

Lung Cancer Screening In Never Smokers & High Risk Populations



Janakiraman Subramanian MD, MPH

Disclosures

- Research funding: Novartis, Merck, CanStem, Helsinn, Biocept, Incyte, Genentech & Paradigm
- Advisory role: Astra Zeneca, Boehringer Ingelheim, Novartis, Eli Lilly, G1 therapeutics, Jazz Pharma & Pfizer
- Speakers bureau: Astra Zeneca, Boehringer Ingelheim, G1 therapeutics & Jazz Pharma

Major LDCT Lung Screening Studies

Powered studies

| | | |
|---|---|---|
| NLST LDCT vs CXR | Age 55–75 years, ≥30 PY smoking, <10 years ex-smoker (n = 53,454) | LDCT reduces lung cancer-related mortality (HR 0.80; $P < 0.004$) |
| NELSON^a LDCT vs no intervention | Age 55–75 years, ≥15 PY smoking, <10 years ex-smoker (n = 15,789) | LDCT reduces lung cancer-related mortality (HR 0.76, 95% CI 0.62–0.94 in men) |

Unpowered studies

| | | |
|---|---|--|
| DANTE LDCT vs no intervention | Age 60–74 years, ≥20 PY smoking, <10 years ex-smoker (n = 2,811) | Non-significant reduction of lung cancer-related mortality (HR 0.99) |
| DEPISCAN LDCT vs CXR | Age 50–75 years, ≥15 PY smoking, <15 years ex-smoker (n = 765) | LDCT enables the detection of more lung cancers than CXR (8 vs 1) |
| DLCST^a LDCT vs CXR | Age 50–70 years, ≥20 PY smoking, <10 years ex-smoker (n = 4,104) | Non-significant reduction of lung cancer-related mortality (HR 1.03) |
| ITALUNG LDCT vs no intervention | Age 55–69 years, ≥20 PY smoking, <10 years ex-smoker (n = 3,206) | Non-significant reduction of lung cancer-related mortality (HR 0.7) |
| MILD LDCT vs no intervention | Age ≥49 years, ≥20 PY smoking, <15 years ex-smoker (n = 4,099) | LDCT reduces cumulative risk of 10 year lung cancer-related mortality (HR 0.61; $P = 0.02$) |
| LUSI^a LDCT vs no intervention | Age 50–69 years ≥15 PY smoking, <10 years ex-smoker (n = 4,052) | LDCT reduces lung cancer-related mortality only in women (HR 0.31; $P = 0.04$) |
| UKLS^a LDCT vs no intervention | Age 50–75 years, LLP _{v2} -defined 5 year lung cancer risk ≥5% (n = 4,055) | LDCT reduces lung cancer mortality (RR=0.65, $P = 0.062$) |

Lung Cancer Screening with LDCT

NLST Trial

- Inclusion Criteria
 - Age 55 – 74 years
 - History of tobacco smoking
 - 30 pack years or more
 - Quit within previous 15 years if a former smoker
- Exclusion Criteria
 - Diagnosis of lung cancer
 - Chest CT in last 18 months
 - Hemoptysis
 - Unexplained weight loss of 15 lbs

NELSON Trial

- Inclusion Criteria
 - History of tobacco smoking
 - > 15 cigarettes/day for > 25 years or > 10 cigarettes/day for > 30 years
 - Quit \leq 10 years
- Exclusion Criteria
 - Diagnosis of lung cancer in last 5 years
 - CT chest in last 12 months
 - Moderate or severe health problems
 - Inability to climb 2 flights of stairs
 - Body weight > 140 kgs
 - Diagnosis of other cancer*.

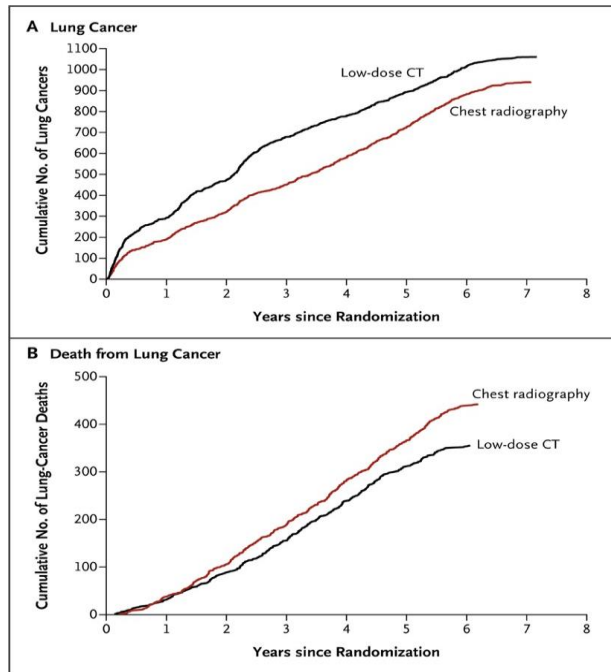
HJ de Koning et al. N Engl J Med 2020;382:503-513.

N Engl J Med 2011;365:395-409.

* renal, breast or melanoma

Lung Cancer Screening with LDCT

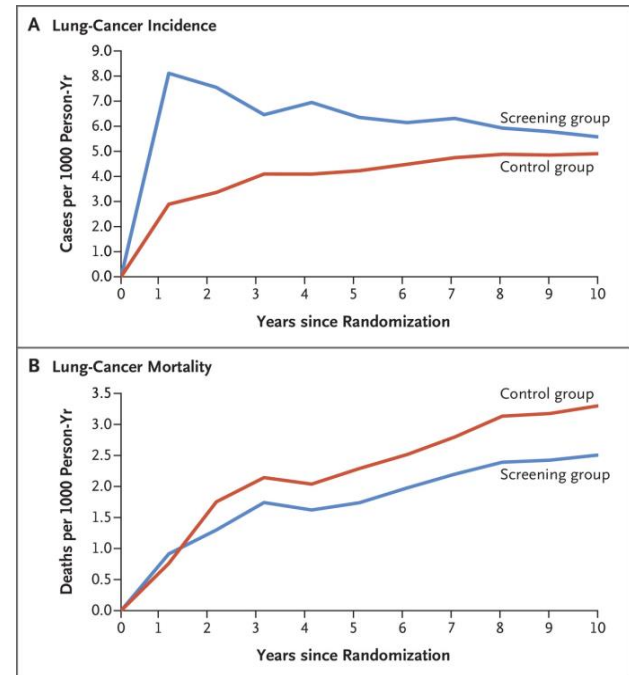
NLST Trial



HJ de Koning et al. N Engl J Med 2020;382:503-513.

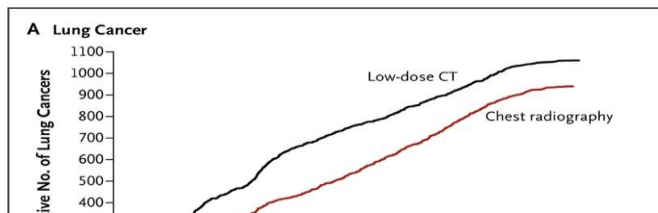
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NELSON Trial

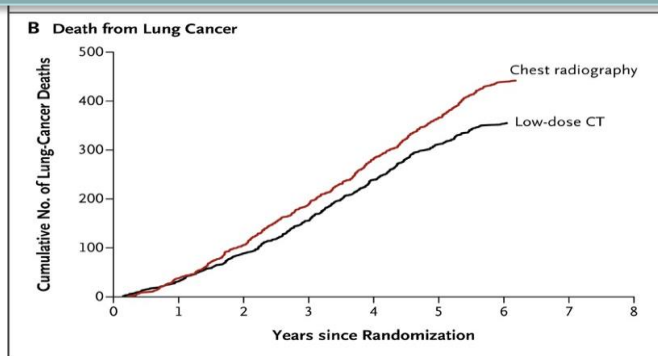


Lung Cancer Screening with LDCT

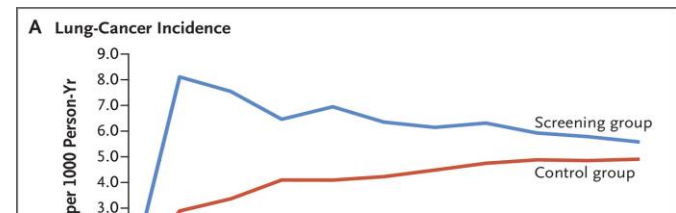
NLST Trial



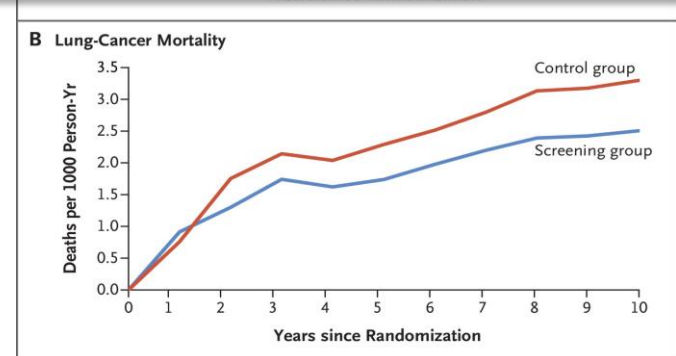
Lung Cancer Mortality Relative Risk Reduction: 20%
All Cause Mortality Risk Reduction: 6.7%



NELSON Trial



Lung Cancer Mortality Cumulative Rate Ratio: 0.76
All Cause Mortality rate ratio: 1.01%



HJ de Koning et al. *N Engl J Med* 2020;382:503-513.

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Final Recommendation Statement

Lung Cancer: Screening

March 09, 2021

Recommendations made by the USPSTF are independent of the U.S. government. They should not be construed as an official position of the Agency for Healthcare Research and Quality or the U.S. Department of Health and Human Services.

Recommendation Summary

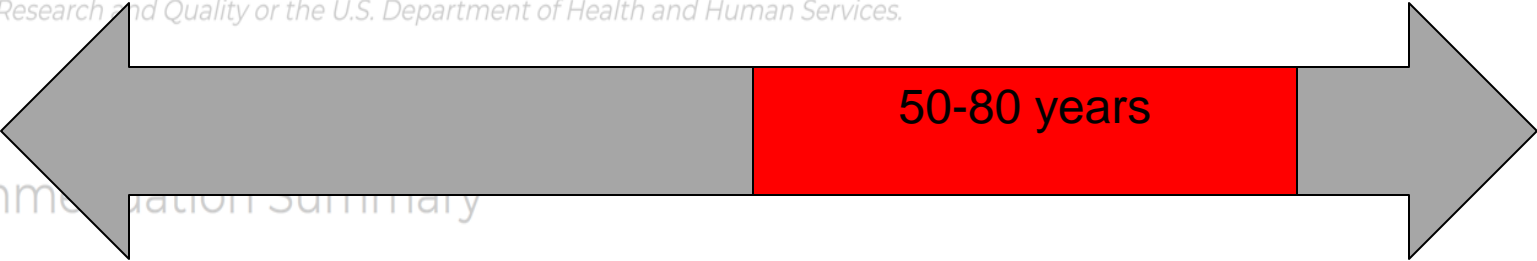
| Population | Recommendation | Grade |
|--|---|----------|
| Adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years | The USPSTF recommends annual screening for lung cancer with low-dose computed tomography (LDCT) in adults aged 50 to 80 years who have a 20 pack-year smoking history and currently smoke or have quit within the past 15 years. 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. | B |

- Who are the screen ineligible but at-risk patients?

- Is LDCT screening effective in this population?

- How do we risk stratify this population?

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| Population | Recommendation | Grade |
|--|--|-------|
| Adults aged 50-80 years who have a ≥ 20 pack year smoking history, currently smoke or have quit in the past 15 years | Offer annual LDCT (low-dose computed tomography) in person or by mail. Do not offer LDCT to individuals with a health problem that substantially limits life expectancy or the ability or willingness to have curative lung surgery. | B |

Should We Screen Never Smokers? Why or Why not?

