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 (chlamyd.
X = P/A & lateral x-ray. (Randomised only if negative)

	CT scan			X-ray only		
	4 yearly 25000	2 yearly 25000	yearly 25000	4 yearly 25000	2 yearly 25000	yearly 25000
Re-randomised (year 0)	×B	×B	×B	×B	×B	×B
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	–	–	–	–	–	–
11 etc.	–	–	–	–	–	–

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

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

Do not do any sputum ≅ do sputum on everybody and if it seems positive then individually randomise whether to recall for extra tests unless already have visual

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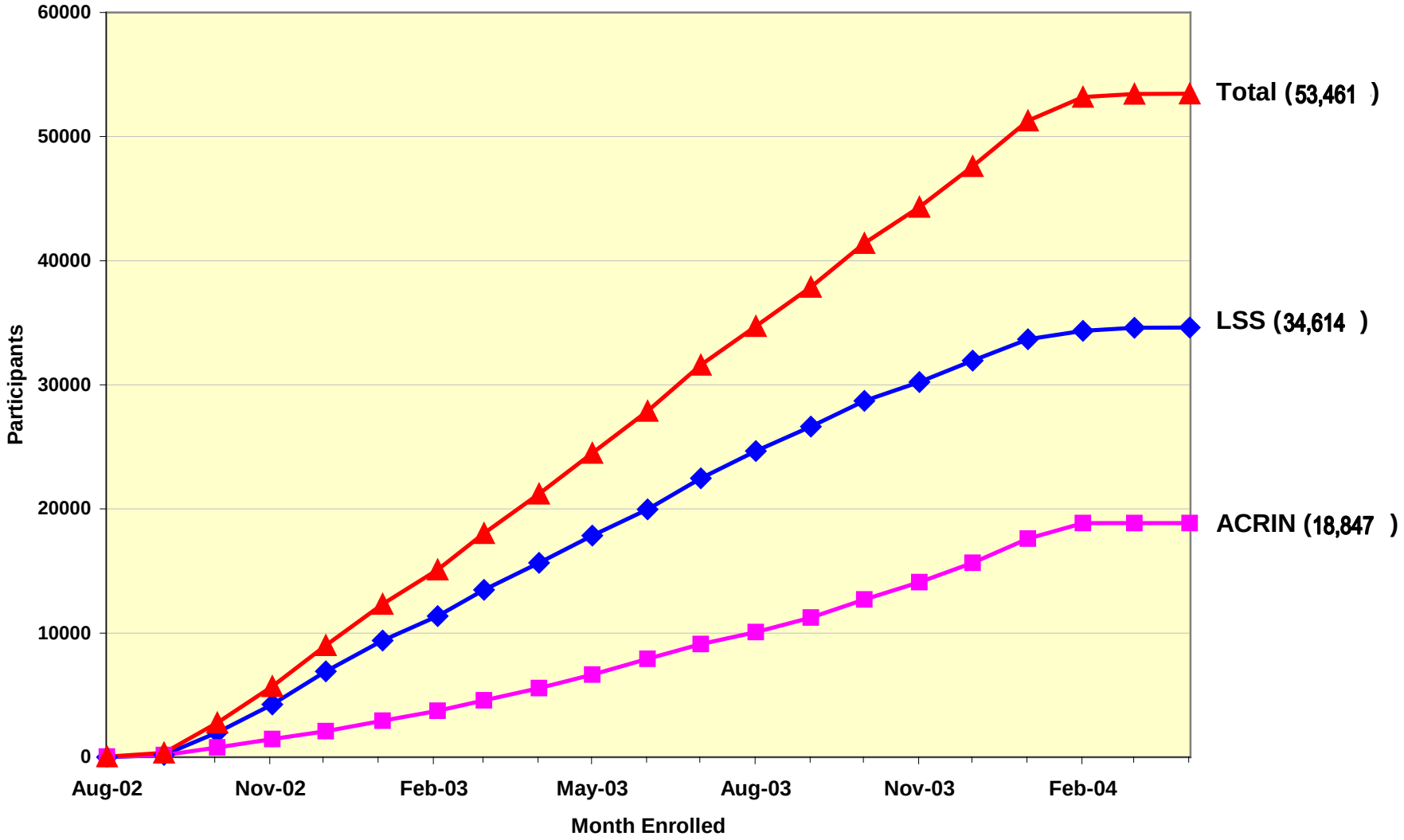
NLST Design

