

Epidemiología y cribado

Bartomeu Massutí MD

Hospital Universitario Alicante Dr Balmis ISABIAL



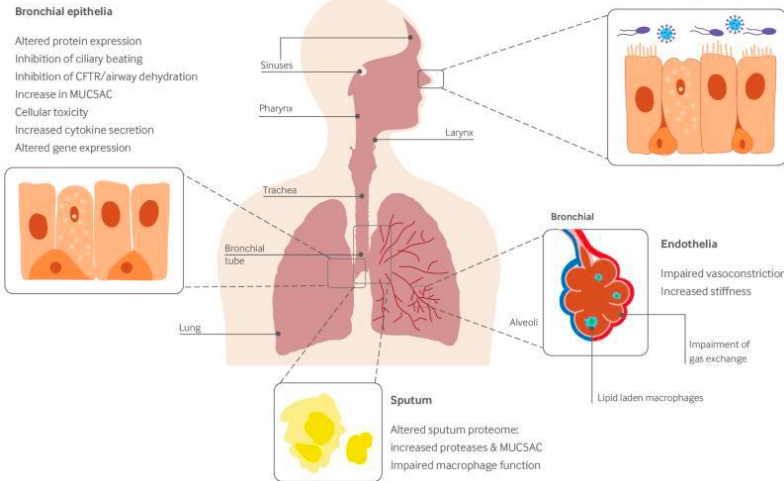
Epidemiología/1

Lung Cancer: Are You at Risk?



- Smoking
- Second-Hand Smoke
- Radon Gas Exposure
- Asbestos Exposure
- Other Carcinogens
- Air Pollution
- Arsenic in Drinking Water
- Previous Lung Radiation
- Personal or Family History

Learn more about lung cancer symptoms, types, and research at www.LCFAmerica.org



Emily Stone / WCLC23

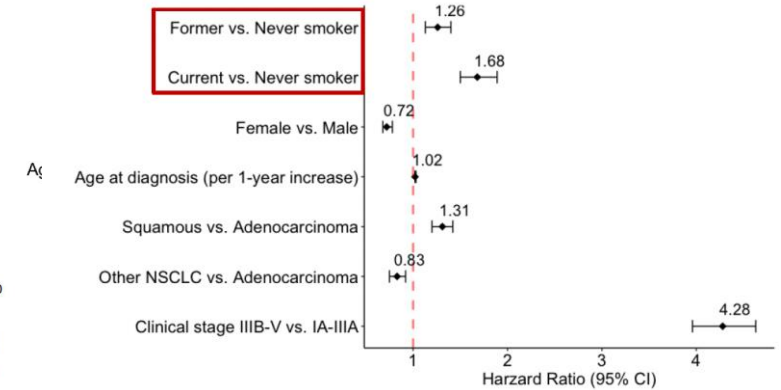
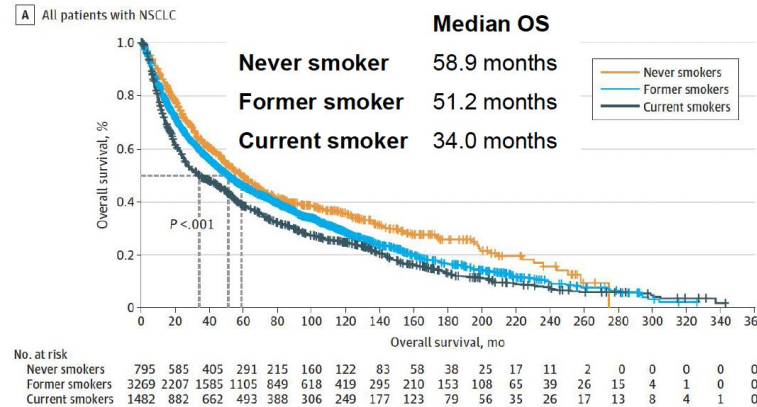
Exposición tabáquica previa al diagnóstico

5.594 pacientes

Análisis impacto en supervivencia

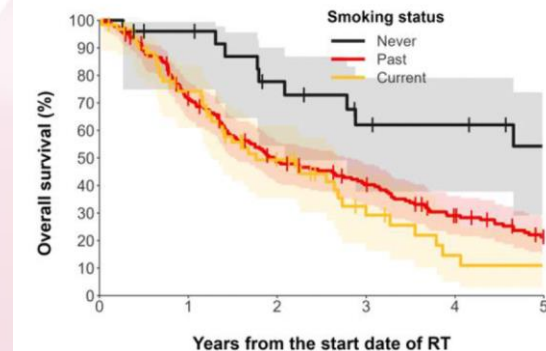
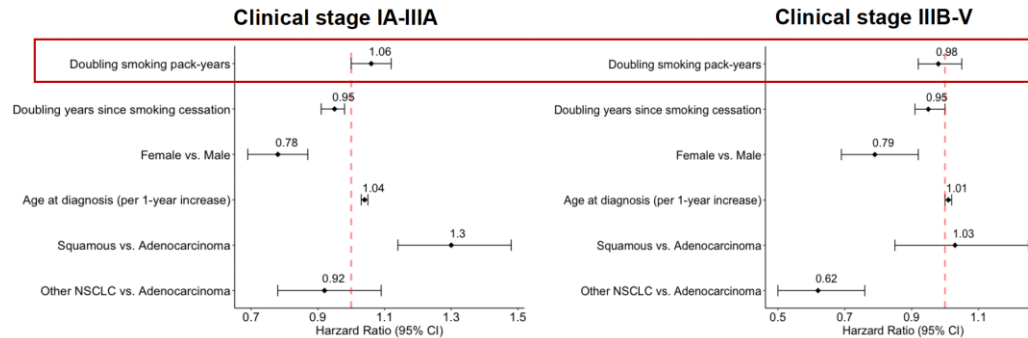
Ex-fum vs. Nunca fum.: HR = 1.26 (95% CI: 1.13 -1.40, P < .001)

Fum. activos vs Nunca fum: HR = 1.68 (95% CI: 1.50 -1.89, P < .001)



Doble IPA HR 1.07 (1.04-1.11)

Doble años abstención tabáquica HR 0.96 (0.93-0.99)



Xinan Wang / WCLC23

Neil Wallace / WCLC23



Contents lists available at ScienceDirect

Environment International

journal homepage: www.elsevier.com/locate/envint

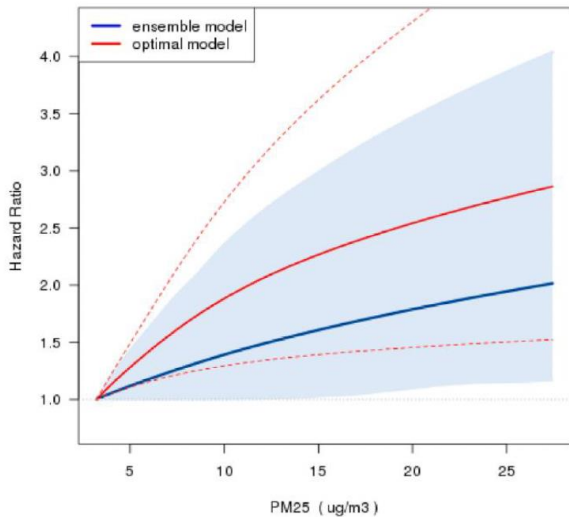


Long-term low-level ambient air pollution exposure and risk of lung cancer – A pooled analysis of 7 European cohorts

Ulla Arthur Hvidtfeldt^{a,*}, Gianluca Severi^{b,c}, Zorana Jovanovic Andersen^d, Richard Atkinson^e, Mariska Bauwelink^f, Tom Bellander^{g,h}, Marie-Christine Boutron-Ruaultⁱ, Jørgen Brandt^{j,k}, Bert Brunekreef^l, Giulia Cesaroni^m, Jie Chenⁿ, Hans Concin^o, Francesco Forastiere^{p,q}, Carla H. van Gils^r, John Gulliver^s, Ole Hertel^t, Gerard Hoek^u, Barbara Hoffmann^v, Kees de Hoogh^{w,x}, Nicole Janssen^y, Karl-Heinz Jöckel^z, Jeanette Therning Jørgensen^{aa}, Klea Katsouyanni^{ab,ac}, Matthias Ketzel^{ad,ae}, Jochem O. Klompmaaker^{af,ag}, Norun Hjertager Krog^{ah}, Alois Lang^{ai}, Karin Leander^{aj}, Shuo Liu^{ak}, Petter L.S. Ljungman^{al,am}, Patrik K.E. Magnusson^{an}, Amar Jayant Mehta^{ao,ap}, Gabriele Nagel^{aq,ar}, Bente Oftedal^{as}, Göran Pershagen^{at,au}, Raphael Simon Peter^{av}, Annette Peters^{aw,ax}, Matteo Renzi^{ay}, Debora Rizzuto^{az,ba}, Sophia Rodopoulou^{bb}, Evangelia Samoli^{bc}, Per Everhard Schwarze^{bd}, Torben Sigsgaard^{be}, Mette Kildevæld Simonsen^{bf}, Massimo Stafoggia^{bg}, Maciek Strak^{bh,bi}, Danielle Vienneau^{bj}, Gudrun Weinmayr^{bk}, Kathrin Wolf^{bl}, Ole Raaschou-Nielsen^{bm,1}, Daniela Fecht^{bn,1}



Long-term ambient PM2.5 exposure is associated with lung cancer incidence even at concentrations below current EU limit values and possibly WHO Air Quality Guidelines.



