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Stakeholder Research Priorities for Smoking Cessation Interventions within Lung Cancer Screening Programs:

An Official American Thoracic Society Research Statement

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Abstract

Rationale: Smoking cessation counseling in conjunction with low-dose computed tomography (LDCT) lung cancer screening is recommended in multiple clinical practice guidelines. The best approach for integrating effective smoking cessation interventions within this setting is unknown.

Objectives: To summarize evidence, identify research gaps, prioritize topics for future research, and propose standardized tools for use in conducting research on smoking cessation interventions within the LDCT lung cancer screening setting.

Methods: The American Thoracic Society convened a multistakeholder committee with expertise in tobacco dependence treatment and/or LDCT screening. During an in-person meeting, evidence was reviewed, research gaps were identified, and key questions were generated for each of three

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research domains: (*1*) target population to study; (*2*) adaptation, development, and testing of interventions; and (*3*) implementation of interventions with demonstrated efficacy. We also identified standardized measures for use in conducting this research. A larger stakeholder panel then ranked research questions by perceived importance in an online survey. Final prioritization was generated hierarchically on the basis of average rank assigned.

Results: There was little consensus on which questions within the population domain were of highest priority. Within the intervention domain, research to evaluate the effectiveness in the lung cancer screening setting of evidence-based smoking cessation interventions shown to be effective in other contexts was ranked highest. In the implementation domain, stakeholders prioritized understanding strategies to identify and overcome barriers to integrating smoking cessation in lung cancer screening settings.

Conclusions: This statement offers an agenda to stimulate research surrounding the integration and implementation of smoking cessation interventions with LDCT lung cancer screening.

Keywords

research priorities; lung cancer screening; smoking cessation; tobacco dependence treatment; LDCT screening

Overview

Smoking cessation counseling and treatment are critical corollaries to low-dose computed tomography (LDCT) screening, offering an opportunity to reduce smoking-related mortality. Although the Centers for Medicare and Medicaid Services (CMS) requires that smoking cessation interventions be delivered in conjunction with lung cancer screening for Medicare reimbursement of LDCT screening, neither the most effective interventions nor the best approach for implementing those interventions with demonstrated efficacy in this setting is known. This research policy statement identifies consensus prioritization of diverse stakeholders regarding three topics for research on smoking cessation interventions in the context of LDCT screening: (*1*) target population to study; (*2*) adaptation, development, and testing of potential interventions; and (*3*) implementation of interventions with demonstrated efficacy. In each of these three domains, we summarize the existing evidence; identify research gaps; and, on the basis of a formal process of consensus development, prioritize research questions. The fourth section presents our committee's recommendations for standardized tools and measures to use in conducting this research. This statement offers a research agenda to inform investigators as well as governmental and nongovernmental funding agencies to generate high-priority, high-quality research surrounding integration of tobacco dependence treatment with LDCT screening.

Key Conclusions and Recommendations

Population domain.

- Although there was little consensus on which questions within the population domain were of the highest priority, research in this area should consider addressing how LDCT screening results (positive or negative test results) affect

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motivation to quit and the resultant impact on effectiveness of cessation, because it was ranked highest by stakeholder representatives.

Intervention domain.

- There is little data on the effectiveness of smoking cessation interventions in the LDCT screening setting, leaving significant knowledge gaps regarding the optimal method of smoking cessation counseling, timing of delivery, and pharmacotherapy approaches in this context.
- Research to evaluate the effectiveness of established, evidence-based interventions for smoking cessation in lung cancer screening settings ranked highest among stakeholder representatives.

Implementation domain.

- There is scant data on the implementation of smoking cessation interventions into lung cancer screening programs.
- A national research agenda should include strategies for implementing tobacco dependence treatment within the lung cancer screening setting.
- Stakeholders prioritized determining the system barriers to integrating smoking cessation in lung cancer screening settings, as well as researching effective strategies to overcome these barriers.

Standardized tools and measures.

- There was strong consensus among committee members that using standardized tools, measures, and outcomes in this research would increase the quality of the science and the ability to interpret and pool results of different studies.
- Applicable standardized measures and tools are outlined in this statement to provide scientists the tools with which to conduct high-quality research in this setting.

