

Subset and Histological Analysis of Screening Efficacy in NLST

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NLST Design

- ~54,000 subjects randomized to low-dose CT (LDCT) or chest radiograph (CXR)
- Eligibility: age 55-74, 30+ pack years, current smoker or quit within 15 years
- 33 screening centers across U.S.
- 3 annual rounds of screening
- 6-7 years of total follow-up
- Primary Outcome: lung cancer mortality

NLST Design, cont.

- Deaths ascertained by Annual Study Update forms and NDI searches
- Endpoint verification process – adjudicated cause of death
- Histology – classifications derived from medical records, as in main paper (NEJM 2011); note diagnosis occurred outside of trial auspices
- Limited centralized pathology available (some tumor specimens collected retrospectively)

Secondary Hypotheses in NLST

- Does LDCT screening efficacy vary by major demographic factors (e.g., age, sex)?
- Does LDCT screening efficacy vary by smoking status (current vs. former)?
- Is LDCT screening efficacy differential across lung cancer histologies?
- If screening varies by demographics/smoking status, can this be explained by histology?

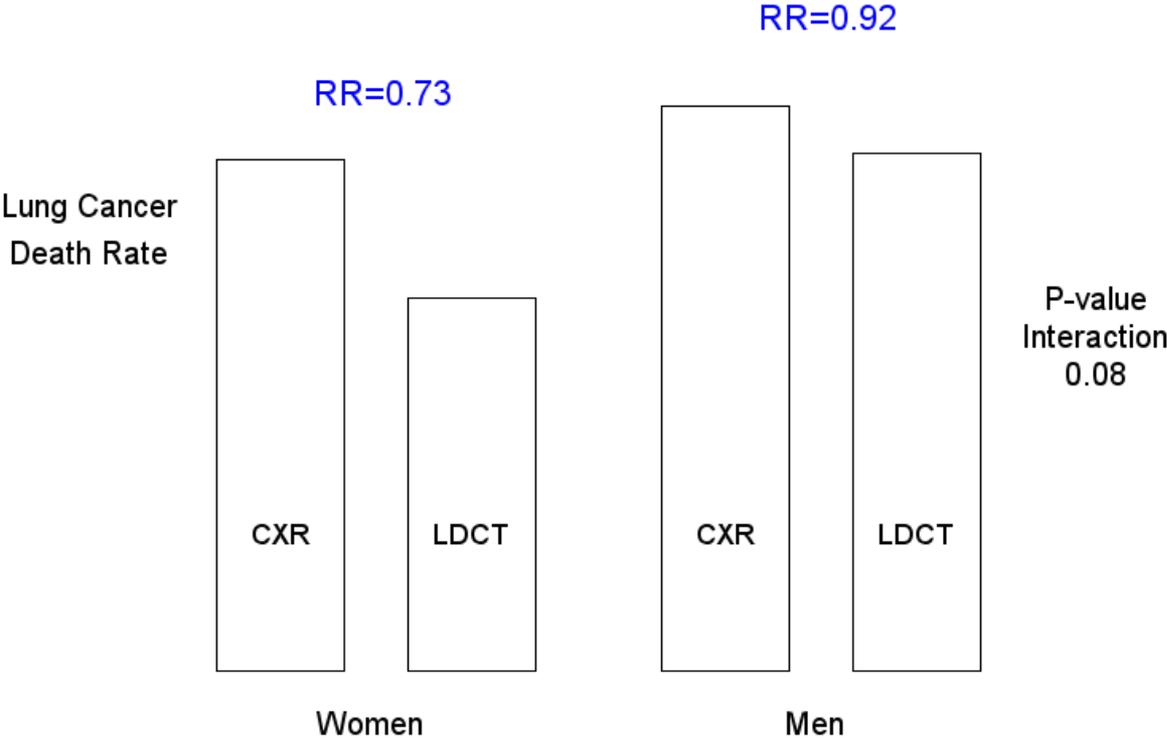
Lung Cancer Screening Mortality Effect by Cutoff Date

	Lung Cancer Deaths (#)		Relative Risk (95% CI)	Number Needed to Screen (95% CI)
	LDCT Arm	CXR Arm		
Jan 15, 2009 Cutoff (NEJM, 2011)	356	443	0.80 (0.73-0.93)	307
Dec 31, 2009 Cutoff (all available data)	469	552	0.84 (0.75-0.95)	322