Lung adenocarcinoma promotion by air pollutants

<https://doi.org/10.1038/s41586-023-05874-3>

Received: 17 June 2022

Accepted: 21 February 2023

Published online: 5 April 2023

Check for updates

William Hill^{1,2,6}, Emilia L. Lim^{1,2,26,27}, Clare E. Weeden^{1,2,6}, Claudia Lee^{1,2,3}, Marcellus Augustine^{1,2,3,4}, Kezhong Chen^{2,5}, Feng-Che Kuan^{6,7}, Fabio Marongiu^{8,9}, Edward J. Evans Jr⁸, David A. Moore^{1,2,10}, Felipe S. Rodrigues¹¹, Oriol Pich¹, Bjorn Bakker¹, Hongui Cha¹², Renelle Myers¹³, Febe van Maldegem^{14,15}, Jesse Boumelha¹⁴, Selvaraju Veeriah², Andrew Rowan¹, Cristina Naceur-Lombardelli², Takahiro Karasaki^{1,2,16}, Monica Sivakumar², Swapnanil De², Deborah R. Caswell¹, Ai Nagano^{1,2}, James R. M. Black^{2,17}, Carlos Martínez-Ruiz^{2,17}, Min Hyung Ryu¹⁸, Ryan D. Huff¹⁸, Shijia Li¹⁸, Marie-Julie Favé¹⁹, Alastair Magness^{1,2}, Alejandro Suárez-Bonnet^{20,21}, Simon L. Priestnall^{20,21}, Margreet Lüchtenborg^{22,23}, Katrina Lavelle²², Joanna Pethick²², Steven Hardy²², Fiona E. McDonald²², Meng-Hung Lin²⁴, Clara I. Troccoli^{8,25}, Moumita Ghosh²⁶, York E. Miller^{26,27}, Daniel T. Merrick²⁸, Robert L. Keith^{28,27}, Maise Al Bakir^{1,2}, Chris Bailey¹, Mark S. Hill¹, Lao H. Saa^{29,30}, Yilun Chen^{29,30}, Anthony M. George^{29,30}, Christopher Abbosh², Nnennaya Kanu², Se-Hoon Lee³¹, Nicholas McGranahan^{2,17}, Christine D. Berg³¹, Peter Sasieni³², Richard Houlston³³, Clare Turnbull³³, Stephen Lam³³, Philip Awadalla¹⁹, Eva Grönroos¹, Julian Downward¹⁴, Tyler Jacks^{34,35}, Christopher Carlsen¹⁸, Ilaria Malanchi¹¹, Allan Hackshaw³⁶, Kevin Litchfield^{2,4}, TRACERx Consortium¹, James DeGregori^{3,17}, Mariam Jamal-Hanjani^{1,16,21,127} & Charles Swanton^{1,2,3,27}



Michelle C. Turner / WCLC23

ARTICLE IN PRESS



REVIEW ARTICLE

Air Pollution and Lung Cancer: A Review by International Association for the Study of Lung Cancer Early Detection and Screening Committee

Christine D. Berg, MD,^{a,*} Joan H. Schiller, MD,^b Paolo Boffetta, MD, MPH,^c Jing Cai, MD,^d Casey Connolly, MPH,^e Anna Kerpel-Fronius, MD, PhD,^f Andrea Borondy Kitts, MS, MPH,^g David C. L. Lam, MD, PhD,^h Anant Mohan, MD, PhD,ⁱ Renelle Myers, MD, FRCPC,^j Tejas Suri, MD,^k Martin C. Tammemagi, PhD,^l Dawei Yang, MD,^m Stephen Lam, MD, FRCPC,ⁿ On behalf of the International Association for the Study of Lung Cancer (IASLC) Early Detection and Screening Committee

UK Biobank –Prospective Cohort Study

- 473,067 eligible participants
- Recruitment 2006 –2010 / Follow-up until 2021
- Self-reported regular medication use (baseline)
- Opioids defined based on WHO ATC codes:
- Analgesic opioids: N02A
- Other opioids: A07DA, N07BC, R05DA, R05FA
- Addressed confounding from comorbidities by adjusting the analysis for a propensity score for opioid-related comorbidities



Group 1
Carcinogenic to humans

There is *sufficient evidence* in humans for carcinogenicity in the:

larynx

lung

**urinary
 bladder**

There is *limited evidence* in humans for carcinogenicity in the:

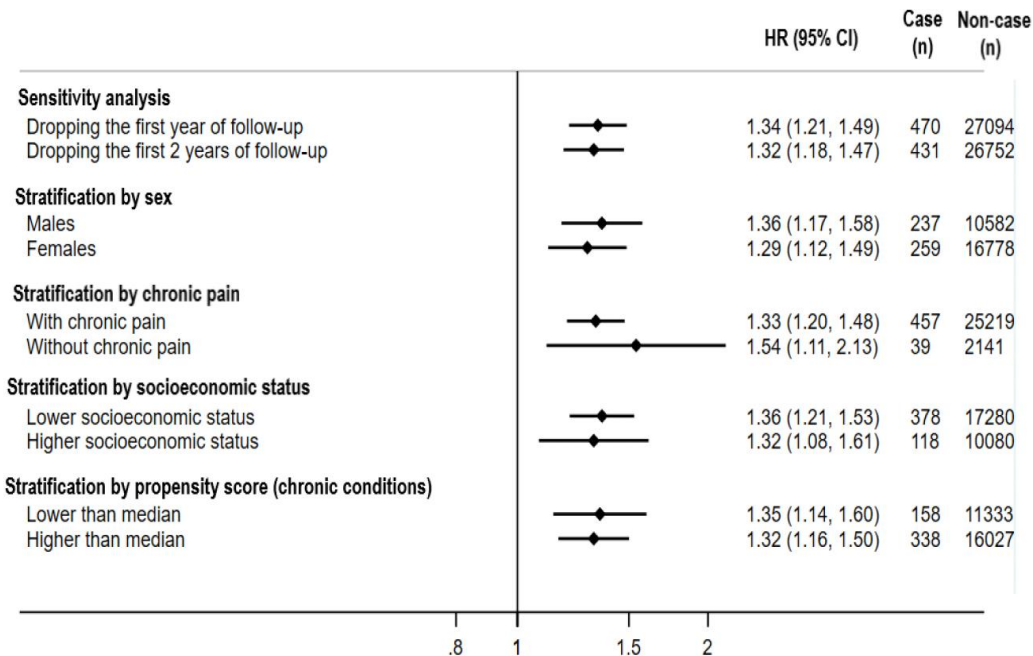
oesophagus

stomach

pancreas

pharynx

Mahdi Sheikh/ WCLC23



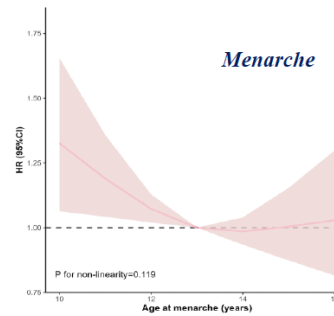
29,266 cases /
 56,450 controls
 • MR Odds Ratio =
1.16 (1.05 –1.28)

Los perfiles de subtipos estrogénicos son diferentes en las mujeres con NSCLC con EGFR mut+ en comparación con las mujeres sin cáncer:

- Mujeres con NSCLC EGFR mut+ muestran niveles E1 y E2 más bajos
- Mujeres con NSCLC EGFR mut+ muestran niveles más elevados de 4-OHE potencialmente carcinogéno con elevación de la proporción 4-OHE/2-OHE

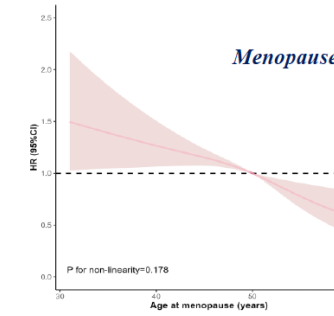
Groups	HR(95%CI)
≤11	1.22 (1.03-1.46)
12	1.07 (0.89-1.29)
13	Ref.
14	0.96 (0.80-1.16)
≥15	1.03 (0.86-1.24)

P trend = 0.088



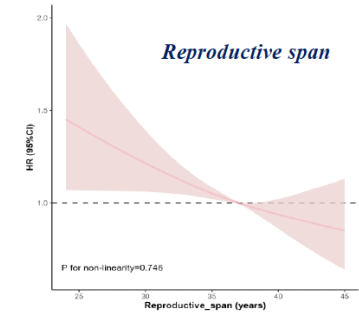
Groups	HR(95%CI)
≤46	1.49 (1.19-1.86)
47-49	1.42 (1.11-1.81)
50-52	Ref.
53-54	1.19 (0.91-1.57)
≥55	0.84 (0.63-1.10)

P trend < 0.001



Groups	HR(95%CI)
≤32	1.42 (1.18-1.71)
33-35	1.24 (1.00-1.53)
36-39	Ref.
40-42	1.01 (0.81-1.25)
≥43	0.84 (0.73-1.24)

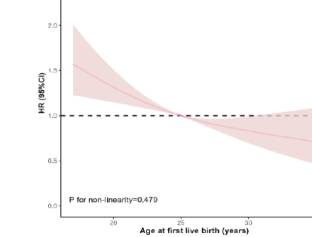
P trend < 0.001



Parity-related factors

- Number of children,
- Number of miscarriage,
- Number of stillbirths,
- Number of abortion

Age at first live birth



Linear relationships using RCS

Groups	HR(95%CI)
≤20	1.63 (1.33-2.01)
21-25	1.31 (1.09-1.58)
26-30	Ref.
31-35	0.89 (0.63-1.26)
≥36	1.03 (0.53-2.01)

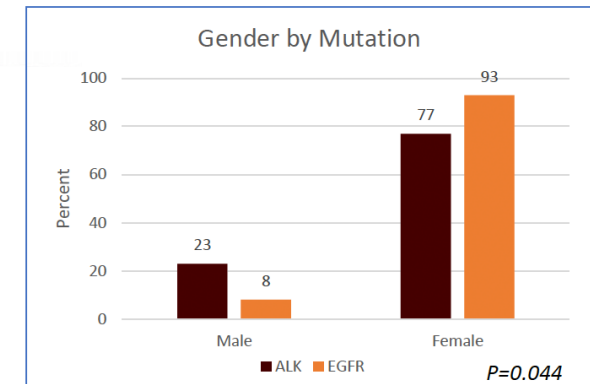
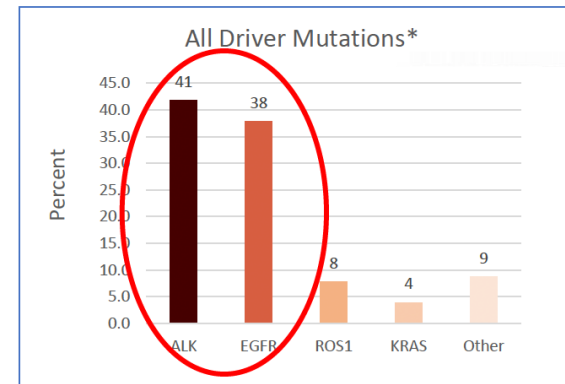
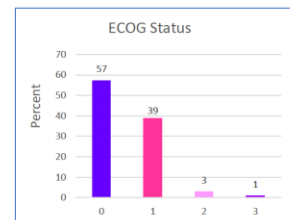
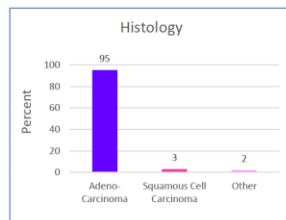
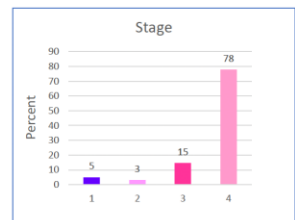
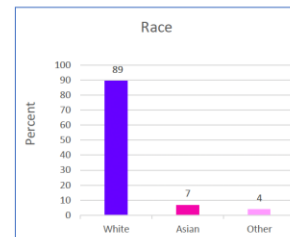
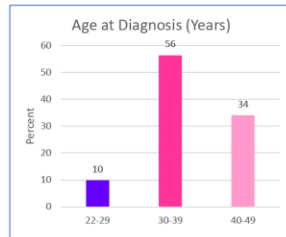
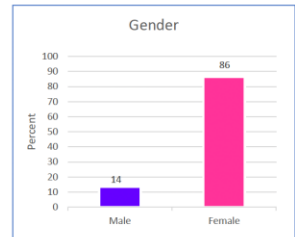
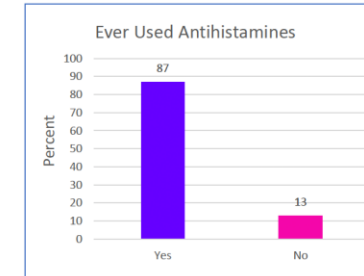
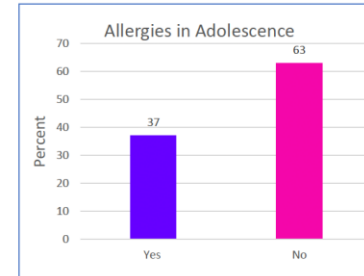
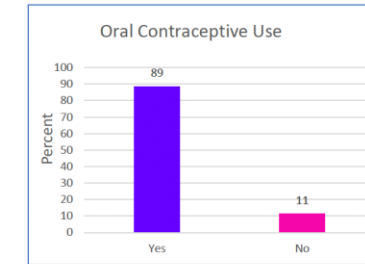
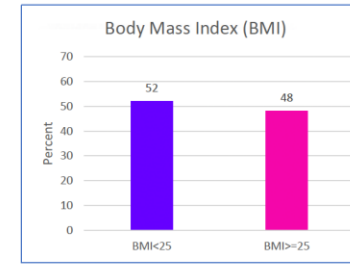
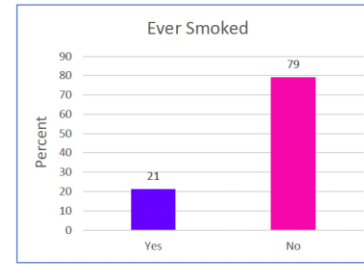
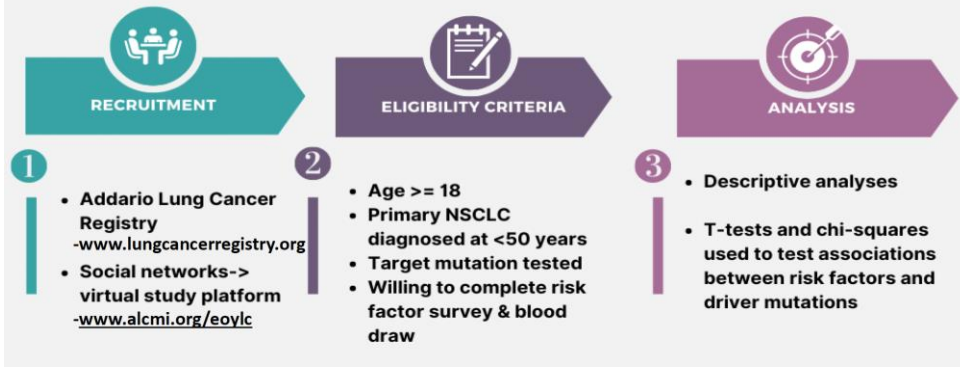
P trend < 0.001

