

U.S. PREVENTIVE SERVICES TASK FORCE LUNG CANCER SCREENING RECOMMENDATION

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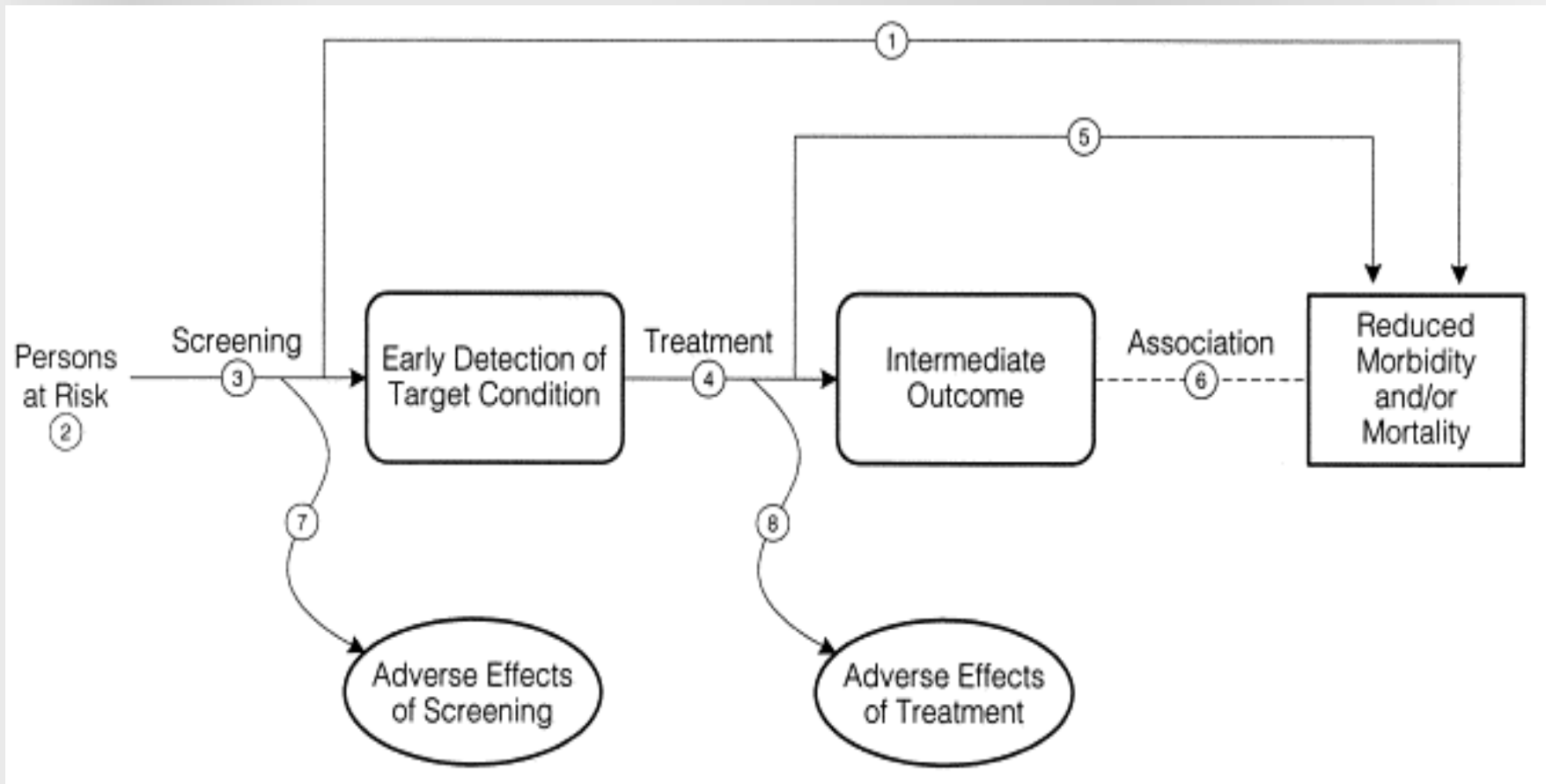
DISCLAIMER

- *This presentation will discuss a recommendation of the U.S. Preventive Services Task Force (USPSTF). Although I served on the Task Force at the time of the release of this recommendation, the views expressed may not reflect the process and recommendations of the USPSTF. For the current findings and recommendations of the USPSTF, please see: www.uspreventiveservicestaskforce.org.*

U.S. PREVENTIVE SERVICES TASK FORCE

- The U.S. Preventive Services Task Force is an independent, volunteer panel of national experts in prevention and evidence-based medicine.
- The Task Force works to improve the health of all Americans by *making evidence-based recommendations about clinical preventive services*

ANALYTIC FRAMEWORK ON SCREENING FOR A DISEASE: WHAT EVIDENCE DO WE SEEK?