TABLE 2. Benefits of Screening

| Scenario | Lung Cancers Detected at an Early Stage (Stage I–II) (%) | Lung Cancer Mortality Reduction (%) | Absolute Number of Lung Cancer Deaths Averted per 100,000 | Life-Years Gained per 100,000 | Life-Years Gained per Lung Cancer Death Averted | Screens per Life-Year Gained | Screens per Lung Cancer Death Averted |
|--|--|-------------------------------------|---|-------------------------------|---|------------------------------|---------------------------------------|
| USPSTF (ever eligible only) | 59.4 | 32.7 | 4,305 | 51,035 | 11.9 | 30 | 353 |
| Never-smokers at average risk | 65.8 | 37.1 | 354 | 3,669 | 10.4 | 594 | 6,162 |
| Never-smokers at two times average risk | 65.9 | 37.0 | 706 | 7,332 | 10.4 | 296 | 3,075 |
| Never-smokers at five times average risk | 65.8 | 37.0 | 1,764 | 18,359 | 10.4 | 117 | 1,216 |
| Never-smokers at 10 times average risk | 65.8 | 37.1 | 3,541 | 36,809 | 10.4 | 57 | 593 |
| Never-smokers at 15 times average risk | 65.8 | 37.1 | 5,322 | 55,247 | 10.4 | 37 | 387 |
| Never-smokers at 20 times average risk | 65.8 | 37.1 | 7,118 | 73,892 | 10.4 | 27 | 283 |
| Never-smokers at 35 times average risk | 65.9 | 37.3 | 12,509 | 129,786 | 10.4 | 15 | 151 |

USPSTF, United States Preventive Services Task Force.

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Microsimulation study of the PLCO cohort identified benefit from lung cancer screening for never smokers at 15-35 times risk from baseline.

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Retrospective Data on Screening Never Smokers

- Retrospective studies for LDCT screening in never smokers
 - Sone et al 3,040 never smokers: lung cancer detection rate of 0.48%
 - Kang et al 12,176 never smokers: lung cancer detection rate of 0.45%

| Variable | Lung Cancer in Never-Smokers | Lung Cancer in Ever-Smokers | <i>p</i> Value |
|--------------|---------------------------------|-----------------------------------|----------------|
| | With Cancer/Total, n/n (%) | | |
| Total | 55 of 12,176 (0.45) | 143 of 16,631 (0.86) | <0.001 |
| Sex | | | |
| Male | 17 of 4432 (0.38) ^a | 139 of 15,883 (0.88) ^b | <0.001 |
| Female | 38 of 7744 (0.49) ^a | 4 of 748 (0.53) ^b | 0.784 |
| Age range, y | | | |
| 40-49 | 8 of 4896 (0.16) | 94 of 8062 (1.17) | <0.001 |
| 50-59 | 21 of 4245 (0.49) | 27 of 5493 (0.49) | 0.982 |
| 60-69 | 22 of 2335 (0.94) | 15 of 2498 (0.60) | 0.173 |
| 70-75 | 4 of 700 (0.57) | 7 of 578 (1.21) | 0.218 |

Early Data on Screening Outcomes in Never Smokers

Table 2. Lung Cancer Detection according to Subgroups and Lung-RADS Categories at Baseline LDCT

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| Lung-RADS category (at baseline LDCT) | | | |
| 1 or S | 3 of 10,958 (0.03) | 57 of 14,315 (0.40) | <0.001 |
| 2 | 15 of 950 (1.58) | 18 of 1914 (0.94) | 0.132 |
| 3 | 20 of 151 (13.25) | 20 of 189 (10.58) | 0.449 |
| 4A | 6 of 70 (8.57) | 23 of 144 (15.97) | 0.138 |
| 4B | 7 of 38 (18.42) | 15 of 55 (27.27) | 0.323 |
| 4X | 4 of 9 (44.44) | 10 of 14 (71.43) | 0.196 |

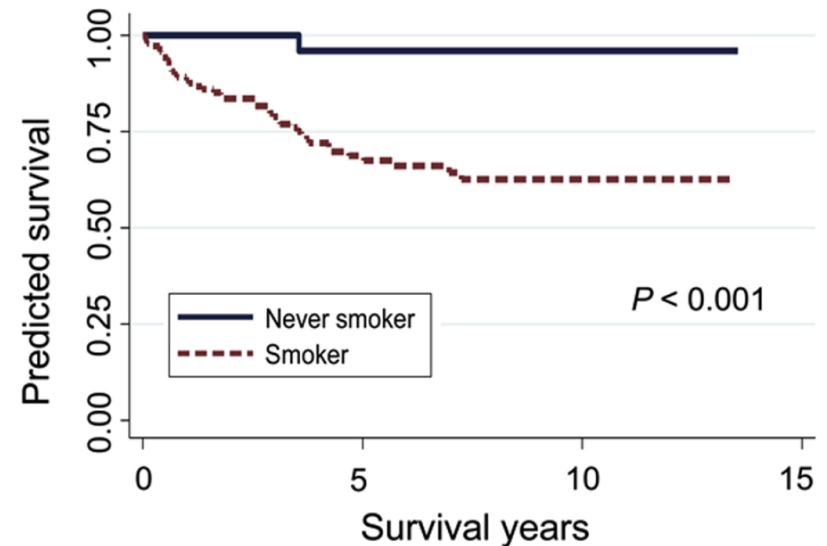


Figure 2. Cumulative survival curves of patients with screening-detected lung cancers, by smoking status.

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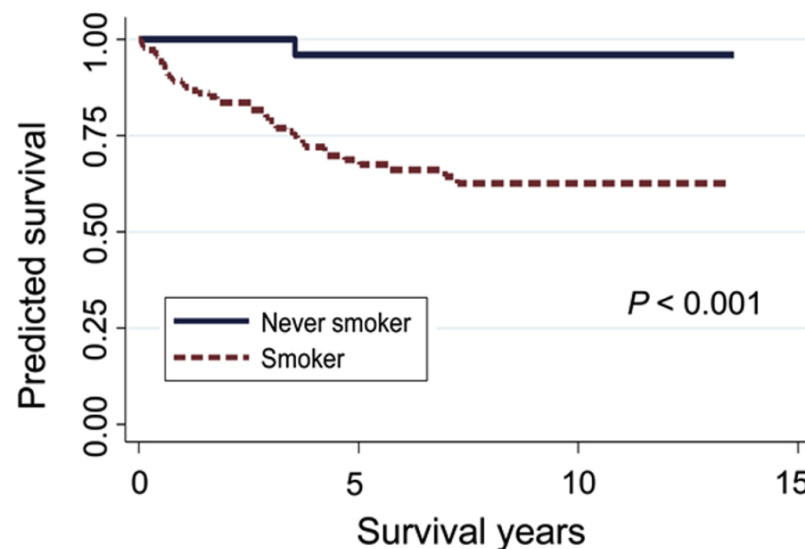
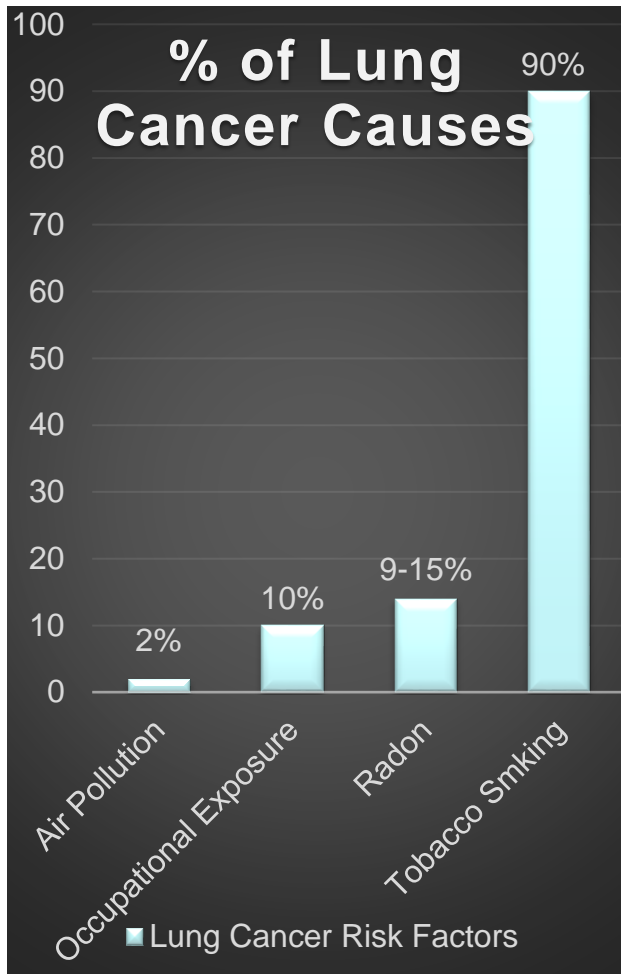
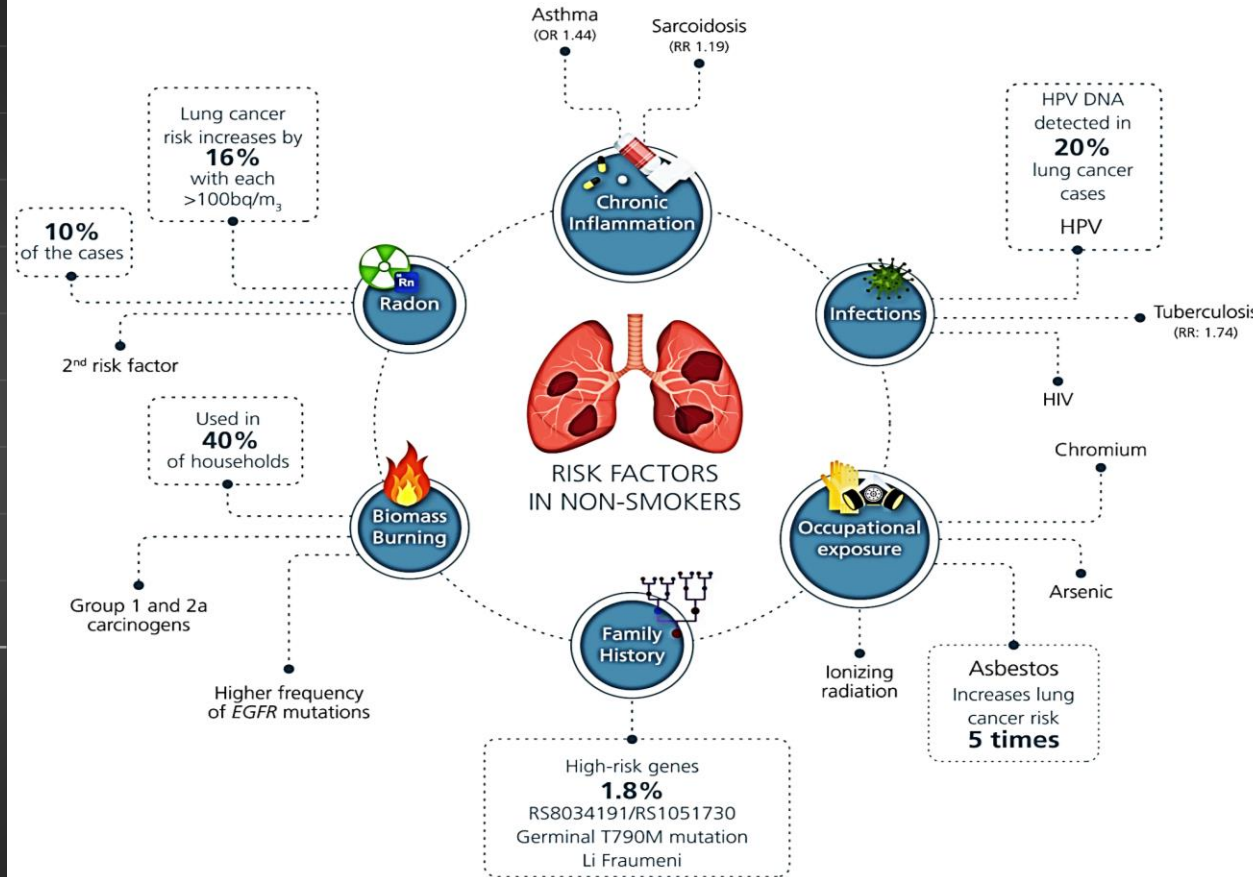