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%
α	5%
Power	90%
Compliance	85% CT | 80% CXR
Contamination	5% CT | 10% CXR
Size	25,000 / arm

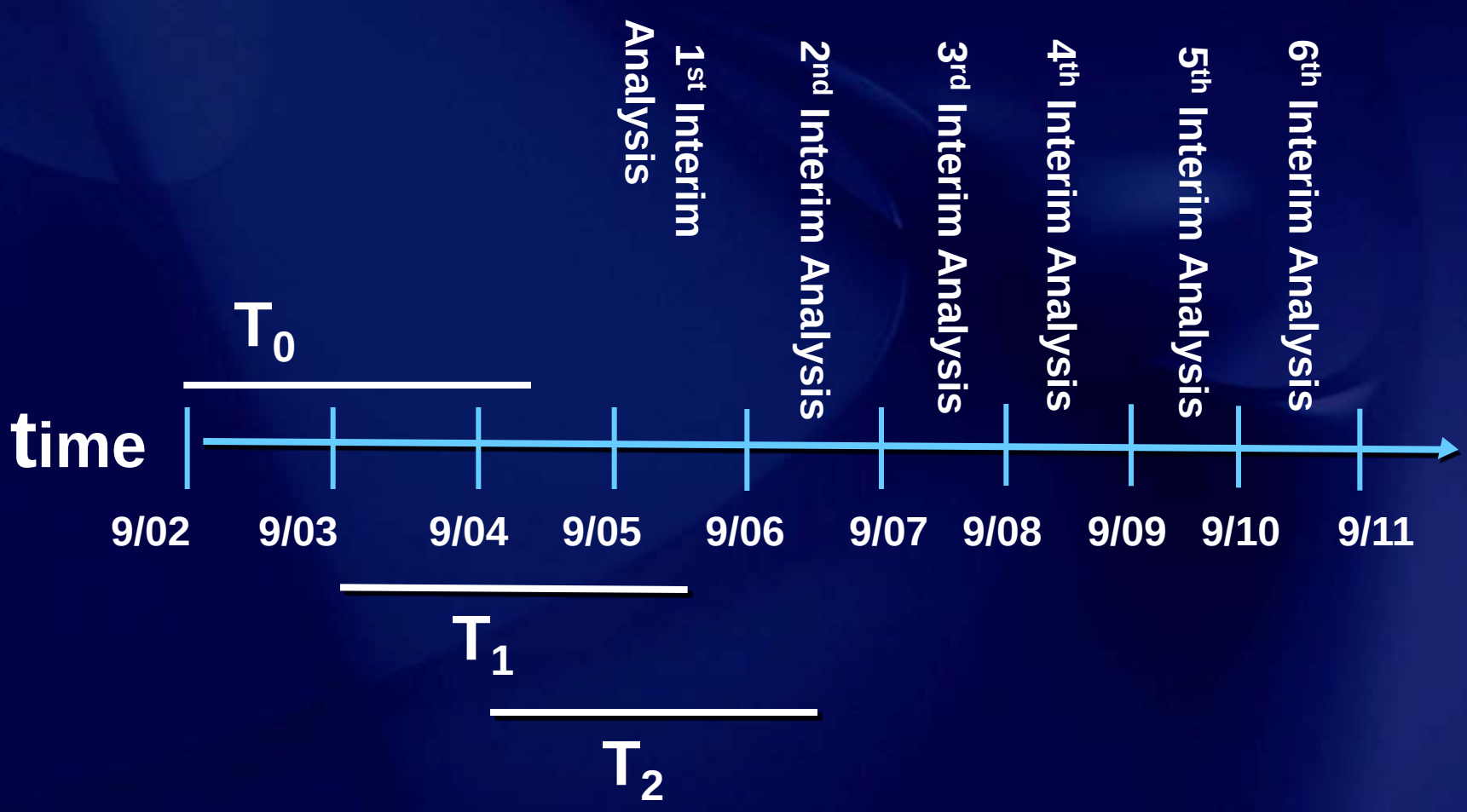
NLST Cumulative Accrual



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

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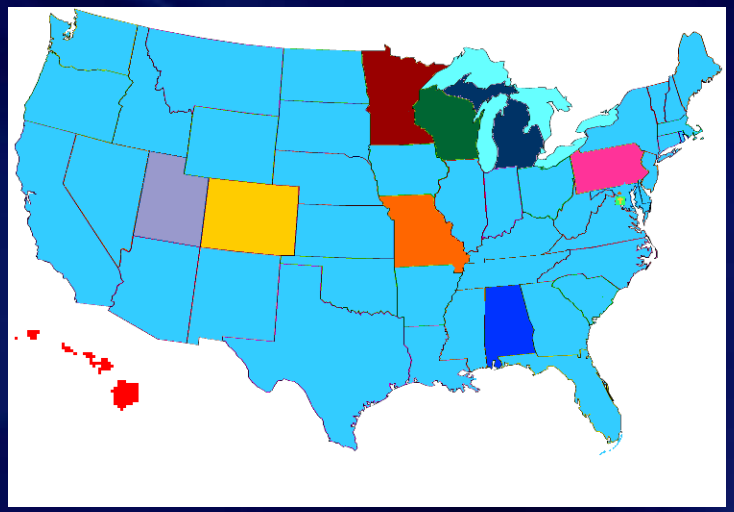
https://www.plcostars.com

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)