Hormone dysfunction

- Oophorectomy (HR 1.25, 95%CI 1.04-1.49)
- Hysterectomy, HRT, OCP, HRT duration

Epidemiologia/5

Epidemiology of YLC (EoYLC) Study Methodology



* Focus on ALK and EGFR due to larger sample size; $n=43$ and 39 , respectively. 'Other' includes MET, RET, p53, HER2, EBBRP

Baja exposición tabáquica. IMC normal. Prevalencia de alergias, antihistamínicos y AOs
 EGFR/ALK: tabaquismo, bajo IMC, sexo femenino, reducido uso AOs y antihistamínicos

Epidemiologia / 6

115 p Adenocarcinomas resecados
 Examen patológico, IHQ PD-L1, NGS Oncomine
 Comparativa: Fumadores (93) vs No-fumadores (22)
No diferencias en Estadio Patológico
Grado: G3 (pobr. dif.): 56% vs 32%

	Total (n=115) n (%)	Smoker (n=93) n (%)	Non-Smoker (n=22) n (%)
< 1%	67 (58%)	49 (53%)	18 (82%)
1-49%	26 (23%)	22 (24%)	4 (18%)
>= 50%	22 (19%)	22 (24%)	0

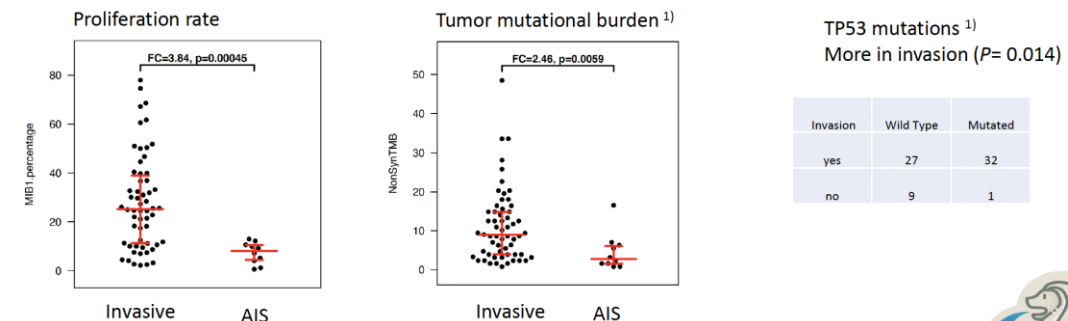
	Total (n=115)	Smoker (n=93)	Non-Smoker (n=22)
Alteration, n (%) Mean/Median Range	3.1/3 0-8	3.5/3 0-8	1.8/2 0-3
Mutation, n (%)			
<i>KRAS/G12C</i>	56 (49%)/19 (17%)	53 (57%)/18 (19%)	3 (14%)/1 (5%)
<i>EGFR</i>	17 (15%)	6 (6%)	11 (50%)
<i>MET</i>	1 (1%)	0	1 (5%)
<i>BRAF/V600E</i>	9 (8%)/5 (4%)	8 (9%)/4 (4%)	1 (5%)/1 (5%)

Guoping. Cai / WCLC23

- AIS: regular pattern (H&E, CK7), monolayer tumor cells on alveolar wall (elastin); growth pattern respects borders of secondary lobule, vessels, bronchi
- Recognition of tangential cutting (DD with micropapillary)
- Minimum criteria for alveolar filling growth pattern: consistent in 3 alveoli
- Grey zone = similar to extensive epithelial proliferation (EEP¹⁾)
- Biological collapse; increase elastin (Noguchi type B²⁾) = non-invasive
- STAS not used (=dissociation characteristic of malignant cells)
- MIA not used

IASLC  Conclusions

- The modified classification (“uncertain competent”) has an essentially higher reproducibility than WHO classification.
- Awareness of morphologic consequences of iatrogenic collapse and more training in modified classification will probably further improve reproducibility.
- Prevalence of AIS in small pulmonary adenocarcinomas with modified classification: 14% (10/70), which are overdiagnosed in WHO classification as invasive adenocarcinoma. These AIS patients have 100% 5 years recurrence free survival.
- Orthogonal biomarker supports the modified classification²⁾



Erik Thunnissen / WCLC23

En 2022, Taiwan HPA propuso un programa nacional para la detección precoz mediante LDCT
Valoración coste-efectividad por el Center for Drug Evaluation: ICER of US\$25,945/LY, comparing to Taiwan's 2022 per capita GDP of US\$32,811.

Lanzamiento del programa el 1 Julio 2022.

■ Eligible populations:

- **Heavy smokers: 50 to 74** yrs old, > 30 pack-yrs, currently smoke or have quitted smoking <15 yrs.
- **Individuals with a family history of lung cancer: male** aged 50 to 74 yrs, and **female** aged 45 to 74 yrs.

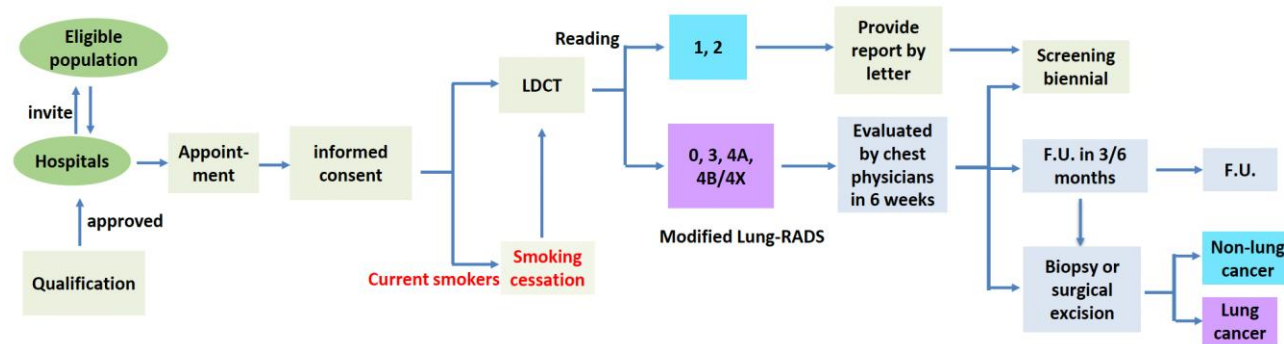
■ Qualification for hospitals: A total of 167 hospitals across all cities/counties participated.

- Staffed with medical professionals: radiologists, radiographer, thoracic surgeons, case managers.
- Certified as cancer care quality hospitals, or cooperating with cancer care quality hospitals.
- Equipped with 64 slice (or more) CT scanners.

■ Quality indicators:

radiation exposure, positive rate, cancer detection rate, positive predictive value, etc..





Performance of the first year after implementation

■ **49,508 cases screened.**

Unit : number (%)

Gender	Family history	Heavy smokers	Both	Total
Male	8,900 (32.0)	17,248 (61.9)	1,708 (6.1)	27,856 (56.3)
Female	19,717 (91.1)	1,722 (7.9)	213 (1.0)	21,652 (43.7)
Total	28,617 (57.8)	18,970 (38.3)	1,921 (3.9)	49,508 (100)

■ **531 lung cancers detected (1.1%), 85.1% stage 0-1**

Unit : number (%)

Gender	Risk factors				Stages of lung cancer				
	Family history	Heavy smokers	Both	Total	0	I	II	III	IV
Male	87(42.7)	100(49.0)	17(8.3)	204	21(10.3)	137(67.2)	8(3.9)	20(9.8)	18(8.8)
Female	309(94.5)	18(5.5)	0	327	48(14.7)	246(75.1)	11(3.4)	11(3.4)	11(3.4)
Total	396(74.6)	118(22.2)	17(3.2)	531	69(13.0)	383(72.1)	19(3.6)	31(5.9)	29(5.5)

■ 49,508 cases screened.