Introduction

Lung cancer is the leading cause of cancer death in the United States (1, 2). Over 90% of lung cancer deaths would be avoided if Americans never initiated cigarette smoking. Quitting smoking is the most effective intervention to reduce lung cancer mortality (3, 4); yet, approximately 36.5 million Americans continue to smoke cigarettes (2, 5). Current smokers between the ages of 55 and 64 years would gain 4 years of life expectancy from avoided lung cancer and other tobacco-related deaths if they quit smoking (6). Among current smokers, the number needed to intervene is as low as 77 because providing cessation interventions to 11 individuals leads to at least 1 additional successful quitter (7), and depending on age and sex, 1 early death from all tobacco-related causes can be avoided by helping as few as 7 individuals quit smoking, even among middle-aged and older adults (8). Despite the fact that nearly 70% of current smokers attempt to quit each year, only 1 to 6% of smokers are successful in quitting (9, 10).

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The other intervention proven to reduce lung cancer mortality is annual LDCT screening of middle-aged and older smokers with a substantial history of tobacco use, which is associated with a gain of 0.04 years of life expectancy from avoided lung cancer deaths (11, 12). The number needed to screen is 320 to prevent 1 early lung cancer death (11, 12). In the NLST (National Lung Screening Trial), individuals in the LDCT screening arm who successfully quit smoking had the lowest rate of lung cancer deaths (13). Thus, providing smoking cessation treatment in conjunction with LDCT screening offers an opportunity to combine two interventions known to reduce smoking-related morbidity and mortality.

Recognizing the importance of helping adults quit smoking, the CMS requires that smoking cessation interventions be offered to receive Medicare reimbursement of LDCT screening. Similarly, multiple professional organizations and the U.S. Preventive Services Task Force recommend that smoking cessation interventions be delivered in conjunction with LDCT screening (14). Yet, neither the most effective interventions nor the best approach for implementing those interventions with demonstrated efficacy in this setting is known.

The National Institutes of Health (NIH); the National Academies of Science, Engineering, and Medicine; the Association for the Treatment of Tobacco Use and Dependence; and the Society for Research on Nicotine and Tobacco have all highlighted the need for research on optimal strategies to integrate smoking cessation interventions within LDCT screening programs (15–17). In this research statement, we discuss the methodology and development of a stakeholder-endorsed research priority agenda relating to tobacco dependence treatment in LDCT screening programs.

Methods

The committee chair (H.K.) and cochair (R.S.W.) convened a team with expertise in LDCT screening and/or tobacco dependence treatment (Table 1). The team included multiple stakeholders representing the perspectives of scientists conducting translational, clinical, cost-effectiveness, implementation science, and health services research; governmental and nongovernmental funding agencies; professional societies; clinicians (physicians, nurses, and health educators specializing in pulmonary medicine, thoracic surgery, and/or tobacco dependence treatment); and patients. To understand diverse contexts and strategies for implementing smoking cessation treatment within LDCT screening programs, we selected individuals representing various clinical settings, including academic centers, community hospitals, integrated health systems, and the Veterans Health Administration. Potential conflicts of interest were disclosed and managed in accordance with the policies and procedures of the American Thoracic Society (ATS).

Our committee met in person at the May 2016 ATS International Conference. Designated moderators led group discussions on four topics: the effect of screening on smoking cessation, interventions for smoking cessation in the LDCT screening setting (not including interventions at the policy level), implementation of smoking cessation interventions in the LDCT screening setting, and standardized tools and measures to conduct research on smoking cessation interventions in the setting of LDCT screening. For each of these topics, the moderator summarized the existing evidence (based on primary literature and recent

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systematic reviews) and identified critical gaps. Through discussion, the committee compiled several draft research questions in three areas: (*1*) target population to study; (*2*) adaptation, development, and testing of potential interventions; and (*3*) implementation of interventions with demonstrated efficacy. For the fourth topic, we discussed existing tools and measures to conduct high-quality research on smoking cessation and compiled lists of resources for investigators working in this area.

Following the in-person meeting, the chairs further refined the draft research questions to eliminate redundancy, with assistance from committee members. We then came to consensus through group discussion on 7 questions in each of the three topics (21 questions total) to be posed to a larger group of stakeholder representatives (Table 1) for prioritization through a subsequent online survey. We identified stakeholders with expertise in tobacco dependence treatment, inviting all members of the ATS Tobacco Action Committee as of August 1, 2016. We also identified stakeholders with expertise in LDCT screening by recruiting from among experts who participated in the July 2016 National Academies of Science, Engineering, and Medicine Workshop on Implementation of Lung Cancer Screening. Finally, stakeholders with expertise in both tobacco dependence treatment and LDCT screening were identified by chairs and committee members and invited to participate in the online survey. In total, 77 stakeholders, who included representatives from payers, government and nongovernment agencies, patient advocacy groups, funding agencies, academic hospitals, government hospitals, integrated health systems, and physician and nonphysician professional organizations, were invited to participate in the online survey. Including our committee members, a total of 43 participants (56%) participated in the online survey (Table 1). Each stakeholder was asked to rank topics from 1 (most important) to 7 (least important) in each of the three topic areas, with no ties between questions within a given topic area (i.e., each question had to be assigned a unique rank). The final prioritization of questions was generated hierarchically on the basis of average rank assigned (lowest to highest).

