Iniciativa científica de:

GECP lung cancer research

Lung Cancer UPDATES

ASCO HIGHLIGHTS

29 MAYO - 02 JUNIO 2026

Chicago, USA

#ASCOUPDATES

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ASCO HIGHLIGHTS

29 MAYO - 02 JUNIO 2026

Chicago, USA

Epidemiología y cribado

Bartomeu Massuti MD

Hospital Universitario Dr Balmis Alicante - ISABIAL

The science and practice of translation: Improving cancer outcomes worlwide

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Mensajes resumen

La incidencia y mortalidad del cancer de pulmón pueden reducirse mediante la prevención primaria y secundaria

Junto al tabaco existen otros factores ambientales y genéticos que incrementan el riesgo de cancer de pulmón

La eficiencia del cribado podria incrementarse mejorando los criterios de selección e integrando tests analiticos y la IA

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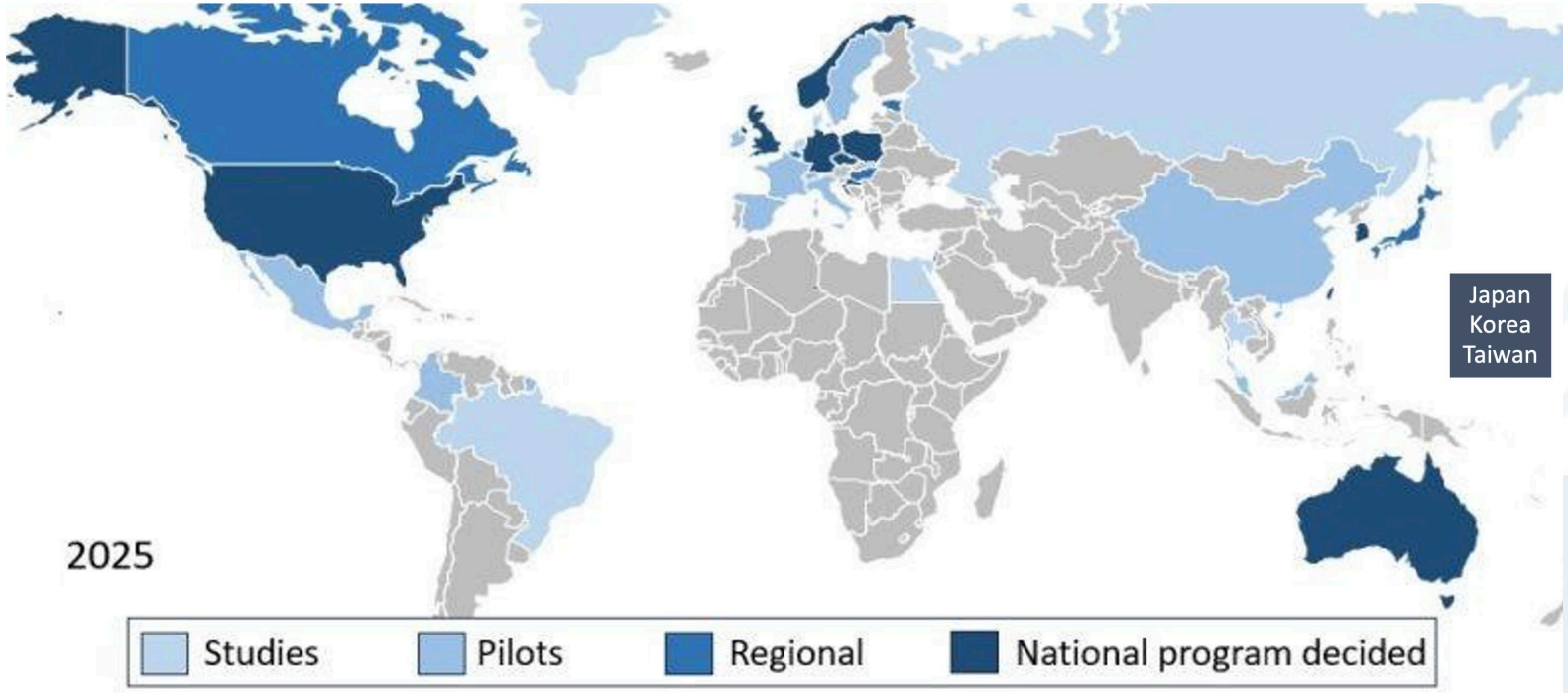
Global National/Regional LDCT Lung Cancer Screening Program



Endogenous Risk Factors

- Family LC History
- Familial Lung Cancer Syndromes
- Polygenetic Risk Score
- SNPs, APOBEC Signature
- Gender (Female)
- Race (Asian)

Exogenous Risk Factors

- Outdoor Air Pollution
- Outdoor & Household
- Second-Hand Smoke
- Occupational Smoke Exposure
- Radon Exposure
- Prior Chest Radiotherapy

Cassandra
Cancer Screening Smoking Cessation and Respiratory Assessment

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Criterios de inclusión

- Fumadores: Edad 50-75 años + Índice de Paquetes-Año > 20.
- Exfumadores: Edad 50-75 años + Índice de Paquetes-Año > 20, y < 15 años de abstinencia.

Guideline expansion helped, but significant gap persists
The 2021 update reduced ineligibility from

57.6% Ineligible | USPSTF 2013 → **40.9%** Ineligible | USPSTF 2021

Still, nearly 4 in 10 lung cancer patients do not meet the USPSTF screening criteria
Failing to meet the pack-year threshold remains the #1 reason for ineligibility (68.2% in 2013; 59.3% in 2021)

USPSTF Criteria	Outcome	Pooled Proportion (95% CI)	I^2 (%)	P-Value
2013	Overall ineligibility	57.6% (48.4–66.2)	97	<0.0001
	Age-based exclusion (<55 or >80 yrs)	34.7% (28.2–41.8)	70	0.018
	Insufficient pack-years (<30 yrs)	68.2% (54.6–79.2)	93	<0.0001
	Quit-year exclusion (>15 yrs)	25.8% (10.8–49.8)	97	<0.0001
2021	Overall ineligibility	40.9% (31.9–50.5)	98	<0.0001
	Age-based exclusion (<50 or >80 yrs)	31.8% (18.4–49.0)	96	<0.0001
	Insufficient pack-years (<20 yrs)	59.3% (45.6–71.6)	89	<0.0001
	Quit-year exclusion (>15 yrs)	49.6% (37.1–62.0)	94	<0.0001

Cigarette smoking duration is a simpler eligibility metric that has been adopted by recent guidelines

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PACK-YEARS (CURRENT)

packs/day × years smoked

Requires patient recall of historical smoking intensity; varies over time; clinically burdensome.

SMOKING DURATION (PROPOSED)

years smoked

Single, easily-ascertained value; prior studies demonstrate better correlated with lung cancer risk.

BIOLOGY

Duration of carcinogen exposure tracks lung cancer risk more closely than intensity.

