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### Authors

Lin, Yannan  
Fu, Mingzhou  
Ding, Ruiwen  
[et al.](#)

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## Patient Adherence to Lung CT Screening Reporting & Data System—Recommended Screening Intervals in the United States: A Systematic Review and Meta-Analysis

Yannan Lin, MD, MPH<sup>a,b,\*</sup>, Mingzhou Fu, MD, MPH, MHI<sup>c</sup>, Ruiwen Ding, BS<sup>a,b</sup>, Kosuke Inoue, MD, PhD<sup>d,e</sup>, Christie Y. Jeon, ScD<sup>e,f</sup>, William Hsu, PhD<sup>a,b</sup>, Denise R. Aberle, MD<sup>a,b,g</sup>, Ashley Elizabeth Prosper, MD<sup>b,g</sup>

<sup>a</sup>Department of Bioengineering, University of California Los Angeles, Los Angeles, California

<sup>b</sup>Medical & Imaging Informatics Group, Department of Radiological Sciences, University of California Los Angeles, Los Angeles, California

<sup>c</sup>Medical Informatics Home Area, Department of Bioinformatics, University of California Los Angeles, Los Angeles, California

<sup>d</sup>Department of Social Epidemiology, Graduate School of Medicine, Kyoto University, Kyoto, Japan

<sup>e</sup>Department of Epidemiology, UCLA Fielding School of Public Health, University of California Los Angeles, Los Angeles, California

<sup>f</sup>Department of Medicine, Samuel Oschin Cancer Institute, Cedars-Sinai Medical Center, Los Angeles, California

<sup>g</sup>Department of Radiological Sciences, David Geffen School of Medicine at UCLA, Los Angeles, California

### Abstract

Lung cancer screening (LCS) is effective in reducing mortality, particularly when patients adhere to follow-up recommendations standardized by the Lung CT Screening Reporting & Data System

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\*Address for correspondence: Yannan Lin, MD, MPH, Department of Bioengineering, University of California Los Angeles, 924 Westwood Boulevard, Suite 420, Los Angeles, CA 90024. [yannanlin@mednet.ucla.edu](mailto:yannanlin@mednet.ucla.edu).

CRedit Authorship Contribution Statement

**Yannan Lin:** Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Project administration, Validation, Writing—original draft, Writing—review and editing.

**Mingzhou Fu:** Data curation, Methodology, Writing—review and editing.

**Ruiwen Ding:** Data curation, Writing—review and editing.

**Kosuke Inoue:** Data curation, Resources, Methodology, Writing—review and editing.

**Christie Y. Jeon:** Conceptualization, Methodology, Writing—review and editing.

**William Hsu:** Conceptualization, Funding acquisition, Writing—review and editing, Supervision.

**Denise R. Aberle:** Conceptualization, Data curation, Funding acquisition, Writing—review and editing, Supervision.

**Ashley Elizabeth Prosper:** Conceptualization, Data curation, Resources, Methodology, Writing—review and editing, Supervision.

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Supplementary Data

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(Lung-RADS). Nevertheless, patient adherence to recommended intervals varies, potentially diminishing benefit from screening. We conducted a systematic review and meta-analysis of patient adherence to Lung-RADS–recommended screening intervals. We systematically searched MEDLINE, EMBASE, Web of Science, the Cochrane Central Register of Controlled Trials, and major radiology and oncology conference archives between April 28, 2014, and December 17, 2020. Eligible studies mentioned patient adherence to the recommendations of Lung-RADS. The review protocol was registered with PROSPERO (CRD42020189326). We identified 24 eligible studies for qualitative summary, of which 21 were suitable for meta-analysis. The pooled adherence rate was 57% (95% confidence interval: 46%–69%) for defined adherence (e.g., an annual incidence screen was performed within 15 mo) among 6689 patients and 65% (95% confidence interval: 55%–75%) for anytime adherence among 5085 patients. Large heterogeneity in adherence rates between studies was observed ( $I^2 = 99%$  for defined adherence,  $I^2 = 98%$  for anytime adherence). Heterogeneous adherence rates were associated with Lung-RADS scores, with significantly higher adherence rates among Lung-RADS 3 to 4 than Lung-RADS 1 to 2 ( $p < 0.05$ ). Patient adherence to Lung-RADS–recommended screening intervals is suboptimal across clinical LCS programs in the United States, especially among patients with results of Lung-RADS categories 1 to 2. To improve adherence rates, future research may focus on implementing tailored interventions after identifying barriers to LCS. We also propose a minimum standardized set of data elements for future pooled analyses of LCS adherence on the basis of our findings.

### Keywords

Lung cancer screening; Patient adherence; Lung-RADS (Lung CT Screening Reporting & Data System); Systematic review; Meta-analysis

### Introduction

The National Lung Screening Trial (NLST), reported in 2011, revealed a 20% relative mortality reduction from lung cancer with chest low-dose computed tomography (LDCT) screening relative to chest radiography.<sup>1</sup> In 2013, the United States Preventive Services Task Force issued a grade B recommendation that smokers aged 55 to 80 years with greater than or equal to 30 pack-year smoking history and less than or equal to 15 years since quitting receive annual screening with LDCT.<sup>2</sup> This was followed by a national coverage decision from the Centers for Medicare and Medicaid Services in 2015. Despite the potential of lung cancer screening (LCS) to identify tumors at earlier, more treatable stages, reports from post-NLST community clinical practices have revealed adherence rates less than 50%,<sup>3,4</sup> far lower than the more than 90% adherence rate found in the NLST.<sup>1</sup> Adherence to annual screening recommendations is critical to realizing mortality benefits found in the NLST, as lung cancer diagnoses on the basis of new nodules at incidence screening revealed shortened survivals, approximating interval diagnoses (cancers diagnosed after a negative screen).<sup>5</sup>

Two recent systematic reviews investigated adherence to LCS. Lam et al.<sup>6</sup> concentrated on patient nonadherence to returning for annual LDCT screening using data from global clinical studies. They reported a pooled nonadherence rate of 28% with a 95% confidence interval (CI) of 20% to 37% at the first annual screen across 12 studies. Lopez-Olivo

et al.<sup>7</sup> reported a pooled LCS adherence rate of 55% (95% CI: 44%–66%) across all follow-up periods for 15 studies in the United States that used any screen-reporting guideline. The Lung CT Screening Reporting & Data System (Lung-RADS) serves as a quality assurance tool to standardize reporting of LCS LDCT results and corresponding management recommendations.<sup>8</sup> Assignment of Lung-RADS scores is based on nodule size, characteristics, and location. Nodule management guidelines are specific to Lung-RADS categories with LDCT in 12 months for Lung-RADS 1 to 2, LDCT in 6 months for Lung-RADS 3, LDCT in 3 months or positron emission tomography (PET)-CT for Lung-RADS 4A, and chest CT, PET-CT, or tissue sampling for Lung-RADS 4B/X (Supplementary Table 1). To date, the literature has lacked systematic evidence on adherence to LCS on the basis of Lung-RADS guidelines. To bridge the gap, this systematic review and meta-analysis highlights patient adherence to Lung-RADS–recommended screening intervals among clinical LCS programs in the United States, with a focus on identifying sources of heterogeneity in adherence rates through subgroup analyses and meta-regression. In addition, on the basis of gaps in data identified through our meta-analysis, we propose a standardized approach to reporting LCS adherence rates.

## Materials and Methods

This systematic review was registered with PROSPERO (CRD42020189326) and was reported following the Preferred Reporting Items for Systematic Reviews and Meta-Analyses statement.<sup>9</sup> We used the Covidence software (Melbourne, Australia)<sup>10</sup> for the title and abstract screening, full-text review, data extraction, and quality assessment.

### Eligibility Criteria

We included studies that reported patient adherence rates to Lung-RADS–recommended screening intervals in the United States. Eligible patients needed to be enrolled in a clinical LCS program located in a US hospital. The screening modality was restricted to LDCT, and the reporting guidelines of the LDCT were limited to Lung-RADS recommendations. There was no restriction on the type of study design for inclusion in this review. Studies published before the release date of Lung-RADS (April 28, 2014) and non-English language publications were excluded.