The chairs drafted the initial version of the manuscript of this document with assistance from committee members. The manuscript was circulated to the full committee and iteratively revised. The final document was approved by the ATS Board of Directors.

Results

The results are organized into four sections designed to help scientists and funding agencies conduct and assess research related to integration of smoking cessation interventions with LDCT screening. The first three sections correspond to the three topics in which questions were prioritized: (*1*) target population to study; (*2*) adaptation, development, and testing of potential interventions; and (*3*) implementation of interventions with demonstrated efficacy. The fourth section presents our committee's recommendations for standardized tools and measures to conduct this research.

Target Population to Study (Who?)

Summary of evidence and research gaps.—The existing literature provides a rationale for studying smoking cessation interventions in specific populations. Within the NLST, current smokers, those with less than a high school education, and black individuals

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had higher rates of lung cancer death (13). Certain groups, including socioeconomically disadvantaged groups, individuals with comorbid substance use or psychiatric disorders, and certain racial and ethnic minorities, are less likely to be offered, to use, and to successfully complete evidence-based tobacco dependence treatment (10, 18–20). It has been suggested that LDCT screening may provide a "teachable moment" for these underserved smokers and an opportunity to offer smoking cessation interventions at a time when these individuals are more cognizant of the potential harms of smoking and thus more likely to be receptive to interventions (21, 22).

Recommendations and clinical practice guidelines to date have not consistently endorsed the allocation of intervention resources to subgroups of smokers on the basis of patient factors such as motivation to quit or self-efficacy. In the Danish Lung Cancer Screening Trial, higher motivation to quit at baseline predicted smoking status both 1 year after screening and at the end of a 5-year screening program (23, 24). Several other factors, such as older age, poorer lung function, greater perceived advantages of quitting, and higher self-efficacy, were associated with abstinence at 1 year (23, 25). Historically, providers and quitlines have been encouraged to identify a patient's willingness to quit and provide cessation treatment only to those patients who have a clear intent to quit (26). However, recent trials have suggested that providing cessation treatment to all smokers, regardless of their current willingness to quit, may help more smokers quit (26).

Other populations that may be of particular interest for study are defined by the results of LDCT screening. Two recent systematic reviews showed that undergoing LDCT screening in itself is not sufficient to achieve long-term smoking abstinence (27, 28). On one hand, however, there is some evidence that positive LDCT screening results (e.g., detection of nodules) are associated with increases in quit rates and in reducing relapse among recent quitters (23, 24, 27, 29). On the other hand, screening may have paradoxical effects because others with a screen-detected nodule may be too scared or anxious to tackle quitting smoking (30), and patients with a normal LDCT screening result may feel little urgency to quit (31). Of note, among all persons screened, 80 to 86% have a normal or low-risk result (American College of Radiology Lung CT Screening Reporting and Data System ["Lung-RADS"] category 1 or 2) (32, 33).

Stakeholder prioritization of research questions.—Of 43 stakeholders, 37 ranked questions relating to "population to study." This first domain includes questions that investigate the subgroups of patients (moderators) with greatest intervention efficacy. Voting results indicated that four of the seven questions were ranked as most or second most important by nearly equal numbers of experts. Mean rank scores across all seven questions showed little variability in mean scores (range, 3.43–4.73; possible range, 1 = most important to 7 = least important) (Table 2).

Adaptation, Development, and Testing of Potential Interventions (What and When?)

Summary of evidence and research gaps.—There is little data on the effectiveness of smoking cessation interventions in the LDCT screening setting (25, 34–39), leaving significant knowledge gaps regarding the optimal method of smoking cessation counseling,

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timing of delivery, and pharmacotherapy approaches in this context. Overall, in screened patients, more intensive interventions appeared to be associated with greater improvement in 6-month smoking abstinence and readiness to quit. In one retrospective case–control study analyzing self-reported physician interventions and quit rates by NLST participants, using the U.S. Public Health Service–recommended "5 A's" approach, the "assist" (connecting smokers with evidence-based treatment) and "arrange follow-up" steps increased the odds of quitting by 40 and 46%, respectively (25). To our knowledge, no studies to date have evaluated the utility and safety of novel approaches such as electronic nicotine delivery systems as a bridge to quitting, financial incentives, mobile technology–based interventions, or patient navigation for smoking cessation in the context of LDCT screening.

