

## **Lung cancer trial results show mortality benefit with low-dose CT:**

*Twenty percent fewer lung cancer deaths seen among those who were screened with low-dose spiral CT than with chest X-ray*

The National Cancer Institute (NCI) is today releasing initial results from a large-scale test of screening methods to reduce deaths from lung cancer by detecting cancers at relatively early stages.

The National Lung Screening Trial (NLST), a randomized national trial involving more than 53,000 current and former heavy smokers ages 55 to 74, compared the effects of two screening procedures for lung cancer—low-dose helical computed tomography (CT) and standard chest X-ray—on lung cancer mortality and found 20 percent fewer lung cancer deaths among trial participants screened with low-dose helical CT. The NLST was sponsored by NCI, a part of the National Institutes of Health, and conducted by the American College of Radiology Imaging Network (ACRIN) and the Lung Screening Study group. A paper describing the design and protocol of the NLST, “The National Lung Screening Trial: Overview and Study Design” by the NLST research team, was published yesterday by the journal *Radiology* and is openly available at <http://radiology.rsna.org/cgi/content/abstract/radiol.10091808.1>.

“This large and well-designed study used rigorous scientific methods to test ways to prevent death from lung cancer by screening patients at especially high risk,” said Harold Varmus, M.D., NCI Director. “Lung cancer is the leading cause of cancer mortality in the U.S. and throughout the world, so a validated approach that can reduce lung cancer mortality by even 20 percent has the potential to spare very significant numbers of people from the ravages of this disease. But these findings should in no way distract us from continued efforts to curtail the use of tobacco, which will remain the major causative factor for lung cancer and several other diseases.”

The NCI’s decision to announce the initial findings from the NLST was made after the trial’s independent Data and Safety Monitoring Board (DSMB) notified the NCI director that the accumulated data now provide a statistically convincing answer to the study’s primary question and that the trial should therefore be stopped. A fuller analysis, with more detailed results, will be prepared for publication in a peer-reviewed journal within the next few months. Participants in the NLST are being notified individually of the findings by the study’s investigators. The participant notification letter, as well as the DSMB letter, can be viewed at <http://www.cancer.gov/clinicaltrials/noteworthy-trials/nlst>.

Starting in August 2002, the NLST enrolled about 53,500 men and women at 33 trial sites nationwide over a 20 month period. Participants were required to have a smoking history of at least 30 pack-years and were either current or former smokers without signs, symptoms, or history of lung cancer. Pack-years are calculated by multiplying the average number of packs of cigarettes smoked per day by the number of years a person has smoked.

Participants were randomly assigned to receive three annual screens with either low-dose helical CT (often referred to as spiral CT) or standard chest X-ray. Helical CT uses X-rays to obtain a multiple-image scan of the entire chest during a 7 to 15 second breath-hold. A standard chest X-ray requires only a sub-second breath-hold but produces a single image of the whole chest in which anatomic structures overlie one another.

Previous efforts to demonstrate that standard chest X-ray examinations can reduce lung cancer mortality have been unsuccessful.

The trial participants received their screening tests at enrollment and at the end of their first and second years on the trial. The participants were then followed for up to another five years; all deaths were documented, with special attention given to the verification of lung cancer as a cause of death. At the time the DSMB held

its final meeting on October 20, 2010, a total of 354 deaths from lung cancer had occurred among participants in the CT arm of the study, whereas a significantly larger 442 lung cancer deaths had occurred among those in the chest X-ray group. The DSMB concluded that this 20.3 percent reduction in lung cancer mortality met the standard for statistical significance and recommended ending the study.

“This is the first time that we have seen clear evidence of a significant reduction in lung cancer mortality with a screening test in a randomized controlled trial. The fact that low-dose helical CT provides a decided benefit is a result that will have implications for the screening and management of lung cancer for many years to come,” said Christine Berg, M.D., NLST project officer for the Lung Screening Study at NCI.

An ancillary finding, which was not the main endpoint of the trial’s design, showed that all-cause mortality (deaths due to any factor, including lung cancer) was 7 percent lower in those screened with low-dose helical CT than in those screened with chest X-ray. Approximately 25 percent of deaths in the NLST were due to lung cancer, while other deaths were due to factors such as cardiovascular disease. Further analysis will be required to understand this aspect of the findings more fully.

The NCI and its partners conducted this trial to obtain the most reliable results possible about the potential benefits of lung cancer screening. Others will begin to use the extensive data from this trial to conduct further analyses and to propose clinical guidelines and policy recommendations for lung cancer screening.

“The results of this trial provide objective evidence of the benefits of low-dose helical CT screening in an older, high-risk population and suggest that if low-dose helical CT screening is implemented responsibly, and individuals with abnormalities are judiciously followed, we have the potential to save thousands of lives,” said Denise Aberle, M.D., NLST national principal investigator for ACRIN. “However, given the high association between lung cancer and cigarette smoking, the trial investigators re-emphasize that the single best way to prevent lung cancer deaths is to never start smoking, and if already smoking, to quit permanently.”

The possible disadvantages of helical CT include the cumulative effects of radiation from multiple CT scans; surgical and medical complications in patients who prove not to have lung cancer but who need additional testing to make that determination; and risks from additional diagnostic work-up for findings unrelated to potential lung cancer, such as liver or kidney disease. In addition, the screening process itself can generate suspicious findings that turn out not to be cancer in the vast majority of cases, producing significant anxiety and expense. These problems must, of course, be weighed against the advantage of a significant reduction in lung cancer mortality.

It should also be noted that the population enrolled in this study, while ethnically representative of the high-risk U.S. population of smokers, was a highly motivated and primarily urban group that was screened at major medical centers. Thus the results may not accurately predict the effects of recommending low-dose helical CT scanning for other populations.

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Copies of the DSMB and NLST participant letters can be found on the NLST site at <http://www.cancer.gov/clinicaltrials/noteworthy-trials/nlst>.

For a Q&A on the NLST, please go to <http://www.cancer.gov/newscenter/qa/2002/nlstqaQA>.

For a Fact Sheet on the NLST, please go to <http://www.cancer.gov/newscenter/pressreleases/NLSTFastFacts> 4.

For more information on lung cancer and screening, please go to <http://www.cancer.gov/cancertopics/types/lung> 5.

“The National Lung Screening Trial: Overview and Study Design” has been published by Radiology. This paper is openly available at <http://radiology.rsna.org/cgi/content/abstract/radiol.10091808>.

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1 <http://radiology.rsna.org/cgi/content/abstract/radiol.10091808>

2 <http://www.cancer.gov/images/DSMB-NLST.pdf>

3 <http://www.cancer.gov/images/ParticipantNLST.pdf>

4 <http://www.cancer.gov/newscenter/pressreleases/NLSTFastFacts>

5 <http://www.cancer.gov/cancertopics/types/lung>