Unit : number (%)

Gender	Family history	Heavy smokers	Both	Total
Male	8,900 (32.0)	17,248 (61.9)	1,708 (6.1)	27,856 (56.3)
Female	19,717 (91.1)	1,722 (7.9)	213 (1.0)	21,652 (43.7)
Total	28,617 (57.8)	18,970 (38.3)	1,921 (3.9)	49,508 (100)

■ 531 lung cancers detected (1.1%), 85.1% stage 0-1

Unit : number (%)

Gender	Risk factors				Stages of lung cancer				
	Family history	Heavy smokers	Both	Total	0	I	II	III	IV
Male	87(42.7)	100(49.0)	17(8.3)	204	21(10.3)	137(67.2)	8(3.9)	20(9.8)	18(8.8)
Female	309(94.5)	18(5.5)	0	327	48(14.7)	246(75.1)	11(3.4)	11(3.4)	11(3.4)
Total	396(74.6)	118(22.2)	17(3.2)	531	69(13.0)	383(72.1)	19(3.6)	31(5.9)	29(5.5)

- 15,440 lung cancer patients from the TTR dataset of the SLCG were analyzed
- 9,616 excluded for unknown family history of cancer and reported no family history of cancer
- Of the remaining 5,824 patients, 939 had a history of cancer and 4,849 did not; 36 patients had an unknown history of cancer
- Genetic susceptibility to lung cancer was higher in women (58.48%)
- 9.53% of the TTR lung cancer patients had EGFR mutation or ALK translocation or HER2 mutation and had at least one relative with cancer
- Familial lung cancer was associated with an increased risk of lung cancer due to smoking habits
- Genetic susceptibility for lung cancer is higher in females
- Young lung cancer patients (≤ 50 years old) have two or more affected relatives with cancer
- Family history of cancer is a potential risk factor and a predictor of an increased risk of developing lung cancer, especially in those aged less than 50 years
- It is very important to have information on patients diagnosed with lung cancer and family history of cancer

327 (62%) cancers discovered in women of which 95% had Family hx only.

Stage distribution differs between sexes:

Female: 90% stage 0,1

Male: 77% stage 0,1



Virginia Calvo / WCLC23

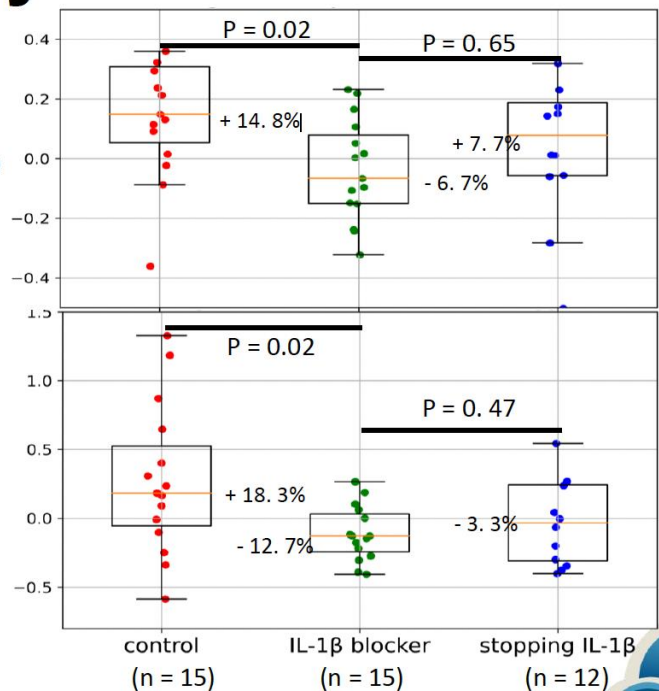
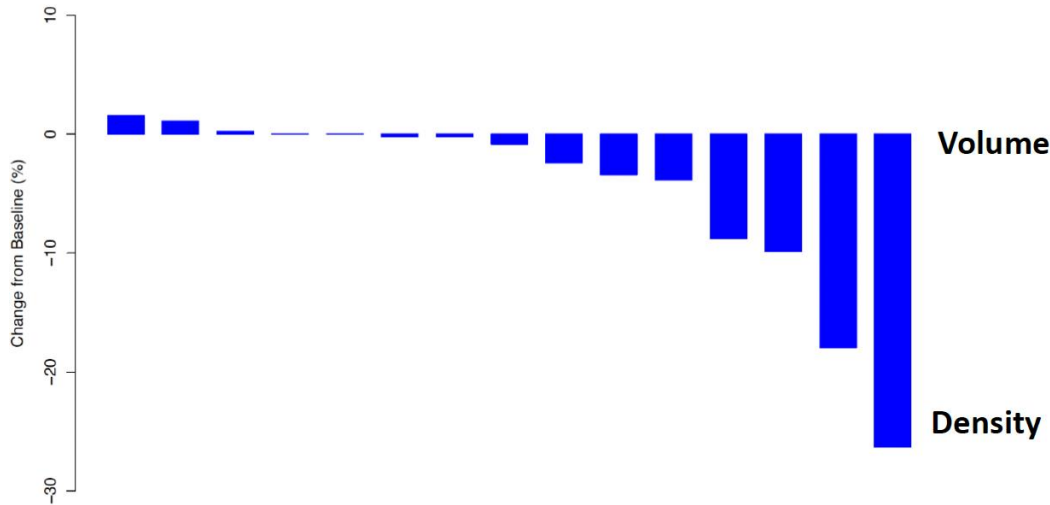
Study Design

N=50
Eligibility:
 -persistent IPNs with estimated cancer probability $\geq 10\%$ if no history of lung cancer
 - Persistent IPNs with estimated cancer probability $>5\%$ if positive for history of state I-IIINSLC

Canakinumab 200mg Q3 weeks for 24 weeks or until progression

Primary Endpoint:
 To determine whether canakinumab increase regression rate of pulmonary nodules at 24 weeks after treatment

CT Chest at 6 weeks, 12 weeks, 24 weeks



Study design

Population: The Lung Cancer Cohort Consortium

- 240,137 people aged 45-80 years with smoking history
- 4 prospective cohorts
EPIC, ATBC, HUNT, CONSTANCES
- 9 European countries
France, Finland, Denmark, Norway,
Germany, Italy, Spain, Sweden, The Netherlands.

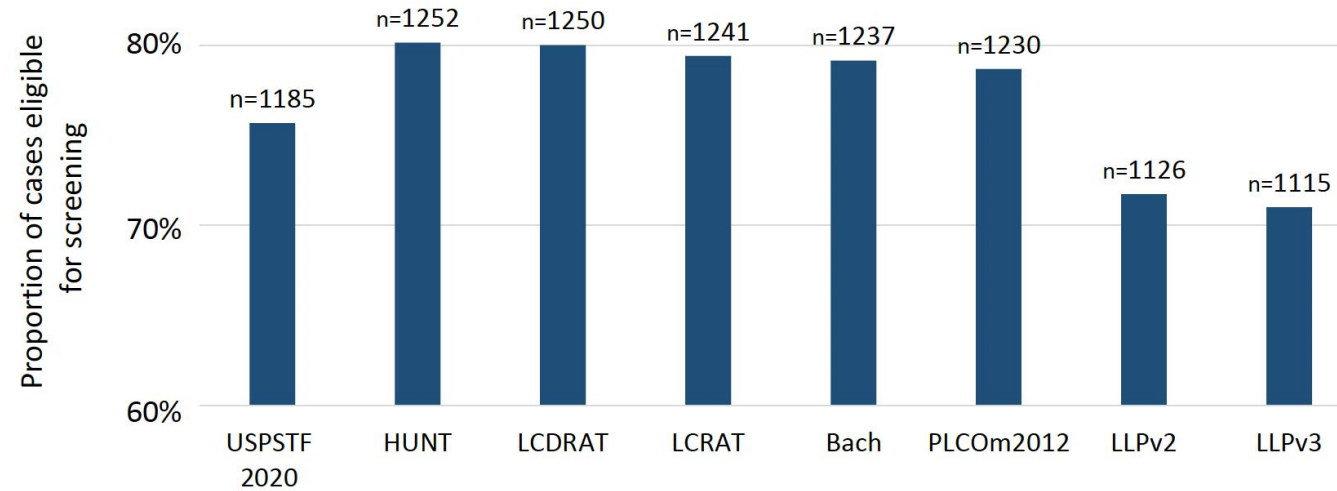
7 lung cancer risk models

- 4 US-based models: Bach, PLCOm2012, LCRAT, and LCDRAT
- 3 European models: LLPv2, LLPv3, and HUNT model

Model evaluation

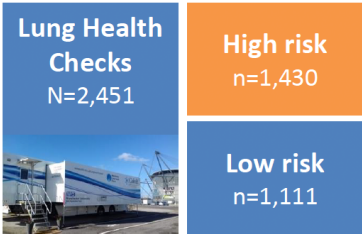
- Calibration: Ratio of expected to observed cases (E/O)
- Discrimination: Area under the ROC curve (AUC)

3. Identifying future lung cancer cases



Results based on thresholds for each model that selected a population of equal size to USPSTF-2020, which selected 34% of ever-smokers aged 45-80.

Cribado/6



CT screening 105 cancers (7.3%)
— $PLCO_{m2012} \geq 1.51\%$ —
No screening 10 cancers (0.9%)

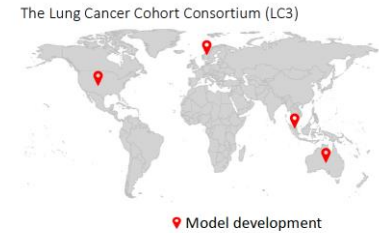
91% of cancers arose in high risk group
83% screen-detected

Sensitivity	91%
Specificity	45%
PPV	7.3%
NPV	99.1%

Case-cohort design
807 cases and 1144 sub-cohort representatives from 7 cohorts

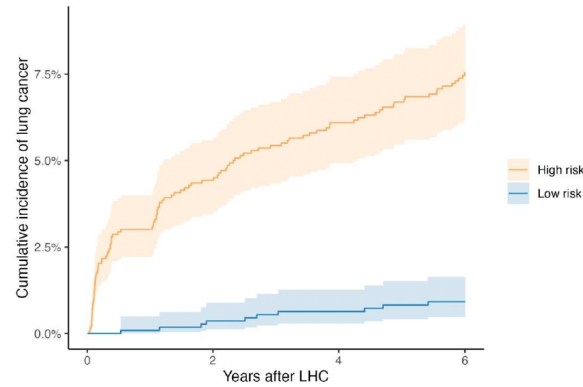
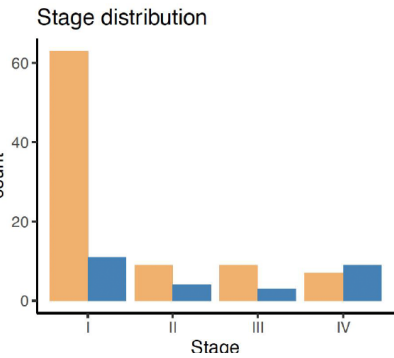
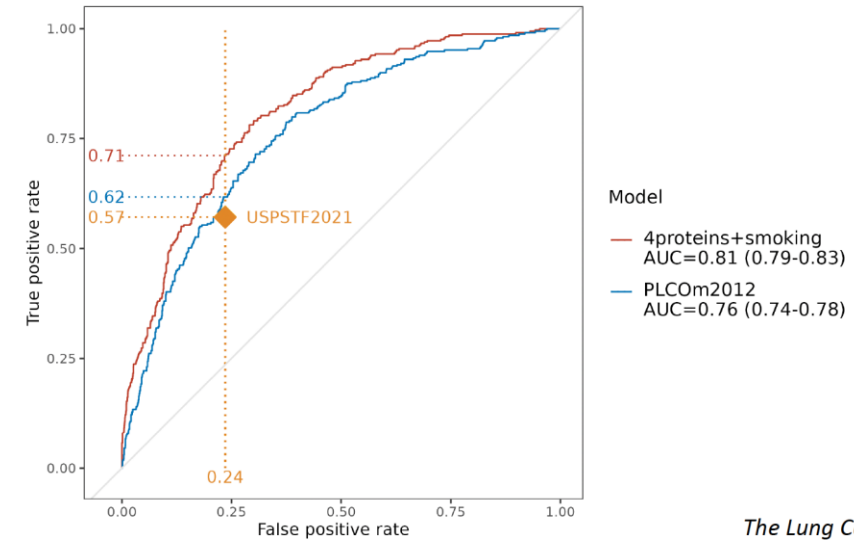
21 proteins assayed
Absolute quantification (Olink)