EQUITY

Duration-based eligibility narrows gaps for women, Black, and Hispanic/Latino patients.

GUIDELINE PRECEDENT

NCCN v1.2025 already incorporates ≥20-year smoking duration into LCS eligibility.

980,399 VETERANS

VHA LARGEST US INTEGRATED HEATLHCARE SYSTEM

2021–2025 STUDY PERIOD

4.89 yrs MEAN FOLLOW-UP

DESIGN

- **Population:** Veterans aged 50–80 with ≥1 outpatient VHA visit in the year prior.
- **Exposure:** Smoking history from VA LCS Health Factors (prospectively-collected, structured).
- **Outcome:** 5-year lung cancer incidence per VHA Central Cancer Registry. "Potentially missed" lung cancer cases (i.e., lung cancers diagnosed in screening-ineligible individuals).
- **Exclusions:** Prior lung cancer, implausible smoking values (<0.1% of cohort).

LCS CRITERIA

USPSTF 2013

≥30 pack-years, quit ≤15 yrs

USPSTF 2021

≥20 pack-years, quit ≤15 yrs

Proposed CSD

≥20 yrs smoking, quit ≤15 yrs

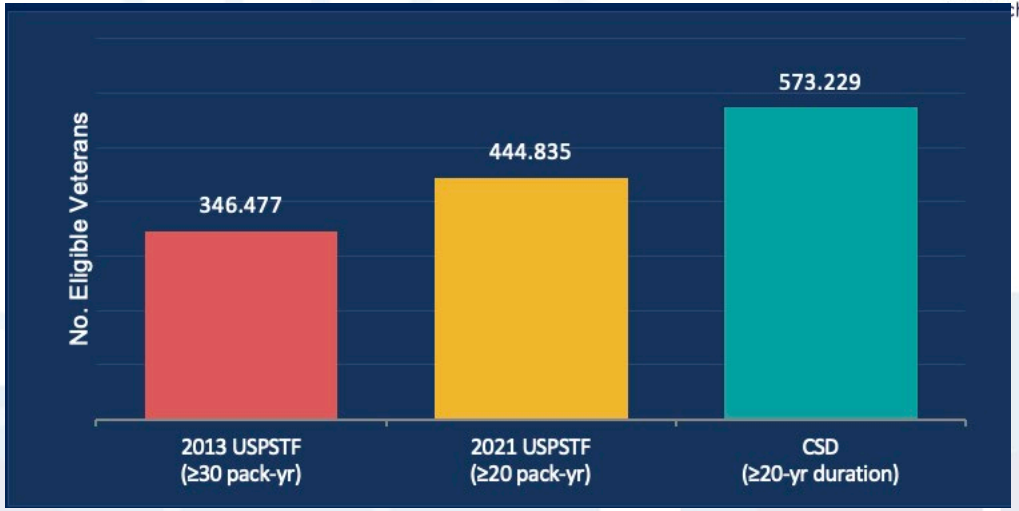
OUTCOME

5-yr lung cancer incidence (2021-2025)

ANALYSES

Stratified by age, sex, race, and ethnicity

Current (n=344,075, 35.1%)	Former (n=315,322, 32.2%)	Never (n=323,802, 33.0%)



	ALL VETERANS	FEMALE VETERANS	BLACK VETERANS
2013 USPSTF	52.8%	38.3%	34.6%
2021 USPSTF	67.8%	55.0%	53.9%
≥20-yr CSD	87.3%	82.7%	82.7%

ELIGIBLE WHO CURRENTLY / FORMERLY SMOKE

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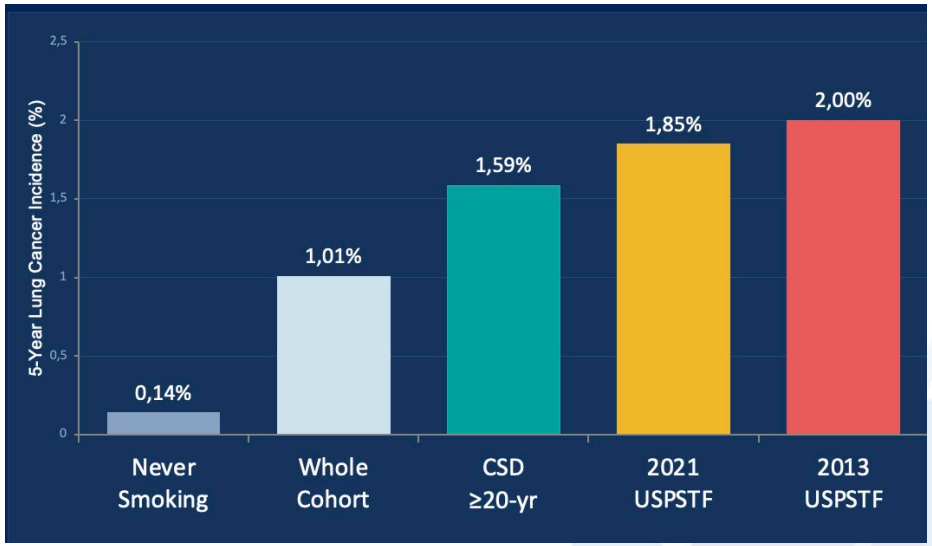
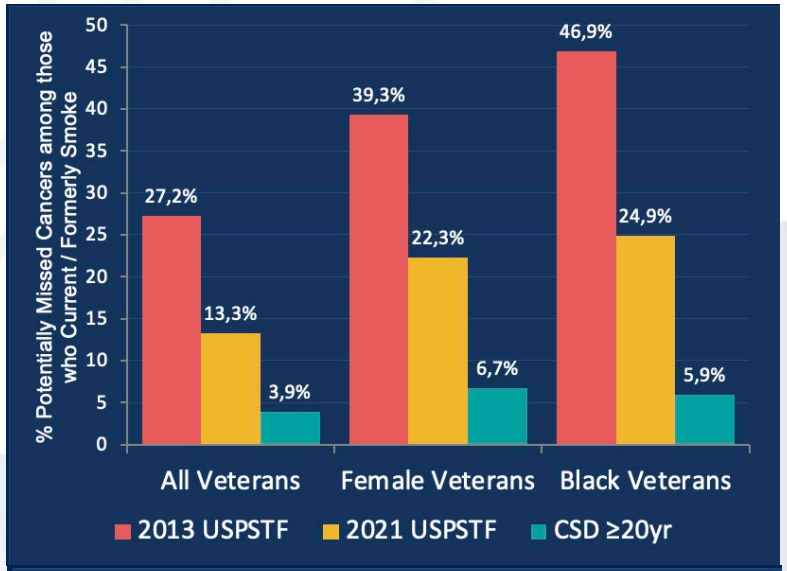
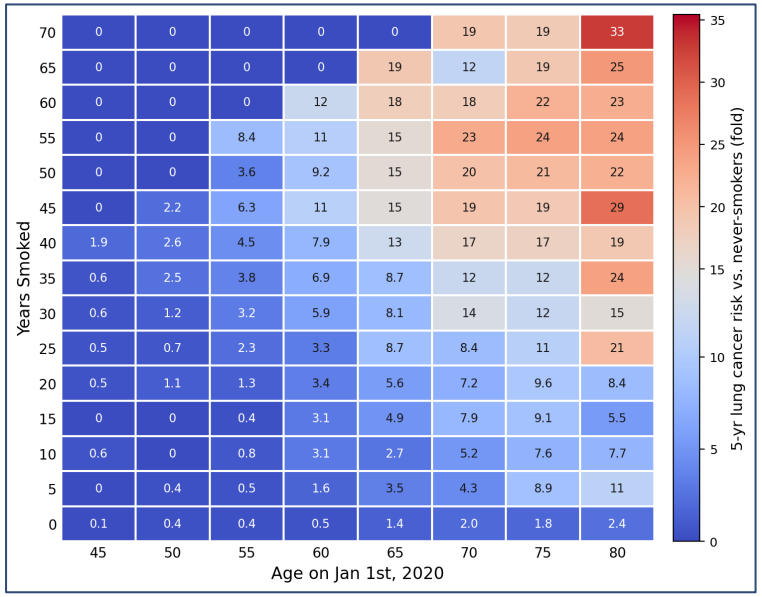
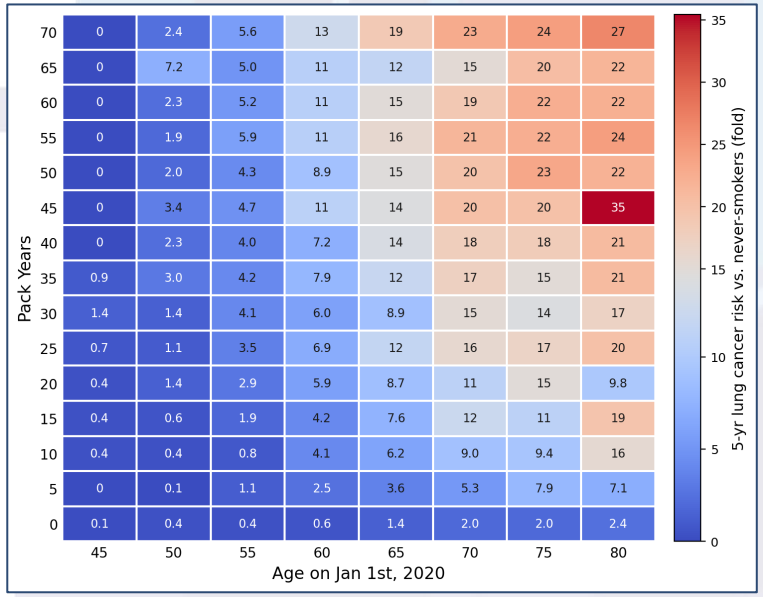




