Lung Cancer Screening in Non-Smokers and High-Risk Populations

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Disclosures

Dr Chiappori has no relevant financial relationships

Lung Cancer Screening
NLST - Reduction in Mortality

- Lung cancer (LC) screening with LDCT compared to CXR, lead to a reduction in LC mortality in (**high-risk**) populations defined by age and smoking history.
- The LC detection rate was 1.1%.
- Relative reduction in mortality from LC with LDCT screening of 20.0% (95% CI, 6.8 to 26.7; P = 0.004).
- The rate of death from any cause was reduced in the LDCT group, by 6.7% (95% CI, 1.2 to 13.6; P = 0.02).

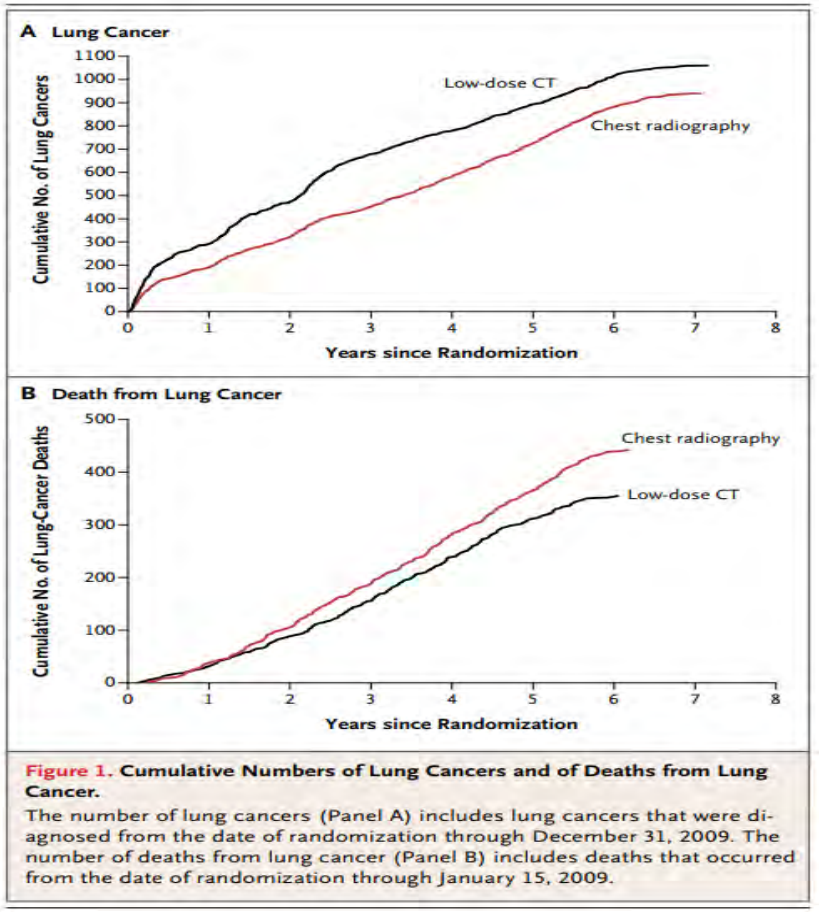
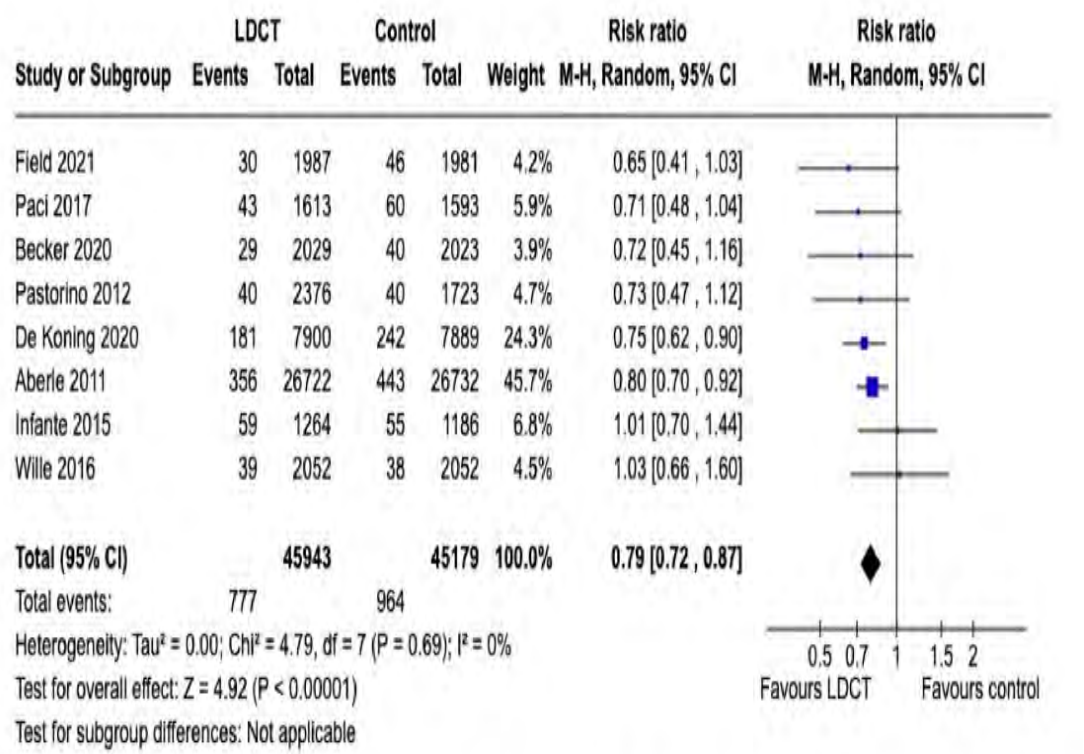


Figure 1. Cumulative Numbers of Lung Cancers and of Deaths from Lung Cancer.
The number of lung cancers (Panel A) includes lung cancers that were diagnosed from the date of randomization through December 31, 2009. The number of deaths from lung cancer (Panel B) includes deaths that occurred from the date of randomization through January 15, 2009.

Aberle DR, et al. NEJM 2011; 365(5):395-409

Lung Cancer Screening
Lung Cancer Mortality (Meta-analyses)



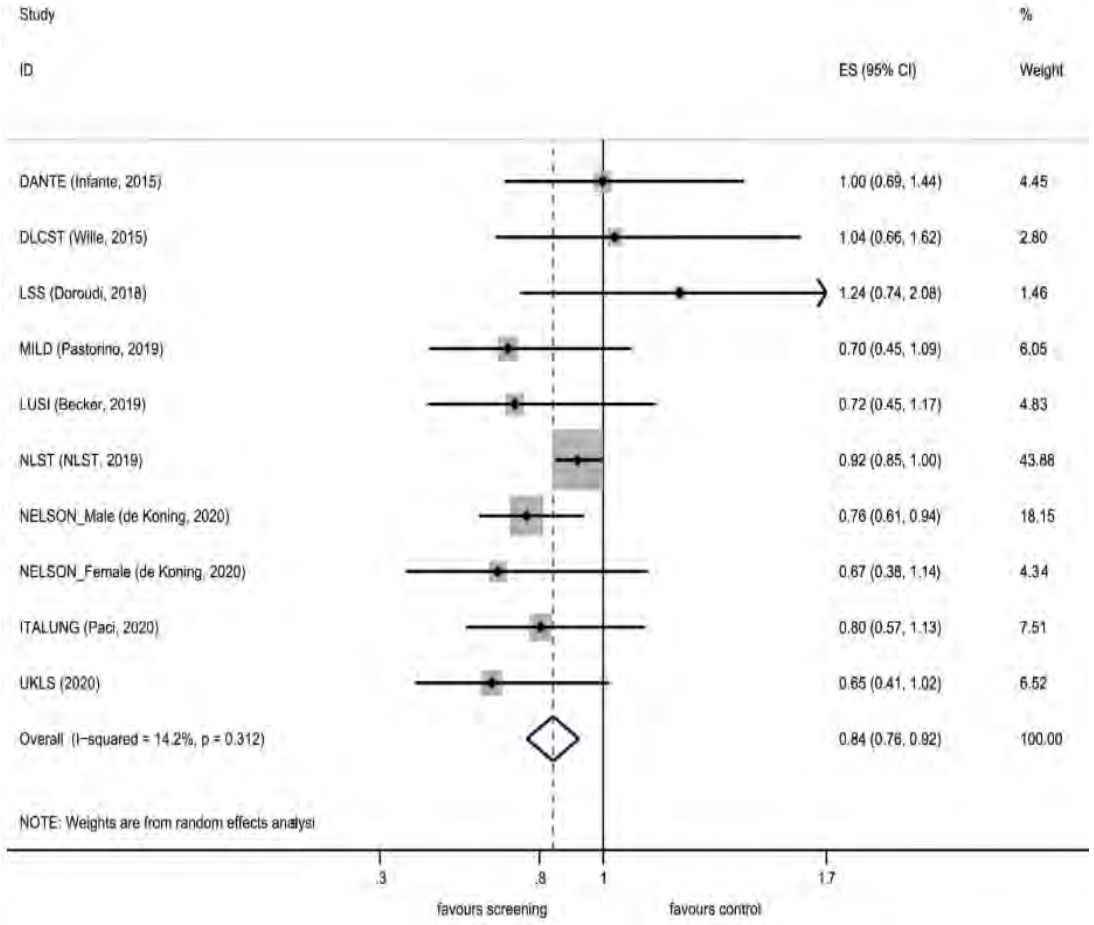
Study or Subgroup	LDCT Events	LDCT Total	Control Events	Control Total	Weight	Risk ratio M-H, Random, 95% CI
Field 2021	30	1987	46	1981	4.2%	0.65 [0.41 , 1.03]
Paci 2017	43	1613	60	1593	5.9%	0.71 [0.48 , 1.04]
Becker 2020	29	2029	40	2023	3.9%	0.72 [0.45 , 1.16]
Pastorino 2012	40	2376	40	1723	4.7%	0.73 [0.47 , 1.12]
De Koning 2020	181	7900	242	7889	24.3%	0.75 [0.62 , 0.90]
Aberle 2011	356	26722	443	26732	45.7%	0.80 [0.70 , 0.92]
Infante 2015	59	1264	55	1186	6.8%	1.01 [0.70 , 1.44]
Wille 2016	39	2052	38	2052	4.5%	1.03 [0.66 , 1.60]
Total (95% CI)		**45943**		**45179**	**100.0%**	**0.79 [0.72 , 0.87]**
Total events:	777		964			

Heterogeneity: Tau² = 0.00; Chi² = 4.79, df = 7 (P = 0.69); I² = 0%
Test for overall effect: Z = 4.92 (P < 0.00001)
Test for subgroup differences: Not applicable

Risk ratio M-H, Random, 95% CI
0.5 0.7 1 1.5 2
Favours LDCT Favours control

Figure 1. Cochrane library: lung cancer-related mortality in eight RCTs. Bonney et al., 2022[2] permission by John Wiley and Sons. CI, confidence interval; LDCT, low-dose computed tomography; M-H, Mantel-Haenszel; RCT, randomized controlled trials; RR, risk ratio.