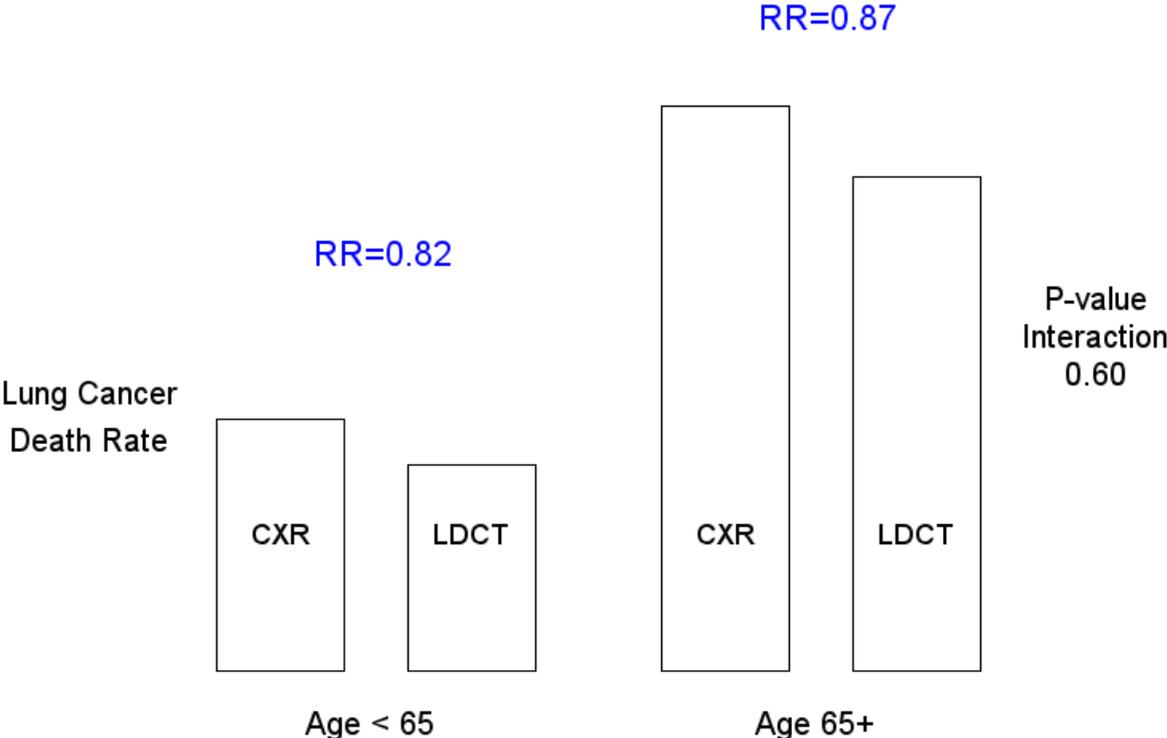
NLST Demographics

	LDCT Arm	CXR Arm
Male	59.0%	59.0%
Age 65+	26.6%	26.6%
Current Smoking	48.1%	48.3%