### Search Strategy and Study Selection

We searched MEDLINE (accessed by PubMed), EMBASE, Web of Science, and the Cochrane Central Register of Controlled Trials (CENTRAL) from January 1, 2014, to December 17, 2020, for eligible original studies. Apart from the electronic literature databases, we searched Google Scholar from January 1, 2014, to December 17, 2020. Moreover, we searched archives of influential conferences in radiology and cancer research for original studies reported in the conference abstract format, which included the American Association for Cancer Research, American Society of Clinical Oncology, American Thoracic Society, Radiological Society of North America, Society of Thoracic Radiology from 2014 to 2020, and American Roentgen Ray Society from 2019 to 2020. In addition, the reference lists of the included studies were manually searched. Three keyword categories (e.g., keywords used in PubMed: Supplementary Table 2) used for the search were lung

cancer, cancer screening, and adherence. For each category, we identified synonyms such as lung neoplasms, early detection of cancer, and patient adherence. Then, the three keyword categories were combined into a comprehensive search strategy. The search strategy was tailored for each database and conference archive (e.g., search in PubMed: Supplementary Table 3). We included both journal articles and conference abstracts. Two independent reviewers (YL and AP) performed literature screening on the basis of the eligibility criteria. Discrepancies were resolved through a group discussion with a third reviewer (DRA).

### Data Items and Data Extraction

Extracted data items were summarized in Supplementary Table 4. Data elements were extracted by two independent reviewers (YL and RD). Discrepancies were resolved through a discussion between the two reviewers.

### Risk of Bias Assessment

Two reviewers (YL and MF) evaluated the quality of the included studies at the study level using relevant items from the Newcastle-Ottawa Scale for cohort studies.<sup>11</sup> Disagreements were resolved through consensus or by a group discussion that involved a third reviewer (KI). The five relevant items were the following: (1) representativeness of the exposed cohort, (2) ascertainment of exposure, (3) demonstration that outcome of interest was not present at start of study, (4) assessment of outcome, and (5) whether follow-up was long enough for outcomes to occur (Supplementary Table 5). The remaining three items in the Newcastle-Ottawa Scale for cohort studies were irrelevant in this context. Because adherence rate is similar to prevalence rate in cross-sectional studies, selection of the unexposed group and comparison between the two cohorts were considered irrelevant. Furthermore, participants who were lost to follow-up were accounted for in the analysis by categorizing into the nonadherent group. Consequently, attrition bias is not a concern for this specific research question.

### Summary Measures

We defined the follow-up examination for Lung-RADS 1 to 2 as an annual incidence screen (i.e., LDCT in 12 mo) and Lung-RADS 3 to 4 as an early follow-up examination (i.e., LDCT in 3–6 mo, chest CT, PET-CT, or tissue sampling). Annual screening time points are labeled T0 (baseline), T1, T2, T3, etc. for annual incidence screens at 1, 2, 3 years, etc., respectively. The patient was considered adherent if they completed an annual incidence screen or early follow-up examination within the time period specified in each study. Adherence rate was the primary outcome, calculated as the number of adherent patients divided by the total number of patients enrolled during the patient enrollment period. As a secondary outcome, adherence rates in subgroups (e.g., adherence rates stratified by Lung-RADS score and demographics) were also extracted from each study, when available. Because of the inconsistent definitions of adherence across the included studies, adherence rates were categorized into defined adherence, when a clear definition of adherence was provided (e.g., annual incidence screen within 15 mo of the initial screen), and anytime adherence, which considered patients as adherent as long as they received a follow-up examination during the course of the study period.

## Statistical Analysis

We summarized study-level characteristics, overall and stratified adherence rates, and factors that were associated with nonadherence. In the meta-analysis, we focused on the adherence rate at the first screen or examination after the T0 screen, because there was insufficient data on the adherence rates at the second annual incidence screen or beyond. We contacted the authors of the four studies<sup>12–15</sup> to clarify which time intervals formed the basis for their calculated adherence rates. We received responses from all authors. We then used random effects models to perform meta-analyses of proportions (adherence rates) using the inverse-variance weighting method with the Freeman-Tukey double arcsine transformation to better approximate to the normal distribution while stabilizing the variances.<sup>16</sup> The statistical heterogeneity in adherence rates across studies was evaluated using the  $I^2$  index<sup>17</sup> (>75% as large heterogeneity) and Cochran's Q test<sup>18</sup> ( $p < 0.05$  indicates significant heterogeneity). Additional sensitivity analyses were conducted to evaluate the influence of adherence rates from conference abstracts on pooled adherence rates by removing them from the meta-analyses. To further understand the causes of heterogeneity, we performed subgroup analyses and bivariate and multivariable mixed effects meta-regression models with the restricted maximum-likelihood estimator<sup>19</sup> and Freeman-Tukey double arcsine-transformed adherence rates to adjust for study-level characteristics, including Lung-RADS, institutional setting, program with coordinators/navigators, shared decision-making, smoking cessation services, interventions for adherence, and publication type. We did not use robust cluster meta-regression because our sample size ( $N < 20$ ) was too small to yield accurate results.<sup>20</sup> Publication bias was evaluated by funnel plots and Egger's test.<sup>21</sup> All analyses were performed in R version 3.6.3 using "meta" and "metafor" packages.<sup>22–24</sup>

## Results

### Search Results

Among the 557 references that underwent title and abstract screen, 510 studies were irrelevant to LCS adherence. Of the 47 studies that underwent full-text review, 24 studies<sup>3,4,12–15,25–42</sup> were included in qualitative synthesis, whereas 21<sup>3,4,12–15,26,27,29–40,42</sup> studies were eligible for quantitative synthesis (meta-analysis) (Fig. 1).

### Quality (Risk of Bias) Assessment

Supplementary Table 6 outlines the risk of bias assessment at the study level. We excluded one study<sup>25</sup> from the meta-analyses because it excluded nonadherent patients who did not come back after the baseline examination. In three studies,<sup>26–28</sup> we assumed that exposure (LCS examination and Lung-RADS information) and outcomes (adherence statuses) data were obtained from patient medical records, although this was not stated explicitly. In two studies,<sup>12,29</sup> patients with a pending follow-up examination were excluded from the adherence rate calculation because their adherence statuses were yet to be determined. Adherence outcomes were unknown at the start of all included studies, as patients undergoing LDCT needed to be followed up to determine adherence.

## Study Characteristics

The characteristics of the 24 included studies<sup>3,4,12–15,25–42</sup> are summarized in Table 1. Among the 24 studies, the distribution of institutional settings was 17 academic,<sup>12–14,25,27,30–38,40–42</sup> four community,<sup>3,4,26,29</sup> two Kaiser Permanente,<sup>28,39</sup> and one Veterans Affairs,<sup>15</sup> with most being retrospective studies.<sup>3,4,12–15,25–30,32–34,36–42</sup> The study period varied for each individual study. Eligibility criteria for LCS mentioned in the studies included guidelines from the American Association for Thoracic Surgery,<sup>12</sup> American Cancer Society,<sup>12</sup> Centers for Medicare and Medicaid Services,<sup>29,31,34</sup> National Comprehensive Cancer Network,<sup>12,14,30,31,33,37</sup> National Cancer Institute,<sup>12</sup> NLST,<sup>4,35,38</sup> and the United States Preventive Services Task Force.<sup>12,15,27,31,37,41</sup> There were 20 studies<sup>4,12,14,15,25–27,29–31,33–42</sup> that described LCS program resources, which included program coordinators/navigators, shared decision-making services, smoking cessation services, and use of a dedicated clinical LCS database. Additional details are reported in Supplementary Table 7, such as publication type, additional inclusion criteria, exclusion criteria, referral types, retrospective assignment of Lung-RADS scores, adherence determination for certain subgroups (e.g., died or became ineligible during follow-up), and reasons for nonadherence.

## Adherence Rates in Specific Lung-RADS Categories

Given that adherence rates were not evaluated for all Lung-RADS categories among all studies, we extracted adherence rates and relevant information in specific Lung-RADS categories for the 24 studies.<sup>3,4,12–15,25–42</sup> There were 10 studies<sup>4,13–15,30,31,34,36,40,42</sup> that reported interventions for adherence, such as reminder letters and phone calls. In addition, there were 14 studies<sup>4,12,15,25,27,30–34,36,39,41,42</sup> that reported Lung-RADS distributions. Heterogeneous definitions of adherence were used for the same Lung-RADS categories across different studies, among which completion of annual screen or early follow-up within 3 months (or 90 d) of recommended date was the most frequently used criterion.<sup>4,14,15,26,28,30,38,40–42</sup> Both overall and Lung-RADS–stratified defined and anytime adherence rates are summarized in Table 2.