JTO 2024; 19(1):36-51



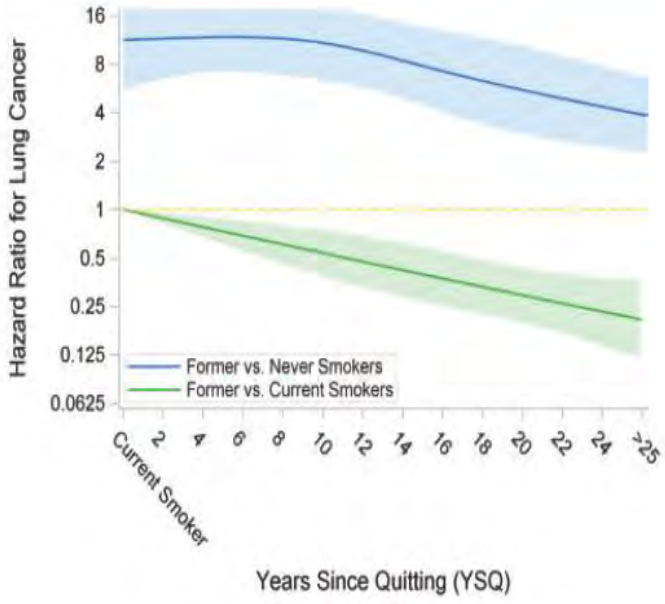
The Lancet Regional Health-Europe,2021; 10:1-11

Lung Cancer Screening
Eligible Population (smoking and age)

Study	Smoking history	Age
NLST	>30py quit<15yrs	55-80
NELSON	>15 or 17,5py quit<10yrs	50-75
ITALUNG	>20py quit<10yss	55-69
JECS	<30yrs	50-64
UKLS	Risk modelling	

Risk Factors for Lung Cancer
Smoking

- Cigarette smoking is most prevalent and reported RF in 75% to 90% of those diagnosed.
- Among ever smokers, the majority of lung cancers (92.7%) occurred among heavy smokers, with 21.3 or more cumulative pack-years of smoking.
- Among current and former smokers with 21.3 or more pack-years, the unadjusted lung cancer risk was more than 10-fold higher than never smokers



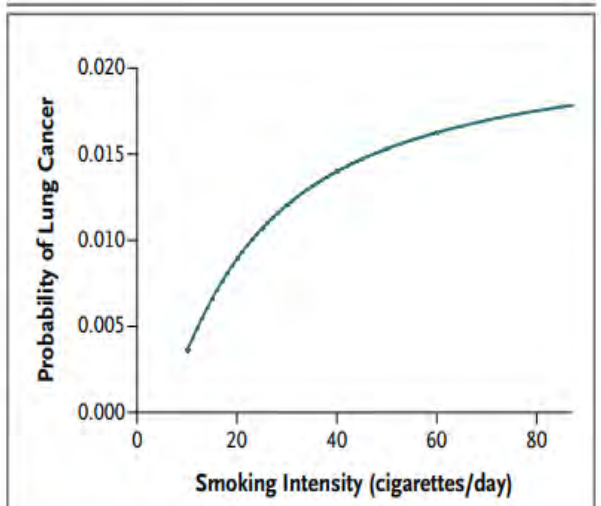


Figure 1. Nonlinear Relationship between Smoking Intensity (Average Number of Cigarettes Smoked per Day) and Lung-Cancer Risk.

Probabilities were calculated on the basis of the following variables: an age of 62 years, white race or ethnic group, some college education, a body-mass index (the weight in kilograms divided by the square of the height in meters) of 27, no chronic obstructive pulmonary disease, no personal history of cancer, no family history of lung cancer, status as a former smoker, smoking history of 27 years, and cessation of smoking 10 years before enrollment.

- Current smoking, increased smoking intensity (average number of cigarettes per day), duration and time since quitting
- MVA modeling:
  - smoking intensity had a significant nonlinear association with lung cancer
  - Lower risk in former heavy smokers after 5-9 years since quitting

J Natl Cancer Inst, 2018; 110(11):

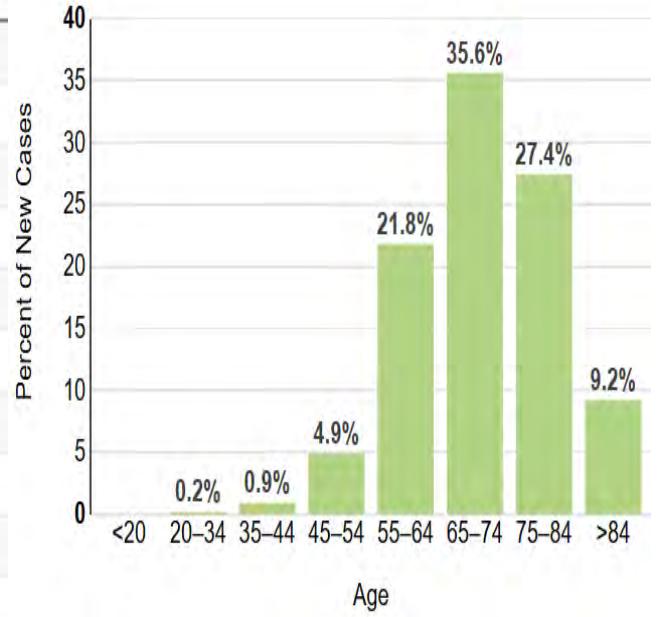
J Thorac Oncol 2024; 19(8):1155–1163

Risk Factors for Lung Cancer
Age

- Lung cancer incidence increases with age.
- Most people diagnosed with lung cancer are 65 or older; a very small number diagnosed are younger than 45
- Incidence rates increase steadily for females and more steeply for males, starting around age 40-44.
- The highest rates are in the 75 to 79 age group for females and the 85 to 89 age group for males.
- The average age of people when diagnosed is about 70.

https://seer.cancer.gov/statfacts/html/lungb.html

Age	Case counts per 100,000 people
15 to 19	0.1
20 to 24	0.3
25 to 29	0.5
30 to 34	1.0
35 to 39	2.5
40 to 44	5.5
45 to 49	14.2
50 to 54	33.2
55 to 59	79.9
60 to 64	140.5
65 to 69	198.4
70 to 74	262.8
75 to 79	334.7
80 to 84	332.6
85+	224.1



Median Age At Diagnosis

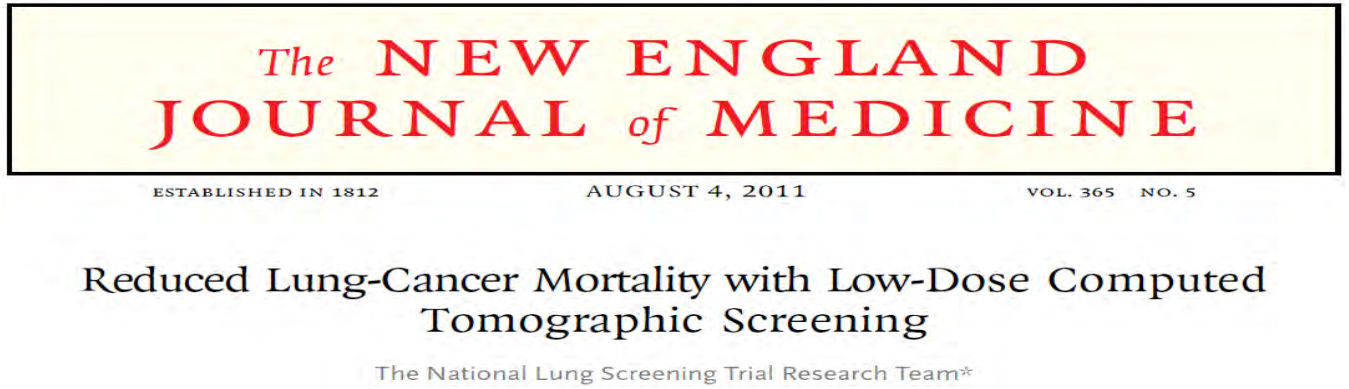
71

Lung Cancer Screening
High Risk Population

Is there a definition?

What is the definition?

Lung Cancer Screening
High Risk Population



- The National Lung Screening Trial (NLST) was conducted to determine whether screening with low-dose CT could reduce mortality from lung cancer.
- Screening with the use of low-dose CT reduces mortality from lung cancer.
- Therefore, the National Cancer Institute (NCI) funded the National Lung Screening Trial (NLST), a randomized trial, to determine whether screening with low-dose CT, as compared with chest radiography, would reduce mortality from lung cancer among **high-risk** persons.

Aberle DR, et al. NEJM 2011; 365(5):395-409

Lung Cancer Screening
USPSTF recommendations

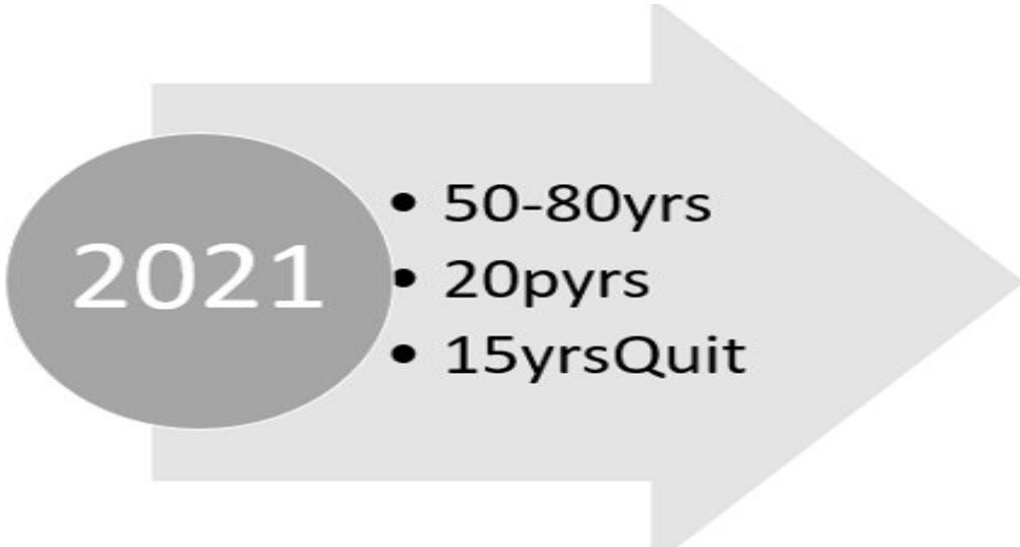
2013

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 the past 15 years

Ann Intern Med 2014; 160(5):330-338.

2021

Annual screening for lung cancer with LDCT in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years



JAMA 2021; 325(10):962-970

NCCN
High Risk Definition

High risk – 50 years of age and over with a 20 pack-year or more history of smoking cigarettes. Lung cancer screening is recommended. People at high risk for lung cancer may benefit from low-dose computed tomography (LDCT) screening.

Lung Cancer Screening
Current Policy

- Current screening policy in the United States is based on age and smoking history.
  - Smoking history and age not the only risk factors however
  - Additional Risk Factors
    - Race/ethnicity, sex, BMI
    - Secondhand smoke
    - Family/personal history of lung cancer
    - Previous radiation therapy to the chest
    - Indoor (cooking and heating fumes) and outdoor air pollution,
    - Exposures to environmental or occupational lung carcinogens, asbestos, silica, radon
    - Socioeconomic status (may be?)
    - Pulmonary diseases, such as tuberculosis, COPD (emphysema/chronic bronchitis), and fibrotic lung diseases.
  - Pack-Year count : Inadequate and biased measure of risk
- It is recognized that these 2 criteria alone miss many individuals who develop lung cancer.
  - A portion of individuals, ineligible by these 2 criteria, are still at high risk for lung cancer

Lung Cancer Screening in High-Risk Populations

Lung Cancer Screening
High Risk Population

- Generally agreed that screening should be limited to high-risk persons for whom the potential benefits of LDCT screening would outweigh its potential harms
  - It is uncertain how a high-risk target population should be defined.
- Many professional societies have endorsed the use of the NLST criteria, however:
  - Recognition that more refined risk assessments, accounting for additional risk factors not considered in the NLST criteria, could improve the selection process for lung-cancer screening.
  - The use of an accurate model that incorporates additional risk factors to select persons for screening may identify more persons with lung cancer or that will develop lung cancer
- Despite theoretical grounds for tailoring screening recommendations to the individual risk of lung cancer death, empirical evidence for risk-based lung-cancer screening is lacking (*early, preliminary, yet to be developed, being developed*).

Lung Cancer Screening Risk Prediction Models

- PLCO: Validated LC risk prediction model from the PLCO screening trial
- Complicated modeling procedures
- Cumbersome to apply
- Inaccurate estimates for NLST

JNCI 2011; 103(13):1058-1068.