THE USPSTF STEPS: BRIEF AND GENERIC

- Assess the evidence across the analytic framework, synthesizing the assessment of each key question:
 - Judge the ***certainty*** of the estimate of benefits and harms
 - Judge the ***magnitude*** of both benefits and harms
 - Determine and judge the *balance* of benefits and harms: the ***magnitude of net benefit***

THE USPSTF STEPS: BRIEF AND GENERIC

- If evidence is not sufficient (low certainty), letter grade is “I”
 - In the context of insufficient evidence, the USPSTF does not use “expert opinion”
- If evidence is sufficient, assign a letter grade:
 - A, B, C or D – reflecting both the certainty and magnitude of net benefit

GRADES OF RECOMMENDATION

Certainty of net benefit	Magnitude of net benefit			
	Substantial	Moderate	Small	Zero/Negative
High	A	B	C	D
Moderate	B	B	C	D
Low	I - Insufficient Evidence			

SCREENING FOR LUNG CANCER

U.S. PREVENTIVE SERVICES TASK
FORCE

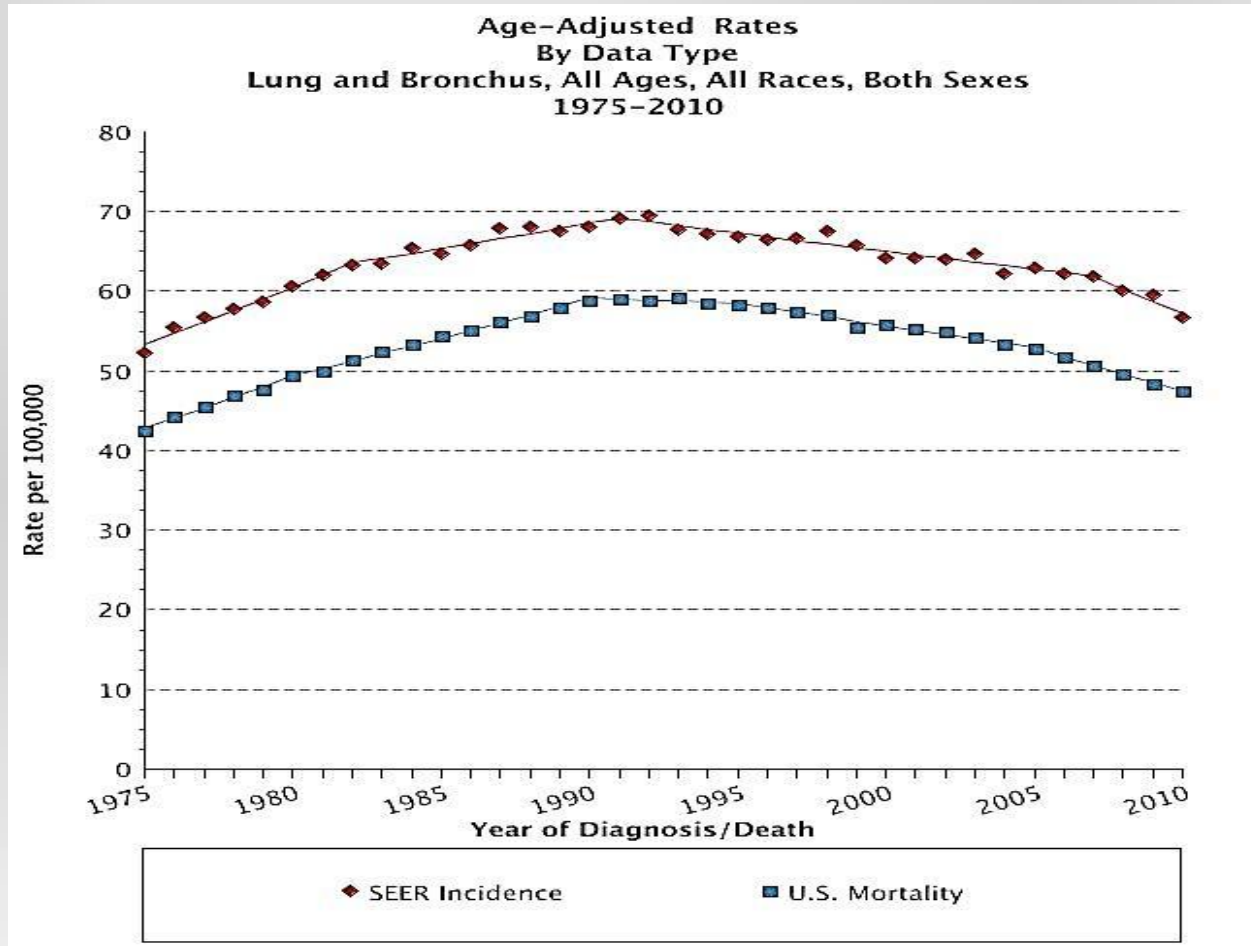
LUNG CANCER IS IMPORTANT

- Leading cause of cancer related death.
- ~ 160,000 deaths per year in the U.S.

LUNG CANCER IS IMPORTANT

- Tobacco related in 85-90%

LUNG CANCER INCIDENCE AND MORTALITY



CXR SCREENING FOR LUNG CANCER

- CXR: 2 trials
 - Mayo Lung Project
 - Prostate, Lung, Colon, Ovarian Screening Trial (PLCO); 1993 - 2001

CXR SCREENING

- Prostate, Lung, Colon, Ovarian Screening Trial (PLCO); 1993 – 2001
 - Males and females ages 55-74 from general population (with a subset of current/former smokers).
 - 77,445 randomized to PA CXR annually.
 - 77,456 randomized to usual care.
 - Evaluation of abnormal tests was done by participants providers.
 - 13-year follow-up.
 - Good-quality.

PLCO

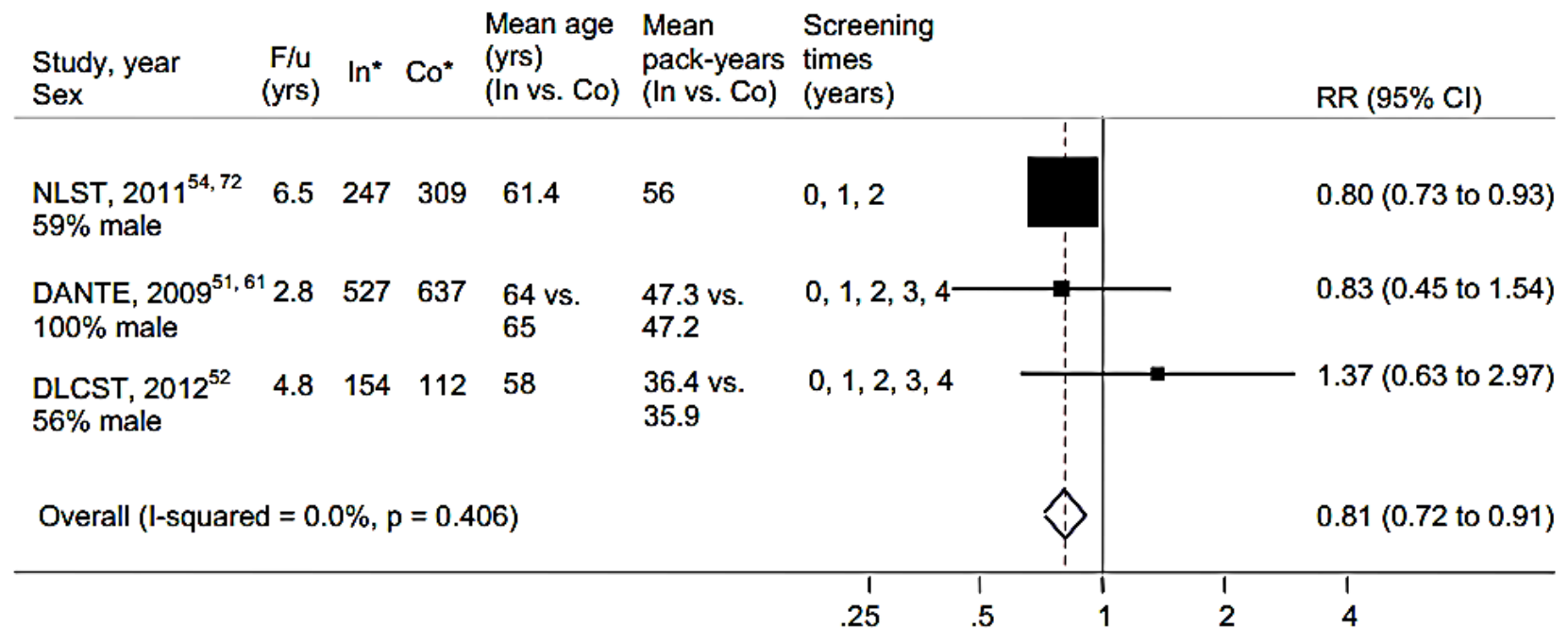
- PLCO results: high-risk population (6-year follow-up)
 - Incidence: RR 1.0 (95 % CI; 0.88-1.13)
 - Lung cancer mortality: RR 0.94 (95% CI; 0.81-1.10)