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Overall Population



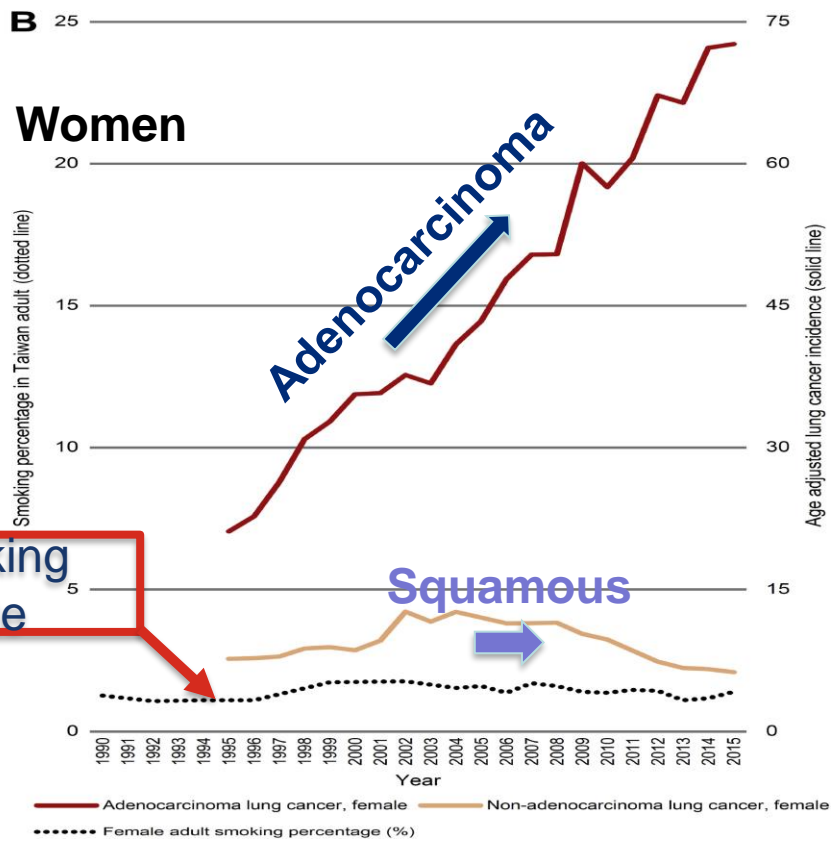
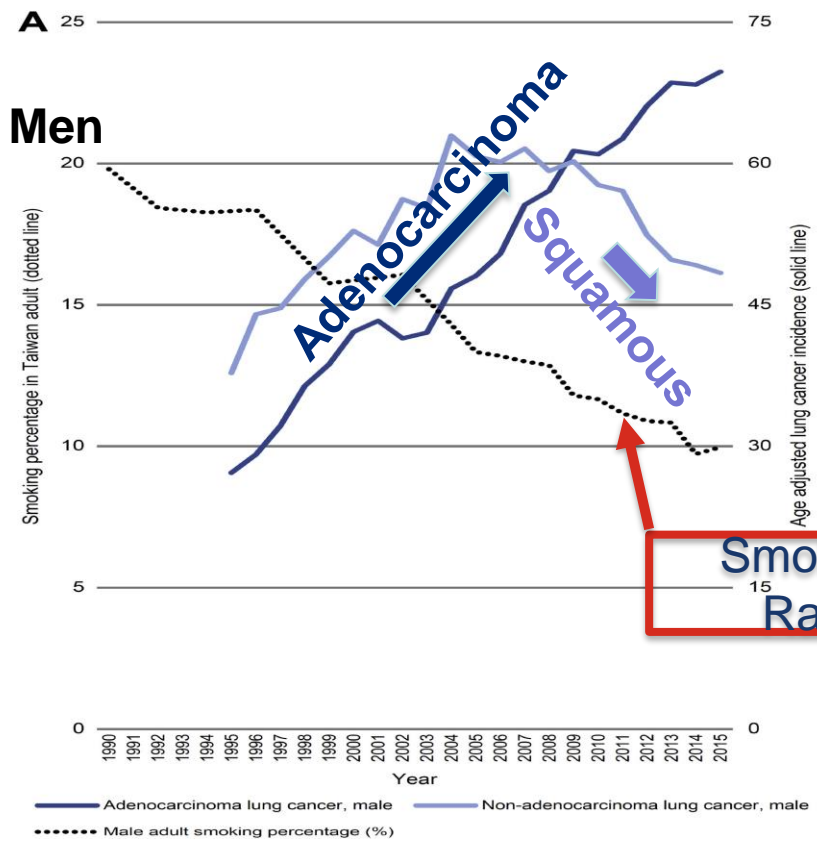
Never Smokers



Corrales Crit Rev Oncol Hematol 2020

Alberg AJ, Samet JM. Chest. 2003

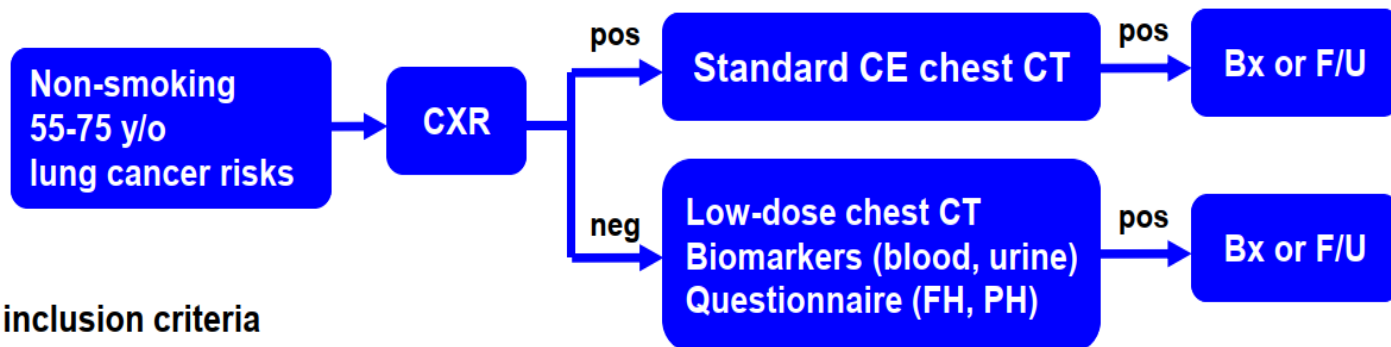
Smoking Rate and Lung Cancer Incidence in Taiwan



Tseng et al. J Thoracic Oncol 2019

Taiwan Lung Cancer Screening in Never Smoker Trial (TALENT)

From Feb 2015 to July 2019, 17 medical centres participated



■ 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 (\leq 3-degree)
 - environmental tobacco smoking history
 - chronic lung disease (TB, COPD)
 - cooking index^b \geq 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

Baseline Characteristics of the Participants

| | | ALL (n, %) | w/ lung cancer family history (n, %) | w/o lung cancer family history (n, %) | P-value |
|----------------------------|--------------------------------|--------------|--------------------------------------|---------------------------------------|---------|
| Gender | Female | 8868 (73.8) | 4322 (71.9) | 4546 (75.7) | <0.001 |
| | Male | 3143 (26.2) | 1687 (28.1) | 1456 (24.3) | |
| Age | Mean (S.D.) | 61.2 (6.2) | 59.6 (6.8) | 62.9 (5.0) | <0.001 |
| | Range | 24 – 75 | 24 – 75 | 55 – 75 | |
| Smoking history | Never smoker | 11201 (93.3) | 5596 (93.1) | 5605 (93.4) | 0.572 |
| | Light ex-smoker | 810 (6.7) | 413 (6.9) | 397 (6.6) | |
| Lung cancer family history | | | | | |
| | 1st-degree family | 5579 (46.4) | 5579 (92.8) | - | |
| | 2nd-degree family | 366 (3.0) | 366 (6.1) | - | |
| | 3rd-degree family | 64 (0.5) | 64 (1.1) | - | |
| Other risk factors | | | | | |
| | Environmental tobacco exposure | 9923 (83.2) | 4492 (75.5) | 5431 (91.0) | <0.001 |
| | Chronic lung disease | 1142 (9.8) | 422 (7.2) | 720 (12.4) | <0.001 |
| | Cooking index ≥ 110 | 4395 (36.7) | 1514 (25.3) | 2881 (48.1) | <0.001 |
| | Cooking without ventilation | 211 (1.8) | 82 (1.4) | 129 (2.1) | 0.001 |

TALENT T0 Lung Cancer Detection Rate

- T0 lung cancer detection rate: 313/12,011= **2.6%**, NLST: 1.1%, NELSON: 0.9%
- Invasive lung cancer: 255/12,011= **2.1%**. Multiple primary lung cancer: **17.9%**
- LDCT positive: 17.4% (GGO > 5mm, S/PS > 6mm) [#]. Invasive procedures: 3.4%
- Lung cancer confirmed: **96.5% stage 0-1**. LDCT features: GGO 47%, S 19%, PS 34%
- Prevalence of lung cancer w/ or w/o family history: **3.2% vs 2.0%** (p< 0.001)

| Histologic Diagnosis | (n) |
|---|------------|
| Adenocarcinoma in situ (AIS) | 58 |
| Minimally invasive adenocarcinoma (MIA) | 71 |
| Invasive adenocarcinoma (INAD) | 183 |
| Adenosquamous carcinoma | 1 |
| Total | 313 |

| | |
|------------|-----|
| Stage 0 | 58 |
| Stage IA | 218 |
| Stage IB | 26 |
| Stage IIA | 0 |
| Stage IIB | 3 |
| Stage IIIA | 2 |
| Stage IIIB | 1 |
| Stage IV | 5 |

GGO: Ground glass opacity; S: Solid; PS: Part solid
Taiwan LDCT Lung Cancer TALENT Study Group, 2020



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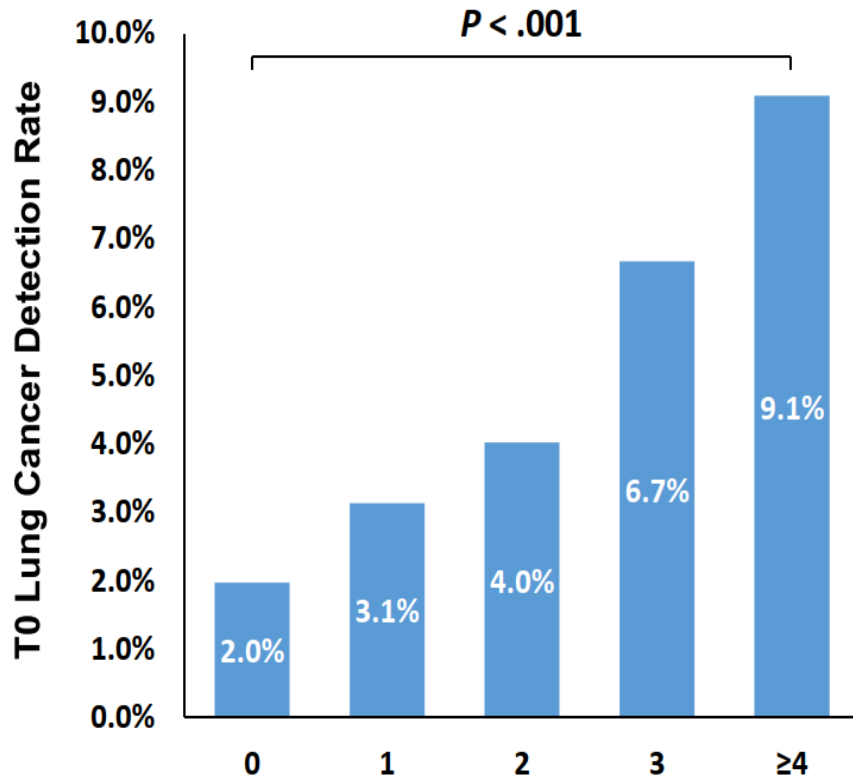
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Prevalence of Lung Cancer in Different Subpopulations

