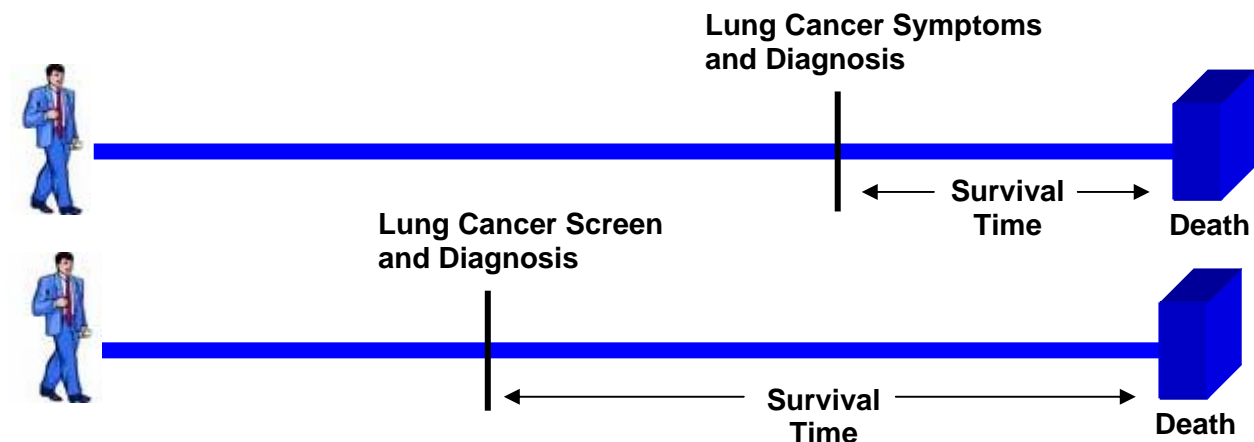


Dear NLST Participant:

Thanks to all of you, NLST is in its third and final year of lung cancer screening for our roughly 53,000 participants. This is a truly remarkable testimony to the dedication of participants such as yourself, upon whom the success of this important study heavily depends. We think we'll be done with the screening phase of NLST by early 2007, and we are beginning an equally important phase of NLST, the follow-up phase. Thank you very much for your ongoing commitment to what is the single largest and most comprehensive lung cancer screening trial ever undertaken.

As you know, the primary goal of NLST is to determine whether lung cancer screening using either chest X-ray or low dose helical computed tomography (CT) will lower deaths from lung cancer (called lung cancer mortality). It seems only logical that the earlier a cancer is found through screening tests, the more likely its treatment will save lives. However, this is not known for many types of cancers, including lung cancer. We only know this: screening can result in the earlier *diagnosis* of a lung cancer. Earlier diagnosis may lengthen “survival time” – the time that an individual lives with the diagnosis. However, survival time may only lengthen, or increase, how long a person knew about the cancer to the degree that the diagnosis occurred earlier, without ever affecting the timing (or likelihood) of death from lung cancer. In short: we have no scientific evidence yet to show that screening for lung cancer can reduce a person’s chance of dying from the disease. To show this another way, let’s look at an example life line of an individual below:



In the first picture, a lung cancer is diagnosed when the individual develops symptoms. In the second picture, the individual is screened, resulting in the earlier diagnosis of lung cancer. With screening, the lead time in diagnosis will increase “survival time” even if death is not delayed. This tendency of screening to extend survival without necessarily providing benefit is called lead-time bias and is one of the many important reasons that the NLST was so carefully designed to look at the real benefits of screening based on *lives saved* and not survival time. The NLST trial will compare chest x-rays and spiral CT, two potentially important methods of lung cancer screening. Through the information participants and their doctors provide us throughout the

NLST, we will be able to know if screening can reduce the death rates from lung cancer. The continued participation of every participant in NLST is essential to reaching our goal.

There has a lot of recent press attention from the ABC-TV News Anchor Peter Jennings' lung cancer announcement. This has caused confusion over the relative effectiveness of chest X-ray and chest CT for screening and for diagnosis.

Mr. Jennings' cancer was discovered after he experienced symptoms that required a diagnostic CT scan. These unfortunate events have led some individuals to recommend CT screening for lung cancer, claiming it is more effective than chest x-rays. These statements have resulted from a misunderstanding of our current knowledge of imaging-based screening benefits. Just as important, these claims confuse the use of CT as a *screening* test in individuals without symptoms versus CT as a *diagnostic* test in individuals with symptoms, such as Mr. Jennings. Screening tests and diagnostic tests are performed for very different reasons and provide very different kinds of information. They must not be confused.

The standards we use to ensure the benefit of a screening test such as chest x-ray or CT are as follows:

- [1] The test must find cancer earlier than if diagnosis occurred because of symptoms.
- [2] The test must not have too many side effects or risks associated with it.
- [3] If cancer is found early through screening, long-term studies must show that treatment of the screening detected cancer will lower the risk of dying from the disease.

An effective screening test must meet all three standards before we can recommend it for widespread use. At this time, we know that both CT and chest x-ray examinations can detect lung cancers before they show symptoms. We will be able to determine through NLST whether either test has side-effects or risks associated with it, such as false-positive results in patients who do not really have lung cancer, an unacceptable number of unnecessary tests or concern, or even non-lung cancer-related findings that put other individuals at risk to potentially other dangerous procedures with their own complications.

Pseudodisease is another possible risk of screening exams that we may be able to gather indirect information about through NLST. There is some evidence that sensitive screening tests such as CT scans may detect small, very slow-growing lung cancers that would never have been diagnosed or become harmful. These lesions, called pseudodisease, have the microscopic appearance of lung cancer, but are so slow growing that they do not behave like lung cancer and do not require treatment. Their diagnosis potentially exposes a person to risks of radiation, lung surgery, chemotherapy, or other treatments with risks.

Ultimately, NLST will provide the evidence we need to assess the true effectiveness of spiral CT scans and chest x-rays for lung cancer screening. We hope one day to establish that screening is an effective way to reduce deaths from lung cancer, but until we know this through the data you provide us as interested and dedicated participants of the NLST, we cannot recommend any one lung cancer screening test as a matter of public policy. This uncertainty remains not only within the NCI and ACRIN, but within virtually all national medical organizations devoted to the

welfare of the American public. In the meantime, you (ACRIN) participants are helping to create an extraordinarily important archive of medical data for ongoing research, which is described in more detail in this newsletter.

We hope to address in this issue of the *NLST Newsletter* questions you may have about lung cancer screening and the NLST. You should also feel free to ask for additional information by contacting your local NLST clinical center or the NCI's Cancer Information Service toll-free number shown below. Specific medical questions should be addressed to your personal health care provider. Questions and/or comments can be sent via U.S. postal mail or e-mail to the following addresses:

E-mail address: NLST@nih.gov

U.S. mailing address: NLST Director of Communications
Early Detection Research Group, DCP, NCI
Executive Plaza North, Room 3100
6130 Executive Blvd. MSC 7346
Bethesda, MD 20892-7346

Cancer Information Service: 1-800-4-CANCER (1-800-422-6237); TTY: 1-800-332-8615.
Toll-free Monday-Friday, 9:00 AM to 4:30 PM. local time

Again, we celebrate your continued participation in the NLST and thank-you for your individual efforts to make this trial a national success!

Sincerely,

Christine D. Berg, M.D.
NLST Co-Director, National Cancer Institute

Denise R. Aberle, M.D.
NLST Co-Director, American College of Radiology Imaging