.6)
High ($>$ median)	950 (48.0)	353 (50.9)	597 (46.4)
ADI state rank ^c			
Low ($\leq$ median)	1072 (54.2)	387 (55.8)	685 (53.3)
High ($>$ median)	907 (45.8)	306 (44.2)	601 (46.7)
Type of referring physician			
Pulmonology, Oncology/Radiology/Surgery	Thoracic 369 (18.6)	176 (25.4)	193 (15.0)
Other ^d	1610 (81.4)	517 (74.6)	1093 (85.0)
Expected follow-up exam			
Pre-COVID	1468 (74.2)	513 (74.0)	955 (74.3)
During COVID pause	53 (2.7)	11 (1.6)	42 (3.3)
Post-COVID pause	458 (23.1)	169 (24.4)	289 (22.5)

Notes: ^a Subcategories in other race: American Indian or Alaska Native, Native Hawaiian or Pacific Islander, more than one race, or other racial and ethnic groups not otherwise stated.

^b Subcategories in other insurance: Veterans Administration (N=1), self-pay (N=27), and other insurance not specified (N=1).

^c Median distance to screening center: 6.84 miles.; median household income: \$73,478; median ADI state rank: 3.

^d Subcategories in other referring physician types: family medicine, general internal medicine, and obstetrics and gynecology.

Abbreviations: Lung-RADS: Lung CT Screening Reporting & Data System; CCI: Charlson Comorbidity Index; ADI: Area Deprivation Index.

Table 2. Multivariable logistic regression analysis on patient non-adherence to baseline Lung-RADS recommendations (Experiment 1, N=1979).

Variable	aOR (95% CI)	p-value
Intercept	9.13 (4.12, 21.65)	
Lung-RADS (Referent: 1-2)		
3	0.35 (0.25, 0.50)	<0.001
4A	0.21 (0.13, 0.33)	<0.001
4B/X	0.10 (0.05, 0.19)	<0.001
Age in years (Referent: <65)		
≥65	1.00 (0.78, 1.28)	0.98
Sex (Referent: Female)		
Male	0.95 (0.77, 1.16)	0.60
Race/ethnicity (Referent: White)		
Asian	0.98 (0.69, 1.41)	0.90
Black	0.84 (0.56, 1.25)	0.37
Hispanic/Latino	1.10 (0.71, 1.73)	0.67
Other ^a	1.55 (0.77, 3.39)	0.24
Education (Referent: College graduate)		
Less than college	0.88 (0.69, 1.11)	0.28
Postgraduate	0.70 (0.53, 0.92)	0.01
Smoking status (Referent: Current smoker)		
Former smoker	0.84 (0.68, 1.03)	0.10
Family history of lung cancer (Referent: No)		
Yes	0.74 (0.59, 0.93)	0.010
Primary insurance (Referent: Medicare/Medicaid)		
Private or Commercial	1.11 (0.88, 1.38)	0.41
Other ^b	1.14 (0.60, 3.70)	0.46
Age-adjusted CCI (Referent: Low (0-1))		
Intermediate (2-3)	0.73 (0.52, 1.02)	0.07
High (≥4)	0.67 (0.46, 0.98)	0.042
Distance to screening center (Referent: Short ≤50 percentile)		
Long (>50 percentile)	1.01 (0.81, 1.25)	0.95
ADI state rank (Referent: Low ≤50 percentile)		
High (>50 percentile)	1.12 (0.90, 1.40)	0.30
Median annual income (Referent: Low ≤50 percentile)		
High (>50 percentile)	0.79 (0.65, 0.98)	0.030

Table 2. Multivariable logistic regression analysis on patient non-adherence to baseline Lung-RADS recommendations (Experiment 1, N=1979) (Continued).