Pre-diagnostic blood
Collected up to 3y prior to diagnosis



Preliminary model
- Fit in 4 cohorts
- Tested in 3 cohorts

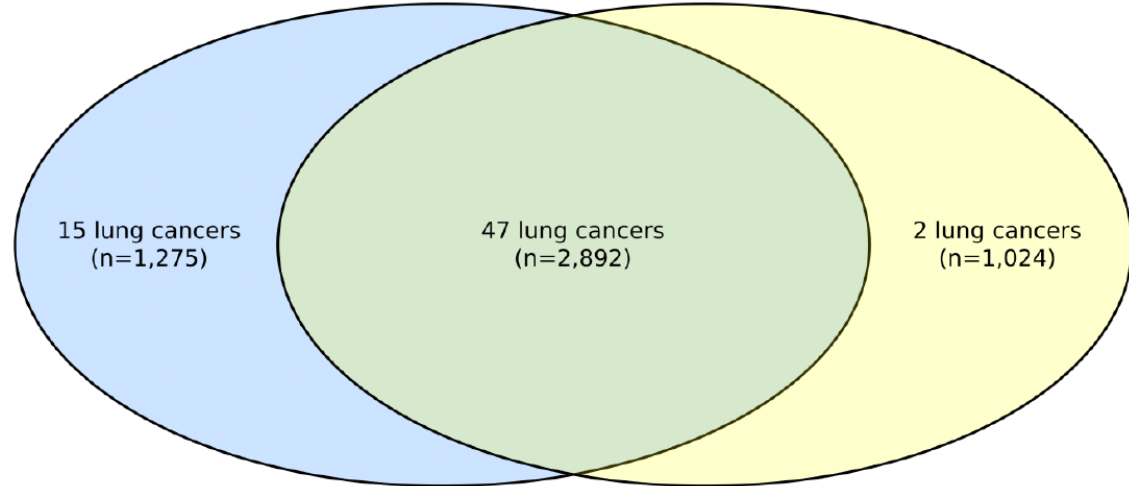
- 4 selected proteins: MMP12, CEACAM5, SCF, LPL
- Age, smoking intensity, smoking duration



Model	Prediction horizon	Expected n (%)	Observed n (%)
$PLCO_{m2012}$	6y	78 (3.1%)	115 (4.5%)
LLPv2	5y	119 (4.7%)	103 (4.1%)
LLPv3	5y	49 (1.9%)	103 (4.1%)
LCRAT	5y	72 (2.8%)	103 (4.1%)

62 lung cancers detected in 4,167 participants in the PLCOM2012 $\geq 1.58\%$ at 6 years group

49 lung cancers detected in 3,916 participants in the NELSON criteria group

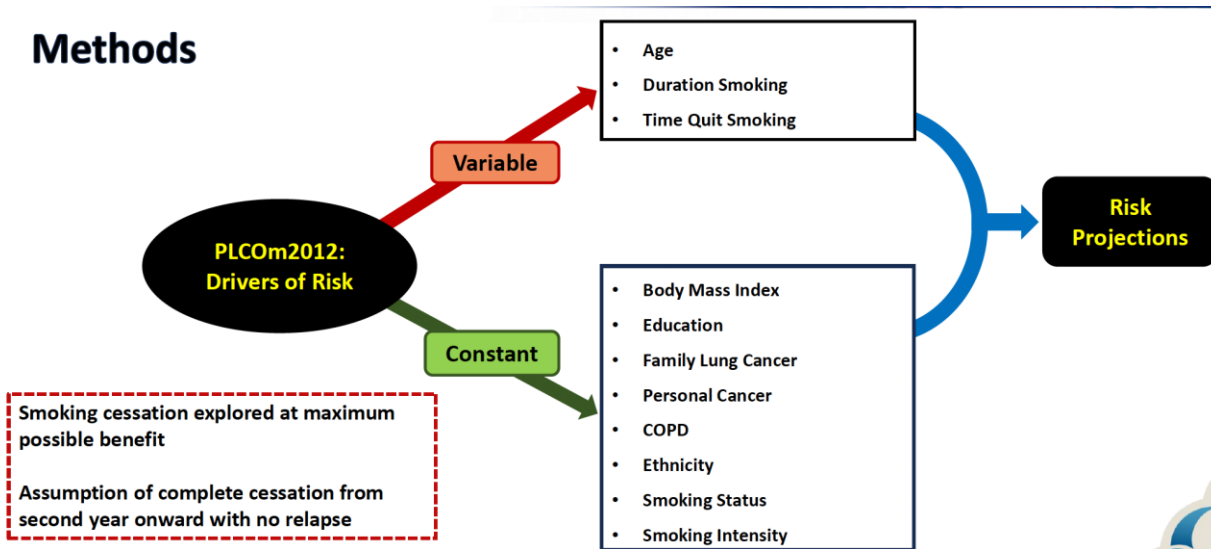


64 lung cancers detected in 5,191 participants who were in the PLCOM2012 $\geq 1.58\%$ at 6 years group, in the NELSON criteria group, or both

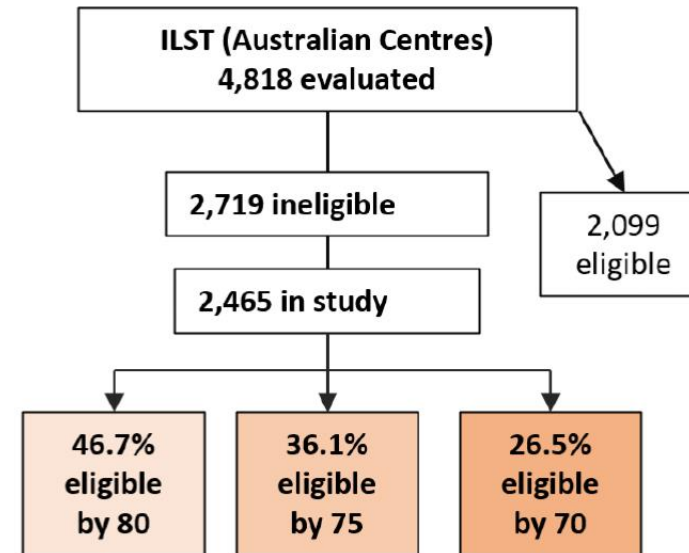
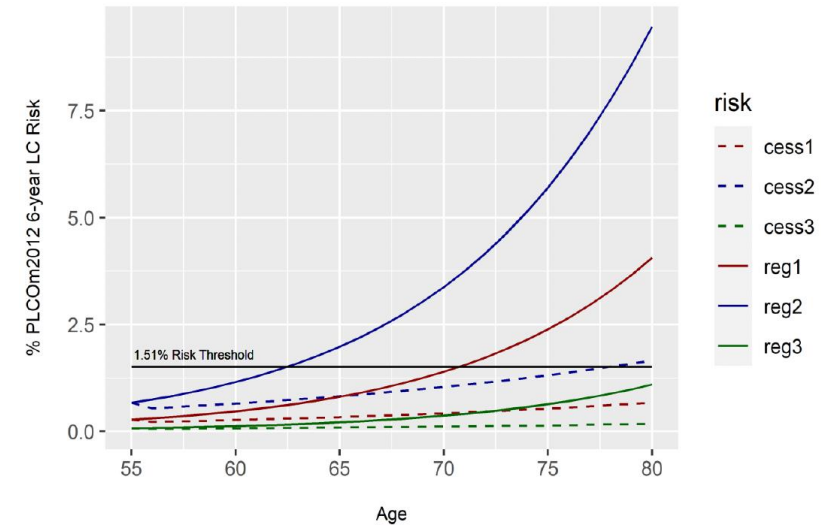
	NELSON-selected (n=3.916)	PLCOM2012-selected (n=4.167)	p value
Cancer detection rate	49/64 (76.6%)	62/64 (96.9%)	0.0036
Positive predictive value	49/3916 (1.25%)	62/4167 (1.49%)	0.02 (relative difference 19.2%)
False-negative proportion	15/1275 (1.18%)	2/1024 (0.20%)	
Negative predictive value	98,8%	99,8%	0.006



Methods



Projections of PLCOm2012 Lung Cancer Risk



- ▶ To evaluate the impact of a **new** proposed guideline that uses a 20-year smoking duration cutoff instead of a 20-pack-year cutoff as a selection criterion for lung cancer screening