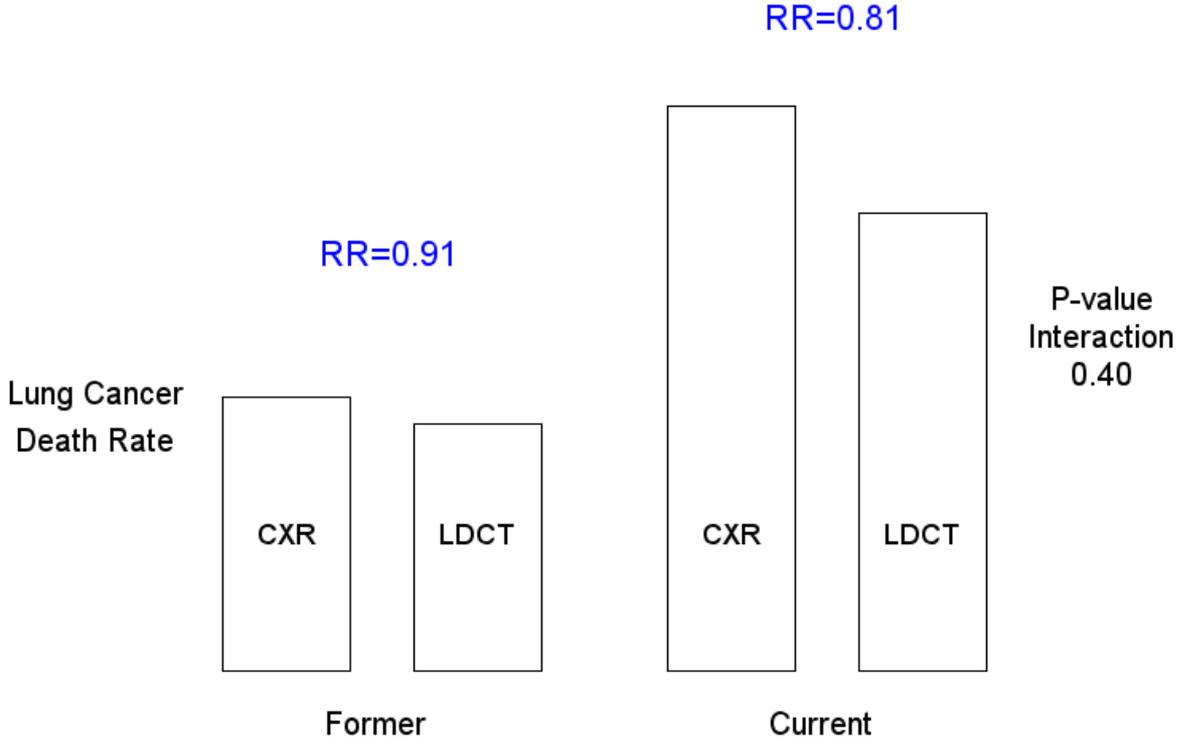
Screening Mortality Benefit by Sex



Screening Mortality Benefit by Age



Screening Mortality Benefit by Smoking Status



Lung Cancer Deaths by Histology

	LDCT Arm	CXR Arm	
	Lung Cancer Deaths	Lung Cancer Deaths	Relative Risk
Adenocarcinoma	136	181	0.75 (0.60-0.94)
Squamous Cell	102	83	1.23 (0.92-1.64)
Other NSCLC	100	144	0.69 (0.54-0.90)
Small Cell	102	113	0.90 (0.69-1.18)
Other/Unk	29	31	0.94 (0.6-1.6)

Global Test for RRs differing
by histology: $p < 0.01$

Survival by Histology

	Start Time of Follow-up	6 Year Survival	6 Year Survival	
Histology		LDCT Arm	CXR Arm	P-value
Adenocarcinoma	Diagnosis	59.1	33.2	<0.0001
	Randomization	71.6	54.5	<0.0001
Squamous Cell	Diagnosis	50.7	48.5	0.82
	Randomization	66.6	65.7	0.68
Small Cell	Diagnosis	14.4	11.5	0.72
	Randomization	39.1	37.8	0.80

LDCT Mortality Benefit by Histology and Sex

Histology	Sex	RR (LDCT vs. CXR)
Adenocarcinoma	Men	0.77 (0.6-1.02)
	Women	0.73 (0.5-1.05)
Squamous Cell	Men	1.31
	Women	1.04
Small Cell	Men	1.10 (0.8-1.6)
	Women	0.67 (0.4-1.03)
All except Small Cell	Men	0.88
	Women	0.76
All except Squamous & Small Cell	Men	0.77 (0.6-0.9)
	Women	0.71 (0.5-0.9)

Conclusions

- LDCT screening efficacy did not vary by age or smoking status in NLST
- LDCT screening efficacy showed borderline significant interaction with sex in NLST, with women having increased benefit
- LDCT screening efficacy appears to vary with lung cancer histology
- Histology may help explain the apparent differential in screening efficacy by sex



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Extra Slides

Lung Cancer Histology Distribution by Sex and Trial Arm

	LDCT	LDCT	CXR	CXR
	Men	Women	Men	Women
	# (%)	# (%)	# (%)	# (%)
BAC	47 (7)	64 (15)	18 (3)	18 (5)
Adenocarcinoma	220 (34)	169 (39)	194 (34)	143 (36)
Squamous Cell	182 (28)	67 (15)	147 (26)	67 (17)
Small Cell	92 (14)	51 (12)	89 (16)	74 (19)
All	665 (100)	434 (100)	574 (100)	395 (100)

Screen Detection by Histology and Trial Arm

	LDCT Arm	CXR Arm
Histology	Screen detected cases #, % of total cases	Screen detected cases #, % of total cases
Adenocarcinoma	258 (68%)	112 (34%)
Squamous Cell	136 (56%)	70 (34%)
Small Cell	49 (36%)	28 (18%)
All Lung Cancer	649 (61%)	279 (30%)

Centralized Pathology Results

Original Histology	# with Centralized Pathology	% Concordant
Squamous Cell	108	88%
Adenocarcinoma	185	81%