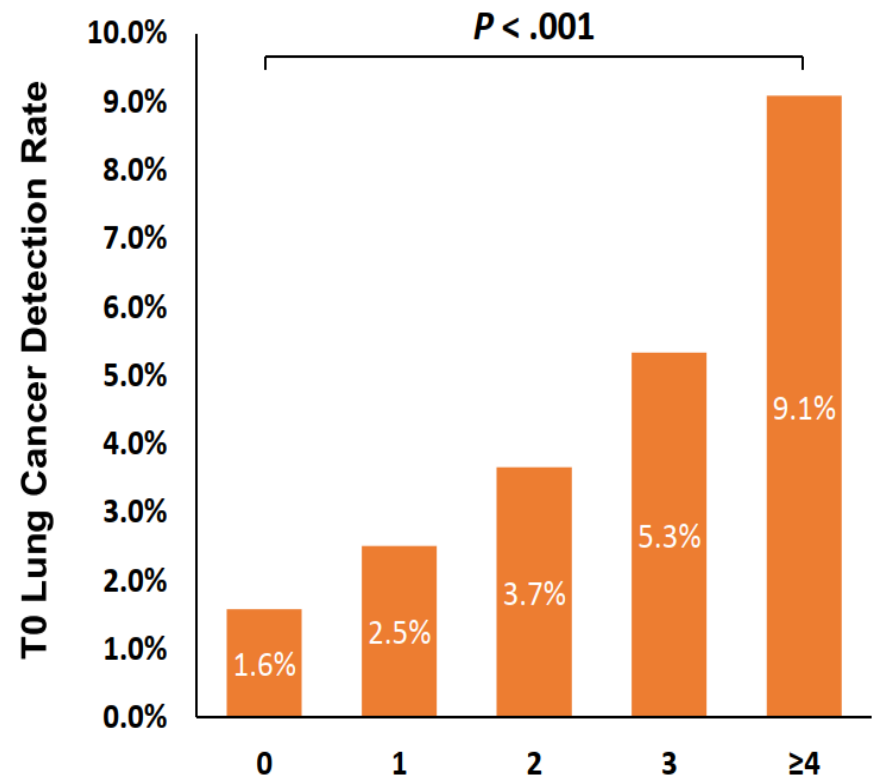
| | Absence | | Presence | | R.R. (95% CI) | | p |
|--|------------------|------------|-----------------|------------|---------------|--------------------|-------------------|
| | n | % | n | % | | | |
| Lung cancer family history | 120/6002 | 2.0 | 193/6009 | 3.2 | 1.61 | (1.28—2.01) | < 0.001 |
| First-degree family | 127/6432 | 2.0 | 186/5579 | 3.3 | 1.69 | (1.35—2.11) | < 0.001 |
| Father | 281/10377 | 2.7 | 32/1634 | 2.0 | 0.72 | (0.50—1.04) | 0.077 |
| Mother | 251/10241 | 2.5 | 62/1770 | 3.5 | 1.43 | (1.09—1.88) | 0.010 |
| Brother | 260/10901 | 2.4 | 53/1110 | 4.8 | 2.00 | (1.50—2.67) | < 0.001 |
| Sister | 244/10367 | 2.4 | 69/1644 | 4.2 | 1.78 | (1.37—2.32) | < 0.001 |
| Second degree family | 307/11645 | 2.6 | 6/366 | 1.6 | 0.62 | (0.28—1.39) | 0.238 |
| Third degree family | 312/11947 | 2.6 | 1/64 | 1.6 | 0.60 | (0.09—4.20) | 1.000 |
| Environmental tobacco exposure | 53/1999 | 2.7 | 254/9923 | 2.6 | 0.97 | (0.72—1.29) | 0.813 |
| Chronic lung disease history | 284/10568 | 2.7 | 19/1142 | 1.7 | 0.62 | (0.39—0.98) | 0.038 |
| Cooking index ≥ 110 | 209/7591 | 2.8 | 104/4395 | 2.4 | 0.86 | (0.68—1.08) | 0.201 |
| Cooking without ventilation | 306/11800 | 2.6 | 7/211 | 3.3 | 1.28 | (0.61—2.67) | 0.513 |

No. of 1st Degree Lung Cancer Family History and Risk of Lung Cancer

All lung cancer



Invasive lung cancer



TALENT vs Other LDCT Lung Cancer Screening Studies

| | TALENT | | | NLST ¹ | NELSON ² | UKLS-pilot ³ | I-ELCAP ⁴ |
|-----------------------------|--|--------------|--------------|-------------------|---------------------|-------------------------|------------------------|
| | w/ FH | w/o FH | ALL | LDCT arm | LDCT arm | LDCT arm | ALL |
| Population | Never or light ex- smoker ⁵ | | | Smoker | Smoker | Smoker ⁶ | Mixed ⁷ |
| Patient number | 6009 | 6002 | 12011 | 26309 | 7557 | 1994 | 31567 |
| LDCT positive rate | 17.7% | 17.1% | 17.4% | 27.3% | 20.8% ⁸ | 13.3% | 26.9% |
| T0 LC detection rate | 3.2% | 2.0% | 2.6% | 1.1% | 0.9% | 1.7% | 1.1% |
| Sensitivity | 91.7% | 92.5% | 92.0% | 93.8% | 94.6% | 97.6% | 98.8% |
| Specificity | 84.7% | 84.4% | 84.6% | 73.4% | 98.3% | 74.6% | 87.9% |
| PPV | 16.6% | 10.8% | 13.8% | 3.8% | 35.7% | 7.6% | 9.7% |
| NPV | 99.7% | 99.8% | 99.7% | 99.9% | 99.9% | 99.9% | 100.0% |
| Stage 0-I (%) | 96.4% | 96.7% | 96.5% | 54.8% | 63.9% | 66.7% | 85%⁹ |

¹ NEJM 2013, ² NEJM 2020, ³ Thorax 2016, ⁴ NEJM 2006,

⁵ 6.7% are light ex-smokers, ⁶ 99.9% are smokers, ⁷ 82.8% are smokers,

⁸ by the first scans, ⁹ including baseline and annual scans

Taiwan LDCT Lung Cancer TALENT Study Group, 2020

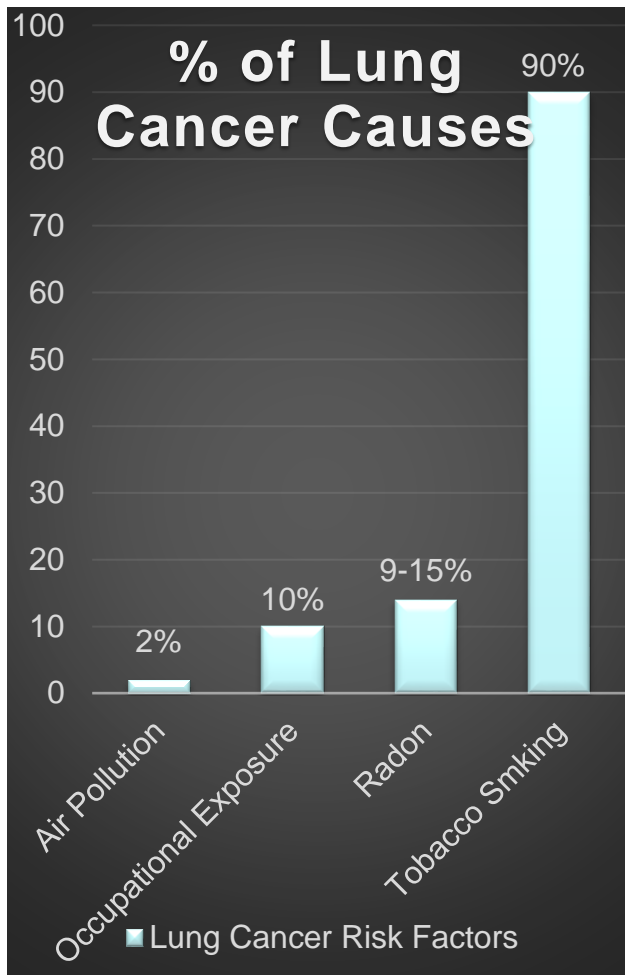


2020 World Conference
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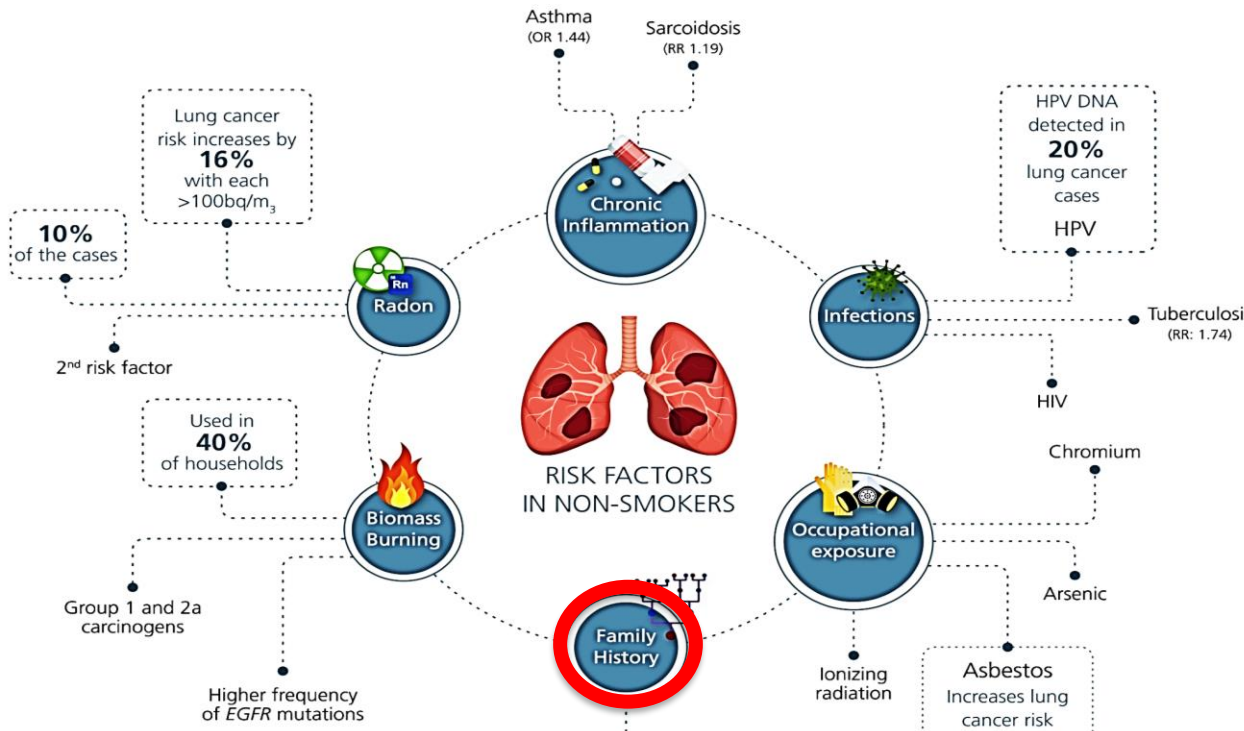
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Conclusions from TALENT

- T0 Lung cancer detection rate is higher than NLST and NELSON.
- 1st degree family history of lung cancer is a significant risk.
- ETS, chronic lung disease and cooking smoke exposure did not reach significance.
- Longer follow-up with mortality data needed.
- Unknown whether findings can be generalized to non-East Asian population.
- Genotyping results are also awaited.



