



National Lung  
Screening Trial

National Cancer Institute

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- I have no conflicts of interest.
- I will be discussing research involving screening for lung cancer utilizing chest x-ray and helical CT. The FDA has not approved either imaging technology for screening.

B = blood sample: store plasma + buffy coat + assay cobin  
 X = P/A & lateral X-ray. (Randomised only if negative)

Re-randomisation (year)	CT Scan			X-ray only		
	4 yearly 25000	2 yearly 25000	yearly 25000	4 yearly 25000	2 yearly 25000	yearly 25000
year 0	C	C	C	-	-	-
1	-	-	C	-	-	X
2	-	C	C	-	X	X
3	-	-	C	-	-	X
year 4	C	C	C	X	X	X
5	-	-	C	-	-	X
6	-	C	C	-	X	X
7	-	-	C	-	-	X
8	C	C	C	X	X	X
9	-	-	-	-	-	-
10	-	-	-	-	-	-

|| etc.

Follow-up continues for at least a few more years,  
 and preferably indefinitely, through  
 National Death Index + coded cause of death (NDEH)

Plan report based on 10-year mortality with  
 3 years of treatment (years 0-8: 9 visits)

Do not do any sputum, or do sputum on  
 every body and if it seems positive then initially  
 randomise whether to recall for extra tests  
 unless absolutely necessary

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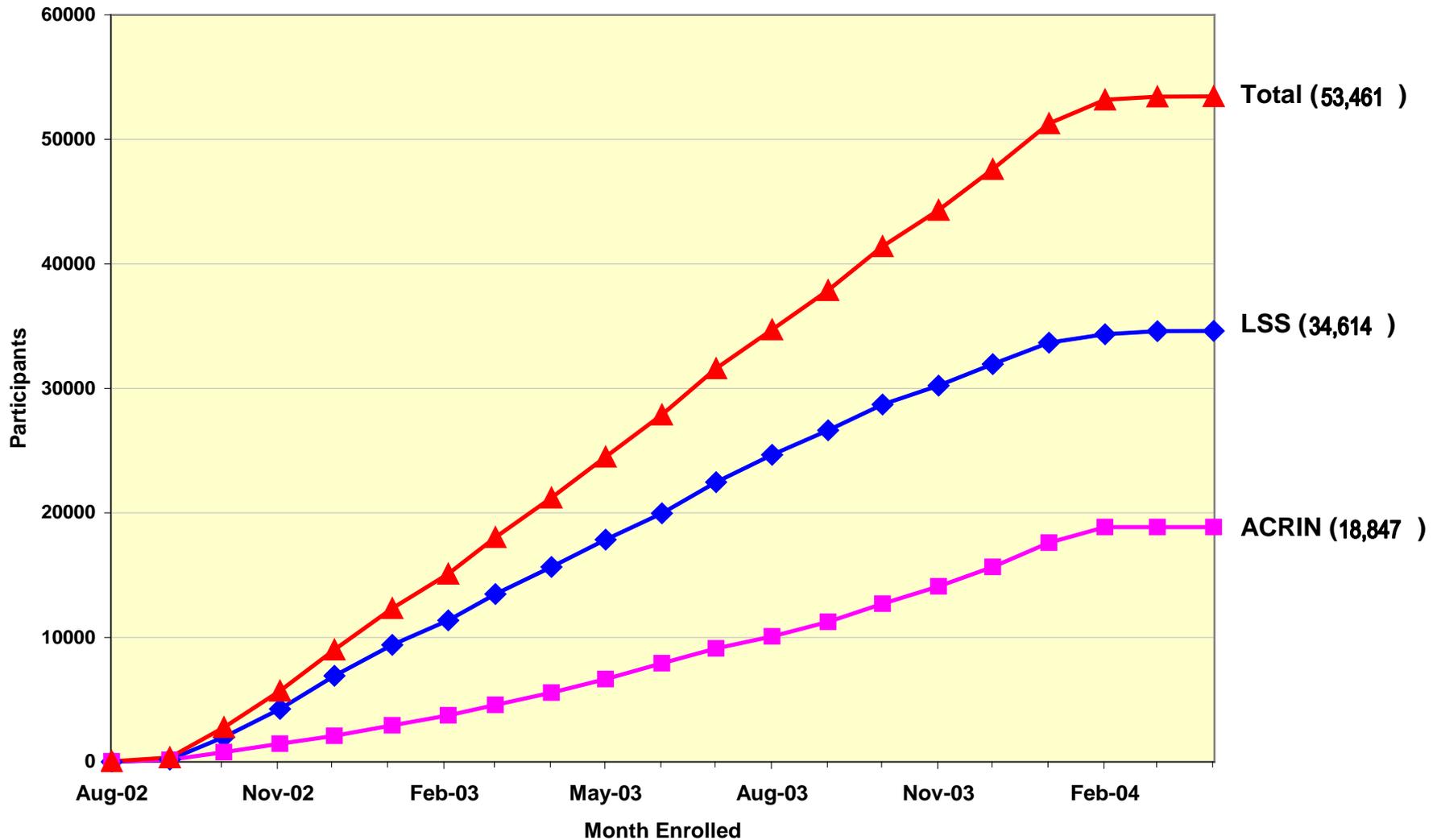
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# NLST Design