SMOKING DURATION (YEARS SMOKED)



PACK-YEARS (CURRENT METRIC)



2013 USPSTF *≥30 pack-years* **27.2%**

2021 USPSTF *≥20 pack-years* **13.3%**

Proposed CSD *≥20-yr CSD* **3.9%**

POTENTIALLY "MISSED" LUNG CANCER CASES

Diagnosed among screen-ineligible Veterans w/ smoking histories

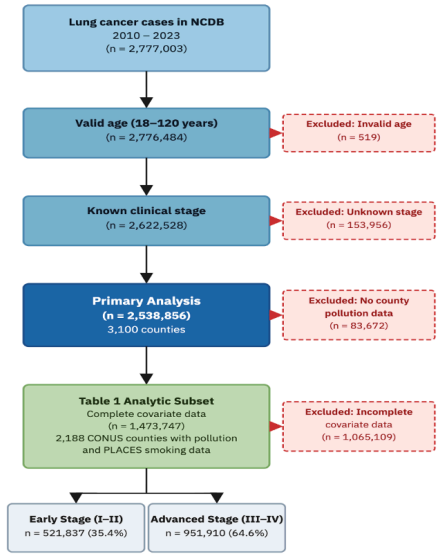
70% CSD reduced potentially missed cancer cases by >70% vs. 2021 USPSTF (13.3% → 3.9%, p<0.001)

Study Cohort Construction

NCDB lung cancer cases, 2010–2023 → analytic subset for pollution analysis

2.78M
Lung cancer cases identified (2010–2023)

2,188
CONUS counties with pollution + smoking data



ANALYTIC OUTCOME

1.47M patients stage-stratified

Early Stage (I–II)
35.4% (n = 521,837)

Advanced Stage (III–IV)
64.6% (n = 951,910)

EXCLUSIONS

- Invalid age: 519
- Unknown stage: 153,956
- No county pollution data: 83,672
- Incomplete covariates: 1,065,109

Source: National Cancer Database (NCDB) | PLACES smoking data | CONUS county pollution data

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KEY FINDINGS

Younger patients present later

74.5% of patients <50 are diagnosed at advanced stage — the highest of any age group.

Racial disparity in stage

Black patients: 69.8% advanced vs White: 63.8%. All race differences significant ($p<0.001$).

PM2.5 not stage-discriminating

PM2.5 levels nearly identical across stages ($p=0.79$); NO_2 shows significant but small gap.

NO2 — Significant

RR = 1.004 (95% CI: 1.001–1.007)
Per SD increase → **+0.4%** advanced-stage rate

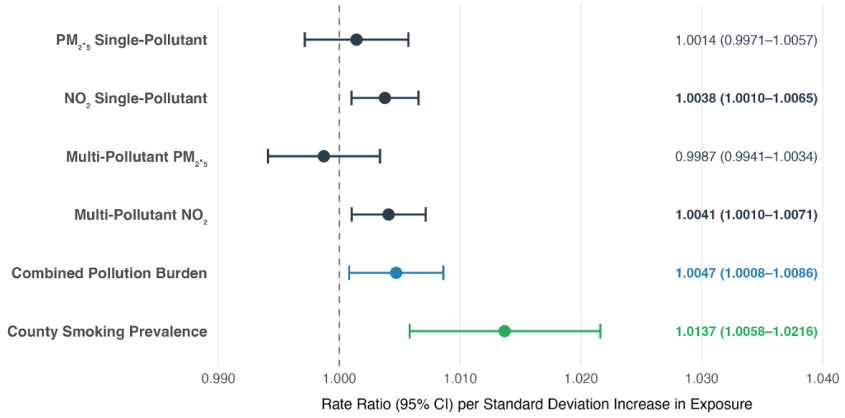
PM2.5 — Null

RR = 1.001 (95% CI: 0.997–1.006)
No significant association after smoking adjustment

Smoking — Dominant

RR = 1.014–1.017 per SD ($p<0.001$)
+1.4–1.7% advanced-stage rate per SD

Rate Ratios (95% CI) per SD increase — all models



Consistent Across Models

Single-pollutant, multi-pollutant, and composite-burden models all confirm: NO_2 is independently associated with advanced-stage presentation after smoking adjustment. Composite burden ($PM_{2.5}$ + NO_2): RR = 1.005 (1.001–1.009), driven by the NO_2 component.

