

# The status of Research on Screening for Lung Cancer

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## Background

A series of observational studies and randomized screening trials have found no benefit from screening for lung cancer with chest X-ray and sputum cytology

## Reasons for uncertainty about lung screening

- Previous screening trials of Chest X-ray and sputum cytology were small and of low power
- New technology (low dose CT scanning) raises hope for screening benefit
- “Single arm” studies suggest good cancer detection but cannot confirm mortality reduction
- CT seems to preferentially detect adenocarcinomas (peripheral lesions)

## Mayo Lung Project (Marcus et al, 2000)

Recruitment: Nov. 1971 to July 1976

Initial follow up, cases and deaths, to July 1, 1983

Follow-up for lung cancers post-screen for 1-5 years

Extended follow-up for deaths to December 31, 1996



## Mayo Lung Project (Marcus et al, 2000)

| <u>Allocation:</u>      | <u>Intervention</u> | <u>Usual Care</u> |
|-------------------------|---------------------|-------------------|
| Lung cancers diagnosed  | 206                 | 160               |
| Death from lung cancer  | 133 (65%)           | 119 (74%)         |
| Death from other causes | 57 (28%)            | 37 (23%)          |
| Alive                   | 16 ( 8%)            | 4 ( 3%)           |

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| <i>Cured</i>            | 41 (20%)            | 41 (26%)          |
| <i>Overdiagnosis</i>    | 32 (16%)            | 0 ( 0%)           |

## Why single arm studies (e.g. ELCAP) cannot provide evidence on efficacy

- Case detection is not equivalent to benefit
- There is no inbuilt comparison group
- Overdiagnosis confounds attempts to use prior experience as a basis of comparison

## The ideal lung screening trial

- Individual randomization with informed consent
- Multicentre, with mechanisms to ensure standardized application of screening and therapy
- Efficient data collection and quality control
- Endpoint: death from lung cancer (mortality) confirmed by a death review committee
- Monitoring of emerging results by independent committee

## The New Lung screening Trials

- PLCO
- NLST
- Europe CT trial (NELSON)

## PLCO screening trial

- a large-scale, randomized trial to determine whether screening will reduce the numbers of deaths from cancers of the prostate, lung, colon and ovary.
- these cancers represent 48% of the incident cancer cases and 49% of the cancer deaths in the United States each year

## Screening tests used

|           |   |
|-----------|---|
| Prostate: | PSA test and DRE (annual)                               |
| Lung:     | PA Chest x-ray (annual)                                 |
| Colon:    | Flexible sigmoidoscopy to 60 cm (x 2)                   |
| Ovary:    | CA 125 blood test and trans-vaginal ultrasound (annual) |

## Enrollment in PLCO trial

- The trial involves over 150,000 men and women ages 55 through 74 at 10 study centers across the United States.
- End date for recruitment was September 30, 2000.
- Screening in the trial comes to an end this year
- Follow up of each participant planned for at least 13 years

## Power of PLCO trial

- Prostate: 90% power to detect a 20% reduction in prostate cancer mortality
- **Lung: 90% power to detect a 10% reduction in lung cancer mortality.**
- Colorectum: 99% power to detect a 20% reduction in colorectal cancer mortality.
- Ovarian cancer: 88% power to detect a 35% reduction in ovarian cancer mortality

## NLST screening trial

- Enrollment September 2002-April 2004
- 53,000 men and women age 55-74, with history of heavy smoking, enrolled
- Randomization to Chest X-ray vs. CT screening
- 3 annual screens, completion this year

## Conclusions on Lung screening trials

- Screening trials are expensive, but essential to evaluate efficacy of lung screening
- The NLST trial accrual is complete, a European trial is beginning
- The trials should have adequate power to detect mortality reduction about 5 years after the intake is completed
- There is no other (easy and cheap) way to evaluate screening