SCREENING WITH LOW DOSE CT

- LDCT: 4 (of 7 total) RCTs with published results in both trial arms.
 - NLST
 - DANTE
 - DLCST
 - MILD: we ultimately agreed should not influence decision

META-ANALYSIS LUNG CANCER MORTALITY

Figure 3. Meta-Analysis of Lung Cancer Mortality



*Per 100,000 person-years

META-ANALYSIS ALL-CAUSE MORTALITY

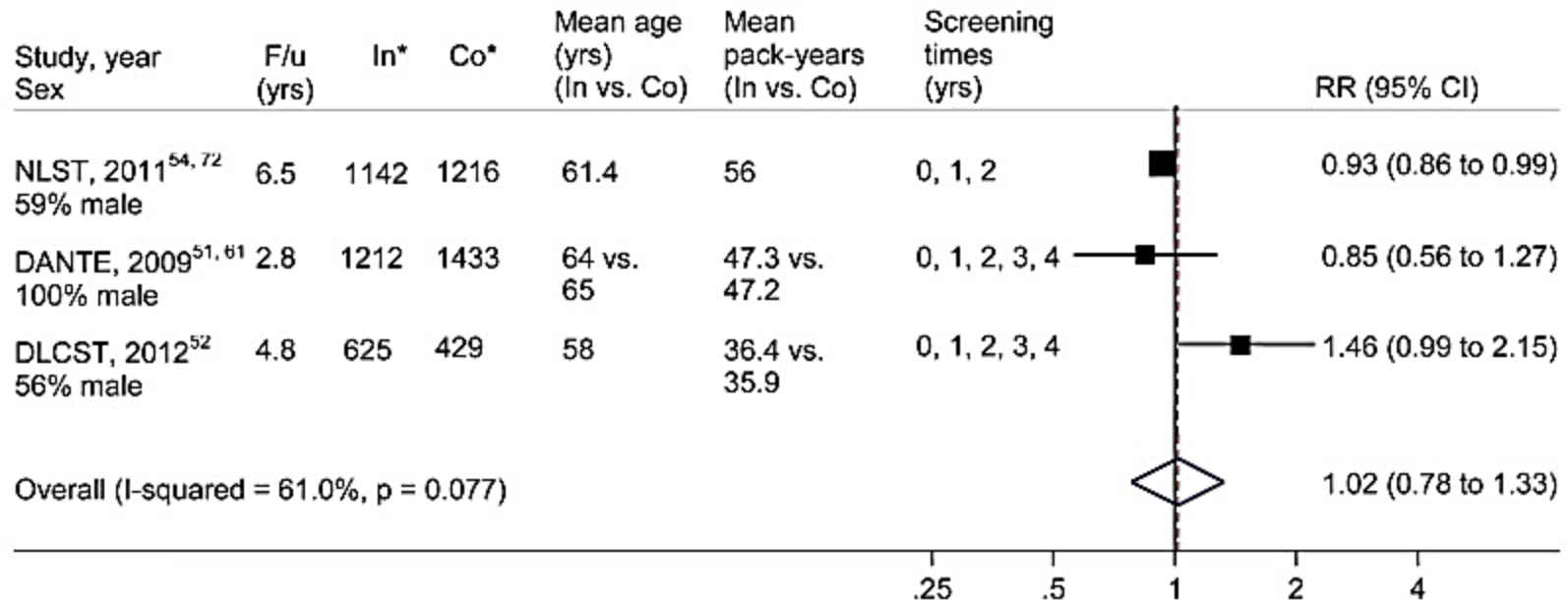


Figure 4 Meta-Analysis of All-Cause Mortality

WHO WAS ENROLLED?

NLST

- N=53,454
- > 30 pack-year history
- Mean age = 61.4

DLCST

- N=4104
- >20 pack-years
- Mean age = 57.9 yrs

LUNG CANCER IS IMPORTANT

- In the three referenced trials of high risk smokers in the previous meta-analysis, in the control groups during the follow-up period there were:
 - 3078 total deaths
 - 1058 deaths from lung cancer (34% of all deaths)
- Contrast that to the ERSPC where over long term follow-up there were:
 - 20, 026 total deaths
 - 522 deaths from prostate cancer (2.6% of all deaths)

SCREENING HELPS

- Per 1000 individuals in the target group, 17 will die of lung cancer over an average of 6.5 years
- With 3 annual screens, can avert 3-4 of those deaths

HARMS

- False positive rate and risks of diagnostic testing
- Radiation
- Overdiagnosis
- Psychological harms, including smoking behavior
- Incidental findings

FALSE POSITIVE SCREEN

- First round of screening: 1000 people screened: 250 positive screens
 - 96% false positive
 - After 3 annual screens, number of individuals with at least one positive screen rises to 390

FALSE POSITIVE SCREEN

- In NLST, a high percentage of false positives resolved with subsequent imaging
 - 8 of the 250 positive screens will have an invasive biopsy to show that they do NOT have cancer
 - Of 17,053 positive results, there were 612 complications and 6 deaths after diagnostic procedure
 - (i.e. approximately 1 in 5000 people screened who do not have lung cancer will die because they were screened in contrast to 15-20 in 5000 who will have lung cancer death averted)