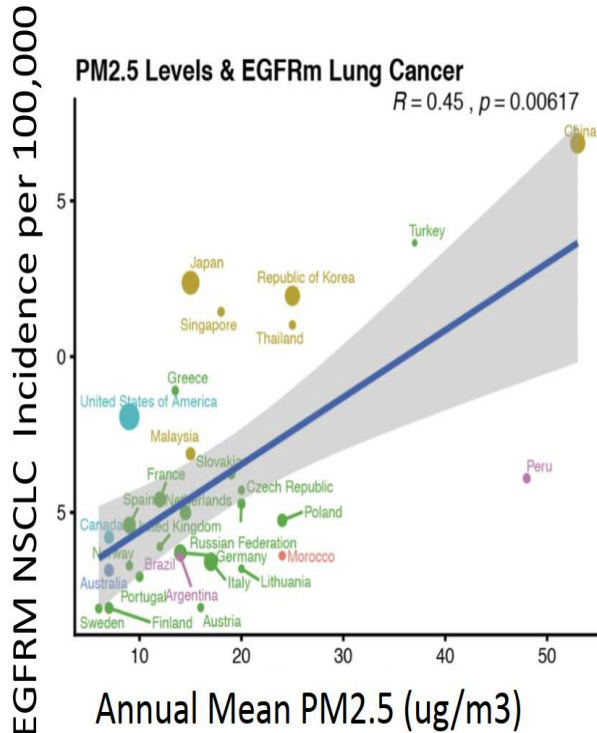
Corrales Crit Rev Oncol Hematol 2020
 Alberg AJ, Samet JM. Chest. 2003
 Oxnard JNCI 2013



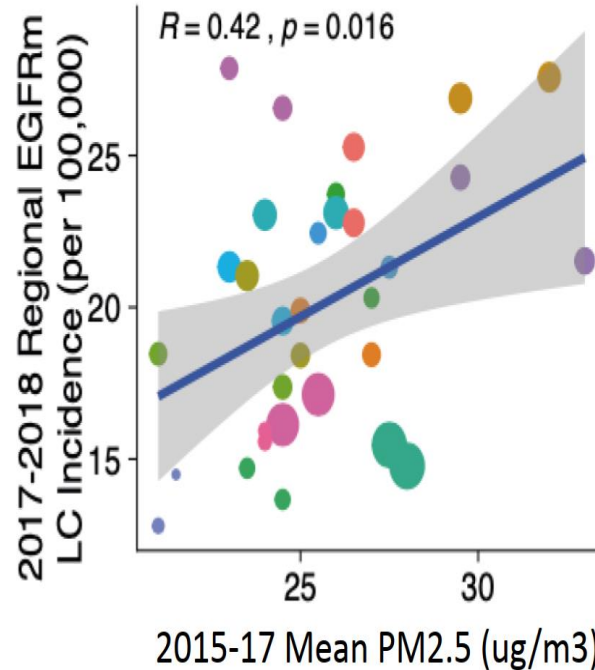
| | | Smoking Associated Lung Cancer | Never Smoker Lung Cancer |
|---|-----------|---|---|
| Genetic Foci Associated with Inherited Susceptibility | Low-risk | 15q25.1 (<i>CHRNA3</i> , <i>CHRNB4</i> and <i>CHRNA5</i>) | 13q31.3 (<i>GPC5</i>) 10q25.2 (<i>VTL1A</i>) |
| | High risk | <i>TP53</i> <i>RB1</i> | <i>EGFR T790M</i> & <i>V843I</i> <i>HER2 G660D</i> |

PM2.5 exposures associated with EGFRm Global Lung Cancer Incidence

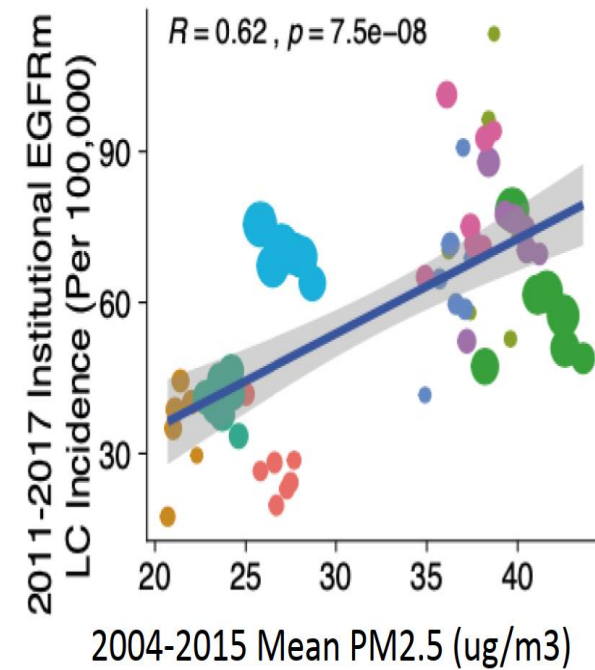
Internationally



South Korea



Taiwan



Geographic Distribution: PM2.5 levels track EGFRm NSCLC incidence

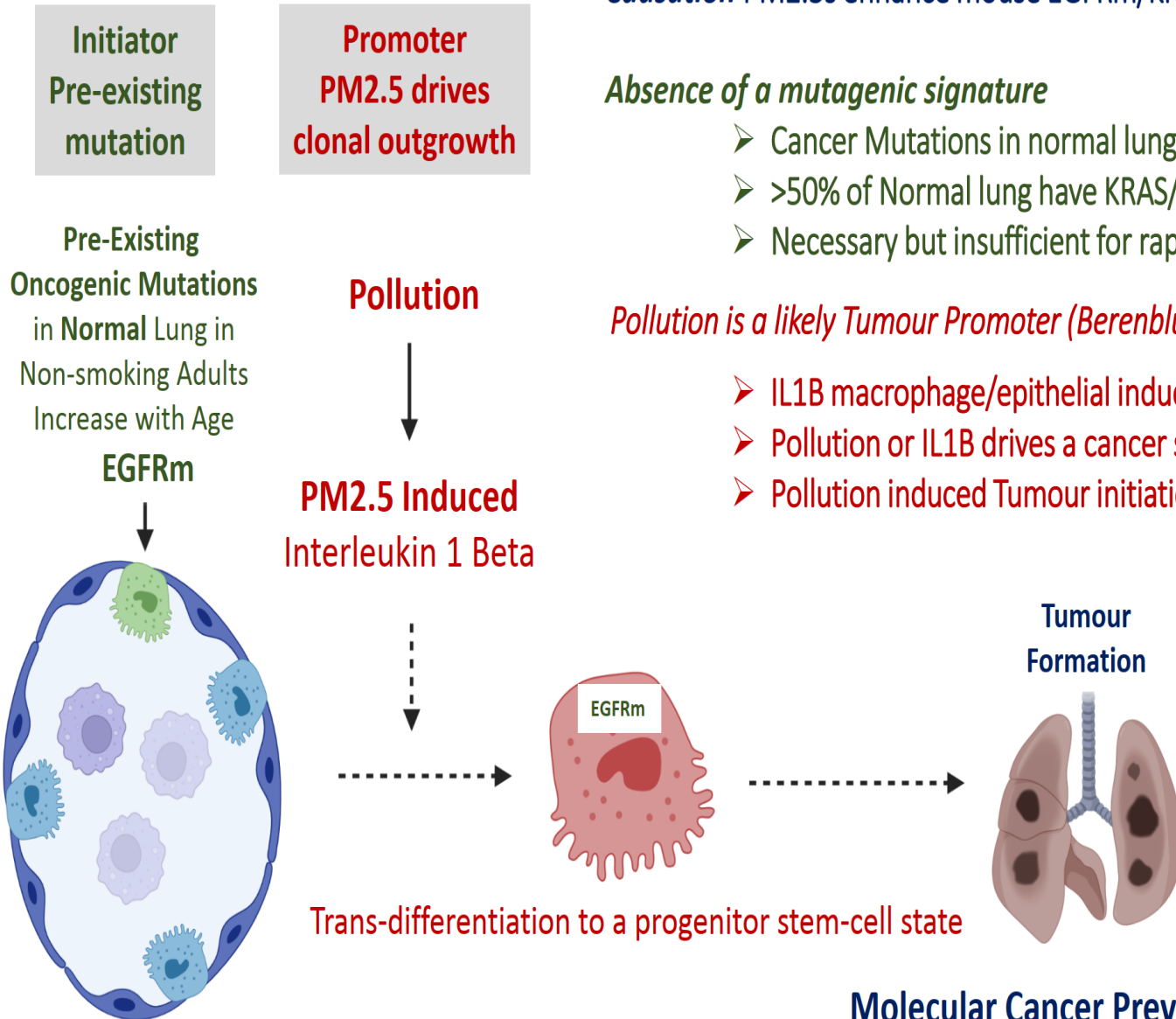
Causation PM2.5s enhance mouse EGFRm/KRASm lung cancer formation

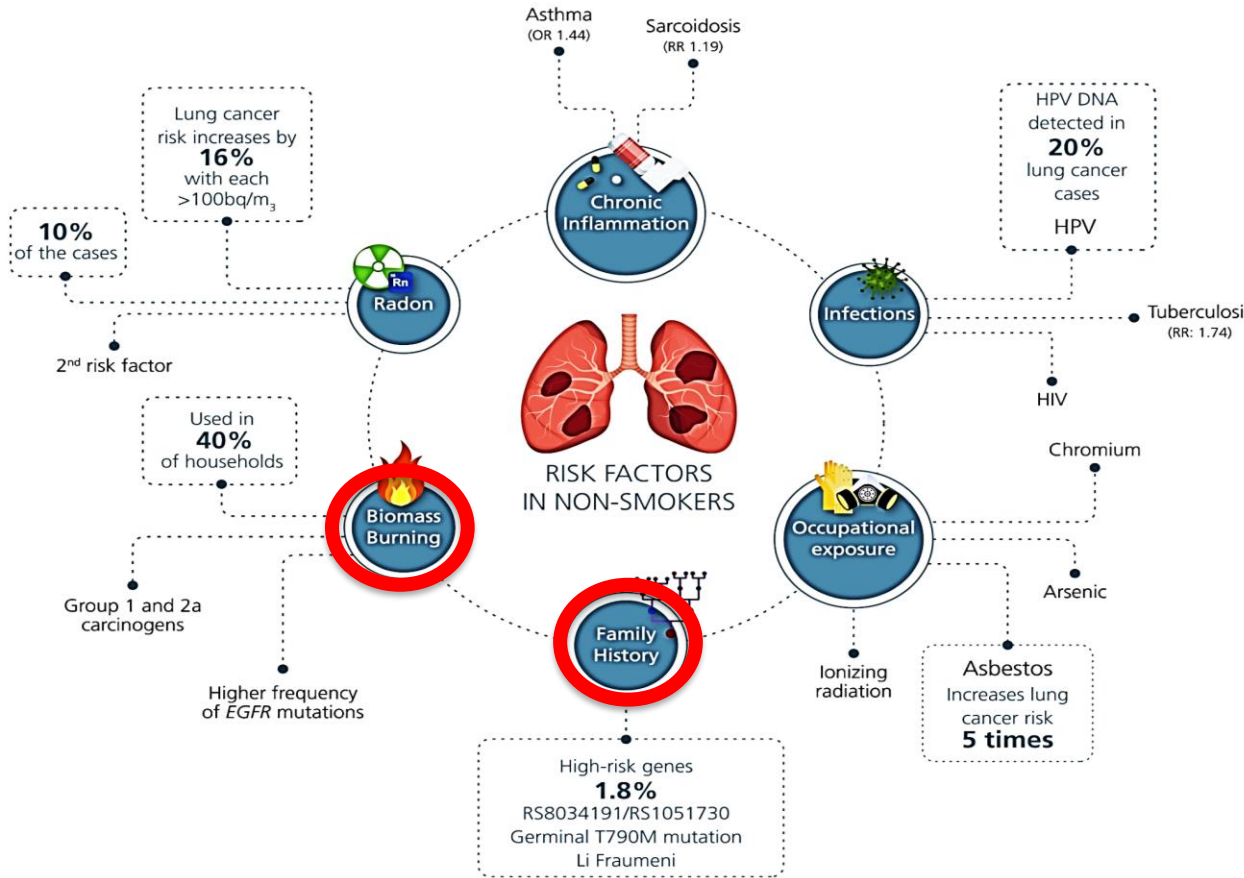
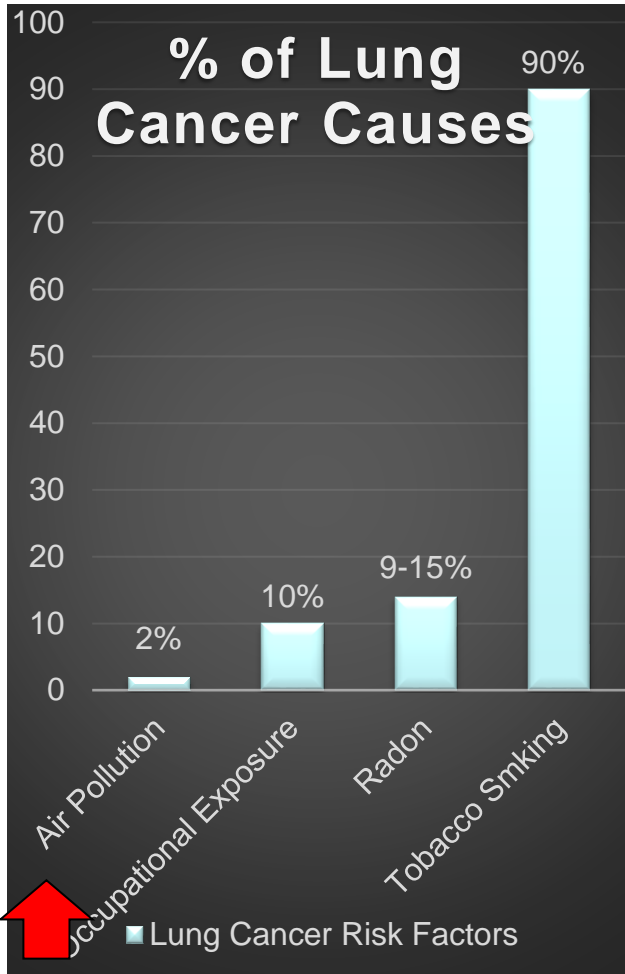
Absence of a mutagenic signature