## Meta-Analysis of Adherence Rates at T1

We performed a pooled analysis of adherence rates at T1 among the eligible studies ( $N = 21$ ).<sup>3,4,12–15,26,27,29–40,42</sup> Three studies were excluded from the meta-analysis because (1) Wernli et al.<sup>28</sup> only reported adherence rates without specifying the total numbers of included and adherent patients and (2) adherence rates at T1 could not be extracted from studies by Barbosa et al.<sup>25</sup> and Stowell et al.<sup>41</sup> In addition, Spalluto et al.<sup>40</sup> reported adherence rates at both 90-day and 180-day windows. To minimize variations in the definition of adherence and be consistent with definitions used by most studies, only 90-day (3 mo) adherence rates were included in the meta-analyses for this study. As found in Figure 2A and B, the pooled adherence rate was 57% (95% CI: 46%–69%) for defined adherence among 6689 patients and 65% (95% CI: 55%–75%) for anytime adherence among 5085 patients. Significant heterogeneity between studies was observed ( $I^2 = 99%$ ,  $p < 0.05$  for defined adherence;  $I^2 = 98%$ ,  $p < 0.05$  for anytime adherence). Sensitivity analyses on



adherence rates from journal articles revealed similar results (Supplementary Fig. 1A and B).

### Subgroup Analyses on Adherence Rates at T1

In the subgroup analysis for Lung-RADS categories, studies that did not report adherence rates in Lung-RADS 1 to 2 or Lung-RADS 3 to 4 were excluded.<sup>13,14,26,27</sup> For defined adherence, the pooled adherence rate was 45% (95% CI: 28%–63%) in Lung-RADS 1 to 2 among 3428 patients and 74% (95% CI: 65%–83%) in Lung-RADS 3 to 4 among 557 patients (test for subgroup differences  $p < 0.05$ ); however, for anytime adherence, the pooled adherence rate was 49% (95% CI: 39%–60%) in Lung-RADS 1 to 2 among 3847 patients and 78% (95% CI: 65%–89%) in Lung-RADS 3 to 4 among 528 patients (test for subgroup differences  $p < 0.05$ ) (Fig. 2C and D). Furthermore, we performed a meta-analysis of defined adherence rates among a subset of the studies in which adherence was defined as completion of the annual screen or early follow-up examination within 3 months (90 d) of the recommended date (Supplementary Fig. 2) and observed significant subgroup differences between Lung-RADS 1 to 2 and Lung-RADS 3 to 4 ( $p < 0.05$ ). In addition, sensitivity analyses removing adherence rates from conference abstracts also revealed significant subgroup differences between Lung-RADS 1 to 2 and Lung-RADS 3 to 4 (Supplementary Fig. 1C and D;  $p < 0.05$ ). Because of limited data, additional subgroup analyses by sex, race, and smoking status did not reveal significant subgroup differences in adherence rates (Supplementary Fig. 3;  $p > 0.05$ ).

### Potential for Publication Bias

Funnel plots of meta-analyses are found in Supplementary Figures 4 to 7. In the Egger's regression tests for funnel plot asymmetry, we found no evidence of the potential publication bias (i.e.,  $p > 0.05$ ) except for the pooled anytime adherence rates from journal articles (Supplementary Fig. 5B;  $p < 0.05$ ).

### Meta-Regression

Because substantial differences were identified between Lung-RADS 1 to 2 and Lung-RADS 3 to 4 for both defined and anytime adherence, studies that reported adherence rate only in Lung-RADS 1 to 4<sup>13,14,26</sup> or a specific Lung-RADS category<sup>27</sup> were excluded from meta-regression analyses (Supplementary Table 8). Detailed information on outcome and independent variables across 17 studies included in this meta-regression analyses is found in Supplementary Table 9. In bivariate meta-regression analyses, Lung-RADS categories (1–2 versus 3–4) were found to be associated with adherence rates for both defined and anytime adherence ( $p < 0.05$  for both). In addition, the mention of smoking cessation services (yes versus not reported) was associated with defined adherence ( $p < 0.05$ ). After adjusting for institutional setting, programs with coordinators/navigators, shared decision-making services, interventions for adherence, and publication type, Lung-RADS categories (1–2 versus 3–4) and mentioning of smoking cessation services (yes versus not reported) were associated with defined adherence rates ( $p < 0.05$ ). Further subgroup analysis revealed a higher adherence rate among studies that reported smoking cessation services as opposed to those that did not (70%, 95% CI: 50%–87% versus 46%, 95% CI: 31%–61%); however, the difference was not significant ( $p > 0.05$ ).



## Predictors of Nonadherence

Table 3 summarizes potential predictors of LCS adherence with  $p$  values derived from the Pearson's chi-square test and ORs derived from bivariate or multivariable logistic regression. Bellinger et al.<sup>31</sup> found that patients with Lung-RADS 3 to 4 were more adherent compared with those with Lung-RADS 1 to 2 ( $p < 0.05$ ). Similar findings were found by Triplette et al.<sup>42</sup> (referent: Lung-RADS 1, Lung-RADS 3: OR = 3.8, 95% CI: 1.9–7.7; Lung-RADS 4: OR = 14, 95% CI: 6.0–32) and Bernstein et al.<sup>26</sup> (referent: Lung-RADS 1, Lung-RADS 2: OR = 2.43, 95% CI: 1.66–3.56; Lung-RADS 3: OR = 5.39, 95% CI: 2.71–10.72; Lung-RADS 4: OR = 28.86, 95% CI: 8.60–96.87). Alshora et al.<sup>30</sup> reported that female patients were more adherent ( $p < 0.05$ ), whereas Seastedt et al.<sup>15</sup> concluded that male patients were more adherent (OR = 2.57, 95% CI: 1.36–4.87). Three studies<sup>15,26,30</sup> revealed that older patients were more adherent than younger patients ( $p < 0.05$  for Alshora et al.<sup>30</sup> and Bernstein et al.<sup>26</sup> and OR = 1.43, 95% CI: 1.03–2.01 for Seastedt et al.<sup>15</sup>). Higher adherence rates were also associated with referral to LCS by pulmonary medicine and thoracic surgery<sup>26</sup> ( $p < 0.05$ ), having a reminder from either a nurse navigator or primary care provider<sup>34</sup> ( $p < 0.05$ ), having a dedicated program coordinator<sup>40</sup> ( $p < 0.05$ ), or being a former smoker<sup>42</sup> (OR = 1.7, 95% CI: 1.2–2.5). On the basis of these findings, when data were available, we further attempted to investigate whether incorporating predictors of nonadherence as fixed effects terms in the random effects meta-analysis models reduced the heterogeneity score,  $I^2$ . Nevertheless, we were not able to perform this analysis owing to the small number of studies reporting mean age, percent of females, percentage of whites, and percentage of former smokers (Supplementary Table 10).

## Discussion

This systematic review and meta-analysis focused on LCS adherence to Lung-RADS recommendations. Lung-RADS guidelines were developed on the basis of findings from the NLST and other screening studies; among the goals was lowering false-positive and false discovery rates<sup>29</sup> while providing standardized management algorithms for clinical practice. Before the release of Lung-RADS, the NLST protocol recommended early follow-up imaging for nodules 4 mm in diameter or larger<sup>43</sup> and the Fleischner 2005 guidelines recommended follow-up for solid nodules greater than 4 mm in diameter.<sup>44</sup> The Lung-RADS threshold for early follow-up is nodules greater than or equal to 6 mm, resulting in fewer positive screens and the number of recommended early follow-up examinations. This decline was not due to a change in adherence patterns, rather, the impact of changing the minimum size threshold for early follow-up examinations. As a result, we purposely excluded studies that reported LCS adherence rates on the basis of other follow-up recommendations.

Highly heterogeneous adherence rates were observed across studies. We found significantly higher adherence rates in patients with Lung-RADS 3 (risk for lung cancer at 1%–2%) and 4 (risk > 5%) than Lung-RADS 1 and 2 (risk < 1%). It is likely that patients and referrers are more concerned on nodules at a higher risk for lung cancer, prompting greater adherence to recommended screening intervals in Lung-RADS 3 to 4. Reporting of smoking cessation services contributed to the heterogeneity in defined adherence rates (bivariate

and multivariable meta-regression:  $p < 0.05$ ), but the test for subgroup differences was insignificant ( $p > 0.05$ ). Regardless, it is crucial that patients and referrers alike understand that screening is most effective when performed regularly, including for those with negative baseline screens, as de novo nodules, those detected after a negative screen, are more aggressive than those detected at baseline screen.<sup>5</sup>

Although adherence rates varied widely across studies, none of them approximated the 95% adherence observed in the LDCT arm in the NLST, which could adversely affect the mortality benefits of LCS. Beyond the more tightly controlled environment of a clinical trial, differences in demographic distributions between the included studies and the NLST could be one of the causes for the differences in adherence rates. Participants in the NLST were greater than 90% white, 59% male, and 52% former smokers at baseline.<sup>1</sup> Only one study<sup>30</sup> had demographic distributions at baseline screen similar to the NLST. Insurance coverage could be another barrier to returning for additional screening examinations because only screen-eligible patients aged 65 years or older qualify for Medicare insurance. Moreover, when retrospectively applying the Lung-RADS criteria to the NLST, the Lung-RADS distribution at baseline screen for Lung-RADS 1 to 2 is 86% and for Lung-RADS 3 to 4 is 14%.<sup>45</sup> Similar distributions were observed in only five studies.<sup>12,31,36,39,42</sup> Perhaps most importantly, the NLST used an active process for patient follow-up by issuing an annual or biannual questionnaire and a study update form; if forms were not completed, participants were contacted by a staff member.<sup>43</sup> In post-NLST clinical practices, despite some sites reporting comparable interventions to ensure adherence that included reminders by means of mail, telephone calls, and involving the patient's primary care provider, the overall adherence rates remain low. This implies that the low adherence rates found in the clinical practices could be caused by multiple factors, including but not limited to patient characteristics, insurance coverage, Lung-RADS category, and interventions for adherence.