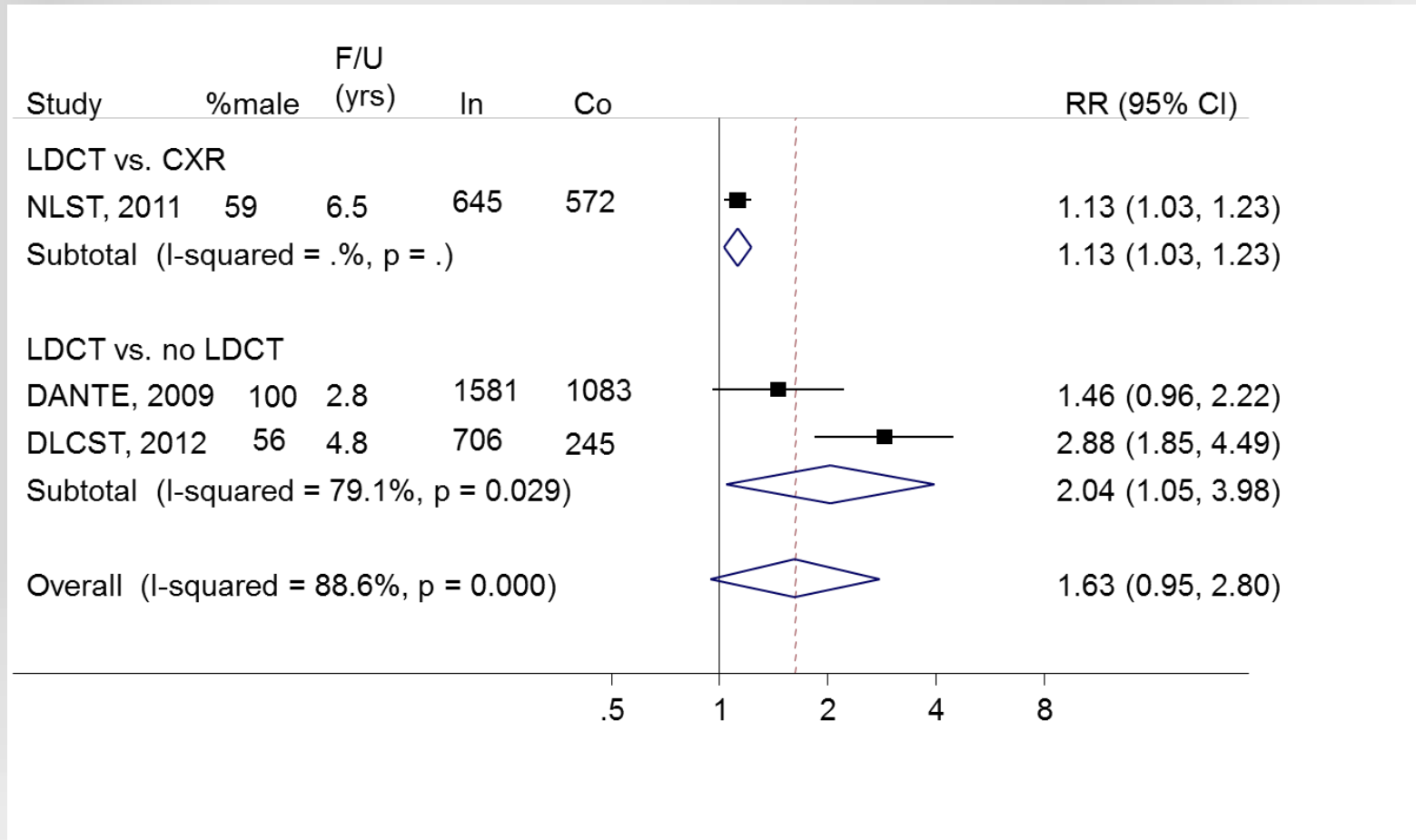
RADIATION

- LDCT radiation ranged from 0.61 to 1.5 mSv per scan
 - Mammogram 0.7 mSv
 - Head CT 1.7 mSv
- Cumulative radiation still a concern
 - F/U scans full dose, not low dose

OVERDIAGNOSIS

- Post recommendation, using NLST data Patz et al reported:
 - Probability that a lung cancer diagnosed on screening is an overdiagnosis is 18.5%
 - Number of overdiagnoses to prevent one death is 1.38
- These estimates are probably high