- Cancer Mutations in normal lung increase with age;
- >50% of Normal lung have KRAS/EGFRm
- Necessary but insufficient for rapid tumour initiation

Pollution is a likely Tumour Promoter (Berenblum 1947)

- IL1B macrophage/epithelial induced inflammation
- Pollution or IL1B drives a cancer stem cell like state in EGFRm clones
- Pollution induced Tumour initiation blocked by anti-IL1B



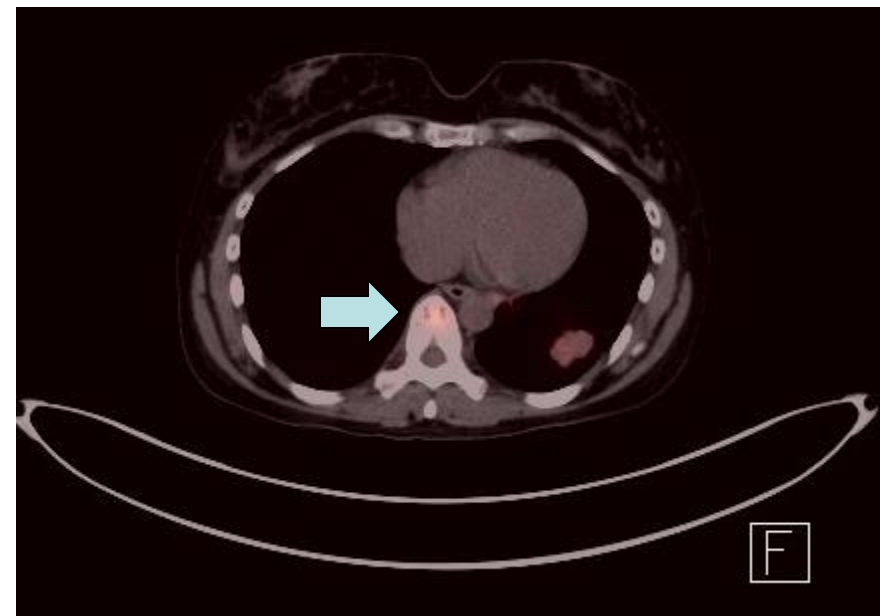
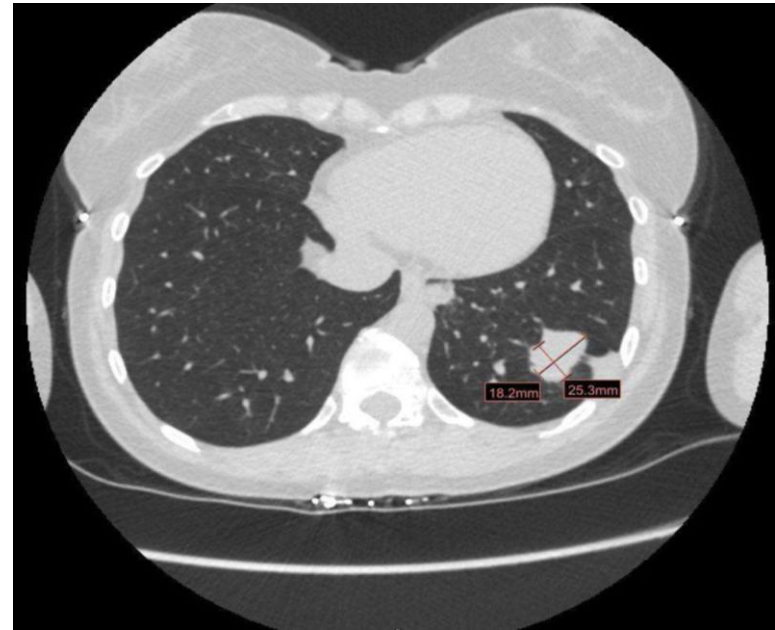


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Alberg AJ, Samet JM. Chest. 2003

Case Presentation

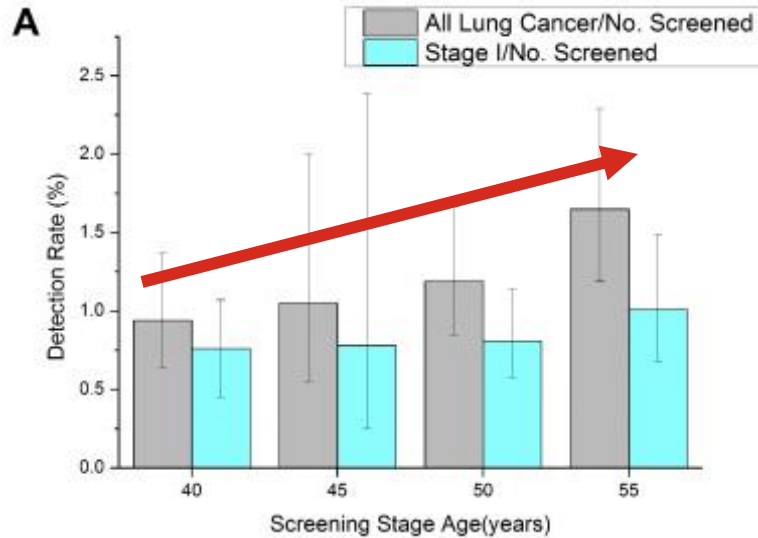
- 46 yo female never smoker with 1-month hx of cough & dyspnea. PMHx of asthma
- Fhx of breast ca in mother, prostate ca in father & paternal grandfather.
- CT chest LLL nodule. EBUS - adenoca in LLL, level 7, 4L & 11L nodes. PET/CT uptake in above sites & abdominal nodes. MRI brain > 20 lesions measuring 2-3 mms.
- Molecular testing identified EGFR exon 20ins mutation.



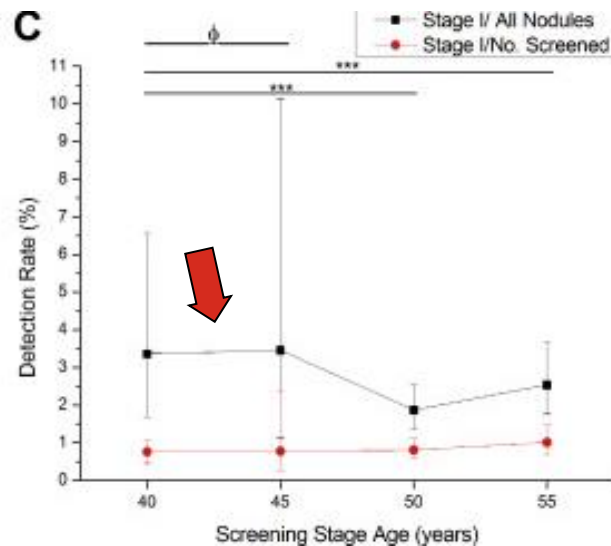
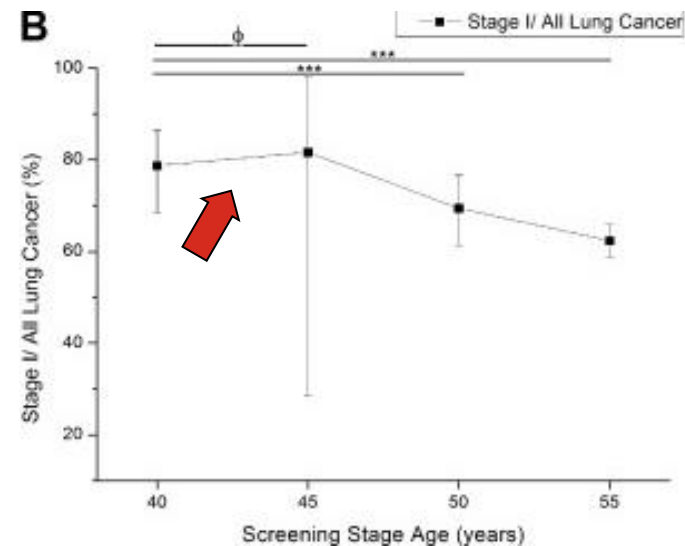
- **Can we better identify at risk patients?**

- Previous patient does not fit any of the current screening criteria for lung cancer.
 - Can LDCT screening help these patients?

What is the optimal age for screening?



- **Meta-analysis of LDCT screening studies including 117,586 participants.**
- There is an increasing detection rate of lung cancer with increasing age.



- There is a higher proportion of stage I cancers vs all stages in the ages 40-45 participants.
- This suggests LDCT screening maybe more effective when started at an earlier age.