Prioritization of research questions.—Of the 43 stakeholders, 36 ranked seven questions relating to "intervention to study." Final voting results indicated that researching "the effectiveness of established, evidence-based interventions for smoking cessation in lung cancer screening settings" was a strong priority based on stakeholder rankings in this area (mean score, 2.86; possible range, 1 = most important to 7 = least important) (Table 3). By contrast, the lowest-ranked question, "What is the optimal intensity of smoking cessation interventions in lung cancer screening setting? What is the comparative effectiveness of interventions that vary in intensity?" received a ranking of 5.03.

Implementation of Interventions with Demonstrated Efficacy (How?)

Summary of evidence and research gaps.—There is scant data on the implementation of smoking cessation interventions into LDCT screening programs; this has been identified as an area for further research (40–42). LDCT screening programs vary in terms of resources and referral pathways for providing smoking cessation interventions. A recent national survey suggested that most LDCT screening programs do not currently offer guideline-based tobacco dependence treatment (42). For example, NLST participants reported that their primary care providers only partially followed the U.S. Public Health Service–recommended "5 A's" recommendations: Whereas the majority "asked," "advised," and "assessed," only half "assisted" smokers in connecting to treatment, and only 10% "arranged follow-up" (25). Little research has been done to explore the barriers to, facilitators of, and most effective implementation strategies for delivering smoking cessation interventions in the LDCT screening setting.

Prioritization of research questions.—Of 43 stakeholders, 35 ranked seven questions relating to implementation. Final voting results indicate that "What are the system barriers to integrating smoking cessation in lung cancer screening settings, and what are the effective strategies to overcome these barriers?" and "What are effective strategies for implementing, disseminating, and scaling up cessation interventions in the real world?" received similar priority rankings (3.06 and 3.17, respectively), with little separation in priority scores between the two (Table 4). By contrast, the lowest-ranked topic had a priority score of 5.49.

Standardized Tools and Measures to Conduct High-Quality Research

There was strong consensus among committee members that using standardized tools, measures, and outcomes in this research would increase the quality of the science and the

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ability to interpret and pool results of different studies. Other professional organizations have issued recommendations about measures of tobacco abstinence and biochemical confirmation in conducting trials of smoking cessation interventions, which our committee agreed would be applicable in the context of LDCT screening as well.

Recommended measures and other considerations for smoking cessation trials.—Standards for measurement are provided in three existing documents issued by other groups: (*1*) the Society for Research on Nicotine and Tobacco Task Force (43), (*2*) West and colleagues (the Russell Standard) (44), and the (*3*) Smoking Cessation at Lung Examination (SCALE) Collaboration (45). The recommendations of the Society for Research on Nicotine and Tobacco and Russell Standard documents on abstinence measures are summarized in Figure 1. The SCALE Collaboration is a National Cancer Institute (NCI)-sponsored initiative to develop and test smoking cessation interventions in the setting of LDCT screening; recommended consensus measures in the domains of demographics and psychological characteristics, medical characteristics and outcomes, tobacco use behavior, implementation, and organizational characteristics from the SCALE Collaboration are summarized in Table E1 in the online supplement. To facilitate research collaboration in this setting, the SCALE panel of 19 funded investigators and NCI scientists formed work groups within content areas. Groups convened in person at facilitated meetings and/or by teleconference over a 2-month period (October–December 2016) to reach consensus on the selection of the most important measures for smoking cessation trials in the LDCT screening context. The following measures are publicly available:

- Demographics (date of birth, sex, race, ethnicity, education, and income)
- Psychological characteristics (depressive symptoms, measured by the K-6 [46])
- Perceived risk of developing lung cancer (“How likely do you think it is that you will develop lung cancer in your lifetime?” and “Compared with other smokers, what do you think your chance of getting lung cancer is in your lifetime?”)
- Lung cancer worry (“How worried are you about getting lung cancer in your lifetime?”)
- Family history of lung cancer
- Family history of any cancer
- The Fagerström Test for Nicotine Dependence (47)
- The cessation Contemplation Ladder (48)
- Confidence/self-efficacy to quit (49)
- History of other tobacco use (50)
- Smoking status (“Have you smoked a cigarette, even a puff, in the past 7 days?” and “Have you smoked a cigarette, even a puff, in the past 30 days?”)

Consensus measures also include implementation measures, medical outcomes, and organizational characteristics (Table E1). The full measure collection is publicly available in the NCI Grid-Enabled Measures Database (45). The NCI Grid-Enabled Measures Database

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is an interactive website that contains behavioral and social science measures organized by theoretical constructs. The NIH-funded Patient-Reported Outcomes Measurement Information System comprises a set of person-centered measures that are used to evaluate and monitor physical, mental, and social health (www.healthmeasures.net). Both are useful resources for developing instruments for smoking cessation trials.

