[ Original Research ]

CHEST

# Tobacco Dependence Predicts Higher Lung Cancer and Mortality Rates and Lower Rates of Smoking Cessation in the National Lung Screening Trial

*Alana M. Rojewski, PhD; Nichole T. Tanner, MD; Lin Dai, PhD; James G. Ravenel, MD; Mulugeta Gebregziabher, PhD; Gerard A. Silvestri, MD; and Benjamin A. Toll, PhD*

**BACKGROUND:** Incorporating tobacco treatment within lung cancer screening programs has the potential to influence cessation in high-risk smokers. We aimed to better understand the characteristics of smokers within a screening cohort, correlate those variables with downstream outcomes, and identify predictors of continued smoking.

**METHODS:** This study is a secondary analysis of the National Lung Screening Trial randomized clinical study. Tobacco dependence was evaluated by using the Fagerström Test for Nicotine Dependence, the Heaviness of Smoking Index, and time to first cigarette (TTFC); descriptive statistics were performed. Clinical outcomes (smoking cessation, lung cancer, and mortality) were assessed with descriptive statistics and $\chi^2$ tests stratified according to nicotine dependence. Logistic and Cox regression models were used to study the influence of dependence on smoking cessation and mortality, respectively.

**RESULTS:** Patients with high dependence scores were less likely to quit smoking compared with low dependence smokers (TTFC OR, 0.50 [95% CI, 0.42-0.60]). Indicators of high dependence, as measured according to all three metrics, were associated with worsening clinical outcomes. TTFC showed that patients who smoked within 5 min of waking (indicating higher dependence) had higher rates of lung cancer (2.07% for $>$ 60 min after waking vs 5.92% $\leq$ 5 min after waking; hazard ratio [HR], 2.56 [95% CI, 1.49-4.41]), all-cause mortality (5.38% for $>$ 60 min vs 11.21% $\leq$ 5 min; HR, 2.19 [95% CI, 1.55-3.09]), and lung cancer-specific mortality (0.55% for $>$ 60 min vs 2.92% for $\leq$ 5 min; HR, 4.46 [95% CI, 1.63-12.21]).

**CONCLUSIONS:** Using TTFC, a one-question assessment of tobacco dependence, at the time of lung cancer screening has implications for personalizing tobacco treatment and improving risk assessment.

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**KEY WORDS:** lung cancer; nicotine dependence; smoking; smoking cessation

**ABBREVIATIONS:** ACRIN = American College of Radiology Imaging Network; FTND = Fagerström Test for Nicotine Dependence; HSI = Heaviness of Smoking Index; HR = hazard ratio; LDCT = low-dose CT; NLST = National Lung Screening Trial; TTFC = time to first cigarette

**AFFILIATIONS:** From the Department of Public Health Sciences (Drs Rojewski, Dai, Gebregziabher, and Toll), Medical University of South Carolina, Charleston, SC; Health Equity and Rural Outreach Innovation Center (HEROIC) (Drs Tanner and Gebregziabher), Ralph H. Johnson VA Medical Center, Charleston, SC; Division of Pulmonary, Critical Care and Sleep Medicine (Drs Tanner and Silvestri), Medical University of South Carolina, Charleston, SC; Hollings Cancer Center (Drs Ravenel, Silvestri, and Toll), Charleston, SC; and the Department of Radiology and Radiologic Sciences (Dr Ravenel), Medical University of South Carolina, Charleston, SC.

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Smoking contributes to 480,000 deaths annually in the United States from causes that include cardiovascular disease and cancer.[1] Lung cancer is the sixth leading cause of death in the United States, with nearly 90% of this cancer caused by cigarette smoking. Tobacco cessation is considered the single most effective primary prevention strategy for reducing the risk of lung cancer death. There is now evidence for secondary prevention, with lung cancer screening as a means to identify lung cancer at an earlier, more treatable stage in patients with extensive smoking histories. Based on the large randomized National Lung Screening Trial (NLST), which reported a 20% reduction in all-cause mortality, the US Preventable Service Task Force now recommends lung cancer screening with low-dose CT (LDCT) scanning for individuals at high risk based on age and smoking history.[2] An estimated eight million Americans are eligible for lung cancer screening.[3]

Many of those presenting for lung cancer screening will be current smokers, as 48% of the 53,454 patients enrolled in the NLST were active smokers at trial entry, and current estimates are that 16.8% of adults smoke cigarettes.[3] A joint policy statement from the American College of Chest Physicians and the American Thoracic Society identified smoking cessation as an essential component of a highly effective and comprehensive lung cancer screening program.[4] Furthermore, to be a lung cancer screening program accredited by the Centers for Medicare & Medicaid Services, smoking cessation must be included. Lung screening is believed to be a teachable moment to promote cessation, but evidence suggests that having a scan increases quit rates only slightly shortly following the scan, and long-term cessation rates are similar for those with both positive and negative lung findings.[5,6] However, detection of a major abnormality from lung cancer screening can lead to higher rates of smoking cessation.[7] It is important to note that one small but potentially troubling study showed that some smokers might view lung cancer screening as a "free pass" to keep smoking.[8] Although the integration of smoking cessation within the context of lung cancer screening has the potential to bolster cessation, little is known about how to best tailor interventions based on screening participants' smoking behaviors.

Cigarette smoking is widely accepted as a dependence disorder,[9] and an individual's level of dependence is predictive of his or her ability to quit smoking.[10,11] The FagerstrÖm Test for Nicotine Dependence (FTND) is a six-item self-report scale commonly used for the measurement of severity of dependence on cigarettes.[12] The Heaviness of Smoking Index (HSI) constitutes two items from the FTND: amount smoked and time to first cigarette (TTFC).[13] All three measures (FTND, HSI, and TTFC) have been shown to predict smoking cessation outcomes, with higher dependence scores corresponding to lower quit rates.[10,11] Greater nicotine dependence may also contribute to lung cancer risk. For example, higher scores on the FTND[14] and, more specifically, the TTFC[15-17] are associated with an increased lung cancer risk, independent of smoking history. Of note, it has recently been shown that assessing nicotine dependence with TTFC can help to classify lung cancer screening patients with regard to their lung cancer risk, which may be helpful in shared decision-making visits and establishing better risk-predictive eligibility criteria for screening.[18]

The present study was conducted to better understand how level of nicotine dependence affects the cessation rates of those undergoing lung cancer screening and to assess its impact on lung cancer diagnosis, all-cause mortality, and lung cancer-specific mortality. By identifying predictors of continued smoking, we aim to inform effective cessation efforts as they are integrated and implemented into lung cancer screening programs.

## Subjects and Methods

This study was approved by the Medical University of South Carolina Institutional Review Board (No. 00054733). It is a secondary analysis of subjects from the American College of Radiology Imaging Network (ACRIN) arm of the NLST randomized controlled trial.

### Participants

The NLST enrolled 53,452 current and former (quit within 15 years) smokers ages 55 to 74 years with a minimum of a 30 pack-year cigarette smoking history.[3] Participants were randomized to three rounds of annual screening with LDCT or chest radiography. The ACRIN arm of the NLST (n = 14,125) was selected for analysis because this subset completed more detailed smoking questionnaires on variables of interest (eg, nicotine dependence) than the other NLST participants. Because the focus of this endeavor was on how current nicotine dependence related to medical outcomes, the

**CORRESPONDENCE TO:** Alana M. Rojewski, PhD, Department of Public Health Sciences, 135 Cannon St, MSC 835, Charleston, SC 29425; e-mail: rojewski@musc.edu

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