Community-based Mass Screening with Low-Dose CT for Lung Cancer in Guangzhou

LUNG-CARE project in Guangzhou

Wenhua Liang, Caichen Li, Jianxing He*, Nanshan Zhong
on behalf of the executive team of LUNG-CARE project



Eligibility criteria:

- 40-74 years old residents in Guangzhou
- Accept to receive LDCT scan,

Exclusion criteria:

- Had a diagnosis of lung cancer or treatment-related to lung cancer within the past 5 years (except for non-melanoma skin cancer)
- Had undergone chest CT within the past year
- Had significant cancer-related symptoms (e.g. hemoptysis, dyspnea, inability to climb two flights of stairs)

Assessed for eligibility (n=12,644)

899 refused CT scans,
28 had a personal history of lung cancer,
9 participants performed a duplicate screenings

LDCT completed (n=11,708)

Negative screening tests (n=9,463)

Solid (subsolid) nodules $\geq 5\text{mm}$ or
pure ground glass $\geq 8\text{mm}$ (n=2,245)

2,026 were suggested to performed serial follow-up LDCT

Invasive diagnostic procedures (n=230)

Lung cancer (n=200), Metastatic cancer (n=10),
Benign nodules (n=20)

Intervention

- One-off LDCT

Control

- Nature cohort from the same communities

Primary objective:

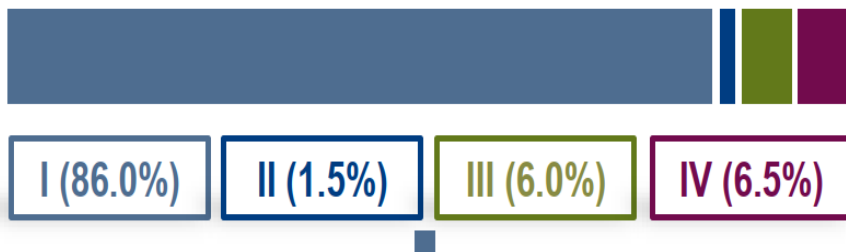
- to evaluate the prevalence of lung cancer in general population in Guangzhou

Secondary objective:

- to compare the prevalence of lung cancer between high-risk and non-high risk groups
- to explore the risk factors for lung cancer in Chinese population
- cost-effectiveness

Lung Nodule & Cancer Detection Rates

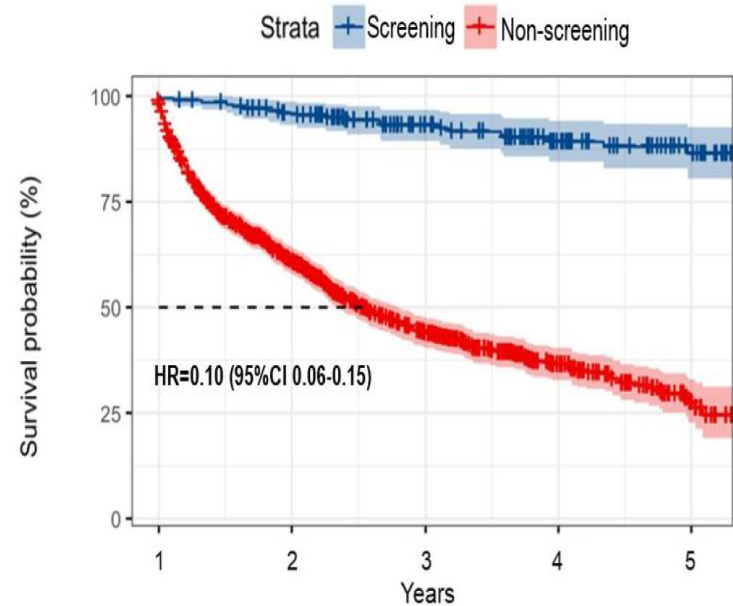
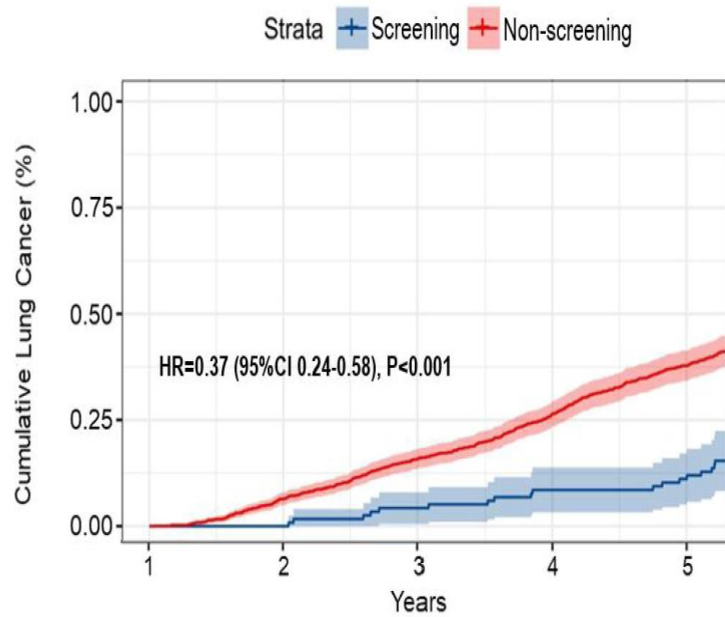
| Group | Detection rate |
|--------------|----------------------|
| 5mm+ nodules | 19.2% (2,245/11,709) |
| Lung cancer | 1.7% (200/11,708) |
| Stage 0-I | 86.0% (172/200) |



| | All Lung cancer | Stage I lung cancer | Stage 4 lung cancer |
|-------------|-----------------|---------------------|---------------------|
| NLST | 6.3% | 62% | 13% |
| NELSON | 3.1% | 71% | 8.1% |
| Liang | 1.7% | 86% | 6.5% |
| Kang | 0.45 | 80% | 3.6% |
| Yang TALENT | 2.6 | 78% | 1.6% |

- Higher proportion of stage I patients compared to NLST and NELSON
 - But included **stage 0**. Possibly due to screening at an earlier age?
- Findings limited by the regional nature of this study
- Control group stage distribution and surveillance status unknown

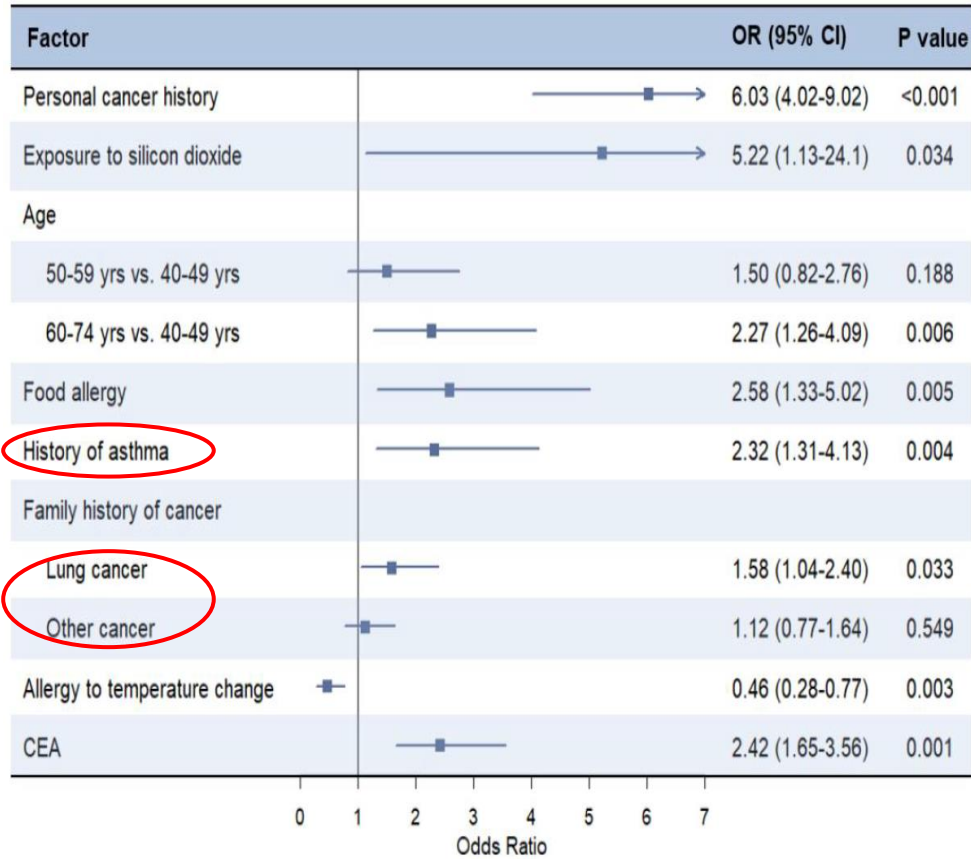
LDCT screening reduced lung cancer deaths of the community and improve prognosis of lung cancer patients

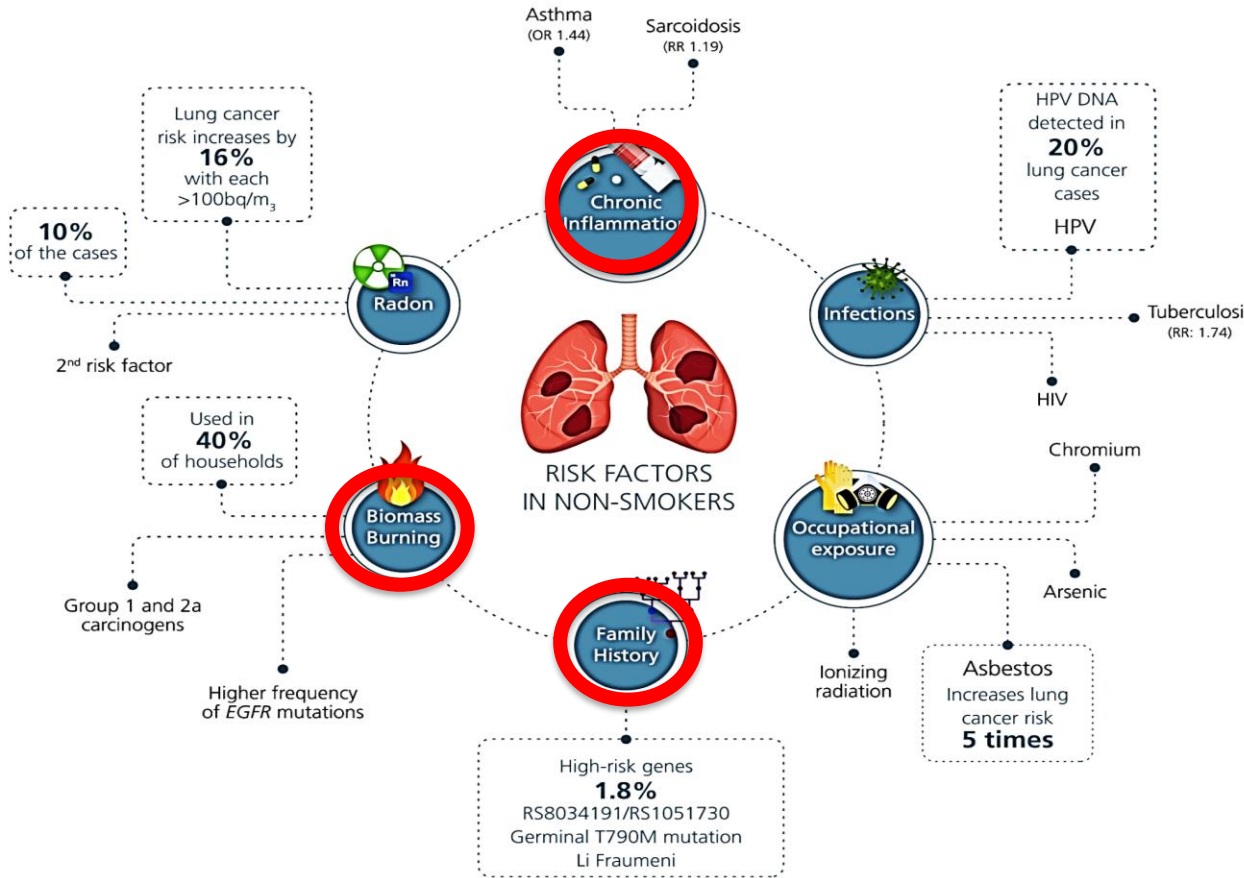
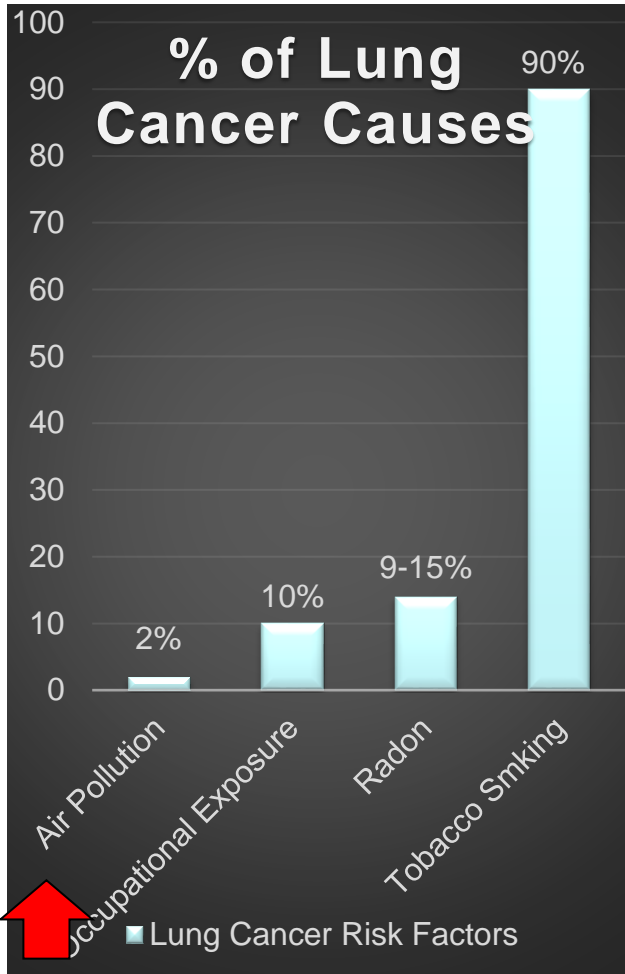


- Limited follow-up and 1- off LDCT
- Is survival the right endpoint, mortality rate is better.
- Subject to bias – selection bias, lead time bias, length time bias, interval cancer bias & over-diagnosis bias

China National Lung Cancer Screening program, HR 0.69, 95% CI [0.53-0.92] Li N et al. Lancet Respir Med. 2022;10(4):378-391.