Variable	aOR (95% CI)	p-value
Type of referring physician (Referent: Other ^c)		
Pulmonology, Thoracic Oncology/Radiology/Surgery	0.56 (0.44, 0.73)	<0.001
Expected follow-up exam (Referent: During COVID pause)		
Pre-COVID	0.56 (0.27, 1.08)	0.10
Post-COVID pause	0.52 (0.24, 1.02)	0.07

Notes: ^a Subcategories in other race: American Indian or Alaska Native, Native Hawaiian or Pacific Islander, more than one race, or other racial and ethnic groups not otherwise stated.

^b Subcategories in other insurance: Veterans Administration, self-pay, and other insurance not specified.

^c Subcategories in other referring physician types: family medicine, general internal medicine, and obstetrics and gynecology.

Abbreviations: Lung-RADS: Lung CT Screening Reporting & Data System; CCI: Charlson Comorbidity Index; ADI: Area Deprivation Index; aOR: adjusted odds ratio; CI: confidence interval.

Table 3. Patient characteristics at baseline, stratified by changes in Lung-RADS scores across three screening time points (Experiment 2, N=830).

Group	Negative Unchanged	Positive Unchanged	Lung-RADS Downgraded	Lung-RADS Upgraded
n (%)	631 (76.0)	26 (3.1)	94 (11.3)	79 (9.5)
Lung-RADS category ^b				
1-2	631 (100.0)	0 (0.0)	0 (0.0)	79 (100.0)
3-4	0 (0.0)	26 (100.0)	94 (100.0)	0 (0.0)
Age in years ^c				
<65	293 (46.4)	5 (19.2)	37 (39.4)	25 (31.6)
≥65	338 (53.6)	21 (80.8)	57 (60.6)	54 (68.4)
Sex (%)				
Female	250 (39.6)	10 (38.5)	33 (35.1)	36 (45.6)
Male	381 (60.4)	16 (61.5)	61 (64.9)	43 (54.4)
Race/ethnicity				
Asian	56 (8.9)	2 (7.7)	10 (10.6)	5 (6.3)
Black	46 (7.3)	2 (7.7)	5 (5.3)	5 (6.3)
Hispanic/Latino	27 (4.3)	1 (3.8)	6 (6.4)	5 (6.3)
White	472 (74.8)	20 (76.9)	69 (73.4)	61 (77.2)
Other ^d	16 (2.5)	0 (0.0)	2 (2.1)	2 (2.5)
Missing	14 (2.2)	1 (3.8)	2 (2.1)	1 (1.3)
Education ^b				
Less than college	281 (44.5)	17 (65.4)	42 (44.7)	43 (54.4)
College Graduate	196 (31.1)	5 (19.2)	34 (36.2)	19 (24.1)
Postgraduate	154 (24.4)	4 (15.4)	18 (19.1)	17 (21.5)
Smoking status (%)				
Current	253 (40.1)	7 (26.9)	42 (44.7)	37 (46.8)
Former	364 (57.7)	19 (73.1)	52 (55.3)	41 (51.9)
Missing	14 (2.2)	0 (0.0)	0 (0.0)	1 (1.3)
Family history of lung cancer ^b				
Yes	140 (22.2)	4 (15.4)	20 (21.3)	21 (26.6)
No	491 (77.8)	22 (84.6)	74 (78.7)	58 (73.4)

Table 3. Patient characteristics at baseline, stratified by changes in Lung-RADS scores across three screening time points (Experiment 2, N=830) (Continued).