2021 USPSTF Lung Cancer Screening Guidelines

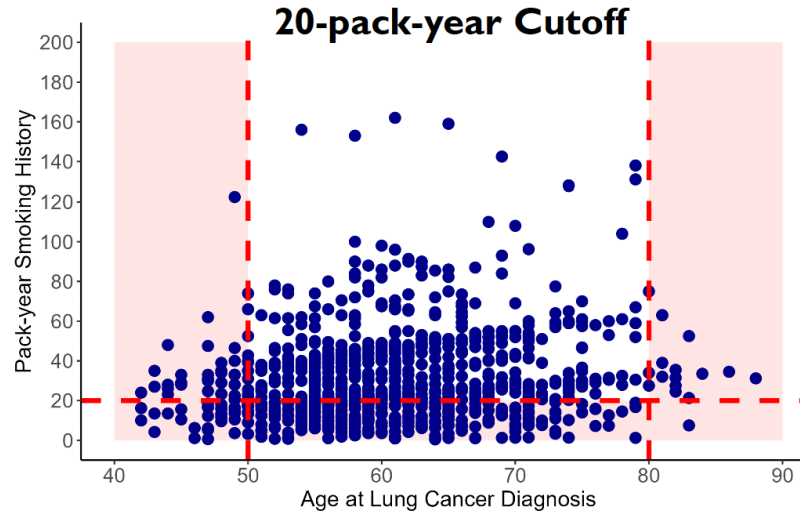
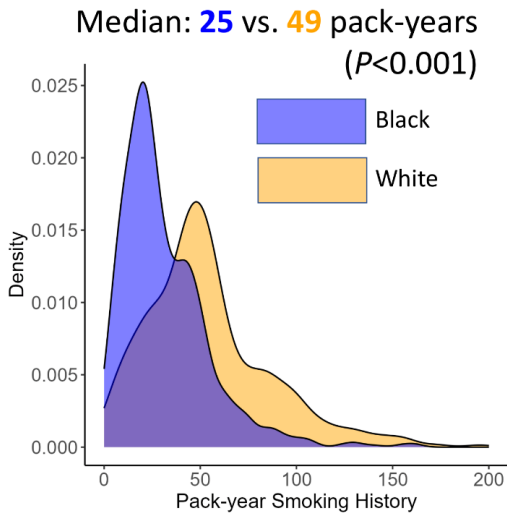
- 1) Aged 50-80, and
- 2) Have a ≥ 20 pack-year smoking history, and
- 3) Currently smoke or have quit within the past 15 years

vs

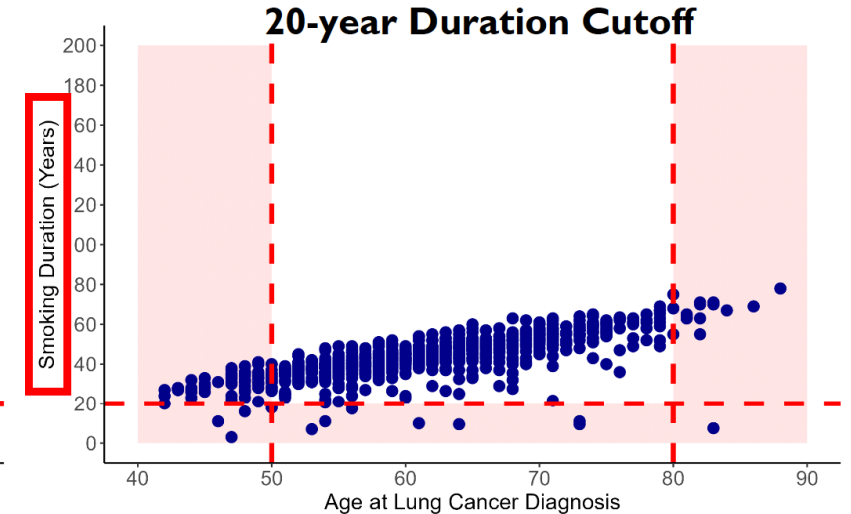
Proposed Duration Guideline

- 1) Aged 50-80, and
- 2) Have a ≥ 20 year smoking duration, and
- 3) Currently smoke or have quit within the past 15 years

Pack-year Smoking History



61.8% of Black Lung Cancer Patients Who Currently Smoked Would Have Qualified



92.0% of Black Lung Cancer Patients Who Currently Smoked Would Have Qualified

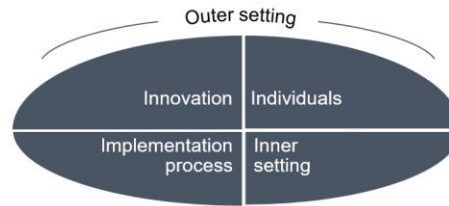
Current qualitative analysis



28 interviews (N=30) with national expert participants in 2022: practitioners, researchers, policymakers

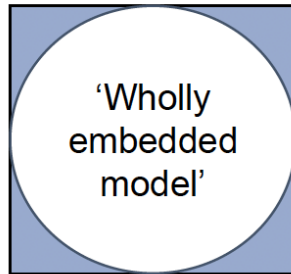


Inductive framework analysis of transcripts (collaborative coding with researchers and patient advocates)



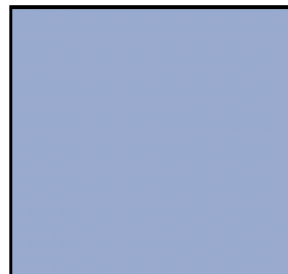
Mapped against the Consolidated Framework for Implementation Research³

Support for delivery models



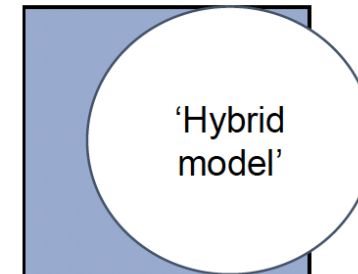
Preference of $n=5$ (17%):

- resource-intensive
 - lower feasibility.
- Partially embedded/ telehealth also suggested*



No outright support:

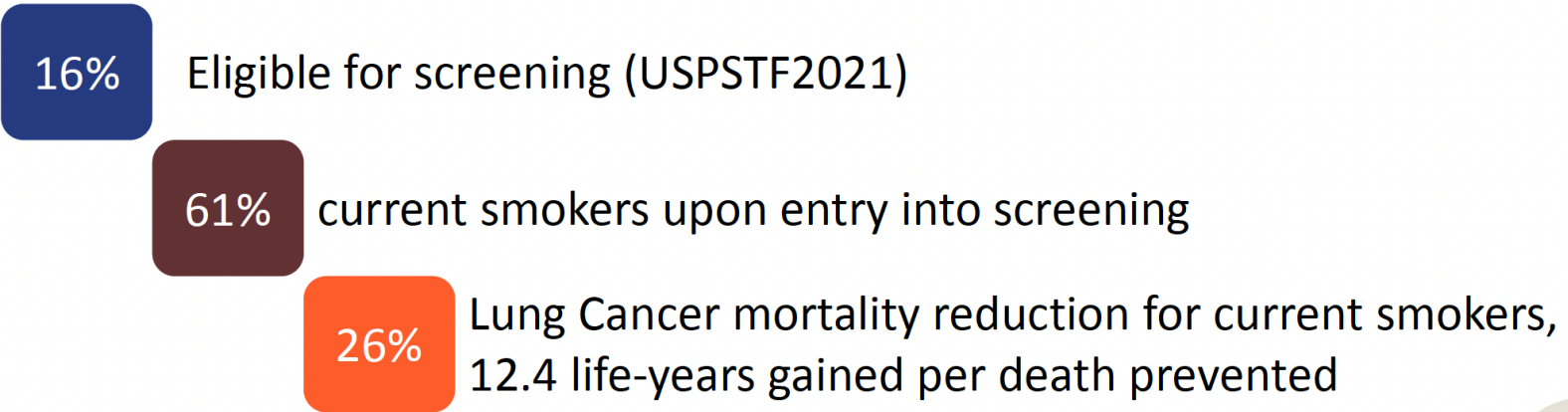
- insufficient to engage participants for uptake
- other models required



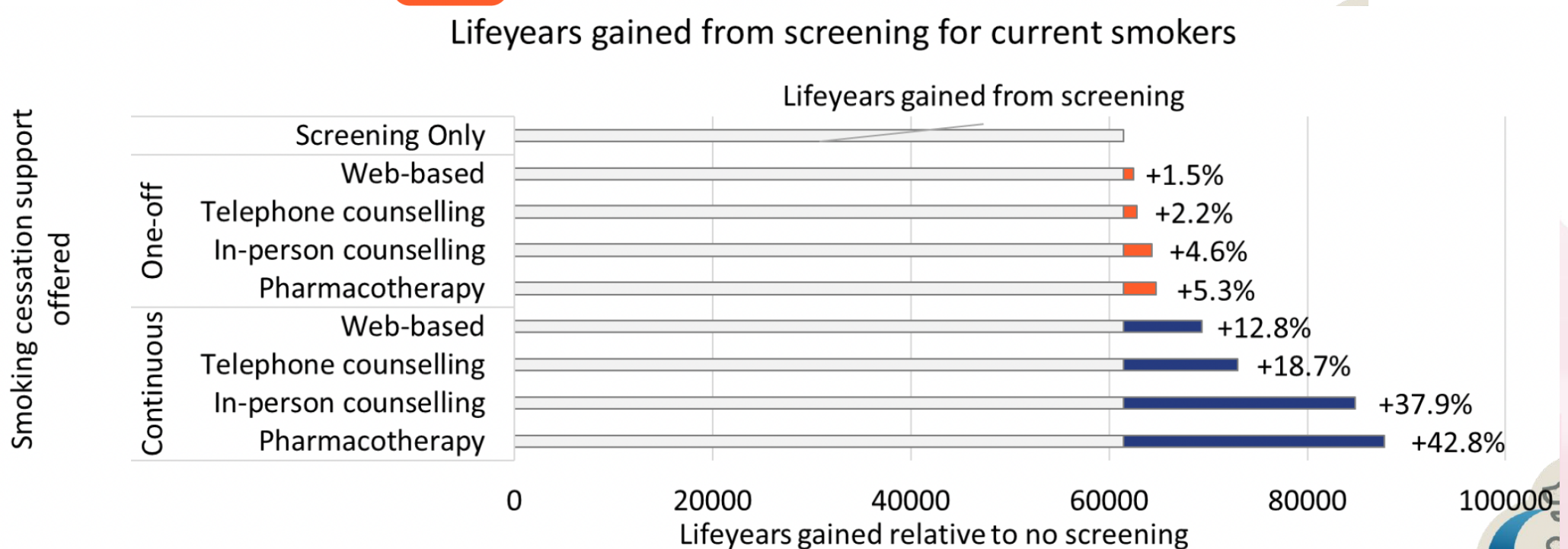
Preference of $n=17$ (57%), to maximise:

- cost-effectiveness
- extent of cessation supports that could be offered

Effectiveness of screening overall (without cessation support):