Table 1 List of Variables in Epidemiological Prediction Models

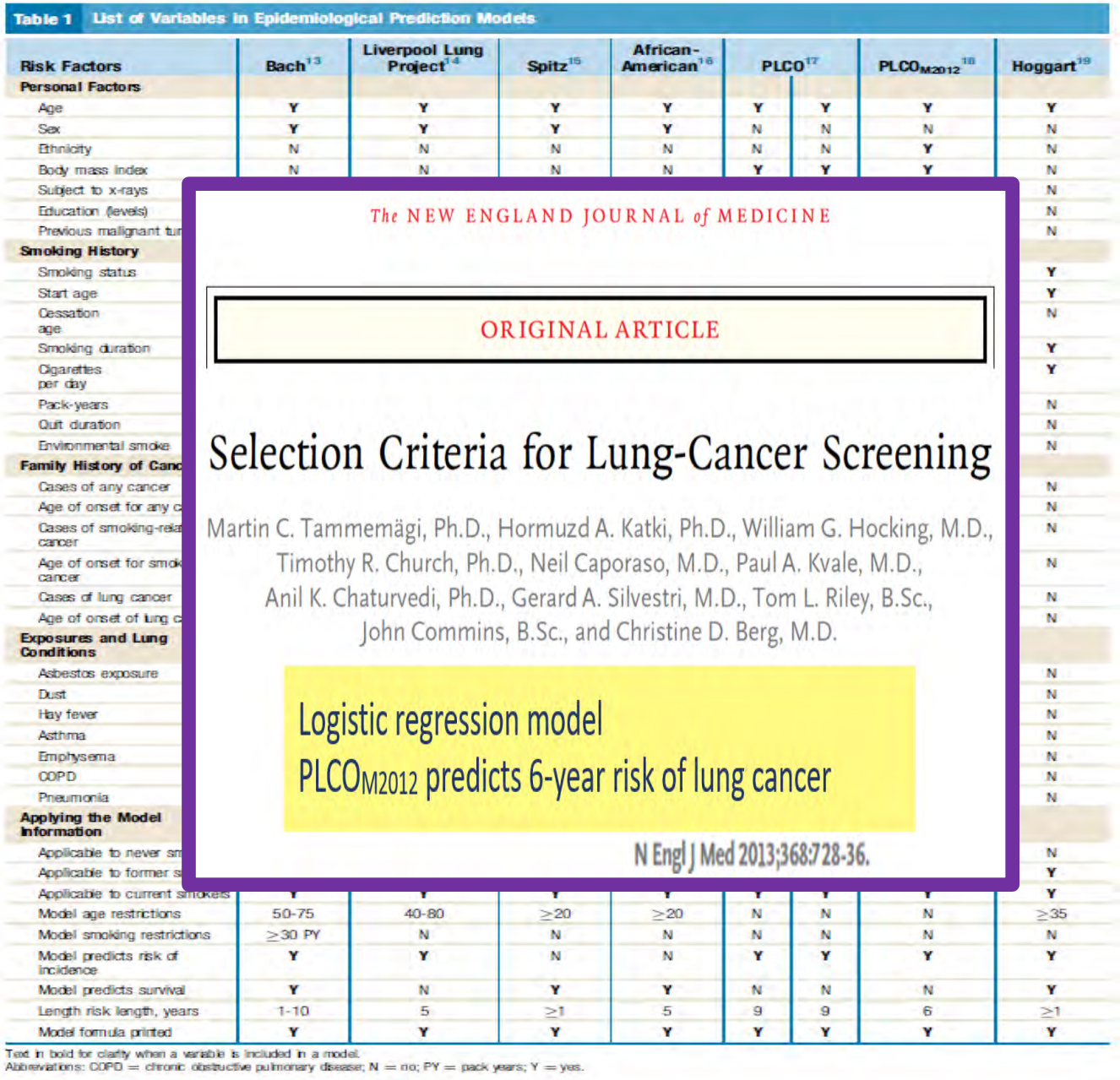
Risk Factors	Bach[13]	Liverpool Lung Project[14]	Spitz[15]	African-American[16]	PLCO[17]		PLCO$_{M2012}$[18]	Hoggart[19]
Personal Factors								
Age	Y	Y	Y	Y	Y	Y	Y	Y
Sex	Y	Y	Y	Y	N	N	N	N
Ethnicity	N	N	N	N	N	N	Y	N
Body mass index	N	N	N	N	Y	Y	Y	N
Subject to x-rays	N	N	N	N	Y	Y	N	N
Education (levels)	N	N	N	N	Y	Y	Y	N
Previous malignant tumor	N	Y	N	N	N	N	Y	N
Smoking History								
Smoking status	N	N	Y	Y	Y	Y	Y	Y
Start age	N	N	N	N	N	N	N	Y
Cessation age	N	N	Y	Y	N	N	N	N
Smoking duration	Y	Y	N	N	Y	Y	Y	Y
Cigarettes per day	Y	N	N	N	N	N	Y	Y
Pack-years	N	N	Y	Y	Y	Y	N	N
Quit duration	Y	N	N	Y	N	Y	Y	N
Environmental smoke	N	N	Y	N	N	N	N	N
Family History of Cancer								
Cases of any cancer	N	N	N	N	N	N	N	N
Age of onset for any cancer	N	N	N	N	N	N	N	N
Cases of smoking-related cancer	N	N	Y	N	N	N	N	N
Age of onset for smoking cancer	N	N	N	N	N	N	N	N
Cases of lung cancer	N	Y	Y	N	Y	Y	Y	N
Age of onset of lung cancer	N	Y	N	N	N	N	N	N
Exposures and Lung Conditions								
Asbestos exposure	Y	Y	Y	N	N	N	N	N
Dust	N	N	Y	Y	N	N	N	N
Hay fever	N	N	Y	Y	N	N	N	N
Asthma	N	N	N	N	N	N	N	N
Emphysema	N	N	Y	N	N	N	N	N
COPD	N	N	N	Y	Y	Y	Y	N
Pneumonia	N	Y	N	Y	N	N	N	N
Applying the Model Information								
Applicable to never smokers	N	Y	Y	Y	Y	N	N	N
Applicable to former smokers	Y	Y	Y	Y	Y	Y	Y	Y
Applicable to current smokers	Y	Y	Y	Y	Y	Y	Y	Y
Model age restrictions	50-75	40-80	≥20	≥20	N	N	N	≥35
Model smoking restrictions	≥30 PY	N	N	N	N	N	N	N
Model predicts risk of incidence	Y	Y	N	N	Y	Y	Y	Y
Model predicts survival	Y	N	Y	Y	N	N	N	Y
Length risk length, years	1-10	5	≥1	5	9	9	6	≥1
Model formula printed	Y	Y	Y	Y	Y	Y	Y	Y

Text in bold for clarity when a variable is included in a model.
Abbreviations: COPD = chronic obstructive pulmonary disease; N = no; PY = pack years; Y = yes.

CLC 2016; 17(2):95-106

Lung Cancer Screening Risk Prediction Models

- PLCO: Validated LC risk prediction model from the PLCO screening trial
- $PLCO_{M2012}$: Modify and update LC model to make it applicable to NLST data



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Sex	Y	Y	Y	Y	N	N	N	N
Ethnicity	N	N	N	N	N	N	Y	N
Body mass index	N	N	N	N	Y	Y	Y	N
Subject to x-rays								N
Education (levels)								N
Previous malignant tu								N
Smoking History								
Smoking status								Y
Start age								Y
Cessation age								N
Smoking duration								Y
Cigarettes per day								Y
Pack-years								N
Quit duration								N
Environmental smoke								N
Family History of Canc								
Cases of any cancer								N
Age of onset for any c								N
Cases of smoking-rela cancer								N
Age of onset for smok cancer								N
Cases of lung cancer								N
Age of onset of lung c								N
Exposures and Lung Conditions								
Asbestos exposure								N
Dust								N
Hay fever								N
Asthma								N
Emphysema								N
COPD								N
Pneumonia								N
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Length risk length, years	1-10	5	≥1	5	9	9	6	≥1
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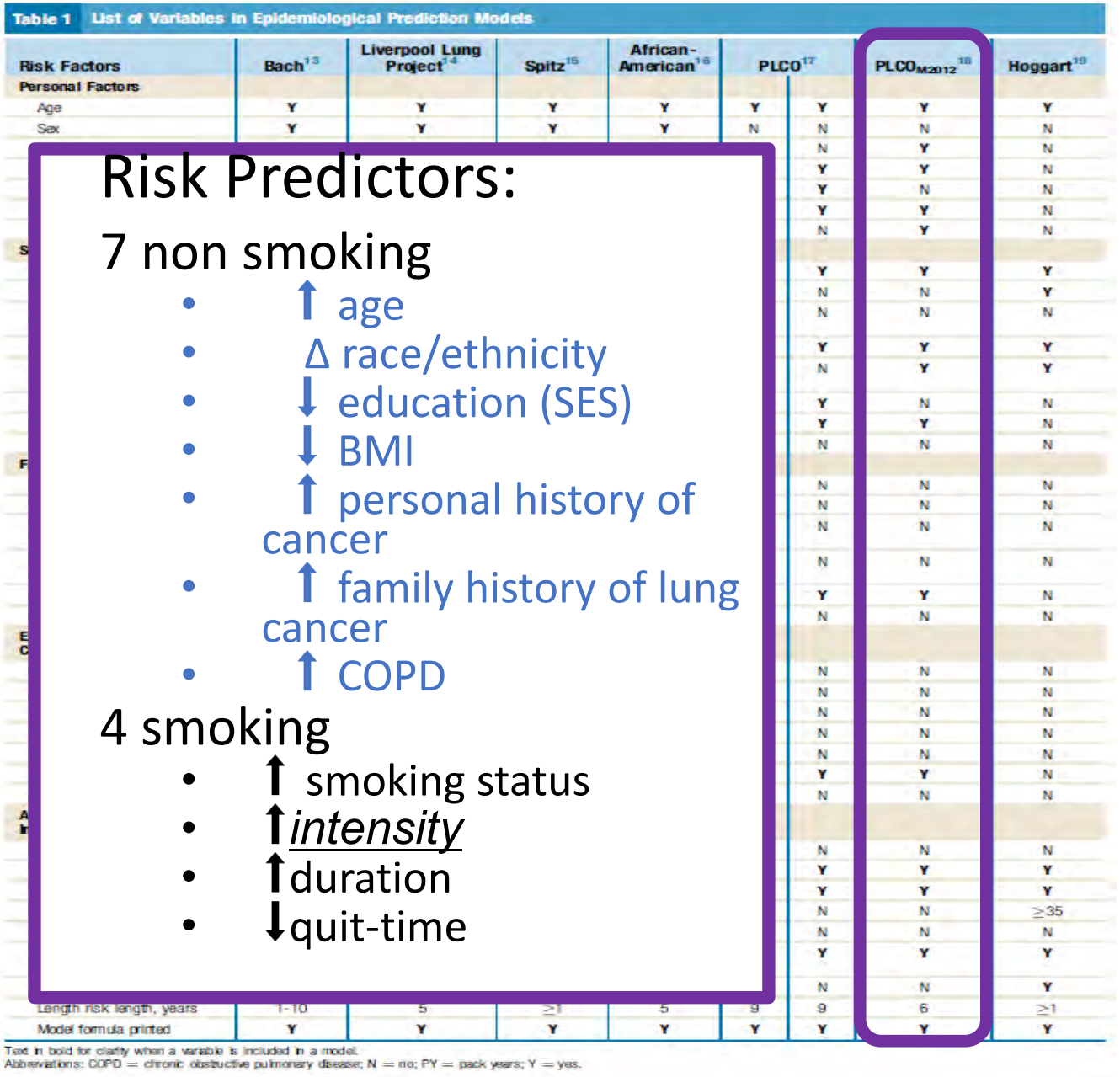