At-risk Population

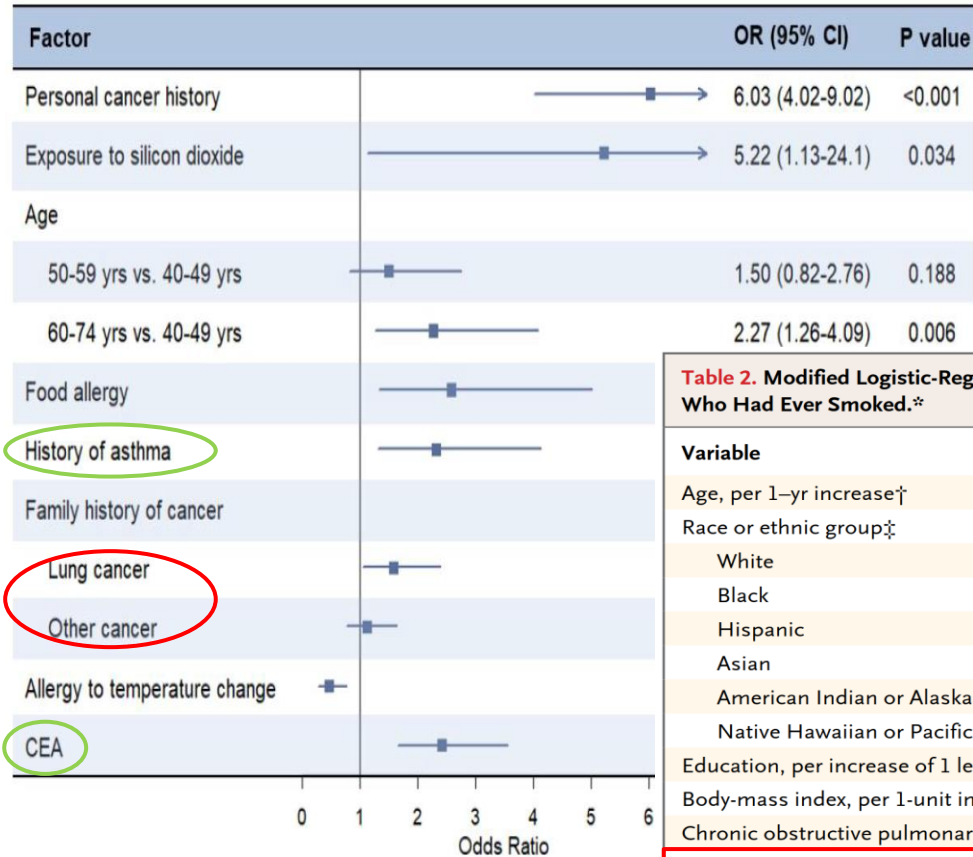




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At-risk Population

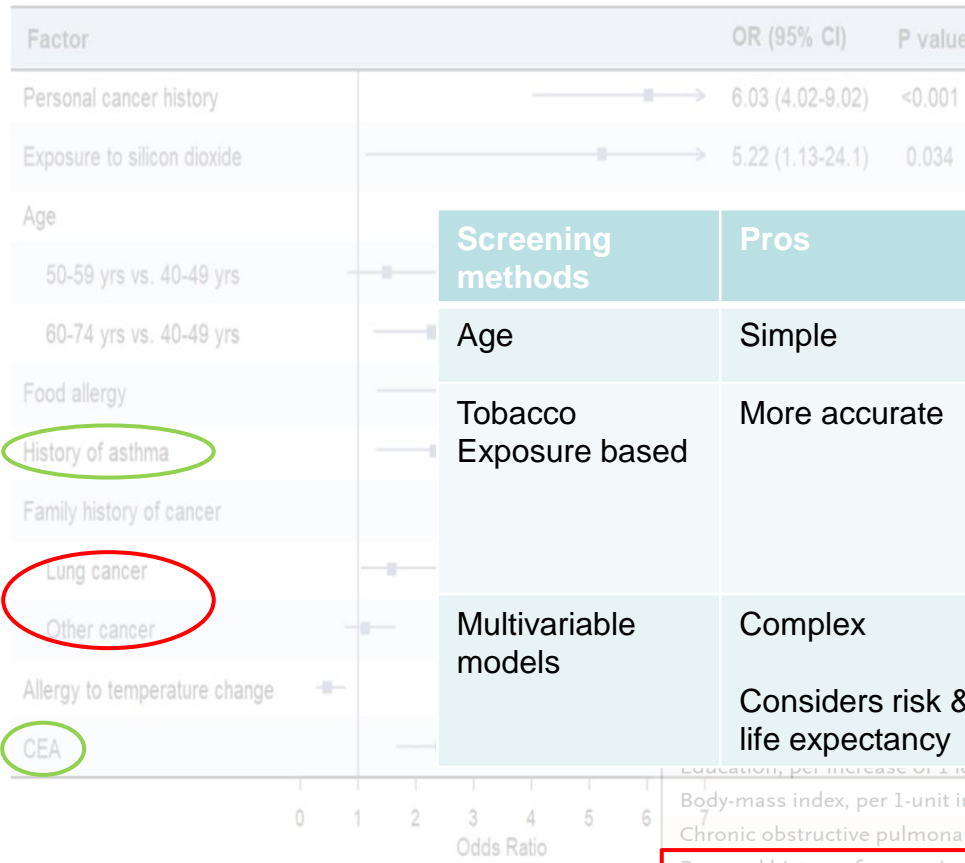


PLCOm2012 model

Table 2. Modified Logistic-Regression Prediction Model (PLCO_{M2012}) of Cancer Risk for 36,286 Control Participants Who Had Ever Smoked.*

| Variable | Odds Ratio (95% CI) | P Value | Beta Coefficient |
|---|---------------------|---------|------------------|
| Age, per 1-yr increase [†] | 1.081 (1.057–1.105) | <0.001 | 0.0778868 |
| Race or ethnic group [‡] | | | |
| White | 1.000 | | Reference group |
| Black | 1.484 (1.083–2.033) | 0.01 | 0.3944778 |
| Hispanic | 0.475 (0.195–1.160) | 0.10 | -0.7434744 |
| Asian | 0.627 (0.332–1.185) | 0.15 | -0.466585 |
| American Indian or Alaskan Native | 1 | | 0 |
| Native Hawaiian or Pacific Islander | 2.793 (0.992–7.862) | 0.05 | 1.027152 |
| Education, per increase of 1 level ^{†§} | 0.922 (0.874–0.972) | 0.003 | -0.0812744 |
| Body-mass index, per 1-unit increase [†] | 0.973 (0.955–0.991) | 0.003 | -0.0274194 |
| Chronic obstructive pulmonary disease (yes vs. no) | 1.427 (1.162–1.751) | 0.001 | 0.3553063 |
| Personal history of cancer (yes vs. no) | 1.582 (1.172–2.128) | 0.003 | 0.4589971 |
| Family history of lung cancer (yes vs. no) | 1.799 (1.471–2.200) | <0.001 | 0.587185 |
| Smoking status (current vs. former) | 1.297 (1.047–1.605) | 0.02 | 0.2597431 |
| Smoking intensity [¶] | | | -1.822606 |
| Duration of smoking, per 1-yr increase [†] | 1.032 (1.014–1.051) | 0.001 | 0.0317321 |
| Smoking quit time, per 1-yr increase [†] | 0.970 (0.950–0.990) | 0.003 | -0.0308572 |
| Model constant | | | -4.532506 |

At-risk Population



| Screening methods | Pros | Cons |
|------------------------|---|---|
| Age | Simple | Low precision |
| Tobacco Exposure based | More accurate | Prioritizes older & sicker patients |
| Multivariable models | Complex Considers risk & life expectancy | Need validation Specific to the population |

2012 model

| 2012 model (M ₂₀₁₂) of Cancer Risk for 36,286 Control Participants | | |
|--|---------|------------------|
| Ratio (95% CI) | P Value | Beta Coefficient |
| (1.057–1.105) | <0.001 | 0.0778868 |
| | | Reference group |
| (-1.083–2.033) | 0.01 | 0.3944778 |
| (0.195–1.160) | 0.10 | -0.7434744 |
| (-0.332–1.185) | 0.15 | -0.466585 |
| (0.992–7.862) | 0.05 | 1.027152 |
| (0.874–0.972) | 0.003 | -0.0812744 |
| 0.973 (0.955–0.991) | 0.003 | -0.0274194 |
| 1.427 (1.162–1.751) | 0.001 | 0.3553063 |
| 1.582 (1.172–2.128) | 0.003 | 0.4589971 |
| 1.799 (1.471–2.200) | <0.001 | 0.587185 |
| 1.297 (1.047–1.605) | 0.02 | 0.2597431 |
| | | -1.822606 |
| 1.032 (1.014–1.051) | 0.001 | 0.0317321 |
| 0.970 (0.950–0.990) | 0.003 | -0.0308572 |
| | | -4.532506 |

Conclusion

- Screen detection rates of lung cancer in never smokers is lower than ever smokers (but still **significant!**)
- Detection rate might be improved by incorporating smoking status (light smokers), inheritable risks & co-morbidities.
- Family history seems to be a consistent risk factor
- Screening program will have to account for geographic & ethnic diversity.
- Major limiting factor is lack of mature data including risk-benefit analysis from randomized studies.

| | NLST | NELSON |
|-----------------------------|------------------|-----------------------------|
| Country | USA | BE/NL |
| Enrollment | 2002–2004 | 2003–NR |
| Number of Centers | 33 | 4 |
| Number of screens | 3 | 3 |
| Screening planned at years | 1, 2 and 3 | 1, 2 and 4 |
| Comparison | LDCT vs Xray | LDCT vs usual care |
| Population | | |
| Age | 55–74 | 50–69 (50–75) |
| Smoking (pack-years) | ≥30 | >15* |
| Sex | both (male 59%) | men ^o (male 84%) |
| Years since quit | ≤15 | ≤10 |
| Patients Screened, <i>n</i> | 26,722 vs 26,732 | 7907 vs 7915 |
| Planned follow-up, <i>y</i> | >7 | 10 |



| | | |
|----------------------------------|------|------------------|
| LC diagnosed at screening, % | 1.02 | 0.9 |
| 5mm Reduction of LC mortality | 20% | 26% ^o |

*, ≥15 cigarettes/day for 25 years or ≥10cigarettes/day for 30 years ; ^o, both in Belgium; VDT, volume doubling time ; ^a, in men.