Prospective, randomized trial comparing low-dose helical CT screening to chest x-ray screening with the endpoint of lung cancer specific mortality in high risk participants

Arms	Helical CT vs. CXR
Difference in lung cancer-specific mortality	20%
$\alpha$	5%
Power	90%
Compliance	85% CT   80% CXR
Contamination	5% CT   10% CXR
Size	25,000 / arm

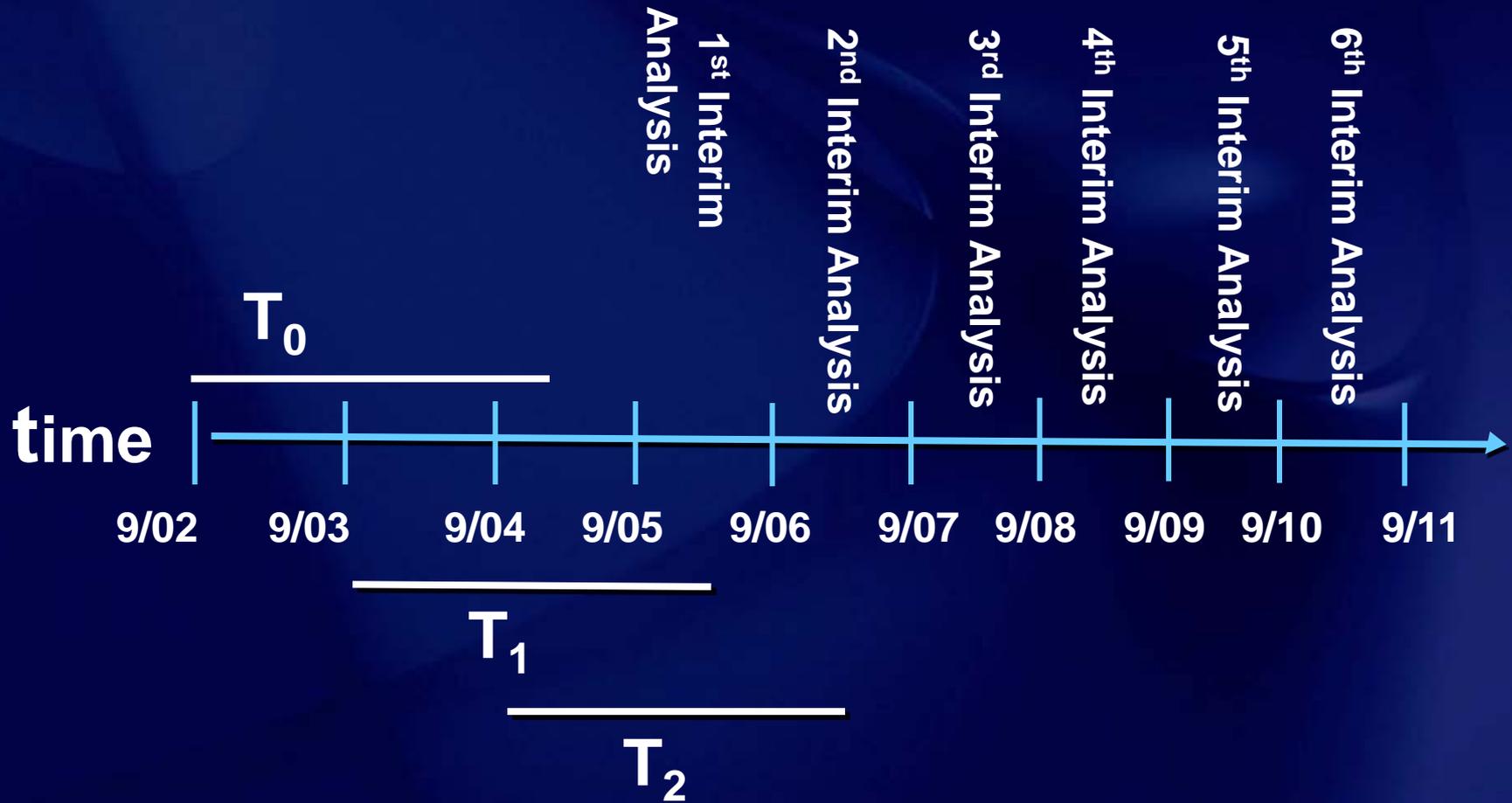
# NLST Cumulative Accrual



# Screening Exam Compliance

Study Year	Helical CT		Chest X-ray		Total	
	Expected	Screened	Expected	Screened	Expected	Screened
T0	26,715	98.5%	26,723	97.5%	53,438	98.0%
T1	26,287	94.0%	26,401	91.3%	52,688	92.6%
T2	25,942	92.9%	26,101	89.5%	52,043	91.2%

# NLST Projected Timeline



**PLCO:**  
**Ovarian Cancer Screening**

**International Cancer Screening Network**

**Biomarkers Workshop**

**June 23, 2010**

**Christine D. Berg, MD**

**Chief, Early Detection Research Group**

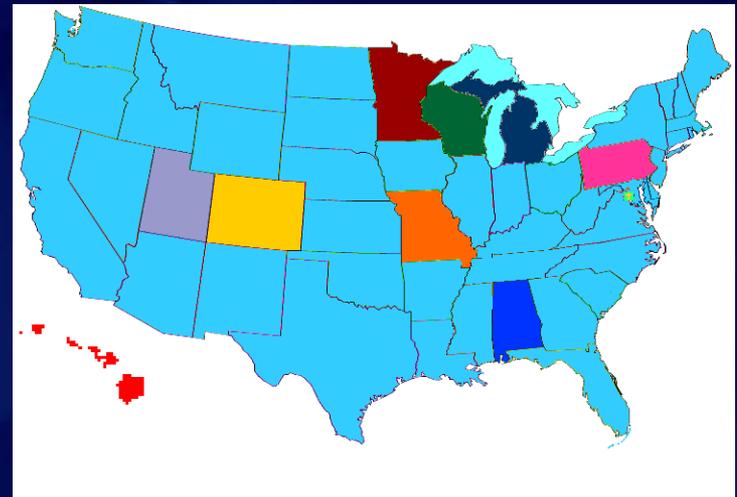
**Division of Cancer Prevention | NCI**

**<https://www.plcostars.com>**

# What is the PLCO?

## Prostate, Lung, Colorectal and Ovarian Cancer Screening Trial

- **Screening Centers: 10**