Furthermore, several studies investigated reasons for nonadherence, including (1) patient declining the annual incidence screen or early follow-up examination,<sup>29,30</sup> (2) screening center's inability to contact the patient,<sup>30</sup> (3) failure of provider to order the annual incidence screen or early follow-up examination,<sup>30</sup> (4) patient completed screening elsewhere,<sup>15,31</sup> (5) patient not contacted to schedule an examination,<sup>15</sup> and (6) LCS was not a priority as opposed to other medical issues.<sup>15</sup> Spalluto et al.<sup>40</sup> reported patient-identified barriers to LCS, such as lack of transportation, lack of communication by physicians, lack of current symptoms (hence the need for screening), and financial costs. Similar barriers to LCS have been reported by Wang et al.<sup>46</sup>

This systematic review and meta-analysis has several limitations. First, we included both conference abstracts and journal articles in the review. Abstracts are more susceptible to missing details that can be used to evaluate potential sources of heterogeneity in adherence rates, such as interventions for adherence, LCS program resources, and adherence rates in subgroups. Second, we were unable to perform a meta-analysis on adherence rates beyond the first annual incidence screen owing to scarcity of data. Capturing adherence rates beyond T1 can provide richer information in that adherence rates at different screen time points may vary. As suggested by Kaminetzky et al.,<sup>35</sup> adherence rates among Lung-RADS 1 to 2 were 46%, 38%, and 28% at T1, T2, and T3, respectively. Third, there were insufficient

data on adherence rates among subgroups for sex, race, and smoking status to reveal the true differences in adherence rates between subgroups. Last but not least, we provided a summary of predictors of nonadherence identified in individual studies (Table 3). Still, we did not perform a meta-analysis on these predictors owing to concerns on their degree of heterogeneity and lack of published data. Such meta-analysis might better inform modifiable factors and effective interventions that can improve adherence rates.

Given the heterogeneity, we observed in reporting adherence to LCS, we have developed a checklist to guide future research and publications (Table 4). These data elements span several categories, such as the following: study period, eligibility criteria, LCS program resources, screening characteristics, and outcome reporting. These data elements provide necessary information to evaluate screening and enable comparisons across programs while also providing data across sex, race/ethnicity, smoking status, and insurance status which may influence adherence. These additional data elements would inform directions for future research, including the following: (1) evaluating patient adherence longitudinally, (2) identifying barriers to LCS and patterns of nonadherence, (3) evaluating tailored interventions to optimize adherence, and (4) applying machine learning-based approaches to realize individualized interventions.

## Conclusions

This study reveals that the overall rates of adherence to Lung-RADS–recommended screening intervals in clinical practices are low as compared with the more than 90% adherence found in the NLST: 57% for defined adherence and 65% for anytime adherence. Meta-analysis of adherence rates reveals significant between-study heterogeneity. Through meta-regression, Lung-RADS categories and reporting of smoking cessation services contribute to this heterogeneity. In subgroup analysis, patients with baseline Lung-RADS 3 to 4 are more adherent than those with baseline Lung-RADS 1 to 2, suggesting tailored interventions on the basis of Lung-RADS categories may be beneficial. Furthermore, inconsistent reporting of adherence rates and supporting details are observed. Standardized reporting of adherence rates to LCS is necessary for the guidance of research and identification of interventions for improving adherence.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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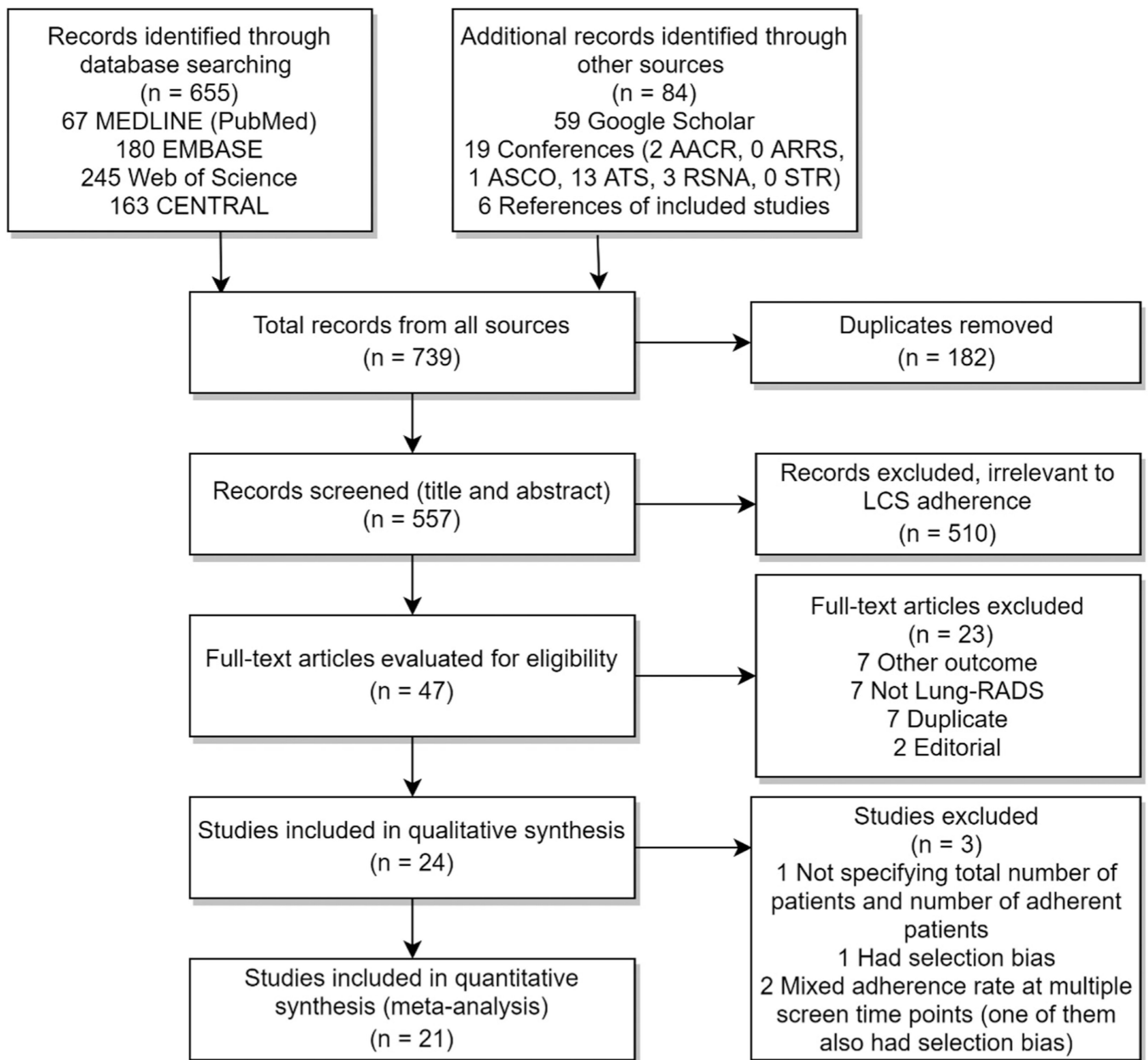
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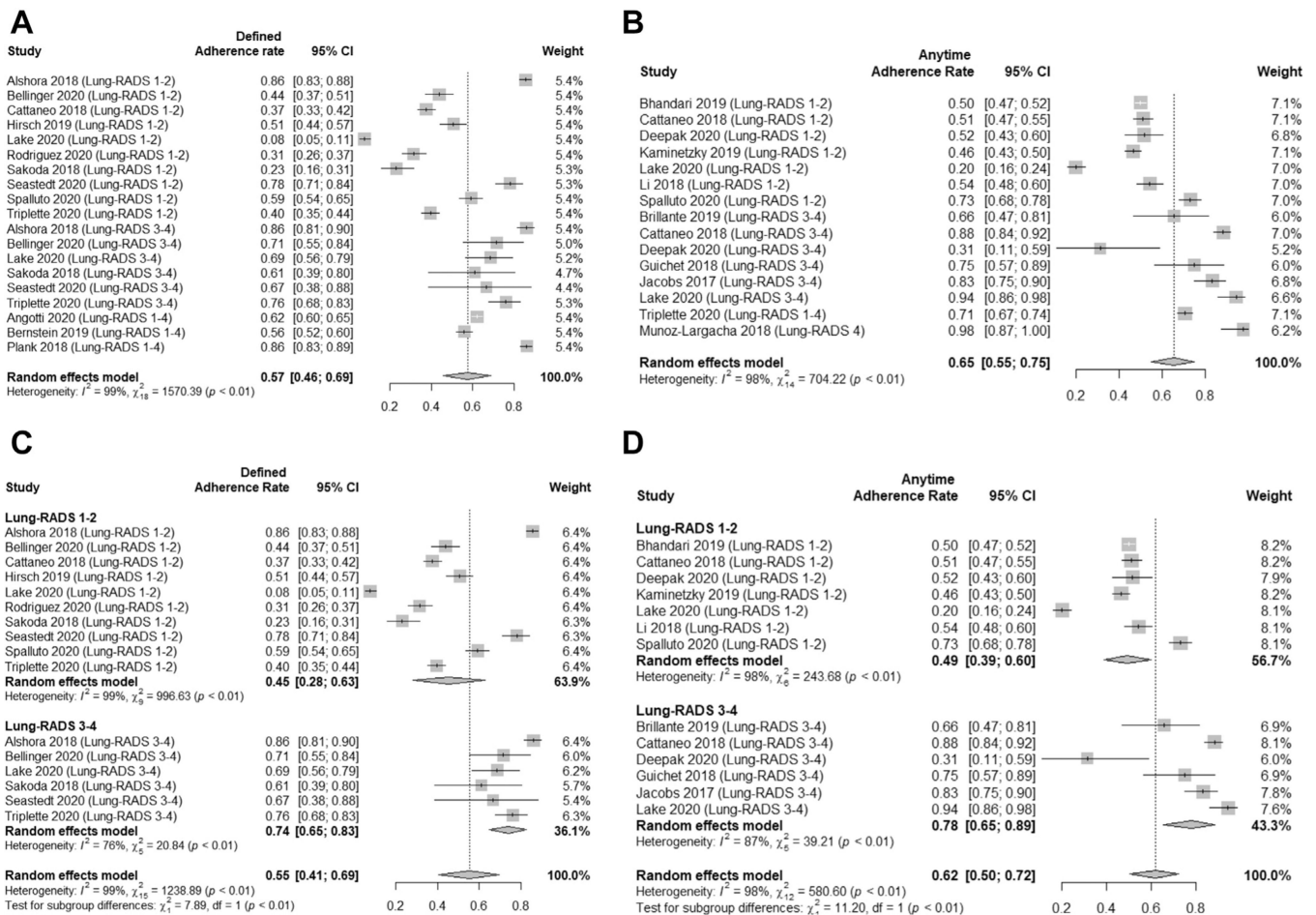