Lifeyears gained from screening for current smokers



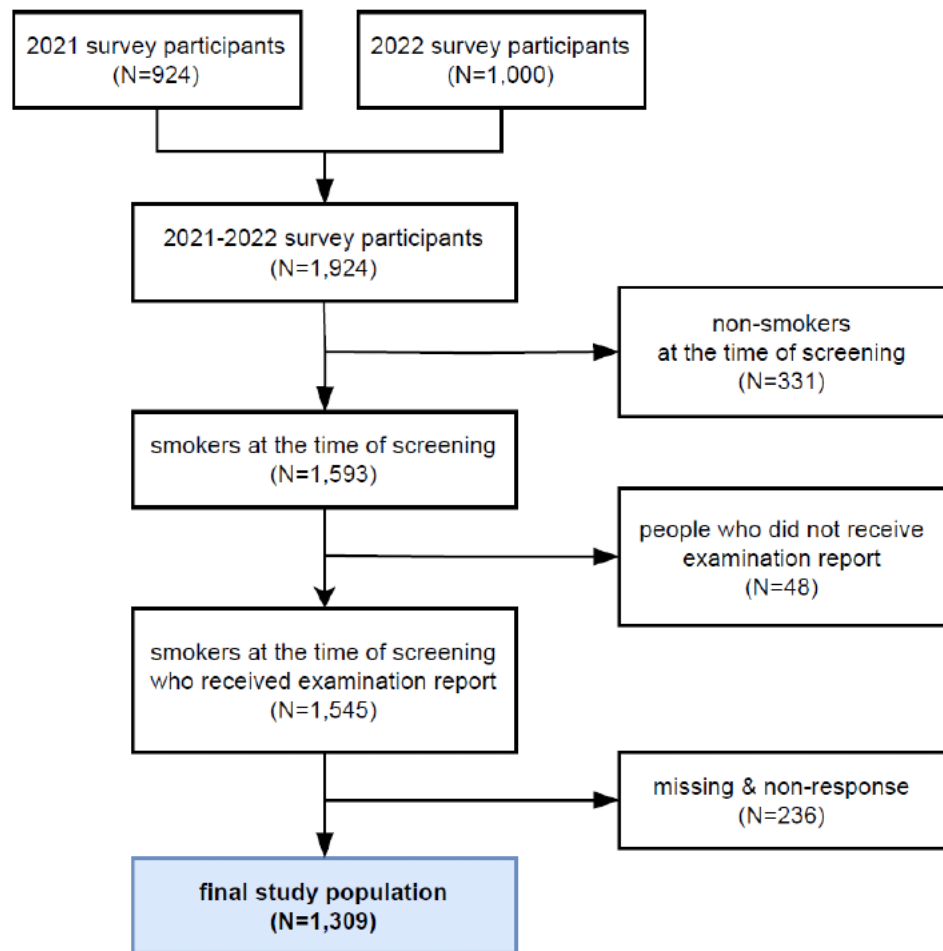
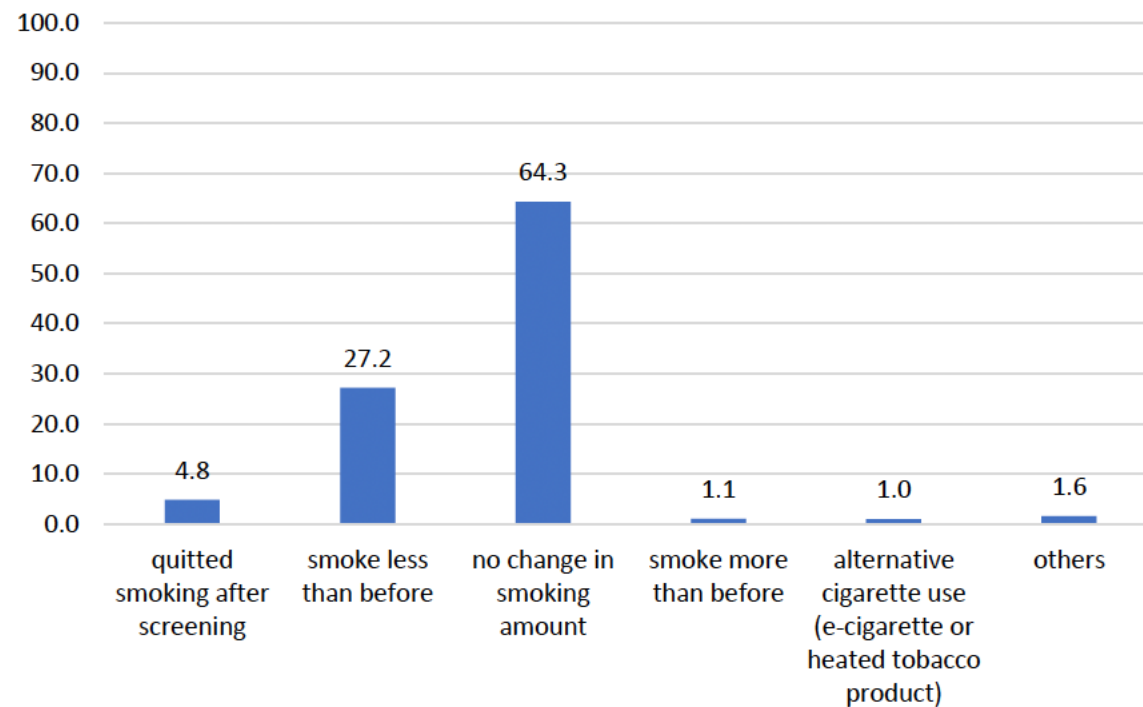
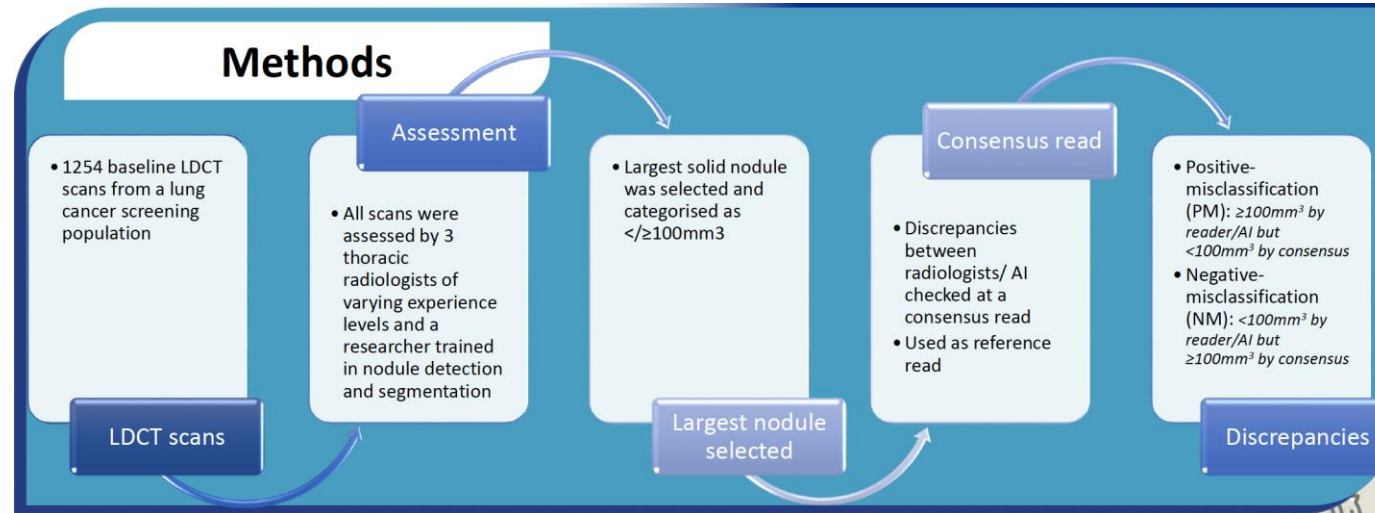


Figure 2. Change in smoking status after lung cancer screening (unit: %)





Results

Consensus: 817 (65%) $< 100\text{mm}^3$, 437 (35%) $\geq 100\text{mm}^3$


	Reader 1	Reader 2	Reader 3	Reader 4	AI
Correct Positives (CP)	232 (19%)	238 (19%)	202 (16%)	218 (17%)	370 (30%)
Correct Negatives (CN)	768 (61%)	809 (65%)	814 (65%)	803 (64%)	758 (60%)
Positive Misclassifications (PM)	49 (4%)	8 (1%)	3 (0.2%)	14 (1%)	59 (5%)
Negative Misclassifications (NM)	205 (16%)	199 (16%)	235 (19%)	219 (17%)	67 (5%)
Total discrepancies	254 (20%)	207 (17%)	238 (19%)	233 (19%)	126 (10%)
Negative predictive value (95% CI)	79,7 (77.4-82.0)	80,3 (81.3-85.5)	77,6 (76.1-79.1)	78,6 (77.0-80.1)	91,9 (90.1-93.4)





- **Inclusion criteria:** aged 60-79 y, $PLCO_{2012} \geq 2.6\%$ or ≥ 35 pack-years; current smoker or < 10 years since cessation.
- **Image acquisition:** first 380 participants were included and screened with one single low dose chest scan on third generation dual-source CT.
- **Image analysis:** scans were evaluated for presence of lung nodules $\geq 30 \text{ mm}^3$ and categorized based on volume and type.

Clinical management

1. **Negative:** next screening round
2. **Indeterminate:** 3-months follow-up scan
3. **Positive:** referral to specialist.

 **1st read:** experienced radiologists as a first independent read.

 **2nd read:** AI based Lung Screen Software (AVIEW, Coreline Soft, Seoul)

 **3rd read:** For participants with a discrepancy in categorization between first and second read, a third unblinded arbitration read was performed by a panel

Agreement for nodule categorization:

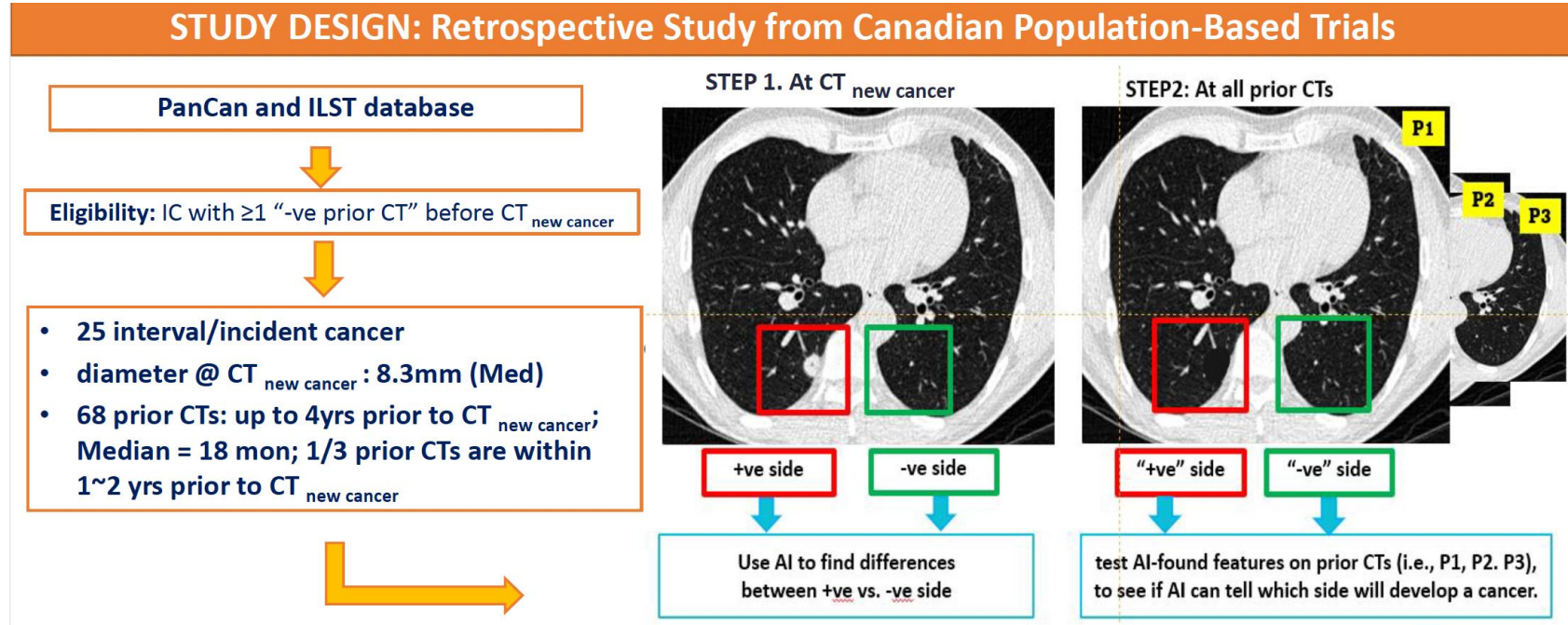
- 78.7% between first and second read.