Squamous Cell

Strongest NO_2 signal
RR = 1.009 (1.005–1.012)
$p < 0.001$

Large Cell

PM2.5 association
RR = 1.021 (1.001–1.042)
$p = 0.042$ ⚠ Small n

Adenocarcinoma

No significant association with either pollutant

Small Cell

No significant association with either pollutant

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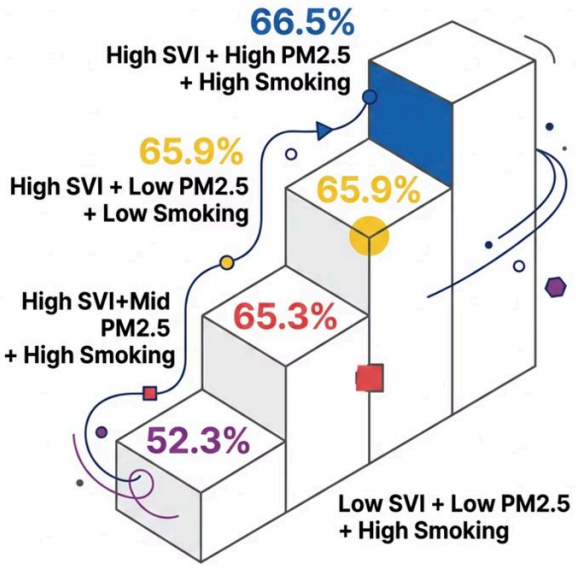
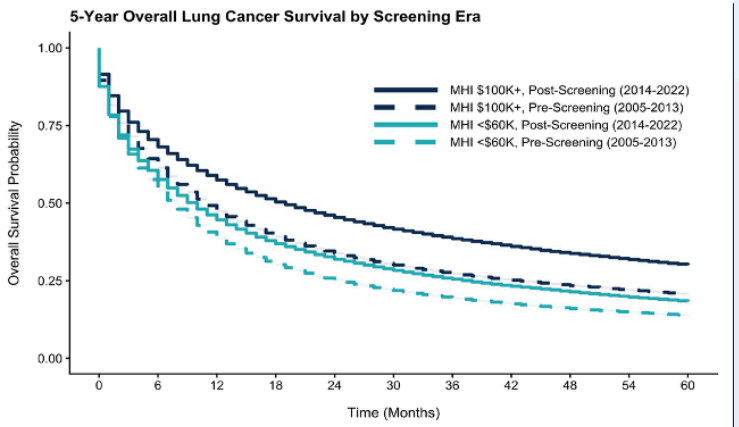


Results



- *Overall survival improved for all MHI groups*
- ***The income-related disparity between the highest and lowest MHI groups widened*** *(era x MHI interaction term HR 1.12, p <0.001)*

NO_2 predicts advanced-stage diagnosis

RR 1.004 per SD (95% CI 1.001–1.007); strongest in squamous-cell carcinoma, consistent with proximal-airway exposure.

$PM_{2.5}$ null reflects ecological confounding, not absence of harm

High-$PM_{2.5}$ counties are urban and have better aggregate healthcare access, offsetting late-stage risk. Narrow US exposure range further limits ecological detection.

Smoking remains the dominant driver

RR 1.014–1.017 per SD ($p < 0.001$); social vulnerability shapes staging disparities more than pollution.

14.2 pp disparity calls for equity-focused action

Pair tighter traffic-related NO_2 controls with targeted screening outreach in high-vulnerability, low-access communities.

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Domain	Key Determinants	Examples	Potential Role in Screening
Biological risk	Genetic susceptibility and molecular alterations	Germline EGFR mutations, DNA repair variants, polygenic risk scores	Identification of high-risk individuals and targeted screening strategies
Imaging biomarkers	Quantitative imaging features derived from LDCT	Pulmonary nodules, emphysema burden, AI-derived risk scores (eg, Sybil)	Risk stratification, screening interval adjustment, early detection
Molecular biomarkers	Circulating tumor markers and liquid biopsy technologies	ctDNA, CTCs, methylation-based assays	Adjunctive risk assessment and evaluation of indeterminate nodules
Environmental and occupational risk	Exposure to carcinogenic environments	Radon exposure, asbestos, silica, biomass fuel exposure	Incorporation into future risk prediction models
Structural determinants of health	Social and health system factors influencing access and outcomes	Insurance status, Medicaid expansion, rural access to imaging centers, language barriers	Identification of populations at risk for underscreening and delayed diagnosis

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Structural determinants of health	Social and health system factors influencing access and outcomes	Insurance status, Medicaid expansion, rural access to imaging centers, language barriers	Identification of populations at risk for underscreening and delayed diagnosis
Integrated risk framework	Combination of biological, imaging, environmental, and structural factors	Multidimensional risk models integrating AI, genetics, and SDOH	Development of personalized screening strategies and equitable implementation

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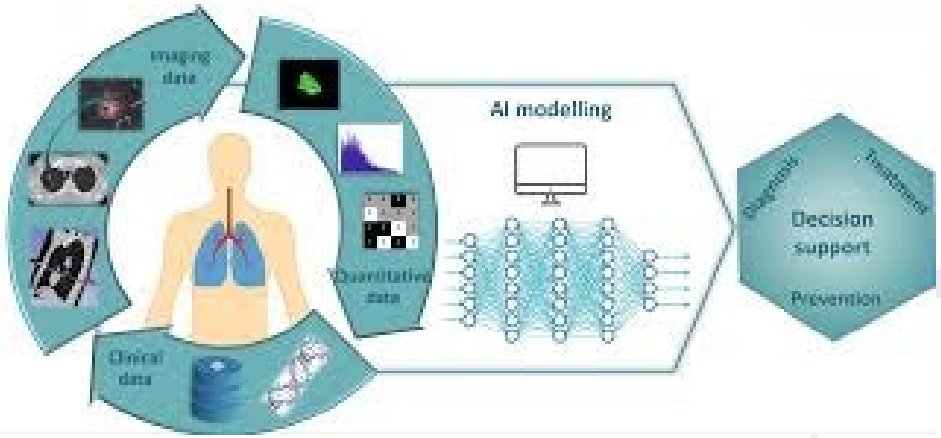