**Figure 1.**

The PRISMA flow diagram for adherence to Lung-RADS-recommended screening intervals. AACR, American Association for Cancer Research; ARRS, American Roentgen Ray Society; ASCO, American Society of Clinical Oncology; ATS, American Thoracic Society; CENTRAL, Cochrane Central Register of Controlled Trials; LCS, lung cancer screening; Lung-RADS, Lung CT Screening Reporting & Data System; PRISMA, Preferred Reporting Items for Systematic Reviews and Meta-Analyses; RSNA, Radiological Society of North America; STR, Society of Thoracic Radiology.





**Figure 2.** The pooled adherence rates to Lung-RADS-recommended screening intervals at T1. (A) Forest plot of defined adherence rates (total N = 6689). (B) Forest plot of anytime adherence rates (total N = 5085). (C) Forest plot of defined adherence rates stratified by Lung-RADS categories (total N = 3985, Lung-RADS 1–2 n = 3428, Lung-RADS 3–4 n = 557). (D) Forest plot of anytime adherence rates stratified by Lung-RADS categories (total N = 4375, Lung-RADS 1–2 n = 3847, Lung-RADS 3–4 n = 528). Defined adherence: adherence was defined as completion of annual incidence screen or early follow-up examination within a specified time interval from recommended date. Anytime adherence: patients are considered adherent as long as they received a follow-up examination anytime during the course of the study period. CI, confidence interval; Lung-RADS, Lung CT Screening Reporting & Data System; T1, annual incidence screen at 1 year.

**Table 1.** Characteristics of Included Studies on Patient Adherence to Lung-RADS-Recommended Screening Intervals (N = 24)

Study	Institutional Setting	Study Design	Study Period	LCS Eligibility Criteria	Program Resources	Cohort Size (Patients)	Patient Characteristics
Aishora et al., 2018 <sup>30</sup>	Academic	Retrospective cohort	Baseline LDCT January 12, 2012–June 12, 2013, followed through September 12, 2014	NCCN	Program coordinators/navigators; SDM; smoking cessation; management system; database; standardized patient discharge protocol	901	Female: 44.2%; White > 95%; current smokers: 45.9%; former smokers: 54.1%
Angotti et al., 2020 <sup>13</sup>	Academic	Retrospective cohort	Baseline LDCT 2016–2018	Not reported	Not reported	1444	Not reported
Barbosa et al., 2020 <sup>25</sup>	Academic	Retrospective cohort	LDCT May 1, 2014–July 11, 2019	Age >50 y and <80 y, 30 pack-years, current smoker or former smoker quit within 15 y	Data maintained in Excel and REDCap	260	Mean age 65.5 y, median age 66 y; female: 51.9%; current smokers 55.0%, former smokers 45.0%; mean pack-years: 51.1 PY, median pack-years: 45 PY
Bellinger et al., 2020 <sup>31</sup>	Academic	Prospective cohort	Baseline LDCT November 2014–March 2016	USPSTF, CMS, NCCN	Program coordinators/navigators	268	Female: 49.6%; White: 76.1%, Black: 22.4%, not reported: 1.5%; current smokers: 62.7%, former smokers: 37.3%
Bernstein et al., 2019 <sup>26</sup>	Community	Retrospective cohort	Baseline LDCT May 1, 2015–May 1, 2018	Not reported	Program coordinators/navigators	631	Female: 48.7%
Bhandari et al., 2019 <sup>3</sup>	Community	Retrospective cohort	LDCT 2016–2017	Not reported	Not reported	3428	Not reported
Brillante et al., 2019 <sup>32</sup>	Academic	Retrospective cohort	Not reported	Not reported	Not reported	32	Mean age: 64.8 y; Black: 75.0%; Medicare/Medicaid: 75.0%
Cattaneo et al., 2018 <sup>4</sup>	Community	Retrospective cohort	Baseline LDCT January 2012–September 30, 2015, followed through December 31, 2016	NLST	Program coordinators/navigators; smoking cessation; database; multidisciplinary program for management	1241	Median age: 66 y; female 52.5%; White: 87.3%, Black: 10.2%, other race: 1.5%, not reported: 1.0%; current smokers 49.1%, former smokers 48.2%, not reported: 2.7%; median pack-years: 40 PY; Medicare: 45.5%, private insurance: 49.7%, Medicaid: 1.4%, not reported: 3.4%
Deepak et al., 2020 <sup>12</sup>	Academic	Retrospective cohort	Not reported	USPSTF, AATS, ACS, NCI, NCCN	Data maintained in Excel	166	Female: 47.0%; White: 15.7%, Black: 81.9%, Asian: 1.2%, not reported: 1.2%
Guichet et al., 2018 <sup>33, a</sup>	Academic	Retrospective cohort	Baseline LDCT July 21, 2015–April 3, 2017, followed through August 1, 2017	NCCN	Program coordinators/navigators; database	275	Mean age: 59 y; female: 47.6%; White: 5.1%, Black: 83.6%, Asian: 0.7%, Hispanic/Latino: 10.5%; current smokers: 81.1%; median pack-years: 40 PY