These three groups (Society for Research on Nicotine and Tobacco Task Force, West and colleagues [44], and the SCALE Collaboration) agree that abstinence from tobacco use is the most important outcome to measure when evaluating the clinical effectiveness of a smoking cessation intervention. Outcomes measured at a longer duration from the intervention (e.g., 6-mo or 1-yr quit rates) are considered more robust than outcomes measured at a shorter interval (e.g., 1-mo quit rates). When feasible, biochemical confirmation should be obtained. Biochemical markers include cotinine, carbon monoxide, 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol (NNAL), or anabasine and anatabine (Table 5).

Use of standardized measures of exposures is also important for interpretation of research results in smoking cessation trials. The National Human Genome Research Institute, with cofunding by the National Institute on Drug Abuse, has developed a publicly available Web-based resource, the PhenX Toolkit (www.phenxtoolkit.org) (51), which compiles high-quality standard measures of phenotypes and environmental exposures for use in biomedical research. The Food and Drug Administration's Center for Tobacco Products and the NIH Tobacco Regulatory Science Program are expanding the tobacco-related measures in the PhenX Toolkit. This toolkit currently includes measures relevant to tobacco research, such as (*1*) demographic measures; (*2*) descriptive, behavioral, or biological measures that characterize tobacco product use; (*3*) measures that characterize intrapersonal factors that influence product use; and (*4*) protocols and assays for tobacco smoke products. Examples of the measures available via this Web-based resource that are relevant to this policy statement are shown in Table E2.

Study design is an important consideration when generating high-quality research. Although the randomized controlled trial are the only study design that can be used to measure efficacy directly, observational designs may be particularly useful in evaluating smoking cessation interventions. For example, randomized controlled trial participants must have enough desire to enroll in the trial, potentially limiting generalizability to the many patients who are not currently interested in quitting. The ATS developed a statement on comparative effectiveness research that may help researchers and funders decide when nonrandomized designs may be most helpful in smoking cessation studies (52).

Discussion

Under the auspices of the ATS, our committee employed a formal process of consensus development to produce a national research agenda for smoking cessation interventions within LDCT screening programs in collaboration with a diverse set of stakeholders. A complete list of stakeholder-endorsed research priorities is available in Tables 2–4. Stakeholder preferences were strongest for the following questions within each domain:

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- *Population*: How do LDCT screening results (positive or negative test results) affect motivation to quit, and what is the resultant impact on the effectiveness of cessation?
- *Intervention*: What is the effectiveness of established, evidence-based interventions for smoking cessation in lung cancer screening settings?
- *Implementation*: What are the system barriers to integrating smoking cessation in lung cancer screening settings, and what are the effective strategies to overcome these barriers?

In comments and discussions with voting members, researching how LDCT screening results affect motivation to quit, as well as the resultant impact on effectiveness of cessation, was prioritized within the population domain because it is likely to influence how screening providers communicate with patients about their results and provide messages about smoking cessation. Whereas the CMS highlights the importance of integrating smoking cessation counseling in the initial shared decision-making conversation about screening, the voting members highlighted that post-screening messaging and interventions related to smoking cessation may also be a critical priority.

Within the intervention domain, the topic of developing an evidence base for understanding how established interventions that have been demonstrated to be effective in other settings perform in the LDCT screening context was prioritized in part because screening providers are eager to ensure that the cessation interventions they provide are effective in this setting. Many voting members emphasized that providing the most effective care possible is a priority and should be guided as much as possible by research evidence. Within the implementation domain, stakeholders identified that a clear challenge to increasing smoking cessation within the LDCT screening setting is ensuring that evidence-based interventions are fully implemented. As highlighted by Park and colleagues, less than 10% of providers fully provided cessation services, in part because of limitations of clinician time and resources (25). To maximally reduce lung cancer mortality, it is critical to overcome barriers to referring high-risk smokers for both LDCT screening and tobacco dependence treatment and to support implementation of full-service LDCT screening programs capable of providing evidence-based tobacco dependence treatment.

Stakeholders were more consistent across rankings for the domains of intervention and implementation, in each case prioritizing one or two questions as clear priorities, whereas rankings were more widely dispersed across the questions within the population domain. Of note, multiple stakeholders contacted the chairs to comment on how difficult it was to rank these questions because they considered all of them important, and not all stakeholders ranked questions in all domains, which may similarly indicate difficulty in assigning relative priority to the questions. Nonetheless, each topic represents the consensus prioritization of diverse stakeholders and provides an agenda for research on smoking cessation interventions in the context of LDCT screening.