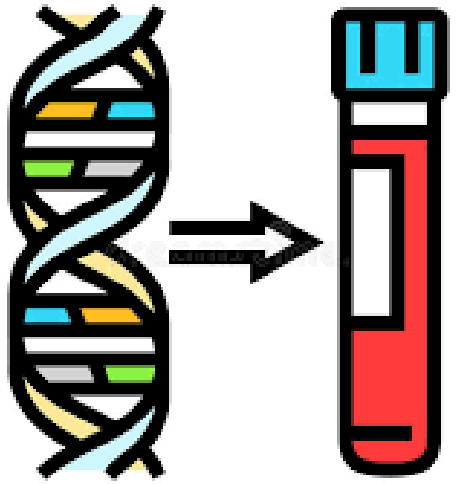

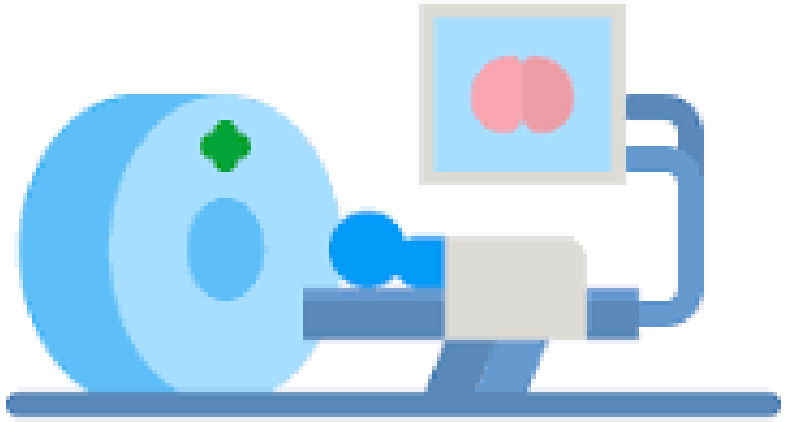

Taiwan National Lung Cancer Early Detection Program

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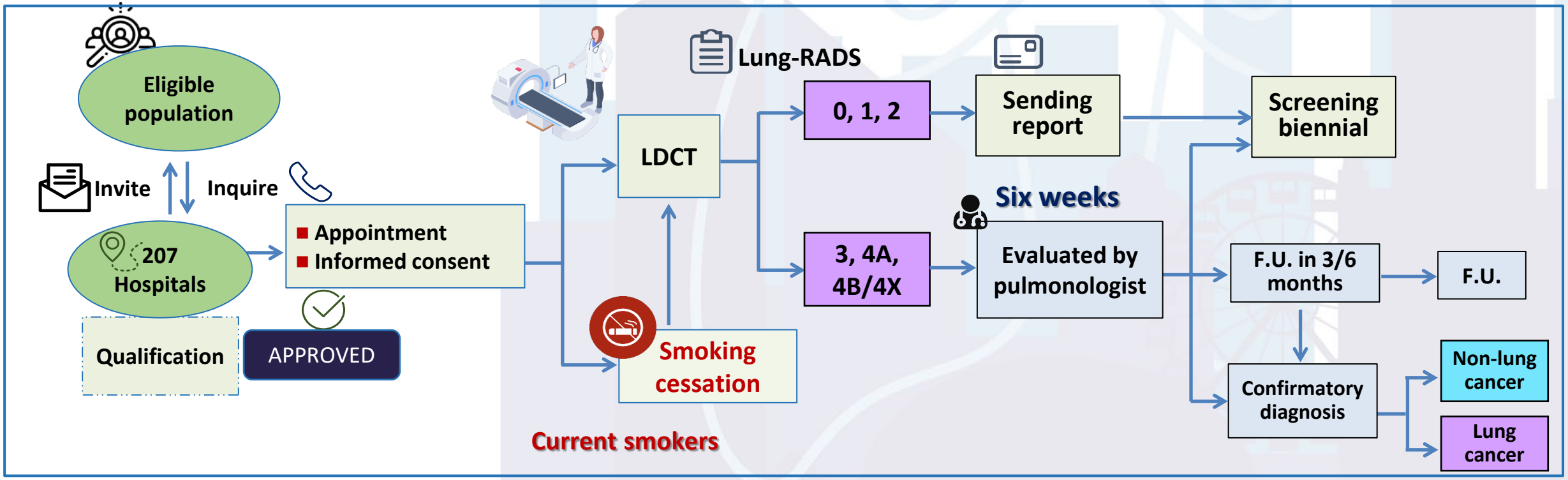
- Aim to double stage 1 disease and 5yr survival by 2030
- Biennial LDCT lung cancer screening for high-risk subjects
  - Smokers, 30 pack/yr, 50-74 yrs, change to 20 pack/yr after 2024
  - LCFH in nonsmokers/light smokers, F:45-74 yrs, M:50-74 yrs, F:40-74 yrs, M:45-74 yrs after 2024



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	TALENT[1]	TNLCEDP[2]	NLST[3]	NELSON[4]
Population	Non-smoker	Smoker & non-smoker[5]	Smoker	Smoker
Subject number	12,011	257,957	26,309	7,557
LDCT positive rate	17.4%	7.5%	27.3%	20.8%
T0 LC detection rate	2.6%	1.2%	1.1%	0.9%
Sensitivity	92.0%	97.8%	93.8%	94.6%
Specificity	84.6%	99.4%	73.4%	98.3%
PPV	13.8%	65.3%	3.8%	35.7%
NPV	99.7%	99.9%	99.9%	99.9%
Stage 0-I (%)	96.5%	81.4%	54.8%	63.9%
NNS[6]	150		320	222

