April 30, 2014

Marilyn Tavenner
Administrator
Centers for Medicare & Medicaid Services
U.S. Department of Health and Human Services
200 Independence Ave, SW
Room 445-G
Washington, DC 20201

RE: Recommendations on Medicare Coverage of Lung Cancer Screening

The American Cancer Society and American Lung Association appreciate the opportunity to provide recommendations and comments regarding the open National Coverage Analysis on Lung Cancer Screening with Low Dose Computed Tomography (LDCT). Our organizations strongly support access to lung cancer screening for all Medicare patients for whom it is appropriate, in order to lead to earlier diagnoses of lung cancer and reduced lung cancer mortality as demonstrated in the National Lung Screening Trial.

The American Lung Association submitted comments to the Centers for Medicare and Medicaid Services (CMS) on March 12, 2014 supporting a National Coverage Determination (NCD) providing full coverage of LDCT scans for lung cancer screening for the high risk population defined in the U.S. Preventive Services Task Force (USPSTF) recommendation.

According to the National Cancer Institute's National Lung Cancer Screening Trial (NLST), the receipt of three annual low dose CT scans was associated with a 20 percent decrease in mortality in those at highest risk of cancer. Recognizing this, the USPSTF released a recommendation on December 30, 2013 that certain high-risk populations be screened for lung cancer using this method. Most of the individuals in the high-risk population identified in the USPSTF recommendation are of the age that qualifies them for Medicare. **Our organizations strongly encourage CMS to include LDCT scans for lung cancer screening among Medicare's covered services for high risk-groups designed by the USPSTF at a minimum.** Coverage of LDCT scans for lung cancer screening under Medicare will give high risk patients access to the only early detection tool for lung cancer currently available.

We also wish to comment on some of the questions that were raised by CMS during an informational phone call, and will likely be part of the discussion at the CMS MEDCAC meeting for lung cancer screening for Medicare beneficiaries. These comments should not be construed as contradicting our strong support for coverage of lung cancer screening for all Medicare patients for whom it is appropriate.

Strength of the Evidence:

The National Cancer Institute's National Lung Screening Trial (NLST), a large randomized control trial with over 50,000 patients, indicated that LDCT scans were effective at reducing mortality from lung cancer by 20 percent compared with chest radiographs in certain high risk populations. The NLST was funded based on many years of data suggesting that finding lung cancers very early in their natural history, earlier than was possible with chest x-ray, could result in significantly improved prognosis and a reduction in lung cancer mortality. The NLST remains the only randomized controlled trial to date to show a benefit from LDCT screening and more evidence is needed. While previous systematic reviews of small trials and pilots conducted in Europe have found null results, these studies were underpowered and used various constructs to assess the benefit of screening. More evidence is needed and we look forward to the completion and results of the NELSON and the UKLS trials, principally because they will compare a group invited to screening with a group that received usual care. Despite the lack of other studies confirming the effectiveness of LDCT in reducing lung cancer mortality, there is widespread acceptance of the NLST results and that the reduction likely is greater than the 20 percent difference in lung cancer mortality rates between two screening arms. In fact, with the exception of one organization, all organizations that have issued recommendations for lung cancer screening have found the NLST findings persuasive.

The purpose of randomized controlled trials is to determine whether a medical strategy is safe and effective in a pre-specified population, such as whether LDCT screening lead to a significant difference in lung cancer mortality rates as in the NLST. Results of clinical trials, like the NLST, can help inform healthcare decision-making but do not provide guidance regarding the implementation of the findings in the real world. For example, current policies for breast and prostate cancer screening do not match the number of screening rounds administered in the initial clinical trials that led to the implementation of these practices. As such, we advise CMS to cover annual LDCT for lung cancer screening according to the recommendations issued by the USPSTF.

Screening Quality:

As with all screenings, access to quality screenings is essential to prevent any harm to patients. Unfortunately, there has been some concern that the quality of lung cancer screening in the community setting will not measure up to highly controlled practices enforced at participating NLST sites, preventing replication of the results and benefits outside of its experimental settings. However, with improvements in imaging technology over the last decade and increasing experience of radiologists in the conduct of LDCT for a variety of diseases, there is little doubt that LDCT for lung cancer screening will be at least of average quality. This is an opportunity for CMS to further improve quality by promoting best practices, accreditation, data collection, medical audits and feedback, and the accumulation of experience. The importance of these program elements has been stressed in most of the organization's guidelines on lung cancer screening. We disagree with providing coverage with evidence determination based on the assumption, not evidence, that the quality of care delivered by the average community imaging facility is substantially below the level of care provided by NLST facilities 10-12 years ago. As was the cases with NLST sites, there will be a range of quality, and through experience over time and quality assurance programs we expect quality to improve steadily, as it has with other cancer screening tests.