Study	Institutional Setting	Study Design	Study Period	LCS Eligibility Criteria	Program Resources	Cohort Size (Patients)	Patient Characteristics
Hirsch et al., 2019 <sup>34</sup>	Academic	Retrospective cohort	Baseline LDCCT July 1, 2014– December 31, 2016	CMS	Program coordinators/navigators; SDM; database	259	Mean age: 64.1 y; female: 42.9%; White: 82.6%; current smokers: 54.8%, former smokers: 45.2%; mean pack-years: 48.6 PY; government insurance: 73.7%, private insurance: 23.2%, other: 3.1%
Jacobs et al., 2017 <sup>29</sup>	Community	Retrospective cohort	Baseline LDCCT June 1, 2014– December 31, 2015	CMS	SDM; smoking cessation	680	Median age: 64 y; female: 44.7%; current smokers: 45.1%; former smokers: 48.4%, not reported: 6.5%; median pack-years: 44.5 PY
Kamietzky et al., 2019 <sup>35</sup>	Academic	Prospective cohort	Baseline LDCCT December 2012– December 2016	NLST	Program coordinators/navigators; data maintained in Excel	1181	Mean age: 64 y; female: 51.8%; White: 22.9%, Black: 31.4%; Hispanic/Latino: 30.9%; Asian: 0.7%, not reported: 14.1%; current smokers: 71.4%, former smokers: 28.6%; median pack-years: 45 PY; Medicare: 55.7%, Medicaid: 21.0%
Lake et al., 2020 <sup>36</sup>	Academic	Retrospective cohort	Baseline LDCCT May 2015– July 2017, followed through September 6, 2019	Not reported	Program coordinators/navigators; SDM; database	477	Mean age: 64.3 y; female: 53.0%; White: 57.9%, Black: 42.1%; current smokers: 57.2%, former smokers: 41.1%, not reported: 1.6%; mean pack-years: 48.5 PY
Li et al., 2018 <sup>37,4</sup>	Academic	Retrospective cohort	Baseline LDCCT July 21, 2015– March 20, 2018	USPSTF, NCCN	Program coordinators/navigators	370	Mean age: 60 y; female: 45.1%; White: 9.0%, Black: 77.0%, Asian: 5.0%, Hispanic/Latino: 8.0%; current smokers: 81.0%; median pack-years: 42 PY
Muñoz-Largacha et al., 2018 <sup>27</sup>	Academic	Retrospective cohort	Baseline LDCCT March 2015– July 2016	USPSTF	Program coordinators/navigators	554	Mean age: 63 y; female: 39.9%; White: 47.8%, Black: 31.4%, Asian/Native American: 5.1%, Hispanic/Latino: 10.1%, not reported: 5.6%; current smokers: 51.6%, former smokers: 24.5%, not reported: 23.8%; Medicare/Medicaid: 64.0%, private insurance: 36.0%
Plank et al., 2018 <sup>14</sup>	Academic	Retrospective cohort	Not reported	NCCN	Smoking cessation; REDCap	825	Mean age: 60 y; female: 40.0%; current smokers: 43.0%; mean pack-years: 46 PY
Rodriguez et al., 2020 <sup>38</sup>	Academic	Retrospective cohort	Baseline LDCCT 2016– 2019	NLST	SDM	421	Black: 15.0%, Hispanic/Latino: 47.3%
Sakoda et al., 2018 <sup>39</sup>	Kaiser Permanente	Retrospective cohort	Baseline LDCCT July 2014– June 2015	Not reported	Database	145	Median age: 66 y; female: 39.0%; White: 71.0%, current smokers: 76.0%
Seastedt et al., 2020 <sup>15</sup>	VA	Retrospective cohort	Baseline LDCCT 2013– June 2019	USPSTF	Smoking cessation; database	242	Median age: 67 y; female: 30.6%; White: 57.9%, Black: 20.2%, other: 21.9%; current smokers: 43.4%, former smoker: 56.6%; mean pack-years: 41 PY
Spalluto et al., 2020 <sup>40</sup>	Academic	Retrospective cohort	Baseline LDCCT January 1, 2014– September 30, 2016, followed through March 31, 2018	Not reported	Program coordinators/navigators; SDM; smoking cessation; database	319	Mean age: 64.1 y; female: 49.2%; White: 86.8%, Black: 7.2%, other or not reported: 6.0%; Hispanic/Latino: 1.3%
Stowell et al., 2020 <sup>41</sup>	Academic	Retrospective cohort	LDCCT January 1, 2016– October 17, 2018	USPSTF	Program coordinators/navigators; SDM; data warehouse	1954	Female: 48.1%; White: 90.9%, non-White: 9.1%; current smokers: 56.0%, Medicaid: 25.8%

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Study	Institutional Setting	Study Design	Study Period	LCS Eligibility Criteria	Program Resources	Cohort Size (Patients)	Patient Characteristics
Triplette et al., 2020 <sup>42</sup>	Academic	Retrospective cohort	Baseline LDCT 2012–September 2017, followed through December 2018	Not reported	Database	668	Median age: 63 Y; female: 32.8%; White: 76.8%, Black: 10.5%, Asian: 4.2%, other: 1.9%, not reported: 6.6%; Hispanic/Latino: 1.8%, non-Hispanic/Latino: 84.7%, not reported: 13.5%; current smokers: 54.5%, former smokers: 45.5%; median pack-years: 47 PY; Medicaid: 15.7%, Medicare: 46.0%, private insurance: 26.8%, Medicare plus private: 7.5%, self-pay: 1.0%, not reported: 3.0%
Wemli et al., 2020 <sup>28</sup>	Kaiser Permanente	Retrospective cohort	Baseline LDCT 2015–July	Not reported	Not reported	2274	Not reported 2019

<sup>2</sup>The two studies were essentially the same cohort that only differed in the end date of the study. They were both included because adherence was evaluated for different Lung-RADS categories with Lung-RADS 1 to 2 for Li et al.<sup>37</sup> and Lung-RADS 3 to 4 for Guichet et al.<sup>33</sup>

AATS, American Association for Thoracic Surgery; ACS, American Cancer Society; CMS, Centers for Medicare & Medicaid Services; LCS, lung cancer screening; LDCT, low-dose computed tomography; Lung-RADS, Lung CT Screening Reporting & Data System; NCCN, National Comprehensive Cancer Network; NCI, National Cancer Institute; NLST, National Lung Screening Trial; PY, pack-year; SDM, shared decision-making; USPSTF, United States Preventive Services Task Force; VA, Veterans Affairs.

**Table 2.**

**Adherence Rates in Specified Lung-RADS Categories**

Study	Cohort Size (Patients)	Interventions for Adherence	Lung-RADS Distribution	Patient Characteristics	Definition of Adherence	Defined Adherence Rate	Anytime Adherence Rate
Aishora et al., 2018 <sup>30</sup>	901	Reminder letters, phone calls, PCP involvement	Lung-RADS 1–2: 69.1% Lung-RADS 3: 27.4% Lung-RADS 4: 3.4%	Lung-RADS 1–4: Female: 44.2%; White: >95.0%; current smokers: 45.9%, former smokers: 54.1%	Completion of an annual incidence screen or early follow-up examination within 3 mo of recommended date	Time point: T1 Lung-RADS 1–4: 85.7% Lung-RADS 1–2: 85.6% Lung-RADS 3: 85.0% Lung-RADS 4: 93.5%	Not reported
Angotti et al., 2020 <sup>13</sup>	1444	Centralized component: phone calls, certified letters; decentralized letters; component: PCP involvement, EMR notifications	Not reported	Not reported	Completion of an annual incidence screen in 12 mo ± 60 d for Lung-RADS 1–2; Completion of an early follow-up examination in 6 mo ± 45 d for Lung-RADS 3; Completion of an early follow-up examination in 3 mo ± 30 d for Lung-RADS 4	Time point: T1 <sup>a</sup> Lung-RADS 1–4: 62.1%	Not reported
Barbosa et al., 2020 <sup>25</sup>	570 (number of LDCT scans from 260 patients)	Not reported	Lung-RADS 1: 36.0% Lung-RADS 2: 56.5% Lung-RADS 3: 4.6% Lung-RADS 4A: 1.6% Lung-RADS 4B: 1.1% Lung-RADS 4X: 0.4%	Not reported	Completion of an annual incidence screen or follow-up CT within ±1 mo of recommended date Completion of a PET/CT examination or biopsy within 3 mo of the radiology report date	Time point: multiple Lung-RADS 1–4: 43.0% Lung-RADS 1: 33.2% Lung-RADS 2: 46.3% Lung-RADS 3: 53.9% Lung-RADS 4A: 77.8% Lung-RADS 4B: 83.3% Lung-RADS 4X: 100.0%	Not reported
Bellinger et al., 2020 <sup>31</sup>	268	Reminder letters	Lung-RADS 1: 31.7% Lung-RADS 2: 52.6% Lung-RADS 3: 11.2% Lung-RADS 4: 4.5%	Lung-RADS 1–4: Female: 49.6%; White: 76.1%, Black: 22.4%, not reported: 1.5%; current smokers: 62.7%, former smokers: 37.3%	Completion of an annual incidence screen or early follow-up examination within 2 mo of recommended date	Time point: T1 Lung-RADS 1–4: 48.1% Lung-RADS 1–2: 43.8% Lung-RADS 3–4: 71.4%	Not reported
Bernstein et al., 2019 <sup>26</sup>	631	Not reported	Not reported	Lung-RADS 1–4: Female: 48.7%	Completion of an annual incidence screen or early follow-up examination within 3 mo of recommended date	Time point: T1 Lung-RADS 1–4: 55.8% Lung-RADS 1: 35.1% Lung-RADS 2: 56.8% Lung-RADS 3: 75.5% Lung-RADS 4: 94.0%	Not reported
Bhandari et al., 2019 <sup>3</sup>	1546	Not reported	Not reported	Not reported	Not reported	Not reported	Time point: T1 Lung-RADS 1–2: 49.9%
Brillante et al., 2019 <sup>32</sup>	32	Not reported	Lung-RADS 3: 65.6% Lung-RADS 4: 34.4%	Lung-RADS 3–4: Mean age: 64.8 y; Black:	Not reported	Not reported	Time point: T1 Lung-RADS 3–4:

Study	Cohort Size (Patients)	Interventions for Adherence	Lung-RADS Distribution	Patient Characteristics	Definition of Adherence	Defined Adherence Rate	Anytime Adherence Rate
Cattaneo et al., 2018 <sup>d</sup>	776	Reminder cards, phone calls, PCP involvement	Lung-RADS 1–2: 65.9% Lung-RADS 3–4: 34.1%	75.0%; Medicare/Medicaid: 75.0%  Lung-RADS 1–2: Female: 54.8%; White: 89.0%, Black: 8.6%, other: 2.3%; current smokers: 44.8%, former smokers: 48.3%, not reported: 6.8%; Medicare: 44.0%, private insurance: 49.5%, Medicaid: 2.0%, not reported: 4.5%	Completion of an annual incidence screen or early follow-up examination within 3 mo of recommended date	Time point: T1 Lung-RADS 1–2: 37.4%	65.6% Lung-RADS 3: 52.4% Lung-RADS 4: 90.9%
Deepak et al., 2020 <sup>12</sup>	146 <sup>b</sup>	Not reported	Lung-RADS 1: 46.6% Lung-RADS 2: 42.5% Lung-RADS 3: 5.5% Lung-RADS 4A: 2.7% Lung-RADS 4B: 2.1% Lung-RADS 4X: 0.7%	Not reported	Not reported	Not reported	Time point: T1 <sup>a</sup> Lung-RADS: 49.3% Lung-RADS 1: 58.8% Lung-RADS 2: 43.5% Lung-RADS 3: 37.5% Lung-RADS 4A: 0 Lung-RADS 4B: 66.7% Lung-RADS 4X: 0
Guichet et al., 2018 <sup>33,c</sup>	32	Not reported	Lung-RADS 3: 53.1% Lung-RADS 4: 46.9%	Not reported	Not reported	Not reported	Time point: T1 Lung-RADS 3–4: 75.0%
Hirsch et al., 2019 <sup>34</sup>	259	Reminders by a nurse navigator or PCP	Lung-RADS 1: 62.9% Lung-RADS 2: 37.1%	Lung-RADS 1–2: Mean age: 64.1 y; female: 42.9%; White: 82.6%; current smokers: 54.8%, former smokers: 45.2%; mean pack-years: 48.6 PY; government insurance: 73.7%, private insurance: 23.2%, other: 3.1%	Completion of an annual incidence screen within 6 mo of recommended date	Time point: T1 Lung-RADS 1–2: 50.6%	Not reported
Jacobs et al., 2017 <sup>29</sup>	113 <sup>b</sup>	Not reported	Not reported	Not reported	Not reported	Not reported	Time point: T1 Lung-RADS 3–4: 83.2%
Kaminezky et al., 2019 <sup>35</sup>	663	Not reported	Not reported	Not reported	Not reported	Not reported	Time point: T1, T2, T3 T1 Lung-RADS 1–2: 46.5% T2 Lung-RADS 1–2: 37.8% T3 Lung-RADS 1–2: 37.8%

Study	Cohort Size (Patients)	Interventions for Adherence	Lung-RADS Distribution	Patient Characteristics	Definition of Adherence	Defined Adherence Rate	Anytime Adherence Rate
Lake et al., 2020 <sup>36</sup>	477	Reminder letters, phone calls, PCP involvement	Lung-RADS 1: 38.2% Lung-RADS 2: 47.2% Lung-RADS 3: 9.0% Lung-RADS 4: 5.7%	Lung-RADS 1-4: Mean age: 64.3 y, female: 53.0%; White: 57.9%, Black: 42.1%; current smokers: 57.2%, former smokers: 41.1%, not reported: 1.6%; mean pack-years: 48.5 PY	Completion of an annual incidence screen or early follow-up examination within ±1 mo of recommended date	Time point: T1 Lung-RADS 1-4: 16.6% Lung-RADS 1: 8.8% Lung-RADS 2: 6.7% Lung-RADS 3: 65.1% Lung-RADS 4: 74.1%	2: 27.8% Time point: T1 Lung-RADS 1-4: 30.8% Lung-RADS 1: 18.7% Lung-RADS 2: 20.9% Lung-RADS 3: 90.7% Lung-RADS 4: 100.0%
Li et al., 2020 <sup>37, c</sup>	271	Not reported	Not reported	Not reported	Not reported	Not reported	Time point: T1 Lung-RADS 1-2: 54.2%
Muñoz-Largacha et al., 2018 <sup>27</sup>	42	Not reported	Lung-RADS 4: 100.0%	Lung-RADS 4: Mean age: 64 y; female: 35.7%; White: 57.0%, Black: 24.0%, Hispanic/Latino: 7.0%, Asian: 10.0%, not reported: 2.4%; current smokers: 57.0%, former smokers: 26.0%, not reported: 17.0%; Medicare/Medicaid: 69.0%, private insurance: 31.0%	Not reported	Not reported	Time point: T1 Lung-RADS 4: 97.6%
Plank et al., 2018 <sup>14</sup>	629 <sup>d</sup>	Reminder letters, phone calls, certified letters <sup>a</sup>	Not reported	Not reported	Completion of an annual incidence screen or early follow-up examination within 3 mo of recommended date	Time point: T1 <sup>a</sup> Lung-RADS 1-4: 86.0%	Not reported
Rodriguez et al., 2020 <sup>38</sup>	258	Not reported	Not reported	Not reported	Completion of an annual incidence screen within 3 mo of recommended date	Time point: T1 Lung-RADS 1-2: 31.4%	Not reported
Sakoda et al., 2018 <sup>39</sup>	145	Not reported	Lung-RADS 1-2: 84.1% Lung-RADS 3-4: 15.9%	Lung-RADS 1-4: Median age: 66 y; female: 39.0%; White: 71.0%; current smokers: 76.0%	Completion of an annual incidence screen within 10 to 14 mo for Lung-RADS 1-2; Completion of an early follow-up examination within ±30 d of the recommended date for Lung-RADS 3-4	Time point: T1 Lung-RADS 1-4: 29.0% Lung-RADS 1-2: 23.0% Lung-RADS 3-4: 61.0%	Not reported
Seastedt et al., 2020 <sup>15</sup>	179	Reminder letters, phone calls	Lung-RADS 1: 18.4% Lung-RADS 2: 73.2% Lung-RADS 3: 4.5% Lung-RADS 4: 3.9%	Not reported	Completion of an annual incidence screen or early follow-up	Time point: T1 <sup>a</sup> Lung-RADS 1-4: 77.1% Lung-RADS 1: 81.8%	Not reported