Blood-Based Targeted Methylation MCED Test

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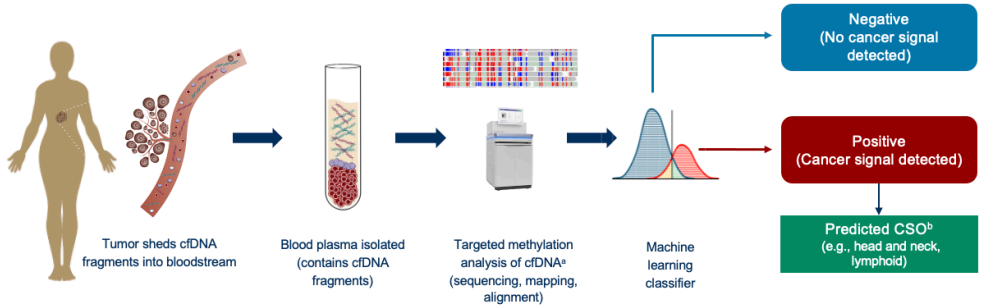
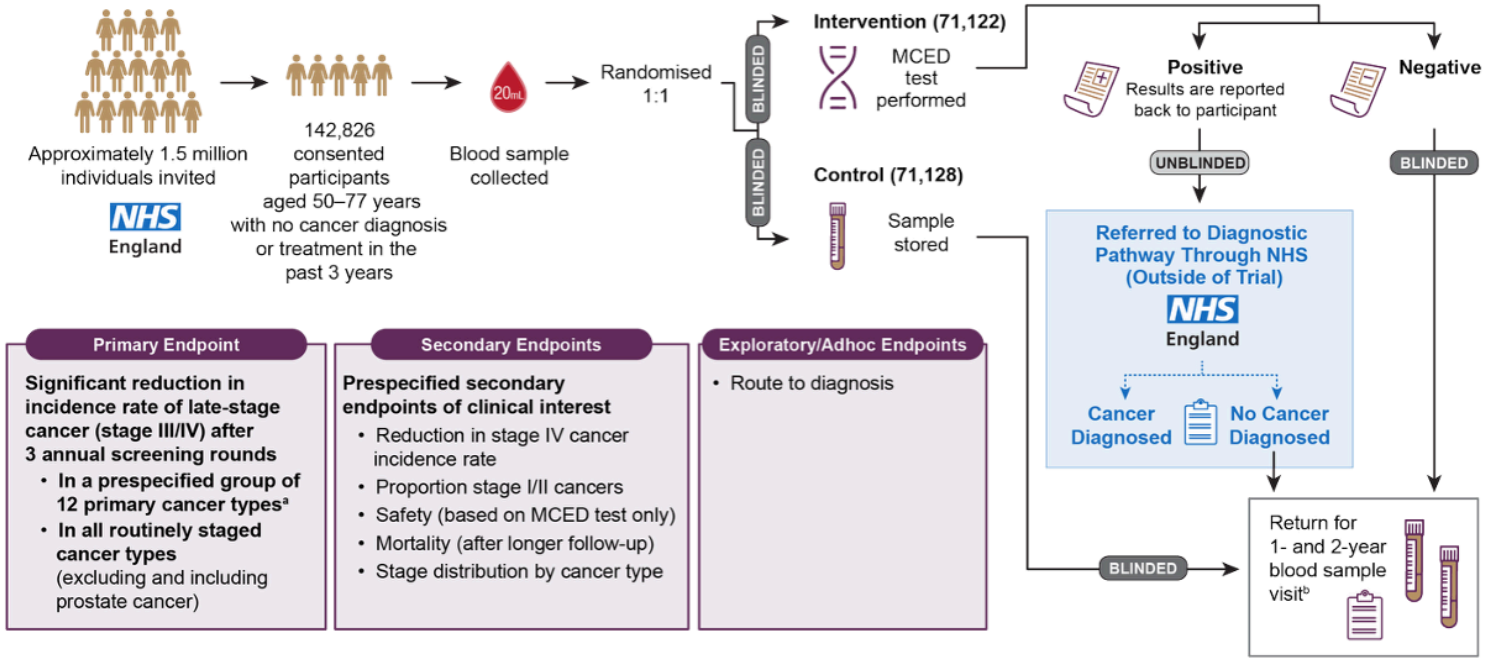
The MCED test detects a cancer signal from cell-free DNA (cfDNA) in blood and predicts cancer signal origin (CSO) to guide diagnostic evaluation



Clinically validated in case-control and population-scale intended-use studies.[1-4]
Clinical evidence program includes >380,000 participants across 9 studies in North America and the UK.

MCED, multi-cancer early detection. [a]Bisulfite treatment; targeted probes pull out fragments matching regions of interest. [b]For a detected signal, this MCED test version predicts 1-2 CSOs that can be either an anatomic site (eg, colorectal) or a cellular lineage (eg, lymphoid). Adapted from Liu MC, et al. 1. Liu MC, et al. *Ann Oncol*. 2020;31(6):745-759. 2. Klein EA, et al. *Ann Oncol*. 2021;32(9):1167-1177. 3. Schrag D, et al. *Lancet*. 2023;402(10409):1251-1260. 4. Nabavizadeh N, et al. Presentation at European Society for Medical Oncology Congress. October 17-21. 2025; Berlin, Germany.



Primary Endpoint

Significant reduction in incidence rate of late-stage cancer (stage III/IV) after 3 annual screening rounds
- **In a prespecified group of 12 primary cancer types[a]**
- **In all routinely staged cancer types** (excluding and including prostate cancer)

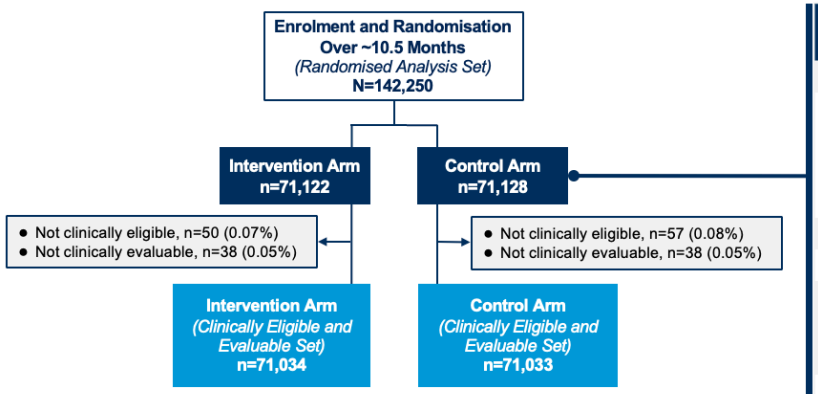
Secondary Endpoints

Prespecified secondary endpoints of clinical interest
- Reduction in stage IV cancer incidence rate
- Proportion stage I/II cancers
- Safety (based on MCED test only)
- Mortality (after longer follow-up)
- Stage distribution by cancer type

Exploratory/Adhoc Endpoints
- Route to diagnosis

Participants passively monitored though national registry datasets

MCED, multi-cancer early detection; NHS, National Health Service.
[a]Lung, head & neck, colorectal, pancreas, myeloma/plasma cell neoplasm, liver/bile duct, stomach, esophagus, anus, lymphoma, ovary, and bladder. [b]Participants who were diagnosed with cancer were not required to return for blood samples.
Sasieni P, et al. *Cancers (Basel)*. 2022;14(19):4818.



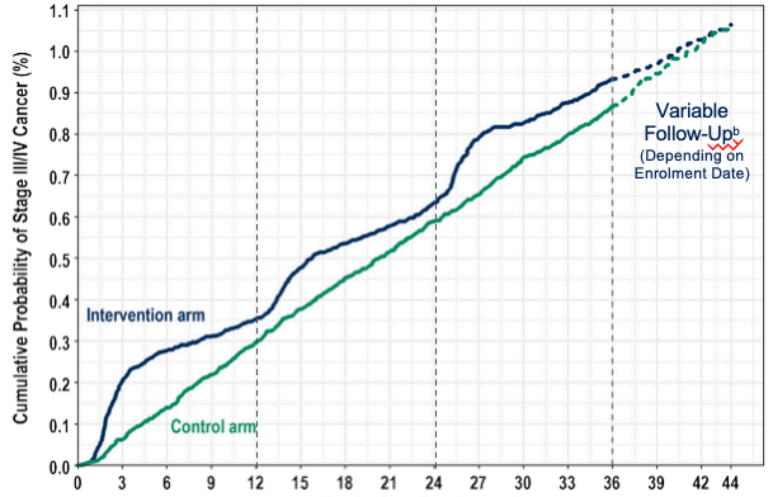
Participants retention was 91% in the second year and 88% in the third year of screening