Arbitration cases (n=81):

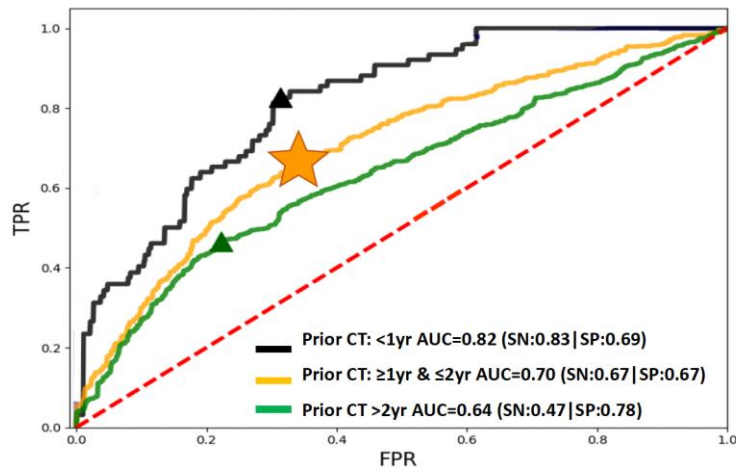
- 45% were classified to the same category as determined by the first radiologist read.
- 34% were classified to the same category as determined by the AI read.
- 21% was classified to another category than the category assigned by either the radiologist or AI.

Final categorization:

- Negative - 72.1%
- Indeterminate - 23.4%
- Positive - 4.5%



AI Model Performance

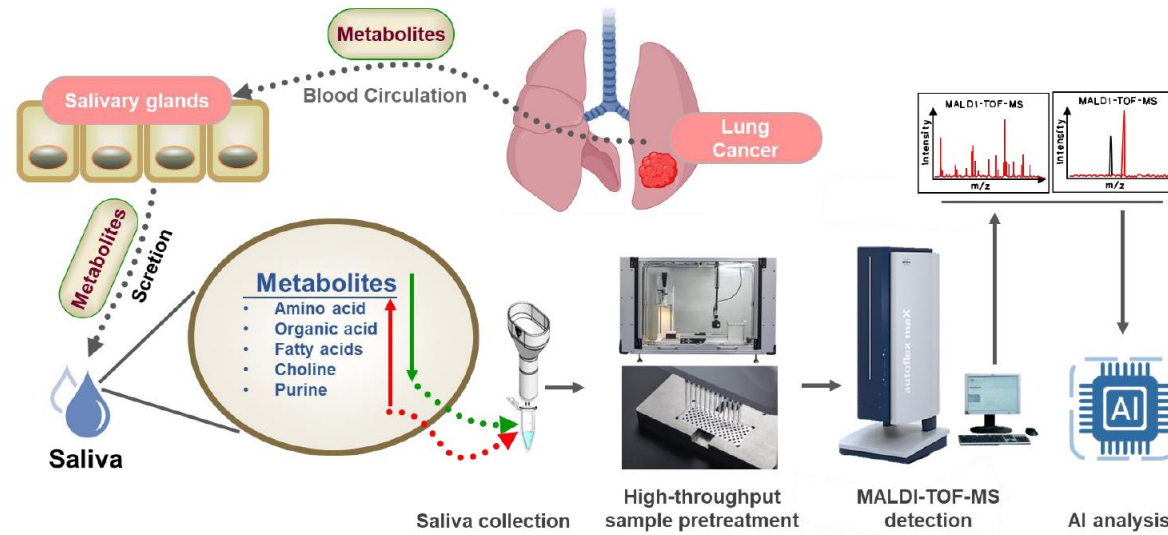


Los modelos desarrollados por la IA ofrecen un potencial para predecir el desarrollo futuro de cáncer pulmón en una imagen de CT pulmonar “normal” y podrían ser utilizados para personalizar los intervalos del cribado

Frequency of Molecular Alterations Based on USPSTF 2021 Screening Eligibility

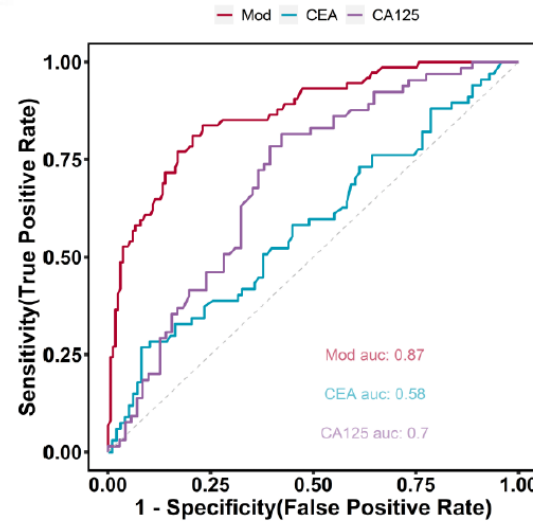
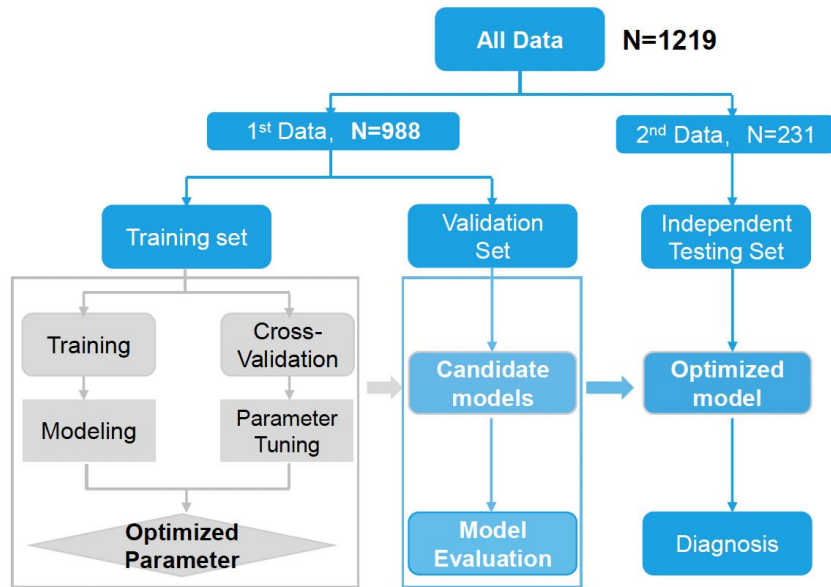
Molecular Alteration	Eligible (N=213)	Ineligible (N=367)	P ^a
Driver Alterations, N (%)	112 (52.6)	252 (68.7)	<0.001
<i>EGFR</i>	13 (6.1)	74 (20.2)	<0.001
<i>ALK</i>	1 (0.5)	5 (1.4)	0.549
<i>ROS1</i>	0 (0.0)	3 (0.8)	0.470
<i>RET</i>	1 (0.5)	4 (1.1)	0.754
<i>BRAF</i>	15 (7.0)	18 (4.9)	0.376
<i>ERBB2</i>	1 (0.5)	9 (2.5)	0.151
<i>KRAS</i>	81 (38.0)	130 (35.4)	0.590
<i>MET</i> ex14	3 (1.4)	13 (3.5)	0.211
Tumor Suppressor Genes, N (%)	145 (68.1)	189 (51.5)	<0.001
<i>TP53</i>	128 (60.1)	158 (43.1)	<0.001
<i>STK11</i>	26 (12.2)	39 (10.6)	0.656
<i>KEAP1</i>	13 (6.1)	13 (3.5)	0.219

^aP value was calculated using Fisher's exact test.



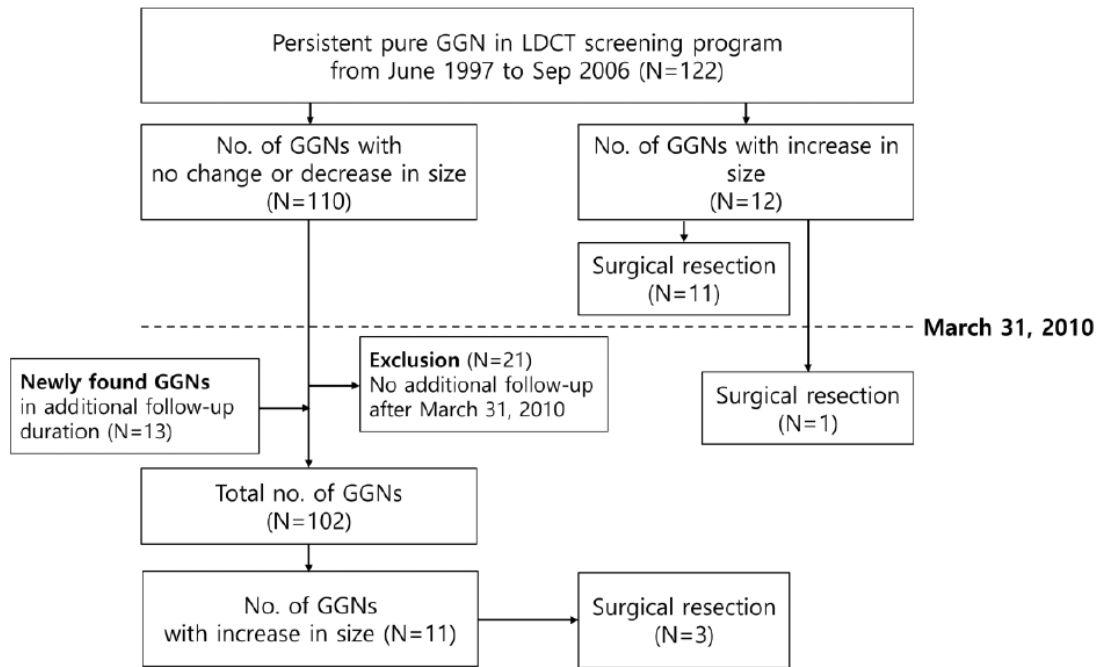
80% Est I

High-throughput MS platform for salivary metabolic profiling and lung cancer detection



✓ Validation Set
Sen. 77%, Spec. 83%, AUC=0.87

✓ Testing Set
Sen. 78%, Spec. 75%, AUC=0.81



- After the initial publication, **102 pGGNs in 71 patients** were further followed up for a median duration of **177 months** and the additional growth was detected in **11 nodules**
 - Histologically confirmed as adenocarcinoma by surgery (N=3)
 - Proton therapy and radiation therapy without histological confirmation (N=2)
- Of 122 pGGNs detected at the initial LDCT scan, 23 grew during follow-up
 - 8 (34.8%) grew within 5 years, 12 (52.2%) grew between 5 and 10 years, and **3 (13.0%) grew after 10 years**
- **Of 76 pGGNs which were stable for 10 years, three (3.9%) increased in size after 10 years**