This research is urgently needed, as recognized by multiple organizations, including the NIH and the National Academies of Science, Engineering, and Medicine (17, 53). The NCI recently awarded six R01 grants to develop and test smoking cessation interventions for

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current smokers undergoing LDCT lung cancer screening (45, 53). The standardized measures and approaches outlined in this document provide scientists the tools with which to conduct high-quality studies using a variety of methods (explanatory trials, pragmatic trials, mixed methods, comparative effectiveness) to answer these questions and to assess mechanisms through which intervention effects may occur (mediators such as psychological characteristics, perceived lung cancer risk, self-efficacy/confidence to quit). This statement provides a road map for scientists and government and nongovernment funding agencies to use in generating high-priority, high-quality research to answer pressing questions surrounding integration of tobacco dependence treatment within LDCT screening screenings. We hope this statement will stimulate the research needed to provide answers to clinicians and administrators seeking to deliver effective smoking cessation interventions to smokers undergoing LDCT screening, thereby improving care and ultimately reducing lung cancer mortality.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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SRNT (43): A workgroup formed by the Society for Research on Nicotine and Tobacco (SRNT) reviewed the literature on abstinence measures used in trials of smoking cessation interventions and recommended that trials report on multiple measures of abstinence, with a minimum of the following:

- Report prolonged abstinence (i.e., sustained abstinence after an initial period in which smoking is not counted as a failure) as the preferred measure, plus point prevalence as a secondary measure
- Use 7 consecutive days of smoking or smoking on ≥1 day of 2 consecutive weeks to define treatment failure
- Include non-cigarette tobacco use, but not nicotine medications in definitions of failure
- Report results from survival analysis to describe outcomes more fully.

The SRNT task force recommends additional considerations in certain circumstances:

- Trials of smokers willing to set a quit date:
  Follow-ups should be tied to the quit date and 6- and/or 12-month abstinence rates should be provided.
  An initial 2-week grace period for prolonged abstinence definitions; however, the period may vary, depending on the presumed mechanism of the treatment.
- Trials of smokers who may not be currently trying to quit:
  Follow-up should be tied to the initiation of the intervention and should report a prolonged abstinence measure of ≥6-month duration and point prevalence rates at 6- and 12-month follow-ups.
  The grace period for these trials will depend on the time necessary for treatment dissemination, which will vary depending on the treatment, setting, and population.
- Trials that use short-term follow-ups (≤3 months) to demonstrate possible efficacy:
  A prolonged abstinence measure of ≥ 4 weeks should be reported.
  Recommend a 2-week grace period; however, that period can vary.

Russell Standard (RS) criteria (44): Applicable to trials of cessation aids where participants have a defined target quit date and there is face to face contact with researchers or clinic staff. *Where there is no face to face contact with participants, the requirement for biochemical verification may be impracticable but the other criteria outlined below should still apply.*

- Follow up for 6 months or 12 months from the target quit date or the end of a pre-defined grace period
- Self-report of smoking abstinence over the whole follow-up period allowing up to 5 cigarettes in total.
- Biochemical verification of abstinence at least at the 6-month or 12-month follow up point.
- Use of an intention to treat approach in which data from all randomized smokers are included in the analysis unless they have died or moved to an untraceable address (participants who are included in the analysis are counted as smokers if their smoking status at the final follow-up cannot be determined)
- Following up protocol violators and using their true smoking status in the analysis
- Collecting follow up data blind to smokers' allocation to trial groups

Figure 1.
Summary of recommendations for trials of smoking cessation interventions.

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Table 1.