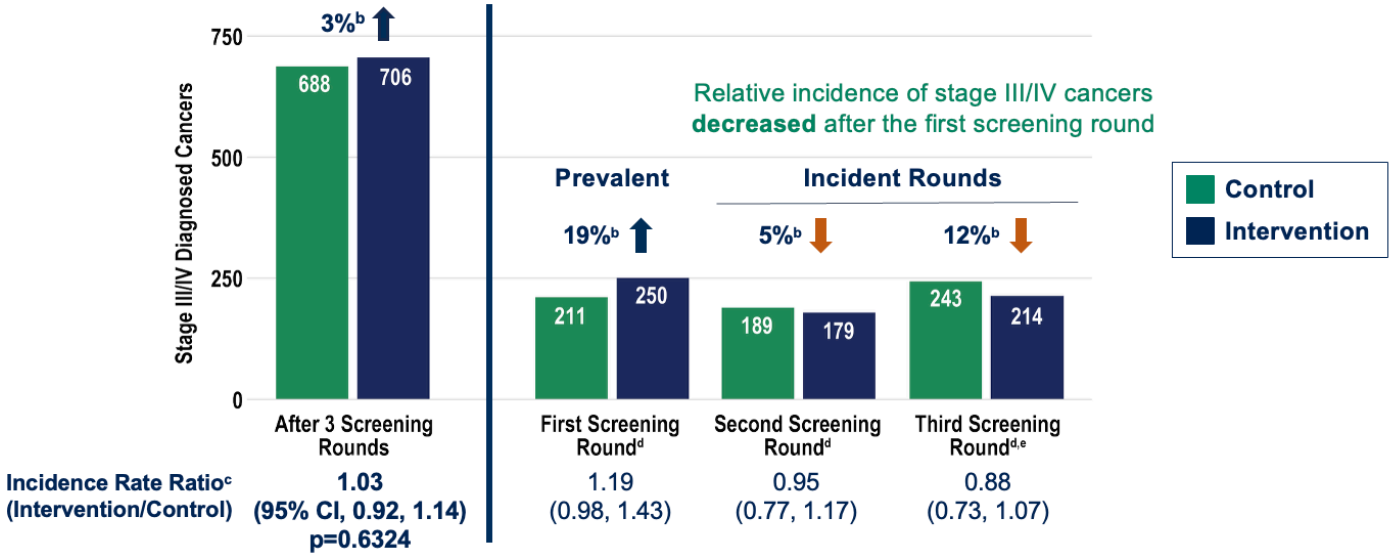
Median follow-up of 17 months after last screen

CSE, certificate of secondary education; IQR, interquartile range; O-levels, ordinary levels.

Baseline Demographics and Characteristics	Intervention Arm (n=71,122)	Control Arm (n=71,128)
Median Age (IQR), years	66 (59, 71)	66 (59, 71)
Age Groups, years		
50-59	26.4%	26.6%
60-69	40.2%	40.5%
70+	33.4%	33.0%
Sex, Female	50.2%	50.2%
Race/Ethnicity, White	93.6%	93.6%
Index of Multiple Deprivation		
Most Deprived	22.6%	22.6%
Least Deprived	16.1%	16.0%
Education		
CSEs, O-Levels, or Lower	44.9%	45.2%
Bachelor's Degree or Higher	25.0%	25.1%
Smoking History		
Former Smoker	38.3%	38.2%
Current Smoker	6.7%	6.6%
Prior Cancer History	7.5%	7.5%

Cumulative Probability of Stage III/IV Cancer





Stage III/IV Cancers Diagnosed	Intervention vs Control	
	Incidence Rate Ratio	% Difference[c] (n vs n)[d]
After 3 Screening Rounds	**1.03 (0.92, 1.14) p=0.6324**	**↑ 3% 706 vs 688**
First Screening Round (Prevalent)	1.19 (0.98, 1.43)	↑ 19% 250 vs 211
Second Screening Round (Incident)	0.95 (0.77, 1.17)	↓ 5% 179 vs 189
Third Screening Round (Incident)[e]	0.88 (0.73, 1.07)	↓ 12% 214 vs 243

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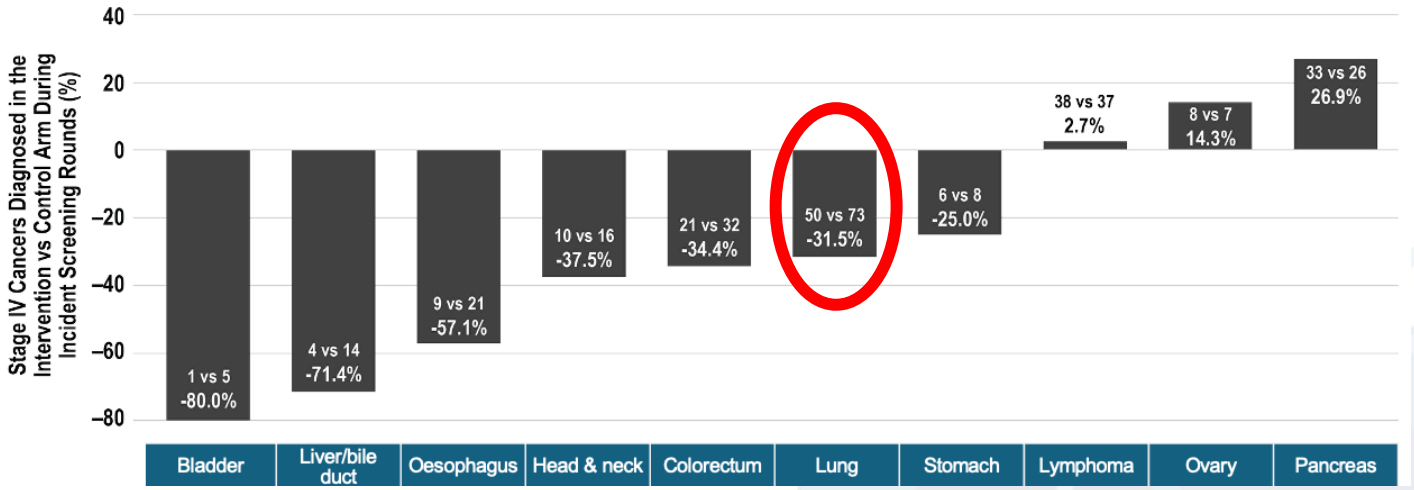
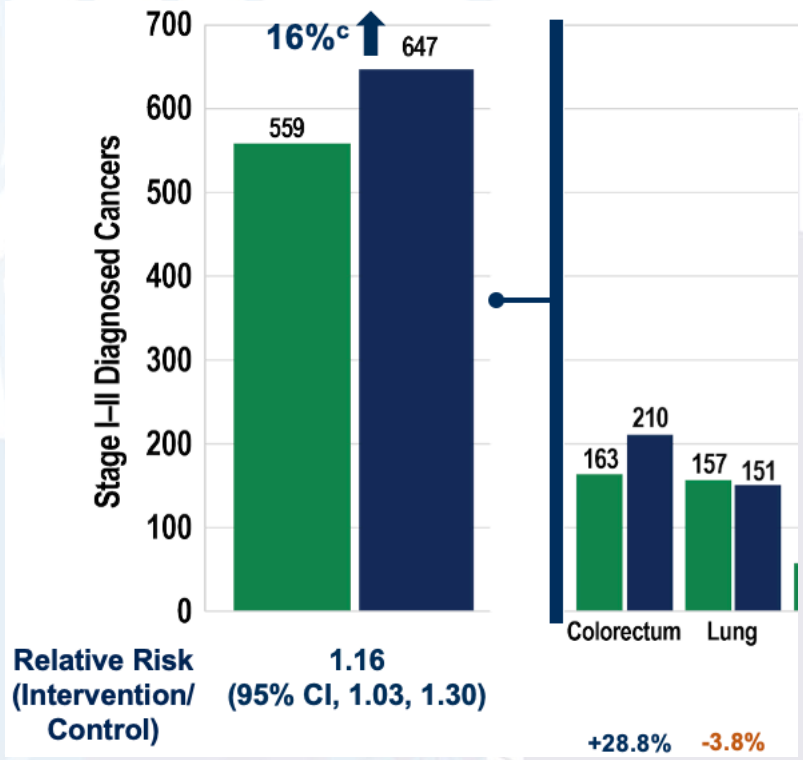