- **Coordinating Center**
- **Participants: 154,935**
- **Gender: 50:50**
- **Age: 55-74 years**
- **Recruitment: 1993-2001**
- **Screening: 1993-2006**
- **Baseline risk factor questionnaire**
- **Dietary questionnaires**
- **Follow-up**
- **Primary Endpoint: Index Cancer Mortality**



# PLCO Trial: Protocol

## Randomization

76,705 Male

78,237 Female

55-74 years of age

13 + year follow-up

## Screened Arm

38,350 Male

39,115 Female

Chest X-ray (T0-T2, T3 for current and former smokers)

Flexible sigmoidoscopy (T0, T5)

## Control Arm

38,355 Male

39,122 Female

Routine medical care

39,115 Female

CA-125 (T0-T5)

Transvaginal ultrasound  
(T0-T3)

38,350 Male

PSA (T0-T5)

Digital rectal examination  
(T0-T3)

# Ovarian Cancer Screening: T0-T3

- 34,261 screening arm women w/o prior oophorectomy
- 89 invasive ovarian or peritoneal cancers; 60 screen detected
- PPV: 1.0 – 1.3% across screening rounds
- Overall ratio of surgeries to screen-detected cancers was 19.5:1
- 72% of screen-detected cancers Stage III/IV
  