Stakeholder Representatives and Affiliations

Representative	Affiliation	Specialty	Expertise	
			Smoking Cessation	LDCT Screening
Individuals with expertise identified by chairs				
Chunxue Bai	Zhongshan Hospital, Fudan University, China	Pulmonology		x
Belinda Borrelli	Boston University	Health psychology	x	
Frank C. Detterbeck *	Yale University	Thoracic surgery		x
Tom Glynn	Stanford University	Tobacco control	x	
Michael K. Gould *	Kaiser Permanente	Pulmonology		x
Joelle T. Fathi *	Swedish Cancer Institute	Nursing	x	x
Denise G. Jolicoeur *	University of Massachusetts Medical School	Health educator	x	
Hasmeena Kathuria *	Boston University	Pulmonology	x	x
Peter J. Mazzone *	Cleveland Clinic	Pulmonology		x
Georgia L. Narsavage	University of South Carolina	Nursing		x
Gerard A. Silvestri *	Medical University of South Carolina	Pulmonology	x	x
Christopher G. Slatore *	VA Portland Health Care System	Pulmonology	x	x
M. Patricia Rivera	University of North Carolina at Chapel Hill	Pulmonology		x
Martin Tammemagi	Brock University, Canada	Epidemiology		x
Anil Vachani *	University of Pennsylvania	Pulmonology	x	x
Carlijn van der Aalst	Erasmus MC, the Netherlands	Pulmonology	x	x
Juan Wisnivesky	Icahn School of Medicine at Mount Sinai	Pulmonology	x	x
Renda Soylemez Wiener *	Bedford VA Medical Center/Boston University	Pulmonology		x
Steven B. Zeliadt *	VA Puget Sound Health Care System	Health economist	x	x
Funding agencies				
Stephanie R. Land *	National Cancer Institute	Tobacco control		
Greta M. Massetti *	CDC			
Patients and patient advocacy groups				
Kathleen Fennig *	Patient representative			
Robert A. Smith *	American Cancer Society			
Additional stakeholders identified through other sources				
ATS Tobacco Action Committee				
Michelle Eakin	Johns Hopkins University			
Harold Farber	Texas Children’s Hospital			
Patricia Folan	Northwell Health			
Frank Leone	University of Pennsylvania			
Farzad Moazed	University of California, San Francisco			
Smita Pakhale	Ottawa Hospital Research Institute			

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Representative	Affiliation	Specialty	Expertise	
			Smoking Cessation	LDCT Screening
National Academy of Sciences Implementation of Lung Cancer Screening Workshop				
Caroline Chiles	Wake Forest Baptist Health Center			
Angela Criswell	Lung Cancer Alliance			
Richard Hoffman	University of Iowa			
Ella Kazerooni	University of Michigan			
Jane Kim	Durham VA Medical Center/Duke University			
Kelly Latimer	U.S. Naval Hospital Sigonella, Italy			
Michael LeFevre	University of Missouri			
Ide Mills	Patient advocate			
Elyse Park	Massachusetts General Hospital			
Joshua Roth	Fred Hutchinson Cancer Research Center			
Jamie L. Studts	University of Kentucky College of Medicine			
Helene Vitella	Bristol-Myers Squibb Co.			
Awardees of NCI Request for Applications on Smoking Cessation Interventions in LDCT Screening				
Kristie Foley	Wake Forest School of Medicine			
David Midthun	Mayo Clinic			
Kathryn Taylor	Georgetown University			
Benjamin Toll	Medical University of South Carolina			

Definition of abbreviations: ATS = American Thoracic Society; LDCT = low-dose computed tomography; NCI = National Cancer Institute; VA = Department of Veterans Affairs.

* Indicates the individual was a member of the American Thoracic Society committee tasked with generating this statement.

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Table 2.

Stakeholder Prioritization of Questions: Population to Study (n = 37)

Final Rank	Question	Mean Score	Percentage Who Ranked 1 or 2
1	How do LDCT screening results (positive or negative test results) affect motivation to quit, and what is the resultant impact on effectiveness of cessation?	3.43	37.8%
2	How do patients' beliefs, attitudes, and perceived or real barriers to quitting impact the effectiveness of cessation interventions in the context of lung cancer screening?	3.49	32.4%
3	How does motivation to quit impact the effectiveness of cessation interventions in lung cancer screening? What approaches are most effective among smokers with low motivation to quit?	3.68	32.4%
4	Who benefits the most from evidence-based interventions for smoking cessation in lung cancer screening? Evidence-based cessation interventions include counseling, nicotine replacement, and other pharmacotherapy, alone or in combination.	4.11	32.4%
5	What are the characteristics of populations for whom evidence-based cessation interventions are not effective? Examples might include smokers with comorbid mental health, physical, or substance use disorders; individuals of low socioeconomic status; or members of racial or ethnic minority groups.	4.14	21.6%
6	For patients who undergo a shared decision-making visit about lung cancer screening and decide not to get screened, what is the effectiveness of smoking cessation interventions, and how does it vary from patients who do undergo lung cancer screening?	4.43	24.3%
7	For patients who recently quit smoking, how does lung cancer screening impact smoking relapse and patients' motivation to stay quit?	4.73	18.9%

Definition of abbreviation: LDCT = low-dose computed tomography.

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Table 3.