Harms associated with LDCT:

Adults seeking testing for early lung cancer detection must be informed that screening will not detect all lung cancers, and the detection of a cancer by LDCT does not guarantee that death from lung cancer will be averted. There is a significant chance of a false-positive result, which will require additional periodic testing and, in some instances, an invasive procedure to determine whether or not an abnormality is lung cancer or some non-lung cancer-related incidental finding. Additional testing will increase lifetime radiation exposure, and increase financial costs, although new algorithms for abnormality thresholds hold great promise to reduce the callback rate, and there has been significant progress in reducing radiation exposure during LDCT screening. Less than 1 in 1,000 patients with a false-positive result will experience a major complication resulting from a diagnostic workup. Death within 60 days of a diagnostic evaluation has been documented, but is rare and most often occurs in patients with lung cancer. Despite these unresolved issues, the NLST demonstrated that the overall benefit exceeds the potential risks as there is a significant opportunity to reduce deaths from lung cancer in a high-risk group of current and former smokers.

Concerns have been raised that individuals will be screened in settings that do not deliver comprehensive care and that the continuum of recommended care ranging from proper risk assessment and informed decisions to testing and follow-up will be highly variable in terms of quality, and therefore harms will be greater. While there is reason to be concerned that there will be growing pains, this is expected with the introduction of a new screening test, although it must be acknowledged that LDCT has been used for a variety of imaging studies over the past several decades. Thus, the learning curve is not as new as it might appear. What is unique today is that all guidelines have stressed the importance of quality, informed decision making, and comprehensive care, and appropriate organizations are becoming increasingly engaged in promoting best practices and visible recognition for sites that support quality programs. The need to identify best practices to reduce the rate of false positives is well appreciated both in the U.S. and abroad. CMS can also show leadership in this area, and CMS and health plans could consider incentives and requirements to insure rapid progress towards achieving high standards of recommended care. We share concerns about quality, but believe that the best strategy to insure high quality is to strive to have sites adhere to quality standards and gain experience. Later in this letter we endorse the general principle that screening sites should participate in registries to provide feedback to the imaging facility and larger practice on outcomes for the purpose of ongoing evaluation and quality improvement.

The Effect of LDCT Screening on Smoking Behavior:

Smoking is the most important avoidable risk factor for lung cancer, accounting for approximately 85 percent of all cases. The best way to prevent lung cancer incidence and death is still to never smoke or quit smoking and avoid exposure to secondhand smoke. Any patient being considered for lung cancer screening who still smokes should be offered cessation treatment. Tobacco cessation is the primary way to prevent lung cancer and lung cancer screening offers an ideal opportunity to provide vigorous screening and cessation services to those at highest risk for lung cancer.

Concerns that normal LDCT screening results in current and even former smokers may be an incentive to keep smoking or abandon cessation has been raised for as long as the potential for LDCT screening has been explored. Probably a very small percentage of adults will feel emboldened by normal test results, but the simple fact is that most smokers want to quit smoking and the current data are at least suggestive that participation in LDCT screening contributes to successful smoking cessation. Further, the

introduction of LDCT screening is an opportunity to establish complementary, state of the art smoking cessation programs directly linked to lung scanning.

The Importance of Registries:

Since LDCT scans are a relatively new screening tool for lung cancer, the evidence base for lung cancer screening is still evolving, and the effectiveness of lung cancer screening in a 'real world' setting remains to be established. However, this only will occur when lung cancer screening is implemented, similar to other screening tests. Thus, it is important to develop simple strategies and incentives to support collection of a common, minimum set of data elements for purposes of evaluation and clinical feedback. Further, it is important to consider the potential for additional at-risk populations, in addition to the NLST population, be included in the target population for lung cancer screening. The NCCN already has endorsed a lower level of cumulative exposure to tobacco smoke if an additional risk factor is present. Therefore, our organizations recommend that the resulting NCD on lung cancer screening should encourage institutions to collect additional data on patients that undergo screening. We also recommend that CMS consider providing coverage with evidence development for the NCCN recommendations that pertain to family history and high-risk occupational exposures. These are important questions to answer, and we believe CMS is in a unique position to lead in this important clinical and public health endeavor.