Group	Negative Unchanged	Positive Unchanged	Lung-RADS Downgraded	Lung-RADS Upgraded
n (%)	631 (76.0)	26 (3.1)	94 (11.3)	79 (9.5)
Age-adjusted CCI ^b				
Low (0-1)	84 (13.3)	2 (7.7)	9 (9.6)	6 (7.6)
Intermediate (2-3)	407 (64.5)	16 (61.5)	58 (61.7)	48 (60.8)
High (≥4)	140 (22.2)	8 (30.8)	27 (28.7)	25 (31.6)
Primary insurance				
Medicare/Medicaid	272 (43.1)	18 (69.2)	47 (50.0)	30 (38.0)
Private or Commercial	348 (55.2)	8 (30.8)	45 (47.9)	47 (59.5)
Other ^c	9 (1.4)	0 (0.0)	2 (2.1)	2 (2.5)
Missing	2 (0.3)	0 (0.0)	0 (0.0)	0 (0.0)
Distance to screening center ^a				
Short (≤ median)	301 (47.7)	14 (53.8)	45 (47.9)	40 (50.6)
Long (> median)	325 (51.5)	12 (46.2)	48 (51.1)	39 (49.4)
Missing	5 (0.8)	0 (0.0)	1 (1.1)	0 (0.0)
Median household income ^{a, b}				
Low (≤ median)	309 (49.0)	15 (57.7)	52 (55.3)	44 (55.7)
High (> median)	322 (51.0)	11 (42.3)	42 (44.7)	35 (44.3)
ADI state rank (%) ^a				
Low (≤ median)	362 (57.4)	14 (53.8)	40 (42.6)	44 (55.7)
High (> median)	231 (36.6)	11 (42.3)	50 (53.2)	31 (39.2)
Missing	38 (6.0)	1 (3.8)	4 (4.3)	4 (5.1)
Type of referring physician ^{b, c}				
Pulmonology, Oncology/Radiology/Surgery	Thoracic 102 (16.2)	4 (15.4)	20 (21.3)	24 (30.4)
Other ^f	529 (83.8)	22 (84.6)	74 (78.7)	55 (69.6)
Expected follow-up exam				
Pre-COVID	595 (94.3)	25 (96.2)	89 (94.7)	69 (87.3)
During COVID pause	8 (1.3)	0 (0.0)	1 (1.1)	2 (2.5)
Post-COVID pause	28 (4.4)	1 (3.8)	4 (4.3)	8 (10.1)

Notes: ^a Median distance to screening center: 5.48 miles; median household income: \$74,011; median ADI state rank: 3

^b Variables adjusted for in Experiment 2 (i.e., significant baseline factors from Experiment 1).

^c p value <0.05 from the Chi-square test.

^d Subcategories in other race: American Indian or Alaska Native, Native Hawaiian or Pacific Islander, more than one race, or other racial and ethnic groups not otherwise stated.

^e Subcategories in Other: Subcategories in other insurance: Veterans Administration, self-pay, and other insurance not specified.

^f Subcategories in other referring physician types: family medicine, general internal medicine, and obstetrics and gynecology.

Abbreviations: Lung-RADS: Lung CT Screening Reporting & Data System; CCI: Charlson Comorbidity Index; ADI: Area Deprivation Index.

Table 4. Summary of findings from generalized estimating equations analysis of non-adherence to Lung-RADS recommendations measured over time (Experiment 2, N=830).

Comparisons of interest	Non-adherence to T1 Lung-RADS recommendations		Non-adherence to T2 Lung-RADS recommendations	
	aOR (95% CI)	p-value	aOR (95% CI)	p-value
Baseline Lung-RADS 1-2				
Unchanged subsequently (Referent: T0)	1.38 (1.12, 1.69)	0.002	1.17 (0.90, 1.52)	0.23
Upgraded subsequently (Referent: T0)	0.29 (0.14, 0.60)	<0.001	0.44 (0.19, 1.01)	0.05
Baseline Lung-RADS 3-4				
Unchanged subsequently (Referent: T0)	1.81 (0.62, 5.22)	0.28	1.34 (0.16, 10.9)	0.78
Downgraded subsequently (Referent: T0)	5.08 (1.28, 20.1)	0.021	6.99 (0.66, 74.1)	0.11

Notes: Adjusted baseline variables included baseline Lung-RADS, family history of lung cancer, education, median household income, age-adjusted Charlson Comorbidity Index, and type of referring physician.

Abbreviations: Lung-RADS: Lung-RADS: Lung CT Screening Reporting & Data System; aOR: adjusted odds ratio; CI: confidence interval, T0: first screening time point, T1: second screening time point, T2: third screening time point.