- Partridge E, Kreimer AR et al *Obstet Gynecol* 2009; 113:775-82

# PLCO Specimens for Prospective Validation of Early Detection Biomarkers

- Serial samples collected at 6 annual screening visits with uniform collection protocol
- Samples collected before cancer diagnosis
- Lifestyle and dietary data collected from all participants
- Thousands of cases in major cancers
- Diagnosis and treatment data available for P, L, C, O cancers, and for colorectal adenomas
- Diagnosis data available for other cancers
- Large participant pool without cancer for control group selection
- Patient consented for etiology and early marker studies

# PLCO Common Sampling Plan

- Cases: 118 invasive ovarian, primary peritoneal and fallopian tube cancers; low malignant potential tumors excluded
- Screen-detected and clinically diagnosed
- Proximate sample, usually at same time as screening except for T3 cases
- Eight controls per case:
  - Four general population
  - Two with family history; two with elevated CA-125 at any time
- Sixty replicate pairs for QC; identical sets sent to six assay sites
- One site not with EDRN/SPORE: Moore L., Pfeiffer R.

## Comparing Phase II and III results\*

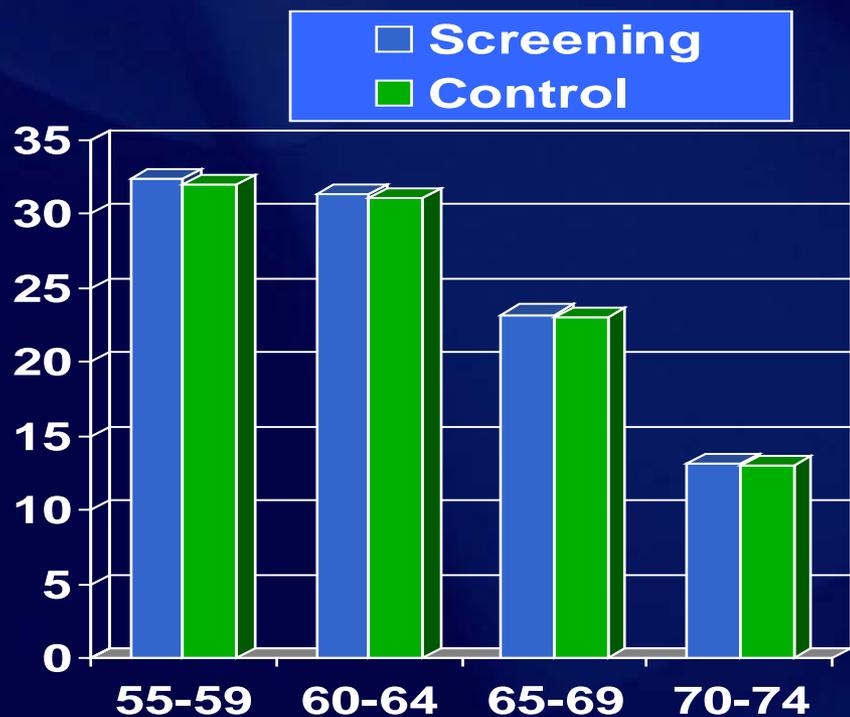
Marker	Phase II	Phase III
CA 125	73%	86%
HE4	57%	73%
CA 72.4	40%	44%
CA 15.3	46%	45%
MSLN	35%	40%
IGFBP2	38%	9%
Prolactin	34%	13%
Transthyretin	47%	2%
Transferrin	23%	9%

\*Sensitivity at 95% specificity for cases within 6 months

PLCO:

Prostate Cancer Screening

# PLCO: Selected Characteristics



Race	Screening	Control
White	86.2	83.8
Black	4.5	4.3
Hispanic	2.1	2.1
Asian	4.0	3.9
Other	0.8	0.9
Missing	2.4	5.0