META-ANALYSIS LUNG CANCER INCIDENCE



OTHER HARMS

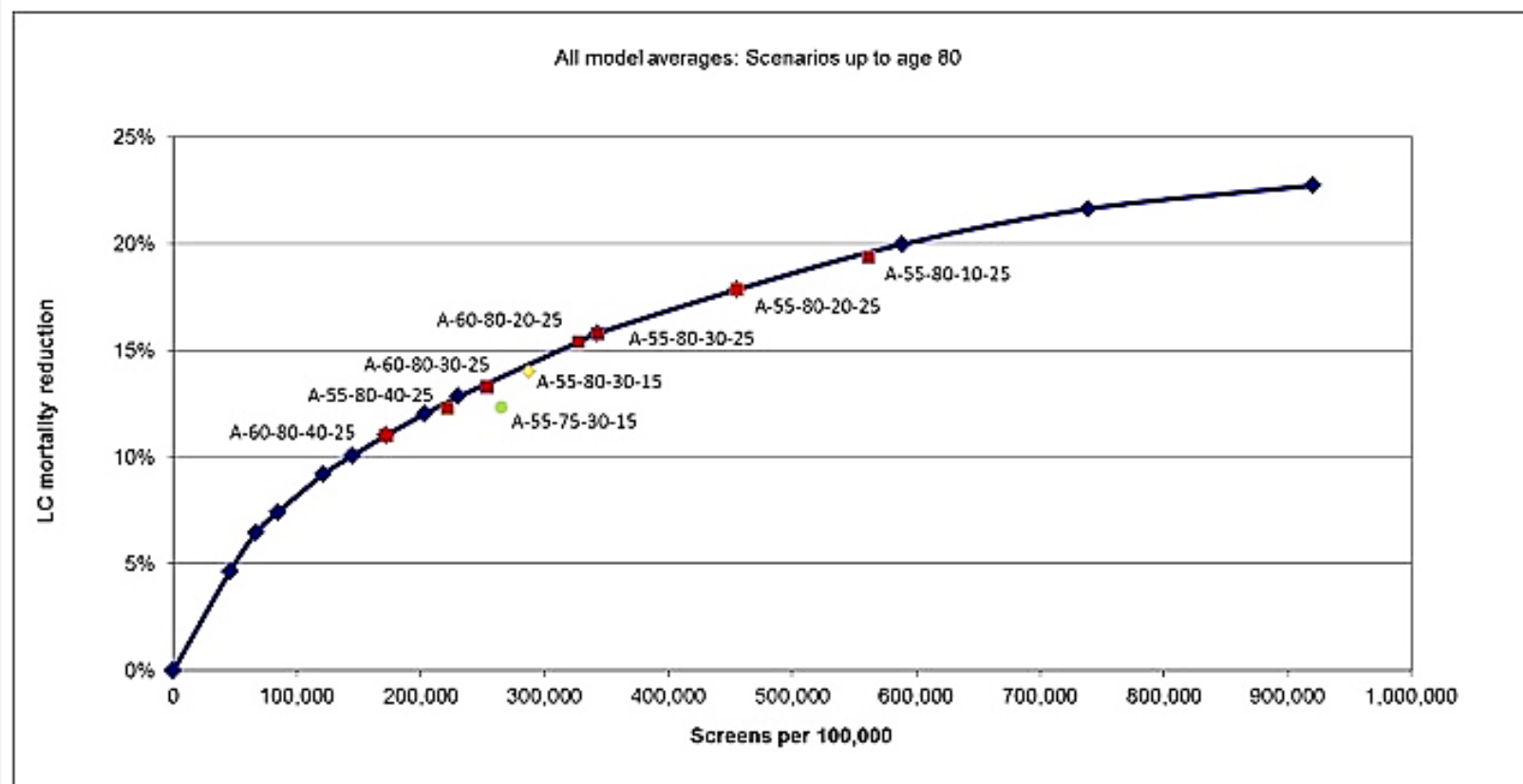
- Psychological harms: overall, no significant impact on quality of life.
- Smoking behavior: no compelling data suggesting either better or worse quit rates
- Incidental findings: 7.5% in NLST had clinically significant, non-lung cancer findings

CISNET MODELING FOR LUNG CANCER SCREENING

WHY MODELING?