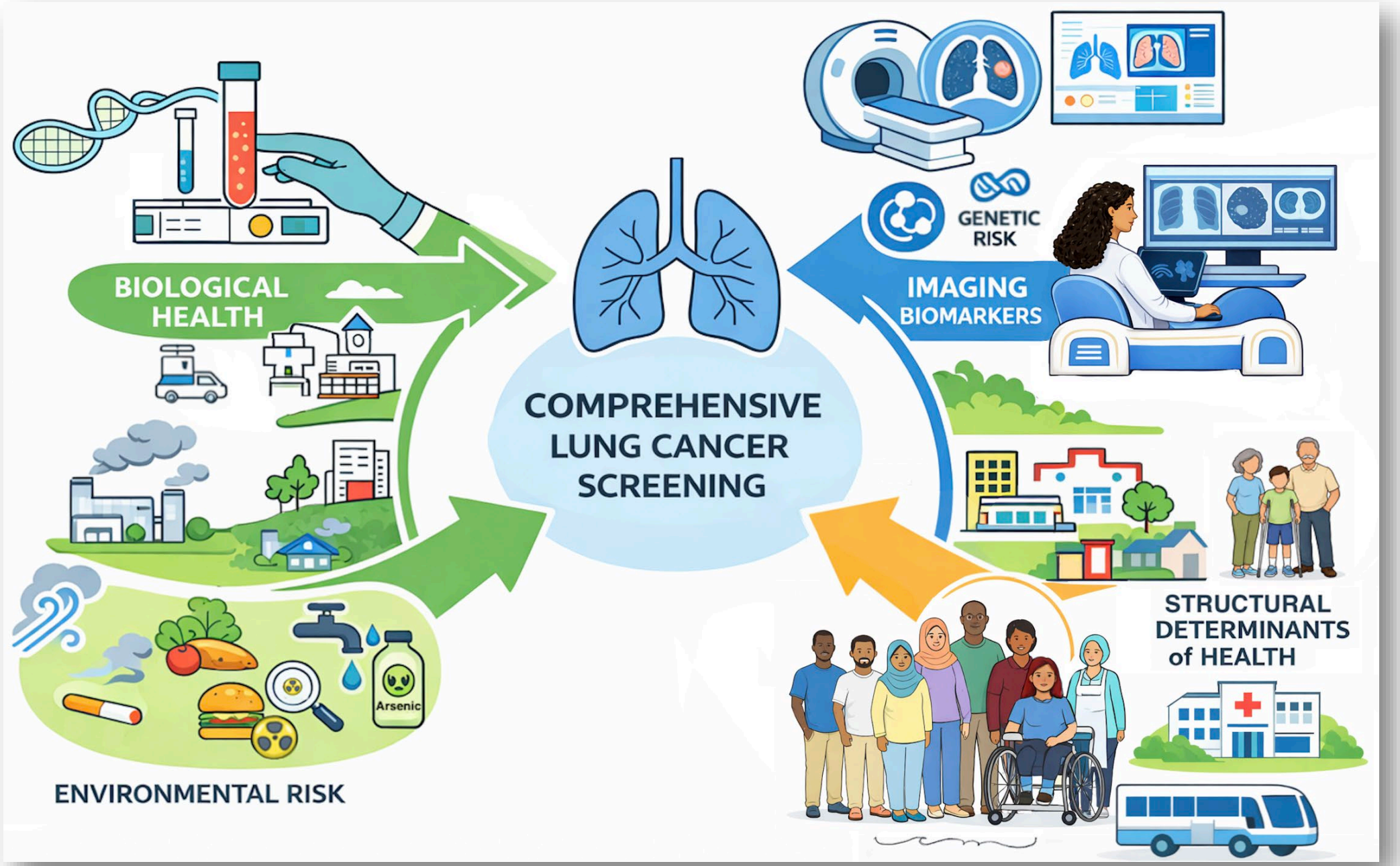
No se alcanza el objetivo primario de reducción significativa de los diagnósticos en Estadio III/IV

Reducción del 20% de los diagnósticos en Est IV (pero no para cáncer pulmón)

VPP 52%; Especificidad 99.55%

Incremento 4x en los diagnósticos generados por el MCED

Reducción 25% diagnósticos originados desde Urgencias



PRESENTED BY: Efrén J. Flores, MD, FACR

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Mensajes resumen

La incidencia y mortalidad del cancer de pulmón pueden reducirse mediante la prevención primaria y secundaria

Junto al tabaco existen otros factores ambientales y genéticos que incrementan el riesgo de cancer de pulmón

La eficiencia del cribado podria incrementarse mejorando los criterios de selección e integrando tests analiticos y la IA

Abstracts utilizados en la presentación

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- Heiden B et al :Abstract 8004. Oral Presentation Session Lung Cancer Non Small Cell Local-Regional
- Yang P: Educational Session Lung Cancer, Prevention, Risk Reduction and Genetics, Global Health
- Qidwai A et al: Abstract 554676 Poster
- Bell R et al :Abstract 8003 Oral Presentation Session Lung Cancer Non Small Cell Local-Regional
- Healy T et al Abstract 80072 Poster
- Swanton RC et al: Abstract LBA100. Oral Presentation Clinical Science Symposium ctDNA in Clinical Practice: From Early Detection to Clinical Decision-Making

Gracias