# Prostate Cancer Detected by 10 years

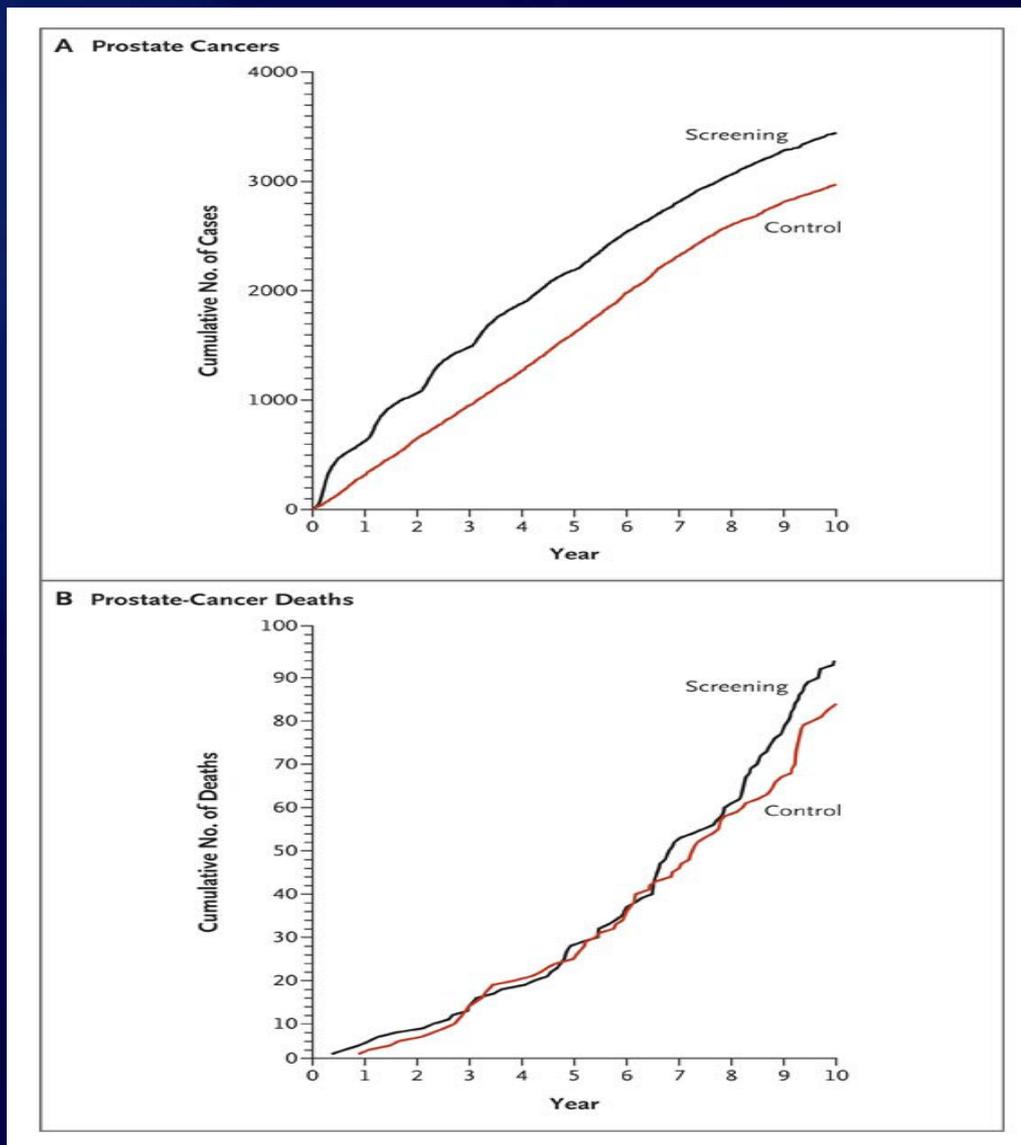
Clinical Stage	Screening	Control
I	18 (0.5)	15 (0.5)
II	3297 (95.5)	2790 (93.8)
III	49 (1.4)	56 (1.9)
IV	73 (2.1)	79 (2.7)
Unknown	15 (0.4)	34 (1.1)

# Comparison of Gleason Scores

Gleason score on biopsy	Screening	Control
2 - 4	222 (6.4)	137 (4.6)
5 - 6	2047 (59.3)	1656 (55.7)
7	815 (23.6)	779 (26.2)
8 - 10	289 (8.4)	341 (11.5)
Unknown	79 (2.3)	61 (2.1)



# Number of Diagnoses of All Prostate Cancers and Number of Prostate-Cancer Deaths



Andriole GL et al. N Engl J Med 2009;360:1310-1319



# PLCO Trial Results

- Annual screening with DRE and PSA results in more prostate cancer compared to community screening practices
  - Seven years: 2820 versus 2322
  - Ten years: 3452 versus 2974
- Few Prostate cancer related deaths in either group
  - 50 screening and 44 controls at 7 years
  - 92 screening and 82 control at 10 years
- Continued follow-up to be done