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Personal Factors								
Age	Y	Y	Y	Y	Y	Y	Y	Y
Sex	Y	Y	Y	Y	N	N	N	N
						N	Y	N
						Y	Y	N
						Y	N	N
						Y	Y	N
						N	Y	N
S								
						Y	Y	Y
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						N	N	N
						Y	Y	Y
						N	Y	Y
						Y	N	N
						Y	Y	N
						N	N	N
F								
						N	N	N
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						Y	Y	N
E C						N	N	N
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						N	N	N
						Y	Y	N
						N	N	N
A								
						N	N	N
						Y	Y	Y
						Y	Y	Y
						N	N	≥35
						N	N	N
						Y	Y	Y
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Risk Predictors:

7 non smoking

- ↑ age
- Δ race/ethnicity
- ↓ education (SES)
- ↓ BMI
- ↑ personal history of cancer
- ↑ family history of lung cancer
- ↑ COPD

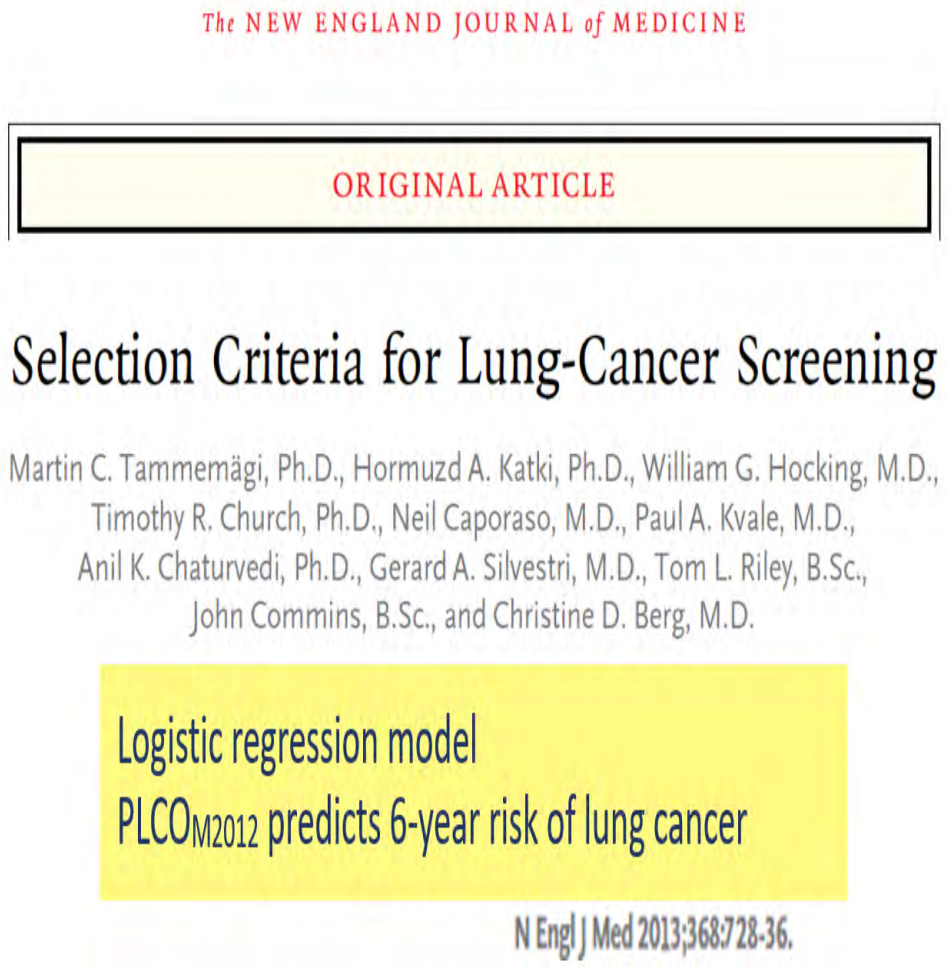
4 smoking

- ↑ smoking status
- ↑ *intensity*
- ↑ duration
- ↓ quit-time

JNCI 2011; 103(13):1058-1068.

CLC 2016; 17(2):95-106

Lung Cancer Screening
Risk Prediction Models – $PLCO_{M2012}$

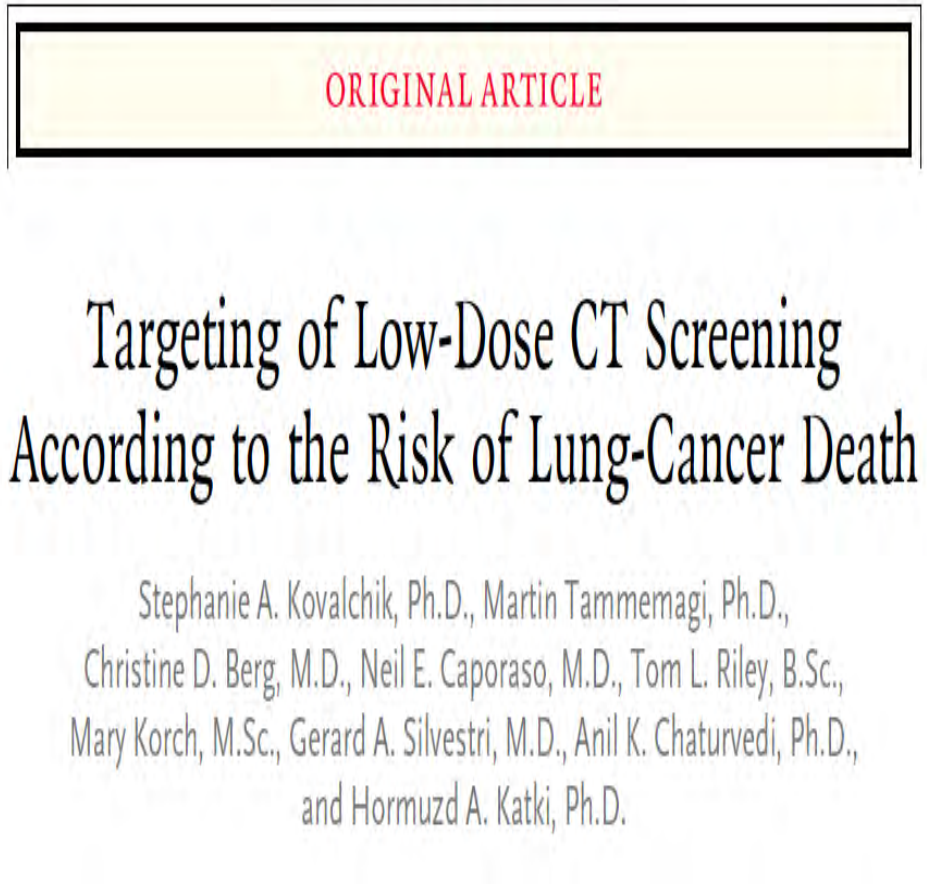


- Cox models used to evaluate whether the reduction in mortality among persons undergoing LDCT screening in the NLST differed according to risk.
- The $PLCO_{M2012}$ prediction rules were evaluated at the 1.3455% risk threshold
- Compared to NLST criteria, $PLCO_{M2012}$ criteria had improved sensitivity (83.0% vs. 71.1%, P<0.001) and PPV (4.0% vs. 3.4%, P = 0.01), without loss of specificity (62.9% and. 62.7%, P = 0.54);
- 41.3% fewer lung cancers were missed. The NLST screening effect did not vary according to $PLCO_{M2012}$ risk (P = 0.61 for interaction).

CONCLUSION

The use of the $PLCO_{M2012}$ model was more sensitive than the NLST criteria for lung cancer detection.

Lung Cancer Screening
High Risk Population



ORIGINAL ARTICLE

Targeting of Low-Dose CT Screening According to the Risk of Lung-Cancer Death

Stephanie A. Kovalchik, Ph.D., Martin Tammemagi, Ph.D., Christine D. Berg, M.D., Neil E. Caporaso, M.D., Tom L. Riley, B.Sc., Mary Korch, M.Sc., Gerard A. Silvestri, M.D., Anil K. Chaturvedi, Ph.D., and Hormuzd A. Katki, Ph.D.

- Assessed: variation in efficacy, number of false positive results, and number of LC deaths prevented among NLST participants who underwent LDCT screening (vs CXR)
- Developed absolute risk-prediction model for LC mortality in the NLST CXR group (PLCO validated)
- Stratified according to: 5-year risk of LC death quintiles (0.15 to 0.55% in the lowest-risk group [Q1] to >2.00% in the highest-risk group [Q5]).
- LDCT screening prevented the greatest number of deaths from LC among participants who were at highest risk and prevented very few deaths among those at lowest risk.

Kovalchick NEJM 2013

Lung Cancer Screening
High Risk Population

Table 3. Outcomes of Three Rounds of Annual Low-Dose CT Screening, According to Risk Quintile.*

Quintile of 5-Year Risk of Lung-Cancer Death	Participants	Lung-Cancer Cases		Lung-Cancer Deaths		Positive Screening Results		Number of False Positives per Prevented Lung-Cancer Death†	Number Needed to Screen†‡
		Total No.	Stage I†	Total No.	Prevented†	Total No.	False Positive†§		
	no. (%)		*no. (%)*		*no. (%)*		*no. (%)*		
All quintiles	26,604 (100)	1083	530 (48.9)	354	88 (24.9)	10,151	9484 (93.4)	108	302
Quintile 1: 0.15–0.55%	5,276 (19.8)	71	40 (56.3)	20	1 (5.0)	1,699	1648 (97.0)	1648	5276
Quintile 2: 0.56–0.84%	5,310 (20.0)	105	59 (56.2)	35	10 (28.6)	1,879	1806 (96.1)	181	531
Quintile 3: 0.85–1.23%	5,396 (20.3)	182	84 (46.2)	45	13 (28.9)	2,024	1911 (94.4)	147	415
Quintile 4: 1.24–2.00%	5,314 (20.0)	263	132 (50.2)	73	31 (42.5)	2,123	1973 (92.9)	64	171
Quintile 5: >2.00%	5,308 (20.0)	462	215 (46.5)	181	33 (18.2)	2,426	2146 (88.5)	65	161

Kovalchick NEJM 2013

Lung Cancer Screening
High Risk Population

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60% at highest risk of developing lung cancer accounted for 88% mortality reduction. Bottom 20% = 1% of the mortality reduction

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		Total No.	Stage I†	Total No.	Prevented†	Total No.	False Positive†§	Death†	
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Kovalchick NEJM 2013

Lung Cancer Screening
High Risk Population

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As quintile of risk increases, more LC are identified with less false positive screens

Quintile of Risk of Death	Participants	Cases		Deaths		Results		Death†	mber ded to Screen†‡
		Total No.	Stage I†	Total No.	Prevented†	Total No.	False Positive†§		
	no. (%)		*no. (%)*		*no. (%)*		*no. (%)*		
All quintiles	26,604 (100)	1083	520 (48.0)	354	88 (24.9)	10,151	9484 (93.4)	108	302
Quintile									5276
Quintile									531
Quintile 3: 0.85–1.23%	5,396 (20.3)	182	84 (46.2)	45	13 (28.9)	2,024	1911 (94.4)	147	415
Quintile 4: 1.24–2.00%	5,314 (20.0)	263	132 (50.2)	73	31 (42.5)	2,123	1973 (92.9)	64	171
Quintile 5: >2.00%	5,308 (20.0)	462	215 (46.5)	181	33 (18.2)	2,426	2146 (88.5)	65	161

Kovalchick NEJM 2013

Risk Based Lung Cancer Screening
Ontario Lung Cancer Screening Pilot ($PLCO_{M2012}$ risk model)

Several countries have adopted a $PLCO_{M2012}$ risk of developing lung cancer >1.5 - 2.0% for screening eligibility

Article https://doi.org/10.1038/s41591-024-02904-z

Risk-based lung cancer screening performance in a universal healthcare setting

Between June 2017 and May 2019, the Ontario Lung Cancer Screening Pilot successfully recruited 7,768 individuals at high risk identified by using the $PLCO_{M2012}$ lung cancer risk prediction model.