Stakeholder Prioritization of Questions: Intervention to Study (n = 36)

Final Rank	Question	Mean Score	Percentage Who Ranked 1 or 2
1	What is the effectiveness of established, evidence-based interventions for smoking cessation in lung cancer screening settings? Evidence-based cessation interventions include counseling, nicotine replacement, and other pharmacotherapy, alone or in combination.	2.86	52.8%
2	What are the most effective strategies for counseling patients to quit smoking in the lung cancer screening setting? (In other words, is it necessary to tailor messaging to this setting, and if so, what are the essential elements to be included in messaging in the lung cancer screening setting?)	3.25	41.7%
3	What is the most effective platform to promote use of evidence-based cessation interventions in lung cancer screening settings? Examples of platforms include patient navigators, health maintenance alerts, and texting.	3.89	33.3%
4	How effective are novel/innovative smoking cessation interventions in lung cancer screening settings compared with established, evidence-based interventions for smoking cessation? Examples of novel innovative interventions include mobile health applications, e-cigarettes, and financial incentives.	4.11	27.8%
5	Among patients who do not benefit from generic evidence-based cessation interventions, is an intervention tailored to their specific needs more effective?	4.22	11.1%
6	How does the effectiveness of smoking cessation interventions in lung cancer screening vary depending on when they are delivered (e.g., before vs. after screening; cessation offered at one time point vs. at multiple time points longitudinally)?	4.64	19.4%
7	What is the optimal intensity of smoking cessation interventions in lung cancer screening? What is the comparative effectiveness of interventions that vary in intensity?	5.03	13.9%

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Table 4.

Stakeholder Prioritization of Questions: Implementation (n = 35)

Final Rank	Question	Mean Score	Percentage Who Ranked 1 or 2
1	What are the system barriers to integrating smoking cessation in lung cancer screening settings, and what are the effective strategies to overcome these barriers? For example, what are the strategies to address issues with time and resource constraints, reimbursement issues, and opportunities to use technology/EMRs?	3.06	45.7%
2	What are effective strategies for implementing, disseminating, and scaling up cessation interventions in the real world? How do feasibility, reach, cost, patient/provider engagement, fidelity, and ease of delivery impact dissemination with quality?	3.17	45.7%
3	Which platforms to promote smoking cessation can be most easily integrated and have the lowest barriers to adoption in the lung cancer screening setting? Examples include texting, phone counseling, quit lines, and in-person visits	3.26	34.3%
4	What are the scalable, reproducible models for training that maximize provider effectiveness for smoking cessation in lung cancer screening?	3.91	25.7%
5	Which professionals are most effective at delivering smoking cessation interventions in lung cancer screening? Examples include primary care providers, peer navigators, nurses, and a team approach.	4.17	22.9%
6	How do provider characteristics influence the effectiveness of smoking cessation interventions in the context of lung cancer screening? Examples of provider characteristics include perceptions of the evidence for cessation interventions; competing priorities; communication skills, bias, and attitudes regarding smoking; and knowledge about and training in smoking cessation interventions.	4.94	14.3%
7	How do site characteristics impact the effectiveness of cessation interventions in lung cancer screening? Examples of site characteristics include comprehensive screening programs versus *ad hoc* screening, sites that permit self-referral compared with those that accept only provider-referred patients, reimbursement for cessation, and demographics and case mix of patients served.	5.49	11.4%

Definition of abbreviation: EMR = electronic medical record.

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Table 5.

Comparison of Biomarkers for Tobacco Use

	Cotinine	Carbon Monoxide	NNAL	Anabasine and Anatabine
What is it?	Major metabolite of nicotine	Combustible byproduct from cigarette smoking	Tobacco-specific nitrosamine metabolite	Two nicotine-related alkaloids present in tobacco
Measured in what samples?	Plasma, saliva, and urine	Expired air	Urine	Urine
Relative sensitivity/specificity	More sensitive than CO, but less specific as it cannot distinguish NRT from tobacco use	Reasonably sensitive for recent or heavy cigarette use; does not detect smokeless tobacco or NRT	Highly tobacco specific; can distinguish NRT from tobacco; detects smokeless tobacco	Specific for tobacco use (not present in NRT); able to detect smokeless tobacco
Suggested cutoff for positive result *	30 ng/ml for urine; 3–5 ng/ml for serum and saliva	5–6 ppm	47.3 pg/ml	2 ng/ml
Half-life	16–18 h; biochemically verifiable window 7 d	2–8 h; biochemically verifiable window 1 d	10–18 d; detected in urine for 6–12 wk	10–16 h

Definition of abbreviations: CO = carbon monoxide; NNAL = 4-(methylnitrosamino)-1-(3-pyridyl)-1-butanol; NRT = nicotine replacement therapy; ppm = parts per million.

Data from References 43, 54, and 55.

* Cutoff points may vary depending on individual's smoking behavior, product, genetic background, and magnitude of secondhand smoke.