Data to Collect in Evidence Development Process:
In response to question by CMS, our organizations considered what data CMS could encourage facilities to collect if CMS were to establish coverage. The collection of the following data items could be encouraged:

- Demographics
- Smoking history, including clear characterization of pack-year history
- Occupational history to cover high-risk jobs and industries
- Pulmonary disease characteristics & applicable comorbidities, particularly COPD
- Prior screening history, including follow-up for positive findings
- Findings and plan (annual vs. short term follow-up)
- Size of lesion at diagnosis
- Adverse events following diagnosis
- Hospitalizations following diagnosis

Additional Populations at Risk:
In response to a question by CMS, our organizations considered which additional populations might eventually be identified as high risk and eligible for screening. They include:

(A) Patients with Reduced Lung Function and Chronic Obstructive Pulmonary Disease (COPD)
Multiple studies have shown that reduced lung function is a general mortality risk factor and an important risk factor for lung cancer.[i, ii] Increasing evidence shows that those at greatest risk for the development of cancer are smokers who develop COPD and have emphysema on their CT scan, although the underlying mechanism for this association is unclear.[iii] New findings suggest that among people with COPD, lung cancer occurs more frequently in older patients with milder airway flow obstruction[iv] and lower body mass index.[v] The risk is gender dependent and appears to be amplified in women.[vi]

(B) Patients with Certain Occupational Histories
Clearly some patients will have combinations of smoking histories and occupational histories that together will result in an additive of super-additive risk that equals or exceeds the absolute risk threshold for NLST eligibility. There is a need to determine the exposures that result in that risk threshold and ways it can be reliably identified when smoking history alone would not qualify someone for screening.

(C) Patients with 30-Pack-Years of Smoking History who Quit More than 15 Years Previously
Questions still remain as to whether all former smokers should be eligible for CMS coverage of lung cancer screening by LDCT if they meet the pack year exposure criteria. We do not agree with the USPSTF recommendation to adults who begin screening should exit screening once 15 years since quitting has elapsed. Since most of these adults will have quit later in life, evidence indicates that risk does not plateau permanently, as it does when adults quit at younger ages, but instead rises steeply after a period of being stable.[vii] Given that NLST absolute risk thresholds were set at a relatively high short term level in order to insure adequate number of cases over a short duration of time, CMS should be open to reconsidering risk thresholds. To determine this, the American Lung Association and the American Cancer Society recommend that CMS collect detailed smoking histories from the people who are screened. This can be done by using the ATS Smoking History questionnaire which would allow for the calculation of pack-years. The core set of questions are as follows:

1. Have you ever smoked as much as 100 cigarettes in your lifetime (if no, then the respondent is a never smoker). If yes, then the sequence is as follows:
2. Are you still smoking cigarettes (if yes, then a current smoker and if no, a former smoker):
3. At what age did you start smoking?
4. On average, how many cigarettes did you smoke per day?
5. For former smokers, at what age did you quit?

Summary
Thank you for the opportunity to share our support for coverage of lung cancer screening for at risk patients in Medicare. The American Cancer Society and American Lung Association strongly encourage CMS to include LDCT scans for lung cancer screening among Medicare's covered services for high risk-groups identified by the USPSTF recommendation so beneficiaries can begin to receive this life-saving preventive annual lung cancer screening with no cost-sharing. We look forward to working closely with CMS as a coverage decision is made. If you have any questions regarding our comments, please contact Robert Smith at Robert.Smith@cancer.org or 404.329.7610 or Elizabeth Lancet at Elizabeth.lancet@lung.org or (212) 315-8788.

---

[i] Lange P, Nyboe J, Appleyard M, Jensen G, Schnohr P. Ventilatory function and chronic mucus hypersecretion as predictors of death from lung cancer. *The American Review of Respiratory Disease*. 1990;141(3):613-7. Available at: http://www.ncbi.nlm.nih.gov/pubmed/2310094. Accessed February 23, 2012.

[ii] Wasswa-Kintu S, Gan WQ, Man SFP, Pare PD, Sin DD. Relationship between reduced forced expiratory volume in one second and the risk of lung cancer: a systematic review and meta-analysis. *Thorax*. 2005;60(7):570-5. Available at: http://www.pubmedcentral.nih.gov/articlerender.fcgi?artid=1747470&tool=pmcentrez&rendertype=abstract. Accessed December 9, 2011.

[iii] Houghton AM, Mouded M, Shapiro SD. Common origins of lung cancer and COPD. *Nature Medicine*. 2008;14(10):1023-4. Available at: http://www.ncbi.nlm.nih.gov/pubmed/18841139. Accessed February 23, 2012.

[iv] From the Global Strategy for the Diagnosis M and P of C. Global Initiative for Chronic Obstructive Lung Disease (GOLD) 2011. 2011:1-90. Available at: Available from: http://www.goldcopd.org/.

[v] de Torres JP, Marín JM, Casanova C, et al. Lung Cancer in patients with COPD: Incidence and predicting factors. *American Journal of Respiratory and Critical Care Medicine*. 2011;184(8):913-9. Available at: http://www.ncbi.nlm.nih.gov/pubmed/21799072. Accessed September 26, 2011.

[vi] Wasswa-Kintu, 2005

[vii] Halpern MT, Gillespie BW, Warner KE. Patterns of absolute risk of lung cancer mortality in former smokers. J Natl Cancer Inst. 1993;85:457–464.