Nat Med 2024; 30:1054-1064

- 7,260 met triage criteria and underwent risk assessment, and 4,918 (67.7%) were eligible for screening ($PLCO_{M2012} \geq 2.0\%$)
- In the Ontario Lung Cancer Screening Pilot, the lung cancer detection rate and the proportion of early-stage cancers were 2.4% and 79.2%, respectively;
- Serious harms were infrequent; and sensitivity to detect lung cancers was 95.3% or more.
- The Ontario Lung Cancer Screening Pilot provides insights into how a risk-based organized lung screening program can be implemented in a large, diverse, populous geographic area within a universal healthcare system.

Risk Based Lung Cancer Screening
UKLS – Pilot Study (Liverpool Lung Project risk model)

Research paper

Lung cancer mortality reduction by LDCT screening: UKLS randomised trial results and international meta-analysis

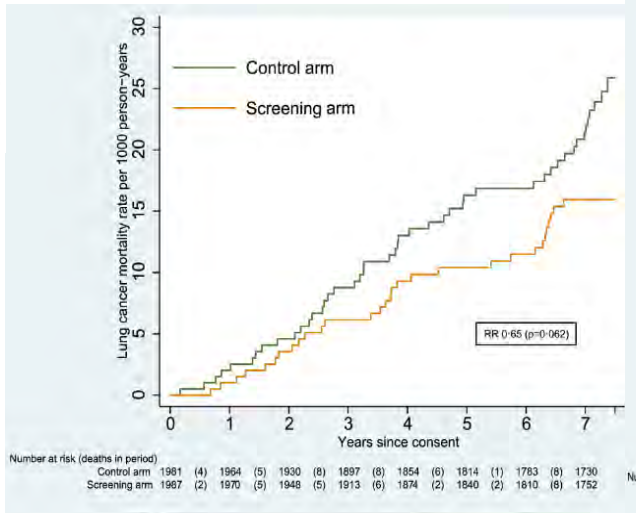
Methods: From 10/2011 to 2/2013, we randomly allocated 4055 participants to either a single LDCT screening or to no screening (usual care). Eligible participants (aged 50-75) had a risk score (LLPv2) ≥4.5% of developing LC over five years. Data were collected on LC cases to 12/2019 and deaths to 2/2020 through linkage to national registries.

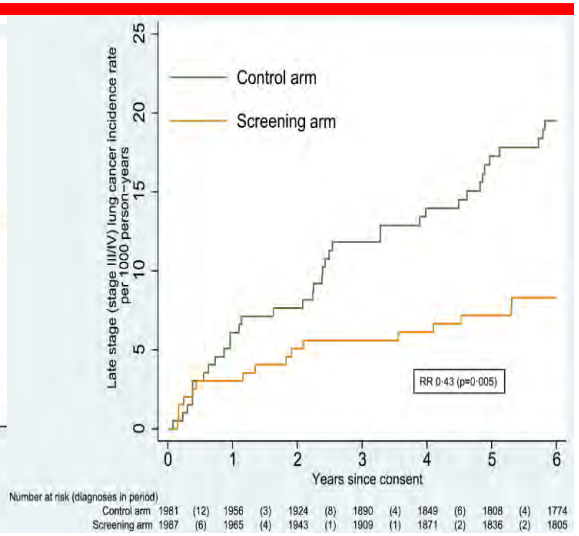
The primary outcome was mortality due to LC.

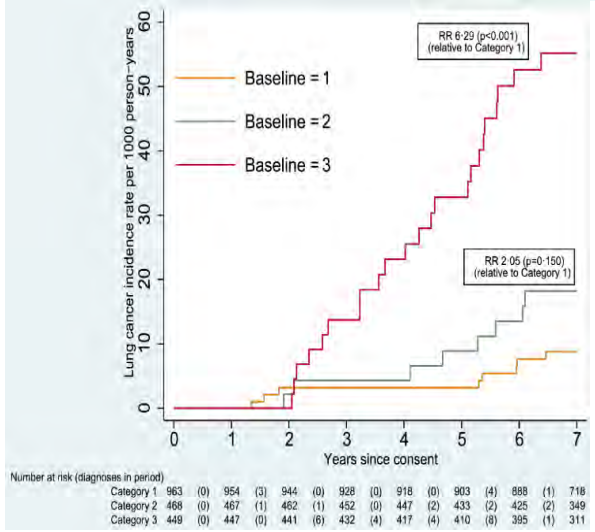
Findings: 1987 participants in the LDCT and 1981 in the usual care arms were followed for a median of 7.3 years (IQR 7.1-7.6), 86 cancers were diagnosed in the LDCT arm and 75 in the control arm. 30 LC deaths were reported in the screening arm, 46 in the control arm, (relative rate 0.65 [95% CI 0.41-1.02]; p=0.062).

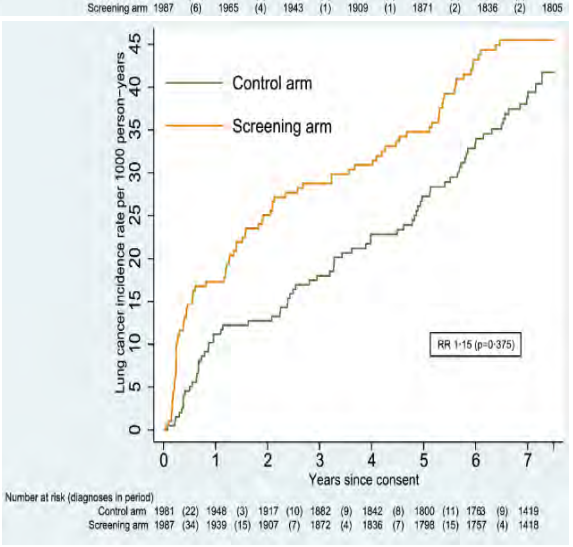
Interpretation: The UKLS trial of single LDCT indicates a reduction of LC death of similar magnitude to the NELSON and NLST trials .

The Lancet Regional Health-Europe,2021; 10:1-11









Lung Cancer Risk Based Modeling
Machine Deep Learning - AI

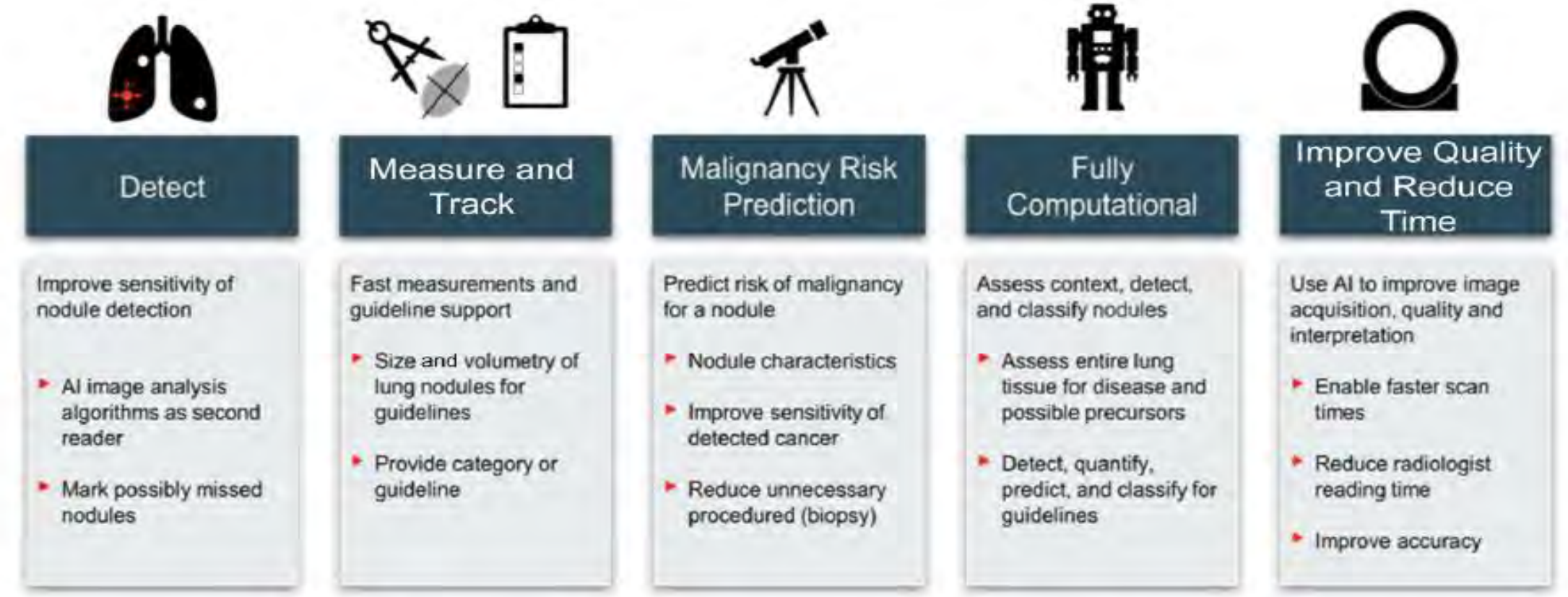


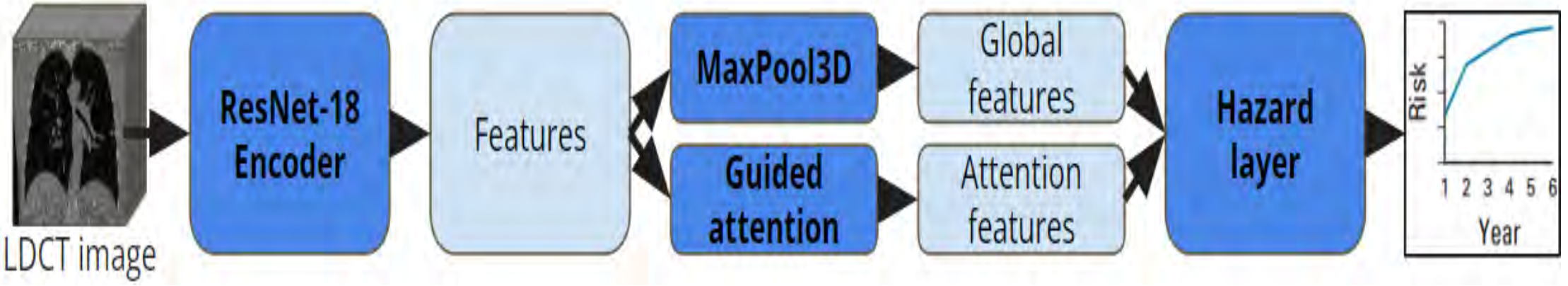
Figure 3. Role of AI in lung cancer screening. AI, artificial intelligence.

JTO 2024; 19(1):36-51

Lung Cancer Risk Based Modeling
Machine Deep Learning - Sybil

- **Relevance:** Sybil, state-of-the-art deep learning model to predict lung cancer risk
- Single LDCT image without segmentation
- Predicting lung cancer risk 1 to 6 years after image acquisition
- Potential to be integrated into the clinical workflow for early cancer detection

- **Conclusions:** Sybil's best performance based on 3 independent validation studies → Predicting lung cancer risk within 1 year
- Decline in predictive accuracy after 3 years
- M may not be able to accurately predict risk without the presence of nodules
  - Limited clinical use for fast-growing nodules, not present at baseline



*Mikhael, Peter G., et al. "Sybil: a validated deep learning model to predict future lung cancer risk from a single low-dose chest computed tomography." *Journal of Clinical Oncology* 41.12 (2023).