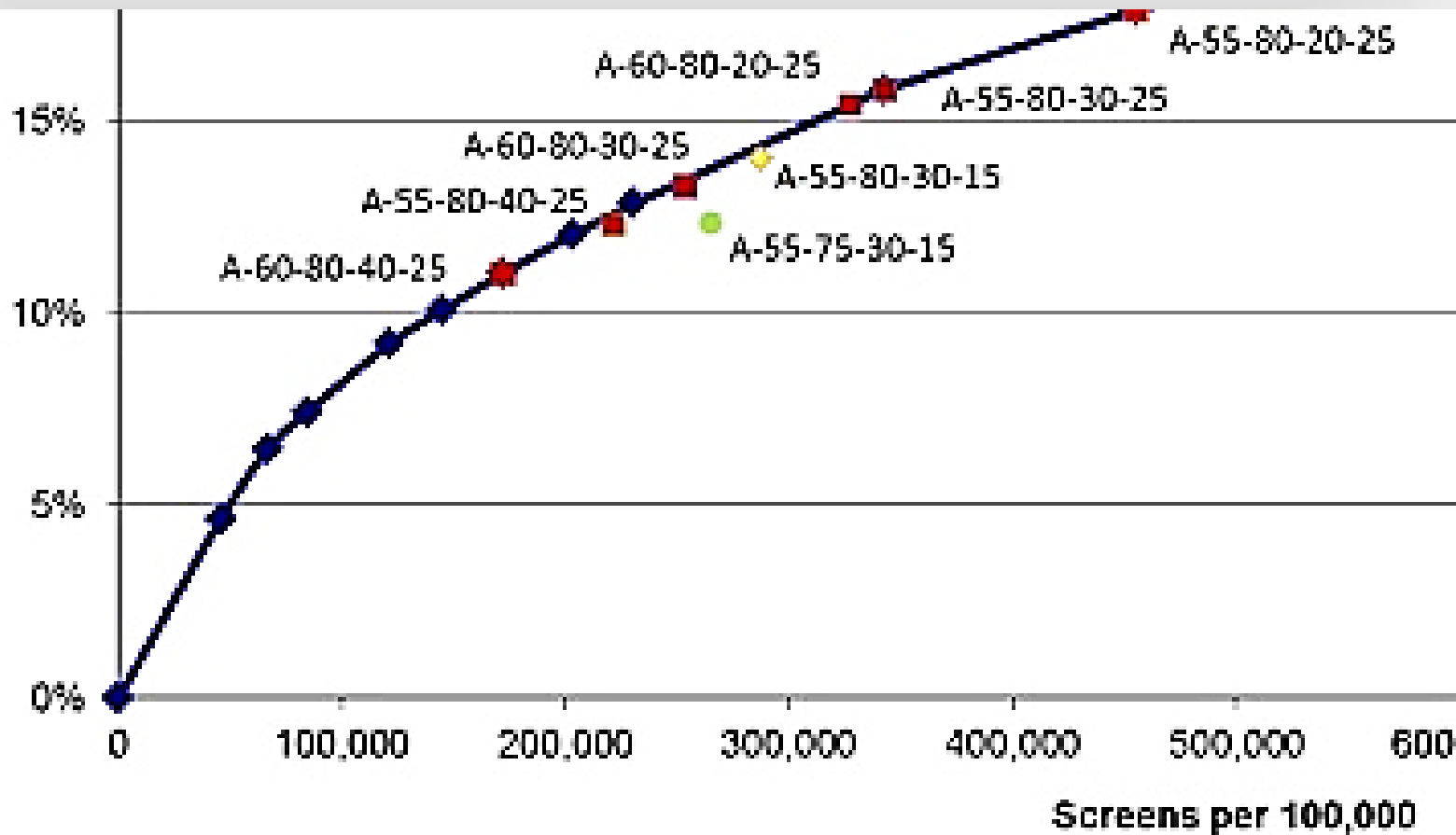
- No trial data for ANY screening test
compare screening across the continuum
of the age ranges recommended for
screening to no screening

Figure 3. Estimated Lung Cancer Mortality Reduction (Average of Five Models) From Annual Computed Tomography Screening in the 1950 Birth Cohort for Programs With Eligible Ages of 55 to 80 Years and Different Smoking Eligibility Cutoffs*



*Highlighted scenarios in Tables 2 and 3 are labeled.

LC mortality reduction



PER 100,000 POPULATION

Scenario	Percentage ever screened	CT screenings	Lung cancer deaths averted	Lifeyears gained
A-60-80-40-25	13.00%	171,924	410	4,211
A-55-75-30-15	19.20%	265,049	459	5,375
A-55-80-30-15	19.30%	286,813	521	5,517
A-55-80-20-25	27.40%	455,381	664	7,092

MODEL RESULTS

55-80-30-15

	Average 5 models	Lower bound	Upper bound
Lung cancer deaths averted	497	177	862
Life-years gained	5,250	2,020	10,153
Screening CT scans	287,000	272,000	301,000
Full dose CT	43,000	23,175	50,100
Surgery/biopsy for benign lesions	910	825	955
Overdiagnosed cancers	190	72	426
Radiation related lung CA death	24		

B RECOMMENDATION

- The USPSTF recommends annual screening for lung cancer with LDCT in adults aged 55 to 80 years who have a 30 pack-year smoking history and currently smoke or have quit within 15 years. Screening should be discontinued once a person has not smoked for 15 years or develops a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery.

IMPLEMENTATION CAVEATS

- Low risk population
- Smoking cessation counseling
- Shared decision making
- Standardization of LDCT screening and f/u abnormal findings
- Registry

QUESTIONS?