Study	Cohort Size (Patients)	Interventions for Adherence	Lung-RADS Distribution	Patient Characteristics	Definition of Adherence	Defined Adherence Rate	Anytime Adherence Rate
Spalluto et al., 2020 <sup>40</sup>	319	Reminder letters, phone calls	Not reported	Lung-RADS 1-2: Mean age: 64.1 y; female: 49.2%; White: 86.8%, Black: 7.2%, other or not reported: 6.0%; Hispanic/Latino: 1.3%	Completion of an annual incidence screen within 3 mo and 6 mo of recommended date	Time point: T1 Within 3 mo Lung-RADS 1-2: 59.2% Within 6 mo Lung-RADS 1-2: 63.9%	Time point: T1 Lung-RADS 1-2: 73.0%
Stowell et al., 2020 <sup>41</sup>	1954	Not reported	Lung-RADS 1: 20.2% Lung-RADS 2: 64.9% Lung-RADS 3: 14.9%	Lung-RADS 1-3: Female: 48.1%; White: 90.9%, non-White: 9.1%; current smokers: 56.0%; Medicaid: 25.8%	Completion of an annual incidence screen or early follow-up examination within 1 mo or 3 mo of recommended date	Time point: multiple Within 1 mo Lung-RADS 1-3: 39.8% Within 3 mo Lung-RADS 1-3: 55.5%	Not reported
Triplette et al., 2020 <sup>42</sup>	668	Reminder letters	Lung-RADS 1: 23.4% Lung-RADS 2: 57.3% Lung-RADS 3: 9.0% Lung-RADS 4A: 6.1% Lung-RADS 4B: 2.8% Lung-RADS 4X: 1.3%	Lung-RADS 1-4: Median age: 63 y; female: 32.8%; White: 76.8%, Black: 10.5%, Asian: 4.2%, other: 1.9%, not reported: 6.6%; Hispanic/Latino: 1.8%, non-Hispanic/Latino: 84.7%, not reported: 13.5%; current smokers: 54.5%, former smokers: 45.5%; median pack-years: 47 PY; Medicaid: 15.7%, Medicare: 46.0%, private insurance: 26.8%, Medicare plus private: 7.5%, self-pay: 1.0%, not reported: 3.0%	Completion of an annual incidence screen or early follow-up examination within 3 mo of recommended date	Time point: T1 Lung-RADS 1-4: 46.6% Lung-RADS 1: 34.0% Lung-RADS 2: 41.8% Lung-RADS 3: 61.7% Lung-RADS 4A: 85.4% Lung-RADS 4B: 89.5% Lung-RADS 4X: 100.0%	Time point: T1 Lung-RADS 1-4: 70.5%
Wernli et al., 2020 <sup>28</sup>	2274	Not reported	Not reported	Not reported	Completion of an annual incidence screen or early follow-up examination within 3 mo of recommended date	Time point: T1 Lung-RADS 1-2: 31.5% Lung-RADS 3: 51.1%	Not reported

Note: Defined adherence: Adherence was defined as completion of annual incidence screen or early follow-up examination within a specified time interval from recommended date. Anytime adherence: Patients are considered adherent as long as they received a follow-up examination anytime during the course of the study period.

<sup>a</sup>Information/confirmation provided by the authors of the study.

<sup>b</sup>Patients with pending/waiting follow-up imaging examinations were excluded (Deepak et al.<sup>12</sup> excluded N = 20; Jacobs et al.<sup>29</sup> excluded N = 20).

<sup>c</sup>The two studies were essentially the same cohort that only differed in the end date of the study. They were both included because adherence was evaluated for different Lung-RADS categories with Lung-RADS 1 to 2 for Li et al.<sup>37</sup> and Lung-RADS 3 to 4 for Guichet et al.<sup>33</sup>

<sup>d</sup>The authors confirmed that the 86% adherence rate was based on 629 patients (of 825) who were due for their follow-up imaging examination.

CT, computed tomography; EMR, electronic medical record; LDCT, low-dose computed tomography; Lung-RADS, Lung CT Screening Reporting & Data System; PCP, primary care provider; PET, positron emission tomography; T1, T2, and T3, annual incidence screens at 1, 2, and 3 years, respectively.

**Table 3.**

Summary of Predictors of LCS Adherence at T1

Study	Adherence Type	Lung-RADS Categories	Main Findings
Aishora et al., 2018 <sup>30</sup>	Defined	Lung-RADS 1–4	(1) Female patients were more adherent compared with male patients ( $p = 0.035$ ). (2) Patients 65–73 y old were more adherent compared with patients 50 to 64 y old ( $p = 0.040$ ).
Bellinger et al., 2020 <sup>31</sup>	Defined	Lung-RADS 1–4	(1) Patients with Lung-RADS 3 and 4 were more adherent compared with those with Lung-RADS 1 and 2 ( $p < 0.01$ ).
Bernstein et al., 2019 <sup>26</sup>	Defined	Lung-RADS 1–4	(1) Compared with patients with Lung-RADS 1, those with Lung-RADS 2, 3, and 4 were more adherent (Lung-RADS 2: OR = 2.43, 95% CI: 1.66–3.56; Lung-RADS 3: OR = 5.39, 95% CI: 2.71–10.72; Lung-RADS 4: OR = 28.86, 95% CI: 8.60–96.87). (2) Age greater than 65 y was associated with increased adherence ( $p = 0.002$ ). (3) Adherence was higher in patients referred by pulmonary medicine and thoracic surgery than for others ( $p = 0.016$ ).
Hirsch et al., 2019 <sup>34</sup>	Defined	Lung-RADS 1–2	(1) Having a reminder from either a nurse navigator or PCP was associated with increased adherence ( $p < 0.001$ ).
Seastedt et al., 2020 <sup>15</sup>	Defined	Lung-RADS 1–4	Adjusting for race, negative screens, smoking status, and rank. (1) older patients were more adherent than younger patients (OR = 1.43, 95% CI: 1.03–2.01); (2) male patients were more adherent than female patients (OR = 2.57, 95% CI: 1.36–4.87).
Spalluto et al., 2020 <sup>40</sup>	Defined	Lung-RADS 1–2	(1) Hiring a dedicated program coordinator was associated with increased adherence ( $p < 0.005$ ).
Triplette et al., 2020 <sup>42</sup>	Defined	Lung-RADS 1–4	Adjusting for age, race, ethnicity, insurance status, origin of referral, CCI, S category, location, year of enrollment, and presence of tracking intervention. (1) patients with Lung-RADS 3 (OR = 3.8, 95% CI: 1.9–7.7) and Lung-RADS 4 (OR = 14, 95% CI: 6.0–32) were more adherent compared with those with Lung-RADS 1; (2) former smokers were adherent than current smokers (OR 1.7, 95% CI: 1.2–2.5).

Note:  $p$  is Pearson's chi-square test  $p$  value; OR from logistic regression. Defined adherence: Adherence was defined as completion of an annual incidence screen or early follow-up examination within a specified time interval from recommended date; S category: a significant non-lung cancer-related finding.

CCI, Charlson Comorbidity Index; CI, confidence interval; LCS, lung cancer screening; Lung-RADS, Lung CT Screening Reporting & Data System; PCP, primary care provider; T1, annual incidence screen at 1 year.

**Table 4.**

**A Checklist for Reporting LCS Adherence**

<b>Adherence Reporting Variables</b>	<b>No.</b>	<b>Item</b>
Study period	1	State the start date of patient recruitment
	2	State the end date of patient recruitment
	3	State the end date of patient follow-up
Eligibility criteria	4	Specify LCS guidelines for patient eligibility (e.g., USPSTF)
	5	Describe any additional inclusion/exclusion criteria
LCS program resources	6	Indicate if a program coordinator/navigator is part of the LCS program and their responsibilities
	7	Report whether shared decision-making is offered by the LCS program
	8	Indicate whether smoking cessation services are provided, including counseling and treatment
	9	Describe any interventions used by the LCS program to increase adherence (e.g., phone calls, reminder letters, clinician communications)
Screening characteristics	10	Present patient characteristics at each screen (e.g., demographics, smoking status, pack-years, insurance status)
	11	Specify Lung-RADS distribution at each screen
Outcome reporting	12	Provide an objective definition of adherence
	13	State whether patients who died or became ineligible for additional screens during follow-up were labeled as adherent or nonadherent, or excluded from the analysis
Additional data elements	14	Specify screen time point for assessing adherence (e.g., T1: first annual incidence screen after initial screen; early 3 mo follow-up scan)
	15	For each adherence rate, give number of adherent patients (numerator) and total number of patients (denominator)
	16	Provide adherence rates for each individual Lung-RADS category
	17	Report adherence rates in other subgroups (e.g., males vs. females, current vs. former smokers)
	18	List any identified predictors of nonadherence
	19	Summarize reasons for nonadherence

LCS, lung cancer screening; Lung-RADS, Lung CT Screening Reporting & Data System; T1, annual incidence screen at 1 year; USPSTF: United States Preventive Services Task Force.