Lung Cancer Risk Based Modeling Biomarkers

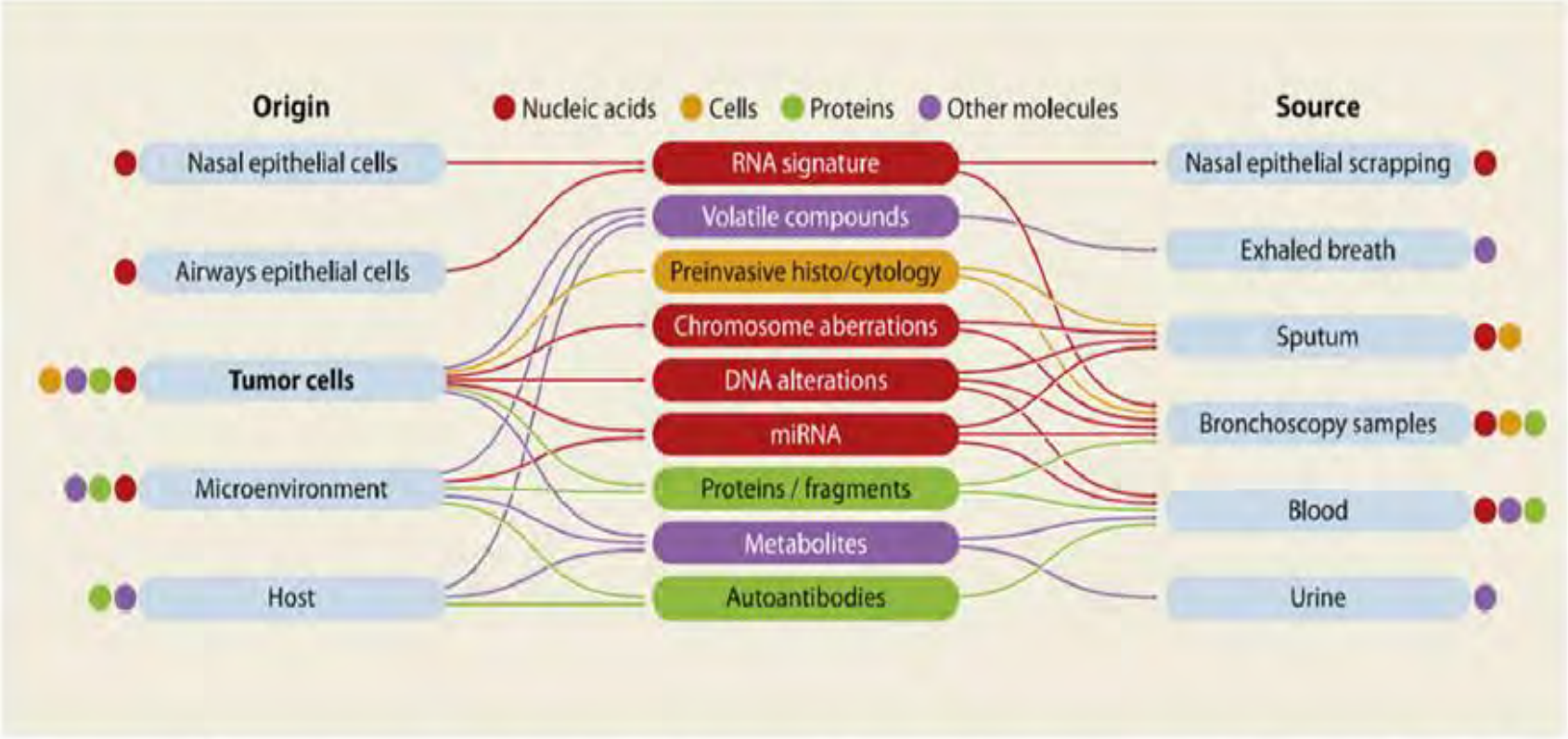


Figure 2. A wide range of biospecimens and approaches proposed for lung cancer screening (Seijo, L.M., et al., Biomarkers in Lung Cancer Screening: Achievements, Promises, and Challenges, 2019). miRNA, microRNA.

JTO 2024; 19(1):36-51

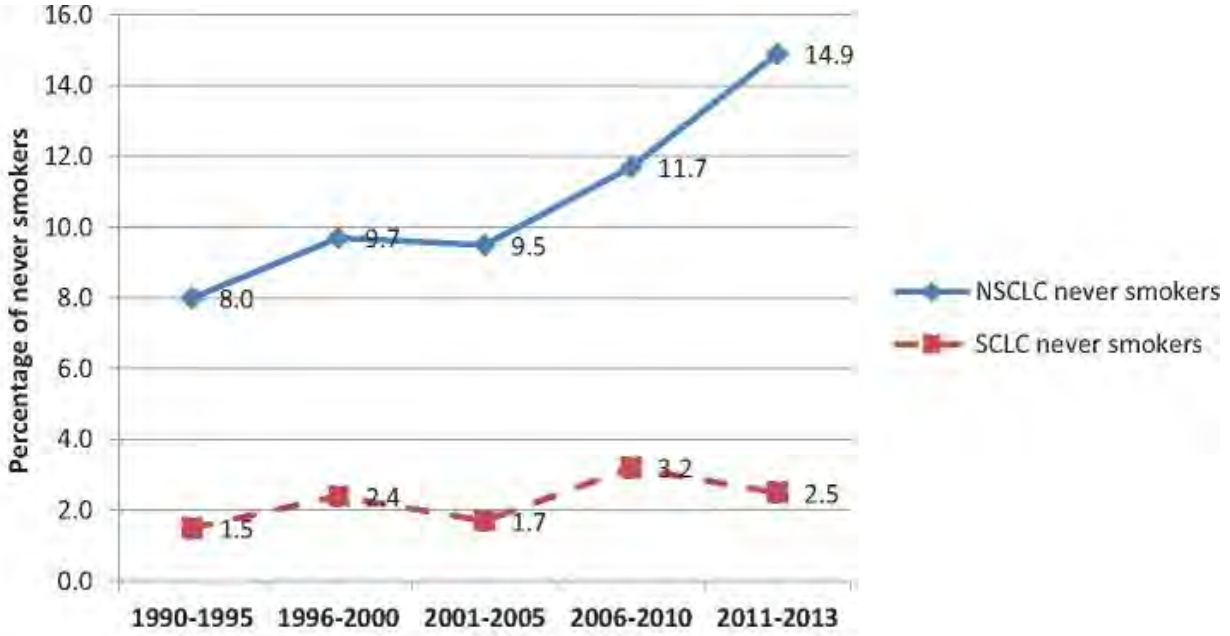
Lung Cancer Screening in Non-Smokers

Risk Factors for Lung Cancer
Individuals who have Never Smoked (LCINS)

”But I never smoked”

There is a growing incidence of lung cancer in never smokers (LCINS)

Never smoker:
history of smoking </=100 cigarettes in a lifetime

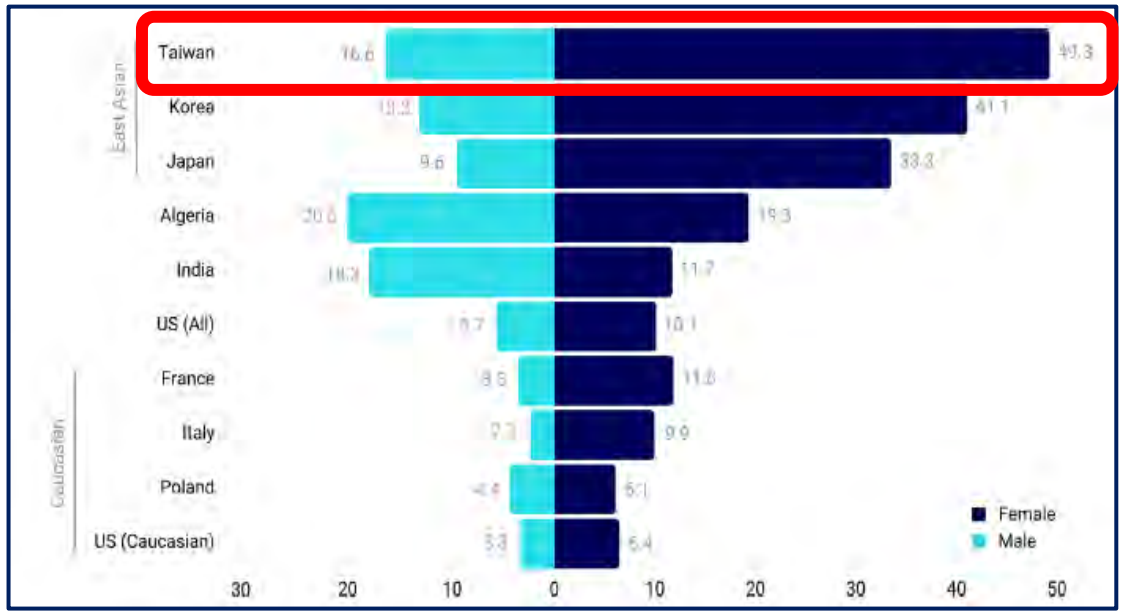


No. of patients						
All NSCLC	677	1726	2391	3182	2617	
Never smoker NSCLC	54	168	228	372	391	P<0.001
All SCLC	136	297	356	404	317	
Never smoker SCLC	2	7	6	13	8	P=0.36

Pelosof ae al. J Natl Cancer Inst. 2017 Jan 28;109(7)

Risk Factors for Lung Cancer
Individuals who have Never Smoked (LCINS)

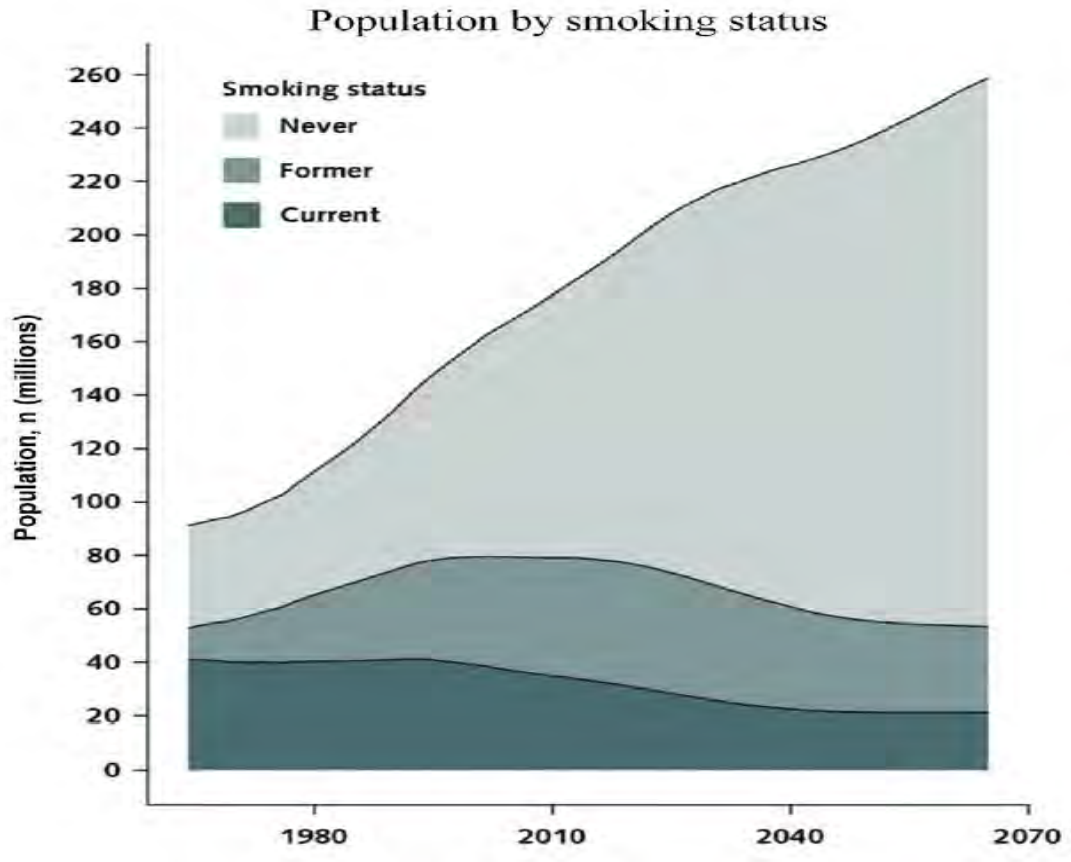
- Because the incidence of lung cancer is so high, lung cancer in individuals who have never smoked (LCINS) is the 7th most frequently detected cancer.
- 5th most common cause of cancer-related deaths worldwide in 2023.
- Occurs more frequently in never-smoking women than men.
  - Twice as likely to develop lung cancer.
  - Proportion of lung cancer in never smoking females varies worldwide.
  - 15-20% in the U.S.
- A different entity from lung cancer in smoking populations:
  - More commonly adenocarcinomas
  - Genomic and molecular differences