39,115 Female

CA-125 (T0-T5)

Transvaginal ultrasound (T0-T3)

38,350 Male

PSA (T0-T5)

Digital rectal examination (T0-T3)

Control Arm

38,355 Male

39,122 Female

Routine medical care

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*

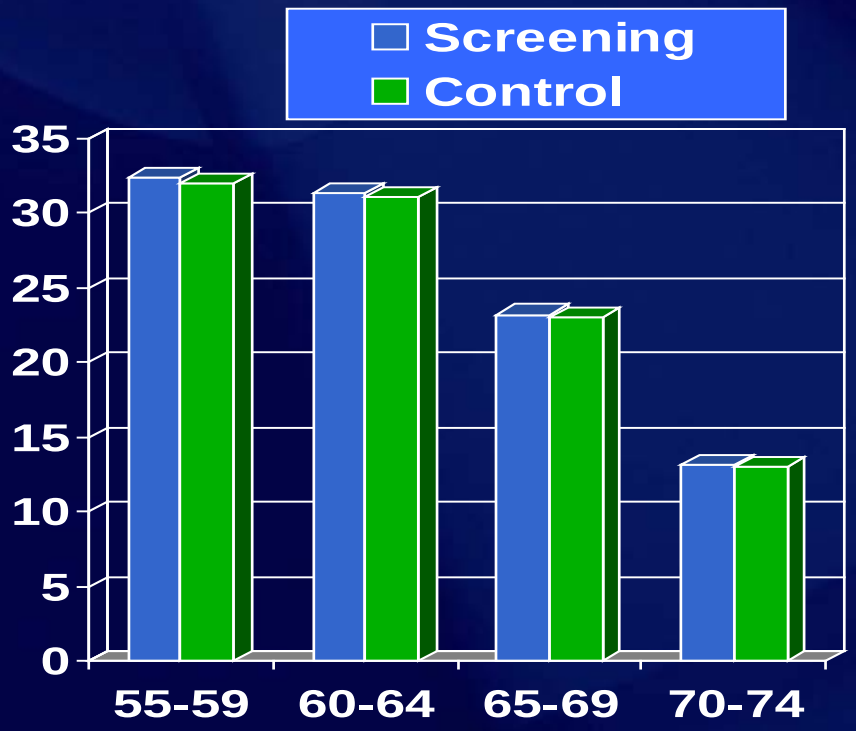
Marker	Phase II	Phase III
CA 125	73%	86%
HE4	57%	73%
CA 72.4	40%	44%
CA 15.3	46%	45%
MSLN	35%	40%
IGFBP2	38%	9%
Prolactin	34%	13%
Transthyretin	47%	2%
Transferrin	23%	9%