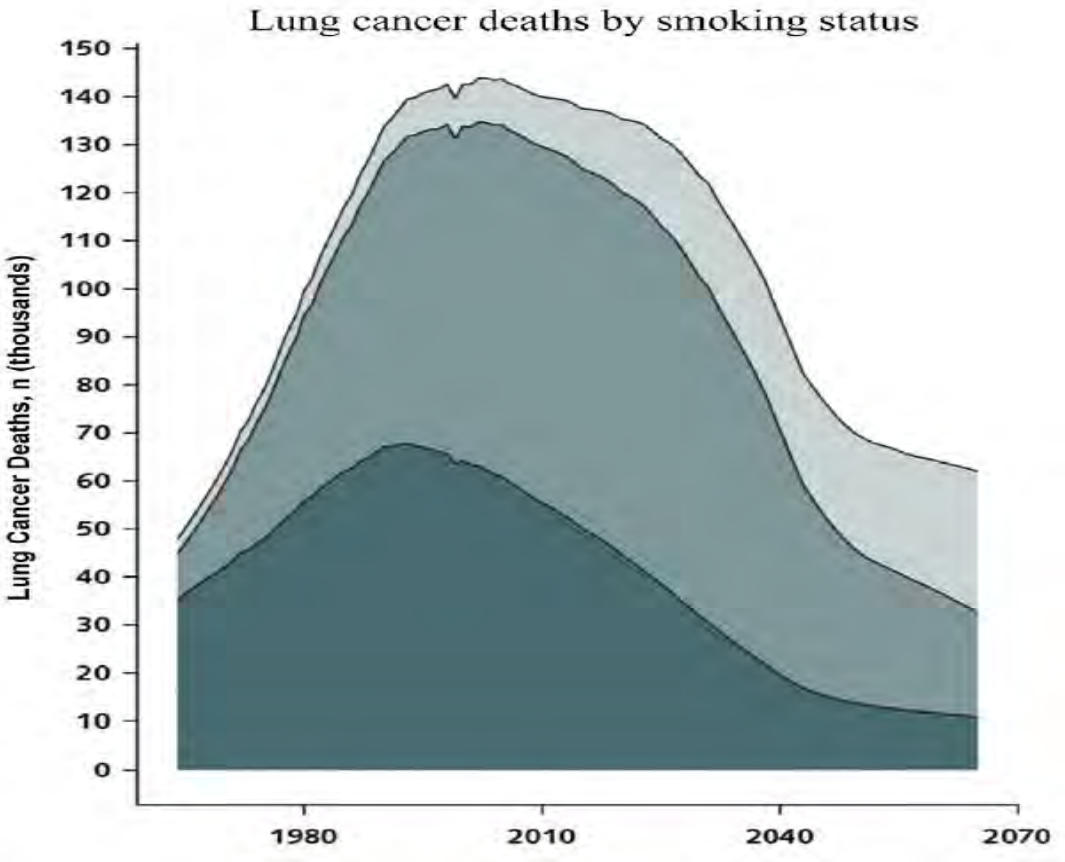


Siegel DA, et al. JAMA Oncology 2023.; Wang P, et al. Journal of Translational Medicine 2023.; LoPiccolo J, et al. Nat Rev Clin Onc 2024.

Risk Factors for Lung Cancer
LCINS - Mortality

Lung cancer deaths in those with no smoking history is increasing.

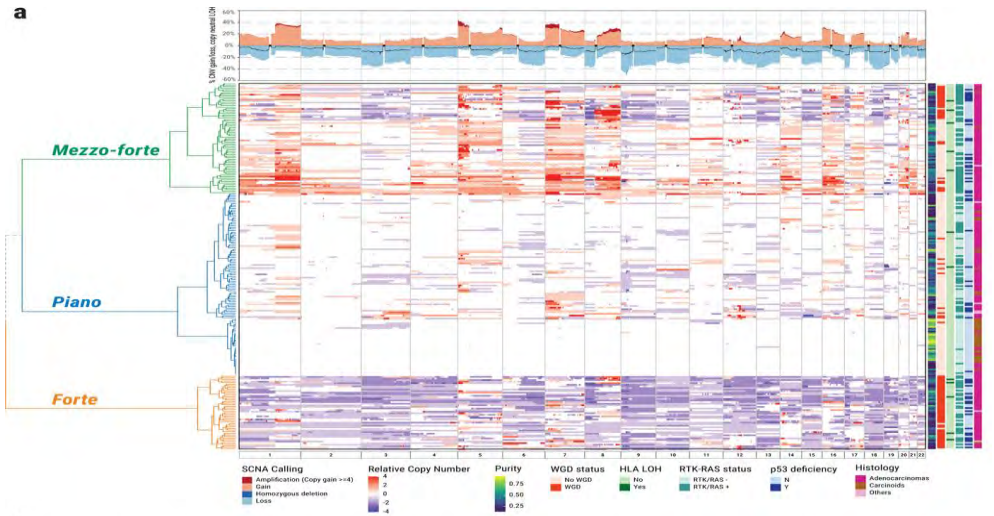




Lam S et al. J Thorac Oncol 2023.

LCINS
A distinct Entity

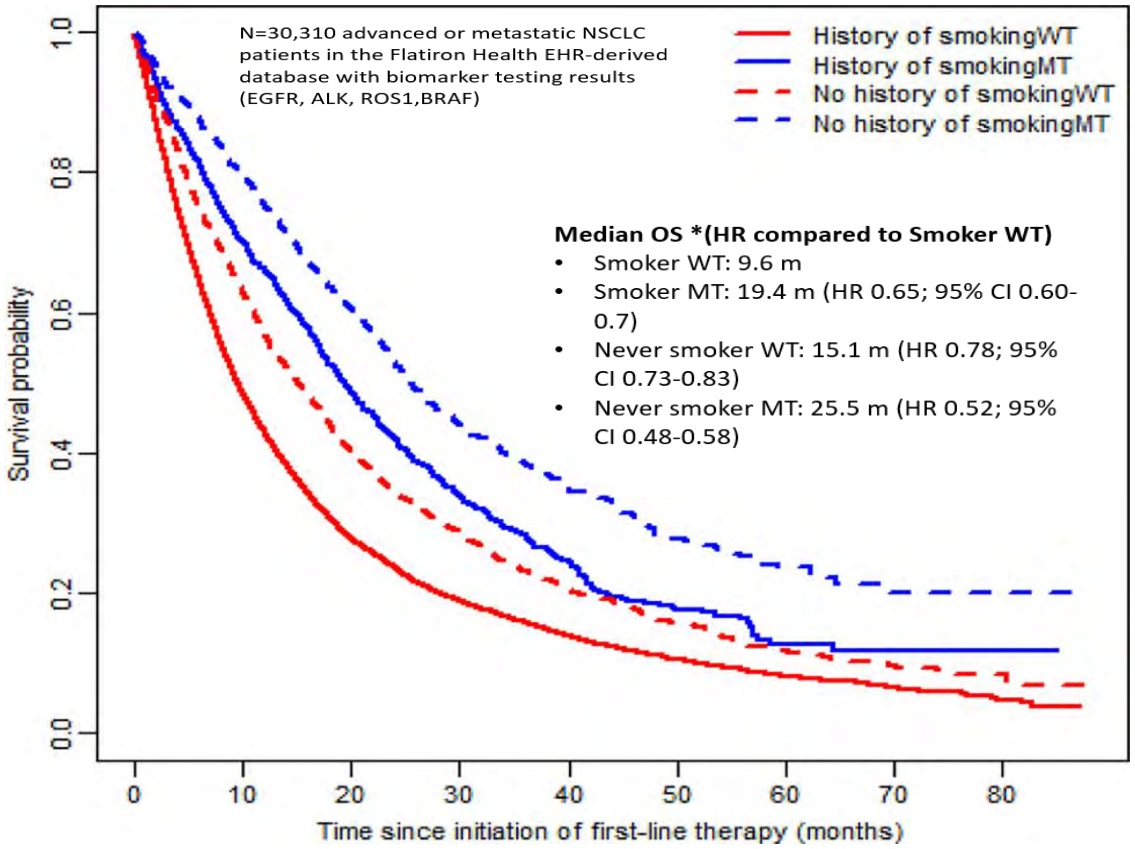
Molecular Level



ARTICLES
https://doi.org/10.1038/s41588-021-00920-0
nature genetics

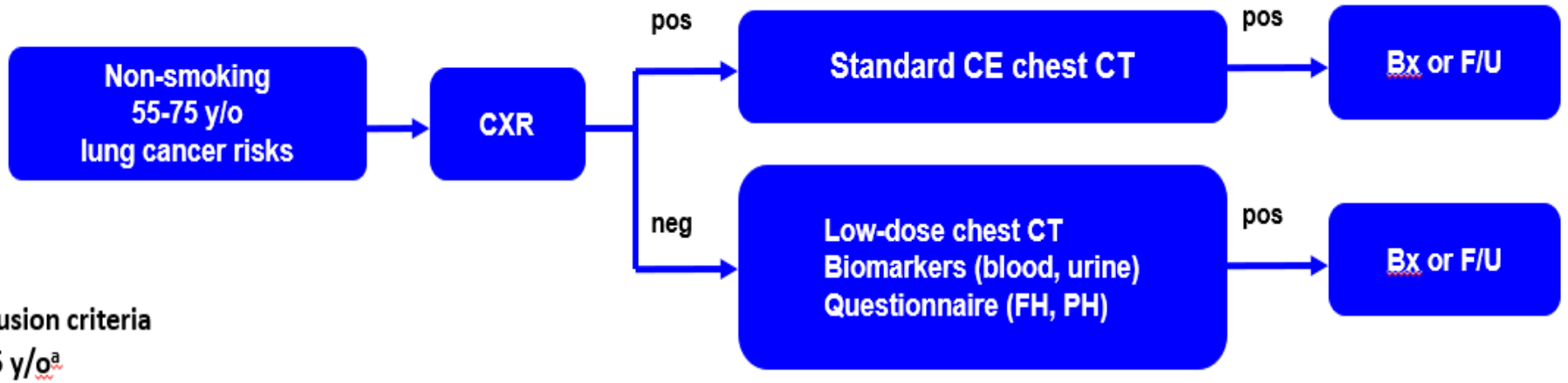
Genomic and evolutionary classification of lung cancer in never smokers

Clinical Level



Kerrigan K,. Real World Characterization of Advanced Non-Small Cell Lung Cancer in Never Smokers by Actionable Mutation Status. Clinical Lung Cancer 2021

Taiwan Lung Cancer Screening in Never Smoker Trial (TALENT)



- Key inclusion criteria
  - 55-75 y/o[a]
  - Never smoking or SI < 10 PY and had quit > 15 yrs
  - Having one of the following risks
    - family history of lung cancer (≤ 3-degree)
    - environmental tobacco smoking history
    - chronic lung disease (TB, COPD)
    - cooking index[b] ≥ 110
    - cooking without using ventilation
  - Negative CXR

- Data cutoff: September 30, 2020
- 13,207 subjects screened, 12,011 enrolled
- 6009 (50%) with family history

[a] Subjects with lung cancer FH: >50 yrs or > the age at diagnosis of the youngest lung cancer case in the family
[b] 2/7 x days with cooking by pan-frying, stir-frying, or deep-frying in 1 week (maximum=21) x Yrs with cooking

From Feb 2015 to July 2019, 17 medical centres participated

Chang GC et al. Lancet Respir Med 2024.

TALENT
Results

- T0 lung cancer detection rate: 2.65%
  - Included invasive adeno, adeno in situ, minimally invasive adeno and adenosquamous carcinomas.
  - Invasive adeno detection rate was 1.52%.
  - The LC detection rate in NLST was 1.1%.
- Lung cancer confirmed: 96.5% Stage 0 or 1
- Prevalence of lung cancer with or without family history:
  - 3.29% vs 2.02%

Histologic diagnosis	n
Adenocarcinoma *in situ*	61
Minimally invasive adenocarcinoma	79
Invasive adenocarcinoma	177
Adenosquamous carcinoma	1
Total	**318**

Stage 0	**61**
Stage IA	**220**
Stage IB	**26**
Stage IIA	0
Stage IIB	3
Stage IIIA	2
Stage IIIB	1
Stage IIIC	0
Stage IV	5

Chang GC et al. Lancet Respir Med 2024.

Lung Cancer Screening
Taiwan National Lung Cancer Early Detection Program

- Biennial LDCT lung cancer screening for high-risk subjects
  - Smoking history either current or quit in last 15 yrs, 30 pack yrs, 50-74yo
  - Light or no smoking history with family hx of lung cancer, F: 45-74 yo; M: 50-74 yo

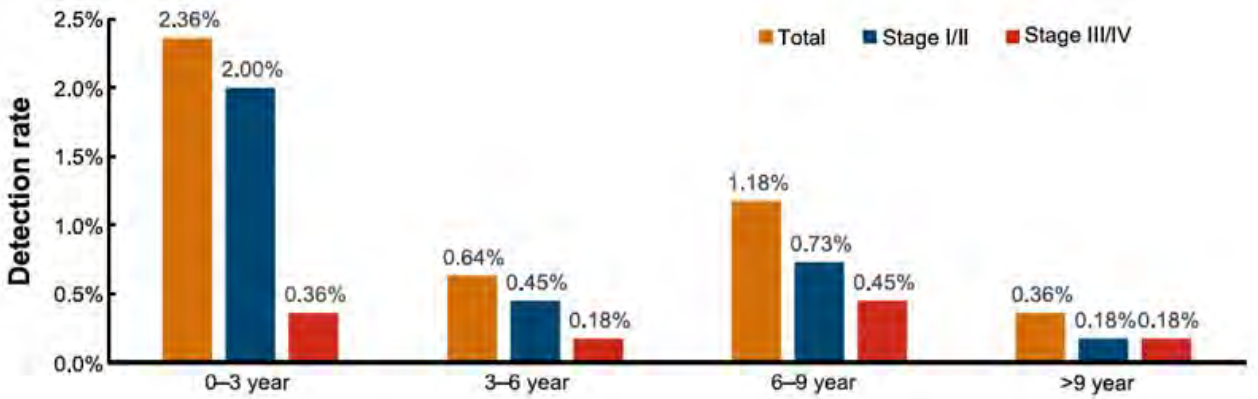
	LCFH			Heavy Smokers	Both	Total
	Non smokers	Light smokers	Overall			
Screened	39,284	4,569	43,853	31,111	3,036	78,000
Diagnostic procedure	858	65	923	433	51	1,407
Lung cancer	653	41	694	228	34	956
Detection rate (%)	**1.7**	**0.9**	**1.6**	**0.7**	**1.1**	**1.2**
Stage 0-1 (%)	**90.5**	**82.9**	**90.1**	**68.9**	**82.4**	**84.7**

Health Promotion Administration. Ministry of Health and Welfare, Taiwan https://www.hpa.gov.tw/EngPages/Index.aspx

Lung Cancer Screening
Individuals with Family History (included never smokers)

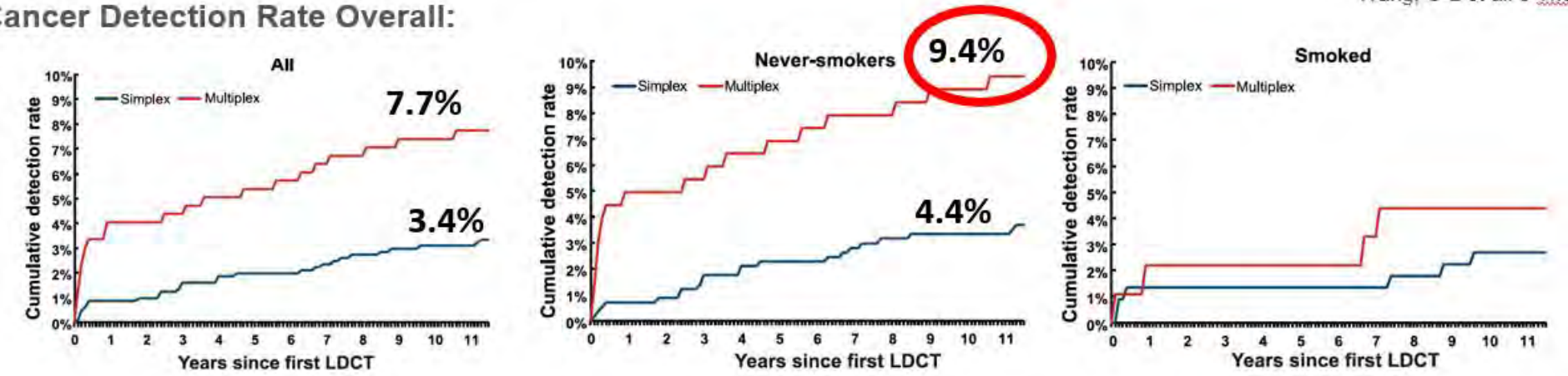
Eligibility: 1st or 2nd degree relatives of patients with lung cancer who were at least 55 yo; or older than the age at onset of LC in the family proband age <54 yo
Method: Annual LDCT for 3 years
Enrollment: 2007-2011, last followup: 5/5/21
Results: n=1102

- 805 from simplex family (SF)
- 297 from multiplex family (MF)
- Never smoker 70% overall, SF and MF

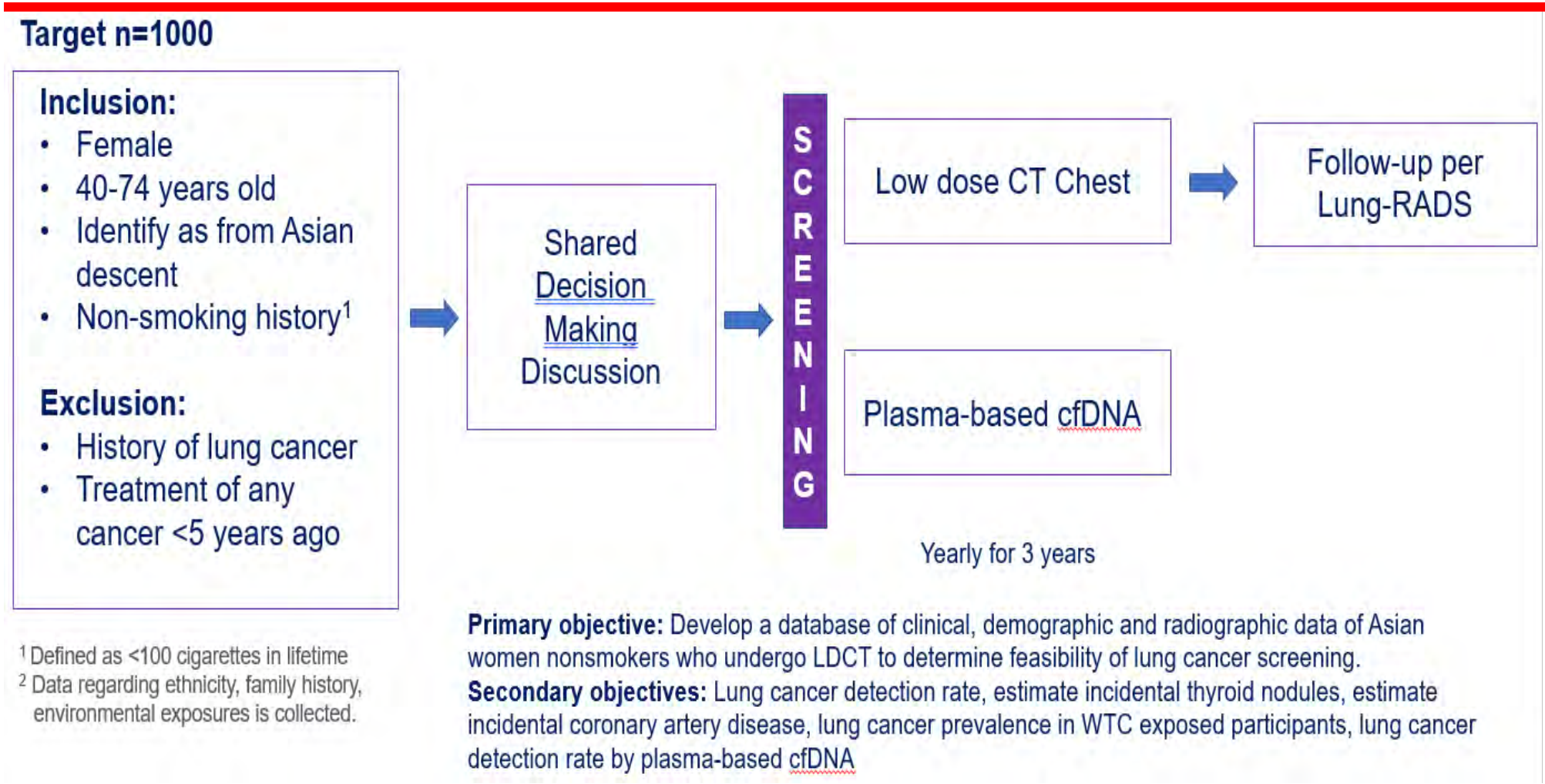


Wang, C-L et al. J Thorac Onc 2023.

Lung Cancer Detection Rate Overall:



Female Asian Nonsmoker Screening Study
FANSS – NYU (**NCT05164757**)



JCO 2024; 41(16): suppl. Abstract 8510

Female Asian Nonsmoker Screening Study
FANSS – NYU (**NCT05164757**)

Results

From 3/1/21 to 1/15/23, 201 baseline LDCT

- Median age: 56.8 yo.
- 83 (41%) reported a family history of LC.
- 87 (43%) were Lung-RADS 1, 101 (50%) were Lung-RADS 2, 6 (3%) were Lung-RADS 3 and 7 (3.5%) were Lung-RADS 4.
- 5 pts with Lung-RADS 3 and 3 pts with Lung-RADS 4 have solid, subsolid or groundglass nodules > 6mm (close followup).
- 3 pts were diagnosed with invasive lung adeno for a LC detection rate of 1.5%;
- 2 are stage IIB and 1 is stage IIIC.
- All pts were surgically resected, EGFR mutation +ive and are receiving adjuvant osimertinib.

Conclusions

LC screening in Asian female nonsmokers is feasible.

- Preliminary results demonstrate an invasive adeno detection rate comparable with TALENT and higher than in NLST.
- Early detection brings new meaning with the recent FDA approval for adjuvant targeted therapy in early stage LC.
- The expansion of LC screening guidelines to other high-risk populations warrants further attention.
- FANSS is continuing to accrue at additional U.S. sites this year.

JCO 2024; 41(16): suppl. Abstract 8510

Lung Cancer Screening
USPSTF recommendations - LCINS

- The US Preventive Services Task Force does not recommend lung cancer screening for people who have never smoked because the potential harms outweigh the benefits.
  - There is no (high-quality) evidence that low-dose CT (LDCT) screening reduces lung cancer mortality in non-smokers.
  - Harms of LDCT screening in this population including overdiagnosis and unnecessary surgical procedures need to be considered