*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)

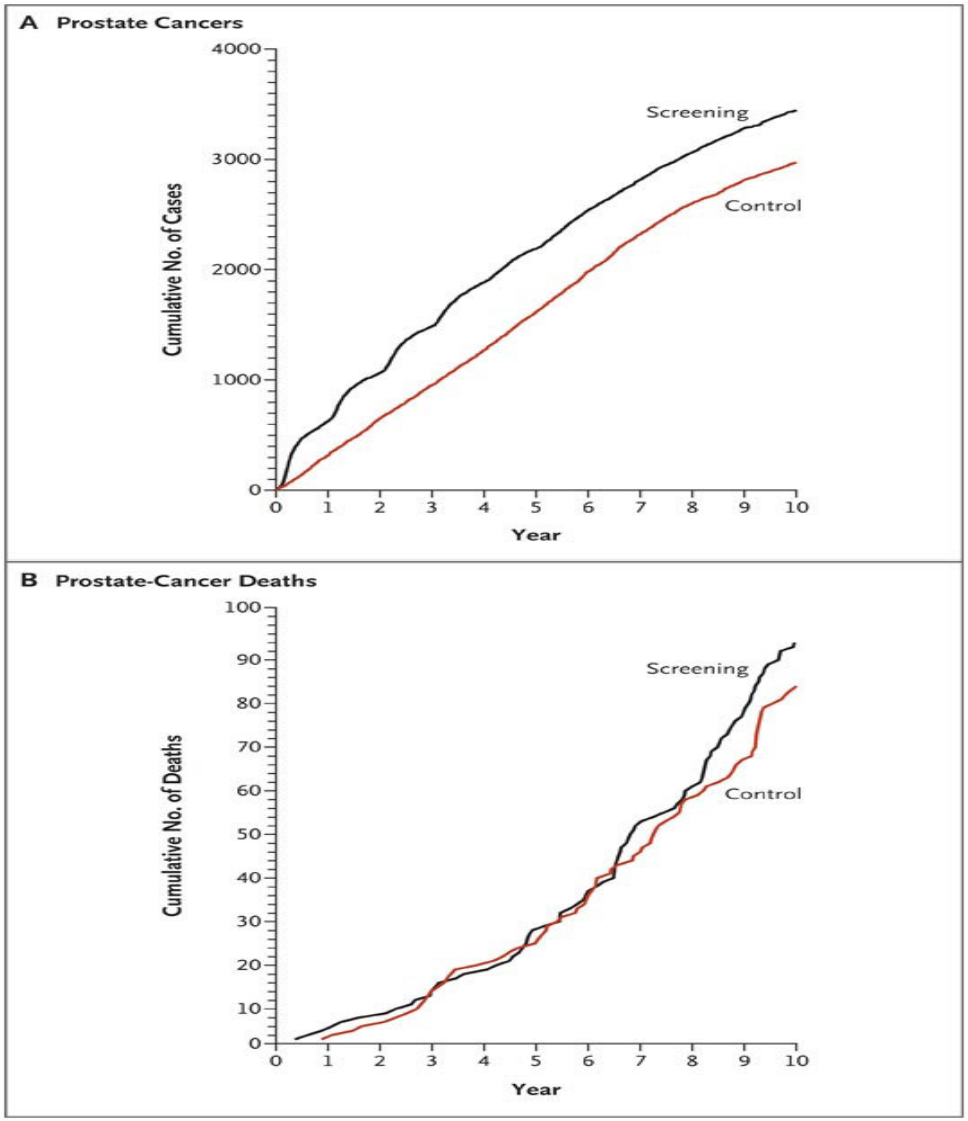
Compliance and Contamination

- Screening before entry (screening/control)
  - PSA test DRE
    - Once: 34.6/34.3 32.8/31/9
    - Two or more: 9.4/9.8 22.2/22.0

- Compliance
  - PSA 85%; DRE 86%

- Testing in the control group
  - PSA: 40% in first year to 52% in sixth year
  - DRE: Range from 41 to 46%

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

The NEW ENGLAND JOURNAL of MEDICINE

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